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The Development, Implementation and Evaluation of Frailty Assessment in Oncology

A THESIS SUBMITTED TO

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Dedicated to the memory of my grandmother, Mary

and

sister-in-law, Sarah

DECLARATION

I declare that this thesis has not been submitted as an exercise for a degree at this or any other university and it is entirely my own work.

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Anita O'Donovan

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SUMMARY OF THESIS

Over the last number of decades, treatment outcomes from cancer care have improved dramatically. However, these improvements have mostly benefitted younger patients, or relatively robust older adults, rather than the entire older patient population. It is well known that the evidence base surrounding oncologic management is mostly extrapolated from a younger patient cohort, or those patients who are considered fit, rather than vulnerable or frail. This is despite the fact that the majority of cancers occur in older people, and there is considerable heterogeneity in terms of health in old age.

Given the predicted demographic changes in many countries, there has been an increased focus on how to more optimally manage older adults with cancer. Since these patients are currently the majority of patients affected by cancer, this area of research might well be considered to be long overdue.

This doctoral thesis was designed to (i) standardise the identification, assessment and reporting of frailty in older adults with cancer, (ii) evaluate this standardised approach in a radiation oncology patient population and (iii) examine survivorship data from The Irish LongituDinal study on Ageing (TILDA) in older to better elucidate the impact of frailty in follow-up care.

The thesis comprises seven chapters. The first chapter discussed the background to the thesis and outlined the research aims and objectives. The second chapter provided a literature review of the field, covering: (i) frailty and ageing, (ii) frailty and cancer and (iii) the role of geriatric assessment (GA) in cancer care, with a particular emphasis on existing research gaps. The review concluded that some research on the optimal method of assessing older adults with cancer has been published, with regard to better integration of geriatric medicine methods. However, many different methods of assessment and frailty screening tools have been employed across different studies, making it difficult to compare the

SUMMARY OF THESIS

literature. In addition, a limited amount of research has occurred identifying the impact of these assessment methods in clinical practice, especially in radiation oncology.

The third chapter aimed to address one of these research gaps, and used the Delphi methodology to gain consensus on the optimal method of GA for older adults with cancer. The Delphi method attempts to achieve a convergence of opinion among experts on a specific topic, over a series of rounds or iterations, using a facilitated group approach. A national and international expert panel was identified to take part in this study.

The fourth chapter investigated the clinical implementation of a consensus-driven approach to GA, using the minimum dataset proceeding from the Delphi method in Chapter 3. This study took place in in Saint Luke's Radiation Oncology Network at St. James's Hospital, Dublin. This study evaluated the feasibility and acceptability of a randomised controlled trial investigating the implementation of GA in radiation oncology.

The remaining chapters examined the longitudinal impact of a cancer diagnosis on older adults, in terms of relevant frailty indicators. The fifth chapter aimed to investigate to what extent community-dwelling older adults with cancer differ from their non-cancer counterparts. Building on the findings of previous chapters, it sought to compare cancer survivors to their non-cancer controls, in relation to physical, cognitive, psychological and social health and wellbeing, using data from The Irish LongituDinal Study on Ageing (TILDA).

The sixth chapter aimed to investigate to what extent older adults with cancer in the community differ from their non-cancer community dwelling counterparts in relation to frailty. Frailty was defined using three commonly used indices, and the prevalence of each type compared.

SUMMARY OF THESIS

The final (seventh) chapter considered the relevance of the research data developed in this thesis, with an emphasis on original contributions to the research field and their implications for clinical practice and health policy. Also, recommendations for future research were made, arising from the research findings and limitations encountered throughout the course of this research, as well as new areas that have emerged as research priorities since the commencement of this PhD.

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ABBREVIATIONS

aCGA	Abbreviated Comprehensive Geriatric Assessment	**CES-D**	Centre for Epidemiological Studies - Depression
ACE-27	Adult Comorbidity Evaluation-27	**CFS**	Clinical Frailty Scale
ADePT	A process for Decision-making after Pilot and feasibility Trials	**CGA**	Comprehensive Geriatric Assessment
ADL	Activities of Daily Living	**CHS**	Cardiovascular Health Study
ADR	Adverse Drug Reaction	**CI**	Confidence Intervals
ADT	Androgen Deprivation Therapy	**CIRS**	Cumulative Illness Rating Scale
AIC	Akaike's Information Criterion	**CIRS-G**	Cumulative Illness Rating Scale for Geriatrics
ASCO	American Society of Clinical Oncology	**CSHA**	Canadian Study of Health and Aging
BMI	Body Mass Index	**ECOG**	Eastern Cooperative Oncology Group
CAPI	Computer-Aided Personal Interview	**ED**	Electoral Division
CCI	Charlson Comorbidity Index	**ELAN-ONCOVAL**	ELderly heAd and Neck cancer-Oncology eValuation

ABBREVIATIONS

ELAN-RT	ELderly heAd and Neck cancer - Radiotherapy	**ESRI**	Economic and Social Research Institute
ELCAPA	Elderly Cancer Patient	**ETF**	Elderly Task Force
ELSA	English Longitudinal Study of Ageing	**EUROCARE**	European Alcohol Policy Alliance
EOL	End Of Life	**EUROSTAT**	European Statistical Office
EONS	European Oncology Nursing Society	**FDR**	False Discovery Rate
EORTC	European Organisation for Research and Treatment of Cancer	**FI**	Frailty Index
EORTC QLQ - ELD15	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire for Elderly cancer patients	**FRAIL**	Fatigue Resistance Ambulation Illnesses and Loss of weight
ESMO	European Society for Medical Oncology	**G8**	Geriatric 8

ABBREVIATIONS

GA	Geriatric Assessment	**KFI**	Kaplan–Feinstein Index
GBM	Glioblastoma Multiforme	**KPS**	Karnofsky Performance Status
GDS	Geriatric Depression Scale	**LFT**	Liver Function Test
GLM	Generalised Linear Model	**MCAR**	Missing Completely At Random
GEE	Generalised Estimating Equations	**MCID**	Minimum Clinically Important Difference
Gy	Gray	**MERGE**	Managing the Elderly in Radiotherapy using Geriatric AssEssment
IADL	Instrumental Activities of Daily Living	**MinDS**	Minimal Dataset
IL-6	Interleukin-6	**MMSE**	Mini-Mental State Examination
IPAQ	International Physical Activity Questionnaire	**MoCA**	Montreal Cognitive Assessment
IQR	Interquartile Range	**MRC**	Medical Research Council

ABBREVIATIONS

MoCA	Montreal Cognitive Assessment	**p-value**	Probability value
MRC	Medical Research Council	**PRO**	Patient Reported Outcome
n	Sample size	**PS**	Performance Status
NCI	National Cancer Institute	**QNHS**	Quarterly National Household Survey
NCCN	National Comprehensive Cancer Network	**QoL**	Quality of Life
NCCP	National Cancer Control Programme	**Q–TWIST**	Quality-Adjusted Time Without Symptoms or Toxicity
NCCS	National Coalition for Cancer Survivorship	**R1**	Round 1
NGT	Nominal Group Technique	**R2**	Round 2
NI	Northern Ireland	**R3**	Round 3
NICE	National Institute for Health and Clinical Excellence (NICE)	**R4**	Round 4
NMSC	Non-Melanoma Skin Cancer	**RAND**	Research and Development
OTU	Overall Treatment Utility	**RCT**	Randomised Controlled Trial

ABBREVIATIONS

RO	Radiation Oncologist	**SLRON**	Saint Luke's Radiation Oncology Network
ROI	Republic of Ireland	**SPSS**	Statistical Package for the Social Sciences
RRR	Relative Risk Ratio	**SRFI**	Self-Reported Frailty Index
SAOP	Senior Adult Oncology Program	**TCD**	Trinity College Dublin
SAGE	Study on Global AGEing and Adult Health	**TILDA**	The Irish LongituDinal Study on Ageing
SCQ	Self-Completion Questionnaire	**TUG**	Timed Up and Go
SE	Standard Error	**VES-13**	Vulnerable Elders Survey 13
SEER	Surveillance, Epidemiology and End Results	**VIF**	Variance Inflation Factor
SHARE	Survey of Health and Retirement in Europe	**WHO**	World Health Organisation

RESEARCH OUTPUTS

PUBLICATIONS

Published

O'Donovan, A., Mohile, S. and Leech, M., Expert Consensus Panel Guidelines on Geriatric Assessment in Oncology. European Journal of Cancer Care, 24, (4), 2015, p574 – 589.

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Managing the Elderly in Radiotherapy Using Geriatric Assessment: "MERGE"', European Oncology Nursing Society (EONS) Spring/Summer Magazine, 2017. [A special joint issue of the EONS magazine with the European SocieTy for Radiotherapy and Oncology (ESTRO)].

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O'Donovan, A. , Gillham, C., Cunningham, C. , Thirion, P. , Cunningham, M. , El Beltagi, N. and Leech, M., Managing the Elderly in Radiotherapy using Geriatric assessmEnt (MERGE): A Pilot Geriatric Oncology Study, International Society of Geriatric Oncology (SIOG) 14th Annual Conference, Lisbon, Portugal, October, 2014.

O'Donovan, A., Mohile, S. and Leech, M., Expert Consensus Panel on Geriatric Assessment Interventions in Oncology: the European Perspective, Annual Scientific Meeting, Faculty of Radiology, Royal College of Surgeons, Dublin, Ireland, September , 2013.

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Chapter 1

1 Introduction

1.1 Ageing Demographics and Cancer

Ireland, like many countries worldwide is in the early stages of a major demographic shift, stemming from the so-called “baby boomers” coming of age. In Ireland alone, excluding non-melanoma skin cancer (NMSC), the number of cancer cases are expected to increase by 81% for females and 108% for males between 2010 and 2040 [1]. This change is also mirrored worldwide [2-4]. The European Statistical Office (EUROSTAT) figures predict an estimated increase in those aged 65 and older in the coming years, and an approximate doubling of those aged 80 and older i.e. the “oldest old” [5]. It is very timely to consider the impact of this projected change, not only on the oncology infrastructure required to effectively manage additional patients, but also the demands of an ageing population and the health service planning changes that may be required to respond to their needs.

There is no widely accepted definition of an “older” or “elderly” person. The United Nations has used 60+ years as a cutoff to define old age; however many developed countries now accept 65+ years as a more suitable definition of old age [6]. This coincides with retirement age in many countries, however, we know that this is changing, and some countries are raising the age of retirement [7] . Many organisations now consider 70 to be a truer reflection of old age in most developed countries [8].

1.2 Current Management of Older Adults with Cancer

Older patients in Ireland are less likely to undergo treatment for their cancer [9], and often present at a later stage, commonly with a presentation at the emergency department [10]. This pattern of undertreatment has also been reported in other countries [11, 12]. As a result, older patients have had poorer outcomes, and this is something that needs to be investigated in order to provide better care.

Taking the most commonly diagnosed cancer in men, prostate cancer, as an example, one study found that in locally advanced disease, the likelihood of patients receiving radical treatment was more than halved with every 10 year age increase [13]. Another study examined the receipt of definitive treatments, including radiotherapy, in intermediate and high-risk older patients with prostate cancer [14]. Among all patients assessed, 92% of intermediate-risk and 87% of high-risk patients received definitive treatment. Age stratification revealed 83% aged 75-79 and only 63% aged ≥80 intermediate-risk patients received definitive therapy, while 81% aged 70-75 and 55% aged ≥80 high-risk patients underwent definitive treatment. An Irish study has demonstrated that age is the main factor in receiving active treatment in older adults, rather than comorbidities, tumour stage and burden [15].

Another common cancer in older people is head and neck cancer. A large retrospective analysis of 14,909 oropharyngeal cancer cases from the Surveillance, Epidemiology, and End Results (SEER) programme assessed the extent of under treatment. Data were categorised by treatment modality, including radiotherapy and age. Their results found that as age increased, the proportion of patients who did not receive any treatment significantly increased, whereas

the number of patients who received a combined treatment approach also significantly decreased [16]. In fact, only approximately half of older patients with head and neck cancer were treated in accordance with standard treatment guidelines and institutional protocols [17]. Likewise for lung cancer, another common cancer in older adults, patients over 70 years of age account for approximately 47% of lung cancer patients, and have been shown to be less likely to receive curative treatment options, such as surgery and radiotherapy [18]. The reasons for the lack of adherence to guidelines are unclear, and may well be related to disease and patient characteristics. However, better clarification and rationalisation of these treatment decisions in older adults is needed.

1.3 Lack of an Evidence Base to Inform Clinical Decision Making

It is a significant problem for evidence-based geriatric oncology, that older adults are under-represented in clinical trials [19-22], despite the incidence of cancer in this age group, estimated to be 60% of all cancer cases [23]. Although approximately 60% of new cancer cases occur in older people, they comprise only a quarter of participants in cancer clinical trials [24].

Clinically, patients will present with variable co-morbidities, performance status, frailty and physiological age [25-27]. Characterising the heterogeneity of the older cancer patient cohort, and their ability to tolerate oncologic treatment, is extremely difficult without the aid of clinical trial information to guide clinicians.

Although survival (overall/progression-free) is recognised as the most valuable outcome of any clinical trial, questions have been raised regarding its significance in older patients, particularly due to patient comorbidities which are likely to be a contributing factor to

patient death. A workshop held by the European Organisation for Research and Treatment of Cancer (EORTC) in 2011 [28] explored methods of improving clinical design and suggested looking at alternative endpoints, such as quality of life (QoL), toxicity and functional independence. Reporting disease-specific survival, rather than overall survival, could also be useful when evaluating treatments for this patient group as it would indicate the number of patients who actually died as a result of their cancer versus other chronic conditions. Overall treatment utility (OTU) is a composite outcome measure, developed within the FOCUS2 trial [29] of frail older patients with colorectal cancer, treated with chemotherapy. It combines both objective and subjective items i.e. clinical/radiological response to treatment, toxicity, adverse events and, importantly, patient-reported acceptability of treatment. This novel composite measure was devised to reflect whether, from the viewpoint of both the patient and the clinician, the treatment had been worthwhile. OTU proved a useful outcome measure in the FOCUS2 trial, in the comparison of treatment groups.

Clinical trial inclusion criteria are an area of much debate. Traditional exclusion criteria based on age, performance status and stringent organ function restrictions have been unhelpful in adding to the evidence base for the management of older patients with cancer [30]. Thus, selection of more appropriate endpoints is also important in "geriatricizing" trial design [31-33]. This has been highlighted by Nipp et al [34], who described the need for pragmatic clinical trials for older adults with cancer. Whereas randomised controlled trials (RCTs) reflect patient outcomes under ideal conditions, there is a large unmet need to investigate older patient outcomes under more realistic conditions i.e. varying degrees of fitness and frailty. In particular, there is limited evidence from clinical trials regarding the toxicity experienced by older patients undergoing radiotherapy, or the

predictive power of comprehensive geriatric assessment (CGA) in linking toxicity to frailty.

1.4 Emergence of Geriatric Oncology as a Discipline

Geriatric oncology, as a discipline, does not exist in Ireland at the present time. Many international models of geriatric oncology exist [35-37], however implementation has been slow due to many factors, such as the lack of consensus as to what should be assessed in oncology, and access to geriatric medicine expertise. An important factor is the time required for proper assessment of older patients, and access to rehabilitation/follow-up care in order to address identified problems [38, 39].Therefore CGA has yet to be fully integrated into oncology, and the optimal format for the assessment to be clarified, as highlighted in a systematic review by Puts et al [40].

Many oncology healthcare professionals feel ill-equipped to deal with these projected demographic changes. Despite the fact that the majority of cancer patients are in older age groups, most oncologists receive little training in the specialised care of older patients [41]. When an older patient presents to oncology, they are often segregated from their co-existing geriatric care, as the oncology and geriatric medicine disciplines often work in isolation, with little collaboration about patients.

One major challenge is that there is a notable shortage of geriatricians worldwide [42]. Traditionally the education of healthcare practitioners has largely taken place in isolation from one another. Recent focus in policy documents on measures to improve the quality of healthcare has resulted in a need to adequately prepare qualified health professionals to work together in a more collaborative manner [43, 44]. In radiation oncology, this would place the onus on the

radiation oncologist, nursing colleagues, allied health professionals and radiation therapists to expand their role and undertake CGA as part of their formal evaluation of their patients.

1.5 Study Rationale and Thesis Scope

A review of the literature has shown little research on the role of CGA in oncology, more so in radiation oncology, however there are numerous calls for its implementation, given the known demographic changes predicted for the coming decades. Currently, there is little appreciation of the prevalence or role of frailty in predicting outcomes for older adults with cancer. One major obstacle at the current time is the lack of standardisation in relation to frailty assessment in oncology.

1.6 Overall Aim and Objectives of Thesis

This thesis arose from an interest in the reported inequities in the provision of cancer care for older adults, and potential ways to address these in clinical practice.

The overall research aim of this thesis is to measure CGA deficits and frailty in an Irish (hospital and community) population with cancer and to study feasibility of CGA in a radiation oncology clinic. This information is important from a health services perspective, as it provides an important baseline for monitoring implementation of policy in relation to geriatric oncology in Ireland.

This aim was achieved through three main approaches. The first was to use consensus-based methods to inform the design of a geriatric assessment (GA) for oncology practice. The second was to undertake a pilot study of this assessment in a clinical setting, while the third investigated the long-term impact of cancer and its

treatment, using information from The Irish Longitudinal Study on Ageing (TILDA).

Chapter 3: A Delphi Consensus Study of Geriatric Assessment in Oncology

The overall aim of this study was to obtain consensus on aspects of CGA in oncology to inform the implementation of an Irish geriatric oncology programme, which would be transferable to other countries and healthcare systems.

The specific objectives of Study 1 were:

1. To determine current practice in relation to CGA in oncology.
2. To establish consensus among a group of Irish Oncologists, with guidance from international experts, in relation to the optimal GA methodology for oncology clinical practice.

Chapter 4: Managing the Elderly in Radiotherapy using Geriatric AssEssment (MERGE): A Pilot Geriatric Oncology Clinic at Saint Luke's Radiation Oncology Network (SLRON)

Part 1

The primary aim of this feasibility study and two-arm, randomised pilot trial was to assess the feasibility of conducting an RCT on the effectiveness of conducting CGA in older patients undergoing radiotherapy.

The specific objectives were:

1) To examine feasibility outcomes, such as recruitment, time and resources, as well as patient completion of study obligations.
2) To describe a process designed to assist researchers in making the best use of the findings from this feasibility study to inform subsequent decisions regarding a follow-on trial.
3) To make recommendations on the resources required in order to implement these management recommendations.

Part 2

The secondary aim was to obtain preliminary data on the prevalence of geriatric impairments in an older patient population undergoing radiotherapy treatment and the efficacy of CGA-driven interventions on patient outcomes (acute radiation-induced toxicity and treatment compliance).

The specific objectives were:

1) To examine the clinical characteristics of older patients with cancer, as part of an initial CGA in the radiotherapy department at Saint Luke's Radiation Oncology Network, at St. James's Hospital.

2) To evaluate the results of patient CGA and identify deficits in various assessment domains, such as physical function, comorbidity, polypharmacy, nutrition, cognition and psychological status.

3) To examine interventions and patterns of referral and subsequent management recommendations for this patient population during this timeframe.

Chapter 5: TILDA Study I

The aim of this study was to investigate to what extent older adults with cancer in the community differ from their non-cancer community dwelling counterparts in relation to key domains of CGA, as determined in the previous chapters.

The study objectives were:

1. To compare cancer survivors to their non-cancer controls, in relation to key aspects of health and wellbeing.

2. To investigate the longitudinal impact of a cancer diagnosis on the overall health and wellbeing of older adults with cancer living in the community across three timepoints: before diagnosis, during the diagnostic/treatment phase, and during the follow-up period.

3. To identify the impact of a cancer diagnosis on the quality of life of cancer survivors.

Chapter 6: TILDA Study II

The aim of the present study was to investigate to what extent older adults with cancer in the community differ from their non-cancer community dwelling counterparts in relation to frailty.

The study objectives were:

1. Define frailty using three commonly used indices, from TILDA data, and compare the prevalence of each type.

2. Describe the prevalence of frailty in community dwelling people with cancer and compare it to those without a cancer diagnosis.
3. Investigate the impact of a cancer diagnosis on the longitudinal development of frailty.

Chapter 2

2 Literature Review

2.1 Frailty, Ageing and Cancer

Frailty forms the basis for the practice of geriatric medicine, but remains poorly appreciated in other aspects of medicine, such as oncology. It has been defined in the gerontology literature as a consequence of (usually) age-related decline in many physiological systems, resulting in a reduced reserve capacity and increased vulnerability to stressors [45, 46]. This vulnerability is related to an inability to maintain homeostasis in the face of a physiological threat e.g. infection, illness and trauma.

In terms of aetiology, frailty and cancer share common risk factors, such as smoking [47], sedentary lifestyle [48], malnutrition and obesity [49]. Recent research efforts have focussed on quantifying the acceleration of frailty that is now known to occur due to cancer and its treatment [50-52]. Accumulation of cellular damage and system dysregulation are common features of both ageing and cancer [51-54]. Long-term follow-up of paediatric and young adult cancer survivors have shown earlier onset of age-related concerns, such as multimorbidity, frailty and functional decline [55-57]. The prevalence of frailty was demonstrated to be similar between younger cancer survivors and adults aged 65 years and older without a diagnosis of cancer [57, 58]. It is thought that aging, and diseases such as cancer, represent different courses, with a common underlying cellular mechanism, which is also influenced by genetics and the environment [59]. This helps in part to explain the considerable differences seen in ageing phenotypes observed in older people e.g. one 70 year old may be frail and use a walking aid, while another may run marathons. Frailty has been associated with

increased mortality in older adults with cancer [60], however the definition of frailty in many studies has been heterogeneous [61].

2.2 Frailty Screening Versus Assessment

There has been a proliferation of frailty assessment tools in both geriatric medicine and in oncology in the past number of years. Many of these lack validation, however [62]. The gold standard in terms of clinical assessment remains the Comprehensive Geriatric Assessment (CGA). CGA is noted to be time consuming and requires specialist training, and therefore frailty screening is considered a more feasible option, or a first step in identifying those who require CGA and associated interventions.

2.2.1 Frailty Screening

Two schools of thought predominate in the gerontology literature, the phenotype of frailty defined by Fried [63], from the Cardiovascular Health Study (CHS), and Rockwood's clinical frailty criteria [64], based on cumulative deficits on various CGA domains.

The frailty model established by Fried and colleagues, in the Cardiovascular Health Study (CHS) study, which studied over 5,000 men and women over the age of 65, is relatively short and easy to use. It focuses on physical frailty, and is assessed using five different components i.e. unintended weight loss, weak grip strength, exhaustion, low physical activity and slow gait speed [63]. People are categorized as robust if no deficits are identified, prefrail if only 1-2 deficits are present, and as frail if there are 3 or more.

There is a moderate degree of correlation between the Fried and Rockwood models [65], however Rockwood's frailty index (FI) has

been deemed more useful in a clinical setting, as it also encompasses cognitive, psychological and social factors, which the Fried model does not (see Figure 2.1 below). It is widely known that that these socio-environmental determinants of health are vital in overall health and wellbeing. The FI was based on the results of a five-year prospective cohort study of over 10,000 people over the age of 65. In the original FI, 92 individual deficits from a wide range of domains, were identified to collectively define frailty [66]. Subsequent work has reduced the number of FI items required to predict frailty from 92 to 30 or so, with no subsequent loss of validity [67, 68]. With a greater number of deficits required to define frailty, the FI is considered to have more in-built redundancy than the phenotypic model i.e. no individual deficit carries a great threat of adverse outcomes.

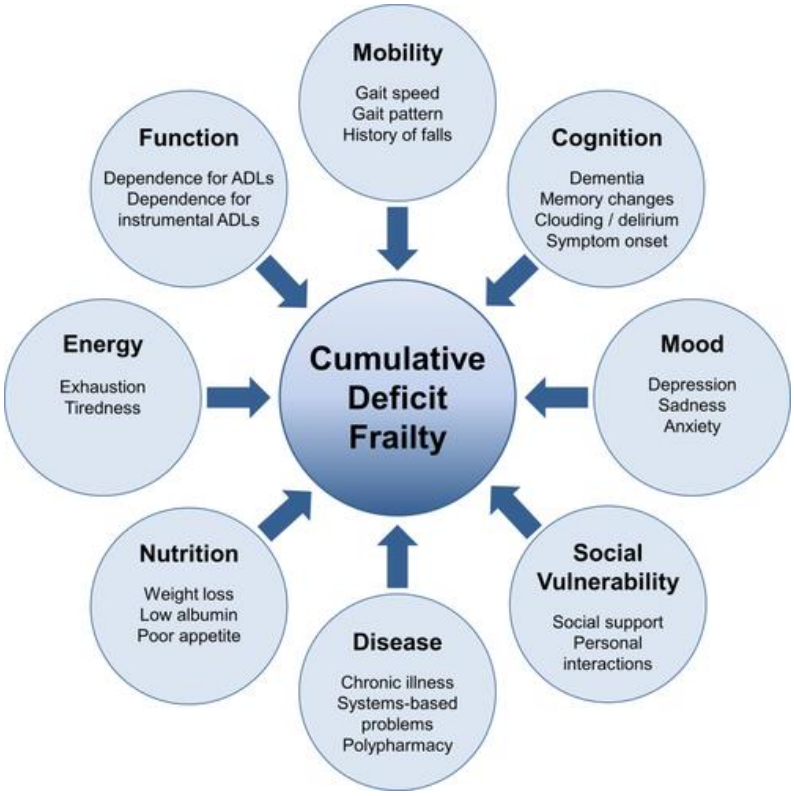


Figure 2.1 The cumulative deficit model of frailty [62]

One way to conceptualise the difference between these two models, is the famous Golden Gate bridge in San Francisco. A recent review [69] has described the phenotypic model as being equivalent to the major structural components of the bridge i.e. the towers or horizontal cables, as seen in Figure 2.2 Loss of even one of these towers would introduce greater instability, while three or more might be detrimental to its existence. Using the FI, or stochastic frailty model, on the other hand, is equivalent to looking at the multiple vertical cables in the bridge. Loss of one of these cables will not threaten the structural strength of the bridge in any way, however the accumulation of numerous insults over time might cause a greater threat to the bridge's integrity, and eventually lead to its collapse. Resilience on the other hand is a measure of the bridge's ability to withstand expected stressors e.g. wind, traffic and water. The Golden Gate bridge is well designed to expect and deal with these stressors, however, unexpected adverse conditions, such as storms, combined with heavy traffic and accumulation of damage over time in the form of the loss of vertical cables, might represent a tipping point, beyond which collapse is inevitable.

Human frailty can be envisaged in much the same way. Under normal conditions, the human body is able to withstand a certain amount of physiological decline, without any great impact on its day-to-day function. However, when a major physiological stressor is introduced, such as a major illness like cancer, and ensuing treatment, this might destabilize an apparently well-functioning individual and lead to a loss of resilience in the face of this physiological threat.

With regard to the phenotype of frailty, and the association with weight, an emerging phenomenon, in the era of higher obesity rates, is the relationship between loss of muscle mass and obesity, rather

than weight loss [70]. Age-related loss of muscle mass and strength, known as sarcopenia, is often used as a surrogate measure of frailty [71, 72]. It has been defined as “a syndrome characterised by progressive and generalised loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor QoL and death” [70]. Skeletal muscle wasting is a phenomenon that may be obscured within the bulk of body weight as patient’s age, and this is known as sarcopenic obesity [73].

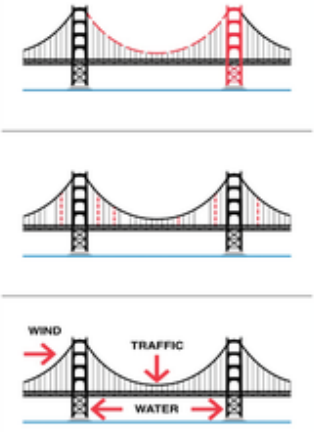
“Frailty” Constructs	Examples	Frailty and Resilience from the Perspective of a Complex Structure (Golden Gate Bridge)	Potential Strengths
A. Phenotypic Frailty (defined state)	Fried CHS Study Sarcopenic Obesity		Capture existence of a clinically defined and measurable phenotypic state Define risk factors and mechanisms with some specificity for given phenotype Measure treatment effect when a degree of treatment specificity is involved
B. Stochastic Frailty (accumulation of deficits)	Rockwood FI Index (e.g. FIclin,FIlab)		Perform prognostication Define cross-cutting risk factors Measure treatment effects when more pleiotropic interventions are studied Measure treatment effects when testing geroscience-guided therapeutics
C. Resilience (Measure of homeostasis in face of stressor)	Orthostasis Vaccine Responses Recovery from infection, surgery, anesthesia, dehydration, bedrest, chemotherapy, trauma or BM transplant		Identify “hidden” vulnerability Identify resilient mechanisms Obtain more individualized risk Design more precise interventions Design earlier interventions Design interventions targeting resilient mechanisms

Figure 2.2 The Golden Gate Bridge as a visual metaphor for the phenotypic and frailty index models of frailty [69]

There are several biomarkers associated with frailty, including cytokines and chemokines, e.g. Interleukin-6 (IL-6), insulin-like growth factor 1, as well as low levels of leptin and abnormal white blood cell counts [74].

The important thing to note in relation to the clinical presentation of frailty, is that compared to disability, frailty is potentially reversible, when managed effectively and appropriate interventions put in place to deal with deficits identified [75, 76]. This has the potential to

prevent falls, hospitalisation, nursing home placement and other important QoL indicators [77].

In oncology, rather than performing a CGA for all older patients, a two-step approach has been recommended by the National Comprehensive Cancer Network (NCCN) [78] and the International Society of Geriatric Oncology (SIOG) [79, 80], the National Comprehensive Cancer Network and European Organisation for Research and Treatment of Cancer (EORTC) [81]. This involves the use of a short screening tool to identify those who would benefit from a full CGA, followed by administration of the CGA to this subgroup.

One of the most acceptable screening methods in the oncology literature is the Geriatric-8 or G8 [82]. Use of a screening tool, such as the G8, enables healthcare professionals to use (scarce) resources more efficiently while ensuring that patients still receive optimum care. The G8 was the first screening tool devised specifically for oncology, and has been validated in the ONCODAGE study of patients with cancer [83]. It has been demonstrated to have high sensitivity (65%-92%) and acceptable specificity [84], and only takes approximately 4 minutes to complete. Poor performance on the G8 is associated with poorer one year survival [83]. A more recent systematic review of the G8, incorporating 46 studies, on the performance of the G8 have also found an association with survival and treatment-related complications [85]. A further development is a self-report version of the G8, with a preliminary analysis demonstrating good concordance with the original G8 [86].

2.3 Comprehensive Geriatric Assessment (CGA)

The gold standard for frailty assessment is the CGA. CGA is a multidimensional, interdisciplinary assessment that includes functional status, comorbidity, cognition, psychological status, nutrition, social support and polypharmacy, amongst others [87]. It is based on the assessment of accumulation of deficits, as mentioned previously. This assessment can provide a broader overall understanding of individual characteristics that affect life expectancy, functional decline, cognition and patient's own wishes, as well as how oncologic treatment might affect them [88]. Many variations in CGA exist, but it is thought that the core domains include physical (comorbidity, mobility, nutrition), psychological (cognition and mood), functional status and social assessments [89]. These domains are interrelated e.g. depressive symptoms may exacerbate lack of appetite and malnutrition, as well as social isolation, lack of physical activity, eventually leading to the development of frailty.

One of the first meta-analyses to demonstrate the benefits of CGA was published in 1993 [90], showing improvements in a range of outcomes, from improved functional status, reduced hospitalisations, greater independence and ability to live at home for longer. Several other studies have further supported these benefits [91, 92], including an updated Cochrane review [93].

2.3.1 Cognition

As an example, cognitive assessment is one of the key components of a CGA, and determines a patient's ability to provide informed consent, as well as their suitability for treatment. Most research in this area, in oncology, has been conducted in patients with breast

cancer receiving chemotherapy, with or without hormone therapy [94, 95]. However, recent studies have also established a tentative link between Androgen Deprivation Therapy (ADT) for prostate cancer and Alzheimer's disease [96, 97]. Testosterone is known to have protective effects on cognition, by promoting hippocampal synaptic plasticity and regulating the accumulation of amyloid proteins [98]. Importantly, declining muscle mass, caused by depletion of testosterone is also linked to frailty [99]. This is an important consideration for men with prostate cancer who are prescribed ADT.

Another emerging challenge for oncologists is treating patients with cognitive impairment. The prevalence of dementia increases exponentially with age, nearly doubling every five years from the age of sixty five [100], with almost half of those in the oldest old category i.e. aged 80 years and over, having a diagnosis of dementia [101]. The probability of being diagnosed with cancer also increases with age, enhancing the probability of co-occurrence of both dementia and cancer [102]. A basic assumption of informed consent for treatment is that patients have capacity. Undiagnosed dementia is very prevalent in the published literature in the acute hospital setting, ranging from 20% to 50% [103, 104], and is expected to increase in the coming years [101]. Early diagnosis of cognitive impairment is important in order to implement earlier treatment and effective management. However, oncologists often feel unable to manage or diagnose cognitive impairment [41].

2.3.2 Functional Status

Functional status can be measured subjectively or objectively. In oncology, function is usually assessed using either the Eastern Cooperative Oncology Group (ECOG) [105] or Karnofsky Performance Status (KPS) scales [106]. This would appear relatively

one dimensional to a geriatrician, who would consider such objective measures as gait speed, balance, grip strength and lower extremity strength, as these are more predictive of patient outcomes [107]. In particular, gait speed has been shown to be a significant predictor of mortality across numerous studies [108], a simple assessment, but with much more predictive value.

Subjective measures, such as Activities of Daily Living (ADLs) and Instrumental Activities of Daily Living (IADLs), provide information on the person's ability to perform basic activities related to self-care, or the ability to function independently in their communities. ADLs were originally devised by Katz et al, as "activities which people perform habitually and universally" [109]. The corresponding IADL scale is derived from a set of validated questions developed by Lawton and Brody [110]. Some of the latter may not be applicable to all individuals e.g. if they were never accustomed to doing housework, or preparing food, then those functions are not taken into account.

Many of these measures are known to exhibit floor and ceiling effects [111]. Ceiling effects (when most participants score the maximum achievable score on a test because the test is unable to distinguish between individuals at the higher score range) are often observed in younger, healthier cancer survivors, while floor effects (when participants typically score the lowest achievable score on a test, because the test is unable to distinguish those at the lower range) typically occur in older, frailer patients. Therefore, a combination of subjective and objective measures is advocated.

The individual components of each are listed in Figure 2.3.

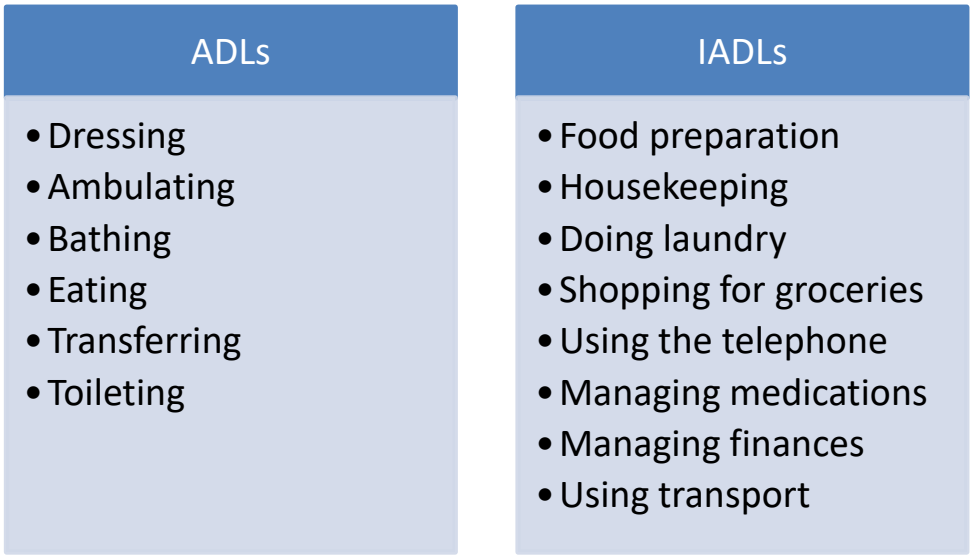


Figure 2.3 Components of Activities of Daily Living (ADLs) and Instrumental Activities of Daily Living (IADLs)

Mohile et al [112], in a study of more than 900 patients with prostate cancer undergoing radiotherapy, found no difference in symptom burden in older patients, but older patients were more likely to report that symptoms interfered with walking after radiotherapy. Again, this underlines the importance of assessing functional status in patients with cancer, and ensuring optimisation of mobility both during and after treatment, in order to prevent further decline. Such decline could increase the risk of falls, which, in conjunction with ADT, contributes another risk factor [113].

2.3.3 Falls

A fall can have various interpretations, however, a common definition from the American and British Geriatrics Society is: “an unexpected event in which the participant comes to rest on the ground, floor or lower level without known loss of consciousness” [114]. Research has demonstrated that older people with cancer, have a 15-20%

greater risk of falling, with occurrence rates of 30-50% of those aged 65 years and older, with a cancer diagnosis [115, 116]. However due to suboptimal reporting the actual rates may be higher [117]. More than one-third of persons, aged 65 and over, fall each year, and in half of these cases the falls are recurrent [118]. In hospitals, patient falls are common and may lead to adverse outcomes, such as physical injury and bruising, fractures and prolonged hospitalisation [119, 120].

Assessment of falls risk is important in all patients over the age of 65, as one in three will experience a fall [121, 122], however it is not routinely assessed in oncology. A comprehensive assessment, such as that advocated by the National Institute for Health and Clinical Excellence (NICE) guidelines [123] and the British and American Geriatrics Societies [114], should be carried out in order to eliminate precipitating factors, such as polypharmacy, poor vision, inadequacy of the home environment etc. Certain types of concurrent chemotherapy, such as taxols, can exacerbate existing risk factors, due to the onset of peripheral neuropathy. ADT can also increase risk, due to its impact on muscle mass in prostate cancer patients [124]. Combined with the side-effects of treatment e.g. fatigue, the patient, at high risk of falling, is increasingly vulnerable. Findings from a Cochrane Review have demonstrated that clinical assessment by healthcare professionals, combined with individualised interventions for identified risk factors, reduced falls rate by 24% [125]. A risk assessment consists of falls history, medication review, physical examination, functional and environmental hazards assessments [126].

2.3.4 Comorbidity

As age increases, so too does the incidence of comorbidity, which is associated with poorer overall survival in older adults with cancer [127]. A Medicare study showed that over two-thirds of older US individuals had two or more medical conditions, and almost a quarter had four or more [128]. Older adults with a diagnosis of cancer are at greater risk of concurrent medical conditions, compared to their age matched counterparts [26].

Many assessment methods for comorbid illnesses are available, and no gold standard exists [127, 129]. One such method is the Charlson Comorbidity Index (CCI) [130], which is also commonly used in oncology. The CCI is the most frequently cited index in the published literature, and is classified as a weighted index. Charlson et al analysed one year mortality as a function of various comorbidities and assigned a weight in relation to their known outcomes. An age-weighted version is also available [131], and the CCI is considered easy to administer in clinical practice.

Another approach is to assess the impact of comorbid illnesses on the function of body organs and systems [129]. The Cumulative Illness Rating Scale (CIRS) classifies comorbidities by organ system and rates them according to their severity (0-4) [132]. Miller et al [133] subsequently modified the CIRS as a way to better reflect the older patient, in the form of the Cumulative Illness Rating Scale for Geriatrics (CIRS-G). Compared to the CCI, the CIRS-G is considered more sensitive, as all coexisting comorbid conditions are recorded, and it appears to provide more prognostic information [134, 135]. The CIRS-G has been validated in older patients with cancer [136] . It is, however, more time-consuming than the CCI and assessment by specifically trained personnel is recommended.

Kaplan–Feinstein Index (KFI) is also a systems based approach, and groups conditions into 12 categories, with a severity rating applied for each one [137]. The original KFI was modified, by adding several health conditions (diabetes, HIV/AIDS, dementia), creating a comorbidity index for newly diagnosed patients with cancer, to become the Adult Comorbidity Evaluation-27 (ACE-27) index [138]. The ACE-27 is a validated instrument that captures comorbidities for cancer patients and grades severity at the time of diagnosis [139]. In total, twenty-seven conditions were identified, based on previous research, as well as clinical judgement.

Comorbid conditions, such as cardiovascular or respiratory disease, as well as diabetes and kidney disease, can pose a potential risk to cancer-directed treatment, and must be carefully evaluated in terms of a risk-benefit analysis, before embarking on a course of treatment [127]. Comorbidity also increases the risk of polypharmacy and adverse drug reactions [140].

2.3.5 Nutrition

Nutritional status is very important in older adults with cancer. As an example, older patients with head and neck cancer are especially susceptible to malnutrition due to anorexia, sequelae of radiotherapy treatment that limit food intake (i.e. xerostomia, odynophagia and dysphagia) as well as metabolic effects due to the inflammatory process (treatment or tumour related) [141, 142]. There is also an increased risk of mucositis in older patients, especially evident when treating cancer of the head and neck region [143]. Weight loss, the main symptom of malnutrition, has independent prognostic value in this group of patients [144], therefore supportive care is of the utmost importance. Symptoms of acute bowel toxicity e.g. diarrhoea, proctitis, rectal urgency, occur in the majority of patients during

treatment of abdominal or pelvic cancers. During radiotherapy, patients should receive individual dietary assessment and counselling, in order to maintain adequate nutrition during treatment, as a basic standard of care. If nutritional requirements cannot be achieved by a regular diet, then nutritional supplements and/or enteral feeding may be prescribed.

2.3.6 Social Support

Lack of social support has been association with frailty and identified as a significant predictor of mortality [145].

Social support is also important for patients who are required to attend daily radiotherapy treatments. Many may already be in a caregiving role, or may require caregivers themselves at some point in the future, as a result of cancer, or its treatment. This is one area where the radiotherapy service in particular can facilitate the patient and offer greater convenience. Considering shorter overall treatment schedules in radiation therapy may be very helpful in such cases, if they provide the appropriate management of course. One example is in the treatment of Glioblastoma Multiforme (GBM). For patients identified as elderly/frail, 25Gy in 5 fractions has been shown to be non-inferior to 40Gy in 15 [146], the previous standard of care for such cases [147]. A further example is hypofractionation in prostate cancer [148] and breast cancer [149].

Social isolation and lack of support have been independently associated with both a greater risk of developing cancer, as well as a higher mortality [150, 151].

2.3.7 Polypharmacy

Polypharmacy has been defined in a number of ways in the published literature. The most common definition is concurrent prescription of five or more medications (excluding supplements), with excessive polypharmacy defined as 10 or more medications [152]. Others have used the criteria of potentially inappropriate medications with a high risk of adverse outcomes for older adults [153]. As the number of comorbid conditions increases, so too does the risk of adverse drug interactions (ADRs) from increased polypharmacy [154]. Older adults with cancer often experience excessive polypharmacy, and recent research efforts have investigated appropriate prescribing and providing clinicians with tools to deprescribe, if necessary [155]. However, it is still problematic that polypharmacy is increasing in recent times, and poses an enhanced risk to patients with cancer, who may be at greater risk of falling, functional impairment [156], fractures [157], hospitalisation [158] and mortality [159], due to inappropriate prescribing. Older patients are already more vulnerable to these adverse effects of medication due to differences in pharmacokinetics and pharmacodynamics in the older population.

2.3.8 Psychological Status

Various studies have looked at the prevalence of depressive symptoms in community dwelling older adults, and estimate a range of 8% to 16% [160-162], with mild depression being even more common, at approximately 23% [163, 164]. For older people diagnosed with cancer, the literature varies in terms of prevalence from 15 to 31% [165, 166]. This variation is due to differences in measurement, type of cancer, age and disease status. Depressive symptoms are linked to healthcare utilisation, with those who are depressed 2-3 times more likely to access services [167].

Psychological status and frailty are inherently linked [168], and depression is also known to affect cognition [169]. Therefore, proper assessment and treatment are of the utmost importance.

2.4 CGA in Oncology

There are many important factors to consider when deciding on a course of cancer treatment for older adults. SIOG and National Comprehensive Cancer Network (NCCN) guidelines for older adults advocate the use of CGA is vital in “staging the ageing” i.e. assessing physiologic and functional capacity, which in turn has implications for being able to predict treatment tolerance and toxicity[170-173]. The potential benefits in oncology are many, and include the identification of geriatric impairments, even in those with a good performance status [136, 174]. CGA can predict toxicity associated with chemotherapy in older adults [175] , as well as mortality [176] . It also predicts postoperative morbidity [177, 178] Reasons put forward to date for the lack of integration of CGA into oncology have included that it is too time consuming . However, it could be argued that those against the use of CGA, citing excessive time consumption and resource implications, have low credibility in a healthcare setting where there are vast amounts of expenditure on high technology for imaging and treatment [179]. CGA by comparison is relatively low cost, as Hamaker et al [179] have highlighted. The cost of CGA, estimated as a nurse’s salary for one hour ($28), is small compared to the cost of dealing with toxicity and treatment complications, and subsequent unplanned hospitalisations. It is also a fraction of the cost of other diagnostic procedures e.g. diagnostic images and genomic testing, commonly used in oncology.

When independence is not maintained and poor outcomes occur, patients require hospital care. Troubleshooting these issues before

they arise by using CGA as part of the diagnostic work-up to determine the most appropriate treatment can prevent reliance on hospital resources in the long-term. Frail patients are more likely to have poor outcomes following surgery, chemotherapy and radiotherapy [62]. In an outpatient setting, CGA-based care has resulted in fewer hospitalisation days and enhanced survival in patients with no associated increase in cost [180]. This not only benefits the patient, but also the health care system as a whole.

CGA also facilitates shared decision-making approaches, as it provides a multidimensional view of the patient's overall health as a potential starting point for risk stratification. Knowledge of current functional and cognitive status, in particular, and the ability of treatment to cause declines in those domains, is especially important to patients, more so than survival [181, 182].

2.4.1 CGA in Radiation Oncology

The current literature on the role of CGA in radiation oncology treatment is particularly limited. A total of twelve non-randomised studies were included in a systematic review by Szumacher et al [183]. Four studies used a screening tool only, while the remaining studies used a combined approach of initial screening, followed by CGA. Two studies demonstrated a significant association between abnormal screening and mortality, while only one study showed that CGA influenced treatment decision making. Half of the studies included did not find an association between screening or CGA, and treatment tolerance. It was highlighted that the majority of these studies included small sample sizes.

2.4.2 The Impact of CGA on Treatment Decision Making in Oncology

The Elderly Cancer Patient (ELCAPA) study, one of the largest studies of older cancer patients published to date, identified subgroups based on CGA that were predictive of overall outcome, hospital admission within 6 months and a fatal outcome within one year, highlighting its clinical utility in oncology [184]. When coupled with targeted interventions, the benefits of CGA in older patients may include prolongation of life, prevention of hospitalisations and admissions to long term care facilities, prevention of geriatric syndromes, recognition of cognitive deficits, and improvement of health status[35].

CGA provides a broader overall understanding of individual characteristics that affect life expectancy [88]. It may be more sensitive than physicians' judgment in classifying patients as "fit" versus vulnerable or frail, and in determining the best choice of cancer treatment [185]. Figure 2.4 depicts a conceptual model of how CGA can be incorporated into oncology assessment and treatment. Fit patients should be candidates for the same treatment as their younger counterparts, while frail patients would benefit from a more palliative approach. Vulnerable patients may need to be offered a tailored treatment in order to avoid decline during/after treatment, or may benefit from a dose adapted approach.

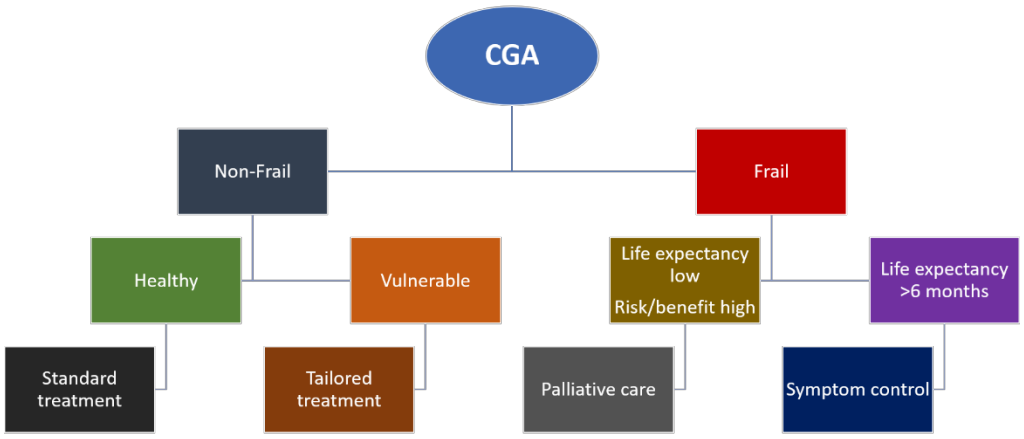


Figure 2.4 Conceptual model of how CGA can be integrated into oncology

In larger studies by Kenis [186] and Decoster [187] treatment modifications were mainly chemotherapy related, and where no CGA was carried out, radiotherapy decisions were only altered in 0.4% of cases. Caillet at al [188] also reported similar results, with the most common change in treatment decision being a switch from chemotherapy to supportive care. Studies similarly suggest that the impact of CGA may be limited to patients undergoing more toxic treatments, such as chemotherapy and targeted therapy [187, 189]. Timing is also important. Horgan et al [190] reported that when the treatment plan was decided before CGA, it altered the decision in only one patient, whereas when the treatment plan was undecided at the time of referral, the CGA impacted the final treatment decision in 83% of cases. The ideal time for intervention is before discussion of the patient case at the multidisciplinary meeting or tumour board, before the patient is referred for radiotherapy/chemotherapy or other modality. It should also be stressed that the majority of studies

looking at decision making were undertaken in medical oncology, and there is a relative lack of information on how CGA may impact radiotherapy related decisions.

Concomitant chemotherapy adds appreciable toxicity in patients aged 70 years and over. They experience more frequent hospitalisations and a lower rate of feeding tube removal at last follow-up or death, as well as worse overall survival [191]. CGA offers important support to patients and could aid treatment decisions in this patient group, especially related to the role of concomitant chemotherapy. The types of interventions, resulting from CGA defined deficits, have been outlined in recent American Society of Clinical Oncology (ASCO) guidelines [192] and are summarised in Table 2.1 below. These interventions are suitable for all treatment modalities.

CGA Domain and Associated Deficit	CGA Driven Interventions
Functional status Instrumental activities of daily living History of falls	Physiotherapy and/or occupational therapy referrals for strength and balance training, home safety evaluation, exercise programme
Comorbidity and Polypharmacy	Involve General Practitioner and/or geriatrician in decision making and disease specialists for management of comorbidities, review medication list and minimise medications as much as is feasible, consider pharmacist review, assess adherence to medications
Cognition Abnormal score on cognitive test	Assess decision-making capacity and ability to consent for treatment, identify healthcare proxy and involve proxy in decision making for treatment, assess delirium risk and counsel patient and family, medication review to minimise medication with a high risk of delirium, consider geriatrician referral
Depression Abnormal score on depression scale	Consider referral to psychotherapy/psychiatry/psycho-oncology, cognitive behavioural therapy, social work involvement and pharmacologic treatment
Nutrition Weight loss >10% in previous months	Dietician referral and nutrition counselling, assess need for additional support for meal preparation and home support interventions e.g. meals-on-wheels

Table 2.1 CGA-driven interventions in oncology [adapted from ASCO guidelines [192]]

2.4.3 The Impact of CGA on Treatment Decision Making in Radiation Oncology

By comparison to medical oncology, the role of CGA in influencing treatment decisions, and in driving interventions for older adults in radiation oncology, is unclear [183]. Soubeyran et al [193], are currently investigating the relationship between CGA-driven interventions and therapeutic outcomes, based on an initial screening with the G8, using an RCT design. Importantly, this study will include patients referred for radiation therapy. Soubeyran and colleagues have highlighted that the number of studies (RCTs) investigating

CGA driven interventions in oncology is currently small (n=9), with only one study of radiation oncology by Lapid et al [194] from 2007. The latter small study (n=33) of newly diagnosed patients with advanced cancer, planned to undergo radiation therapy, investigated a quality of life intervention with patients randomised to either the intervention group or standard care. The intervention consisted of eight sessions, devised to address five QoL/CGA domains, i.e. cognitive, physical, emotional, spiritual, and social functioning, and found a significant improvement in QoL scores.

The ongoing multicentre ELAN trial [195] aims to stratify patients according to whether or not they are fit or unfit, and select treatment accordingly. Unfit patients will be randomised in the ELAN-RT trial, to a hypofractionated split course schedule (30 Gy/10 fractions, with a two-week gap for toxicity management, followed by 25Gy/10 fractions). This trial could potentially support a change of practice in relation to the role of baseline CGA in determining appropriate treatment for older adults with head and neck cancer.

Identification of previously unknown deficits is one of the major advantages of frailty screening and accompanying CGA, allowing some intervention in order to optimise patient care and potentially to reverse frailty. A limited number of other, non-randomised, studies, exist in radiation oncology. Goineau et al [196], in a study of 100 patients with localised prostate cancer, aged 75 and older, undergoing radiotherapy treatment, found no association between CGA and quality of life. However, they found Instrumental Activities of Daily Living (IADL) impairments at baseline in approximately half of all patients enrolled in the study, as well as ADL impairments in 16% of patients. One fifth of patients presented with cognitive decline (defined as MMSE<27), 31% with depressive symptoms and more than two-thirds with significant co-morbidities, especially

cardiovascular comorbidities, which may obviously affect ADT tolerance. Malnutrition was virtually absent, suggesting that nutrition based screening tools, such as the G8 [82], would be of little relevance in this particular patient cohort. Spyropoulou et al [197], in a radiotherapy patient population (n=230) found that patients >75 years with higher Vulnerable Elders Survey-13 (VES-13) [198] scores were less likely to complete radiotherapy, independent of other factors that might affect radiotherapy completion. VES-13 is largely based on functional status, an integral part of CGA. Keenan et al [199] did not find any correlation between the Edmonton frailty score and radiotherapy toxicity. Neve et al [200], in a small study of older patients with head and neck cancer, also undergoing radiotherapy, found that patients identified as vulnerable at baseline, were less likely to complete radiotherapy.

A further study [201] investigated whether an objective measure of physical function, the Timed Up and Go (TUG) test, as well as the G8, had an association with acute toxicity and ability to comply with treatment. This showed no relationship between the two tests and treatment tolerance. The other was a prospective cohort study focusing on patients with head and neck cancer [31], in which those who reported pre-radiotherapy functional limitations were more likely to show both reduced health-related QoL during treatment, as well as a longer recovery afterwards.

These studies signal some of the potentially useful interventions for patients receiving radiation therapy, albeit not directly investigated or mentioned in most of the aforementioned studies which have focussed exclusively on assessment, often without mention of follow-up care. This area has been one of the gaps in the current literature in oncology generally, but more so in radiation oncology.

Some of the ways in which CGA might alter treatment decisions in radiation oncology include omission of concomitant chemotherapy for example, which contributes considerable toxicity for the patient. Another adaptation is altering the type and modality of radiation treatment offered to patients. Although radiation therapy is usually well tolerated in older patients [112], hypofractionated radiotherapy could be considered in older patients with poor supports, lack of mobility, lack of transportation, in active caregiver roles or with social frailty, for example. This would limit the burden of travel for such patients, especially those not living adjacent to regional cancer centres. This is one area where the radiotherapy service can facilitate the patient and afford greater convenience. One example of this is in the treatment of Glioblastoma Multiforme (GBM). For patients identified as elderly/frail, 25Gy in 5 fractions has been shown to be non-inferior to 40Gy in [146], the previous standard of care for such cases [147]. Alternatively, the CGA may help to identify frail patients who are not candidates for conventional, daily radiotherapy but may benefit from other (curative) modalities, such as stereotactic body radiotherapy, with fewer hospital visits and potentially less toxicity [202]. Accelerated Partial Breast Irradiation (APBI) is another option to simultaneously limit toxicity and afford greater convenience for the patient [203]. APBI uses larger radiation doses to the localised tumour bed (as opposed to the entire breast) over a shorter period of time.

Pottel et al [204] have highlighted the need for regular re-evaluation of CGA domains during radiotherapy as the toxicity of chemoradiation results in multidimensional decline, necessitating supportive care and intervention. Again, this highlights the need for ongoing assessment and appropriate interventions. Some of these interventions are congruent with those listed in Table 2.1, but more

radiotherapy specific interventions, as well as those mentioned above, warrant further investigation.

2.4.4 The Lack of Standardised Approaches to Assessment

Consensus papers in geriatric medicine have recommended that frailty assessment should include the core domains of physical activity, mobility, strength, endurance, balance, nutrition, cognition, the senses, mood and coping, as well as social support [205, 206]. However, cognition is not included in the Fried phenotypic model and is included in approximately 50% of frailty measures in the gerontology literature [207]. SIOG recommend the inclusion of the following domains in CGA: functional status, comorbidity, cognition, mental health status, nutrition, social status and support, fatigue, polypharmacy, and geriatric syndromes [79].

When it comes to oncology, the lack of consensus is even more pronounced. Understandably, as CGA was never intended to predict how patients will respond to cancer therapy. Puts et al [40] have highlighted this lack of standardisation with regard to CGA domains and assessments in the published literature to date. This limitation further hinders the advancement of the field of geriatric oncology, due to an inability to compare studies from the published literature.

Few studies have looked at radiotherapy alone as a treatment modality, the vast majority including medical oncology patients. In general, there do not appear to be significant differences between younger and older patients in relation to reported toxicity during radiotherapy, although older patients were more likely to report difficulty with walking after completion of radiotherapy and greater

distress [112]. Again, this reinforces the need for CGA to estimate baseline function and optimise function where possible.

2.4.5 Providing More Holistic Care for Patients with Cancer

A patient-centred approach is crucial. While therapy may increase survival rates, a reduction in patient's health-related QoL potentially negates any benefits. Sekeres et al. state that QoL was more important to patients than the duration of life when making treatment decisions [208]. Another study showed that maintenance of physical and cognitive function was more important to older patients than traditional survival endpoints [181]. Survivors of haematological cancer are known to be at increased risk of depression and a variety of physical impairments compared to a control population [209]. Tools for measuring QoL such as the elderly specific European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire for Elderly cancer patients – the QLQ-ELD15 [210] and Q–TWIST (Quality-Adjusted Time Without Symptoms or Toxicity) [211] can be used to determine time with/without significant toxicity experienced until death and can be used to compare treatments.

Although overall survival is an important outcome in most patient groups, compromising a patient's QoL to achieve this could cause the patient to lose his or her independence at home or lose the ability to carry out daily activities. CGA-based allocation has been proven to reduce toxicity and thus results in a better QoL for the patient after treatment, which is a valuable endpoint for older patients [21, 212]. CGA should be used to assess the patient's frailty status and estimate the severity of expected side effects and the impact these would have on a patient's QoL. Should the patient be rendered too

frail, their QoL could be negatively impacted or their functional reserve could be depleted after intense treatment. Overall survival should not be the only goal when designing clinical trials or treatment for older patients, as QoL is equally as important. Regular CGA assessment throughout the course of treatment ensures the patient's frailty status can be monitored.

2.5 Implementation of CGA in Clinical Practice

As alluded to in Section 1.4, geriatric oncology does not exist in Ireland at the current time, but there are many international models to use as exemplars as to how it may be implemented in clinical practice [35-37]. One major challenge is that there is a notable shortage of geriatricians worldwide [42]. However, international models of geriatric oncology are based upon upskilling oncologists, nurses and allied health professionals to be able to implement, understand and interpret the findings of a CGA and how they may impact patient care [213]. Patient and/or caregiver self-report is also feasible for many of the domains of CGA, including electronic methods [86]. Some components however, i.e. cognitive assessment and physical performance measures (e.g. TUG test), require additional time in the clinic. A two-step model with a brief initial screening, followed by full assessment allows a better allocation of resources in the oncology setting [35].

These assessments can be carried out by a nurse or other allied health professional, and don't necessarily require oncologist's time. Estimates of the total time required for a basic CGA in oncology range from 22 - 27 minutes in total [36, 214], with only a fraction of that time needed by the healthcare professional [215]. In terms of cost-effectiveness, the relative cost of CGA—approximately a nurse's

salary—is minute by comparison to the various diagnostic tests and scans that are used in oncology [179].

Other members of the allied health professional groups have also been identified as key contributors to the multidisciplinary team in geriatric oncology [216]. Occupational therapists and physiotherapists are uniquely positioned to provide supportive services for patients in danger of functional decline. Dietician collaboration is essential for nutritional issues. Pharmacists can provide much needed insight into polypharmacy and potentially inappropriate prescribing, while psycho-oncology services and social workers can assist with psychological or social issues. Harnessing the skills and expertise of the existing multidisciplinary team is essential in geriatric oncology. Not every department will have access to the full array of specialists, but it is important to remember that CGA and screening can be provided by physicians, nurses and any other healthcare professional.

Although the literature has shown the approach to geriatric oncology is feasible in clinical practice, there is currently no evidence on the clinical and cost-effectiveness of this approach. The current evidence to suggest that geriatric interventions have a positive impact on survival and QoL in older patients with cancer is limited, and RCT data are required. There is one large study currently underway that will evaluate the cost-effectiveness of geriatric oncology programmes, by Puts et al in Canada [217]. Cost-effectiveness of CGA has been well established in other settings [218-220].

There are many models of geriatric oncology programmes, such as those providing ongoing geriatric oncology management throughout the cancer trajectory, one-time consult programmes, site specific

models and those based on age, rather than tumour site [221]. Geriatric oncology remains a niche service in many countries internationally [213]. In a European context, significant heterogeneity exists among geriatric oncology programmes.

For example the use of a screening tool is a quality indicator for patients with colorectal cancer in the Netherlands [222]. The Italian system of geriatric oncology is organised through The Italian Geriatric Oncology Group (GIOGER) [223], which is similar to the Spanish system [224], with a few geriatric oncology programmes in some of the biggest centres. Similarly, in the UK, a number of pilot programmes have been initiated [225].

France has a relatively coordinated system of geriatric oncology and serves as one of the exemplars worldwide. This coordination has been facilitated by funding through Institute National du Cancer (INCa), who have funded consecutive cancer plans [226]. This has led to a more coordinated network of geriatric oncology units across the country, which are led by both an oncologist and a geriatrician. Ultimately, this has enhanced access for older patients and resulted in organised geriatric oncology research programmes and increased awareness among both the general population and health professionals.

A geriatric oncology programme requires this kind of infrastructure and administrative support to lay the foundations for a sustainable programme in the longer term. Difficulties sustaining these requirements have been explored in the published literature [227]. Defining clinical referral pathways for identified deficits and ensuring access to appropriate interventions are important tasks to address before implementing CGA [228]. This requires good communication with other disciplines as part of the multidisciplinary pathway, which

has historically been quite poor, with both professions traditionally working in a separate capacity, with little collaboration [229]. General Practitioners (GPs) are another untapped resource that could potentially be better utilised in geriatric oncology. GPs often feel excluded during cancer treatment, despite being a main point of contact for the patient, and often the best gatekeeper for access to support services in the local community [230, 231].

Bagayogo et al [232] outlined ways in which oncologist-geriatrician collaboration could be enhanced, such as institutions mandating the presence of the geriatrician at multidisciplinary meetings, or tumour boards. Oncologists indicated that this would be useful, and also that physical proximity of geriatricians would be ideal. Health technology was also identified as a good facilitator of communication and collaboration [229], and having “geriatric oncology champions” in academic oncology [233]. Four recent pilot studies (three RCTs and one cohort study) examined the role of a multidisciplinary collaborative approach to CGA and associated interventions in oncology [234-237]. These studies have demonstrated a positive impact from a multidisciplinary geriatric oncology team with regard to patient outcomes, such as QoL.

To implement CGA into clinical practice, there are educational requirements in the medical, nursing and allied health curricula that need to be addressed. Studies have highlighted there is an unmet need in this regard [41, 238]. In order to address this, efforts to devise a core curriculum in geriatric oncology have been undertaken by several societies. ASCO [192] and the European Society of Medical Oncology (ESMO) [239] have both developed recommendations for geriatric oncology as a part of their global curricula. Likewise, the European Oncology Nursing Society (EONS) has also published recommendations for a core curriculum for geriatric oncology for the

nursing profession [240]. Similar efforts are underway in radiation oncology [241]. SIOG have developed the Treviso Advanced Geriatric Oncology course [242] in order to enhance education and clinical practice for both the geriatrics and oncology disciplines . Initiatives such as these are vital to address the existing knowledge gap.

2.6 Conclusion

Many aspects of the care of older patients receiving cancer-directed treatment are under-served compared to the evidence base and rigour applied to other patient cohorts. This is a result of the traditional exclusion of older patients from oncology clinical trials. A direct consequence of this practice is that the current evidence base only serves to define treatment for the fittest category of older adults. We generally lack clear guidance on other patient groups, i.e. those who are vulnerable or frail. While intuition can guide clinicians to a certain extent, there is an urgent need for more defined research to allow us to better understand the heterogeneous group of patients presenting to us for treatment.

There is a growing need for increased collaboration between the disciplines of oncology and geriatric medicine. CGA is a multidimensional assessment used to assess an older patient's cognitive function, co-morbidities, physical function, psychological function, nutritional status and the patient's social support system. It allows oncologists to have a better estimation of the patient's overall health status i.e. is the patient fit, vulnerable or frail [243]? This can potentially inform treatment decision making and allow a more patient-centred process of care.

Commonly used ECOG based inclusion criteria have been shown to poorly define the extent of frailty in the older patient population[244]. Therefore, study findings cannot be fully extrapolated to clinical practice. A CGA can also be used to allocate patients to various treatment arms in clinical trials. One such example is the phase III ELderly heAd and Neck cancer-Oncology eValuation (ELAN-ONCOVAL) trial which used CGA to allocate patients into treatment arms depending on whether they were fit, vulnerable or frail [245]. Unfortunately, there is a lack of consensus on the ideal CGA based evaluation to use in oncology, which makes comparison between studies difficult at present [246, 247]. CGA was initially devised for a geriatric medicine setting in order to diagnose and intervene as appropriate. It was not designed for an oncology setting, where the intention for its use may be to guide treatment and predict survival, toxicity and QoL.

Research examining the role of frailty in oncology remains inconclusive in many key areas, and more studies are needed to determine the role of frailty assessment in treatment decision making and impact on other outcomes, such as toxicity, quality of life and survival.

Chapter 3

3 A Delphi Consensus Study of Geriatric Assessment in Oncology

3.1 Introduction

It is widely reported that older patients with cancer are undertreated compared to their younger counterparts [248-250]. Survival data from national cancer registries and institutions such as the European Alcohol Policy Alliance (EUROCARE) [251], have highlighted significantly poorer outcomes for older patients. There is a lack of empirical data related to tolerability of cancer-directed treatment in older patients, due to the traditional exclusion of older patients from cancer clinical trials [19, 20, 24, 212, 252]. Existing level 1 evidence and treatment guidelines tend to favour fitter older patients, and it remains uncertain what approach to take towards more vulnerable patients [253-255]. Also, ageism may exist in cancer care [256], and indeed patients themselves may choose not to undergo aggressive treatment, especially if treatment could affect their quality of life [181, 257].

The Institute of Medicine's 2013 report on cancer care [258] highlighted an urgent need to gain more evidence regarding effective remedial action for the undertreatment of older adults with cancer. Guidelines have advocated for a more objective pre-treatment assessment of older cancer patients [79]. The ability to stratify patients according to their physiological age to help guide cancer treatment decisions for older patients is of paramount importance. It is thought that integration of geriatric medicine principles into oncology might better assist clinicians in making complex treatment decisions. It may also help to overcome issues of inequity of access, undertreatment and indeed overtreatment.

A comprehensive geriatric assessment (CGA) is defined as a "multidimensional interdisciplinary diagnostic process focussed on determining an older person's medical, psychological and functional capability in order to develop a coordinated and integrated plan for treatment and long term follow up" [87]. This is often abbreviated to GA (geriatric assessment) in the geriatric oncology literature.

GA has been shown to improve outcomes in older adults in the geriatric medicine setting, with regard to reduced hospital admissions, improved functional status and better survival [90, 259]. The evidence for the benefits of GA in oncology include prediction of treatment related toxicity [189, 260, 261], treatment adherence [197, 262, 263], quality of life [204, 264], ability to inform oncologist's treatment decisions [186-188, 190, 265, 266] and overall survival [176, 267-269]. However, much of the current knowledge base for the effectiveness of GA in oncology is based on smaller retrospective studies of heterogeneous cancer patients, and better prognostic models are needed [79].

Despite consensus guidelines from The International Society of Geriatric Oncology (SIOG) [79, 80], the National Comprehensive Cancer Network (NCCN) [78] and European Organisation for Research and Treatment of Cancer (EORTC) [81], who have recommended GA be performed in all cancer patients, it has yet to be optimally integrated into the field of oncology in most countries. One difficulty in the published literature in relation to GA, lies with the lack of standardisation of assessment approaches to date [40]. In the absence of evidence-based guidance, the Delphi method is frequently employed in healthcare to formulate expert consensus guidelines in a particular field [270-272]. There is also a knowledge gap amongst many oncologists in relation to the objectives and methods of GA [41, 273].

3.1.1 The Current Study

No research to date has been carried out to examine the optimal method of frailty assessment in oncology and how best to implement GA into radiation oncology clinical practice, in particular. The current study sought to address this gap in the literature by examining how best to implement GA for older cancer patients. In addition, the study sought to address the lack of research about assessment methods and care pathways.

The overall aim of this study was to obtain consensus on aspects of GA in oncology to inform the implementation of an Irish geriatric oncology programme, which would be transferable to other countries and healthcare systems.

The specific objectives of Study 1 were:

1. To determine current practice in relation to GA in oncology.

2. To establish consensus among a group of Irish Oncologists, with guidance from international experts, in relation to the optimal GA methodology for oncology clinical practice.

3.2 Methodology

This study used the Delphi method in order to achieve its primary aim of gaining consensus among a group of participants. The Delphi method attempts to reach a convergence of opinion among experts on a specific topic, over a series of rounds or iterations, using a facilitated group approach. It was developed in the 1950s by the Research and Development (RAND) Corporation, for a US military project [274]. The basic process has evolved over the years, but still comprises a number of key steps i.e. convening an expert group, discussion and iteration with regard to a particular topic, and condensing data from this expert body in order to achieve consensus, using various statistical methods [275-277]. All of these steps are important in maintaining the methodological rigour of the approach [278]. While survey methodology defines the current status of events, the Delphi technique is used to define "what should be" [279]. It has been used extensively in healthcare, in order to set goals, policies or predict future events, and is especially useful where the relevant evidence base is lacking, as in the current study [280, 281].

There are a number of benefits to using the Delphi method [282, 283]. Usually participants can remain anonymous (though this isn't feasible in face-to-face rounds), and thus may change their opinions without peer pressure [275] . Interpersonal difficulties, often inherent in committee based decisions, are eliminated, and dominant members of a group are less intrusive [284]. Subject bias is thus potentially reduced, as participants are anonymous, and greater transparency is achieved through more open communication. Using the Delphi method overcomes geographical boundaries to participation, as in the current study, where it would not otherwise be feasible to convene such a range of stakeholder groups.

3.2.1 Different Types of Delphi

There are a number of ways in which the Delphi technique can be facilitated. The Classical Delphi technique is delivered over a period of time (often months), in a series of structured "rounds", which are used to reach consensus from a group of experts in a particular topic, usually through the use of questionnaires. Feedback from successive rounds is provided to participants in an iterative process, with the potential for altered opinions to emerge over time. Feedback is incorporated into the design of subsequent rounds, e.g. by eliminating items that have reached consensus. When consensus has been achieved, the process ends. However, consensus may not always be possible.

Other methods use face-to-face meetings or focus groups in the first round. Some take the opportunity to capitalise on a group of experts presenting for a specific purpose e.g. a conference, to gather expertise in a room via a "consensus conference". More recent studies have concentrated on web-based implementation. Online Delphi is mainly administered via the internet, using anonymous online surveys, which is the methodology chosen for the current study. Questionnaires are circulated for each round, whereby participants rank their agreement, or lack thereof, with particular questions or statements. The next round then incorporates this feedback in its design, and participants are invited to reconsider their initial judgements, based on the collective feedback received. This process continues until agreement is reached. A four round Delphi was chosen for the purpose of this study.

3.2.2 Alternatives to the Delphi Technique

There are a number of other methodologies that were considered for the current study. One of these, another consensus-seeking method, was the nominal group technique (NGT). The NGT Is a structured face-to-face group interaction comprising four key stages [285]. These are: 1) silent generation round, 2) round robin, 3) clarification and 4) voting (ranking or rating). Using this method, a maximum of seven participants is recommended for the entire process, and it usually involves one or two questions, which are circulated to participants in advance of the meeting. For the silent generation round, participants are

given approximately 20 minutes at the beginning of the group meeting to answer the specific questions asked. The facilitator then invites each participant to say a single idea to the entire group in a “round robin” fashion. Study participants might think of new ideas during this process, but must wait their turn before sharing with the entire group. This round proceeds until no new ideas are formed i.e. saturation is reached, and no discussion is allowed at this stage, ideas are merely recorded on either a flip chart, or a board. During the clarification stage, similar ideas are grouped together and discussed. Participants may also choose to add or omit certain ideas and are also involved in generating overall group themes. Finally, participants are asked to rate or rank the resultant ideas from the process and to select their top preferences. Usually this number is specified by the facilitator as a maximum number of ideas that may be chosen in the final selection process. One of the disadvantages of NGT is the lack of anonymity for participants and the possibility of influence from other participants. However, individual scoring is confidential. The NGT also has the advantage of being time efficient in that everything is decided in one meeting, however the number of questions posed may dictate the time taken to complete it.

The NGT was deemed unsuitable for the current study, as it wasn’t feasible to arrange this type of meeting, given the geographic spread of the participants and a desire for anonymity.

3.2.3 Participants

3.2.3.1 Eligibility Criteria

In keeping with best practice in Delphi methodology, the expert panel was purposively sampled upon individual expertise and knowledge, as follows: 1) recognised scientific expertise in geriatric oncology research or clinical experience, demonstrated by publication or clinical activities and participation in guideline development; 2) multidisciplinarity to facilitate diversity of views and expertise from a geriatric medicine and oncology perspective; and 3) both a national and international context to facilitate a global representation and exchange of state-of-the-art knowledge, with the aim of implementing an Irish geriatric oncology programme.

Purposive sampling methods are usually employed in Delphi studies [286], i.e. participants are selected for a specific purpose, as outlined below. This is particularly useful in areas where there are a limited number of individuals with the required expertise in relation to the research topic, as is the case with geriatric oncology.

3.2.3.2 Expert Panel Sampling and Recruitment

Guidelines for composition of Delphi panels indicate that their membership should reflect the stakeholders involved in a particular area [276, 280, 287]. This is important to ensure content validity of the resultant consensus document. Given the multidisciplinary nature of geriatric oncology, it was important that the panel for this study reflected both oncology and geriatric medicine stakeholder groups. Heterogeneous stakeholder groups can result in better performance in Delphi studies [281] and may help to overcome issues related to bias. There is no definitive number for the optimal composition of a Delphi panel [276, 288]. Likewise, the literature is inconclusive in relation to the number of stakeholder participants. However, most Delphi panels comprise 15-20 members [276].

The international expert panel was identified through active International Society of Geriatric Oncology (SIOG) affiliation. SIOG is considered a niche organisation, promoting the discipline of geriatric oncology through education, clinical practice and research. A follow-up search of Pubmed was used to verify clinical and research activity of the SIOG panel.

For the current study, whose focus was the implementation of a geriatric oncology programme in Ireland, it was deemed important to include a national panel of stakeholders also. The SIOG affiliated panel was mainly European-based. All Irish (Consultant) Radiation and Medical Oncologists and Geriatricians were identified through the relevant professional body and invited to participate also. Consultant level participation was deemed appropriate, as this indicated the highest level of expertise in each discipline. The national panel also had relevant expertise in the clinical management of older patients with cancer.

Surgeons were excluded from this study, as although it is appreciated that there are some commonalities, the pre-operative assessment of patients is necessarily different to the pre-

treatment assessment of patients undergoing chemo-radiotherapy. It would therefore constitute a separate panel of expertise with different aims and objectives.

3.2.3.3 Expert Panel Composition

One hundred and fifty eight experts, in total, were contacted via email and provided with information regarding the study. Response rate varied per professional group, as follows: SIOG affiliated 55% (n=24/44), radiation oncology 31% (n=9/29), medical oncology 23% (n=6/26) and geriatric medicine 17% (n=10/59).

3.2.4 Study Procedures

3.2.4.1 Ethical Considerations

Ethical approval was granted by the Research Ethics Committee of the Faculty of Health Sciences in Trinity College Dublin and Saint Luke's Radiation Oncology Network, Research Management Committee (Appendix 1). All participants provided informed consent to participate in the study (Appendix 2). All data collection and storage were compliant with data protection regulations. No identifiable patient data were collected as part of the study.

3.2.4.2 Survey Design

Initial survey items were based on a review of the literature. As is often the case in Delphi studies, the first round (R1) also consisted of unstructured open questions whereby participants were invited to put forward their opinions on various aspects of GA. This data was then collated and summarised in the round two (R2) survey, and so on for each successive round.

R1 comprised 49 members, encompassing four disciplines: radiation oncology (n=9), medical oncology (n=6), geriatric medicine (n=10) and SIOG-affiliated (n=24).

3.2.4.3 Number of Delphi Rounds

There is no clear guidance on the optimum number of Delphi rounds that should be used. The original Delphi traditionally used four rounds [289]. However, a 2011 systemic review [290] found that most Delphi studies used two rounds and that three rounds should allow consensus to be achieved in most studies [276, 281, 291]. Extending past three rounds carries the risk of attrition, and often there is little to be achieved after this point, apart from an assessment of stability. Stopping rules for Delphi studies vary between those who stress that consensus should be achieved on the matter under discussion [281], versus those who recognise the importance of stability of responses [292], indicating that opinion is at saturation point, and that further rounds will do little to change that. It should also be recognised that consensus is not always possible.

In the present study, four Delphi rounds were undertaken, as it was envisaged that consensus would be difficult to achieve, due to the multidisciplinary nature of the group, and the novel nature of GA in oncology for some participants (i.e. the Irish panel). It was also hoped that this would allow stability to be assessed.

3.2.4.4 First Delphi Round

All four rounds of the study were facilitated online using "Survey Monkey" *(Survey Monkey Inc., Palo Alto, CA, U.S.A*), and consisted of open-ended questions related to GA. Open-ended statements, designed to capture the breadth of opinion within the multidisciplinary group, were combined with 10 point Likert scales. The generation of statements was carefully considered to limit bias. Questionnaires were accessed via a secure URL link, generated by Survey Monkey, and sent via email.

A quasi-anonymous approach was used, whereby each participant used a unique study ID when completing each round, whose identity was known only to a designated gatekeeper who secured the study code. This allowed participant's anonymity to be protected, and compliance/attrition to be monitored between rounds. Other studies have used self-

generated codes, whereby participants combine the letters and numbers of key demographic personal data to form a unique number or code [293-296].

The R1 survey consisted of information on the demographic profile of the expert panel (see Appendix 3) and qualitative development of guidelines (see Appendix 4a to 4d) relating to use of GA, organisation of geriatric oncology activity, use of GA tools and interventions, stratification of patients for full GA and perceived importance of GA in the decision-making process. The demographic survey was common to all disciplines. In the first round, individual R1 surveys were designed for each discipline, with identical statements included, but tailored to that particular discipline. This allowed for the language to be different, reflecting differing levels of familiarity between the disciplines, as advocated in similar Delphi studies [297]. Sample questions used included: “What staff members participate in the interpretation of GA?”, “who is offered GA (i.e. characteristics of patients)?” and “please list any GA tool(s) that you currently use in your clinical practice”. As per the classical Delphi approach, the rationale for the use of open-ended questions in R1 is to reduce bias, allowing participants relative freedom in their responses [282]. Surveys were piloted in advance to ensure comprehension and promote clarity, in keeping with best practice in Delphi studies [274].

3.2.4.5 Iteration

An important feature of Delphi studies is iteration or feedback between rounds. For this purpose, summary statements were amalgamated after each round, grouping related content together and then distributed to participants in an anonymised report before each successive round. Participants were requested to review the report of reach round, before proceeding to the next round of the study.

It is recommended that this feedback include descriptive statistics of the combined results and a summary of qualitative data received from participants [281]. Simple descriptive statistics were included in the feedback summary of each round in the current study, and open responses from additional comment text boxes were included in appendices (ensuring anonymity), with broad summaries and synopses in the main text. Experts were asked to

consider their responses in the context of the group response, along with the summarised report and then re-rate the statements. Where items reached consensus they were re-introduced once more to ensure stability, as per the pre-defined methodological approach. Box and whisker plots were also displayed in the feedback report for certain aspects, to display the distribution of responses and to highlight outliers, who were identified by study ID. It was anticipated that this would aid convergence towards group consensus.

Delphi studies are time consuming processes, both for the participants and the researcher, who has to collate and analyse the data from each round in an efficient manner in order to ensure timely feedback of information [276]. Reminder emails were sent before the pre-defined deadline for completion in all cases, in order to enhance participation.

The first round report is provided in Appendix 5. The second, third and fourth round surveys are included in Appendix 6, 8 and 10, respectively. The second, third and fourth round feedback reports are included in Appendix 7, 9 and 11, respectively.

3.2.4.6 Second Delphi Round

In R2, the goal was to design a questionnaire, with quantifiable ranking/rating scales, using information put forward by participants in the first round. This formed the basis for subsequent rounds, whereby items were eliminated only through consensus and stability. Participants were asked to rate or rank certain aspects of the geriatric oncology process, under the aforementioned broad headings i.e. selection of patients for GA, appropriate assessments and interventions for older oncology patients, implementation strategies as well as education and training requirements. Participants “voted” to indicate the level of importance attributed to a particular statement, or to rank order items presented to them, or by simply answering yes or no to a given question. The method of voting chosen depended on the type of information sought. Some statements required a simple yes or no answer, while others were ranked in order of preference, from a selection of choices e.g. assessment tools/interventions. A 10 point Likert scale was used to measure level of agreement with a statement, or the level of importance attributable to it.

3.2.4.7 Third Delphi Round

For R3, survey items remained unchanged. The expert panel was invited to consider their opinions on each topic, in light of the second round summary report. In order to assess stability, it was necessary to produce a duplicate round of all items used in R2. Each member of the panel was provided with an anonymous summary of the experts' opinion from the previous round in order to aid decision making.

3.2.4.8 Final Delphi Round

Items that had not achieved consensus and stability in the previous rounds were presented in R4. Only the top three options (identified by mean rank/rating) were presented in the final round where consensus had yet to be achieved, in a final effort to "force" consensus.

Open comments were encouraged throughout in a combined qualitative and quantitative approach. The Delphi process is summarised in Fig. 3.1. The number of participants completing each round is summarised in Table 3.1.

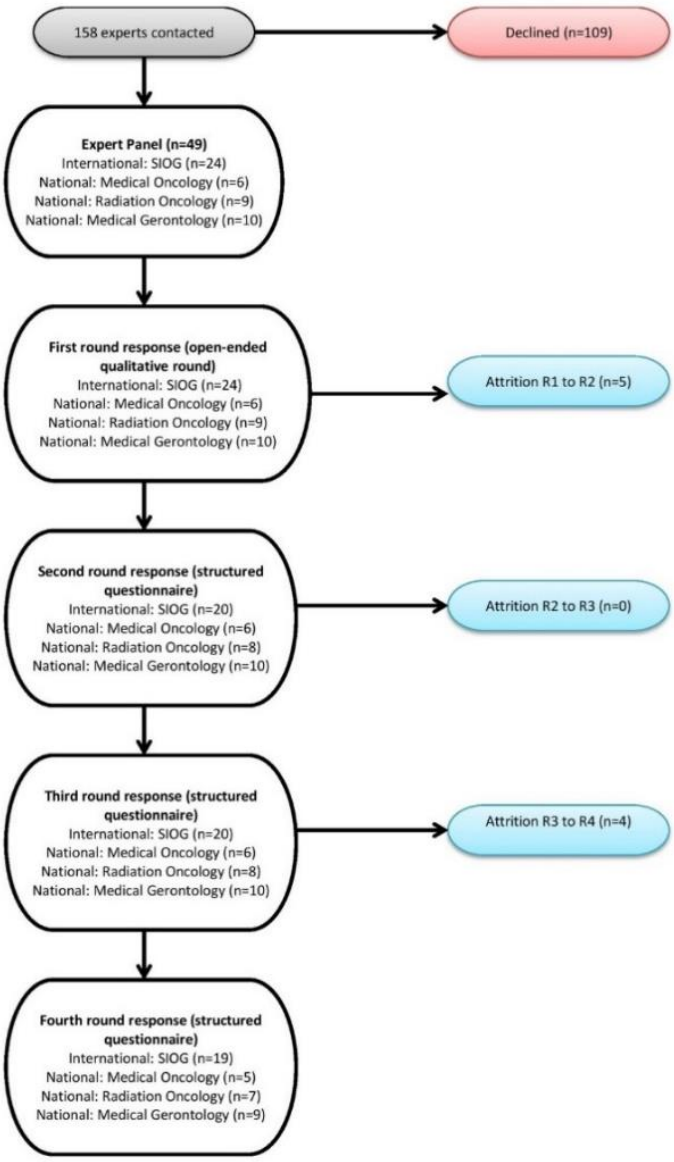


Figure 3.1 Participant flow through the Delphi process

Expert Panel	Group/ Discipline	Study Population (i.e. invited to participate)	Sample (positive response to invitation)	Consent forms received & Round 1 circulation	Round 1 completion	Round 2 completion	Round 3 completion	Round 4 completion	Completed at least one round
International	SIOG Affiliated Group	44	24	24	24	20	20	19	24
National	Consultant Medical Oncologists	26	6	6	6	6	6	5	6
	Consultant Radiation Oncologists	29	9	9	9	8	8	7	9
	Geriatricians	59	10	10	10	10	10	9	10
	Total	158	49 (30%) of study pop.	49 (30% of study pop.)	49 (100% of consented participants)	44 (90% of consented participants)	44 (90% of consented participants)	40 (82% of consented participants)	49 (100% of consented participants)

Table 3.1 Summary of attrition and participant numbers for each Delphi round

3.2.4.9 Attrition

Poor response rates and attrition are often a feature of Delphi studies [298]. Attrition between rounds in the current study was minimal, with five panel members choosing not to participate further after R1 (one from radiation oncology, four from the SIOG affiliated group). There was no further attrition between rounds two (R2) and three (R3), while four participants did not proceed to the final round (R4), one member from each of the respective professional subgroups. A nonrespondent bias check was conducted after the first Delphi round, which verified that nonresponders did not differ demographically from responders.

3.2.5 Data Analysis

Both qualitative and quantitative data analysis were undertaken of the results of each round of the Delphi process.

Data were analysed anonymously by encoding panel members with their survey ID numbers, provided by a gatekeeper. Data were exported from Survey Monkey and analysed using Statistical Package for the Social Sciences (*SPSS) v20.0*. Demographic characteristics were analysed using descriptive statistics. The stratification of patients for GA, ranking of GA domains and assessments/interventions was reported as ordinal data. The median was used to measure the group aggregate rating. The median rating was interpreted along with the interquartile range (IQR) to determine consensus of the statements, as outlined previously. The median and IQR were calculated based on all participating respondents. Missing answers were regarded as nonparticipation, and the panel was directed not to provide guidance on items it was unsure about. This

was considered important due to the heterogeneous nature of the expert panel.

Non-parametric tests were used to test consensus, differences between stakeholder groups and stability of responses.

Data produced from the open ended questions were entered verbatim onto an excel spreadsheet where it was arranged into common themes for the purpose of the feedback report. As the volume of data produced from these questions was extremely small, it was not subject to further qualitative analysis.

3.2.5.1 Defining Consensus

There is large variation in the measurement of consensus in Delphi studies. A predetermined threshold for consensus was chosen in the current study, before initiation, as per best practice in Delphi studies [299]. This serves to eliminate researcher bias. For nominal data, consensus was defined as 67% i.e. two-thirds majority. Some studies have used a threshold of 70% [297, 300], 75% [287, 288, 301] and 80% [276], with a systematic review of Delphi studies demonstrating a median level of consensus defined at 75% [302].

Consensus for Likert data is often calculated by using the IQR [276, 292, 303], which measures the variability of responses. It is widely accepted as an objective and rigorous method of defining consensus in Delphi studies [292, 304]. An IQR ≤1 can be considered as good consensus on a five-point Likert scale, signifying that at least half of participants agreed to within one point on the scale. An IQR ≤2 is recommended for a ten-point scale, indicating that at least half of responses are within two points on the scale [274]. The latter was employed for the majority of the current study, whereby 10 point

scales were used. However, for the final round, many items were reduced to <5, therefore an IQR of 1 was used in this instance.

Kendall's coefficient of concordance W was performed to measure the degree of consensus among experts [305]. Kendall's W ranges from 0 (no agreement) to 1 (complete agreement). A high and significant W means that participants are applying the "same standard in judging the importance of the issues" [306]. The Kendall's coefficient of concordance was reported for the final round ratings.

3.2.5.2 Defining Stability

For Likert scales, items reaching consensus, based on a priori IQR definitions, were re-presented in the following round to ensure stability of responses in two successive rounds. Stability reflects the permanence of participants' vote distribution over successive rounds [307], an important indicator that is often not reported in the literature [308]. Changes of less than 15% offer a working definition of stability in the literature, when the responses obtained in two successive rounds are shown to be not significantly different from each other [307]. Group stability, rather than individual stability was assessed in this study.

In this study, group stability (as opposed to individual stability) was tested between the final two rounds in which consensus was achieved for ordinal responses, using a Wilcoxon matched-pairs signed rank test on all items that reached a pre-determined consensus level. In each of these rounds, the same question was posed, using an identical Likert scale. This facilitated analysis of the response data between the two rounds. For some items the resultant analysis was of rounds 2 and 3, whereas for others it was rounds 3

and 4. A statistically significant *Z* score indicates that the median score for the two rounds is different, and therefore lacking in stability.

Strictly speaking, from a statistical perspective, the mean is not considered an appropriate central tendency measure for ordinal data [292], such as the Likert scales used in Delphi studies. However, the mean was used in the present study, for prioritisation and ranking purposes, as is common in other Delphi studies [292].

3.2.5.3 Comparison of Ratings by Different Disciplines in the Expert Panel

The Kruskal Wallis H test was used to analyse differences in independent variables among the different subgroups of experts.

The significance level for determining statistical difference on all tests was defined at $p \leq 0.05$.

3.3 Results

Four Delphi rounds were used in total. The first round presented relevant areas from the literature and invited participants to contribute others. Various items were rated in the rounds that followed, with a final consensus achieved for most items by the final round. The data collection involved quantitative data from a series of Likert scales in each Delphi round (and associated descriptive and inferential statistics) and qualitative data in the form of comments from participants. A feedback report was circulated to participants after each round, before commencement of the next round. All data were collected online. The sections below describe the main findings of the process, which took place over a seven month period from December 2012 to June 2013.

3.3.1 Study Participant Profile

Demographics of study participants are presented in *Table 3.2*, by professional group i.e.(a) SIOG affiliated panel (representing 49% of the entire expert panel), (b) Irish radiation oncologists (18% of the expert panel), (c) Irish medical oncologists (12% of the expert panel) and (d) Irish geriatricians (18% of the expert panel). Apart from medical oncology, which showed a marked male preponderance, the gender and age distribution of participants were approximately equal. Years of clinical experience varied between groups, with the SIOG group and radiation oncology groups having slightly more than the other groups.

Participants were asked to rate the current evidence base in geriatric oncology, on a ten point Likert scale, as part of the initial demographics round. Overall, this was rated at an overall mean

value of 4.3 (1.8). For the SIOG affiliated panel, this increased marginally to 4.6 (2.1).

3.3.2 Current Use of GA

All of the SIOG group stated that they perform GA on their patients (always or sometimes), validating their selection for the Delphi process. The Irish Geriatrician group, as expected, also employ GA.

For those who answered “sometimes”, specified reasons included clinical judgement, when radical treatment is proposed, as part of a research protocol, when there is evidence of comorbidities or cognitive impairment and when time allows. Please see the R1 feedback report, Appendix 5, for detailed responses.

The majority of Irish Oncologists (Radiation and Medical) did not perform GA on their older patients (53%). 41% of participants stated that they “sometimes” perform GA, under specific conditions, such as “obvious frailty”, concerns about ability to give consent for treatment and for curative treatment.

SIOG participants were asked to specify how GA is integrated into clinical practice in their institutions. Many different approaches were demonstrated. For some institutions, GA was considered routine practice and the standard of care was to offer all older patients GA on initial consultation. Some used an initial screening tool, such as the G8 to identify patients who required full CGA. Geriatrician review was available upon request, or by provision of dedicated oncology clinics at regular intervals in some centres. Nurse-led assessments were also used to provide the initial screening of patients, which was followed up, if required. Institutions participating in research performed full CGA routinely for older trial patients.

SIOG Group (n=24)

Characteristics	n	% Entire Expert Panel	Mean(SD)	Median	Range
Age (y)	24	49	44.8(9.4)	43	34-73
Female gender	11	22			
Male gender	13	27			
Years in clinical practice	24	49	12.8(11.0)	11	1-48
Current evidence base in GO (scale 1-10)	24	49	4.6(2.1)	4.5	1-9
In receipt of funding for GO research	8	16			
Caseload Older Patients with Cancer Seen/Week	22	45	24(30.5)	18	1-150
Additional Expertise of the SIOG group					
	Yes n(%)	No n(%)			
I do more clinical work than research	18 (82%)	4 (18%)			
I mentor others in GO	18 (86%)	3 (14%)			
I describe myself as a geriatric oncologist	10 (48%)	11 (52%)			
Profession:					
Geriatrician	5 (10%)				
Medical Oncologist	19 (39%)				

*One participant declined to complete the demographic summary

(a) Demographic Characteristics SIOG Panel

Radiation Oncology Group (n=9)					
Characteristics	**n**	**% Entire Expert Panel**	**Mean (SD)**	**Median**	**Range**
Age (y)	**9**	**18**	**45.4(8.1)**	**43**	**35-62**
Female gender	**4**	**17**			
Male gender	**5**	**21**			
Years in clinical practice	**9**	**18**	**12(8.7)**	**9**	**3-29**
Current evidence base in GO (scale 1-10)	**9**	**18**	**4.1(1.8)**	**4**	**2-7**
In receipt of funding for GO research	**0**	**0**			
Caseload Older Patients with Cancer Seen/Week	**9**	**18**	**8.7(12.4)**	**4**	**2-40**

(b) Demographic Characteristics Radiation Oncologists

Medical Oncology Group (n=6)					
Characteristics	**n**	**% Entire Expert Panel**	**Mean(SD)**	**Median**	**Range**
Age (y)	**6**	**12**	**42(7.6)**	**39**	**36-56**
Female gender	**1**	**4**			
Male gender	**5**	**21**			
Years in clinical practice	**6**	**12**	**10(8.4)**	**8**	**2-12**
Current evidence base in GO (scale 1-10)	**6**	**12**	**4.2(1.0)**	**4**	**1-5**
In receipt of funding for GO research	**0**	**0**			
Caseload Older Patients with Cancer Seen/Week	**6**	**12**	**16.2(6.3)**	**16**	**10-25**

(c) Demographic Characteristics Medical Oncologists

Geriatric Medicine Group (n=10*)					
Characteristics	**n**	**% Entire Expert Panel**	**Mean(SD)**	**Median**	**Range**
Age (y)	**9**	**18**	**43.4(3.5)**	**44**	**39-48**
Female gender	**5**	**10**			
Male gender	**5**	**10**			
Years in clinical practice	**9**	**18**	**7.9(3.2)**	**8**	**2-12**
Current evidence base in GO (scale 1-10)	**9**	**18**	**3.8(1.4)**	**4**	**1-5**
In receipt of funding for GO research	**2**	**4**			
Caseload Older Patients with Cancer Seen/Week	**9**	**18**	**2.4(1.4)**	**2**	**1-5**

(d) Demographic Characteristics Geriatricians

Table 3.2 Demographic characteristics of study participants by professional group i.e. SIOG affiliated panel (a), radiation oncologists (b), medical oncologists (c) and geriatricians (d)

3.3.3 Feasibility of Geriatric Oncology in Ireland

It was found that 93% of Irish participants believed that geriatric oncology, as a discipline, was feasible in Ireland. One participant stated:

"But very challenging because of an already extensive commitment to numerous MDTs and dwindling resources. (RO)"

Reasons given by those who did not think geriatric oncology was feasible were also related to time/resources:

"The resources at Consultant level are probably insufficient in both geriatrics and oncology to achieve this."

3.3.4 Use of Self-Report Items to Complement Assessments

In R1, the majority of participants (81%) felt that GA should be completed by face-to-face interview. This opinion changed slightly in R2. Thirty-four percent of participants felt that completion of *all or part of* GA at home by the patient/family was desirable, while the remaining 66% felt that it was not. This may represent different attitudes towards different assessment types, some of which participants felt were feasible by self-report methods and others which were not.

Using expert panel guidance, this was re-examined in R3 to gain clarity, and the question was rephrased as follows:

"Should part of the GA be completed at home by the patient/family prior to the initial oncology consultation? Please note that this includes assessments that the panel feel (by consensus) are feasible by self-report only."

In R3, sixty-six percent of participants felt that this option was feasible (the reverse of R2). This represented borderline consensus, even though this was in opposition to rounds 1 and 2, and was thus reintroduced in the final round.

In R4, 83% of participants felt that completion of part of the GA at home by the patient/family prior to an oncology consultation was feasible, thereby representing clear consensus on this item.

3.3.5 Selection of Patients for GA

R1 sought the opinion of the contributing professional groups regarding which patients should be routinely referred for GA. This item represented the most dissensus in the Delphi panel, and only the top three ranking items were reintroduced in R4, in an effort to force consensus. There was no consensus in the first three rounds regarding this aspect of GA. Consensus was finally reached in R4 that all patients aged 70 and over, and those who are younger with age-related issues or concerns, should be referred for GA. See *Table 3.3* for a summary of descriptive statistics per round.

For the final round age cutoff variable, W was calculated ($W = 0.452$) and found to be statistically significant ($p < 0.001$). This indicates moderate agreement with the final ranking. The Kruskal Wallis test demonstrated that there was no significant difference in relation to how ranks were applied among the four subgroups.

Wilcoxon's matched-pairs signed-rank test was used to test stability of responses by analysing whether there was any statistical difference in participants' responses from the final two rounds in which consensus was achieved.

Taking all of the participants' rankings as a whole, their views on the optimal age stratification changed significantly between rounds, indicating relative instability. Details of the results of Wilcoxon's test are provided in *Table 3.4* below.

Rank	Mean Rank	Median	Interquartile Range	Consensus [R4 W=0.452, 2 df, p<0.001)
1. All patients aged 70 and over, and those who are younger with age-related issues or concerns	**R2:** 3.16	**R2:** 3.00	[1.00, 5.00]	**No**
	R3: 2.68	**R3:** 2.00	[1.00, 3.50]	**No**
	R4: 1.28	**R4:** 1.00	[1.00, 2.00]	**Yes**
2. All patients aged 75 and over, and those who are younger with age-related issues or concerns	**R2:** 3.60	**R2:** 3.00	[2.00, 5.00]	**No**
	R3: 3.51	**R3:** 3.00	[2.00, 5.00]	**No**
	R4: 2.10	**R4:** 2.00	[1.00, 3.00]	**No**
3. All patients aged 70 and over	**R2:** 5.72	**R2:** 6.00	[3.00, 8.00]	**No**
	R3: 4.63	**R3:** 4.00	[2.00, 7.00]	**No**
	R4: 2.62	**R4:** 3.00	[2.00, 3.00]	**No**
An IQR <2 was applicable for consensus in rounds 2 and 3 (8-10 options), with an IQR of <1 for the final round (<5 options)				

Table 3.3 Results for patient stratification for GA (in order of mean rank per individual round).

Age Cut-off	Median		Z	p-value
	R3	R4		
1.All patients aged 70 and over, and those who are younger with age-related issues or concerns	2.00	1.00	-4.079	<0.001
2. All patients aged 75 and over, and those who are younger with age-related issues or concerns	3.00	2.00	-3.608	<0.001
3. All patients aged 70 and over	4.00	3.00	-4.094	<0.001
Z: Wilcoxon's signed-rank test				

Table 3.4 Results of Wilcoxon signed-rank test for age cut-off

3.3.6 Appropriate Assessment and Interventions for Oncology

3.3.6.1 Screening Tools

Consensus was not reached on the use of a shorter screening tool that would identify those patients who could potentially benefit from GA, versus those who would not. In R2, 89% agreed that screening with a shorter geriatric-based measure should be instituted as standard practice, in order to help determine who should undergo full GA. This increased to 93% in R3. However, a number of stipulations were given (see Appendix 11).

In R2, 53% of participants felt that no specific screening measure should be recommended, and that any measure could potentially be used. The remaining 37% of the panel recommended a specific screening tool to identify patients who could potentially benefit from full GA. Of these, four participants recommend the use of the G8

tool, while others recommend the use of the VES13 or G8 (n=1), ADL or IADL (n=1), the aCGA (n=1), SAOP (n=1) and the SHARE frailty instrument (n=1).

In R3, clarity was sought on whether or not participants were satisfied with their recommendations of using a short screening tool, given the current lack of discriminative power for the commonly recommended tools in oncology, as articulated by many members of the expert panel. Forty-nine percent of participants (a decrease of 4%) felt that no specific screening measure should be recommended, and that any measure could potentially be used. Equally, the remaining 49% of the panel recommended a specific measure to identify patients who could potentially benefit from full GA. Six participants chose not to answer this question.

In R4, this question was further explored. Fifty percent of participants (an increase of 1%) felt that no specific screening measure should be recommended, and that any measure could potentially be used. Forty percent of the panel recommended a specific measure to identify patients who could potentially benefit from full GA. Of these, four recommended the G8, two the abbreviated CGA, and the remainder varied as documented below. Four participants chose not to answer this question.

Only the top three screening options were presented in the final round in an effort to force consensus. The abbreviated CGA (aCGA) was ranked highest overall, however it did not achieve consensus. As the degree of familiarity with the screening tools under consideration was specific to the field of geriatric oncology, and many of the tools were relatively new by comparison to other GA domains, subgroup analysis of the SIOG affiliated group was also carried out. This analysis of the SIOG affiliated group indicated an overall preference

for the G8 screening tool, but this did not reach consensus. However, there was consensus among the SIOG group in R3 and R4 regarding the lower ranked (3rd place) VES-13, with a mean rank of 2.13 and IQR of 1. See *Table 3.5* for further details.

Screening Tool	Round (Group)	Mean	Median	Interquartile Range	Consensus (R4 All:W=0.002, 2df, p=0.957; R4 SIOG:W=0.016, 2df, p=0.779)
1. aCGA	**R2 (All):**	4.14	3.00	[1.00, 7.00]	**No**
	R2 (SIOG):	3.44	2.50	[1.00, 4.50]	**No**
	R3 (All):	3.69	3.00	[1.00, 4.50]	**No**
	R3 (SIOG):	4.06	3.00	[1.50, 6.00]	**No**
	R4 (All):	1.96	2.00	[1.00, 3.00]	**No**
	R4 (SIOG):	2.00	2.00	[1.00, 3.00]	**No**
2. G8	**R2 (All):**	3.62	3.00	[1.00, 5.00]	**No**
	R2 (SIOG):	2.50	2.00	[1.00, 3.00]	**Yes**
	R3 (All):	2.92	2.00	[1.00, 4.00]	**No**
	R3 (SIOG):	2.47	2.00	[1.00, 3.00]	**Yes**
	R4 (All):	2.00	2.00	[1.00, 3.00]	**No**
	R4 (SIOG):	1.88	1.50	[1.00, 3.00]	**No**
3. VES-13	**R2 (All):**	3.62	3.00	[2.00, 4.00]	**No**
	R2 (SIOG):	3.17	2.50	[2.00, 4.00]	**No**
	R3 (All):	2.73	2.00	[1.75, 3.25]	**No**
	R3 (SIOG):	2.53	2.00	[2.00, 3.00]	**Yes**
	R4 (All):	2.04	2.00	[1.00, 3.00]	**No**
	R4 (SIOG):	2.13	2.00	[2.00, 3.00]	**Yes**
Others under consideration	Groningen Frailty Indicator (GFI), functional status, objective physical performance (OPP), self-rated health, ECOG performance status, Karnofsky performance status, Cancer and Aging Research Group (CARG), Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH), self-rated health				
Please note that consensus was defined as an IQR of 2 for rounds 2 and 3, and 1 for Round 4 (as only 3 items presented to participants in final round) Subgroup analysis of the SIOG affiliated group is also presented					

Table 3.5 Best choice of screening tool in oncology (in order of preference: 1=1st place etc)

Wilcoxon's signed-rank test was used to test stability of responses by analysing whether there was any statistical difference in participants' responses from R3 to R4. Taking all of the participants' rankings as a whole, their views on the relative ranking of screening tools did not change significantly between rounds, indicating good stability for the G8 and VES-13. However, the relative ranking of the aCGA did change significantly, as indicated by a z score of -2.818 (p=0.005). This did not achieve consensus. Details of the results of Wilcoxon's test are provided in Table 3.6 below.

Screening Tool	Median		Z	p-value
	R 3	R 4		
aCGA	3.00	2.00	-2.818	0.005
G8	2.00	2.00	-1.706	0.088
VES-13	2.00	2.00	-1.628	0.103

Z: Wilcoxon's signed-rank test

Table 3.6 Results of Wilcoxon signed-rank test for screening tools

Statistical tests for concordance and intergroup variability proved insignificant for the selection of screening tools.

3.3.6.2 Geriatric Assessment and Interventions

A recent systematic review [40] was used as the basis for selection of relevant GA domains in oncology, which were used for this Delphi study. Panellists were also invited to contribute other domains and assessments. The importance of each domain was ranked in each

round, as can be seen in *Table 3.7.* For the final round, *W* was calculated ($W = 0.427$) and found to be statistically significant ($p < 0.001$), indicating moderate agreement among the expert panel in relation to the importance of each domain.

Kruskal Wallis tests found a statistically significant difference between the four subgroups, only in relation to social support status (H=11.35, 3 df, p=0.01). Significant difference in mean rank was found between the SIOG group and radiation oncology (H=9.053, 1 df, p=0.003). Radiation oncology ranked this aspect of GA much lower (mean=5.08) than their SIOG colleagues (mean=14.97).

Overall, panellists rated functional status (subjective and objective measures) as the most important domain in influencing oncology decisions, followed by comorbidities and cognition. Other domains did not reach consensus in relation to overall importance. Wilcoxon's signed-rank test (*Table 3.8*) was used to test stability of responses by analysing whether there was any statistical difference in participants' responses from R3 to R4. Taking all of the participants' rankings as a whole, their views on the relative ranking of each domain did not change significantly between rounds, indicating good stability for the items reaching consensus. It was relatively unstable for other items, not reaching consensus.

Domain and Rank	Round	Mean Rank	Median	Interquartile Range	Consensus [R4:W=0.427, 8df, p<0.001]
1. Functional status	R2:	8.91	10.00	[8.00, 10.00]	Yes
	R3:	9.23	10.00	[8.25, 10.00]	Yes
	R4:	9.31	10.00	[9.00, 10.00]	Yes
2. Objective physical performance status	R2:	8.52	9.00	[7.25, 10.00]	No
	R3:	8.70	9.00	[8.00, 10.00]	Yes
	R4:	8.82	9.00	[8.00, 10.00]	Yes
3.Comorbidities	R2:	8.07	9.00	[6.25, 10.00]	No
	R3:	8.60	9.00	[7.25, 10.00]	No
	R4:	8.74	9.00	[8.00, 10.00]	Yes
4. Cognitive status	R2:	8.79	9.00	[8.00, 10.00]	Yes
	R3:	8.98	9.50	[8.00, 10.00]	Yes
	R4:	8.54	9.00	[8.00, 10.00]	Yes
5.Nutritional status	R2:	7.66	8.00	[7.00, 9.00]	Yes
	R3:	7.75	8.00	[6.00, 9.00]	No
	R4:	7.59	8.00	[6.00, 9.00]	No
6.Social support status	R2:	6.93	7.00	[6.00, 9.00]	No
	R3:	7.03	8.00	[6.00, 9.00]	No
	R4:	7.38	8.00	[6.00, 9.00]	No
7.Polypharmacy	R2:	6.82	7.00	[5.00, 9.00]	No
	R3:	6.88	7.50	[5.00, 9.00]	No
	R4:	6.77	7.00	[5.00, 9.00]	No
8.Psychological status - depression	R2:	**6.48**	**6.00**	**[5.00, 8.00]**	No
	R3:	**6.30**	**7.00**	**[5.00, 8.00]**	No
	R4:	**6.54**	**7.00**	**[5.00, 9.00]**	No
9.Psychological status - anxiety	R2:	**6.02**	**6.00**	**[4.25, 8.00]**	No
	R3:	**6.13**	**7.00**	**[4.00, 8.00]**	No
	R4:	**6.03**	**6.00**	**[5.00, 8.00]**	No

Table 3.7 Importance of each domain in rank order (1=1st place etc.)

Domain	Median		Z	p-value
	R3	R4		
1. Functional status	10.0	10.0	-0.486	0.627
2. Objective physical performance status	9.00	9.00	-0.528	0.598
3.Comorbidities	9.00	9.00	-1.101	0.271
4. Cognitive status	9.50	9.00	-0.956	0.339
5.Nutritional status	8.00	8.00	-2.610	0.009
6.Social support status	8.00	8.00	-3.135	0.002
7.Polypharmacy	7.50	7.00	-3.993	<0.001
8.Psychological status - depression	7.00	7.00	-1.018	0.309
9.Psychological status - anxiety	7.00	6.00	-4.030	<0.001

Z=Wilcoxon's signed-rank test

Table 3.8 Results of Wilcoxon signed-rank test for the relative importance of each domain

Consensus was reached on the optimal assessment method and interventions required for the commonly employed domains of GA, apart from polypharmacy assessment.

Table 3.9 outlines the consensus achieved for selected domains of GA in oncology, including the round(s) in which consensus was reached. There was significant agreement among the expert panel with respect as to how they ranked the relative importance of each assessment and intervention. There was no consensus regarding polypharmacy assessment, but the expert panel agreed that geriatricians should be consulted regarding management of medications. The strength of agreement varied from weak agreement (functional status, nutritional status and depression

assessments), to moderate (interventions for comorbidities, social support and anxiety/depression) to strong (cognition, comorbidities and nutritional status assessments). See Table 3.9 for further details.

There were no significant differences in the Kruskal-Wallis H-test results for items reaching consensus, thereby indicating expert agreement in variable ranking among the four professional subgroups.

Functional Status Assessment [R3 W=0.266, 8df, p<0.001]					
Item	**Mean Rank**	**Median**	**Mode**	**Interquartile Range**	**Consensus**
1. ADL/IADL in combination	R3: 1.86	1.00	1.00	[1.00, 2.00]	Yes
Functional Status Interventions [R4 W=0.189, 2df, p=0.001]					
1. Physiotherapy referral	R4: 1.59	1.00	1.00	[1.00, 2.00]	Yes
Physical Performance Impairment: Assessment (R4 W=0.267, 2df, p<0.001)					
1. Timed Up and Go (TUG)	R4: 1.67	1.00	1.00	[1.00, 2.00]	Yes
Physical Performance Impairment: Interventions (R3 W=0.266, 8df, p<0.001)					
1. Physiotherapy Referral	R3: 1.24	1.00	1.00	[1.00, 1.00]	Yes
Cognitive Status: Assessment (R3 W=0.667, 14df, p<0.001)					
1. Mini Mental State. Examination (MMSE)	R3: 1.55	1.00	1.00	[1.00, 2.00]	Yes
Cognitive Status: Interventions (R4 W=0.222, 2df, p=0.001)					
1. Geriatrician referral	R4: 1.46	1.00	1.00	[1.00, 2.00]	Yes
Co-morbidities: Assessment (R3 W=0.662, 4df, p<0.001)					
1. Charlson Comorbidity Index	R3: 1.53	1.00	1.00	[1.00, 2.00]	Yes
Co-morbidities: Interventions (R3 W=0.356, 2df, p<0.001)					
1. Geriatrician Referral	R3: 1.43	1.00	1.00	[1.00, 2.00]	Yes
Polypharmacy: Assessment (R4 W=0.003, 2df, p=0.90)					
1. List of Medications	R4: 1.95	2.00	1.00	[1.00, 3.00]	No
Polypharmacy: Interventions (R4 W=0.186, 2df, p=0.001)					
1. Geriatrician Referral	R3: 1.54	1.00	1.00	[1.00, 2.00]	Yes
Nutritional Status: Assessment (R4 W=0.203, 2df, p=0.002)					
1. Mini Nutritional Assessment (MNA) Short form	R4: 1.50	1.00	1.00	[1.00, 2.00]	Yes
Nutritional Status: Interventions (R3 W=0.605, 1df, p<0.001)					
1. Dietician Referral	R3: 1.11	1.00	1.00	[1.00,1.00]	Yes

Social Support Status: Assessment (R3 W=0.732, 3df, p<0.001)					
Item	**Mean Rank**	**Median**	**Mode**	**Interquartile Range**	**Consensus**
1. Patient History/caregiver interview	R3: 1.27	1.00	1.00	[1.00, 1.00]	Yes
Social Support: Interventions (R3 W=0.309, 4df, p<0.001)					
1. Social work referral	R3: 1.57	1.00	1.00	[1.00, 2.00]	Yes
Anxiety: Assessment (R3 W=0.345, 2df, p<0.001)					
1. Patient history/ Interview	R3: 1.62	2.00	1.00	[1.00, 2.00]	Yes
Anxiety: Interventions (R3 W=0.492, 5df, p<0.001)					
1. Referral to a Psychiatrist/ Psychologist /Cognitive Behavioural Therapy	R3: 1.63	1.00	1.00	[1.00, 2.00]	Yes
Depression: Assessment (R3 W=0.117, 3df, p=0.006)					
1. Geriatric Depression Scale (GDS) Short form	R3: 1.86	2.00	1.00	[1.00, 2.00]	Yes
Depression: Interventions (R3 W=0.451, 5df, p<0.001)					
1. Referral to a Psychiatrist /Psychologist /Cognitive Behavioural Therapy	R3: 1.50	1.00	1.00	[1.00, 2.00]	Yes
Kendall's W is also indicated for each domain					

Table 3.9 Top 3 assessments and interventions for older patients with cancer (in order of preference)

Wilcoxon's signed-rank test was used to test stability of responses by analysing whether there was any statistical difference in participants' responses from the final two rounds where consensus was achieved. Taking all of the participants' rankings as a whole, their views on the relative ranking of assessments did not change significantly between rounds, indicating good stability for the assessments that were agreed upon as the basis for GA in oncology. However, the relative ranking of nutritional status assessment did change significantly, as indicated by a z score of -2.389 (p=0.017).

Finalising interventions for each domain showed greater instability, as indicated by significant z scores for most of the interventions agreed upon in the final round.

Details of the results of Wilcoxon's test for assessments and interventions are provided in *Tables 3.10* and *3.11,* respectively.

Assessment	Rounds in which consensus was reached Rx Ry	Mdn Rx	Mdn Ry	Z	p-value
Functional Status: ADL/IADL in combination	R2 R3	1.00	1.00	-0.894	0.372
Physical Performance: TUG	R3 R4	2.00	1.00	-0.827	0.408
Cognition: MMSE	R2 R3	1.00	1.00	-1.469	0.142
Comorbidity: Charlson Comorbidity Index	R2 R3	1.00	1.00	-1.667	0.096
Polypharmacy: List of medications	R3 R4	2.00	2.00	-0.775	0.439
Nutritional Status: MNA Short Form	R3 R4	2.00	1.00	-2.389	0.017
Social Support: Patient/ caregiver interview	R2 R3	1.00	1.00	-1.604	0.109
Anxiety: Patient history/ interview (anxiety)	R2 R3	2.00	2.00	0.000	1.000
Depression: GDS Short Form	R2 R3	1.00	2.00	0.000	1.000

Table 3.10 Results of Wilcoxon signed-rank test for assessments

Intervention	Rounds in which consensus was reached Rx Ry	Mdn Rx	Mdn Ry	Z	p-value
Functional Status: Physiotherapy referral	R3 R4	2.00	1.00	-2.074	0.038
Physical Performance: Physiotherapy referral	R2 R3	1.00	1.00	-2.691	0.007
Cognitive Impairment: Geriatrician Referral	R3 R4	1.50	1.00	-2.003	0.045
Comorbidity: Geriatrician Referral	R2 R3	1.00	1.00	-0.711	0.477
Polypharmacy: Geriatrician Referral	R2 R3	1.00	1.00	-0.876	0.381
Nutritional status: Dietician Referral	R2 R3	1.00	1.00	-0.577	0.564
Social support: Social Work Referral	R2 R3	1.00	1.00	-1.628	0.103
Anxiety: Referral to a Psychiatrist/ Psychologist /Cognitive Behavioural Therapy	R2 R3	1.00	1.00	-2.232	0.026
Depression: Referral to a Psychiatrist/ Psychologist /Cognitive Behavioural Therapy	R2 R3	1.00	1.00	-0.254	0.799

Table 3.11 Results of Wilcoxon signed-rank test for interventions

3.3.6.3 Who Should Carry Out GA?

In R2, clear consensus existed for most items with regard to who could carry out the assessment, apart from polypharmacy and psychological status. In R3, stability was maintained for all items, but nutritional status did not meet consensus at 65%, compared to 68% in R2. Only these domains were represented in R4. Finally in R4, it was agreed that any healthcare professional with sufficient training could undertake nutritional assessment, but not assessment of polypharmacy or psychological status (see Table 3.12 below).

Domain	R2	R3	R4
Functional Status	Yes (98%)*	Yes (93%)*	-
Objective Physical Performance	Yes (98%)*	Yes (88%)*	-
Cognitive Status	Yes (80%)*	Yes (73%)*	-
Comorbidity	Yes (73%)*	Yes (68%)*	-
Polypharmacy	No (57%)	No (53%)	Yes (43%)
Nutritional Status	Yes (68%)*	Yes (65%)	Yes (82%)*
Social Support Status	Yes (82%)*	Yes (85%)*	-
Psychological Status	No (52%)	Yes (53%)	Yes (56%)

[Consensus items *]

Table 3.12 Can any healthcare professional perform this assessment?

3.4 Discussion

Currently, formal GA tools are rarely employed by oncologists, not only in Ireland, but internationally. Underutilisation of GA may be due to the lack of consensus in relation to the application of geriatric assessments and interventions in oncology, as well as the lack of level 1 evidence for the efficacy of this approach. The current Delphi study aimed to gain consensus from an expert panel of national and international stakeholders regarding the optimal assessment methods in oncology.

Strengths of the Delphi technique include a contribution to participant's knowledge base through the use of multiple rounds, promotion of decision-making, and achieving consensus on topics where little empirical evidence exists [298, 309]. It is an inexpensive way to share knowledge from various experts and stakeholders, from various countries, for whom face-to-face meetings would not be possible [298] It is for these reasons that the Delphi technique was used in this study.

The expert panel employed, included a diversity of participants, which can assist in the reduction of bias [310] and the development of a geriatric oncology programme that was inclusive of all relevant stakeholders. The range of Irish stakeholders included reflected those who would potentially be implementing a geriatric oncology service, which brought a level of "authenticity" to the process, which would not have been achievable through the use of the SIOG panel alone [311].

The panellists in this study clearly identified the criteria that should be included in a clinical geriatric oncology programme. Patient stratification and essential assessments and interventions to be

included were identified through expert consensus. As the panellists in this study vocalised, the current evidence base in geriatric oncology (rated 4/10) is insufficient to advise on the optimal assessment of older oncology patients, and guidance of an expert panel with related expertise is an appropriate alternative.

Content validity is ensured in Delphi studies when the expert panel has appropriate expertise and clinical experience [312]. As geriatric oncology is considered to be a specialised area, selection of this expert panel was well considered, and included contributions from a wide range of experts. Overall, during the consultation process, attrition rates were low, ensuring the validity of the final results [282, 313].

Poor response rates and attrition pose a substantial risk to the success of Delphi studies [283, 298], owing to the need for repeated rounds. This may lead to concerns about the validity of the results of the consensus process [308]. Some attrition is to be expected as the study progresses, especially with a four round process [311]. However, for the current study, response rates were consistent across rounds (R1 n=49, R2 n=44, R3 n=44 and R4 n=40). The response rate was highest in R1, which was the most time-consuming for participants to complete, with the associated demographics survey included in this round. There was a slight drop-off in responses to the final round, which was the critical decision stage for many items. A response rate of 70% is recommended throughout the Delphi process, in order to maintain validity [282, 314, 315]. The response rates in the current study were 100%, 90%, 90% and 82% for rounds 1, 2, 3 and 4, respectively, thus maintaining the rigour of the Delphi technique.

There is large variation in defining consensus in Delphi studies [316]. Consensus for Likert data is often calculated by using the interquartile range (IQR) [276, 292, 303], which measures the variability of responses. A lower IQR signifies less dispersion in participant ratings. It is widely accepted as an objective and rigorous method of defining consensus in Delphi studies [292, 304]. The repetition in subsequent rounds, of items that had reached consensus in previous rounds, was an important aspect of the Delphi process. This allowed participants to reconsider their answers in light of guidance from other members of the expert panel [317]. Examining the IQR for most items under consideration demonstrated that the IQR decreased from R2 to R4, indicating that convergence of opinion was very strong. However, it must be borne in mind that for many items consensus was “forced” in the final round by only presenting the top three items. It is very obvious when looking at the IQR ratings for screening tools from round to round that there was dissensus. This did not improve in the final round. This can be as revelatory in Delphi studies, as a high level of consensus is [292] and certainly reflects the lack of acceptability with relation to a screening tool for geriatric oncology [61], as discussed below.

Kendall’s coefficient of concordance (W) is commonly used in Delphi studies, in order to measure the degree of consensus among experts [305]. Kendall's W ranges from 0 (no agreement) to 1 (complete agreement). A high and significant *W* means that participants are applying the "same standard in judging the importance of the issues" [305, 306]. The Kendall's coefficient of concordance was carried out on the final round in which consensus and stability had been established. Application of this test to the final round data found that there was mostly moderate agreement on the finalised list of items for implementation of geriatric oncology. Again, the rating of screening tools showed relative disagreement (W=0.002, p=0.779).

Strong agreement can be difficult to achieve in heterogeneous Delphi panels, with different disciplines thinking about the feasibility of implementation in their own clinical setting [271, 287].

Group stability in this study was measured using the Wilcoxon matched-pairs signed rank test, which indicates the internal reliability of results [291]. Measuring stability shows whether there was a change in responses from one round to the next [291]. Taking all of the participants' rankings as a whole, their views on the relative ranking of assessments did not change significantly between rounds, indicating good stability for the assessments that were agreed upon as the basis for GA in oncology. Finalising interventions for each domain showed greater instability, however, as indicated by significant z scores for most of the interventions agreed upon in the final round. Likewise, the selection of an age cut-off for GA and screening tools also showed relative instability. This highlights the importance of examining consensus and stability separately, as they assess two different concepts [316]. For example, while consensus was reached on a suitable age cut-off for GA, participants' ratings on this item were inconsistent and unstable.

The term GA, is a derivative of CGA, which has been defined as "a multi-dimensional, interdisciplinary, diagnostic process to identify care needs, plan care, and improve outcomes of frail older people" [89]. The core components of CGA include an assessment of physical health (comorbidities and associated medications), functional status (ADLs, IADLs and mobility), psychological health (including cognition and mood), as well as socioenvironmental factors (social supports, home safety etc.). Fundamental to CGA is the development of a treatment plan and associated implementation of interventions for remedial care of identified deficits, and it is this aspect that is often not reported in the geriatric oncology literature

[318]. This may offer an explanation for the instability found in the definition of interventions for each domain in the current study. The term GA is widely used in the geriatric oncology literature, and indeed is advocated by SIOG [79]. It usually reflects a shorter assessment in oncology ranging from 10 to 45 min, compared to geriatric medicine where it would typically take 1-2 hours. Some academics would argue that the term GA is inaccurate and that selected domains of assessment, or screening be used instead [318].

The first task of the expert panel was definition of an age cutoff for routine referral for GA. An age cutoff for older adults with cancer is difficult to define due to the considerable heterogeneity in the ageing process. Some organisations, such as SIOG [79] and the EORTC [81] use an age cut-off of 70, others use 65 [319]. The European Medicines Agency [320] considers 65 years of age as a cut-off for the definition of "old", from a regulatory perspective. In the current study, consensus was finally reached in R4 that all patients over the age of 70, and those who are younger with age related issues or concerns, should be referred for GA. In the final round the overall level of agreement was good ($W=0.452$, $p<0.001$). The expert panel may have been reluctant to provide an age cut-off in previous rounds, as it contradicts the basic principle on which geriatric medicine is founded i.e. definition of physiological age, rather than chronological age. In the words of one participant, *"it is pragmatic to choose an age above which the incidence of issues is high enough for a routine policy, but this should not preclude the younger patients being assessed. To some degree the choice of age should reflect local patterns of age related problems."* This comment is in line with SIOG recommendations at the time of the study [79] which may have biased the results, given the relatively large proportion of SIOG affiliated members. Another factor to consider when defining an age threshold, and something to investigate in future larger studies, is the

need to acquire objective data on the proportion of prefrail and frail patients per age category to inform decision making in oncology. This could highlight important site-specific differences, and also depend on the aggressiveness of selected treatment. Population based data are important in definitively selecting an age threshold for GA.

Consensus was not reached on the use of a shorter screening tool that would identify those patients from an oncology clinical practice who could potentially benefit from GA, versus those who would not. However, there was consensus among the SIOG panel in relation to the VES-13, although this was ranked the lowest of the three options presented in the final round. It may suggest suitability in the absence of alternatives, and reflects the literature in this area which has yet to reveal a tool sufficiently sensitive and specific enough for use in oncology [61]. A GA is time-consuming and resource intensive, which is one of the recognised barriers to the more widespread implementation of geriatric oncology. To mitigate this, a number of studies have been conducted, focussing on screening tools that may be used to distinguish fit older patients who are able to tolerate standard treatment versus those who may be considered more vulnerable or frail [35, 321, 322] The majority of the expert panel felt that screening should be implemented, but were divided approximately 50:50 between those who would recommend a particular screening tool, versus those who could not identify an appropriate choice. In a 2012 systematic review [61], Hamaker and colleagues concluded that none of the currently available frailty screening methods have sufficient sensitivity or specificity for predicting outcome on GA. Many of the screening tools included in the Hamaker review were rated by the expert panel, who failed to reach consensus. While the pursuit of a shorter screening tool is worthwhile, especially for centres lacking dedicated geriatric

oncology services, its investigation may be premature in some respects. Many of the current screening tools are broadly based on one or more domains of GA e.g. the G8 is mainly based on nutritional status, while the VES-13 is based on functional status. Greater knowledge of the impact of these individual domains on patient outcomes in oncology is needed for various patient groups and endpoints of interest.

The lack of consensus regarding which domains to be included in a GA, and what assessments and interventions should be used, was identified as one of the main barriers to advancing the field of geriatric oncology at the current time [40]. This Delphi study aimed to address that with the rating of all domains identified by the expert panel as relevant, and selection of appropriate assessment tools. Consensus was reached on all GA assessments and interventions considered to be important, apart from polypharmacy assessment, with significant agreement achieved, and no individual differences between the professional subgroups. It could be argued that continuation of the study to a fifth round may have secured consensus for items such as polypharmacy, or use of a screening tool. There are no guidelines in relation to the optimal number of Delphi rounds that should be employed in a study of this kind, but generally four is a maximum [281]. It is advised to exercise caution with excessive rounds, at the expense of expert panel attrition [274, 282]. Due to the repetitive nature of this study, and the substantial time demands required, it was deemed appropriate to only use four rounds, in order to minimise respondent fatigue. Other studies have used a *modified Delphi* approach, with the integration of a face-to-face meeting, with subsequent ranked rounds. As a multinational expert panel was employed in the current study, this was not feasible. However, there are also recognisable limitations to face-to-face meetings, due to the dominance of certain individuals [323], different personalities [324],

as well as time limitations. The Delphi method affords other advantages such as anonymity [284], democracy [325] and structured conformity [312]. A comparison of both the Delphi method and the nominal group technique highlighted greater consensus and depth of understanding for the latter, but much higher reliability for the Delphi method [326]. This reliability can be further enhanced by the use of appropriate, standard feedback [327] as well as multiple professional groups, both illustrated in this study, where subset analysis was used as appropriate.

A number of "voting" methods were used in the current study, depending on the type of information sought e.g. yes/no responses, versus ordinal scales, with different definitions of consensus applied. This may also have affected the inability to reach agreement on some items, however it must be acknowledged that dissensus is equally meaningful [292]. Defining consensus is one of the most contentious aspects of the Delphi method, and its measurement varies greatly in the literature [316, 328]. The more stringent the criteria, the more difficult it is to achieve consensus among the expert panel, while less stringent criteria can also limit the meaningfulness of the consultation process. In addition to measuring consensus, it is also important to measure the relative strength and stability of that agreement, for which Kendall's *W* and Wilcoxon's signed rank test [305] may be used, as calculated in this study.

The final assessment and intervention algorithm may be considered a minimum dataset, but importantly, it is not all-inclusive. There are additional domains that would greatly benefit patients from a holistic care perspective, if time and resources permitted e.g. spiritual care, sexuality issues, quality of life, amongst others. The EORTC Elderly Task Force (ETF) has previously established an Elderly Minimal Dataset (MinDS) with the proposed aim of harmonisation of data

collection with regard to geriatric oncology studies. This included four elements, the Instrumental Activities of Daily Living (IADL), Charlson Comorbidity Index (CCI), G8 (Geriatric-8) Screening Tool (which includes a set of questions from the Mini Nutritional Assessment (MNA)) and social status. Apart from the G8, all of these have been selected by the expert panel, in addition to the following: Activities of Daily Living (ADLs), Mini Mental State Examination (MMSE), Timed Up and Go test (TUG), MNA and psychological assessment using patient interview and the Geriatric Depression Scale (GDS). The scope of a GA will therefore be broader than the EORTC's MinDs.

In relation to the relative importance of each domain, functional status was rated as the most important, followed by comorbidities and cognition. This is reflected by the literature to date [176, 264, 329, 330]. However, lower ranked domains, such as psychological status are also important. Studies suggest that older age may not predispose to increased anxiety levels in patients with cancer, but may be associated with higher rates of depression [331]. Depressive symptoms have been associated with poorer outcomes [332, 333], and even a higher suicide risk [334]. The evidence is growing that resilience [335], defined as the ability to maintain or restore stable psychological and physical functioning, is more important than depression or psychological deficits, per se. Some studies suggest, especially in older adults, that a large proportion of those who experience serious illnesses, such as cancer, report high levels of QoL, following their diagnosis and treatment [336]. This phenomenon has been variously described as personal or posttraumatic growth [337, 338], adaptation [339], positive illusions [340], thriving [341], or benefit finding [342]. Perhaps clinicians rated psychological outcomes lower for this reason.

A measure of resilience was not discussed in the current study, but it has been linked to QoL and survival in patients with cancer. Further studies are needed to examine the impact of psychological distress and outcomes of older patients with cancer, as well as the relative importance of GA domains in decision making in oncology. Polypharmacy was also rated lower than other domains, even though it has been identified as a significant cause of adverse drug events, greater hospital admission rates, reduced quality of life and increased falls risk in older patients in the acute care setting [343-345]. However, there are little data to date regarding polypharmacy and its potential effects in cancer patients. Shedding light on this little known area, Maggiore et al [140], in a recent study of 500 patients, found that polypharmacy and potentially inappropriate medication use were common in older adults with cancer, but not associated with additional morbidity or hospitalisation.

Many assessment methods for comorbid illnesses are available, and no gold standard exists [127, 129]. The Charlson Comorbidity Index (CCI) [130], was recommended in the consensus outcomes of the current study, and is the most frequently cited index in the published literature. However, other approaches also have merit. The Cumulative Illness Rating Scale (CIRS) classifies comorbidities by organ system and rates them according to their severity (0-4) [132]. The original version was subsequently modified to better reflect the older patient, in the form of the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) [133]. Compared to the CCI, the CIRS-G is considered more sensitive, as all coexisting comorbid conditions are recorded, and it appears to provide more prognostic information [134, 135]. It is, however, more time-consuming than the CCI and assessment by specifically trained personnel is recommended. A further option, discussed during the Delphi process, was the the Adult Comorbidity Evaluation-27 (ACE-27) index [138]. The ACE-27 is a

validated instrument that captures comorbidities for cancer patients and grades severity at the time of diagnosis [139]. In total, twenty-seven conditions were identified, based on previous research, as well as clinical judgement, building on the original Kaplan–Feinstein Index (KFI) which grouped conditions into 12 categories, with a severity rating applied for each one [137]. The original KFI was modified, by adding several health conditions (diabetes, HIV/AIDS, dementia), creating a comorbidity index for newly diagnosed patients with cancer, to become the Adult Comorbidity Evaluation-27 (ACE-27) index.

Interventions that were identified for deficits in each domain underline the importance of multidisciplinary team collaboration, particularly close collaborative links with the geriatric medicine team. U.S. based geriatric oncologists similarly reached consensus on multidisciplinary input to design interventions for older adults [346]. While employment of a geriatrician dedicated to oncology patients is highly desirable, this is not always feasible. However, the results of this Delphi study highlight the importance of having a geriatrician participate in the care of older patients with cancer and thus incorporating geriatricians into multidisciplinary oncology care should be the ultimate aim of every organisation.

Finally, in order to implement geriatric oncology services in Ireland, a number of educational needs were frequently cited in the qualitative responses of the current study. Oncologists and healthcare professionals must have the underlying knowledge to assess and intervene in order to optimise the usage of GA in clinical practice.

There are identified deficits in knowledge in the undergraduate curricula for Oncologists and allied health professionals in relation to GA implementation. A recent study [41] investigated the knowledge,

attitudes and clinical practice of Radiation Oncologist trainees in geriatric oncology. This study highlighted that trainees were poorly informed regarding key aspects of GA tools and implementation. Other studies have demonstrated similar inadequacies in geriatric oncology competencies and medical curricula [347-350].

As Irish oncology services to transition to an increasingly aging population in the coming years, it is imperative that greater focus is placed on age appropriate care and preparing for these changing demographics. This consultation process shed valuable light on the current shortcomings in services and education.

3.5 Strengths and Limitations

3.5.1 Advantages and Disadvantages of the Delphi Technique

This first study of the doctoral thesis provided much needed insight into the application of commonly used GA methods to oncology practice. It sought consensus where none existed, on the best method of GA in oncology, using an international expert panel, in collaboration with a national multidisciplinary panel.

There are a number of limitations to this study. Given the aforementioned absence of high quality studies to date [40], the use of a Delphi panel is justified. However, bias is an inherent risk in such an approach [282]. This may be overcome to a certain extent by the adoption of a heterogeneous panel [323, 351], such as the four groups consulted here. In relation to the Delphi method itself, there are a lack of methodological guidelines and differences in the approaches taken, however a number of evidence-based approaches were taken in the current study to try to overcome this.

Each group added a valuable perspective for clinical practice, while simultaneously benefitting from the opinions of others. However, the SIOG group had the greatest expertise in geriatric oncology, and the other groups may have been disadvantaged by a relative lack of experience in GA, especially the Irish oncology group. In additionr, the SIOG group was the larger one, in the hope that their expertise would prove influential in the provided feedback. Another important limitation of this process is that new relevant data may have been published subsequent to the Delphi study, and a substantial time commitment from participants is required. Also, the response rate was low, which may also influence the results.

The panel was mainly European-based, as a similar study was devised, in collaboration with the researcher, to run concurrently in the United States [346]. The results may therefore represent a bias towards European practice. However, the fact that both studies yielded broadly similar results is a testimony to the reliability of the approach taken.
This study did not include a face-to-face meeting, as per the modified Delphi approach often employed in guideline development, which would have facilitated greater discussion and elaboration of views. However, the approach used avoids the disadvantages inherent in group processes, where one panellist might dominate discussions and may unduly influence consensus [281], as previously discussed.

While panelists agreed on the assessments and interventions that are important in oncology, the subsequent usefulness of the information provided depends on the individual organisation. Resources are a key concern, hence the desire to find a shorter screening tool to avoid lengthy consultations. Collaboration with geriatric medicine colleagues is essential, and employment of at least one dedicated geriatrician for oncology should be a primary aim for

every oncology department. However, several members of the expert panel have alluded to the shortage of geriatricians for this purpose, and there is a known shortage of geriatricians worldwide [352]. It must also be acknowledged that decision making in oncology is inherently complex, and that complexity could not be captured in a study of this kind. A more detailed analysis of decision making in older adults warrants further investigation under more controlled, site-specific conditions.

It is advisable that patients should be included as much as possible, as partners in the process of designing, delivering, assessing and improving their own care [353, 354]. However, involvement of patient advocates was not considered feasible in the current study.

3.6 Conclusion

The study provides a framework for the consensus-based development of geriatric assessments and interventions for oncology which may be extrapolated to other areas, similarly lacking in evidence.

In the absence of evidence-based guidelines, this Delphi expert consensus on geriatric oncology design and implementation provides a useful template for clinicians regarding multidimensional assessment of older patients with cancer, although more data are needed to clarify the clinical efficacy of this approach. GA as a model of care for patients with cancer is currently under investigation, and will contribute to the development of existing guidelines and practices. In addition, as highlighted previously [40], the instruments that have been selected as part of this Delphi process were validated in the geriatric medicine setting, although their psychometric properties have yet to be established in oncology

Without level 1 evidence for the benefits of GA in oncology, one should still endeavour to incorporate its principal components into clinical practice. There is a wealth of evidence for its benefits in the non-oncologic setting. These outcomes and the provision of a more holistic approach to the care of older patients should be a key pursuit in cancer care.

This Delphi study will help to inform the future development and implementation of a pilot geriatric oncology programme in Ireland, in Part 2 of this thesis.

Chapter 4

4 Managing the Elderly in Radiotherapy using Geriatric AssEssment (MERGE): A Pilot Geriatric Oncology Clinic at Saint Luke's Radiation Oncology Network (SLRON)

4.1 Introduction

The findings of the previously described Delphi study (Chapter 3) informed the rationale for this pilot study of the implementation of geriatric assessment (GA) in radiation oncology.

In Ireland, there will be a 50% increase in the number of cancer cases by 2025, with 60% of these in patients aged 65 and older [355]. Approximately 50% of these patients will require radiotherapy as part of their disease management [356]. This presents the radiation oncology community with unique challenges, especially in the face of unclear guidelines and limited research on the optimal approach in terms of caring for older patients.

The daily nature of external beam radiotherapy over the course of a few weeks, depending on treatment site, is a significant undertaking for older patients in particular. However, as radiotherapy is a localised treatment, its toxic effects are unique to the treatment site and modality employed, and are usually more tolerable than systemic treatment [357]. Depending on the area being treated, site-specific toxicity may be more evident in the older adult, which can impact quality of life, the need for treatment interruptions, and the need for additional supportive care or hospitalisations. For example, there have been concerns for the older patient when employing whole brain

irradiation due to the risk of neurologic sequelae, including dementia [358, 359]. Also, there is an increased risk of mucositis in older patients, especially evident when treating cancers of the head and neck region [143]. This can lead to symptoms such as pain and local discomfort, with feeding difficulties and nausea, with the consequential risk of nutritional impairment. Older adults can also experience significant fatigue over the course of radiotherapy treatment [360] . Overall, radiotherapy appears to be well tolerated in older adults, however [112].

GA has the potential to influence treatment decisions in older patients with cancer [186-188, 190, 361-363] with varying degrees of influence reported in the published literature to date, ranging from 21% to 49% of treatment approaches, either by decreasing or increasing treatment intensity. However, while a GA could greatly enhance the preliminary assessment of older patients and distinguish for whom curative-intent treatment is appropriate or not, it is widely recognised as resource-intensive and is not integrated into the model of care in Irish oncology institutions at the current time.

The current literature on the role of GA in radiation oncology treatment is particularly limited. A total of twelve non-randomised studies were included in a systematic review by Szumacher et al [183]. Four studies used a screening tool only, while the remaining studies used a combined approach of initial screening, followed by GA. Two studies demonstrated a significant association between abnormal screening and mortality, while only one study showed that GA influenced treatment decision making. Half of the studies included did not find an association between screening or GA, and treatment tolerance. It was highlighted that the majority of these studies included small sample sizes.

Also, by comparison to medical oncology, the role of GA in influencing treatment decisions, and in driving interventions for older adults with cancer, is unclear [183]. The number of studies (RCTs) investigating GA-driven interventions in oncology generally, is small (n=9) [193], with only one study of radiation oncology by Lapid et al [194] from 2007. The latter small study (n=33) of newly diagnosed patients with advanced cancer, planned to undergo radiation therapy, investigated a QoL intervention with patients randomised to either the intervention group or standard care. The intervention consisted of eight sessions, devised to address five QoL/CGA domains, i.e. cognitive, physical, emotional, spiritual, and social functioning, and found a significant improvement in QoL scores.

Identification of previously unknown deficits is one of the major advantages of frailty screening and accompanying GA, allowing some intervention in order to optimise patient care and potentially to reverse frailty. A limited number of other, non-randomised, studies, exist in radiation oncology. Goineau et al [196], in a study of 100 localised prostate cancer patients, aged 75 and older, undergoing radiotherapy treatment, found no association between CGA and quality of life. However, they found Instrumental Activities of Daily Living (IADL) impairments at baseline in approximately half of all patients enrolled in the study, as well as ADL impairments in 16% of patients. One fifth of patients presented with cognitive decline (defined as MMSE<27), 31% with depressive symptoms and more than two-thirds with significant co-morbidities, especially cardiovascular comorbidities, which may affect ADT tolerance. Malnutrition was virtually absent, suggesting that nutrition-based screening tools, such as the G8 [82], would be of little relevance in this particular patient cohort. Spyropoulou et al [197], in a radiotherapy patient population (n=230) found that patients >75 years with higher Vulnerable Elders Survey-13 (VES-13) [198] scores were

less likely to complete radiotherapy, independent of other factors that might affect radiotherapy completion. VES-13 is largely based on functional status, an integral part of CGA. Keenan et al [199] did not find any correlation between the Edmonton frailty score and radiotherapy toxicity. Neve et al [200], in a small study of older head and neck cancer patients, also undergoing radiotherapy, found that patients identified as vulnerable at baseline, were less likely to complete radiotherapy.

A further study [201] investigated whether an objective measure of physical function, the Timed Up and Go (TUG) test, as well as the G8, had an association with acute toxicity and ability to comply with treatment. This showed no relationship between the two tests and treatment tolerance. The other was a prospective cohort study focusing on patients with head and neck cancer [31], in which those who reported pre-radiotherapy functional limitations were more likely to show both reduced health-related QoL during treatment, as well as a longer recovery afterwards.

These studies signal some of the potentially useful interventions for patients receiving radiation therapy, albeit not directly investigated or mentioned in most of the aforementioned studies which have focussed exclusively on assessment, often without mention of follow-up care. This area has been one of the gaps in the current literature in oncology generally, but more so in radiation oncology.

Some of the ways in which GA might alter treatment decisions in radiation oncology include omission of concomitant chemotherapy for example, which contributes considerable toxicity for the patient. Another adaptation is altering the type and modality of radiation treatment offered to patients. Although radiation therapy is usually well tolerated in older patients [112], hypofractionated radiotherapy

could be considered in older patients with poor supports, lack of mobility, lack of transportation, in active caregiver roles or with social frailty, for example. This would limit the burden of travel for such patients, especially those not living adjacent to regional cancer centres. This is one area where the radiotherapy service can facilitate the patient and afford greater convenience. One example of this is in the treatment of Glioblastoma Multiforme (GBM). For patients identified as elderly/frail, 25Gy in 5 fractions has been shown to be non-inferior to 40Gy in 15 [364], the previous standard of care for such patients [365]. Alternatively, the CGA may help to identify frail patients who are not candidates for conventional, daily radiotherapy but may benefit from other (curative) modalities, such as stereotactic body radiotherapy, with fewer hospital visits and potentially less toxicity [202]. Accelerated Partial Breast Irradiation (APBI) is another option to simultaneously limit toxicity and afford greater convenience for the patient [203]. APBI uses larger radiation doses to the localised tumour bed (as opposed to the entire breast) over a shorter period of time.

Pottel et al [204] have highlighted the need for regular re-evaluation of CGA domains during radiotherapy as the toxicity of chemoradiation results in multidimensional decline, necessitating supportive care and intervention. Again, this highlights the need for ongoing assessment and appropriate interventions.

Guidelines on best practice from the International Society of Geriatric Oncology (SIOG) [79], the National Comprehensive Cancer Network (NCCN) [78] and European Organisation for Research and Treatment of Cancer (EORTC) [81] have recommended GA be integrated into the care of older adults with cancer, for optimal patient management. However, there remain many unanswered questions as to its efficacy and predictive power, sufficient to translate to

incorporation of geriatric medicine principles in many centres [366, 367]. The current lack of high level evidence may be due to the complexities with regard to the conduct and interpretation of trials in older patients, where there may be multiple underlying factors to consider that may affect response to treatment [368, 369], as well as biological factors that change with age [370]. Many authors have advocated for more focussed research efforts and older-specific trial endpoints in order to “geriatricise” trial design [31, 371].

Medical Research Council (MRC) guidelines on complex intervention evaluation, advise a phased approach to the implementation of complex interventions in medicine [372]. This includes feasibility studies (whether the study can be carried out effectively) and pilot trials (a scaled down version of the trial), with the aim of optimising aspects of study design for consideration during a larger scale implementation of in the future. This ensures both internal validity in one’s own institution and aids external validityalso as some of the issues are common to both.

Due to the complex nature of GA, and its implications for older patients, which involves multiple patient/healthcare contacts and clinical judgement as to its relevance, it was considered appropriate to pilot the current proposed geriatric oncology programme, before progression to a larger trial.

Another difficulty in the published literature in relation to GA, lies with the lack of standardisation of assessment approaches to date [40]. In order to address the current lack of consensus as to the optimal method of GA to be undertaken, a national consultation process and Delphi study were carried out seeking consensus from Irish radiation and medical oncologists and geriatricians, as well as a team of international experts in the field of geriatric oncology (Chapter 3).

This provides the basis and rationale for the current chapter, which aims to establish its clinical feasibility and significance.

Studies to date have largely focussed on treatment decisions in surgical/medical oncology, with fewer studies attempting to relate GA assessment and outcomes to radiotherapy related endpoints, although some smaller studies have been carried out [200, 373].

In relation to the study itself, it was hypothesized that implementation of GA has the potential to affect patient outcomes and radiotherapy treatment decisions for older patients. The results section of this chapter are presented in two sections. Part 1 will focus on feasibility, while Part 2 will focus on patient outcomes.

4.1.1 Study aims

Part 1

The primary aim of this feasibility study and two-arm, randomised pilot trial was to assess the feasibility of conducting an RCT on the effectiveness of conducting GA in older patients undergoing radiotherapy.

The specific objectives were:

1) To examine feasibility outcomes, such as recruitment, time and resources, as well as patient completion of study obligations.
2) To describe a process designed to assist researchers in making the best use of the findings from this feasibility study to inform subsequent decisions regarding a follow-on trial.

3) To make recommendations on the resources required in order to implement these management recommendations.

Part 2

The secondary aim was to obtain preliminary data on the prevalence of geriatric impairments in an older patient population undergoing radiotherapy treatment and the efficacy of GA-driven interventions on patient outcomes (acute radiation-induced toxicity and treatment compliance).

The specific objectives were:

1) To examine the clinical characteristics of older patients with cancer, as part of an initial GA in the radiotherapy department at Saint Luke's Radiation Oncology Network, at St. James's Hospital.

2) To evaluate the results of patient GA and identify deficits in various assessment domains, such as physical function, comorbidity, polypharmacy, nutrition, cognition and psychological status.

3) To examine interventions and patterns of referral and subsequent management recommendations for this patient population during this time-frame.

4.2 Methodology

4.2.1 Pilot Study Design

A two-arm, randomised, controlled trial was chosen.

The two treatment arms were as follows:

- **Arm 1** =Usual care. Primary Oncologist was only notified with abnormal cognitive or depression screening results that ethically could not be withheld. The ability to provide informed consent for the study would be reassessed at this stage, if appropriate. Usual care does not typically include GA domains.

- **Arm 2** = Usual care plus GA results and recommendations. These were conveyed to the primary oncologist in written form within 2 days of assessment completion.

4.2.2 Participant Selection and Recruitment

Potential participants were recruited from a single institution oncology outpatient clinic of participating radiation oncologists (ROs) before a radiotherapy treatment decision had been finalised. This study took place at a Dublin radiotherapy centre (St. James's Hospital), which forms part of a wider network of radiotherapy departments as part of Saint Luke's Radiation Oncology Network. The centre currently treats approximately 1,400 patients each year, of which 32% are aged 70 and older. The majority of cases are outpatients, however there are some inpatient facilities also. There is no dedicated

geriatrician provided for oncology, however referral pathways exist if required, and were defined as part of the preparatory work for this study.

Study participants were screened via new patient clinic lists, and the study outline was provided initially by the treating RO, who referred interested parties to the study co-ordinator for further information and consent procedures.

4.2.3 Selection Criteria

4.2.3.1 Inclusion Criteria

Participants were deemed eligible for the study if they met the following criteria at pre-screening: age ≥70 years old, diagnosis of solid tumour malignancy or lymphoma, initially planned to undergo radiotherapy treatment of at least 3 weeks duration (with or without chemotherapy), life expectancy with treatment of 6 months or greater (as judged by their RO), receiving follow-up care in St. James's Hospital and able to provide written informed consent for the study.

4.2.3.2 Exclusion Criteria

Exclusion criteria were patients who were currently under the continuous care of a geriatrician or who had moderate/severe dementia, symptomatic brain metastases, or pre-existing major neurological or psychiatric disorders (impacting ability to consent).

4.2.4 Pilot study procedures

Recruitment occurred, on a part-time basis, between August 2014 and September 2015.

All participants underwent GA at baseline, before randomisation to the intervention/control arm and before commencement of radiotherapy treatment planning procedures. Randomisation procedures are an important aspect of any pilot study, to determine any issues going forward to full trial. This is in keeping with the published literature [374, 375]. All face-to-face assessments were completed by the same individual, who was a radiation therapist with specific training in the methods of GA used. The results of GA were relayed to the Radiation Oncologist (RO) for the intervention arm only, unless significant psychiatric/cognitive/other issues were identified. The results of this assessment and impact on radiotherapeutic decision making were then noted for the intervention arm, including any unknown issues identified and additional referrals for followup/remedial care.

4.2.5 Intervention Delivery

Once the participants agreed to take part in the study and informed consent was received, all assessments were completed in a quiet room in the radiotherapy department of Saint Luke's Radiation Oncology Network at St. James's Hospital. The room contained a desk, chairs and the appropriate space for the completion of the assessments, especially a 3 metre space for the performance of the timed up and go test (TUG). All participants underwent GA at baseline during one of their planned radiation oncology appointments (usually the pre-treatment planning appointment), to avoid extra travel on days that they had no hospital appointment. The study investigator conducted all assessments. Where possible, some patients were able to complete self-completion questionnaires ahead of the schedule GA, and were asked to bring it with them on the day of the assessment. GA details are listed below (Section 4.2.8).

A summary of GA findings was sent within two working days both in writing and verbally to the patient's RO (please see Appendix 13 for a copy of the summary assessment template). The findings on the individual domains were summarised, and recommendations made regarding further referrals and supportive care. Based on the GA, predefined evidence-based interventions deemed necessary were recommended and discussed with the clinician at the time of presentation of the findings. These were based on the previous Delphi study and a corresponding US version [247]. The patient's consultant reviewed the summary of the findings and the interventions that were recommended and agreements were made on the necessary referrals. Permission had been secured to contact the patient's GP, and the patient was consulted if any GP referrals were deemed necessary. In addition, a clinical care pathway had been defined for referrals to the medical gerontology department, based on patient need and GA outcomes.

GA was repeated for each participant, by the study investigator, approximately three months after the completion of radiotherapy. Again, every effort was made to coincide with other scheduled appointments, in order to reduce the burden of travel for patients.

4.2.6 Sample Size

In keeping with pilot and feasibility study methodology [375, 376], no formal sample size calculation was performed, as the objectives related to recruitment, retention, feasibility and acceptability of the trial. Also, there were no previous completed trials of this intervention in this population and investigations of changes in key trial parameters relating to patient outcomes and impact on decision making were exploratory only. The total number of participants recruited was small (n = 30), but consistent with recommendations

for feasibility studies in the published literature [376], with recommendations of at least 12 participants per arm [377].

4.2.7 Blinding

In order to reduce the risk of bias in randomised controlled trials, a double blind design is recommended, whereby neither the participant nor the researcher are aware of the allocation arm [378]. This may eliminate both performance and detection bias when analysing the outcomes measured. However, blinding isn't always feasible, as was the case in the current study, which involved interaction between the researcher and the patient, as well as interventions for the non-control arm.

4.2.8 GA Details

As described previously, the methodological basis for the current pilot study was based on the results of a prior consensus process (Chapter 3), please see Table 4.1 for a brief summary. The following sections discuss the various outcome measures used in this pilot study. Please see Appendix 12 for a full version of the assessments used.

Eight domains were selected as part of the GA, including functional status and mobility, nutrition, mood, comorbidity, cognition, number of medications, and social support status.

DOMAIN	ASSESSMENT TOOL	DOMAIN	ASSESSMENT TOOL
Functional status	ECOG ADL* IADL* Falls history*	**Social support**	Patient history/caregiver interview*
Objective physical performance	TUG	**Polypharmacy**	Number of total medications*
Comorbidity	Charlson Comorbidity Index (age-adjusted)	**Psychological status**	GDS* Patient history/interview
Nutrition	MNA-SF	**Cognition**	MMSE
Screening tool	G8	**Additional Frailty Measures**	Balducci criteria Clinical Frailty Scale

ECOG PS indicates European Cooperative Oncology Group Performance Status; ADL, Activities of daily living; IADL, Instrumental Activities of Daily Living; .TUG, Timed Up and Go test; MMSE, Mini Mental State Examination; MNA SF, Mini Nutritional Assessment Short Form; GDS, Geriatric Depression Scale; G8, Geriatric 8.
*Indicates eligible for self-completion

Table 4.1 Summary of GA

4.2.8.1 Functional Status

The need for functional assistance (measured by ability to complete activities of daily living) is predictive of treatment toxicity and survival [177, 379, 380], and there are a number of ways to assess function.

4.2.8.1.1 Activities of daily living (ADL)

ADLs are measures of basic self-care. ADL independence was assessed using the Katz Index of Independence in Activities of Daily Living [381], commonly referred to as the Katz ADL, which is the most commonly used instrument to assess functional status as a measurement of the person's ability to perform activities of daily living independently. Clinicians typically use the tool to detect problems in performing activities of daily living and to plan care accordingly. The index ranks adequacy of performance in the six basic functions of bathing, dressing, toileting, transferring, continence, and feeding. Patients are scored yes/no for independence in each of the six functions. Continence is usually considered an impairment, rather than a disability, and it is not taken into account to measure ADL limitations [382].This is especially important for patients on active treatment, who may be experiencing transient/permanent side-effects related to their cancer and its management. ADL limitation was therefore measured based on the remaining five items.
For the purpose of the current study, patients were categorised as dependent if they could not perform at least one activity of the scale without assistance, as defined by the authors of the original scale [381].

4.2.8.1.2 Instrumental Activities of Daily Living (IADL)

Self-reported functional status or level of independence in the community was assessed using the IADL scale [110]. This scale consists of eight questions rated on a three-point Likert scale. It measures the degree to which an activity can be performed independently. The eight items on the IADL scale include using a telephone, shopping, preparing meals, cleaning the house, doing laundry, using transport, managing one's medications, and handling finances. Traditionally, some of these were thought to only apply to

women e.g. preparing meals, cleaning the house and doing the laundry. The option of "not applicable" is thus very important here as some categories may not be relevant for some patients, and they were only rated out of those that were considered relevant for their unique circumstances.

For the purpose of the current study, patients were categorised as dependent if they could not perform at least one relevant activity of the IADL scale without assistance, as defined by the authors of the original scale [110].

4.2.8.1.3 Falls History

A self-reported history of falls in the past six months was also recorded for information on geriatric syndromes, considered important for Balducci classification of frailty [243] (see Appendix 12). A history of a recent fall has been demonstrated to be independently predictive of increased risk of treatment toxicity in older cancer patients [175].

4.2.8.2 Objective Physical Performance

The Timed Up and Go (TUG) test is a reliable and valid test for quantifying an older person's mobility [383]. The original purpose of the Timed Up and Go (TUG) test was to assess basic mobility skills of frail older persons. It is a very simple test that times the ability to stand from a seated position and walk a set distance (3 metres), and back to the original starting point to resume a sitting position [383]. It has been found to be predictive of further functional decline in community-dwelling individuals and cancer patients alike [176, 384]. It has also been associated with mortality in older patients with cancer

[385], with a score of ≥20 seconds indicating higher risk (hazard ratio 1.90, *P*=0.001) .

4.2.8.3 Comorbidity

Among patients with cancer, comorbidity is associated with poorer overall survival, due to competing causes of mortality [134, 135, 139, 386, 387]. Comorbidity may also impact cancer treatment tolerance [388-390]. Furthermore, these comorbid conditions may predispose patients to the risk of polypharmacy and potentially adverse drug interactions [391].

The Charlson Comorbidity Index (CCI) was used to quantify patients' number of comorbid conditions [130]. The CCI encompasses 19 medical conditions weighted 1–6 with total scores ranging from 0–37. It takes into account both the number and severity of co-morbidities. The CCI is known for its ease of use, short rating time and widespread use in oncology.

4.2.8.4 Cognition

A cognitive assessment is needed to determine if the patient has the decisional capacity to consent and adhere to treatment and understand the indications to seek attention. In the presence of cognitive impairment, the involvement of the patient's family or caregiver is required to maintain safety [392-395]. Cognitive impairment is common in the older population, with the most common underlying cause being Alzheimer's Disease [396].

The MMSE [397] is often used to assess global cognition, and is one of the most commonly employed tools to measure cognitive impairment [397]. The MMSE is a 20 item tool, scored out of 30, used to screen orientation to time and place, registration, recall,

attention and calculation. The MMSE has demonstrated validity and reliability in many different populations [398].

Scores of less than 24 are indicative of mild (18-23) or severe (0 to 17) cognitive impairment. In terms of the psychometric properties of the MMSE, the sensitivity increases with increasing levels of impairment, while specificity was found to be between 80-100% [399]. Disadvantages of the MMSE include difficulty to identify mild cognitive impairment, for which the Montreal Cognitive Assessment or MoCA [400] is deemed more appropriate and difficulty in recording changes in cases of severe dementia [401]. The MMSE is sensitive to demographic variables, such as age, highest educational attainment, race and sex [402-404]. However, normative data from The Irish Longitudinal stuDy of Aging (TILDA) did not find a sex difference in the Irish population [401].

In preparation, MMSE training was undertaken by the lead investigator in Saint James's Hospital, in order to ensure correct administration and interpretation of the MMSE assessment tool. The MMSE was conducted so as to minimise distress for the patient. Errors were not indicated and, in general, mistakes were not corrected.

4.2.8.5 Nutritional Status

Both aging and cancer increase the risk of malnourishment, and approximately a third of older European adults, admitted to hospital, are considered to be undernourished [405-407]. The latter is associated with greater morbidity and mortality, as well as adverse outcomes from oncologic therapy [408-412].

Screening for nutritional deficits is therefore of the utmost importance and was performed with the Mini-Nutritional Assessment Short Form (MNA-SF) in the current study [413]. The MNA SF is a well-validated nutrition screening and assessment tool that can identify older patients who are malnourished or at risk of malnutrition. It is recognised by the European Society of Parenteral and Enteral Nutrition as the nutritional screening of choice in older adults [405].
In the current study, a score of 8-11 points indicated a risk of malnutrition, while a score of 7 or less indicated that the individual was malnourished.

4.2.8.6 Psychological Status

In a study of older adults with cancer, significant distress was identified in 41% of older adults, and poorer physical function correlated with higher distress [395]. Depressive symptomatology was assessed using the Geriatric Depression Screen Short Form (GDS SF) [414]. This is a 15-item questionnaire, shortened from the original 30 item version [415], which has been shown to have adequate sensitivity and specificity in screening for depression in older adults with cancer [416]. Anxiety was assessed via patient interview.

On the GDS SF scale, a score of:

- 0 to 4 is considered a normal score.
- 5 to 8 suggests mild depression.
- 9 to 11 suggests moderate depression.
- 12 to 15 suggests severe depression.

4.2.8.7 Social Support status

In both the geriatric and oncology literature, social isolation has been linked to an increased risk of mortality [417, 418]. Patient's social support status was assessed by patient interview.

4.2.9 Screening tool

Given the high prevalence of cancer in the geriatric population, it is not feasible for all geriatric patients with cancer to be evaluated by a geriatric oncologist. Ideally, a method of screening could be employed to identify the patients who would benefit most from a geriatric evaluation.

The subject of screening gave rise to the most dissensus in the Delphi study, completed as preliminary work for this project by the study co-ordinator (Chapter 3 of this thesis). This is an evolving area of research, which requires further investigation. The current lack of discriminative power for the commonly recommended tools in oncology, has been articulated by many members of the expert panel and summarised in a systematic review [61]. However, the Geriatric 8 (G8) has since emerged as a potentially useful predictive tool for those who require full CGA versus those who do not.

The G8 questionnaire consists of 8 questions and its development was based on items from the Mini Nutritional Assessment [82]. A score of ≤ 14 (score range: 0–17) corresponds to an abnormal screening test. Completing the 8 questions of the G8 takes about 5 minutes. The sensitivity of the G8 to predict abnormal scores on the CGA in cancer patients has been reported as 76.5%, and the specificity as 64.4% [83]. Patients with a score of less than or equal

to 14 points are considered to be frail [82] and associated with poorer one year survival [83].

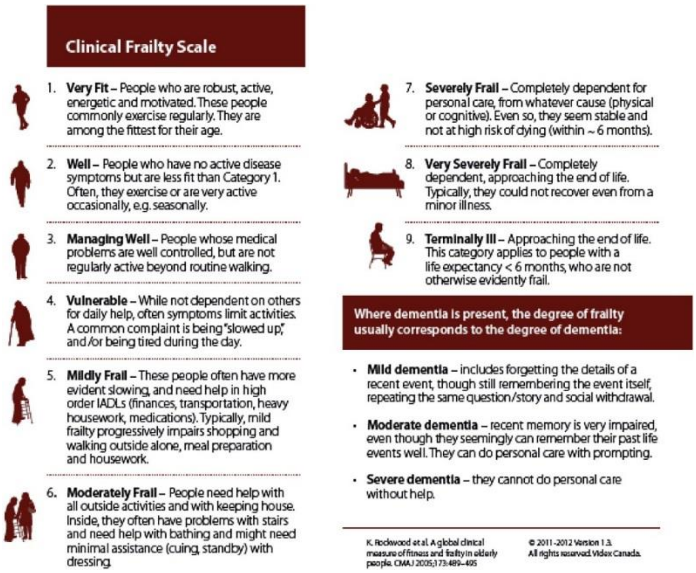
4.2.10 Additional Measures of Interest

4.2.10.1 Additional Frailty Measures

Frailty was further categorised according to cumulative deficits as summarised by Balducci frailty criteria [243] and the Clinical Frailty Scale (CFS) [64]. The latter was added to the list of assessments due to participating geriatrician referral guidelines and institutional protocol.

The CFS (Figure 4.1) is a brief (7 item) measure of frailty based on clinical judgement, and ranges from 1 (in robust health) to 7 (complete functional dependence on others). It is a well established, quick and easy, scale to define frailty, and the most popular tool used in geriatric medicine in Canad and the UK, as well as in published research [419]. Its evaluation, thus far, in a cancer patient population, is limited to one small surgical series of patients with pancreaticobiliary and melanoma cancers . In this study, the CFS was deemed to have greater discriminatory power than the more commonly used ECOG performance status [420].

A validation study in community-dwelling older people demonstrated that it was a better predictor of mortality than simple measures of cognition, function or comorbidity [64]. Its obvious advantage in a clinical setting is its relative ease of use, compared to other longer assessments of cumulative deficits, such as the 70 item Frailty Index [421], to which it has correlated well, in terms of validity and reliability.



Clinical Frailty Scale

1. **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.
2. **Well** – People who have no active disease symptoms but are less fit than Category 1. Often, they exercise or are very active occasionally, e.g. seasonally.
3. **Managing Well** – People whose medical problems are well controlled, but are not regularly active beyond routine walking.
4. **Vulnerable** – While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up," and /or being tired during the day.
5. **Mildly Frail** – These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.
6. **Moderately Frail** – People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.
7. **Severely Frail** – Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).
8. **Very Severely Frail** – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.
9. **Terminally Ill** – Approaching the end of life. This category applies to people with a life expectancy < 6 months, who are not otherwise evidently frail.

Where dementia is present, the degree of frailty usually corresponds to the degree of dementia:

- **Mild dementia** – includes forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.
- **Moderate dementia** – recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.
- **Severe dementia** – they cannot do personal care without help.

K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489–495

Figure 4.1 Clinical frailty scale (CFS) [64]

The following information was also collected:

Sociodemographic information, including patient age, race and ethnicity, highest level of education achieved and marital status were abstracted from the medical record.

The tumour stage, previous surgery, radiation therapy dose and schedule (intended and received), chemotherapy type, dose and schedule (intended and received) were also collected.

Please see Table 4.2 below for a full list of assessments used, including threshold values signifying impairment.

The associated assessment forms are included in Appendix 12.

DOMAIN	TOOL	SCORE SIGNIFYING IMPAIRMENT
Physical function	➢ ADL ➢ IADL ➢ Falls history	➢ Any ADL or IADL impairment ➢ Any history of falls
Objective physical performance	➢ TUG	➢ <10s Freely mobile ➢ <20s Mostly independent ➢ 20-29s Variable mobility ➢ >20s Impaired mobility ➢ 13.5s threshold for increased falls risk
Comorbidity	➢ Charlson Comorbidity Index	➢ Evaluated on a case-by-case basis
Nutrition	➢ MNA-SF	➢ Normal nutritional status 12-14 ➢ At risk of malnutrition (8-11 points) ➢ Malnourished (0-7 points)
Social support	➢ Patient history/caregiver interview	➢ Any deficit noted
Polypharmacy	➢ Number of total medications	➢ ≥5 medications
Psychological Status	➢ GDS ➢ Patient history/interview	➢ 10-19 mildly depressed ➢ 20-30 severely depressed
Cognition	➢ MMSE	➢ 24-30=normal
Screening	➢ G8	➢ ≤ 14

Table 4.2 Assessments used in the pilot study and scores signifying impairment

4.2.11 Outcome Measures

4.2.11.1 Feasibility

For self-administered items, feasibility was assessed via the percentage of patients able to complete certain aspects of the assessment on their own, or with the assistance of a carer before appointments, was recorded. Consultation times and referrals were also documented.

4.2.11.1 Moving from Feasibility to Full Trial

Feasibility was assessed via the methodological issues identified by Shanyinde et al [375] as an analytic framework. Subsequently the ADePT (A process for Decision-making after Pilot and feasibility Trials) framework [422] was employed to support recommendations for clinical practice in moving from feasibility study to full trial. This framework entails (1) categorising feasibility outcomes of the study according to whether they affect real world implementation only, the trial itself only, or both; (2) coming up with potential solutions according to changes in the intervention, trial design, or the study context (3) assessing these potential solutions in terms of effectiveness and ability to implement; and (4) selecting the best solutions based on effectiveness, feasibility, cost implications and how these solutions could be applied and improved upon in a future definitive trial.

4.2.11.2 Treatment Tolerance and Compliance

Treatment tolerance and compliance were defined as follows:

- Rate of (one or more fractions) unplanned radiotherapy interruptions or radiotherapy incompletion (one or more fraction less than the prescribed radiation dose)
- Radiotherapy/chemotherapy dose reduction during a course of treatment
- Chemotherapy withdrawal
- Hospital admission (not elective) rate

4.2.11.3 Assessment of Factors Determining the Treatment Plan

A summary of GA findings was sent within two working days both in writing and verbally to the patient's RO (please see Appendix 13 for a copy of the summary assessment template). Recommendations were made based on previous research [246, 247], which represents consensus on best supportive care for each GA deficit, as well as the patient's own unique circumstances.

Any changes to the treatment plan were noted, as well as any unidentified issues that the RO had previously been unaware of, and additional referrals made. ROs were asked if GA results influenced their decision-making in order to identify factors that influenced the patient's subsequent treatment (i.e. age, stage of disease, performance status, GA measures used). Clinicians ranked each factor, on a ten point Likert scale (see Appendix 14), to determine which were the most influential in their decision making process. ROs also noted any additional interventions/referrals made as a result of GA recommendations. This was completed for each individual patient in the treatment arm (n=15). In total, four ROs participated in this study.

4.2.11.4 Quality of Life

Health-Related Quality of Life (HRQoL) is a major concern for cancer patients, and it can be affected by symptoms caused by cancer, as well as by treatment-induced toxicity [423]. Older patients are less willing to compromise their HRQoL for the potential for increased survival [257]. HRQoL was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 (QLQ-C30) [424].

4.2.11.5 Toxicity

Toxicity was assessed using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 [425], as this was the toxicity grading system employed in the participating radiotherapy department.

4.2.12 Statistical analysis

In this pilot study, patient outcomes were analysed on the entire cohort of enrolled patients rather than according to the two treatment groups. This was deemed appropriate due to the negligible influence on treatment decisions (reported below) and minimal intervention beyond routine care in the control arm. Also, as it was a pilot study, it was not sufficiently powered to determine the relative benefit of GA between arms.

Descriptive statistics for patient characteristics, health and functional status measurements, and outcome characteristics were calculated. Normally distributed data were summarised using means and SD; non-normally distributed data were summarised using medians and ranges.

Normality tests were conducted using the Shapiro-Wilk test, recommended for small sample sizes [426]. The student's t test (metric data) was used to analyse differences between baseline and followup assessments, or Wilcoxon signed rank test (non-parametric data).

Data were analysed using IBM Statistical Package for Social Sciences Version 22 (SPSS Inc., Chicago, IL, USA). All p values presented are two-sided using an alpha of 0.05.

4.2.13 Data Protection

All hardcopy research records were stored onsite in the Discipline of Radiation Therapy, in locked research files. Offices were secured by key and data kept in locked file cabinets. Electronic research records were stored on the Discipline of Radiation Therapy's password secured and firewall protected networks. These were the same methods of security used for patient medical records.

The study coordinator assigned a numerical Study ID to each participant once they signed the consent form. All study forms and questionnaires used this number to ensure data integrity. Other identifying information was eliminated from these forms. A complete list of study participants with study ID, name, and contact information was maintained separately. This linkage information was only accessible to the study coordinator, study investigators, and the individual responsible for maintaining the database.

4.2.14 Ethical Considerations

This study was conducted in accordance with the ethical principles derived from the Declaration of Helsinki [427]. Written informed

consent was obtained from all participants (please see Appendix 15 for a copy of the participant information leaflet, and Appendix 16 for the consent form).

The study was approved by the Saint Luke's Radiation Oncology Network (SLRON) and Faculty of Health Sciences, Trinity College Dublin (TCD), Faculty of Health Sciences Research Ethics Committees. Written and verbal informed consent were obtained from all patients before inclusion.

Please see Appendices 17 and 18 for a copy of ethics approval from TCD and SLRON, respectively.

4.3 Part 1 Results: Feasibility

4.3.1 Patient Participation and Characteristics

Among 58 eligible inpatients, 30 (52%) agreed to participate and were randomised, 15 to the intervention group and 15 to usual care (control) group. Baseline characteristics are presented in Table 4.3. The median age (range) was 73 (70-89) and the majority (77%) were male, and had a diagnosis of prostate cancer (63%).

Characteristics	Control arm	Intervention arm	Total (n=30) n(%)
Age: median(range)	72(70-79)	75(71-89)	73(70-89)
Gender: Male	14(46.67)	9(30)	23(76.67)
Female	1(3.33)	6(20)	7(23.33)
Marital Status: Married	12(40)	9(30)	21(70)
Single	0(0)	1(3.33)	1(3.33)
Widowed	3(10)	5(16.67)	8(26.67)
Highest Educational Attainment:			
Primary	8(26.67)	11(36.67)	19(63.33)
Secondary	5(16.67)	4(13.33)	9(30)
Third Level	2(6.67)	0(0)	2(6.67)
Type of Cancer (Primary Site):			
Prostate	13(43.33)	6 (20)	19 (63.33)
Rectum	1(3.33)	2(6.67)	3(10)
Endometrium	0(0)	1(3.33)	1(3.33)
Cervix	0(0)	2(6.67)	2(6.67)
NHL	1(3.33)	2(6.67)	3(10)
Vulva	0(0)	1(3.33)	1(3.33)
Bladder	0(0)	1(3.33)	1(3.33)
Type of Treatment:			
Radiotherapy alone	2(6.67)	4(13.33)	6(20)
Concurrent chemo-radiation (CRT)	0(0)	4(13.33)	4(13.33)
Neo-adjuvant CRT	1(3.33)	1(3.33)	2(6.67)
Radiotherapy and Androgen Deprivation Therapy (ADT)	12(40)	6(20)	18(60)

Note: Listed as proportions n(%), apart from age

Table 4.3 Patient characteristics

The majority of participants were educated to primary level (63%) only and in receipt of radiotherapy alone, or in combination with Androgen Deprivation Therapy (80% in total). Six patients were

commenced on chemoradiation, two of these in the neo-adjuvant setting.

4.3.2 Feasibility

Self-completion was possible (for items identified with an asterix on Table 4.1) for the majority (n=26/30, 87%) of participants.

The average length of time taken for the study co-ordinator to complete (face-to-face) assessments was 31.2 minutes.

When calculating the cost of this per department, overheads and level of expertise of the person conducting the assessment need to be taken into account, as well as the cost of referral to geriatric medicine and supportive care services (as judged on an individual patient basis). These cost calculations are therefore complex, and dependent on the level of frailty identified, considered beyond the scope of the study.

Recruitment rates were lower than anticipated. The mean rate of recruitment per month at the study site was 2.5. This may have resulted from an underestimate of the number of eligible patients at the start of the study.

Of the 58 patients approached to take part, 28 were unwilling at the outset to be contacted by the study team. Of those whose eligibility was confirmed, reasons provided for non-participation were mainly related to the timing of recruitment at the initial appointment with the RO, with many patients reporting feeling overwhelmed and anxious. There were also some competing larger studies that were prioritised within the centre. Better representation of clinical trial staff at the

study centre may have avoided some of the issues encountered with recruitment, as this study was undertaken on a part-time basis.

As patients were recruited at a point when they may have been very anxious about their upcoming treatment, this might have affected their motivation to agree to being recruited to a clinical trial. This was less of an issue for patients with prostate cancer, who generally had a number of pre-treatment visits to their RO, especially if undergoing ADT.

There was an indication that participants who entered the study were relatively young in terms of the target patient group that was initially aimed for (median age 73) i.e. the majority of patients were in the "young old" category.

Once participants were randomised, follow-up was generally good, in terms of completion of questionnaires, suggesting that this part of the methodology would be transferrable to a larger trial. Attendance at follow-up appointments was poorer however, with 4/30 patients unable to attend due to distance to the oncology centre and inconvenience.

Acceptability was not assessed directly but adherence to study procedures gives an indication, as does the initial rate of willingness to participate. One participant refused cognitive assessment, due to a previous negative experience. However, all other patients reported no issues with the assessment itself.

The results of applying the methodological issues identified by Shanyinde et al. [375], as an analytic framework to the current study findings, are presented under each of the 14 items summarized below in Table 4.4.

Methodological issues	Findings	Evidence
1. Did the feasibility study allow a sample size calculation for the main trial?	Not achieved/recommended from pilot work [428, 429]	As this was a pilot study no formal sample size calculations have been conducted
2. What factors influenced eligibility and what proportion of those approached were eligible?	Ineligibility for randomisation was mainly due to age (<70)	30 out of 58 (52%) patients approached were recruited
3 Was recruitment successful?	Recruitment was slower than anticipated. Issues due to timing, centre and participant were identified	The mean rate of recruitment per month at study site was 2.5 Possibly due to an underestimation of the number of eligible patients at the start of the study. The timing of recruitment was not ideal in terms of patients' anxiety due to diagnosis/treatment The median age of patients recruited was relatively young (73; range 70-89)
4. Did eligible participants consent?	Suboptimal conversion to consent	30 (52%) randomized out of 58 eligible participants
5. Were participants successfully randomised and did randomisation yield equality in groups?	Randomisation procedures worked well	Baseline comparability of the two groups was adequate (Table 1). Minimisation based on age may be appropriate in a larger trial however due to age imbalance per arm
6. Were blinding procedures adequate?	Blinding was possible only at baseline assessment, as randomisation to the study arm was conducted after this	Blinding of the research team was possible only at baseline assessment

Methodological issues	Findings	Evidence
7. Did participants adhere to the intervention?	Adherence to baseline assessment was high. However, there was poor adherence to followup appointments that did not coincide with medical appointments	Data for all 30 patients were available for the intention-to-treat analysis re: impact on decision making. Four patients were considered protocol violators, and consequently a per-protocol analysis of 26 patients was completed for pre-/post- GA measures. One patient was withdrawn from the study during radiotherapy treatment, but was eligible for inclusion in baseline data analysis
8. Was the intervention acceptable to the participants?	Overall, there was good acceptability with study procedures	One participant refused cognitive assessment, due to a previous negative experience. However, the majority of patients reported no issues with the assessment itself, which was non-invasive The inconvenience of attending follow-up appointments was an issue
9. Was it possible to calculate intervention costs and duration?	Aspects of feasibility e.g. self-completion and time to complete assessments were calculated and judged to be reasonable	The mean duration of assessments was 31.2 minutes. 87% of patients could complete questionnaires before clinic appointments. When calculating the cost of this per department, overheads and level of expertise of the person conducting the assessment need to be taken into account, as well as the cost of referrals (as judged on an individual patient basis)

Methodological issues	Findings	Evidence
10. Were outcome assessments completed?	The most appropriate outcomes to use were decided beforehand based on previous work. Rate of completion was lower at followup	Both trial arms were comparable at baseline with regard to demographic variables. Overall, there may have been a slight selection bias towards younger patients however
11. Were outcomes measured those that were the most appropriate outcomes?	Outcome measures used did assess main areas of interest	Some outcome measures could be altered/further explored in future research e.g. impact on treatment decisions (negligible) and aspects of the EORTC QLQ-C30 which were more fully addressed through GA (see Part 2)
12. Was retention to the study good?	Once recruited, retention was generally good	Follow-up was generally good, in terms of completion of questionnaires. Attendance at follow-up appointments in order to complete objective assessments was poorer however, with 4/30 patients unable to attend due to various reasons
13. Were the logistics of running a multicentre trial assessed?	This was not assessed for logistical reasons	Many issues raised were department specific, therefore a pilot study is recommended for all additional sites
14. Did all components of the protocol work together?	Overall, components had strong synergy	No significant differences identified with trial processes or the researcher's abilities to implement them

Table 4.4 Summary of feasibility findings mapped to Shanyinde et al [375], analytic framework

4.3.3 Recommendations for a Definitive Trial: Application of ADePT (A process for Decision-making after Pilot and feasibility Trials)

In terms of the ADePT approach [422], the problems identified related to aspects of trial process, most of which were classified as “Type B”, i.e. with application for both the trial/institution and the real world [422]. These are summarised in Figure 4.2 below.

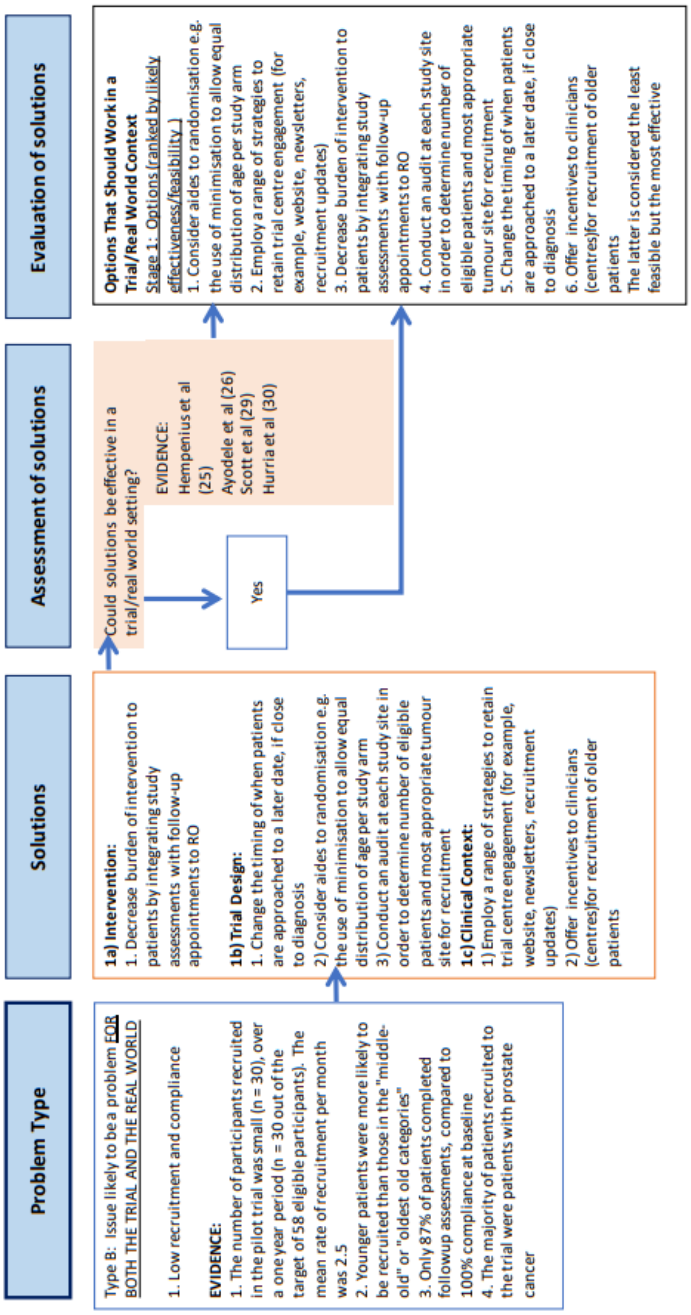


Figure 4.2 A process for Decision-making after Pilot and feasibility Trials (ADePT)

4.4 Part 2 Results: Patient Outcomes and Treatment Decision Making

All randomised patients completed the baseline GA assessment. The impact of decision making was recorded for the intervention arm only, after presentation and discussion of GA results with the referring consultant. See Figure 4.3 below for study schema.

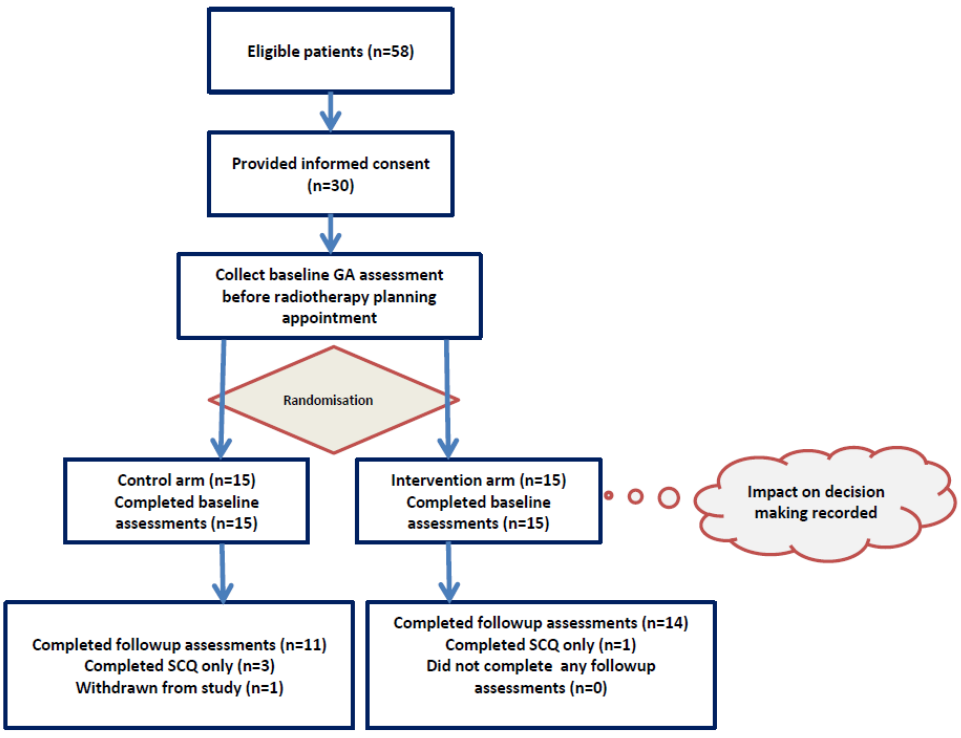


Figure 4.3 Study schema

4.4.1 GA: Patient Outcomes

4.4.1.1 Baseline GA

Most patients (n=29; 97%) had an ECOG status of 0–1. One patient had an ECOG status of 2 and none had a score of 3. GA outcomes are presented in Table 4.5 (a) below. All patients were independent for ADLs at baseline and 83% for IADLs. The mean TUG score was 10.64 (SD=2.3) and 7% (n=2) of patients had experienced two falls in the previous six months. The median MMSE score was 27 (range 20-30; normal range >24). One patient reported symptoms suggestive of mild depression (Geriatric Depression Scale >4/15), with the majority of patients reporting no significant signs. The mean number of medications taken per patient was 3.76 (2.63), with 37% (n=11) taking >5 medications i.e. polypharmacy.

The majority of patients had good nutritional status at baseline (83%, n=25), four patients were identified as being at risk of malnutrition, and one malnourished. The majority of patients had an age-adjusted Charlson score of 4-7 (n=29, 97%).

Domain	Baseline (n=30)		3m Followup (n=29 SCQ, 25 All)		Difference Between Baseline and 3mFollowup (p values)
	n	%	n	%	
Functional Status					
Independent in both ADLs/IADLs	25	83	21	72	
Dependent in >1 ADL	0	0	1	3	0.32
Dependent in >1 IADL	5	17	8	28	0.08
Objective Physical Performance					
Timed Up and Go (TUG)					0.871
Mean TUG score in seconds (SD)	10.64	2.3	11.24	3.76	
>13.5s High falls risk	3	10	4	16	
Number of falls in the previous 6 months					
0	24	80	27	93	
1	4	13	2	7	
> 2	2	7	0	0	
Co-morbidities					0.317
Charlson score 0-3	0	0	0	0	
Charlson score 4-7	29	97	27	93	
Charlson score 8-11	1	3	2	7	
Cognitive Status					
Median MMSE score (out of 30: >24=normal cognition)(range)	27	(20-30)	27	(20-30)	0.432
Psychological Status					0.075
GDS 0-4 (normal)	29	97	24	83	
GDS 5-8 (mild depression)	1	3	4	14	
GDS 9-11 (moderate depression)	0	0	1	3	
GDS 12-15 (severe depression)	0	0	0	0	
Number of Medications					
Mean number per patient (SD)	3.76	2.63	3.48	2.5	0.073
Polypharmacy (>5 medications)	11	37	10	34	
Nutritional Status (MNA)					0.98
12-14 points: Normal nutritional status	25	83	21	84	
8-11 points: At risk of malnutrition	4	13	3	12	
0-7 points: Malnourished	1	3	1	4	

(a)

Domain	Baseline (n=30)		3m Followup (n=29 SCQ, 25 All)		Difference Between Baseline and 3m Followup (p values)
	n	%	n	%	
Screening (G8 Score)					0.434
Score indicating impairment G8 ≤ 14	7	23	6	24	
Score not indicating impairment G8 > 14	23	77	19	76	
Mean (SD)	14.83	2.26	15.06	1.95	
Balducci Frailty					
Fit	21	70	19	73	
Vulnerable	7	23	4	15	
Frail	2	7	3	12	
Clinical Frailty Scale					
1. very fit	4	13	2	8	
2. well	12	40	11	42	
3. managing well	6	20	6	24	
4. vulnerable	2	7	1	4	
5. mildly frail	5	17	5	20	
6. moderately frail	0	0	1	4	
7. severely frail	0	0	0	0	
8. very severely frail	0	0	0	0	
9.terminally ill	0	0	0	0	

(b)

Table 4.5 GA outcomes at baseline and followup (a) GA domains (b) screening tools and frailty criteria

Patients were classified by their G8 scores (Table 4.5 (b)) as fit (G8 > 14, n = 23, 77%) or vulnerable (G8 ≤ 14, n = 7, 23%). The majority of patients (n=21, 70%) were considered fit by Balducci criteria [243], and only 24% (n=7) as vulnerable or frail on the CFS.

4.4.1.2 Three Month Followup GA

GA outcomes at three month followup were not significantly different from baseline, as seen in Table 4.5. There was some evidence of increasing dependence in ADLs and IADLS, slower walking speed (TUG score), higher GDS scores and increased vulnerability. However, these were not statistically significant.

4.4.1.3 Treatment Compliance

Of those enrolled, 100% completed baseline measures and 83% completed the full post-intervention assessment.

One patient with prostate cancer only completed 6 out of 37 planned radiotherapy treatments due to concerns regarding loops of small bowel in the treatment area observed on daily imaging, and was therefore withdrawn from the study at this stage as it was considered more appropriate to continue the patient on ADT alone. Another patient had their chemoradiation treatment terminated after 25 (out of 28) treatments due to development of a subdural haematoma necessitating surgery. A female patient undergoing chemo-radiotherapy for endometrial cancer had a dose reduction of taxol based chemotherapy due to the development of peripheral neuropathy.

One patient missed one day of treatment due to illness (non-treatment related). A patient with prostate cancer experienced a delay commencing radiotherapy due to his wife's bereavement. A further patient with prostate cancer who had been on ADT had their Casodex terminated due to concerns re: Liver Function Test (LFT) results. One female patient experienced a significant fall (tibia

fracture) between CT planning and the start of radiotherapy, however this did not incur any delay in starting RT.

4.4.1.4 Acute Toxicity

Acute toxicity was evaluated weekly in all patients. Maximum toxicity recorded was grade 2 (8/30 patients, 27%). The majority of patients experience mild (grade 1) toxicity.

4.4.2 RO Outcomes

4.4.2.1 Modifications to Radiotherapy Treatment Plan

All patients underwent their predefined radiotherapy treatment plan, without modification. Any changes with respect to chemotherapy were unrelated to GA results, as these were only communicated to participating ROs.

4.4.2.2 Factors Influencing Treatment Decision

For the treatment arm, ROs were asked if GA results influenced their decision-making in order to identify factors that impacted the patient's subsequent treatment (i.e. age, stage of disease, performance status, GA measures used). Clinicians ranked each factor, on a ten point Likert scale (see Appendix 14), to determine which were the most influential in the decision making process. Overall, ROs ranked stage of disease, PS and chronological age as the most influential factors in determining patient's treatment (see Table 4.6).

Factors Affecting Decision Making (in order of influence)	Mean Rank (SD)
1. Disease stage	8.8 (2.33)
2. ECOG PS	8.33 (2.16)
3. Chronological Age	6.33 (2.82)
4. Functional Status (ADL/IADL)	5.33 (3.33)
5. Comorbidities	5.07 (2.99)
6. Cognition	4.8 (2.88)
7. Psychological Status	4.73 (3.06)
8. Objective physical performance	4.27 (2.4)
9. Social support status	4.13 (2.83)
10. Nutritional status	3.93 (2.81)
11. Polypharmacy	3.53 (2.61)

Table 4.6 Factors affecting treatment decisions

4.4.2.1 Additional Information Revealed by GA

A summary of the GA findings was sent within two working days both in writing and verbally to the patient's RO. Results of GA revealed new information, previously not known to the referring RO, in 7/15 (47%) patients (intervention arm) assessed at baseline. This included multiple GA deficits (functional status, history of falls, cognition and nutritional status), a history of falls for two patients, poor cognition for two patients (one of whom had been lost to followup with the dementia services), mild depression and falls risk for a patient with poor mobility related to the onset of peripheral neuropathy while on chemotherapy.

4.4.2.2 Patient Referrals and Interventions

As a result of GA outcomes, one patient underwent extensive rehabilitation in the geriatric medicine department, including detailed assessment in the Falls and Blackout unit. A diagnosis of dementia was also made for the latter patient. Another patient, who had been lost to follow-up with the dementia services, was reinstated under their care. One patient who had a history of falls was referred to her GP for vision correction. Psycho-oncology services were consulted for the patient with queried depression. For the patient identified as being at risk of falling, the local General Practitioner and community nurse were contacted in order to provide support and assistance in the home.

4.5 Discussion

To our knowledge, this is the first study to attempt to systematically investigate the feasibility and acceptability of a randomised controlled trial regarding the implementation of GA in radiation oncology. RCTs are considered the gold standard in clinical trial design, yet there has been a relative lack of such trials in geriatric oncology until recent times. This may reflect methodological issues, such as those highlighted in this feasibility study.

The aim of this pilot study was to obtain preliminary data on the efficacy of a novel GA intervention on patient outcomes and treatment decisions in radiation oncology. Studies to date have focussed predominantly on medical and surgical oncology [186, 187, 190], and little is known about the impact of GA on the radiotherapy decision making process and patient outcomes [183].

It is a significant problem for evidence-based oncology care, that older adults are under-represented in oncology clinical trials [19, 20, 22], despite the incidence of cancer in this age group, estimated to be 60% of all cancer cases [23]. A greater focus on phased introduction of trials, in keeping with MRC guidelines [430] and appreciation of institutional issues may help to increase the success of future trials. Selection of more appropriate endpoints is also important in “geriatricising” trial design[31-33]. This has recently been highlighted by Nipp et al [34], who described the need for “pragmatic” clinical trials for older adults with cancer. There is a large unmet need to investigate older patient outcomes under more realistic conditions i.e. varying degrees of fitness and frailty. Inclusion criteria need to be broader to facilitate this, and have been used in other studies [431].

This trial provided important data to inform a definitive trial. The sample size was purposely small owing to the focus of the trial objectives. Despite some aspects of the study proving quite effective (for example, randomisation, intervention costs and adherence to baseline study requirements), data revealed the existence of a number of feasibility issues to consider going forward to a full trial.

Using the framework proposed by Shanyinde et al et al [375] and the ADePT process [422] provided greater transparency in deciding what to change in the light of the pilot study findings (see Fig 2). The suggested modifications, include refinement of trial design features and adaptations to older patients, such as facilitating convenience, giving greater consideration to the timing of recruitment and offering incentives to clinicians to recruit a larger percentage of older patients.

With regard to patient related factors in trial recruitment, Hempenius et al [432], in a randomised controlled trial of a geriatric liaison intervention also found under-recruitment of frail older adults to be related to the burden of additional hospital visits for patients, as well as insufficient awareness of the study by medical personnel. While the majority of patients in our pilot study were fit, rather than frail, the same issues were found. Hempenius et al adapted their design to facilitate home visits in order to overcome this. To enhance awareness, promotional material with the study logo was used and the study protocol was continuously presented to new staff. While these measures were effective, they incurred additional resource investment in terms of time, budget and staffing, which may not be feasible in every centre.

It must be acknowledged there was suboptimal conversion to consent amongst eligible patients in the current study. Reasons offered for non-participation were generally related to the timing of

information provision, which is an important consideration. Another possibility is that the study information was provided by the clinician, rather than the study investigator, as the first point of contact. Also, other studies were ongoing in the department at the time, which may have taken priority. At the time, there were also some issues with inpatient bed capacity, which impacted the number of vulnerable or frail patients undergoing treatment in the St. James's centre. Acceptability of trial procedures did not seem to be a factor for patients. In a similar (Irish) patient population, little difference between younger and older patients was found with regard to willingness to participate in clinical trials [433]. Furthermore, a similarly designed Phase II study, by Puts et al [235], has demonstrated the ability to recruit 60 patients over a one-year period, for a similar trial protocol. However, the infrastructure and experience with recruitment in geriatric oncology are much greater in that particular centre. There is also some evidence to suggest that older patients are less likely to be offered a clinical trial by their clinician [434, 435].

Traditionally, trials in geriatric oncology tend to include mixed patient populations. Given the difficulties in data interpretation and the multiple confounding factors that may present themselves, there is a great need to develop site specific guidelines for patient care and a greater body of research on how age-related differences manifest and interact with (radiotherapy) treatment. In our study, there was a preponderance of patients with prostate cancer, which highlights the suitability of focussing on this patient group in our institution for the more definitive trial. Minimisation [436] by age is an additional measure that aids equal distribution of patients between the control and intervention arms of randomised controlled trials (31).

In this study, GA had no effect on radiotherapy decision making in this small sample of radiotherapy patients from a mixed patient population, the majority of whom were prostate cancer patients. The study sample included predominantly fit and relatively young patients, which undoubtedly impacted these results. There were no significant differences between the study groups in terms of baseline and followup GA results, however there was a trend towards greater dependence and increased vulnerability. The inability to impact treatment decisions may be attributed in part to a lack of experience with GA, as well as a known lack of education on geriatrics in medical curricula. Many oncology professionals therefore feel ill-equipped to interpret the findings of a GA. Despite the fact that the majority of patients with cancer are older, most oncologists receive little training in the specialised care of older patients [41]. When an older patient presents to oncology, they are often segregated from their co-existing geriatric care, as the oncology and geriatric medicine disciplines often work in isolation, with little collaboration about patients. There were no issues identified in the current study with regard to radiotherapy treatment compliance or toxicity. A similar study (n=30) of radiotherapy patients [373], concluded that vitamin D deficiency and decreased gait speed correlated to radiotherapy toxicity in older patients with cancer, however given the study sample, these results require further investigation in specific populations.

GA has been shown to impact treatment decisions in cancer care, with variations in the literature extending from 20% to 49% impact [437]. Commonly, less aggressive treatments are offered, especially with regard to systemic treatments, and this is independent of who conducts the GA. In larger trials by Kenis et al [186] and Decoster et al [187] modifications were mainly chemotherapy related and where no GA was carried out, radiotherapy decisions were only altered in 0.4% of cases. Caillet at al [188] also reported similar results, with

the most common change in treatment decision being a switch from chemotherapy to supportive care. Studies similarly suggest that the impact of GA may be limited to patients undergoing more toxic treatments, such as chemotherapy and targeted therapy [187, 189].

Neve et al [200], in a small study of head and neck cancer patients undergoing radiotherapy, found that patients identified as vulnerable by G8, were less likely to complete radiotherapy. On a larger scale, Pignon et al [438] reported that there should be "no age limit for radical radiotherapy in head and neck tumours" in a pivotal meta-analysis, in 1996, collating data from 1,589 patients (26% of whom were over the age of 65 years) enrolled in five EORTC trials. No differences were observed in overall survival, locoregional control, acute objective mucosal reactions, weight loss, and late effects. However, mucositis was much more pronounced in older adults, as well as other acute toxicities requiring timely and efficacious supportive care, including GA. It could be argued that this meta-analysis is now somewhat outdated, but subsequent studies have testified to the significance of toxicity in older head and neck cancer patients [439]. We did not ascertain the predictive power of the G8 screening tool in the current study, however as stated previously, our patient population was predominantly fit to begin with and did not include head and neck cancer patients, who could potentially benefit more from GA, as demonstrated in other studies [204, 440].

Spyropoulou et al [197], in a general radiotherapy patient population (n=230) found that patients >75 years with higher VES-13 scores were less likely to complete radiotherapy, independent of other factors that might affect radiotherapy completion. VES-13 is largely based on functional status, which correlates somewhat with the results of the current study, that demonstrated greater functional dependence over time.

Context is also important in terms of integrating GA into oncology. It would be ideal if every department had regular access to a geriatrician. This may afford greater credibility and influence in the treatment decision making process. Unfortunately, the current worldwide shortage of geriatricians [441] means that most centres must attempt to integrate GA, using existing resources and expertise. Timing is also important. Horgan et al [190] found that when the treatment plan was decided before GA, it altered the decision in only one patient, whereas when the treatment plan was undecided at the time of referral, the GA impacted the final treatment decision in 83% of cases. The ideal time for intervention is before discussion of the patient case at the multidisciplinary meeting, before the patient is referred for radiotherapy/chemotherapy or other modality.

The most significant finding in the current study, was the number of previously unknown issues that were identified by GA that clinicians may not have detected by routine assessment. These were identified and relayed to the medical team in 7 out of 15 patients in the intervention arm. Previous studies looking at the impact of GA on treatment decisions, reported intervention rates in the region of approximately 70% [437]. Social support and management of polypharmacy were the most commonly reported concerns, followed by nutritional deficits and finally psychological/ cognitive/mobility/falls risk/comorbidities in the remaining 20% of cases.

Adequate social support is important for a range of physical and mental health outcomes [442, 443], including cancer survival [444-446] and is closely related to quality of life. Social support is also important for those who are required to attend oncology treatments e.g. attending daily radiotherapy treatments. Many may already be in a caregiving role, or may require caregivers themselves at some point in the future, as a result of cancer, or its treatment.

Polypharmacy is most likely linked to the treatment of both cancer and other comorbidities and should be assessed to ensure the appropriateness of all medications [140]. It is widely recognised that polypharmacy is common in patients with cancer [447, 448], and more attention should be paid to assessing and optimising polypharmacy which could potentially lead to improvements in adverse drug reactions, medical costs, and quality of life [449]. Polypharmacy is also linked to increased risk of falls, which is another outcome that has significant implications for older patients [450].

Most oncology departments do not employ routine screening for falls risk. Screening for falls is recommended for all older adults with cancer [451], as research suggests that falls have a negative impact on quality of life, due to traumatic injury, subsequent fear of falling, and increased dependence. Screening for and correcting reversible risk factors, in combination with falls prevention education, are considered essential in reducing falls.

One of the most important findings in the current pilot study was in relation to cognitive status. One patient with an MMSE score of 20 had been lost to followup with the dementia services. Another patient (aged 89) who was referred to geriatric medicine for numerous deficits, was diagnosed with dementia. While these findings did not impact on the radiotherapeutic approach, they are important. A basic assumption of informed consent for treatment is that patients have capacity. Undiagnosed dementia is very prevalent in the published literature in the acute hospital setting, ranging from 20% to 50% [103, 452], and is expected to increase in the coming decades [101]. Early diagnosis of cognitive impairment is important in order to implement earlier treatment and effective management [453]. However, oncologists often feel unable to manage or diagnose cognitive

impairment. Therefore, baseline measurement of cognition should be included for all older patients at a minimum.

4.5.1 Recommendations for a Full Trial

Traditionally, trials in geriatric oncology tend to include mixed patient populations. Given the difficulties in data interpretation and the multiple confounding factors that may present themselves, there is a great need to develop site specific guidelines for patient care and a greater body of research on how age-related differences manifest and interact with (radiotherapy) treatment. In our study, there was a preponderance of prostate cancer patients, which highlights the feasibility of focussing on this patient group in our institution for a more definitive trial. It also highlights the need to expand inclusion criteria and recruitment to other sites, typically in greater need of GA and supportive care, e.g. head and neck cancer patients. Minimisation [436] by age is an additional measure that aids equal distribution of patients between the control and intervention arms of randomised controlled trials in order to overcome unequal allocation, as observed in the current study.

This study included mostly fit patients, future research efforts should broaden inclusion criteria in order to represent the wider spectrum of patients encountered in a clinical setting, and have been used in other studies[431].

Using the framework proposed by the ADePT process [422] provided greater transparency in deciding what to change in the light of the pilot study findings (see Fig 4.2). The suggested modifications, which can be considered to have internal validity only, as this was a single institution study, include refinement of trial design features and adaptations to older patients, such as facilitating convenience, giving

greater consideration to the timing of recruitment and offering incentives to clinicians to recruit a larger percentage of older patients.

Other institutional factors influenced the recruitment rate e.g. the introduction of the study by the clinician rather than the researcher, as well as competing studies in the same centre. At the time, there were also some issues with bed capacity, which have since been resolved, which almost definitely impacted the number of vulnerable or frail patients undergoing treatment in the St. James's centre. All of these factors should be investigated in future studies in order to ensure inclusion of a broader range of frailty.

4.5.2 Strengths and Limitations

This first pilot geriatric oncology programme highlighted a number of unknown limitations in relation to GA for patients undergoing radiotherapy treatment. It also highlighted the feasibility of implementing GA in radiation oncology.

The results of this small heterogeneous sample of radiotherapy patients need to be interpreted with caution, however. The impact on decision making may reflect a lack of experience and familiarity with GA and how to interpret it, as well as an obvious gap in the literature as to how it affects radiotherapy patient outcomes.

Due to the nature of the pilot study, full blinding was not possible. In addition, as this study included a variety of cancer sites, it is possible that numerous confounding factors existed, limiting interpretation of results.

A further limitation of this study is the small sample size and low recruitment rate.

Primary tumour type and radiotherapy doses employed were not directly comparable by virtue of the heterogeneous nature of our sample. The general performance status of all patients was good and the majority would be considered fit by CGA.

There was an indication that participants who entered the study were relatively young in terms of the target patient group that was initially aimed for (median age 73) i.e. the majority of patients were in the "young old" category.

4.6 Conclusion

GA had no effect on radiotherapy decision making in this small sample of radiotherapy patients from a mixed patient population, the majority of whom were prostate cancer patients. The study sample included predominantly fit and relatively young patients, which undoubtedly impacted these results. There were no significant differences between the study groups in terms of baseline and followup GA results, however there was a trend towards greater dependence and increased vulnerability. There were no issues identified with regard to radiotherapy treatment compliance or toxicity. The most significant finding in the current study, was the number of previously unknown issues that were identified by GA, that clinicians may not have detected by routine assessment.

Based on these preliminary results, recommendations for future research include investigation of: 1] longitudinal changes in GA domains and whether there is evidence of decline after radiotherapy completion and 2] identification of the prognostic factors indicative of poor outcome for selected and more defined patient groups undergoing radiotherapy, incorporating previous recommendations on consideration of optimal trial design in an older patient population.

Chapter 5

5 TILDA Study 1

5.1 Introduction

This chapter presents the methodology, results and discussion of the third study undertaken as part of this thesis. The findings of the previously described Delphi study (see Chapter 3) and pilot geriatric oncology study (see Chapter 4) informed this followup study investigating the impact of a cancer diagnosis on key domains of geriatric assessment (GA), using longitudinal data from The Irish LongituDinal Study on Ageing (TILDA). The initial studies undertaken for this thesis set out to identify the important factors to assess in older adults with cancer from a theoretical and clinical context. As part of the Delphi study, panellists rated functional status (subjective and objective measures) as the most important domain in influencing oncology decisions, followed by comorbidities and cognition. Other domains i.e. nutritional status, social support, polypharmacy and psychological status, did not reach consensus in relation to overall importance. Therefore the aim of this chapter is to ascertain the prevalence of impairments in these domains in cancer survivors, versus non-cancer controls, and investigate the overall impact of a cancer diagnosis on QoL. QoL may be broadly defined as “an individual’s or group’s perceived physical and mental health over time” [454]. All GA domains will be investigated for the purpose of this study, in order to ascertain the importance of those reaching consensus, as well as those that did not. This is justified as it seeks to verify previous studies undertaken as part of this PhD.

Cancer is increasingly recognised as a chronic disease, with appropriate survivorship care needed in order to enhance the quality of life of patients with cancer. Improvements in treatment and enhanced access to oncologic treatment has improved survival in Ireland [455]. Ireland’s five year survival rate increased by 33%

between 1994 and 2012. In the UK, half of people diagnosed with cancer are now reaching 10 year survival [456]. In 2016, approximately 60% of the 16 million cancer survivors in the USA were aged 65 and over [457]. By 2040, it is expected that this will increase to about two-thirds of all cancer survivors [458].

Enhanced survivorship care will become more of an issue in the future, with recent predictions from the National Cancer Registry of Ireland estimating an approximate doubling in the number of cancer cases by 2045 [9]. Cancer is predominantly a disease of older people [459], therefore considerations of more age appropriate care in the survivorship phase are greatly needed.

The term “cancer survivor” is ill-defined at present. The US National Coalition for Cancer Survivorship (NCCS) states that an individual is a cancer survivor from the time of diagnosis, through to the remainder of his or her life [460]. The European Organisation for Research and Treatment of Cancer (EORTC) provides an alternate definition of someone who has received a cancer diagnosis, has completed their primary treatment (not including any ongoing maintenance therapy), and has no evidence of active disease [461]. For the purpose of this study, the former definition is preferred, in the absence of confirming clinical evidence of disease status.

Cancer survivors bear a greater burden of illness compared to their age-matched equivalents [462, 463]. In addition to the physical health burden, there is an increase in mental health issues and decreased QoL. There is some evidence to suggest that cancer and its management may accelerate the aging process [464], but the patient characteristics of those at greatest risk are currently unknown [465].

Comprehensive Geriatric Assessment (CGA) is defined as a “multidimensional interdisciplinary diagnostic process focussed on determining an older person’s medical, psychological and functional

capability in order to develop a coordinated and integrated plan for treatment and long term follow up" [87]. It is based on the assessment of accumulation of deficits, on CGA domains. This assessment can provide a broader overall understanding of individual characteristics that affect life expectancy, functional decline, cognition and patient's own wishes, as well as how oncologic treatment might affect them [88].

It is often abbreviated to GA in oncology, and has utility in the survivorship phase, as well as during treatment. Although there is an increased focus on the need for survivorship data, research to date has been scant, compared to that of the active treatment phase [466, 467]. Recently, patient-reported outcomes (PROs), as an adjunct to clinical data, are used in follow-up. These help us to understand the patient's trajectory through survivorship care. PROs are defined as "any report of a patient's health status, provided directly by the patient without amendment or interpretation from a clinician or others"[468] .

From a research perspective, there is little follow-up information with respect to GA measures and how the level of function impacts the everyday lives of patients after a diagnosis of cancer. The emphasis in current studies is often on CGA deficits during the treatment period, without regard for patient function at follow-up. There is an associated health policy implication for long-term CGA deficits, with a known association with healthcare utilisation in the general population [469], which is as yet, largely unknown or unexplored in the published literature for those affected by cancer.

The Institute of Medicine (USA), the American Society of Clinical Oncology (ASCO) and other institutions have specifically identified survivorship issues for older adults with cancer as a key research priority [258, 465].To inform policy, additional evidence is required about the relationship between more age appropriate research endpoints, as defined by CGA, e.g. physical function and cognitive

performance, and their impact on daily life for cancer survivors. Longitudinal studies are the perfect resource to investigate survivorship care.

TILDA, in particular, is an invaluable resource from an Irish perspective. A major advantage of TILDA is the objective information provided e.g. Mini Mental State Examination (MMSE), Timed Up and Go (TUG), grip strength, as well as self-reported symptoms, physical function, self-rated health, mental health status and QoL. This chapter focuses on the outcomes of interest, as identified in Chapter 3 (consensus and non-consensus items), and the prevalence of impairments in (older) cancer survivors, using objective and subjective measures from TILDA.

5.1.1 Study Aims

The aim of this study was to investigate to what extent community-dwelling older adults with cancer different from their non-cancer community dwelling counterparts. This thesis chapter used data from Waves 1 to 4 of TILDA, which were collected between 2009 and 2016, at approximately two-yearly intervals.

The study objectives were:

1. To compare cancer survivors to their non-cancer controls, in relation to physical, cognitive, psychological and social health and wellbeing, using data from Wave 1 of TILDA.

2. To investigate the acute and longitudinal impact of a cancer diagnosis and treatment on the overall health and wellbeing of older adults with cancer living in the community during the diagnostic/treatment phase, and the follow-up period, using the pre-diagnostic phase as a baseline measure of function.

5.2 Methodology

5.2.1 The Irish Longitudinal Study on Ageing (TILDA) Design

TILDA is a population based study of adults aged 50 and over, with the aims of (1) providing comprehensive baseline data on older people living in Ireland, (2) investigating factors influencing age-related health, (3) empowering older people to have a voice in Irish society and (4) providing the infrastructure for gerontological research. The overarching aim is to provide an evidence base which can be used to influence policy and practice, to examine biomarkers of ageing and to investigate how economic and social factors affect health and wellbeing. The three main domains of TILDA are health, economics and social function.

5.2.2 TILDA Data Collection

In order to ensure a nationally representative sample was achieved, the 'RANSAM' sampling procedure, initially developed by the Economic and Social Research Institute (ESRI) based on the Irish GeoDirectory, was used [470]. A comprehensive mapping of all residential addresses in Ireland was compiled by Ordnance Survey Ireland. Clusters were formed based on district Electoral Divisions (EDs), with 500-1180 addresses in each cluster. Of the total 3,155 clusters, 640 were stratified according to socioeconomic status, age and geographical location. Forty addresses in each of the 640 clusters were then chosen as the initial sample in Wave 1.

Invitation letters were issued to all addresses selected. Each of the selected addresses was then visited by a trained social interviewer, who ascertained eligibility of all persons aged 50 or over to participate in the survey. The response rate was 62% and 8,504 people agreed to participate in Wave 1. The major inclusion criterion for the study

was being aged 50 years or older (although spouses/partners of any age were also included), community-dwelling and cognitively capable of providing informed consent to participate. Therefore, the study excludes those resident in nursing homes and other institutions in Wave 1. These individuals were included in subsequent waves as part of follow-up. Further detail of the study design are described elsewhere [471].

5.2.3 TILDA Study Procedures

TILDA data collection consists of three main components:

(1) A structured Computer Aided Personal Interview (CAPI) with a trained professional social interviewer in the participant's home.

(2) A 'self-completion questionnaire' (SCQ) to be completed and returned to TILDA by mail. A summary of data collected via CAPI and SCQ is provided in Figure 5.1.

(3) At Waves 1 and 3, each participant was invited to undergo a health assessment, either a full health assessment at a specialised TILDA health centre, or a modified partial assessment in their own home where travel to a designated centre was not feasible, or desired.

The health assessment was carried out in either Dublin or Cork in Wave 1, and Dublin only in Wave 3, and took approximately three hours in total to complete. Participants were reimbursed for the cost of attending TILDA health centres, and the time period between waves was approximately two years for CAPI and SCQ.

From Wave 2 onwards, a proxy interview was completed by a close family member or friend if a participant was unable to complete the interview themselves, due to physical or cognitive impairment. If a

participant had passed away between waves, a family member or close friend was asked to complete an End-of-Life (EOL) interview on their behalf. The latter could also be deferred to the next wave. Only self interviews (i.e. excluding proxy and EOL interviews) were deemed eligible for inclusion in the current study, due to the largely subjective nature of most outcomes of interest.

Summary of data collected in TILDA CAPI and Self-completion Questionnaire (SCQ)

- **Demographic data**
  - Education
  - Childhood health
  - Migration history
  - Marital status and marriage history
- **Social circumstances**
  - Transfers to (and from) children
  - Transfers to (and from) parents
  - (Instrumental) activities of daily living
  - Helpers
  - Social connectedness
  - Participation in social/recreation activities
  - Relationship quality (SCQ)
- **Employment and lifelong learning**
  - Employment situation
  - Job history
  - Lifelong learning
- **Retirement and expectations**
  - Planning for retirement
  - Expectations
- **Income and assets**
  - Sources of income
  - Assets
- **Transport**
  - Transportation
  - Driving
- **Medications**
- **Health-care utilization**
- **Physical health**
  - Self-rated health
  - Limiting long-standing illness/disability
  - Sensory function
  - Cardiovascular disease
  - Non-cardiovascular chronic illness
  - Falls/fear of falling/steadiness
  - Chronic pain
  - Incontinence
  - Medical screening
- **Mental health**
  - Self-reported mental health
  - Depression
  - Life satisfaction
  - Anxiety (SCQ)
  - Worry (SCQ)
  - Loneliness (SCQ)
  - Perceived stress (SCQ)
  - Stressful life events (SCQ)
  - Quality of life (SCQ)
- **Cognitive health**
  - Self-rated memory
  - Orientation
  - Word-list learning (immediate and delayed recall)
  - Verbal fluency
  - Prospective memory
- **Behavioural health**
  - Smoking
  - Physical activity
  - Sleep
  - Alcohol (SCQ)
- **Ageing perceptions (SCQ)**

Figure 5.1 Summary of data collected in TILDA CAPI and Self-Completion Questionnaire (SCQ)

5.2.3.1.1 Wave 1

Data collection for Wave 1 on 8,504 participants took place between October 2009 and February 2011, with 85% (n=7,196) and 72% (n=6,150) completing the SCQ and health assessment, respectively. All participants completed the CAPI.

5.2.3.1.2 Wave 2

Data collection for Wave 2 commenced in February 2012 and was completed in March 2013. 7,375 (88%) participants in Wave 2 completed the CAPI, while 6,274 (85%) completed the SCQ. Wave 2 data collection consisted of the CAPI and SCQ items only, with no health assessment. However, some aspects of the health assessment were included in the CAPI assessment from Wave 2 onwards i.e. the Mini Mental State Examination (MMSE) and Timed Up and Go (TUG) test.

5.2.3.1.3 Wave 3

The third wave began in March 2014 and was completed in October 2015. In total, 6,566 (85%) participants completed the CAPI, while 81% (n=5,391) completed the health assessment. The majority of health assessments were completed in the Dublin centre (n=4,307) and 20% opted for a home assessment (n=1,057). The corresponding SCQ response rate was 85% (n=5,565).

5.2.3.1.4 Wave 4

The fourth wave took place from January to December 2016, and included 5,856 home interviews (CAPI), representing an 84% response rate. A total of 5,064 SCQs were returned, representing an 86% response rate. As for Wave 2, there was no health assessment,

but some measures e.g. TUG and grip strength, were taken in the home.

Figure 5.2 provides a summary of the data collection and timeframes in TILDA.

Figure 5.2 Summary of data collection and timeframes in TILDA

5.2.3.2 Cross-Sectional Analysis

The cross-sectional sample used data on health and well-being from participants reporting a cancer diagnosis in Wave 1, comparing them to control participants who were cancer-free. A cancer diagnosis was defined as answering 'yes' to the question: "Has a doctor ever told you that you have any of the following conditions?", with the option of "cancer or a malignant tumour". If they said yes they were asked 'In which organ or part of the body have you or have you had cancer?" with various options presented for the most common cancer types, and "other" or "don't know".

Due to the limitations of self-report, and in the absence of pathological confirmation of cancer type, all cancer diagnoses were

included. All ages were included due to the relatively small sample size (n=522) for those diagnosed with cancer.

5.2.3.1 Longitudinal Analysis

In order to ascertain the acute impact of a cancer diagnosis and treatment, and to control for time since diagnosis, a longitudinal analysis was also conducted. The longitudinal sample used data from participants reporting a new cancer diagnosis in Wave 2 or 3, comparing them to control participants who were cancer-free. Again, for this analysis, all cancer types were included.

The first wave in which the participant reported a cancer diagnosis became the 'peri-diagnosis' point (T1), the previous wave was their baseline point (T0), and the subsequent wave was their post-diagnosis point (T2). Thus Wave 1 represented the baseline for those with a new cancer diagnosis in Wave 2, with Wave 3 used for follow-up data. Wave 2 was used as baseline measures for those reporting a new cancer diagnosis in Wave 3, with Wave 4 used as the follow-up period. Therefore, three timepoints were required for data analysis.

The comparison or control group was composed of participants who did not report a cancer diagnosis in any wave. Data from Waves 1, 2 and 3 were used as T0, T1 and T2, respectively, for the control group. These were chosen as there was more information available in terms of health assessment in Waves 1 and 3, compared to Waves 2 and 4. All four waves were not used, as this might introduce a bias related to a longer follow-up time period, compared to the cancer group. For both samples, only individuals with data available in three consecutive waves for at least one variable of interest, were deemed eligible for inclusion.

Participants who had reported a cancer diagnosis at Wave 1 were excluded, as well as those who went on to report a new cancer diagnosis at Wave 4, because of the absence of baseline or post-

diagnosis data, as well as the possible influence on the control group analysis.

5.2.4 Exclusion Criteria for Longitudinal Analysis

Exclusion criteria for the longitudinal sample included individuals with:

- A diagnosis of cancer in excess of two years for the cancer group in the longitudinal sample analysis.
- Proxy interviews at any wave.
- Incomplete data for the outcomes of interest at three successive waves.
- Anyone with a previous cancer diagnosis was excluded from the control arm for Waves 1 and 4.

5.2.5 Study Measures

5.2.5.1 Sociodemographics

Age, gender and education were all collected by self-report during the CAPI. Education was categorised as primary only, secondary education or third level education and above.

Following on from the previous analyses (Chapters 3 and 4), the below domains of GA (see Table 5.1) were investigated as part of this TILDA study. Where the corresponding measure was not available, another item was chosen that represented a reasonable alternative and validated measure.

Domain	Assessment tool	Corresponding TILDA measure
Functional status	ADL IADL Falls history	ADL (CAPI) IADL (CAPI) Falls history (CAPI)
Objective physical performance	TUG	TUG (health assessment Waves 1 and 3, CAPI Waves 2 and 4)
Comorbidity	Charlson Comorbidity Index (age-adjusted)	Range of chronic conditions derived from TILDA data (CAPI)
Nutrition	MNA-SF	No comparable indicator-therefore excluded
Social support	Patient history/caregiver interview	Social connectedness score (CAPI)
Polypharmacy	Number of total medications	Polypharmacy (CAPI)
Psychological status	GDS Patient history/interview	CES-D (CAPI)
Global Cognition	MMSE	MMSE (health assessment Wave 1, CAPI Waves 2-4)

ADL, Activities of daily living; IADL, Instrumental Activities of Daily Living; TUG, Timed Up and Go test; MNA SF, Mini Nutritional Assessment Short Form; GDS, Geriatric Depression Scale; CES-D, Center for Epidemiologic Studies Depression scale; MMSE, Mini Mental State Examination; CAPI, Computer-Assisted Personal Interview

Table 5.1 List of study measures to be used in TILDA compared to Delphi study

5.2.5.1 Physical Function Measures

5.2.5.1.1 Activities of Daily Living (ADLs)

Activities of daily living (ADLs) were assessed in the CAPI by asking participants if they had difficulty performing six everyday activities, including dressing, bathing, feeding, getting in and out of bed, toileting and walking across a room [110]. A binary (yes/no) response was used for each item, with scores ranging from 0 to 6 according to

the number of ADLs with which a participant reported difficulties. A dichotomous variable was created to distinguish between participants reporting any ADL impairment (score of 1 or more) and those with no ADL impairment (score of 0).

5.2.5.1.2 Instrumental Activities of Daily Living

Instrumental activities of daily living (IADLs) were also assessed in the CAPI, by asking participants whether they had difficulty preparing a hot meal, doing household chores, shopping for groceries, making telephone calls, taking medications or managing finances [110]. A binary (yes/no) response was used, with scores ranging from 0 to 6 according to the number of IADLs with which a participant reported difficulties. A dichotomous variable was created to distinguish between participants reporting any IADL impairment (score of 1 or more) and those with no IADL impairment (score of 0).

5.2.5.1.3 Falls History

A history of falls was captured by asking respondents in the CAPI, whether they had fallen in the previous year (new participant) or since the last interview (subsequent waves), with a binary yes/no response used in all analyses.

5.2.5.2 Objective Physical Performance

5.2.5.2.1 Timed Up and Go (TUG)

The Timed Up and Go (TUG) task involves rising from a chair, walking 3 metres at the participant's normal pace, turning around, and walking back to the chair to sit down again [383]. It is a measure of walking speed, balance and coordination. The time elapsed between hearing the "Go" command to returning and sitting with the participant's back to the chair, was recorded with a stopwatch.

In TILDA health centres, a chair with armrests and seat height of 46 cm was used for the TUG tests. For home-based assessments, a similar chair height was sought (seat height 40–50 cm), but not always feasible. For the purpose of this analysis, only TUG values with a corresponding chair height between 40-50cm, if conducted in the home, were included.

TUG values were examined for the presence of extreme values, and possible coding error, and those that were deemed to appear significantly different to other physical function measures were excluded as possible errors.

5.2.5.3 Comorbidity

Comorbidity was assessed by answering 'yes' to the question: "Has a doctor ever told you that you have any of the following conditions?" i.e. lung disease, asthma, arthritis, osteoporosis, Parkinson's disease, liver disease, stroke, heart failure, diabetes and high blood pressure. For this variable, a composite measure was generated at each wave of these ten chronic conditions, which was then subcategorised as one of three categories: a) 0, b) 1, c) 2 or more. Four of these (lung disease, liver disease, heart failure and diabetes) are represented in the commonly used Charlson Comorbidity Index, however the latter could not be reproduced directly across four waves. As Charlson also includes "solid tumour, leukaemia and lymphoma", which were already included in the analysis of the cancer group, these three categories were not deemed eligible for inclusion. Other items were selected for inclusion for comparison with similar, previously published studies.

5.2.5.4 Social Support

As patient interview regarding social support was not feasible, a corresponding measure of social support status was used from

TILDA dataset. The Berkman-Syme Social Network Index [472] is a four item scale, which uses marital status, sociability (frequency of contact with children, relatives and friends), membership of church groups, and membership of voluntary organisations. Aggregated scores from each of these four items provide an indicator of social connection from most isolated (0-1), moderately isolated (2), moderately integrated (3) to most integrated (4).

5.2.5.5 Polypharmacy

In TILDA, participants were asked to provide a list of medications. Polypharmacy was defined as the regular use of five or more medicines (excluding dietary supplements) [473]. This definition was chosen instead of the list of medications as it is commonly used to estimate the risk of frailty, disability, mortality, and falls.

5.2.5.6 Psychological Status

The Center for Epidemiologic Studies Depression Scale (CES-D) was used to measure depressive symptoms across all waves. In Waves 1 and 2 the long form of the CES-D was used [474]. This is a 20 item scale, which measures various depressive symptoms, experienced during the previous week, and forms part of the CAPI assessment. A cutoff score of ≥ 16, out of a possible 60, is used to define clinically significant depressive symptoms. For the purpose of this analysis, a dichotomised variable was created, using this cutoff score, which is associated with 100% sensitivity and 88% specificity for major depression in community dwelling older adults [475].

In Waves 3 and 4, the short form of the CES-D was used. This is an 8 item scale, with a score of 9/24 recommended for case level depression. The corresponding sensitivity and specificity, using this cut-off, are 98% and 83% respectively [476]. For comparison with

the longer CES-D using in previous waves, the short form was also dichotomised.

5.2.5.7 Global Cognition

The MMSE was used to assess global cognition [397]. This is a 20 item test, commonly used in clinical practice to screen for dementia, and includes the assessment of orientation to time and place, recall, attention, calculation, language abilities and visuospatial perception. The cut point established for the MMSE defines 'normal' cognitive function and is usually set at 24, however, it's known to have floor and ceiling effects [399]. Therefore, MMSE errors i.e. the number of participant errors, subtracted from the total score of 30, were calculated and used in this analysis.

5.2.5.8 Quality of Life

QoL was measured using the CASP-19 [477] for Waves 1 and 2, and a shorter version for Waves 3 and 4 – the CASP-12. The latter version used 12 items from the original CASP-19. Thus it was possible for the purpose of this analysis to deduce a CASP-12 score for Waves 1 and 2, by scoring the 12 items used in CASP-12. The CASP-12 consists of 12 statements such as: I can do the things that I want to do, I look forward to each day, and I feel that life is full of opportunities. These statements are part of the SCQ and participants are asked to indicate how often (often, sometimes, not often, or never) they feel each statement to be true for their current lives. Each item is scored from 0 to 3 and summed to give an overall score (range 0 to 36), with higher scores indicating better QoL.

5.2.6 Statistical Analysis

This study comprises both cross-sectional and longitudinal information.

5.2.6.1 Cross-sectional Analysis

Participants from Wave 1 only were analysed to ascertain the difference between those with a cancer diagnosis and without, with respect to the outcomes of interest. Descriptive statistical data were summarised as frequencies and percentages for categorical variables, and means (standard deviations, SD) for other continuous variables. T-tests and chi-square tests were used to ascertain the difference between the cancer and control group at each timepoint, as mandated by variable type and associated tests of normality. Non-parametric equivalents were carried out for skewed data i.e. the Mann-Whitney U test for continuous data.

5.2.6.2 Longitudinal Analysis

Participants with a cancer diagnosis in Wave 2 or 3 were included in the longitudinal analysis, in order to ascertain the impact of a cancer diagnosis. Differences in function for both groups over time (longitudinal data) were assessed using generalised estimating equations (GEEs).

GEEs, developed by Liang and Zeger [478] for repeated measures research design, were used to investigate differences between the control and cancer group over successive waves of TILDA i.e. the group x time interaction. For the purpose of this analysis, those reporting a cancer diagnosis for the first time in Waves 2 and 3, were combined.

5.2.6.2.1 Generalised Estimating Equations (GEE)

The GEE methodology is based on the quasi-likelihood theory and takes into account that there are multiple valuations reported by the same participants, and unlike traditional regression methods, the assumption of independence is not required for GEE models. GEEs

were considered the most appropriate multivariate modelling technique, as unlike conventional repeated measures approaches, it is able to incorporate baseline data as well as all available data including those from participants with missing data over time. It is an especially useful analysis for clinical and epidemiological longitudinal data where within subject correlated data are relatively common. GEE modelling allows the analysis of data without transforming it and therefore produces easily interpretable and communicable results.

GEE models are partial-likelihood, rather than full-likelihood, methods. The main advantage of this is that a wide variety of outcome measures with different distributional forms may be used with ease in GEE analysis [479]. GEEs represent an extension of generalized linear models (GLMs) to allow for regression analyses of both normally and non-normally distributed dependent variables, and can be used to evaluate both categorical and continuous independent variables. The focus of GEE analysis is to provide a population-averaged, or marginal model, rather than prediction based on a given individual [479]. Therefore, for every unit increase in a covariate across the population, GEEs estimate the effect on the average population response, and it is assumed that the data are of a clustered structure i.e. there are independent clusters of dependent observations. This clustering of observations is especially applicable to the design of TILDA. GEE can also provide comparisons for unequal sample sizes [478].

Unlike a standard regression, a GEE model requires a number of specifications to be made at the analysis stage, these are detailed in Appendix 20.

5.2.6.2.2 Specification of the Working Correlation Matrix

The advantage of GEEs is that standard errors are correctly estimated, even if the correlation structure is misspecified. However,

correct specification of the correlation structure aids efficiency. While GLMs are based on the maximum likelihood theory for independent observations [480], GEE is based on quasilikelihood theory [481] with no assumption about the distribution of response variables. Therefore, the widely used method for model selection in GLM, Akaike's information criterion (AIC) [482], cannot be used in GEE. Model fit in the current study was therefore evaluated with the use of the model selection criteria originally described by Pan [483] the quasi-likelihood under the independence model criterion (QIC), an extension of the AIC method. Selecting the correct correlation structure is an important step in GEE analysis, as an inappropriate choice may lead to inefficient parameter estimation i.e. with large sampling variability. The QIC score is commonly used as a statistical basis for comparing model fit. In general, the smaller the value, the better the fit of the predictor combinations [483, 484]. Three variables (age, sex and education) were included, as well as the cancer group, because they were selected for subsequent GEE analysis. Models were selected for each variable, using the method outlined by Cui [484].

5.2.6.2.3 Sensitivity Analysis and Goodness of Fit

As the responsiveness of GEE estimates to various correlation structures differs from one application to the next, sensitivity analyses are recommended [485]. One means by which this can be done is to estimate several GEE models, each time changing the correlation specification. This was carried out for the current analysis.

5.2.6.2.4 Robust Estimation for the Standard Error

Robust standard errors (SEs), calculated using an empirical variance estimator, were also reported for the current study. The robust option specifies that the Huber/White/sandwich estimator of variance be used in place of the traditional calculation. Robust SE calculation

does not affect the working correlation matrix that is selected in the process of fitting the model. However, it changes the standard error of the coefficients. This is an appropriate safeguard against choosing the incorrect working correlation structure, as using the Huber/White/sandwich estimator will remedy this to a certain extent [485].

5.2.6.3 Application of GEE to the Current Study

To investigate the effect of a cancer diagnosis on GA domains, separate GEEs were used. This allows the estimation of differences between the cancer and control group for the GA domain of interest, including any changes over time i.e. from pre-diagnosis to post-diagnosis, and group-by-time interactions. Each GEE model included the effect of group, and the effect of time (wave from which the data was taken i.e. T0, T1 or T2). This group-by-time interaction provides an estimate of the change from baseline for the cancer group, versus the change from baseline for the control group.
Unadjusted analysis estimating change from baseline to follow-up in the cancer group was followed by an analysis with age, sex and education as control variables. Age and outcomes of interest were categorized as time varying, while gender, educational attainment and cancer status, were entered as factor variables in all analyses.

For the outcomes of interest, univariate and multivariate GEE models were specified with a distribution specific to the variable type, a link function and the relevant correlation matrix, chosen as per the method above (these are indicated with the relevant results below). Crude and adjusted Beta coefficients with 95% confidence intervals are presented for all variables. All analyses were performed using Stata version 12.1 (Stata Corporation, College Station, TX, USA).

5.2.6.4 Missing Data

There are several approaches to dealing with missing data in longitudinal data analysis, including complete data analysis, available data analysis and multiple imputation methods. Complete data analysis only includes participants who have data at all timepoints. Available data analysis includes all participants, whether they have complete data or not. The last approach is to impute missing responses. Generally GEE analysis takes the approach of available data analysis, and the assumption is that data are missing completely at random (MCAR) [486]. In the current study, complete case analysis was chosen, and therefore no missing data were imputed.

5.2.7 Sampling Weights

In addition, TILDA sampling weights were applied in order to ensure the results were nationally representative [487]. These account for differences in response rates by subgroups of the population and have been estimated by comparing demographic characteristics of TILDA study cohort (CAPI Wave 1) to the national population, as described by the 2011 census. Sociodemographics such as age, sex, educational attainment, marital status and urban/rural location were used in this calculation to ensure a nationally representative sample and reduce selection bias. Data from the 2006 and 2011 census, as well as the 2010 Quarterly National Household Survey (QNHS) were used to construct a TILDA sampling weight based on age, sex and education [488]. The 2011 census weight was used in the current analysis, as it is more recent. Variations in response rate are specific to TILDA, as demonstrated earlier, therefore sampling weights have been devised for the CAPI, SCQ and health assessment (centre or home based). Therefore, CAPI weights were applied for measures obtained in CAPI, health assessment weights for those obtained during a health assessment and SCQ weights for outcomes of interest from SCQ. It isn't feasible to apply survey

weights to GEE analysis in STATA, and using this approach already produces population averaged results, as described above. Likewise, it isn't feasible to include similar sampling weights by cancer type, as the population with cancer was too small, and relatively heterogeneous.

5.2.8 Correction for Multiple Comparisons

In instances of multiple comparisons, which increase the risk of Type I error i.e. rejecting the null hypothesis when it is true, a Benjamini-Hochberg correction [489], was applied to control the false discovery rate (FDR). This provided an adjusted $\alpha = 0.005$ i.e. values of less than or equal to 0.005 were considered significant. For further details, the calculation of the FDR (set at 0.25 for all calculations) is contained in Appendix 21. Both unadjusted p values and indicators of statistical significance following Benjamini-Hochberg adjustment are presented in tables for ease of interpretation. This correction was applied for both cross-sectional and longitudinal analyses.

5.2.9 Ethical Approval

Ethical approval for all waves of the study was obtained from the Faculty of Health Sciences Research Ethics Committee at Trinity College Dublin.

TILDA is compliant with Trinity College Dublin (TCD) policy in relation to data protection, and all relevant data protection legislation.

5.3 Results

5.3.1 Cross Sectional Analysis

5.3.1.1 Wave 1 Study Sample

The demographic characteristics of the cross-sectional (Wave 1) study sample are shown in Table 5.2. In total, there were 522 participants with cancer in Wave 1, and 7,982 without. The cancer group was marginally older ($p<0.001$), with a mean age of 65.77, in comparison to the control arm, whose mean age was 62.97. The sample included mostly females; 60.34% of the cancer group was female, compared to 55.24% of the control arm.

Characteristic	Cancer group		Control group		Difference
	n (%)	Mean (SD)	n (%)	Mean (SD)	p value
Age	522 (6.15%)		7,970 (93.85%)		
		65.77 (9.68)		62.97 (10.22)	<0.001*
Sex					0.02
Female	315 (60.34)		4,409 (55.24)		
Male	207 (39.66)		3,573 (44.76)		
Education Level					0.62
Primary	167 (31.99)		2,354 (29.49)		
Secondary	206 (39.46)		3,225 (40.40)		
Third Level	149 (28.54)		2,399 (30.06)		
Marital Status					0.13
Married	351 (67.24)		5,615 (70.35)		
Not married	171 (32.76)		2,367 (29.65)		

*indicates significance at adjusted p value following Benjamini-Hochberg correction
n=12 of the control group were missing data for age variable, and 4 for education variable

Table 5.2 Demographic characteristics of the cancer and control group at Wave 1

Marital status was similar in the cancer and control arms, with over two-thirds of both groups being married.

5.3.1.2 Disease and Treatment Characteristics Wave 1

The average time since diagnosis was 21.6 years, with a range of 0-53 years (median 20.5). With regard to cancer type, the majority of cases were breast cancer in women (n=174), followed by prostate cancer in men (n=93). Other sites, in order of prevalence, included: colon/rectum (n=68), melanoma(skin) (n=48), Non-Hodgkin's Lymphoma (n=15), bladder (n=13), lung (n=13), cervix (n=12), ovary (n=12), stomach (n=8), leukaemia (n=7), brain (n=7), oral cavity (n=7), kidney (n=6), larynx (n=5), endometrium (n=5), liver (n=5), oesophagus (n=4), thyroid (n=3), testicle (n=3), pancreas (n=1). Thirteen were classified as "other".

Surgery was the most commonly used treatment modality (n=324), followed by radiotherapy (n=225) and chemotherapy (n=173). These modalities were employed on their own, or in combination. There was not a specific category for hormone therapy, but 120 reported receiving "medication", 7 were classified as "other" and 29 did not receive any cancer-directed treatment.

Sixty-four participants received trimodality treatment of surgery, chemotherapy and radiotherapy, 113 chemotherapy combined with surgery, 115 surgery combined with radiation therapy and 116 chemo-radiation. In relation to monotherapy, 28 received chemotherapy alone for their cancer, 159 surgery alone and 77 radiation therapy alone.

5.3.1.3 GA Outcomes Wave 1

A cross-sectional comparison of the outcomes of interest may be viewed in Table 5.3. Both ADL and IADL disability were higher in the cancer arm, compared to the control group, however, this was not statistically significant.

Falls were also more common in those with a history of cancer (25.5% versus 19.4%), as well as having two or more chronic conditions (33.8% versus 26.5%). A significantly greater proportion of participants diagnosed with cancer experienced polypharmacy (29.3% versus 19.8%). Social connectedness, depression, global cognition (measured by MMSE errors) and QoL did not differ greatly between both groups.

	Cancer group % [CI]	Control group % [CI]	Difference between both groups P value
ADL Disability	11.55 [8.58,15.37]	8.21 [7.50,8.97]]	0.03
IADL Disability	9.23 [6.57,12.81]	6.88 [6.20,7.62]	0.10
TUG (sec)	9.02 [8.67,9.37]	9.02 [8.91,9.13]	0.53
History of Falls (in previous year)	25.49 [21.20,30.32]	19.38 [18.35,20.45]	0.005*
Chronic conditions (2 or more)	33.82 [28.93,39.07]	26.46 [25.32,27.63]	<0.001*
Social connectedness (Berkman-Syme Social Network Index)			0.45
Most isolated (0)	-	0.37 [0.22,0.61]	
Most isolated (1)	9.35 [6.29,13.69]	7.13 [6.37,7.97]	
Moderately isolated (2)	28.03 [23.26,33.35]	28.32 [27.04,29.63]	
Moderately integrated (3)	37.90 [32.67,43.43]	40.79 [39.44,42.16]	
Most integrated (4)	24.72 [20.52,29.45]	23.39 [22.29,24.53]	
Polypharmacy (≥5 medications)	29.32 [24.75,34.35]	19.83 [18.80,20.90]	<0.001*
Depression (CES-D)	13.63 [9.97,18.37]	12.84 [11.83,13.92]	0.71
Global cognition (number of MMSE errors)	1.87 [1.56,2.18]	1.72 [1.65,1.79]	0.36
Quality of Life (CASP-12 score)	27.25 [26.59,27.90]	27.84 [27.68,28.00]	0.08

*indicates significance at adjusted p value following Benjamini-Hochberg correction
All are adjusted for age, sex and education with TILDA weights applied

Table 5.3 Differences between the cancer and control group (Wave 1) for the outcomes of interest, with TILDA weights applied

5.3.2 Longitudinal Analysis

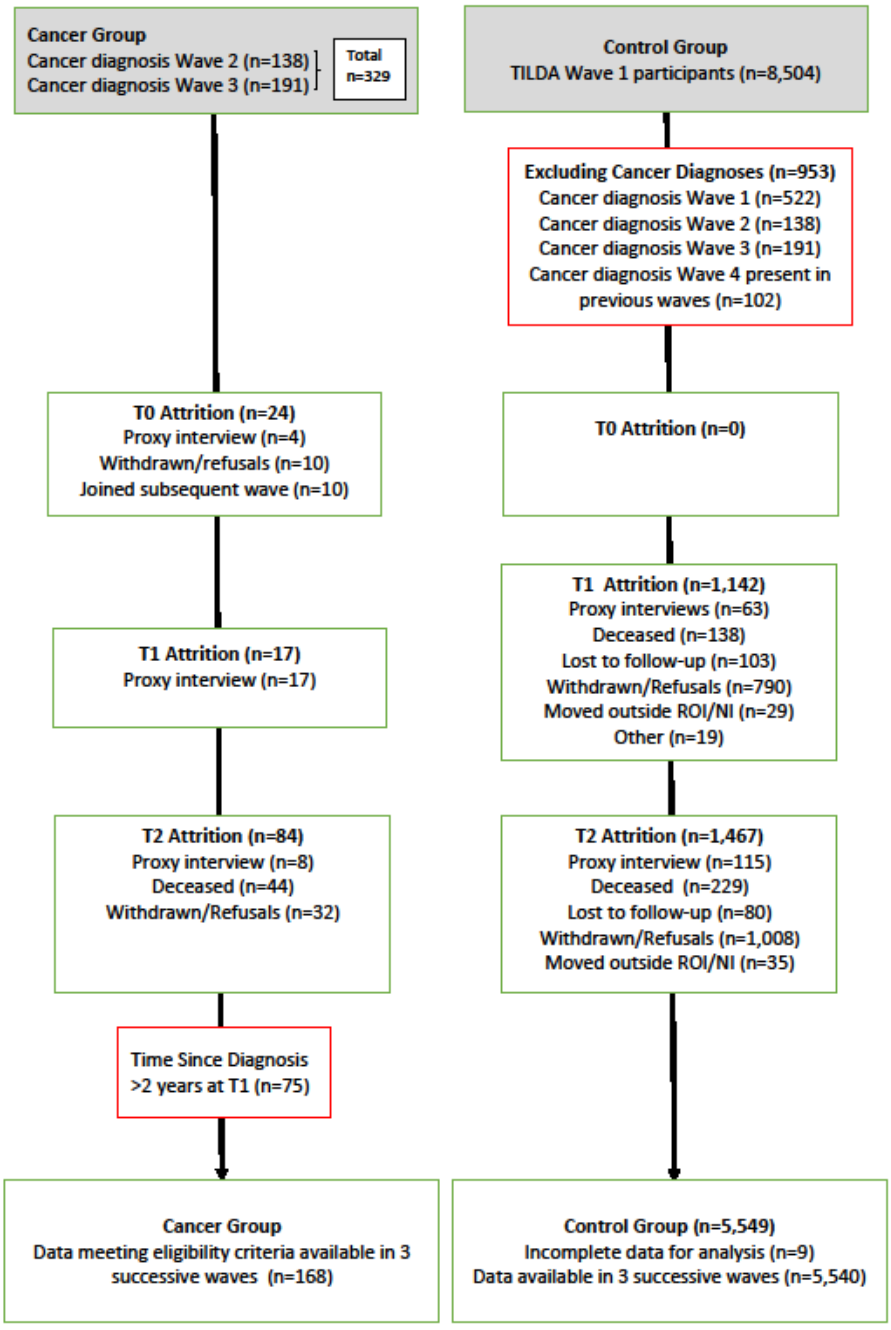
5.3.2.1 Longitudinal Study Sample

The study cohort, with sufficient follow-up time to enable analysis of at least one outcome of interest across all three timepoints was 5,708. The cancer group comprised 168 participants altogether, and the control group consisted of 5,540 individuals. The selection of study participants and attrition is shown in Figure 5.3. Some participants "skipped" a wave in data collection. Common reasons provided for non-participation included illness, personal circumstances, lack of interest or lack of time.

Anyone with a cancer diagnosis at Wave 1 (n=522) or Wave 4 (n=102) were excluded. In total, 138 new cancer cases were recorded in Wave 2 and 191 in Wave 3. Time since cancer diagnosis was calculated by subtracting a participant's age at cancer diagnosis from the participant's age at interview. In total, 64 were excluded from the cancer group based on this criterion of a recent cancer diagnosis. The final number of participants available for analysis, with data on at least one outcome of interest in three successive waves, was 81 for Wave 2 diagnoses and 87 for Wave 3 diagnoses.

For the control group, there was no attrition at T0 i.e. in Wave 1. For the cancer group, 24 participants were excluded at T0 due to exclusion criteria, proxy interview, withdrawals/refusals or joining at a subsequent wave.

At T1 and T2, participants in both groups were either excluded or did not participate due to proxy interviews, withdrawals/refusals, deaths, loss to follow-up or moving to another country (see detailed information below).



[ROI=Republic of Ireland, NI= Northern Ireland. Note: some participants had attrition in two waves]

Figure 5.3 Selection of study participants

5.3.2.2 Longitudinal Demographic Characteristics

The cancer diagnosed group was older (65.24 versus 61.75; $p<0.001$), and comprised more males than females (56% versus 44%), compared to the control group, where females represented 56% of the study sample.

There were no significant differences in terms of education level, with the majority of both groups having received secondary level education and approximately one third proceeding to third level, as shown in Table 5.4. Likewise for marital status, approximately 70% of both groups were married.

5.3.2.1 Disease and Treatment Characteristics

The majority of cancer cases consisted of prostate cancer in men (n=53), followed by breast cancer in women (n=32). Other sites, in order of prevalence, included: colon/rectum (n=20), melanoma(skin) (n=12), lung (n=7), Non-Hodgkin's Lymphoma (n=6), ovary (n=6), bladder (n=3), stomach (n=3), endometrium (n=3), larynx (n=3), leukaemia (n=2), liver (n=2), kidney (n=1), oesophagus (n=1), thyroid (n=1), testicle (n=1), Ten were classified as "other". Two didn't know. Surgery was the most commonly used treatment modality (n=99), followed by radiotherapy (n=64) and chemotherapy (n=34). These modalities were employed on their own, or in combination. Six did not receive any of the previous modalities.

Twelve participants received trimodality treatment of surgery, chemotherapy and radiotherapy, 14 chemotherapy combined with surgery, 21 surgery and radiation and 6 chemo-radiation. In relation to monotherapy, 5 received chemotherapy alone for their cancer, 51 surgery alone and 27 radiation therapy alone.

There was not a specific category for hormone therapy, but 33 reported receiving "medication".

Characteristic	Cancer group		Control group		Difference between both groups
	n (%)	Mean (SD)	n (%)	Mean (SD)	p value
	168 (2.94%)		5,540 (97.06%)		
Age		65.24 (7.99)		61.75 (9.61)	<0.001*
Sex					0.003*
Female	74 (44.05)		3,092 (55.72)		
Male	94 (55.95)		2,457 (44.28)		
Education Level					0.27
Primary	50 (29.76)		1,353 (24.39)		
Secondary	67 (39.88)		2,337 (42.12)		
Third Level	51 (30.36)		1,858 (33.49)		
Marital Status					0.58
Married	118 (70.24)		4,045 (72.90)		
Not married	50 (29.76)		1,504 (27.10)		

*indicates significance at adjusted p value following Benjamini-Hochberg correction
n=9 of the control group were missing data for age variable, and 1 for education variable

Table 5.4 Demographic characteristics of the cancer and control group at baseline (T0)

5.3.2.2 Differences Between Both Groups at Each Timepoint

A comparison between the cancer and control groups, at each timepoint, is presented in Table 5.5.

There were no significant differences between both groups in relation to the proportion with one or more ADL or IADL impairments at each timepoint.

Likewise, there were no significant differences between both groups in relation to the number of falls, or TUG time.

Compared with the comparison group, participants with cancer were more likely to report (>2 chronic conditions) comorbidity, at all time points. However, these differences were not statistically significant. The cancer group experienced more polypharmacy than the control arm, and this was statistically significant at T2 (Figure 5.4), whereby 40.39% of the cancer group experienced polypharmacy compared to 27.02% of the control arm.

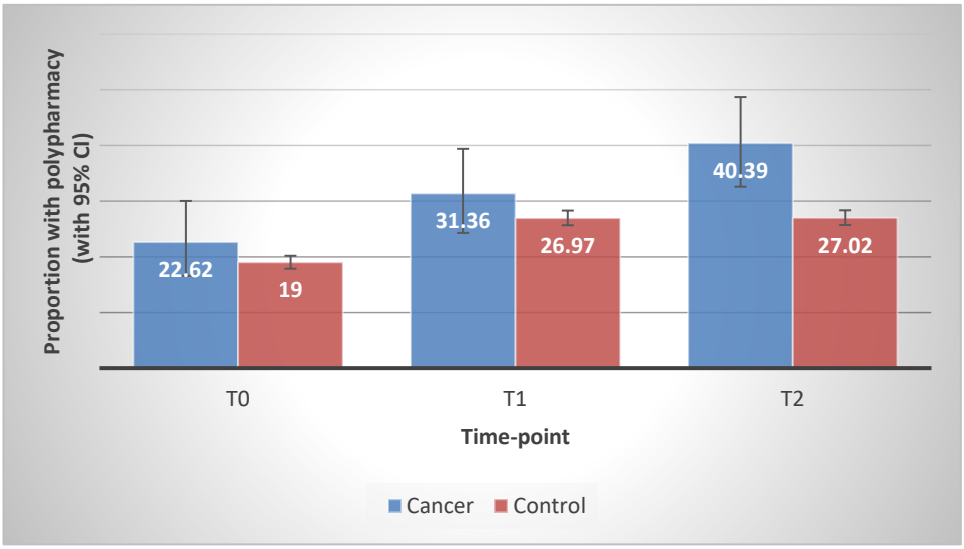


Figure 5.4 Proportion with polypharmacy at each time-point (adjusted for age, sex and education)

In relation to the social, psychological, cognitive and quality of life outcomes, there were no statistically significant differences between the two groups over time.

	T0			T1			T2		
	Cancer group	**Control group**	**P value**	**Cancer group**	**Control group**	**P value**	**Cancer group**	**Control group**	**P value**
ADL Disability	5.15 [2.40,10.70]	7.73 [6.96,857]	0.28	3.59 [1.56,8.03]	5.45 [4.77,6.22]	0.31	6.62 [3.56,11.99]	6.52 [5.77,7.35]	0.96
IADL Disability	3.13 [1.24,7.67]	6.08 [5.36,6.88]	0.14	5.76 [2.86,11.25]	6.67 [5.91,7.51]	0.68	4.30 [1.98,9.09]	7.75 [6.92,8.66]	0.12
TUG	9.02 [8.67,9.37]	9.02 [8.91,9.13]	0.53	9.83 [9.37,10.30]	10.11 [9.96,10.25]	0.15	9.88 [9.42,10.33]	10.17 [10.00,10.33]	0.29
History of Falls	18.21 [12.83,25.20]	19.40 [18.24,20.60]	0.72	17.97 [12.62,24.95]	22.04 [20.84,23.30]	0.23	18.09 [12.69,25.13]	24.59 [23.33,25.90]	0.07
Chronic conditions (2 or more)	31.79 [24.75,39.78]	25.95 [24.68,27.26]	0.10	31.36 [24.28,39.43]	29.69 [28.36,31.06]	0.08	35.35 [27.94,43.55]	32.19 [30.83,33.58]	0.44

Social connectedness			0.16			0.34			0.65
Most isolated (0)	-	0.43 [0.24,0.76]		0.60 [0.08,0.42	0.25 [0.12,0.55]		-	0.78 [0.53,1.15]	
Most isolated (1)	2.39	7.12		10.93	8.36		11.14	10.28	
Moderately isolated (2)	[0.76,7.25]	[6.28,8.06]		[6.48,17.86]	[7.44,9.38]		[6.39,18.71]	[9.32,11.33]	
Moderately integrated (3)	31.00	27.21		28.88	27.07		25.00	29.21	
Most integrated (4)	[23.14,40.14]	[25.81,28.65]		[21.62,37.42]	[25.66,28.53])		[18.33,33.10]	[27.87,30.59]	
	36.82	41.22		31.78	39.67		39.53	38.77	
	[28.82,45.62]	[39.72,42.74]		[24.62,39.92]	[38.16,41.20]		[31.88,47.74]	[37.37,40.19]	
	29.78	24.02		27.81	24.65		24.33	20.95	
	[22.77,37.90]	[22.80,25.29]		[21.31,35.40]	[23.40,25.95]		[18.18,31.76]	[19.86,22.08]	
Polypharmacy	22.62 [16.60,30.04]	19.00 [17.87,20.19]	0.27	31.36 [24.30,39.40]	26.97 [25.67,28.31]	0.24	40.39 [32.60,48.70]	27.02 [25.71,28.36]	<0.001*
Depression	8.86 [4.86,15.61]	12.95 [11.81,14.17]	0.19	10.79 [6.32,17.82]	11.44 [10.37,12.61]	0.83	10.45 [5.81,18.09]	15.06 [13.82,16.38]	0.20
Global cognition	1.50 [1.19,1.80]	1.62 [1.55,1.70]	0.42	1.35 [1.10,1.61]	1.55 [1.48,1.62]	0.14	1.43 [1.11,1.74]	1.71 [1.63,1.78]	0.09
Quality of Life	28.82 [27.99,29.65]	27.87 [27.69,28.04]	0.03	26.77 [25.85,27.69]	26.96 [26.78,27.14]	0.69	27.05 [26.10,28.01]	26.67 [26.48,26.86]	0.44

TUG, cognition and Quality of Life are presented as mean [CI]. All other (categorical) variables are presented as proportions [CI].
*indicates significance at adjusted p value following Benjamini-Hochberg correction
All are adjusted for age, sex and education with survey weights applied

Table 5.5 Differences between the cancer and control group (all ages) at each timepoint for the outcomes of interest

Across all timepoints, the level of cognitive impairment in both groups, was low, and did not differ greatly between groups.
There were no significant differences between groups in relation to quality of life, which remained relatively high and mostly stable over time. The lowest mean value (26.77) was observed in the cancer group at T1, however this was not statistically significant.

5.3.2.1 Longitudinal GA Outcomes

A GEE model was applied to accommodate the correlated data of repeated measurements (three successive waves, at two year intervals) in the same patient. All the models computed regression coefficients of the various dependent variables (GA domains) on the main predictor variable (cancer status) followed by analysis with cancer status and potential confounders (age, sex and education).
The results from the univariate and multivariate GEE analyses, investigating longitudinal differences between the cancer and control group, with details of the working correlation matrix chosen from the QIC analysis, are presented in Tables 5.6 and 5.7. A binomial variance distribution, a common logit link function and an independent working correlation were specified for most variables as those models with this covariance structure had the lowest quasi-likelihood under the independence model criterion [484]. For the TUG variable, a gaussian distribution, with an identity link function and independent working correlation was applied. For the analysis of social connectedness and number of chronic conditions, a poisson distribution with a log link function and independent working correlation were applied. The results of the QIC analysis are contained in Appendix 19.

Domain	Cancer Group ß coefficient	Robust Standard Error (SE)	95% Confidence interval Lower	Upper	P value
ADLs	-0.11	0.25	-0.61	0.38	0.66
IADLs	-0.21	0.25	-0.71	0.28	0.40
History of Falls	-0.07	0.13	-0.33	0.19	0.61
TUG	-0.02	0.15	-0.31	0.28	0.90
Number of chronic conditions	0.13	0.05	0.02	0.24	0.02
Social connectedness	0.02	0.02	-0.02	0.07	0.29
Polypharmacy	0.43	0.14	0.16	0.71	0.002*
Depression	-0.20	0.21	-0.62	0.22	0.35
Cognition	-0.07	0.09	-0.24	0.10	0.43
Quality of life	0.26	0.36	-0.45	0.96	0.48

For the above items, a matrix with a binomial variance distribution**,** a common logit link function and an independent working correlation were specified for most variables.
For the TUG variable, a gaussian distribution, with an identity link function and independent working correlation was applied.
For the analysis of social connectedness and number of chronic conditions, a poisson distribution with a log link function and independent working correlation were applied.
Interpretation: For most variables (logit link), the likelihood to report a positive/worse outcome increases exp(coefficient) times more from baseline to follow-up for the cancer group versus control group. For the TUG variable (identity link), the coefficient reflects the additional increase in TUG from baseline to follow-up for the cancer group versus control group. For social connectedness and number of chronic conditions (log link), the number increases exp(coefficient) times more from baseline to follow-up for the cancer group versus control. A more technical description of the logit and log coefficients is provided in the Appendix 20.
*indicates significance at adjusted p value following Benjamini-Hochberg correction

Table 5.6 Results from the unadjusted GEE regression analyses

The likelihood to report polypharmacy at follow-up compared to baseline increased more for those with a cancer diagnosis compared to the control group in univariate analysis. Cancer patients showed a 1.5 (95% CI 1.2-2, p=0.002) times increase in odds ratio follow-up vs baseline compared to the control group. However, this effect diminished and became non-significant in multivariate analysis. This means that, although in this study cancer patients as a whole show a difference, this is not explained by their cancer diagnosis but by an effect of covariates associated with cancer diagnosis. Cancer patients were not significantly different in their likelihood to report polypharmacy from control subjects with the same covariate profile.

When adjusting for covariates, TUG changes on average 0.63 seconds less from baseline to follow-up for cancer patients compared to the control group (95%CI -0.92--0.28, p<0.001). This means that cancer patients have a smaller TUG change from baseline compared to control subjects with the same covariate profile. This effect was not evident in univariate analysis, meaning that the small true effect of a cancer diagnosis is cancelled out by an opposite effect of covariates associated with a cancer diagnosis on TUG change from baseline.

For other variables of interest, the group-by-time interaction was not significant (see Tables 5.6 and 5.7).

Domain	ß coefficient	Robust Standard Error (SE)	95% Confidence interval Lower	Upper	P value
ADLs					
Cancer diagnosis	-0.24	0.25	-0.74	0.26	0.35
Age	0.05	0.004	0.04	0.05	<0.001*
Sex(male reference)	0.02	0.08	-0.15	0.19	0.82
Education (primary level reference)					
Secondary	-0.23	0.099	-0.42	-0.04	0.02
Third level	-0.51	0.11	-0.73	-0.29	<0.001*
IADLs					
Cancer diagnosis	-0.29	0.26	-0.79	0.21	0.26
Age	0.06	0.005	0.05	0.07	<0.001*
Sex(male reference)	0.64	0.09	0.46	0.82	<0.001*
Education (primary level reference)					
Secondary	-0.40	0.10	-0.60	-0.20	<0.001*
Third level	-0.59	0.11	-0.82	-0.37	<0.001*
History of Falls					
Cancer diagnosis	-0.12	0.13	-0.38	0.14	0.38
Age	0.03	0.002	0.02	0.03	<0.001*
Sex(male reference)	0.33	0.05	0.24	0.42	<0.001*
Education (primary level reference)					
Secondary	0.21	0.06	-0.09	0.14	0.72
Third level	0.11	0.06	-0.01	0.23	0.08
TUG					
Cancer diagnosis	-0.63	0.14	-0.92	-0.35	<0.001*
Age	0.15	0.006	0.14	0.16	<0.001*
Sex(male reference)	0.26	0.07	0.13	0.39	<0.001*
Education (primary level reference)					
Secondary	-0.54	0.11	-0.74	-0.33	<0.001*
Third level	-0.82	0.11	-1.03	-0.61	<0.001*
Chronic conditions					
Cancer diagnosis	0.08	0.05	-0.03	0.18	0.14
Age	0.03	0.001	0.02	0.03	<0.001*
Sex(male reference)	0.24	0.02	0.20	0.28	<0.001*
Education (primary level reference)					
Secondary	-0.11	0.02	-0.15	-0.06	<0.00
Third level	-0.16	0.03	-0.21	-0.11	<0.001*
Social connectedness					
Cancer diagnosis	0.02	0.22	-0.02	0.07	0.27
Age	0.001	0.0004	-0.003	0.002	0.009
Sex(male reference)	-0.008	0.008	-0.02	0.007	0.29
Education (primary level reference)					
Secondary	0.08	0.01	0.06	0.10	<0.001*
Third level	0.11	0.01	0.09	0.13	<0.001*
Polypharmacy					
Cancer diagnosis	0.25	0.15	-0.03	0.54	0.09
Age	0.07	0.003	0.07	0.08	<0.001*
Sex(male reference)	0.17	0.06	0.06	0.28	0.003*
Education (primary level reference)					
Secondary	-0.33	0.07	-0.47	-0.19	<0.001*
Third level	-0.49	0.07	-0.64	-0.34	<0.001*

Domain	ß coefficient	Robust Standard Error (SE)	95% Confidence interval Lower	Upper	P value
Depression					
Cancer diagnosis	-0.14	0.22	-0.56	0.28	0.52
Age	-0.02	0.004	-0.03	-0.01	<0.001*
Sex(male reference)	0.38	0.07	0.23	0.52	<0.001*
Education (primary level reference)					
Secondary	-0.41	0.09	-0.58	-0.25	<0.001*
Third level	-0.66	0.10	-0.85	-0.47	<0.001*
Cognition					
Cancer diagnosis	-0.19	0.08	-0.36	-0.03	0.02
Age	0.03	0.002	0.03	0.03	<0.001*
Sex(male reference)	-0.10	0.03	-0.15	0.05	<0.001*
Education (primary level reference)					
Secondary	-0.52	0.03	-0.58	-0.45	<0.001*
Third level	-0.99	0.04	-1.06	-0.92	<0.001*
Quality of life					
Cancer diagnosis	0.40	0.36	-0.31	1.10	0.27
Age	0.002	0.007	-0.01	0.01	0.81
Sex(male reference)	0.19	0.13	-0.06	0.45	0.14
Education (primary level reference)					
Secondary	1.15	0.18	0.80	1.50	<0.001*
Third level	1.93	0.18	1.57	2.28	<0.001*

For the above items, a matrix with a binomial variance distribution, a common logit link function and an independent working correlation were specified for most variables.
For the TUG variable, a gaussian distribution, with an identity link function and independent working correlation was applied.
For the analysis of social connectedness and number of chronic conditions, a poisson distribution with a log link function and independent working correlation were applied.
Interpretation: For most variables (logit link), the likelihood to report a positive/worse outcome increases exp(coefficient) times more from baseline to follow-up for the listed level versus reference level (of for a one unit increase in age). For the TUG variable (identity link), the coefficient reflects the additional increase in TUG from baseline to follow-up for the listed level versus reference level (of for a one unit increase in age). For social connectedness and number of chronic conditions (log link), the number increases exp(coefficient) times more from baseline to follow-up for the listed level versus reference level (of for a one unit increase in age). A more technical description of the logit and log coefficients is provided in Appendix 20.
*indicates significance at adjusted p value following Benjamini-Hochberg correction

Table 5.7 Results from the adjusted GEE regression analyses

5.4 Discussion

These data elucidate the burden of a cancer diagnosis and treatment among Irish cancer survivors, in relation to the accumulation of deficits, as measured by CGA, and to our knowledge is the first comprehensive analysis of community dwelling adults with cancer in Ireland to date. A cross-sectional analysis of Wave 1 participants demonstrated that falls were more common in those with a history of cancer, as well as multimorbidity. In addition, a significantly greater proportion of participants diagnosed with cancer reported polypharmacy. This TILDA analysis evaluated three distinct timepoints: before diagnosis (T0), during the peri-diagnostic period (T1) and post-diagnosis (T2), with two year intervals between each one. The cancer group experienced more polypharmacy than the control arm at T0, T1 and T2, and this was statistically significant at T2. A longitudinal analysis demonstrated that those with a cancer diagnosis were more likely to report polypharmacy, compared to those with no diagnosis of cancer. However, this effect was not significant when controlling for confounders (age, sex and education) in multivariate analysis. The longitudinal analysis only included those diagnosed with cancer in the previous two years, and therefore serves to highlight more clearly the impact of a cancer diagnosis and treatment in more controlled conditions, compared to the Wave 1 cross-sectional analysis, which included various intervals since a diagnosis of cancer was made.

Both the cross-sectional and longitudinal analyses highlighted an increased prevalence of polypharmacy. In recent times, both the incidence and prevalence of polypharmacy has been increasing steadily in both the general population [490], and especially in those diagnosed with cancer [491]. While this study looked at the number of medications i.e. 5 or more, in categorising polypharmacy, some

would argue that polypharmacy is “the administration of one medication or more that is not clinically indicated” [492]. Polypharmacy is known to increase with age [491]. It may be completely necessary to control comorbid conditions, however it also increases the risk of adverse drug reactions that are often predictable and preventable [493, 494]. Taking five or more medications is viewed as a reasonable cut-point, however, as it’s been demonstrated to be associated with falls, disability and frailty in both a geriatric medicine and geriatric oncology population [473, 495]. Turner et al, in a study of 385 patients with cancer, found a fourfold increased risk of frailty (measured by Fried criteria) in older (>70 years) adults, who reported polypharmacy, defined as five or more medications [491]. Therefore, polypharmacy should be assessed in order to ensure the appropriateness of all prescribed medications [140]. One of the barriers in the management of polypharmacy and potential deprescribing interventions, are that oncologists may feel they lack the expertise to evaluate polypharmacy [496], and close liaison with disease specialists, pharmacists and geriatricians is vital in order to limit the harms that polypharmacy may cause for someone with a diagnosis of cancer.

A diagnosis of cancer was also associated with a faster longitudinal mean TUG time, equating to a marginal reduction of 0.63 seconds in TUG time for those diagnosed with cancer. A recent systematic review has found that poorer TUG performance is associated with lower overall survival from cancer, as well as treatment related complications [497]. TUG has also been established as a good surrogate marker for frailty in older adults [498].

The results from TILDA may be explained by the selection of participants for longitudinal analysis, whereby attrition may have resulted in frailer individuals being excluded from the analysis. Or it could also be related to the age profile of participants, which is slightly younger. However, the small difference observed in the current

analysis is not considered to be clinically meaningful, as the mean Minimum Clinically Important Difference (MCID) established in the published literature is 3.4 seconds [499]. The numbers completing this assessment were also lower, which may exclude those who were not fit to travel to the health centre, or who declined a home assessment due to an inability to complete the assessment. However, lack of uptake for health assessment was not only linked to ability. Other studies of patients with cancer report significant associations between TUG and such endpoints as survival, treatment-related complications and functional decline [497].

Polypharmacy and multimorbidity are inherently linked. Multimorbidity, as defined in the current study, is the co-occurrence of two or more chronic conditions in the same person [500].The prevalence of multimorbidity in the general population is estimated to range from 55% to 98%, according to a 2011 systematic review in those aged 65 years and older [501]. A lower prevalence was found in the current study, possibly due to a slightly younger cohort. However, the prevalence was increased in cancer survivors, who are known to bear a greater burden of illness compared to their peers [462, 463]. This is significant in terms of treatment decisions, as patients with cancer and significant comorbidity are known to have poorer overall survival [26, 502]. They also have greater needs in relation to healthcare, and there may also be a link between multimorbidity and (chemotherapy) treatment toxicity [503], as well as treatment incompletion [504]. It is thought that over half of older adults with cancer have at least one comorbid condition that may impact their oncologic treatment [505]. The evidence base in oncology treatment is particularly poor for those with multimorbidity due to their traditional exclusion from clinical trials [212]. This has increasingly been recognised as a major issue in oncology, and will

become even more significant in the coming decades, unless clinical trial exclusion criteria are changed.

Some of the potential harms of multimorbidity, and polypharmacy in particular, include a substantial risk of falling, functional and cognitive decline, increased hospitalisations, healthcare utilisation and mortality [496]. Results from the cross-sectional analysis have demonstrated a greater prevalence of falls in older adults with cancer. Other adverse reactions from polypharmacy, in patients with cancer, include neutropenia, diarrhoea or constipation, nausea and vomiting, fatigue, alopecia, myelosuppression, skin irritation, anorexia and mucositis [506]. These avoidable consequences of medical management can negatively impact a patient's QoL. Assessment of falls risk is important, especially in those over the age of 65 in particular, as one in three will experience a fall [121, 122]. A comprehensive assessment, such as that advocated by the National Institute for Health and Clinical Excellence (NICE) guidelines [123] and the British and American Geriatrics Societies [114], should be carried out in order to manage precipitating factors, such as polypharmacy, poor vision, inadequacy of the home environment etc. Certain types of concurrent chemotherapy, such as taxols, can exacerbate risk factors, due to the onset of peripheral neuropathy. Androgen deprivation therapy (ADT) can also increase falls risk, due to its negative impact on muscle mass in patients with prostate cancer [124]. Combined with the side-effects of treatment, e.g. fatigue, management of falls risk and assessment of polypharmacy are important during treatment and in follow-up care.

To date, there have been few studies on the prevalence of polypharmacy and multimorbidity in the Irish oncology population. This is something that will become even more pressing in the coming years, due to the increasingly older population presenting for cancer treatment. Lavan et al [507], in a study of 350 patients with cancer,

aged 70 years and older, in an Irish oncology centre, found that approximately 20% of hospital admissions in oncology were related to adverse drug reactions. The majority of these were found to be predictable, and more than 60% were preventable. These adverse outcomes were found to be related to systemic anticancer therapies (SACTs) in about half of cases identified, and to non-cancer medications in 45% of cases.

Previous studies have reported cross-sectional results which are difficult to interpret as they often include a very heterogeneous group in terms of the time of diagnosis and cancer type. In relation to other aspects of physical and mental wellbeing, there is evidence of resilience among Irish community dwelling cancer survivors, who mostly appear to be doing as well as their peers two years after diagnosis and treatment. This is similar to the findings of other studies [508, 509]. However, it should be highlighted that this is a select sample, comprised of those who survive at least two years after their diagnosis and treatment, and who are relatively young compared to the typical age profile of many cancer types, with what could be considered as mostly favourable prognosis cancers.

These results contrast with a similar analysis from Waves 1-6 of the English Longitudinal Study of Ageing (ELSA), that found poorer health outcomes in a cancer cohort (n=444;mean age 67) with regard to self-rated health, QoL and life satisfaction, as well as a higher incidence of depression, mobility problems and limitations with ADLs [510]. All of the studied outcomes became gradually worse over time, with the exception of depression, although the group x time interaction was insignificant for most, similar to our findings from the GEE analysis. Comorbidity was also higher in the cancer group in the ELSA study (cross-sectional analysis), however the prevalence of polypharmacy, TUG and falls were not analysed. In contrast, the ELSA cohort seemed to report a lower baseline level in many domains, and a recent ELSA publication has found declines in health

from four to six years preceding a cancer diagnosis [511]. It should be noted however, that the study cohort used in the latter ELSA analysis was older, with a mean age of 71.4, versus 65.7 in TILDA study.

A recent systematic review of ADL disability estimates that approximately a third of adults with cancer experience difficulties with ADLs, which is higher than the current study, but includes (but not limited to) studies of older patients and increased follow-up times [512]. This is something that may be a more significant concern for older adults with cancer, but this study was unable to undertake this analysis. Similarly for IADL impairment, larger numbers and longer follow-up may be required to ascertain the long term impact of treatment, the prevalence of which is reported to be 50% in some studies [512, 513]. Disability relating to housework is the most prevalent IADL reported in a review of patients with cancer followed by disability related to shopping and transportation. The latter is an important consideration for travel to care during the treatment phase and for follow-up appointments in oncology.

A French study (n=486), which used cancer registry data on older adults with cancer from three prospective cohort studies, found a number of factors to be related to ADL and IADL impairments [514]. These included the oldest old (>85 years) (OR = 18.3; 95% CI = 3.7–90.9), those with cognitive impairment or dementia at the pre-diagnosis visit (OR = 8.3; 95% CI = 2.6–27.0) and participants with advanced stage at diagnosis (OR = 4.7; 95% CI = 1.3–16.7). In the current study, ADL impairments were slightly higher at baseline in those diagnosed with cancer, which is unusual, however the difference was quite small. As most of these factors were notably absent in the longitudinal analysis of TILDA, it may be assumed that the proportion with ADL and IADL impairments may increase in future years as the population ages.

Physical function is usually assessed in oncology using either the Eastern Cooperative Oncology Group (ECOG) or Karnofsky Performance Status [106, 515] scales. This is relatively one dimensional when you consider such things as gait speed, balance, grip strength and lower extremity strength, as these are more predictive of patient outcomes [107]. Grip strength, which is included in the next chapter as part of the phenotype of frailty analysis, is associated with sarcopenia [516, 517]. Sarcopenia refers to decreased muscle mass and quality, the latter also associated with poorer outcomes in patients with cancer [518-520].

There were no significant differences between both groups in relation to QoL, which remained relatively high and mostly stable over time. This is in contrast to the ELSA study which reported significant declines in QoL over time, and a low QoL at baseline [510]. Some studies suggest, especially in older adults, that a large proportion of those who experience serious illnesses, such as cancer, actually report enhanced QoL and other positive life changes following their diagnosis and treatment [336]. This phenomenon has been variously reported as personal or posttraumatic growth [337, 338], adaptation [339], positive illusions [340], thriving [341], and benefit finding [342]. As an example, Goineau et al [196], in a study of 100 patients with localised prostate cancer, aged 75 and older, attending for radiotherapy, found IADL impairments at baseline in approximately half of all patients enrolled in the study, as well as ADL impairments in 16% of patients. One fifth of patients presented with cognitive decline (defined as MMSE<27), 31% with depressive symptoms and more than two-thirds with significant co-morbidities, especially cardiovascular comorbidities, which may obviously affect ADT tolerance. The most important finding was that despite numerous impaired geriatric domains, more than 70% of older patients undergoing radiotherapy for prostate cancer maintained their overall

QoL immediately after completion of radiotherapy, consistent with the findings of the current study.

Many oncology healthcare professionals feel ill-equipped to deal with the projected demographic changes in years to come. Despite the fact that the majority of patients with cancer are older, most oncologists receive little training in the specialised care of older patients [41]. When an older patient presents to oncology, they are often segregated from their co-existing geriatric care, as the oncology and geriatric medicine disciplines often work in isolation, with little collaboration about patients. This seems unusual, given the known importance of the multidisciplinary team in oncology, seen as the cornerstone of patient management. The geriatrician is notably absent from such meetings in many institutions, something that should change in order to provide more holistic care to the older person. The geriatrician's involvement is essential in identifying and potentially reversing frailty, as well as providing recommendations on overall care. The results of this study suggest the importance of multimorbidity, polypharmacy and associated falls risk as important considerations for patients with cancer. These need to be assessed and managed effectively in order to avoid functional decline and other adverse outcomes, such as mortality and hospitalisation, in the general population. Future studies should investigate these factors in specific cancer types, including older ages and those with varying degrees of frailty.

5.4.1 Strengths and Limitations

This study has several strengths. A large nationally representative population with objective health measures was used to compare community dwelling adults with cancer, to those without. Both a cross-sectional and longitudinal analysis were conducted, and a range of GA measures compared. This makes our findings more

robust, and, to our knowledge, is the first such analysis of this group in community dwelling adults with cancer in Ireland.

There are some limitations to this study. TILDA excludes nursing home residents and those resident in other institutions in Wave 1. This potentially excludes some of the most vulnerable and frail members of the population from the cross-sectional analysis, many of whom may have become dependent due to a cancer diagnosis. In addition, those who completed the SCQ and health assessment were likely to be in better health than those who did not, and were thus excluded from the analysis. Analysis of complete cases means that those with poorer outcomes were more likely to be excluded. This is a potential source of selection bias in the study.

There is not a widely accepted or adopted definition of an “older” person. The United Nations generally uses 60+ years to refer to the older population with most developed world countries accepting the age of 65+ years [6]. The 65 years threshold is used in many scientific publications, including clinical trials. Unfortunately, the numbers were considered too small for any meaningful analysis of an older population with cancer in the current TILDA analysis.

Another limitation to using longitudinal data is attrition. Attrition may bias results as the oldest and most unwell participants are the least likely to be included in follow-up, leading to an unrepresentative sample. This is especially relevant for those diagnosed with cancer, and was evident in the results of the current study, as longitudinal results demonstrated fewer health concerns, compared to the cross-sectional data.

The cancer sample consisted of heterogeneous cancer types, and it was not possible to assess cancer stage for these, or current disease

status. The risk profile associated with some of these diagnoses is likely to be substantially different from that of a good prognosis cancer. In addition, the majority of those diagnosed with cancer were female, which reflects the TILDA sample as a whole, whereby female participants have outnumbered males in every wave [487].
In addition, the number of patients with some cancer subtypes was small, and therefore, a subgroup analysis was not feasible as it would be underpowered to detect statistically significant associations. Site specific studies provide more insight into how the unique disease and treatment characteristics influence health and wellbeing.
Also, in TILDA, skin cancer is classified as “malignant melanoma (skin cancer)”. This is a relatively broad classification that is usually separated in studies of cancer into “melanoma” and “non-melanoma skin cancer (NMSC)” as the latter is associated with a much more favourable diagnosis. Previous studies have excluded NMSC on the basis that it is so treatable, however it wasn’t possible to do so in the current analysis.

It was not possible to reproduce a nutritional outcome in TILDA [471], as the food frequency variable was only included from Wave 3.

Disclosure of a cancer diagnosis, and of other comorbid conditions, was self-reported and it was not possible to verify the accuracy of these reports.

5.5 Conclusion

The current TILDA longitudinal analyses spanning pre- and post-cancer diagnosis, suggest that cancer survivors bear a greater burden of multimorbidity, polypharmacy and falls, compared to their counterparts without a cancer diagnosis. This has implications for oncology clinical practice, as these deficits are known to be

associated with greater healthcare utilisation and adverse outcomes for older adults. Non-significant effects can never be interpreted as proof of absence of effect. It is possible that in reality there is an effect, but because of insufficient power (low sample size, large variation) it was not possible to demonstrate this in the current study. These findings warrant further investigation, incorporating these domains at a minimum, not only during the treatment phase, but in follow-up care in order to ascertain their true effect in a more clinically relevant patient population, incorporating all degrees of fitness and frailty. Future studies should also include an older population (>75 years), as the current study included a relatively young population, with fewer health concerns, as nursing home residents were excluded in Wave 1. Longer follow-up periods are also required in order to clarify the survivorship concerns of older adults with cancer. This is something that will become even more pressing in the coming years as the population ages. Future studies, with longer follow-up may enhance our understanding of the more long term impact on patient function.

Chapter 6

6 TILDA Study 2

6.1 Introduction

The ageing demographic shift in Ireland and most countries internationally will result in a corresponding increase in the incidence of chronic conditions, such as cancer, as well as frailty [63]. In the medical gerontology literature, frailty is a consequence of age-related decline in many physiological systems, resulting in a reduced reserve capacity and increased vulnerability to stressors [45]. This vulnerability is related to an inability to maintain homeostasis in the face of a physiological threat e.g. cancer and its treatment [521]. Frailty leads to an increased risk of adverse events, such as falls, disability and death [63, 522, 523]. Some of the clinical manifestations of frailty include fatigue, unexplained weight loss, infections, falls, delirium and fluctuating disability [45]. The development of frailty represents a complex interplay between genetic and environmental factors, leading to an accumulation of damage in several physiological systems, as seen in Figure 6.1. Faced with a stressful life event, frailty may manifest via the clinical manifestations mentioned before, and lead to dependency, hospitalisation and a requirement for long term care [63, 524, 525].

There are a number of frailty models in existence, but the two most common operationalisations are the phenotypic and cumulative deficit models. The first of these was established by Fried and colleagues, in the Cardiovascular Health Study (CHS) study, which studied over 5,000 community dwelling men and women over the age of 65. Using this data, a phenotype of frailty was operationalized from five different components i.e. unintended weight loss, weak grip strength, exhaustion, low physical activity and slow walking speed

[63]. People were categorized as robust if no deficits were identified, prefrail if only 1-2 deficits were present, and as frail if there were 3 or more.

Using this definition, approximately 7% of the CHS study population were considered frail, 47% pre-frail and 46% robust. The risk of adverse outcomes and mortality was much greater for those considered frail. The phenotypic model has been criticized for lacking important information, such as cognition, and as a research study, was not designed to validate a frailty measure.

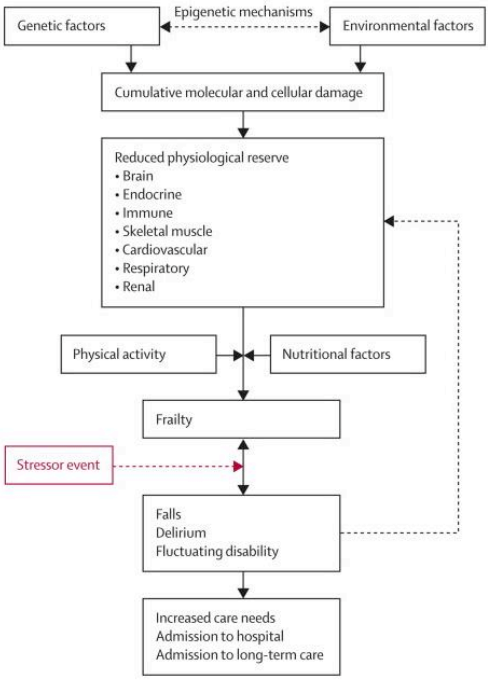


Figure 6.1 Schematic representation of the pathophysiology of frailty [45]

It is thought that the cumulative deficit model, such as the Frailty Index (FI) developed as part of the Canadian Study of Health and Aging (CSHA) has greater clinical utility [64]. The FI was based on the results of a five year prospective cohort study of over 10,000 people over the age of 65. In the original FI, 92 individual deficits from a wide range of domains, were identified to collectively define frailty [66] – "the more individuals have wrong with them, the more likely they are to be frail" [526]. With a greater number of deficits required to define frailty, the FI has more in-built redundancy than the phenotypic model i.e. no individual deficit carries a great threat of adverse outcomes. However, with an increasing accumulation of deficits, there is an enhanced risk, which allows a gradual "grading" of frailty, rather than just a present/absent type classification, which is thought to be more clinically meaningful. A value of 0.67 has been identified as a FI score that indicates a high likelihood of dying [527], known as the "tipping point" in frailty research [528]. Subsequent work has reduced the number of FI items required to predict frailty from 92 to 30 or so, with no corresponding loss of validity [67, 68].

Other operational definitions of frailty lie somewhere between the above two approaches i.e. the phenotype and FI approaches [529]. In addition, different scales report different estimates of frailty prevalence [529]. The FI approach provides a higher estimate of pre-frailty and frailty compared to the CHS classification. However, the European Male Aging Study [530] and others [531] have demonstrated that prefrail and frail status on the CHS, FI and Morley FRAIL scale are all predictive of mortality.

An example of this is the FRAIL scale [532], which is a five item questionnaire, used in diverse older populations and known to be predictive of disability and mortality [533, 534]. It combines the following items: fatigue, resistance, ambulation, illness and loss of

weight (FRAIL). Scores range from 0 to 5, with 0 representing robustness, 1-2 prefrail and 3-5 frailty, similar to the Fried categorisation. The advantages of the FRAIL scale are that it only includes interview questions and is therefore very feasible in clinical practice [535].

There is a distinction between frailty, disability and multimorbidity, as shown in the CHS by Fried et al [63]. Frailty and comorbidity were present in approximately 46% of the population, while frailty and disability (restriction in at least one activity of daily living) were present in approximately 6% of the population. All three were present in about a fifth of the population. However, frailty alone, without disability or comorbidity, was identified in 27% of the study group. Estimates from more recent studies, suggest that the overlap may even greater than previously estimated [536].

Frailty is a dynamic process, and is potentially reversible, therefore early identification is very important [537, 538]. The gold standard for the assessment of frailty and follow-up care is Comprehensive Geriatric Assessment (CGA). CGA has been extensively described in the previous chapters. However, CGA is noted to be time consuming and requires specialist training, and therefore frailty screening is often a more feasible option, using either the phenotype model and frailty indices.

There is a known relationship between cancer and aging. Age is the number one risk factor for the development of cancer [539, 540] and current research efforts are focussing on quantifying acceleration of aging due to cancer and its treatment [50-52]. Accumulation of molecular and cellular damage and dysregulation is a common feature of both aging and cancer [51-54]. Long-term follow-up of paediatric and young adult cancer survivors have shown earlier onset

of age-related conditions, such as multimorbidity, frailty and functional decline [55-57]. The prevalence of pre-frailty and frailty were demonstrated to be similar between younger cancer survivors and adults aged 65 years and older without a diagnosis of cancer [57, 58].

The consideration of an older adults' frailty status should be fundamental to their cancer care, as it is in other aspects of medicine [541]. If a frail 70-year old is diagnosed with lung cancer, for example, they should not be considered as a surgical candidate, or for concurrent chemotherapy, and will likely benefit more from a less aggressive approach. On the other hand, if a fit 80 year old is in the same situation, they should not be denied the standard of care based on age alone. Frailty assessment, as part of routine work-up of older patients adds valuable information, not appreciated through the use of a standard assessment [188]. In addition, patient follow-up should aim to understand the development of frailty over time, after a cancer diagnosis and treatment.

Frailty prevalence rates vary by country and setting, with wide variation seen in published studies [542-544], ranging from 2% to 59%. Two large longitudinal studies, the Survey of Health and Retirement in Europe (SHARE) and the Study on Global AGEing and Adult Health (SAGE), reported the lowest mean FI scores were found in Ireland, the Netherlands and Greece, with the highest levels in Spain, Italy and Poland [545]. One of the lowest rates (2%) has previously been reported in TILDA [542], using the Fried phenotype approach. In another analysis, using the FI approach, for all (n=3,069) participants (with data at four waves), the prevalence of frailty was 12.7% in Wave 1 and pre-frailty was estimated to be 30.9% [546].

Frailty is more common with age, female sex and is also associated with lower educational attainment and socioeconomic deprivation [545]. Most studies on frailty prevalence to date have focused on community dwelling populations, with limited analysis of those living with and beyond cancer in the community.

The application of the commonly used models of frailty in patients with cancer is poorly understood, and much research effort has been invested in developing new frailty indices, without fully investigating the usefulness of existing models from the medical gerontology literature. There is no “gold standard” used to measure frailty at present, and there is limited information on the prevalence of frailty in community dwelling people with cancer.

A recent National Cancer Institute (NCI) think thank was convened in order to address the current lack of an evidence base for aging-related sequelae of cancer treatment [50]. Recommendations were put forward on measures to consider when researching aging-related consequences of cancer and its management, including Fried frailty phenotype, deficit accumulation indices/frailty indices and CGA. In particular, the need to leverage existing resources such as longitudinal studies, to describe aging trajectories over time, was highlighted as a priority. This has also been recommended in previous studies [547-549]. Healthcare providers should be aware of the long term needs of cancer survivors to ensure the delivery of appropriate care [550].

While the previous chapter looked at some aspects of CGA, the current chapter will look at the application of frailty models in more detail, with the aim of quantifying aging trajectories over time in Irish community dwelling cancer survivors.

6.1.1 Study Aims

The aim of the present study was to investigate to what extent older adults with cancer in the community differ from their non-cancer community dwelling counterparts in relation to frailty.

The study objectives were to:

1. Define frailty using three commonly used indices, from TILDA data, and compare the prevalence of each type.
2. Describe the prevalence of frailty in community dwelling people with cancer and compare it to those without a cancer diagnosis.
3. Investigate the impact of a cancer diagnosis on the longitudinal development of frailty.

6.2 Methodology

6.2.1 The Irish Longitudinal Study on Ageing (TILDA) Design

TILDA is a population based study of adults aged 50 and over, with the aims of (1) providing comprehensive baseline data on older people living in Ireland, (2) investigating factors influencing age-related health, (3) empowering older people to have a voice in Irish society and (4) providing the infrastructure for gerontological research. The overarching aim is to provide an evidence base which can be used to influence policy and practice, to examine biomarkers of ageing and to investigate how economic and social factors affect

health and wellbeing. The three main domains of TILDA are health, economics and social function.

6.2.2 TILDA Data Collection and Study Procedures

Details of TILDA data collection methods and study procedures are detailed in Chapter 5. In brief, participants completed a Computer-Aided Personal Interview (CAPI) in their homes, and were subsequently invited to attend a supraregional health centre for a comprehensive health assessment [551]. For those who were unable to travel to the health centre, modified health assessments could be carried out in the participant's home.

In Wave 1, 72% of participants (n = 6,150) completed the health assessment in the designated health centre (n=5,275; 86%) or in their own home (n= 876; 14%) assessment [487]. All participants completed the CAPI.

6.2.3 Current Study Design

This thesis chapter used data from Wave 1 of the Irish Longitudinal Study on Ageing (TILDA), which were collected between October 2009 and February 2011.

6.2.4 Current Study Participants

This retrospective, longitudinal study compared individuals with cancer to those without cancer. The analysis sample used data from participants reporting a cancer diagnosis in Wave 1, comparing them to control participants who were cancer-free. A cancer diagnosis was defined as answering 'yes' to the question: "Has a doctor ever told you that you have any of the following conditions?", with the option of

"cancer or a malignant tumour". If they said yes they were asked 'In which organ or part of the body have you or have you had cancer?" with various options presented for the most common cancer types, and "other" or "don't know". For these analyses, all cancer types were included.

Analysis consisted of both cross-sectional and longitudinal components. For cross-sectional analysis, prevalence of frailty at Wave 1 was investigated, and compared to those without a cancer diagnosis. A separate longitudinal analysis was also conducted to ascertain the frailty status of those who had reported a cancer diagnosis in Wave 1. Due to the limitations of self-report, and in the absence of pathological confirmation of cancer type, all cancer diagnoses were included. The comparison or control group was composed of participants who did not report a cancer diagnosis in any wave. All ages were included due to the limitations of sample size.

6.2.5 Study Measures

6.2.5.1 Sociodemographics

Age, sex and educational attainment were compared for all study participants.

6.2.5.2 Frailty Measures

Frailty was defined from TILDA data, as closely as possible, to three commonly used measures of frailty, as described below.

6.2.5.2.1 Phenotype of Frailty

A phenotype of frailty was devised, as closely as possible, to the definition provided by Fried and colleagues [63]. Five components were derived in order to ascertain frailty status. The first was handgrip strength, which was calculated as the mean of two measures taken from the dominant hand taken by nurses in the health centre and the home.

Readings below the 20th percentile of handgrip strength were then used, based on those aged 65 years and older, and adjusted for sex and BMI, to categorize those with low grip strength. The cutoffs applied are detailed in Table 6.1.

Male	Female
BMI≤26: 22.5kg	BMI ≤25: 13kg
BMI 27-29: 24.5kg	BMI 26-28: 13.5kg
BMI 30-32: 24kg	BMI 29-31: 13.5kg
BMI>32: 23.5kg	BMI>31: 13kg

Table 6.1 Cutoffs applied for hand grip strength calculations stratified by sex and BMI

Slowness was measured by the Timed Up and Go (TUG) task, which involves rising from a chair (of seat height 46cm), walking 3 metres at the participant's normal pace, turning around, and walking back to the chair to sit down again [383]. It is a measure of walking speed, balance and coordination. The time elapsed between hearing the "Go" command to returning and sitting with the participant's back to the chair, was recorded with a stopwatch. In TILDA health centres, a chair with armrests and seat height of 46 cm was used for all TUG tests.

Those in the lowest 20th percentile of the population, calculated based on those over the age of 65, stratified by median height, were categorized as having slow walking time. The sex-specific cutoffs applied are outlined in Table 6.2.

Male	Female
≤:171.5cm: 12.4 s	≤157.8cm: 13.4s
>171.5cm: 11.19s	>157.8cm: 11.35s

Table 6.2 Cutoffs applied for TUG time calculation stratified by sex and median height

Exhaustion was measured using two items from the Centre for Epidemiological Studies Depression scale [552], "I could not get going" and "I felt that everything I did was an effort". Of the four

possible responses: never, rarely, sometimes or often, a response of "sometimes" or "often" was considered to indicate exhaustion.

Physical activity was measured from the International Physical Activity Questionnaire (IPAQ). Energy expenditure in kilocalories (kcal) per week was calculated using the time reportedly spent walking, and in vigorous/moderate physical activity, weighted against the participant's weight in kilograms. Again, the 20th percentile was used (<675 kcal/week for men and <223 kcal/week for women) to categorise low physical activity for men and women.

Finally weight loss information was provided by answering yes/no to the following question from the CAPI: "in the past year, have you lost 10 pounds (4.5kg) or more in weight when you were not trying to?"

In order to define frailty, the sum total of the above components was added, and those with one or two components were considered "prefrail", while those with three, four, or five components were classified as "frail".

6.2.5.2.2 Frailty Index

Frailty in Wave 1 was also assessed using a deficit accumulation FI approach [66], as described by Theou et al [68] and previous studies [469, 553]. Items were first screened from the CAPI questionnaire in order to identify FI deficits. Deficits were defined as "any symptom, sign, disease, disability or laboratory abnormality that is associated with age and adverse outcomes, present in at least 1% of the population, covers several organ systems and has <5% missing data" [68, 553]. Valid FIs require at least 30 deficits, and for the FI, a 32-item index was devised, based on self-report (self-reported FI or SRFI). The individual items, from several health domains, which

comprised the SRFI index are shown in Table 6.3 below. Each was coded as present or absent. Deficits with more than two categories were coded as a proportion of the number of categories present, from 0-1 e.g. five categories for excellent, very good, good, fair and poor were coded as 0, 0.25, 0.5, 0.75 and 1.0.

A mixture of binary, ordinal or continuous variables were used to construct the SRFI, and these were recoded as binary measures with 0 indicating no deficit, 0.5 a half deficit and 1 indicating that the full deficit was present. For continuous variables with no known cut-off, percentiles were used. For those in the lowest 5th percentile, a full deficit was assigned, while those between the 5th and 20th percentile were assigned a half deficit. The resultant FI score was defined by dividing the number of deficits by the total number of variables used i.e. 32. Participants missing more than a fifth of FI items were excluded from the analysis. As per previous studies, a cut-off score of 0.25 was used to define frailty [65, 554]. The categorical cut-points were: FI score <0.099: Robust, FI score 0.10-0.2499: Pre-frail and FI score ≥0.25: Frail.

Self-Reported Frailty Index (SRFI) variables	1.Difficulty walking 100m	17.Urinary incontinence
	2.Difficulty rising from a chair	18.Hypertension
	3.Difficulty climbing stairs	19.Angina
	4.Difficulty stooping, kneeling or crouching	20.Heart attack
	5.Difficulty reaching above shoulder height	21.Diabetes
	6.Difficulty pushing/pulling large objects	22.Stroke & Transient ischemic attack
	7.Difficulty lifting/carrying weights ≥10lb	23.High cholesterol
	8.Difficulty picking up coin from table	24.Irregular heart rhythm
	9.Feeling lonely	25.Other cardiovascular disease
	10.Poor self-rated physical health	26.Cataracts
	11.Poor self-rated vision	27.Glaucoma & age-related macular degeneration
	12.Poor self-rated hearing	28.Arthritis
	13.Difficulty following a conversation	29.Osteoporosis
	14.Daytime sleepiness	30.Liver disease
	15.Polypharmacy	31.Varicose ulcer
	16.Knee pain	32.Poor self-rated memory

Table 6.3 Items included in the construction of the 32-item FI [68]Note: cancer was replaced by liver disease for this analysis

6.2.5.2.3 Morley

Five indicators, based on self-reported measures from CAPI, were used to construct the Morley FRAIL scale [532]. Variables included:

Fatigue: “How much of the time during the past 4 weeks did you feel tired?” Responses included: 1=all of the time, 2=most of the time, 3=some of the time, 4=a little of the time and 5=none of the time. Responses of 1 or 2 were categorised as fatigue, by creation of a dichotomous variable, and all others categorised as no fatigue.

Resistance: “By yourself and not using aids, do you have any difficulty walking up one flight of stairs without resting?” Responses were either “yes” or “no”.

Ambulation: “By yourself and not using aids, do you have any difficulty walking several hundred yards?” Responses were either “yes” or “no”.

Illnesses: Illnesses included a composite measure based on 16 chronic conditions, i.e. heart attack, heart failure, angina, cataracts, high blood pressure, high cholesterol, stroke, diabetes, lung disease, asthma, arthritis, osteoporosis, Parkinson’s disease, peptic ulcer, hip fracture and liver disease (not cancer) for the purpose of this analysis.

Loss of weight: Weight loss information was provided by the answering yes/no to the following question from the CAPI: “in the past year, have you lost 10 pounds (4.5kg) or more in weight when you were not trying to?”

The categorical cut-points were: 0: Robust, 1-2: Pre-frail and ≥3: Frail.

6.2.6 Statistical Analysis

6.2.6.1 Cross-Sectional Analysis

Descriptive statistical data were summarised as frequencies and percentages for categorical variables, and means (standard deviations, SD) for other continuous variables. T-tests and chi-square tests were used to ascertain the difference between the cancer and control group, as mandated by variable type and associated tests of normality. Non-parametric equivalents were carried out for skewed data.

To determine the differences between non-frail versus pre-frail and non-frail versus frail, separate unadjusted multinomial regression analyses were conducted. The non-frail group was used as the reference group for all analyses, and cancer diagnosis was used as the predictor variable. This was followed by a multinomial regression model adjusted for age, sex and education, and TILDA survey weights (described below) were applied. Potential multicollinearity was assessed by Person correlation and analysis of variance inflation factor (VIF) between covariates (VIF>5).

Both unadjusted and adjusted models, including relative risk ratios (RRR) and 95% confidence intervals (CIs) were produced.

6.2.6.2 Longitudinal Regression Analysis

Participants who declared a cancer diagnosis in Wave 1 were followed up at Wave 3, to determine the change in frailty status over

time. Only those participants with frailty data in both waves were included in this analysis i.e. those who survived approximately four years from Wave 1 to Wave 3. All Wave 3 participants were included in this analysis, regardless of interview status i.e. proxy or self. Multinomial logistic regression was used to evaluate the longitudinal association between frailty and cancer. A multinomial logistic regression model was fitted (using non-frail as the reference group) to assess the odds of frailty and pre- frailty at Wave 3 in the context of a cancer diagnosis. This was followed by an adjusted analysis, controlling for age, sex and education, and TILDA weights (described below) were applied.

6.2.7 Correction for Multiple Comparisons

In instances of multiple comparisons, which increase the risk of Type I error i.e. rejecting the null hypothesis when it's true, a Benjamini-Hochberg correction [489], was applied to control the false discovery rate (FDR). This provided an adjusted $\alpha = 0.05$ i.e. values or less than or equal to 0.05 were considered significant. For further details, the calculation of the FDR (set at 0.25 for all calculations) is contained in Appendix 22.

All analyses were performed using Stata version 12.1 (Stata Corporation, College Station, TX, USA).

6.2.8 Sampling Weights

In TILDA, participants were selected according to a multistage sampling design, which has been described in the previous chapter and elsewhere [488]. The response rates may vary for certain subgroups of the population, and thereby introduce a source of bias. In order to overcome this, calibration weights were applied in the

analysis stage to ensure that subgroups were nationally representative.

For cross-sectional analysis, a health assessment weight was applied to the measurement of Fried frailty, while CAPI weights were applied to the FI and Morley measures.

The CAPI weight was derived from a comparison of individuals (sample versus true population) using age, sex and highest educational attainment. This information was provided by the Quarterly National Household Survey (QNHS 2010) and more recently the 2011 Census data.

The health assessment weight includes a probability weighting for those who completed the CAPI, in terms of going on to complete the health assessment in the regional health centres, or in the home. This probability is calculated for each participant, based on age, sex and education, using multivariable logistic regression.

For longitudinal analysis, the corresponding Wave 3 weights were applied to the relevant dependent variable for regression analysis.

6.3 Results

6.3.1 Cross-sectional Analysis

6.3.1.1 Demographic Characteristics of Study Sample

The demographic characteristics of the cross-sectional (Wave 1) study sample are shown in Table 6.4. In total, there were 522 participants with cancer in Wave 1, and 7,982 without. The cancer group was marginally older ($p<0.001$), with a mean age of 65.77, in

comparison to the control arm, whose mean age was 62.97. The sample included mostly females; 60.34% of the cancer group was fem6ale, compared to 55.24% of the control arm. Marital status was similar in the cancer and control arms, with over two-thirds of both groups being married.

6.3.1.1 Disease and Treatment Characteristics

The disease and treatment characteristics of the Wave 1 analysis sample are reported in the previous chapter (Chapter 5).

Characteristic	Cancer group		Control group		Difference
	n (%)	Mean (SD)	n (%)	Mean (SD)	p value
Age	522 (6.15%)		7,970 (93.85%)		
		65.77 (9.68)		62.97 (10.22)	<0.001*
Sex					0.02*
Female	315 (60.34)		4,409 (55.24)		
Male	207 (39.66)		3,573 (44.76)		
Education Level					0.62
Primary	167 (31.99)		2,354 (29.49)		
Secondary	206 (39.46)		3,225 (40.40)		
Third Level	149 (28.54)		2,399 (30.06)		
Marital Status					0.13
Married	351 (67.24)		5,615 (70.35)		
Not married	171 (32.76)		2,367 (29.65)		

*indicates significance at adjusted p value following Benjamini-Hochberg correction
n=12 of the control group were missing data for age variable, and 4 for education variable

Table 6.4 Demographic characteristics of study sample

6.3.1.2 Participants

In Wave 1, 72% of participants (n = 6,150) completed the health assessment in the designated health centre (n=5,275; 86%) or had a home (n= 875; 14%) assessment [487]. Of those, 149 of the 522 participants with cancer did not have a health assessment in Wave

1, while 308 had a health centre assessment, and 65 opted for a home assessment instead. In the control group, 2,205 had no health assessment, 4,967 had a health centre assessment and 810 opted for a home assessment. The participant flow chart and final numbers for analysis of each frailty measure in each group are presented in Figure 6.2.

Figure 6.2 Participant flow chart

6.3.1.3 Prevalence of Frailty

The overall prevalence of frailty for each of the three frailty measures used, is presented in Table 6.5. For all three frailty measures, the prevalence of frailty was significantly greater in the cancer group compared to the control group.

With regard to the Fried criteria, there was a greater incidence of weight loss in the cancer group compared to the control group ($p<0.001$). There was also a statistically significant difference in the low activity and slowness, with the cancer group reporting more adverse features. Overall, the incidence of prefrailty at Wave 1 was 40.42% in the cancer group, versus 33.70% in the control arm. The corresponding frailty categorization was 7.13% for the cancer arm, versus 4.64% in the control arm.

The prevalence of frailty according to FI criteria was 23.44% in the cancer arm, versus 13.98% in the control arm, while 35.44% and 29.33% of the cancer and control arm, respectively, were characterized as pre-frail.

Using Morley FRAIL scale criteria, there were lower levels of frailty in both groups, compared to the other measures. Frailty levels for the cancer and control arm, were 6.45% versus 3.04%. Pre-frailty categorization was also lower: 29.96% versus 21.8%, again with higher levels of pre-frailty reported in the cancer group.

A comparison of the prevalence of frailty and pre-frailty, for all three measures, is shown in Table 6.5. A further break-down by age >65 and <65 is included in Appendix 23. Please note: weight loss information is different for Fried and Morley criteria due to the differing numbers of participation, as displayed in Figure 6.2.

Frailty Measure	Group	Cancer group weighted proportion % [95% CI]	Control group weighted proportion % [95% CI]	Difference between both groups (p value)
Fried	Exhaustion	10.26 [7.24,14.34]	9.72 [8.90,10.61]	0.76
	Weight loss	12.77 [9.53,16.89]	7.14 [6.43,7.93]	<0.001
	Low activity	21.40 [17.05,26.50]	16.09 [15.02,17.22]	0.018
	Slowness	18.89 [14.56,24.14]	11.66 [10.68,12.72]	<0.001
	Low grip	18.00 [13.80,23.12]	14.05 [13.03, 15.14]	0.08
	Prefrail	40.42 [34.93,46.15]	33.70 [32.32,35.10]	0.005
	Frail	7.13 [4.61,10.87]	4.64 [4.00,5.38]	
Frailty Index	**Prefrail**	35.44 [31.27,39.85]	29.33 [28.28,30.40]	<0.001
	Frail	23.44 [19.71,27.65]	13.98 [13.17,14.84]	
Morley	Fatigue	11.05 [8.48,14.29]	10.11 [9.42,10.85]	0.52
	Resistance	12.96 [10.05,16.54]	7.86[7.23,8.54]	<0.001
	Ambulation	13.25 [10.33,16.85]	8.35 [7.70,89.05]	<0.001
	Illnesses	7.48 [5.38,10.33]	4.56 [4.08,5.09]	0.005
	Loss of weight	15.59 [12.53,19.23]	7.23 [6.63,7.86]	<0.001
	Prefrail	29.96 [25.91,34.35]	21.80 [20.84,22.80]	<0.001
	Frail	6.45[4.46,9.26]	3.04 [2.65,3.49]	

Table 6.5 Prevalence of frailty for all three measures and all participants (adjusted for age, sex and education

6.3.1.4 Cross-sectional regression analysis of frailty

Multinomial logistic regression was used to model the association between frailty and cancer, both unadjusted and adjusted, as seen in Table 6.6. Upon adjustment for demographic variables and TILDA survey weights, a cancer diagnosis was associated with frailty, as measured by FI and Morley criteria, but not the Fried phenotypic classification. The highest relative risk was in relation to predicting frailty, rather than pre-frailty. In most analyses, increasing age, female sex and low educational attainment (primary level) were also predictive of worsening frailty.

		Unadjusted model				Adjusted model	
		Non-frail versus		Non-frail versus		Non-frail versus[a]	
		Pre-frail RRR (CI)	Frail RRR(CI)	Pre-frail RRR(CI)	Frail RRR(CI)	Pre-frail RRR(CI)	Frail RRR(CI)
Fried	Cancer diagnosis	1.39* [1.11,1.74]	2.00* [1.26,3.17]	1.17 [0.93,1.49]	1.47 [0.91,2.38]	1.16 [0.90,1.50]	1.30 [0.77,2.22]
	Age			1.05** [1.04,1.06]	1.11** [1.10,1.14]	1.06** [1.05,1.06]	1.13** [1.11,1.15]
	Sex						
	Male			reference	reference		
	Female			1.14* [1.01,1.27]	1.05 [0.79,1.39]	1.16* [1.03,1.32]	1.10 [0.81,1.49]
	Education Level						
	Primary			reference	reference		
	Secondary			0.64* [0.68,0.91]	0.78* [0.47,0.89]	0.76** [0.66,0.88]	0.64* [0.47,0.89]
	Third Level			0.60** [0.52,0.70]	0.32** [0.21,0.48]	0.61** [0.52,0.71]	0.32** [0.21,0.49]
Frailty Index	Cancer diagnosis	1.69** [1.33,2.14]	2.36** [1.78,3.13]	1.40* [1.10,1.80]	1.77** [1.30,2.41]	1.43* [1.09,1.87]	2.09** [1.52,2.88]
	Age			1.07** [1.07,1.08]	1.12** [1.11,1.13]	1.07** [1.06,1.08]	1.11** [1.10,1.12]
	Sex						
	Male			reference	reference		
	Female			1.34** [1.19,1.51]	1.82** [1.54,2.17]	1.31** [1.15,1.49]	1.96** [1.62,2.36]
	Education Level						
	Primary			reference	reference		
	Secondary			0.71** [0.60,0.82]	0.52** [0.43,0.64]	0.69** [0.59,0.81]	0.50** [0.40,0.61]
	Third Level			0.70** [0.60,0.82]	0.36** [0.29,0.46]	0.68** [0.58,0.80]	0.36** [0.29,0.46]
Morley FRAIL scale	Cancer diagnosis	1.66** [1.31,2.11]	2.88** [1.74,4.75]	1.42* [1.12,1.81]	2.27* [1.36,3.79]	1.40* [1.07,1.82]	2.50* [1.46,4.28]
	Age			1.04** [1.03,1.05]	1.06** [1.04,1.08]	1.04** [1.03,1.05]	1.06** [1.04,1.08]
	Sex						
	Male			reference	reference		
	Female			1.15** [1.33,1.73]	1.13 [0.80,1.59]	1.56** [1.35,1.79]	1.26 [0.87,1.82]
	Education Level						
	Primary			reference	reference		
	Secondary			0.71** [0.61,0.83]	0.43** [0.29,0.64]	0.70** [0.60,0.82]	0.41** [0.27,0.62]
	Third Level			0.55** [0.47,0.66]	0.28** [0.17,0.46]	0.57** [0.48,0.68]	0.28** [0.17,0.47]

**P<0.001 *p<0.05 [a] adjusted for age, sex and education with TILDA survey weights applied
RRR = relative risk ratio – greater than 1 means an increased risk equivalent to the ratio provided e.g. 1.39 is equivalent to a 0.39 increased risk, 2.0 to a doubling in relative risk etc.

Table 6.6 Unadjusted and adjusted associations between a cancer diagnosis and three measures of frailty

6.3.2 Longitudinal Analysis

For those participants who disclosed a previous history of cancer at Wave 1, a follow-up analysis of their frailty trajectory was performed with a regression analysis at Wave 3. The demographic characteristics of the longitudinal sample are provided in Table 6.7.

6.3.2.1 Demographic Characteristics

	Statistic	Cancer group (n=358)	Control Group (n=6,155)	P value
Age	Mean (SD)	64.65 (9.50)	62.21(9,64)	<0.001*
Sex	n (%)			0.03*
Male		137 (38.27)	2,728 (44.26)	
Female		221 (61.73)	3,436 (55.74)	
Education	n (%)			0.36
Primary		105(29.33)	1,597 (25.91)	
Secondary		136 (37.99)	2,440 (39.58)	
Third level		117(32.68)	2,126 (34.49)	
Marital Status	n (%)			0.60
Married		254(70.95)	4,452 (72.23)	
Unmarried		104 (29.05)	1,712 (27.77)	

*indicates significance at adjusted p value following Benjamini-Hochberg correction

Table 6.7 Demographic characteristics of study sample (Wave 1) included in the longitudinal analysis

Multinomial logistic regression was used to evaluate the longitudinal association between frailty and cancer. A multinomial logistic regression model was fitted (using non-frail as the reference group) to assess the odds of pre- frailty and frailty at Wave 3 in the context of a cancer diagnosis. This was followed by an adjusted analysis, controlling for age, sex and education, and TILDA weights.

A cancer diagnosis was not a significant predictor of longitudinal frailty, when either the Fried or Morley criteria were used (results not presented here). However, it was significant when combined with the FI measure, on univariate analysis, for pre-frailty only, as shown below in Table 6.8.

		Unadjusted model				**Adjusted model**	
		Non-frail versus		**Non-frail versus**		**Non-frail versus[a]**	
		Pre-frail RRR (CI)	**Frail RRR(CI)**	**Pre-frail RRR(CI)**	**Frail RRR(CI)**	**Pre-frail RRR(CI)**	**Frail RRR(CI)**
Frailty Index	Cancer diagnosis	1.52* [1.13,2.03]	1.18 [0.76,1.83]	1.32 [0.98,1.78]	0.979 [0.62,1.54]	1.37 [0.96,1.97]	0.83 [0.48,1.46]
	Wave 1 FI group						
	Non-frail	reference	reference	reference	reference	reference	reference
	Prefrail	7.89** [6.79,9.16]	22.12** [16.78,29.15]	6.44** [5.52,7.51]	15.50** [11.66,20.62]	6.13** [5.08,7.39]	13.60** [9.40,19.68]
	Frail	46.19** [26.14,81.63]	803.64** [441.79,1461.86]	37.36** [21.06,66.27]	526.33** [286.63,966.48]	48.95** [24.68,97.07]	706.37** [336.6,1482.6]
	Age			1.06** [1.05,1.07]	1.10** [1.08,1.11]	1.06** [1.04,1.07]	1.10** [1.08,1.12]
	Sex						
	Male			reference	reference		
	Female			1.26* [1.09,1.45]	1.91** [1.52,2.40]	1.24* [1.04,1.48]	1.72** [1.29,2.28]
	Education Level						
	Primary			reference	reference		
	Secondary			0.77* [0.63,0.93]	0.53** [0.40,0.69]	0.72** [0.57,0.91]	0.53** [0.38,0.74]
	Third Level			0.65** [0.53,0.79]	0.32** [0.24,0.43]	0.565** [0.51,0.82]	0.35** [0.24,0.51]

**P<0.001
*p<0.05
[a] adjusted for age, sex and education with health assessment survey weights applied
FI=Frailty Index
RRR = relative risk ratio – greater than 1 means an increased risk equivalent to the ratio provided e.g. 1.39 is equivalent to a 0.39 increased risk, 2.0 to a doubling in relative risk etc.

Table 6.8 Unadjusted and adjusted associations between a cancer diagnosis at Wave 1 and three measures of frailty at Wave 3

6.4 Discussion

In this study of TILDA Wave 1 participants, frailty was defined using three measures, Fried phenotype of frailty [63], a deficit accumulation FI as described by Theou et al [68] and the Morley FRAIL scale [532]. Comparing all three measures of frailty, the prevalence of frailty criteria was higher in the cancer arm, compared to the control arm, for all participants and all ages combined. Similar to previous studies of older adults, the cumulative deficits approach provided a higher estimate of frailty, compared to the phenotype model. The highest prevalence of frailty was provided by the FI approach. The lowest overall prevalence of frailty was provided by the FRAIL scale. A cancer diagnosis resulted in a greater risk of developing frailty when using the cumulative deficits and FRAIL scale approaches. However, there was no longitudinal association with frailty at Wave 3, when controlling for baseline frailty at Wave 1, or age, sex and education.

In terms of aetiology, frailty and cancer share common risk factors, such as smoking [47], sedentary lifestyle [48], malnutrition and obesity [49]. Recent research efforts have focussed on defining the acceleration of frailty that is known to occur, due to cancer and its treatment [50-52]. Accumulation of cellular damage and system dysregulation are common to both ageing and cancer [51-54]. Follow-up of paediatric and young adult cancer survivors have shown earlier onset of age-related concerns, such as multimorbidity, frailty and functional decline [55-57]. The prevalence of frailty has previously been demonstrated to be similar among younger cancer survivors and adults aged 65 years and older, without a cancer diagnosis [57, 58]. It is thought that aging and cancer represent different courses, with a common underlying cellular mechanism, which is also influenced by genetics and the environment [59]. This helps in part to explain the considerable differences seen in ageing

phenotypes observed in older people e.g. one 70 year old may be frail and use a walking aid, while another may run marathons.

Although frailty is usually studied in older adult populations, a lower age cutoff was used for the current study, using data from TILDA. Previous studies have reported greater than expected rates of frailty in populations of adult survivors of childhood and adolescent cancers several years after treatment [56-58]. A recent longitudinal study of phenotypic frailty and cognition in women aged 50 years and older, with breast cancer, similarly found a greater prevalence of frailty before, during and after receiving chemotherapy. Although frailty status had resolved 6 months after completing chemotherapy, it remained higher than age-matched controls. Thus, the inclusion of younger patients with a history of cancer was justified in the current analysis. The average time since diagnosis was 21.6 years, with a range of 0-53 years. Indeed, it was observed that despite including a "younger" population on average, frailty characteristics were more prevalent and mean frailty scores were higher in those diagnosed with cancer, compared with controls. These findings provide some leverage for reconsideration of the traditional age cut-offs advocated in oncology of 65 and 70 [80, 555].

A recent study, one of the largest to date using phenotype frailty criteria, and 418 patients aged 66-100 years, found that 37% were pre-frail and 55% were frail [556].This included all cancer types, and was measured before active treatment, however it included older individuals referred to a "geriatric frailty clinic", with an under representation of good prognosis cancers, such as prostate and breast cancer. The corresponding proportions for pre-frailty and frailty in the current study for those aged 65 and over and a previous diagnosis of cancer, using phenotypic criteria, were lower. However, the two study cohorts are very different with regard to age and

disease type. Other smaller studies of the Fried phenotype, mostly in surgery, have shown associations with post-operative risk [557, 558] and chemotherapy toxicity [559]. A further study (retrospective) investigated the association between preoperative frailty and the onset of surgical complications in patients (n=587) diagnosed with non-melanoma skin cancer, undergoing plastic and reconstructive surgery [560]. It was found that increasing FRAIL scores were associated with worsening surgical outcomes.

Frailty assessment in radiation oncology research has been relatively sparse, by comparison to medical and surgical oncology [183]. Comparison to published series is difficult as no consensus on optimal frailty assessment exists in either geriatric medicine [45] or oncology [61, 561]. Some of the frailty assessment tools developed in oncology to date have been criticised as they lack assessment of physical function, which is seen as a central element of frailty [561]. The two most common frailty assessments in medical gerontology are the Fried phenotype and FI approaches. Thus, their use in the current analysis is considered justified. One of the many obstacles to implementing CGA in oncology has been the argument that it is too time consuming [179]. The FI used in this analysis consisted of self-report items only, and is easily replicated in other settings. It is based on established criteria for FI construction [553]. Previous studies have demonstrated good agreement with a corresponding FI based on test-based measures [68].

The highest prevalence of frailty in the current analysis was in relation to the accumulation of deficits, as measured by FI. Frailty models, such as the FI, may be used to make better treatment decisions for patients with cancer, as it is related to a host of adverse outcomes, such as hospitalisation, disability and death [66, 562, 563]. Knowing the risk of such adverse outcomes in advance is important in making

life affirming decisions. In oncology, impairment in geriatric domains is predictive of such things as chemotherapy toxicity [564], postoperative complications [558], functional decline [565] and overall survival [566]. A previous TILDA analysis has shown that frailty, independent of other health and socioeconomic factors, is associated with increased healthcare utilisation among those aged 65 and over [469], in the areas of General Practitioner visits, use of homecare services and unplanned hospital visits. Reported healthcare expenses related to frailty are estimated to be approximately €3500 over 3 months for older adults, which is about 5 times the cost for those who are nonfrail [567]. It therefore has an economic impact, and may be more of a concern for those diagnosed with cancer, although it was not investigated in the current study.

It is also imperative to investigate and diagnose frailty in older adults with cancer, as frailty is potentially reversible [568, 569], and presents an opportunity for appropriate interventions if detected at an earlier stage i.e. pre-frailty. Without regular assessment of frailty, it isn't possible to respond to the more complex healthcare needs that someone with cancer and frailty may have. Functional reserves of frail patients may preclude them from benefitting from active cancer treatment, and thus it should form the basis of a diagnostic workup, especially in older patients, to ensure adequate reserve capacity. Change in frailty status over time, based on the (continuous) FI approach, is also associated with mortality risk, and thus regular assessment is advocated [562].

The predictive capacity of frailty scores generally has mainly been studied with morality endpoints. Their ability to predict other important outcomes in the older population, such as cancer occurrence and cardiovascular events, are not currently available in the published

literature, as highlighted by a recent comparative analysis of the relationship between 35 frailty measures and cancer events [570].

Having completed this research, the question now arises as to which of the three measures used might be the most useful in clinical practice? Of the three measures used in this study, the FI provided the highest estimate of frailty, due to its multidimensional nature. Both Fried and Morley scales are based on physical frailty, and are therefore seen as less sensitive to longitudinal changes, from a clinical perspective [45]. Therefore, the FI may be more useful to investigate the effectiveness of an intervention and to describe health trajectories over time [571]. The most widely used frailty measures in clinical practice are undoubtedly the FP and FI approaches [572]. These two frailty models are well validated in many populations and settings [573]. The aforementioned secondary analysis of ELSA studies, by Aguayo et al [570], analysed 35 different frailty scores in their review and found that multidimensional measures, such as the FI, may have a stronger association with mortality and cardiovascular events. The FI has the added advantage of being eligible for self-completion. It is essential to choose a frailty screening tool, which is has sufficient predictive power for other adverse outcomes, but is simple to use, and validated, in a specific clinical setting [45]. Ideally, combined use of the FP and FI instruments is advised, as they provide separate and complementary clinical information about the individual's risk profile [571].

In order to overcome some of the stigma associated with a diagnosis of frailty, a recent construct that has been proposed is the idea of intrinsic capacity, which emphasises the physical and mental capabilities of an individual, rather than their losses, as characterised by frailty measures [574]. This has been endorsed by the WHO, but has not been validated in clinical practice.

A recent report from the National Cancer Control Programme (NCCP) has highlighted the survivorship needs of those living with and beyond cancer in Ireland [575]. Cancer survivors comprised 4% of the Irish population in 2016, and greater recognition of the physical and psychological consequence of a cancer diagnosis were highlighted as key priorities from this report. Most follow-up care is currently delivered in hospitals, and it was suggested that this be reviewed so that a model of more integrated care may be provided. This is especially important in the context of longitudinal assessment and management of frailty. It was also stressed that meeting the needs of cancer survivors would require more detailed information from research in the post-treatment phase. Longitudinal studies, such as TILDA are useful resources to help fill this important gap.

6.5 Strengths and Limitations

This study had several strengths. Firstly, validated measures were used to provide a comprehensive assessment of frailty in cancer survivors, using both objective and self-report items. While the aim of this study was to investigate the prevalence of frailty in community dwelling older adults with cancer, it also described the construction of a FI which may have relevance for clinical practice and is feasible in terms of implementation. Also, the study sample is nationally representative of adults aged 50 years and over living in the community in Ireland.

With regard to limitations, TILDA excludes individuals in hospital, nursing home residents and those resident in other institutions in this wave (these were facilitated by proxy interviews in subsequent waves). This potentially excludes some of the most vulnerable and frail members of the population, many of whom may have become dependent due to a cancer diagnosis.

Frailty measures were constructed using available data, obtained within TILDA, and extracted from various questionnaires, but nevertheless retain their validity.

The cancer sample consisted of heterogeneous cancer types, and it wasn't possible to assess cancer stage for these, in order to ascertain disease status. The risk profile associated with some of these diagnoses is likely to be substantially different from that of a good prognosis cancer. Also, it wasn't possible to report if participants with cancer were undergoing active treatment, or not.

In addition, the number of participants with some cancer subtypes was small, and therefore, a subgroup analysis was not feasible as it would be underpowered to detect statistically significant associations. Site specific studies provide more insight into how the unique disease and treatment characteristics influence health and wellbeing.

Disclosure of a cancer diagnosis, and of other comorbid conditions, was self-reported and may not always be accurately reported e.g. someone might report they have brain cancer, for brain metastases, while their primary cancer may be breast cancer. Likewise for "liver cancer" and colorectal disease.

Also, in TILDA, skin cancer is classified as "malignant melanoma (skin cancer)". This is a relatively broad classification that is usually separated in studies of cancer into "melanoma" and "non-melanoma skin cancer (NMSC)" as the latter is associated with a much more favourable diagnosis. Previous studies have excluded NMSC on the basis that it is so treatable, however it wasn't possible to do so in the current analysis.

The absolute numbers of participants with cancer, compared to those without, was relatively low. However, this forms the basis for

generation of hypotheses to be further investigated in larger scale studies of cancers under more controlled conditions.

6.6 Conclusion

In conclusion, in this secondary analysis of a large nationwide study, it was determined that participants with cancer had higher frailty scores compared with noncancer controls. Given that frailty is a known risk factor for adverse outcomes for older patients in particular, consideration of this aging-related syndrome needs to be taken into account by all healthcare practitioners treating patients with cancer. Interventions are needed to minimize the progression of frailty and to possibly reverse onset of premature frailty. These data could inform treatment decision making and survivorship care planning.

Chapter 7

7 Discussion and Conclusions

7.1 Thesis Aims and Structure

The overall aim of this thesis was to measure geriatric assessment (GA) based deficits and frailty in an Irish (hospital and community) population with cancer and to study the feasibility of GA in a radiation oncology clinic. This information is important from a health services perspective, as it provides an important baseline for monitoring implementation of policy in relation to geriatric oncology in Ireland. This chapter will provide an overall discussion of these results, with an emphasis on original contributions to the research field and their implications for clinical practice and health policy. Also, recommendations for future research are made, arising from the research findings and limitations encountered throughout the course of this research, as well as new areas that have emerged as research priorities since the commencement of this PhD.

7.1.1 Literature Review Main Findings

Chapters 1 and 2 of this doctoral thesis provided a background to the research area, including relevant literature and importantly identified existing research gaps.

In Chapter 1, the context for this research was established, through highlighting the predicted demographic changes that are expected in Ireland, and internationally, over the coming decades. In Ireland alone, the number of cancer cases are expected to increase by 81% for females and 108% for males between 2010 and 2040 [1]. The various challenges that this represents in oncology were highlighted, namely poorer outcomes for older adults with cancer at the present

time [11, 12], inequities in access to treatment [13, 14], with undertreatment a common occurrence [17], as well as the traditional exclusion of older patients from cancer clinical trials [19-22]. Although approximately 60% of new cancer cases occur in older people, they comprise only a quarter of participants in cancer clinical trials [24]. The latter is particularly problematic, as the evidence base for treatment of older adults is poor, particularly those who may be pre-frail or frail. There is virtually no guidance on appropriate treatment for those in the "oldest old" category i.e. 80 years and older, which is projected to double in the coming decades [576].

Ireland's National Cancer Strategy 2017–2026 [577], has recognised for the first time that geriatric oncology is a priority area for development in Ireland. The strategy focuses on three main areas to prioritise – education, clinical practice and research. It states that "formalised geriatric input needs to be built into the multidisciplinary assessment of the care of older patients with solid and haematological malignancies". This recommendation has also been mirrored internationally. Major organisations, such as the Institute of Medicine (USA) and American Society of Clinical Oncology (ASCO) have specifically identified older adults with cancer as a key research priority group [258, 465]. Additionally, the International Society of Geriatric Oncology (SIOG) [79], and the National Comprehensive Cancer Network (NCCN) [78] have advocated for the implementation of Comprehensive Geriatric Assessment (CGA) in older adults with cancer in order to better determine the appropriate course of treatment, and to assess patient outcomes. It is well established in the literature, and from the major advisory and advocacy organisations, that in order to inform policy, additional evidence is required about the relationship between more age appropriate endpoints, as defined by CGA, e.g. physical function and cognitive performance, and their impact on a patient's daily life.

Many international models of geriatric oncology exist [35-37], to provide guidance. Ironically, geriatric oncology is a relatively young, but increasingly important field in oncology. Since the first geriatric case for geriatric oncology as a discipline was put forward in the 1980s [578] the field has grown, with most of that growth taking place in developed nations, and often in very select regional centres of those developed countries [213]. There are many models of geriatric oncology programmes, such as those providing ongoing geriatric oncology management throughout the cancer trajectory, one-time consult programmes, site specific models and those based on age, rather than tumour site [221]. Geriatric oncology remains a niche service in many countries internationally [213]. In a European context, significant heterogeneity exists among geriatric oncology programmes.

For example the use of a screening tool is a quality indicator for patients with colorectal cancer in the Netherlands [222]. The Italian system of geriatric oncology is organised through The Italian Geriatric Oncology Group (GIOGER) [223], which is similar to the Spanish system [224], with a few geriatric oncology programmes in some of the biggest centres. Similarly, in the UK, a number of pilot programmes have been initiated [225].

France is known to be at the forefront of geriatric oncology and has a relatively coordinated system which serves as one of the exemplars worldwide. This coordination has been facilitated by funding through Institute National du Cancer (INCa), who have funded consecutive cancer plans [226]. This has led to a more coordinated network of geriatric oncology units across the country, which are led by both an oncologist and a geriatrician. Ultimately, this has enhanced access for older patients and resulted in organised geriatric oncology research programmes and increased awareness among both the

general population and health professionals. Such funding initiatives would greatly enhance current provision in an Irish context.

National support is necessary to provide the kind of infrastructure and administrative support to lay the foundations for a sustainable programme in the longer term. Difficulties sustaining these requirements have been explored in the published literature [227]. Defining clinical referral pathways for identified deficits and ensuring access to appropriate interventions are important tasks to address before implementing CGA [228]. This requires good communication with other disciplines as part of the multidisciplinary pathway, which has historically been quite poor, with both professions traditionally working in a separate capacity, with little collaboration [229]. General Practitioners (GPs) are another untapped resource that could potentially be better utilised in geriatric oncology. GPs often feel excluded during cancer treatment, despite being a main point of contact for the patient, and often the best gatekeeper for access to support services in the local community [230, 231].

The literature review (Chapter 2) outlined the main schools of thought in relation to frailty, which lacks consensus in the medical gerontology literature, as well as in oncology. The two main schools of thought were outlined, i.e. the phenotype of frailty defined by Fried [63], from the Cardiovascular Health Study (CHS), and Rockwood's clinical frailty criteria [64], based on cumulative deficits on various CGA domains. The metaphor of the Golden Gate Bridge best describes the differences between these two operationalisations of frailty, and is depicted in Figure 2.2 in Chapter 2. Both of these models of frailty were investigated in the final study of this doctoral thesis.

The association between frailty and cancer was then explored, as well as the importance of assessing frailty in older adults with cancer.

There is now a well-known acceleration of frailty linked to cancer and its treatment [50-52]. Accumulation of cellular damage and system dysregulation are now established features of both ageing and cancer [51-54]. Frailty has been associated with increased mortality in older adults with cancer [60], however the definition of frailty in many studies has been heterogeneous [61]. Very few studies have investigated the association between the phenotypic or FI approaches in oncology, which was later explored in the second TILDA study of this PhD research.

The literature review also demonstrated that identification of previously unknown deficits is one of the major advantages of a CGA, allowing some intervention in order to optimise patient care. This is more beneficial for older adults with cancer, but younger frail patients may also benefit. CGA or Geriatric Assessment (GA) as it's commonly abbreviated to in oncology, is a multidimensional, interdisciplinary assessment that includes functional status, comorbidity, cognition, psychological status, nutrition, social support and polypharmacy, amongst others [87]. This assessment can provide a broader overall understanding of individual characteristics that affect life expectancy, functional decline, cognition and patient's own wishes, as well as how oncologic treatment might affect them [88]. These are important factors to consider when deciding on a course of treatment. GA is vital in "staging the ageing" i.e. assessing physiologic and functional capacity, which in turn has implications for being able to predict treatment tolerance and toxicity [170-173]. Accumulation of deficits, as defined by CGA, was investigated in both Chapters 4 and 5.

When it comes to oncology, the lack of consensus in relation to frailty assessment has been considered a major impediment to the advancement of the field of geriatric oncology. Puts et al [40] have

highlighted this lack of standardisation with regard to CGA domains and assessments in the published literature. The initial study (Chapter 3) of this PhD sought to overcome this barrier, by seeking consensus on the optimal form of frailty assessment for Irish oncology practice.

Having considered the published literature, and known research gaps, the thesis aims were formed through three main approaches. The first was to use consensus-based methods to inform the design of a GA for oncology practice. The second was to undertake a pilot study of this assessment in a clinical setting, while the third investigated the long-term impact of cancer and its treatment, using information from The Irish Longitudinal Study on Ageing (TILDA).

7.1.2 Summary of Study Findings

7.1.2.1 Delphi Study

Traditionally, the definition of frailty has lacked consensus in geriatric medicine, and needless to say, there is even less consensus in oncology regarding an appropriate adaptation from our colleagues in medical gerontology. This posed a first challenge in the PhD process, and the initial question was therefore how to optimally assess older adults with cancer, in order to identify frailty in a clinically meaningful manner. This was addressed in Chapter 3, with a Delphi study whose main aim was to establish consensus among a group of Irish Oncologists, with guidance from international experts, in relation to the optimal GA methodology for oncology clinical practice.

The underlying premise for this investigation was that the consensus achieved, through the input of a national panel, as well as an international panel of experts in geriatric oncology, would provide a

clinically acceptable assessment template for oncology practice in Ireland. This contribution of a standardized approach to the existing literature was an important step towards the clinical investigation of GA in oncology.

This first study of the doctoral thesis used the Delphi method in order to achieve its primary aim of achieving consensus. The Delphi method attempts to achieve convergence of opinion among experts on a specific topic, over a series of rounds or iterations, using a facilitated group approach. The basic process comprises a number of key steps i.e. convening an expert group, discussion and iteration with regard to a particular topic, and condensing data from this expert body in order to achieve consensus, using various statistical methods [275-277]. All of these steps are important in maintaining the methodological rigour of the approach [278]. While survey methodology defines the current status of events, the Delphi technique is used to define "what should be" [279]. It has been used extensively in healthcare, in order to set goals, policies or predict future events, and is especially useful where the relevant evidence base is lacking, as in the current context [280, 281].

Strengths of the Delphi technique include contribution to participant's knowledge base through the use of multiple rounds, promotion of decision-making, and achieving consensus on topics where little empirical evidence exists [298, 309]. It is an inexpensive way to share knowledge from various experts and stakeholders, from various countries, for whom face-to-face meetings would not be possible [298] It is for these reasons that the Delphi technique was used in this study.

Four Delphi rounds were undertaken, as it was envisaged that consensus would be difficult to achieve, due to the multidisciplinary

nature of the group, and the novel nature of GA in oncology for some participants (i.e. the Irish panel). The Delphi study achieved a reasonably low level of attrition throughout four rounds, perhaps highlighting the importance that participants felt would emerge from the process, and a growing interest in geriatric oncology. The panelists in this study clearly identified the criteria that should be included in a clinical geriatric oncology programme. Patient stratification and essential assessments and interventions to be included were identified through expert consensus.

Consensus was reached on all GA assessments and interventions considered to be important, apart from polypharmacy assessment, with significant agreement achieved, and no individual differences between the professional subgroups. Consensus was not reached on the use of a shorter screening tool that would identify those patients from an oncology clinical practice who could potentially benefit from GA, versus those who would not. This minimum dataset was further investigated in Chapter 4, via a pilot study in radiation oncology. It was anticipated that having a consensus-driven approach to implementation of geriatric oncology in Ireland, where no such model already existed, with inclusion of all of the relevant stakeholders from oncology and geriatric medicine, would aid in the implementation of this major change in practice. This was one of the first attempts in the literature to standardise the approach to frailty assessment, to our knowledge, and the approach was replicated in a subsequent US study [346]. Both studies were important research outputs from this doctoral thesis.

7.1.2.2 Pilot Geriatric Oncology Study

The acronym for this pilot study was Managing the Elderly in Radiotherapy using Geriatric AssEssment (MERGE). It should be

highlighted that towards the latter stages of this doctoral research, the term “elderly” was outruled as a term to describe older adults, as advocated by one of the most prominent journals in ageing research, the Journal of the American Geriatric Society or JAGS [579]. This recommendation is in keeping with the American Medical Association (AMA) style guide, as terms such as elderly “connote discrimination and certain negative stereotypes that may undercut research-based recommendations for better serving our needs as we age”. The thesis as a whole reflects this recommendation on language, where possible.

Chapter 4 aimed to use the results of the Delphi study to obtain preliminary data on the feasibility of implementing GA in clinical practice and the prevalence of geriatric impairments in an older patient population undergoing radiotherapy treatment in terms of GA-driven interventions on patient outcomes (acute radiation-induced toxicity and treatment compliance).

For the purpose of this doctoral thesis, the main advantage of the pilot study research setting in Saint Luke’s Radiation Oncology Network, was that it offered a clinical environment to investigate the feasibility and utility of the consensus-driven GA approach. In addition, it allowed the research to be conducted, predominantly in radiation oncology, which has been identified as an area that has lagged behind in terms of geriatric oncology research to date. It also had the advantage of being situated in a large academic hospital, with access to a multidisciplinary team, including geriatric medicine.

However, as explained in Chapter 4, the research design imposed limitations on the study. First, the recruitment rate was low over the designated time period of the study, which precluded the inference of causality. Second, the recruitment strategy used resulted in a

heterogeneous, non-random, convenience sample, which does not guarantee the external validity of the study findings. However, it may be interpreted as a pilot, that serves to inform the design of future, larger studies, as discussed in the future research section below.

In addition, Medical Research Council (MRC) guidelines on complex intervention evaluation advise a phased approach to the implementation of complex interventions in medicine [372]. This includes feasibility studies (whether the study can be carried out effectively) and pilot trials (a scaled down version of the trial), with the aim of optimising aspects of study design for consideration during a larger scale implementation of in the future. This ensures both internal validity in one's own institution and external validity, with real world relevance. This pilot study could be considered an important first step in evaluating how best to incorporate GA into Irish oncology clinical practice.

To our knowledge, this was the first study to attempt to systematically investigate the feasibility and acceptability of a randomised controlled trial investigating the implementation of GA in radiation oncology. The results of this small pilot study did not show a significant impact on treatment decisions in radiation oncology. This may reflect a lack of experience and familiarity with GA and how to interpret it, as well as an obvious gap in the literature as to how it affects radiotherapy patient outcomes. In addition, the study sample included predominantly fit and relatively young patients, which undoubtedly impacted these results.

The most significant finding of this pilot study was the number of previously unknown issues that were identified by GA, that clinicians may not have detected by routine assessment. These were identified and relayed to the medical team in 7 out of 15 patients in the

intervention arm. Inadequate social support and management of polypharmacy were the most commonly reported, followed by nutritional support, and finally psychological/ cognitive/mobility/falls risk/comorbidities.

7.1.2.3 TILDA Study I

The aim of this first analysis from The Irish LongituDinal Study on Ageing (TILDA) was to investigate to what extent community-dwelling older adults with cancer different from their non-cancer community dwelling counterparts. Building on the findings of previous chapters, it sought to compare cancer survivors to their non-cancer controls, in relation to physical, cognitive, psychological and social health and wellbeing, using data from Wave 1 of TILDA. It also sought to investigate the acute and longitudinal impact of a cancer diagnosis and treatment on the overall health and wellbeing of older adults with cancer living in the community during the diagnostic/treatment phase, and the follow-up period, using the pre-diagnostic phase as a baseline measure of function.

Although there is an increased focus on the need for survivorship data, research to date has been scant, compared to that of the active treatment phase [466, 467]. From a research perspective, there is little follow-up information with respect to GA measures and how the level of function impacts the everyday lives of patients after a diagnosis of cancer. Longitudinal studies are the perfect resource to investigate survivorship care, and to our knowledge, this was the first analysis of the TILDA cohort, which adds valuable information to the existing body of knowledge that TILDA has produced, much of which has had a substantial impact on health policy in Ireland.

This study investigated a range of common GA outcomes and their impact on those with and without cancer. A cross-sectional analysis of Wave 1 participants, followed by a longitudinal analysis of those with a new cancer diagnosis at Waves 2 and 3, both demonstrated a significantly higher burden of comorbidity and polypharmacy in those diagnosed with cancer, compared to non-cancer controls. In addition, in Wave 1, a greater proportion of participants diagnosed with cancer experienced a fall in the previous year. Multimorbidity is significant in terms of treatment decisions, as patients with cancer and significant comorbidity are known to have poorer overall survival [26, 502]. They also have greater needs in relation to healthcare, and there may also be a link between multimorbidity and (chemotherapy) treatment toxicity [503], as well as treatment incompletion [504].

Polypharmacy and multimorbidity are inherently linked, and in recent times, both the incidence and prevalence of polypharmacy have been increasing steadily in both the general population [490], and especially in those diagnosed with cancer [491]. There is a fourfold increased risk of frailty (measured by Fried criteria) in older (>70 years) adults, who report polypharmacy, defined as five or more medications [491]. To date, there have been few studies on the prevalence of polypharmacy and multimorbidity in the Irish oncology population. This is something that will become even more pressing in the coming years, due to the increasingly older population presenting for cancer treatment. One of the few studies from an Irish perspective, by Lavan et al [507], in a study of 350 patients with cancer, aged 70 years and older, in an Irish oncology centre, found that approximately 20% of hospital admissions in oncology were related to adverse drug reactions. The majority of these were found to be predictable, and more than 60% were preventable. This makes a convincing case for medication review as part of a CGA in oncology. Identification of previously unknown deficits is one of the

major advantages of a CGA, allowing some intervention in order to optimise patient care.

These results contrast with a similar analysis from Waves 1-6 of the English Longitudinal Study of Ageing (ELSA), that found poorer health outcomes in a cancer cohort (n=444;mean age 67) with regard to self-rated health, QoL and life satisfaction, as well as a higher incidence of depression, mobility problems and limitations with ADLs [127]. All of the studied outcomes became gradually worse over time, with the exception of depression. It should be noted however, that the study cohort used in the latter ELSA analysis was older, with a mean age of 71.4, versus 65.7 in the TILDA study. Even though the findings of this TILDA analysis were not significant for some domains related to physical and psychological health, variations in functional status [580, 581] and cognition [582, 583] are prevalent with advancing age, and represent competing causes of mortality in the face of a cancer diagnosis. The TILDA group was relatively young, and this first analysis serves as important baseline data to evaluate health and wellbeing over time.

A limitation imposed by the research was that the analysis was retrospective, therefore some measures from the Delphi consensus study could not be directly extrapolated from TILDA. However, other well validated measures were used instead (see Table 5.1 Chapter 5). Polypharmacy is a risk factor for frailty.

A further limitation to the longitudinal analysis in this study is, as is common to all longitudinal studies, attrition. Attrition can bias results as the frailest and oldest members of the population are less likely to be included in follow-up, leading to an unrepresentative sample. As demonstrated in Chapter 5, the longitudinal sample excluded those with poorer prognosis cancers, as a result of the time period under

investigation, spanning six years. The sample was already relatively young at baseline and thus attrition rates signified a further reduction in older adults. However, the use of attrition weights partially compensated for this attrition.

7.1.2.4 TILDA Study II

The aim of the final TILDA study (Chapter 6) was to investigate to what extent older adults with cancer in the community differ from their non-cancer community dwelling counterparts in relation to frailty. Frailty was characterised using three commonly used indices, using the TILDA data, and the prevalence of each type compared. For cross-sectional analysis, prevalence of frailty at Wave 1 was investigated, and compared to those without a cancer diagnosis.

A separate longitudinal analysis was also conducted to ascertain the frailty status of those who had reported a cancer diagnosis in Wave 1.

A phenotype of frailty was defined, as closely as possible, to the definition provided by Fried and colleagues [63]. A deficit accumulation frailty index (FI) was compiled [66], as described by Theou et al [68] and previous studies [469, 553]. Finally, five indicators, based on self-reported measures from TILDA CAPI questionnaire data, were used to construct the Morley FRAIL scale [532]. Comparing all three measures of frailty, the prevalence of frailty criteria was higher in the cancer arm, compared to the control arm, for all participants and all ages combined. Similar to previous studies of older adults, the cumulative deficits approach provided a higher estimate of frailty, compared to the phenotype model. The highest prevalence of frailty was provided by the FI approach 23.44% versus 13.98% in the cancer versus control group. The lowest overall

prevalence of frailty was provided by Morley criteria. A cancer diagnosis resulted in a greater risk of developing frailty when using the cumulative deficits and Morley approaches.

There are a number of other limitations to this work which must be highlighted. It was not possible to derive a comparable frailty measure in Waves 2 or 4 for comparison purposes, due to the lack of a health assessment in this wave, Therefore the longitudinal component of this analysis was small.

7.2 Implications for Policy and Practice

In considering the results of this thesis, it must be noted that the observed effects were small for some measures, perhaps due to the considerable differences between the cancer group and the control group for the TILDA analyses.

Although these changes are small, however, some results were over a short follow-up period of two years after a diagnosis of cancer, and it is of interest that there is any such difference in a community dwelling sample of relatively young older adults. It will, of course, be necessary to follow these participants in future waves to determine whether various aspects of frailty becomes progressively worse, and how it impacts the QoL of TILDA participants as they age.

SIOG and National Comprehensive Cancer Network (NCCN) guidelines for older adults advocate the use of CGA is vital in “staging the ageing” i.e. assessing physiologic and functional capacity, which in turn has implications for being able to predict treatment tolerance and toxicity[170-173]. The potential benefits in oncology are many, and include the identification of geriatric impairments, even in those with a good performance status [136, 174]. CGA can also predict

toxicity associated with chemotherapy in older adults [175] , as well as mortality [176] and postoperative morbidity [177, 178] Reasons put forward to date for a lack of integration of CGA into oncology have argued that it is too time consuming . However, it could be argued that those against the use of CGA, citing excessive time consumption and resource implications, have low credibility in a healthcare setting where there are vast amounts of expenditure on high technology for imaging and treatment [179]. CGA by comparison is relatively low cost, as Hamaker et al [179] have highlighted. The cost of CGA, estimated as a nurse's salary for one hour ($28), is small compared to the cost of dealing with toxicity and treatment complications, and subsequent unplanned hospitalisations. It is also a fraction of the cost of other diagnostic procedures e.g. diagnostic images and genomic testing, commonly used in oncology.

When independence is not maintained and poor outcomes occur, patients require hospital care. Troubleshooting these issues before they arise by using CGA as part of the diagnostic work-up to determine the most appropriate treatment can prevent reliance on hospital resources in the long-term. Frail patients are more likely to have poor outcomes following surgery, chemotherapy and radiotherapy [62]. In an outpatient setting, CGA-based care has resulted in fewer hospitalisation days and enhanced survival in patients with no associated increase in cost [180]. This not only benefits the patient, but also the health care system as a whole.

To implement CGA into clinical practice, there are educational requirements in the medical, nursing and allied health curricula that need to be addressed. Studies have highlighted there is an unmet need in this regard [41, 238]. In order to address this, efforts to devise a core curriculum in geriatric oncology have been undertaken by

several societies. ASCO [192] and the European Society of Medical Oncology (ESMO) [239] have both developed recommendations for geriatric oncology as a part of their global curricula. Likewise, the European Oncology Nursing Society (EONS) has also published recommendations for a core curriculum for geriatric oncology for the nursing profession [240]. Similar efforts are underway in radiation oncology [241]. SIOG have developed the Treviso Advanced Geriatric Oncology course [242] in order to enhance education and clinical practice for both the geriatrics and oncology disciplines . Initiatives such as these are vital to address the existing knowledge gap.

A recent report from the National Cancer Control Programme (NCCP) has highlighted the survivorship needs of those living with and beyond cancer in Ireland [575]. Cancer survivors comprised 4% of the Irish population in 2016, and greater recognition of the physical and psychological consequence of a cancer diagnosis were highlighted as key priorities from this report. Most follow-up care is currently delivered in hospitals, and it was suggested that this be reviewed so that a model of more integrated care may be provided. This is especially important in the context of longitudinal assessment and management of frailty. It was also stressed that meeting the needs of cancer survivors would require more detailed information from research in the post-treatment phase. Longitudinal studies, such as TILDA are useful resources to help fill this important gap. Although the overall numbers with a cancer diagnosis in TILDA are small, they are indicative of areas of clinical priority.

To that end, and as recommended by national policy, implementation of GA in oncology should be prioritised. This should not only be limited to the treatment phase, but continue through to survivorship

care to provide more robust evidence for the specific concerns of older adults with cancer.

7.3 Recommendations for Future Research

Throughout the period of this doctoral thesis (2012-2019), there have been parallel developments in the field of geriatric oncology that have been greatly encouraging.

Based on some of the limitations encountered throughout this research, some themes for future research are outlined below:

The pilot study findings of identified deficits from GA, as well as the first TILDA study requires further exploration, under more controlled conditions of time and setting, as well as in more homogeneous cancer groups. In particular, the role of CGA-driven interventions in enhancing patient care in radiation oncology is a key priority. Inclusion of more vulnerable and frail patients will also help to elucidate this area.

The TILDA study findings of increased polypharmacy in those with a diagnosis of cancer requires further exploration. As polypharmacy is a risk factor for falls, which were also elevated in Wave 1 in the cancer group, falls risk assessment and a review of medications should become part of the ongoing assessment of those diagnosed with cancer.

The development of evidence-based guidelines is important to facilitate clinical practice improvements regardless of the resource setting in which they are applied. As geriatric oncology is

underdeveloped in Ireland at the moment, this is a research priority for Irish institutions and funding organisations. Guidelines should recognize that care of older adults is multidisciplinary, and that attention to age-related concerns forms an integral part of oncology clinical practice.

These guidelines, and the evidence to underpin them, should cover the whole spectrum of care: GA assessment and interventions to inform treatment decisions, toxicity prevention, approach to specific disease types, pre- and re-habilitation, through to survivorship care. While the majority of analyses in this doctoral thesis comprised a heterogeneous cancer group, future studies should aim to investigate specific disease subtypes and develop appropriate age-related guidelines. More research in radiation oncology in particular is a key priority.

Further to the aforementioned recommendations to develop evidence to improve care, there is a great need to develop novel trial designs in geriatric oncology research, and to make current research more relevant to older adults. Although survival is recognised as the most valuable outcome of any clinical trial, it may not be the most valued outcome for older adults with cancer [181], who have been shown to place greater importance on their functional and cognitive health. A workshop held by the European Organisation for Research and Treatment of Cancer (EORTC) in 2011 [28] explored methods of improving clinical design and suggested looking at alternative endpoints, such as QoL, toxicity and functional independence. These endpoints need to be incorporated into future research. Selection of more appropriate endpoints is important in “geriatricizing” trial design [31-33]. This has been highlighted by Nipp et al [34], who described the need for pragmatic clinical trials for older adults with cancer. Whereas RCTs reflect patient outcomes under ideal conditions, there

is a large unmet need to investigate older patient outcomes under more realistic conditions i.e. varying degrees of fitness and frailty. Incorporating some form of frailty assessment is essential in better quantifying outcomes for older adults with cancer.

As determined in the initial stages of this PhD, reaching a consensus on a minimum dataset for GA in oncology is important, but remains elusive, in order to enhance the interpretation of existing research.

7.4 Conclusions

The overall aim of this thesis was to measure geriatric deficits and frailty in an Irish (hospital and community) population with cancer and to study feasibility of geriatric assessment in a radiation oncology clinic. In order to achieve that aim, four individual studies were conducted.

The first Delphi study provided a valuable framework for a consensus-based development of geriatric assessments and interventions for oncology which formed the basis for this PhD research. In the absence of evidence-based guidelines in the initial stages, this Delphi expert consensus on geriatric oncology design and implementation provided a useful template for clinicians regarding multidimensional assessment of older patients with cancer, although more data are needed to clarify the clinical efficacy of this approach. This Delphi study helped to inform the future development and implementation of a pilot geriatric oncology programme in Ireland, the first such programme in Ireland.

The pilot study did not have a significant effect on clinical practice and decision making in oncology. However, it highlighted a number of issues in relation to feasibility and recommendations to be made

going forward to a more extensive study. This is important groundwork for future research which should aim to investigate the impact of GA under more controlled conditions, and in better refined, and older patient populations.

The first TILDA longitudinal analyses spanning pre- and post-cancer diagnosis, suggested that cancer survivors bear a greater burden of multimorbidity, compared to their counterparts without a cancer diagnosis. The prevalence of polypharmacy and falls was also higher. This has implications for oncology clinical practice, as these deficits are known to be associated with greater healthcare utilisation and adverse outcomes for older adults. These findings support the recommendation for implementation of GA in oncology, not only during the treatment phase, but during follow-up care.

Finally, in the second TILDA study, a secondary analysis of a large nationwide study of frailty in cancer patients, it was determined that patients with cancer had higher frailty scores compared with noncancer controls. Given that frailty is a known risk factor for patients with cancer, and older patients in particular, consideration of this aging-related phenotype needs to be considered by all healthcare practitioners treating patients with cancer. Interventions are needed to minimize the progression of frailty and to possibly reverse onset of premature frailty.

Collectively, these data have the potential to inform treatment decision making and survivorship care planning for older adults with cancer, bearing in mind the aforementioned caveats in relation to the limitations encountered during this doctoral thesis, and recommendations for future work.

Chapter 8

8 References

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583. Plassman, B.L., et al., *Prevalence of dementia in the United States: The aging, demographics, and memory study.* Neuroepidemiology, 2007. **29**(1-2): p. 125-132.

Appendices

Appendix 1: Study 1 Ethical Approval

Coláiste na Tríonóide, Baile Átha Cliath
Trinity College Dublin
Ollscoil Átha Cliath | The University of Dublin

Anita O'Donovan
Discipline of Radiation Therapy
Trinity College Dublin, the University of Dublin
Dublin 2,
Ireland.

Title of Study: **Feasibility study of the implementation of comprehensive geriatric assessment in Irish Oncology Departments.**

Date & Duration of Study: August 2012 – February 2013

Dear Anita,

Further to a meeting of the Faculty of Health Sciences Ethics Committee held in June 2012. We are pleased to inform you that the above project has ethical approval to proceed.

Yours sincerely,

pp Síne Bowan

Prof. Jacintha O'Sullivan
Chairperson
Faculty Research Ethics Committee

Dámh na nEolaíochtaí Sláinte
Foirgneamh na Ceimice,
Coláiste na Tríonóide,
Ollscoil Átha Cliath,
Baile Átha Cliath 2, Éire.

Faculty of Health Sciences
Chemistry Building,
Trinity College Dublin,
The University of Dublin,
Dublin 2,Ireland.

www.healthsciences.tcd.ie

Valerie Owens<Valerie.owens@slh.ie>

Fri 06/07/2012, 12:00

Re: A Delphi Consensus Study of Geriatric Assessment in Oncology

Dear Anita,

Just a note to let you know your research proposal was reviewed and approved at a meeting of the SLRON Research Management Committee yesterday.

Regards,

Valerie.

Appendix 2: Delphi Participant Informed Consent form

INFORMED CONSENT FORM

PROJECT TITLE: Feasibility Study of the Implementation of Comprehensive Geriatric Assessment in Irish Oncology Departments: Phase 1 Delphi Investigation of Geriatric Oncology Experts.

PRINCIPAL INVESTIGATOR: Anita O'Donovan

BACKGROUND

The aims and objectives of this study are to carry out a qualitative study of Irish Geriatricians and Oncologists (both Radiation and Medical),as well as International Society of Geriatric Oncology (SIOG) members, to evaluate what should be incorporated into a Comprehensive Geriatric Assessment for the older oncology patient population. A series of Delphi rounds will be conducted to achieve the study objectives. These will be submitted via a series of online surveys, with the participant's consent, and all data collected as part of this research will be anonymised and stored securely in the Discipline of Radiation Therapy. Research data will be used to design an assessment method for older Oncology patients that will subsequently be piloted in selected Irish Oncology departments. Data collected as part of this research may be used in research publications.

DECLARATION:

I have read, or had read to me, the information leaflet for this project and I understand the contents. I have had the opportunity to ask questions and all my questions have been answered to my satisfaction. I understand that I will remain anonymous to the other participants (or experts) throughout this Delphi study, and that my responses will be anonymised via the use of online surveys and an assigned study ID. I freely and voluntarily agree to be part of this research study, though without prejudice to my legal and ethical rights. I understand that I may withdraw from the study at any time and I have received a copy of this agreement.

I consent to being acknowledged as part of the expert panel for this study:

YES ■ NO ☐

PARTICIPANT'S NAME:.

CONTACT DETAILS:

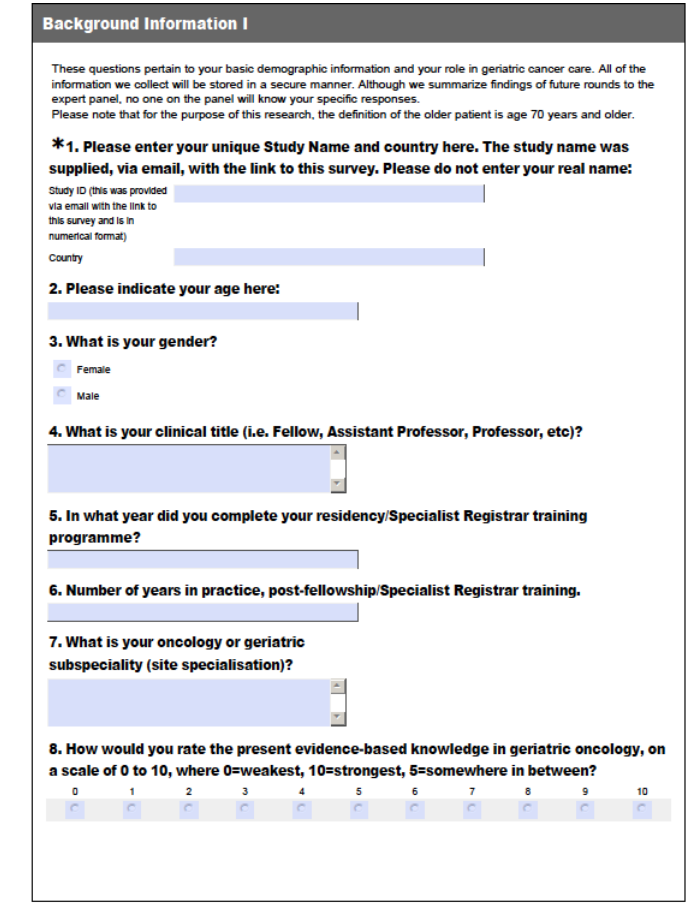
PARTICIPANT'S SIGNATURE:

Statement of investigator's responsibility: I have explained the nature and purpose of this research study, the procedures to be undertaken and any risks that may be involved. I have offered to answer any questions and fully answered such questions. I believe that the participant understands my explanation and has freely given informed consent.

INVESTIGATOR'S SIGNATURE:..... Date:.....

(Keep the original of this form in the investigator's file, give one copy to the participant, and send one copy to the sponsor (if there is a sponsor).

Appendix 3: Study 1 Demographic Survey of Participants



Background Information I

These questions pertain to your basic demographic information and your role in geriatric cancer care. All of the information we collect will be stored in a secure manner. Although we summarize findings of future rounds to the expert panel, no one on the panel will know your specific responses.
Please note that for the purpose of this research, the definition of the older patient is age 70 years and older.

***1. Please enter your unique Study Name and country here. The study name was supplied, via email, with the link to this survey. Please do not enter your real name:**

Study ID (this was provided via email with the link to this survey and is in numerical format)

Country

2. Please indicate your age here:

3. What is your gender?

- Female
- Male

4. What is your clinical title (i.e. Fellow, Assistant Professor, Professor, etc)?

5. In what year did you complete your residency/Specialist Registrar training programme?

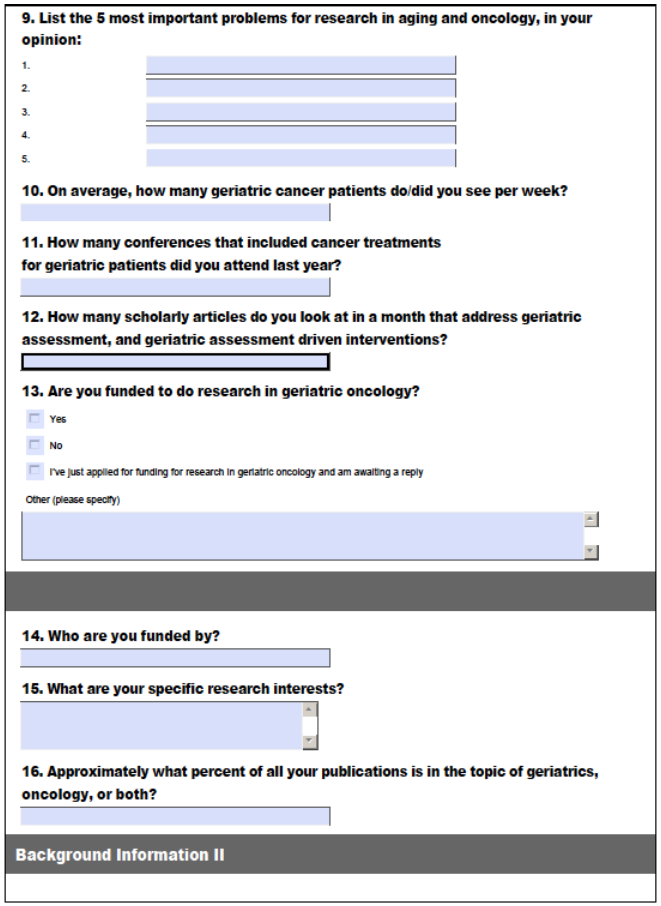
6. Number of years in practice, post-fellowship/Specialist Registrar training.

7. What is your oncology or geriatric subspeciality (site specialisation)?

8. How would you rate the present evidence-based knowledge in geriatric oncology, on a scale of 0 to 10, where 0=weakest, 10=strongest, 5=somewhere in between?

0 1 2 3 4 5 6 7 8 9 10

Page 1



9. List the 5 most important problems for research in aging and oncology, in your opinion:

1.
2.
3.
4.
5.

10. On average, how many geriatric cancer patients do/did you see per week?

11. How many conferences that included cancer treatments for geriatric patients did you attend last year?

12. How many scholarly articles do you look at in a month that address geriatric assessment, and geriatric assessment driven interventions?

13. Are you funded to do research in geriatric oncology?

- Yes
- No
- I've just applied for funding for research in geriatric oncology and am awaiting a reply

Other (please specify)

14. Who are you funded by?

15. What are your specific research interests?

16. Approximately what percent of all your publications is in the topic of geriatrics, oncology, or both?

Background Information II

Page 2

This section pertains to the role of geriatric cancer care in your practice/institution.

17. Is your principal clinical institution:

- General Multi-specialty hospital
- Specialty Cancer Center
- Outpatient Care only

Other (please specify)

18. Is your institution a:

- University Affiliated Teaching Hospital
- Private Practice/Private Non-teaching Hospital
- National Health Service/Public Hospital

Other (please specify)

19. Does your institution have: (Check all that apply)

- A geriatric medicine department/service
- An outpatient clinic in geriatrics
- A designated outpatient clinical program for older cancer patients
- A designated inpatient unit for older cancer patients
- A designated inpatient consult service for older cancer patients
- Designated fellowship training program in geriatrics
- Designated fellowship training program in haematology/oncology
- Designated dual training program in geriatrics and oncology

20. Approximately how many geriatricians (MD) are at your centre?

21. Approximately how many oncologists with geriatric interests are at your centre?

22. Do you have regularly scheduled case conferences or tumor boards to discuss geriatric oncology cases?

- Yes
- No
- I don't know

23. Is there a regularly scheduled interdisciplinary team meeting (medical oncology, geriatrics, social work, nutritionist, etc)to discuss elderly care at your hospital?

- Yes
- No
- I don't know

24. Excluding this study, do you have a forum to present geriatric oncology research concepts (at your institution or elsewhere), where you can obtain feedback from both oncologists and geriatricians?

- Yes
- No
- I don't know

25. If yes, please describe:

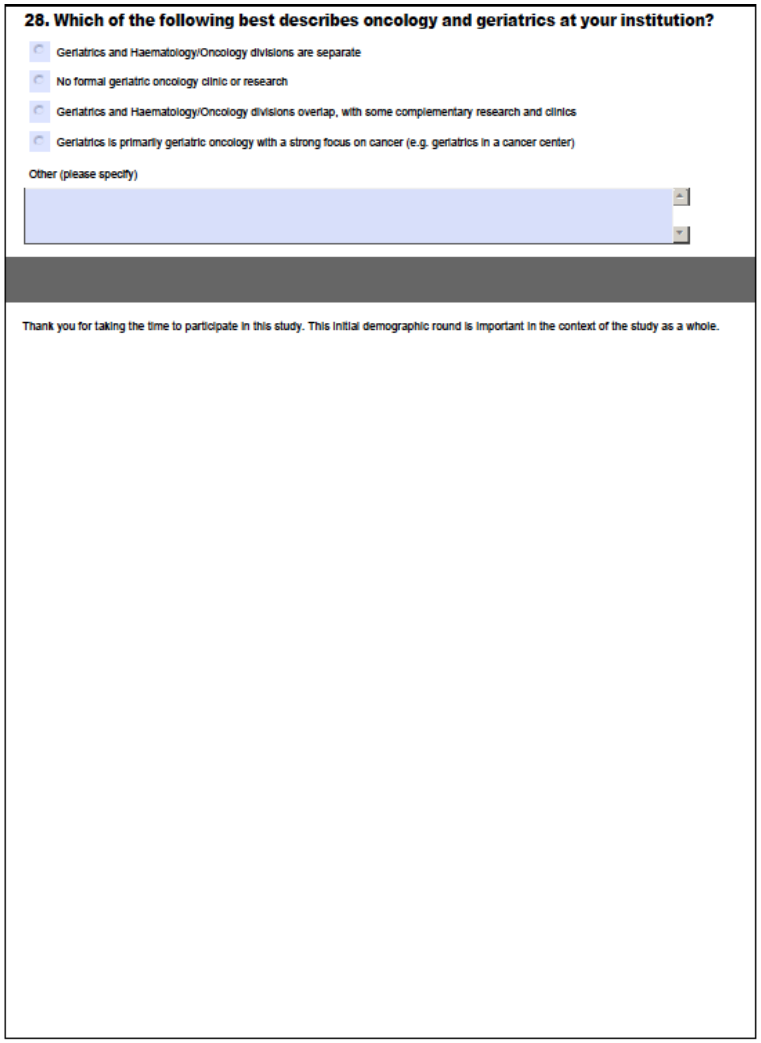
26. At your institution, would you consider anyone in the following disciplines as a contact person who specialises in older patients? (Check all that apply)

- Nutrition
- Physiotherapy
- Occupational Therapy
- Pharmacy
- Nursing
- Medical Oncology
- Radiation Oncology
- Surgery

Other (please specify)

27. My institution supports my geriatric-oncology research (if applicable):

- Strongly Agree
- Somewhat Agree
- Somewhat Disagree
- Strongly Disagree
- NA



28. Which of the following best describes oncology and geriatrics at your institution?

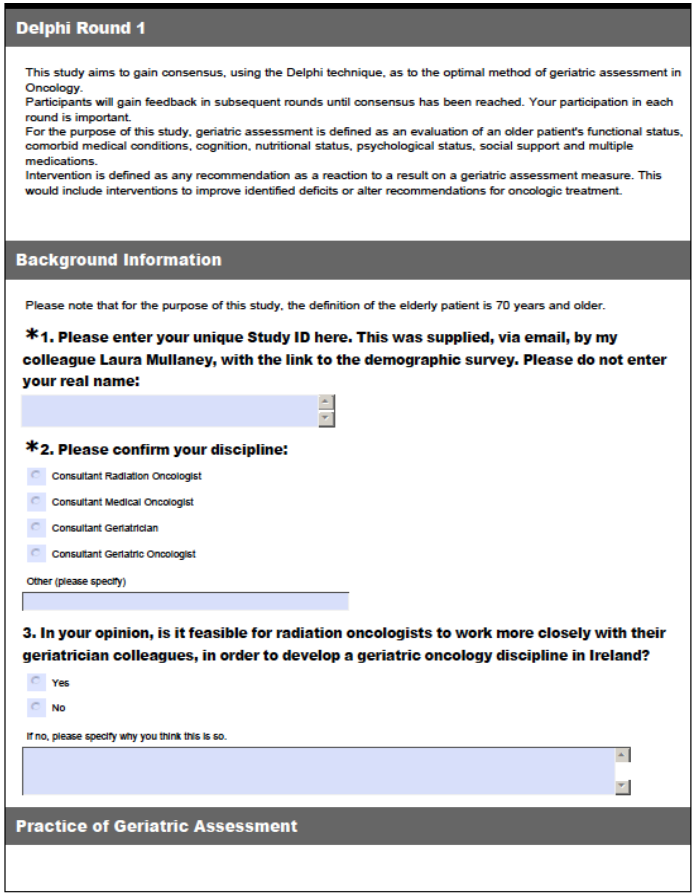
- Geriatrics and Haematology/Oncology divisions are separate
- No formal geriatric oncology clinic or research
- Geriatrics and Haematology/Oncology divisions overlap, with some complementary research and clinics
- Geriatrics is primarily geriatric oncology with a strong focus on cancer (e.g. geriatrics in a cancer center)

Other (please specify)

Thank you for taking the time to participate in this study. This initial demographic round is important in the context of the study as a whole.

Page 5

Appendix 4a: Study 1 Round 1 Survey Radiation Oncologists



Delphi Round 1

This study aims to gain consensus, using the Delphi technique, as to the optimal method of geriatric assessment in Oncology.
Participants will gain feedback in subsequent rounds until consensus has been reached. Your participation in each round is important.
For the purpose of this study, geriatric assessment is defined as an evaluation of an older patient's functional status, comorbid medical conditions, cognition, nutritional status, psychological status, social support and multiple medications.
Intervention is defined as any recommendation as a reaction to a result on a geriatric assessment measure. This would include interventions to improve identified deficits or alter recommendations for oncologic treatment.

Background Information

Please note that for the purpose of this study, the definition of the elderly patient is 70 years and older.

***1. Please enter your unique Study ID here. This was supplied, via email, by my colleague Laura Mullaney, with the link to the demographic survey. Please do not enter your real name:**

***2. Please confirm your discipline:**

- Consultant Radiation Oncologist
- Consultant Medical Oncologist
- Consultant Geriatrician
- Consultant Geriatric Oncologist

Other (please specify)

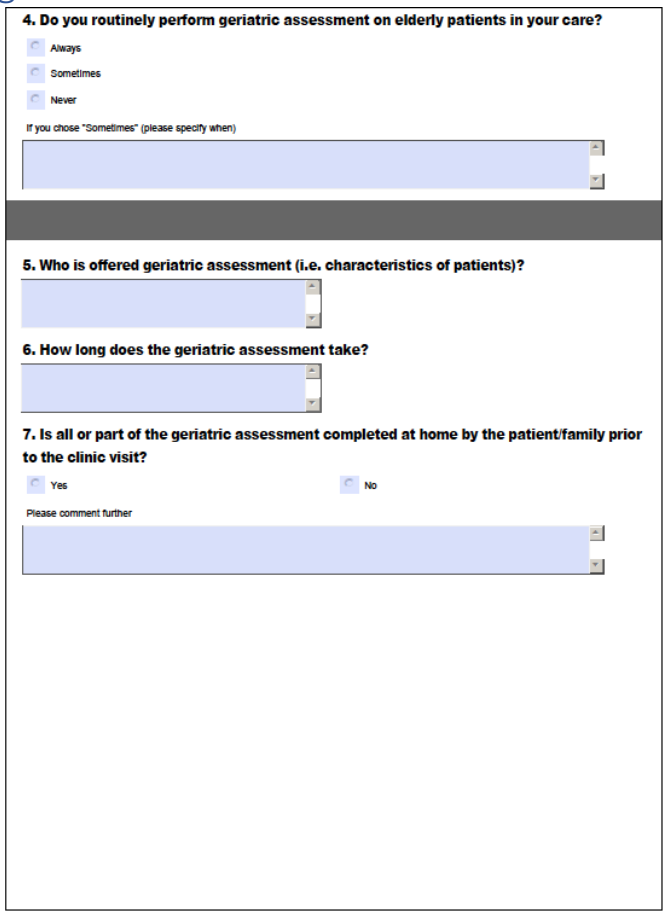
3. In your opinion, is it feasible for radiation oncologists to work more closely with their geriatrician colleagues, in order to develop a geriatric oncology discipline in Ireland?

- Yes
- No

If no, please specify why you think this is so.

Practice of Geriatric Assessment

Page 1



4. Do you routinely perform geriatric assessment on elderly patients in your care?

- Always
- Sometimes
- Never

If you chose "Sometimes" (please specify when)

5. Who is offered geriatric assessment (i.e. characteristics of patients)?

6. How long does the geriatric assessment take?

7. Is all or part of the geriatric assessment completed at home by the patient/family prior to the clinic visit?

- Yes
- No

Please comment further

Page 2

8. What staff members participate in the interpretation of geriatric assessment? (Choose all that apply)

- Geriatric Oncologist
- Geriatrician
- Radiation Oncologist
- Medical Oncologist
- Palliative Care team
- Social worker
- Dietician
- Physiotherapist
- Occupational therapist
- Psychologist
- Psycho-oncology liaison nurse
- Pharmacist
- Nurse
- Nurse Practitioner

Other (please specify)

9. In your opinion, what are the educational needs required to implement geriatric assessment in your institution?

10. Do you use assessment results to identify patients at high risk for adverse outcomes in your practice?

- Yes
- No

11. Do you use a fit/vulnerable/frail model?

- Yes
- I don't know what this is
- No

12. How do you determine patients for each category of the model?

13. How do you use geriatric assessment to identify patients at high risk for adverse outcomes?

14. Do you recommend interventions based on geriatric assessment (please see definitions at the beginning of the survey)?

- Yes
- No

15. How do you currently estimate life expectancy in your elderly patient population?

16. What are the potential barriers that you anticipate regarding implementation of geriatric assessment for older patients at your institution?

Process

17. In your opinion, is there an age cut-off that should be used to establish a standard for who should undergo geriatric assessment in Oncology?

- Yes
- No

18. What age?

- 65 and over
- 70 and over
- 75 and over
- 80 and over
- 85 and over

Why did you choose this age?

19. If you do not have an age cut-off, please explain why not?

20. In your opinion, what patient characteristics should be used to establish guidelines for who should undergo geriatric assessment in Oncology?

21. Please rate the importance of using geriatric assessment to help inform the following oncology treatment decisions:

	Not important 0	1	2	3	4	5	6	7	8	9	very important 10	I don't know
Screening for cancer												
Undergoing invasive diagnostic procedures for cancer												
Prior to radiotherapy (for curative intent)												
Prior to palliative radiotherapy												
During a course of radiotherapy												
Survivorship care (after completion of treatment)												
Deciding on dose and fractionation in radiotherapy												

What other kinds of treatment decisions in oncology do you think geriatric assessment could help inform?

22. Please rate the importance of including the following team members for developing recommendations based on geriatric assessment results in an Oncology setting:

	Not Important 0	1	2	3	4	5	6	7	8	9	Very Important 10
Radiation Oncologist											
Medical Oncologist											
Geriatrician											
Radiation therapist											
Palliative care team											
Social worker											
Dietician											
Physiotherapist											
Occupational therapist											
Psychologist											
Pharmacist											
Nurse											
Nurse practitioner											
Psycho-oncology liaison nurse											

You may add other important team members, comments and thoughts:

23. What is the ideal process for patients to complete geriatric assessment (e.g. mailed, web-based, ipads, in person)?

24. Rate the importance of the following domains to be included in geriatric assessment of oncology patients:

	Not Important 0	1	2	3	4	5	6	7	8	9	Very Important 10
Functional status	○	○	○	○	○	○	○	○	○	○	○
Objective physical performance (e.g. gait, speed, balance, strength)	○	○	○	○	○	○	○	○	○	○	○
Comorbidity	○	○	○	○	○	○	○	○	○	○	○
Medications	○	○	○	○	○	○	○	○	○	○	○
Nutrition	○	○	○	○	○	○	○	○	○	○	○
Social support	○	○	○	○	○	○	○	○	○	○	○
Psyhological status - Anxiety	○	○	○	○	○	○	○	○	○	○	○
Psychological status - Depression	○	○	○	○	○	○	○	○	○	○	○
Cognition	○	○	○	○	○	○	○	○	○	○	○

You may add comments of other domains that you believe are important in geriatric assessment:

25. What do you believe are the three most important domains and why?

Screening Tools and Interventions in Geriatric Assessment

26. Do you currently assess each of the following domains of geriatric assessment in clinical practice?

	Yes	No
Functional impairment	○	○
Physical performance impairment (eg gait speed, balance, strength)	○	○
Cognitive impairment	○	○
Co-morbidities	○	○
Polypharmacy	○	○
Nutritional impairment	○	○
Social support impairment	○	○
Anxiety	○	○
Depression	○	○

Please specify any other assessment that you use:

27. Please list any assessment tool(s) that you currently use in your clinical practice, to screen for the following:

Functional impairment	
Physical performance impairment (eg gait speed, balance, strength)	
Cognitive impairment	
Co-morbidities	
Polypharmacy	
Nutritional impairment	
Social support impairment	
Anxiety	
Depression	
Other (please specify)	

28. Please list interventions, if any, that you would recommend for impairments in the following:

Functional status	
Physical performance status (eg gait speed, balance, strength)	
Cognitive status	
Co-morbidities	
Polypharmacy	
Nutritional status	
Social support	
Anxiety	
Depression	
Other (please specify)	

29. Are there any other healthcare professionals who would be essential in developing interventions for the following:

Functional status	
Physical performance status (eg gait speed, balance, strength)	
Cognitive status	
Co-morbidities	
Polypharmacy	
Nutritional status	
Social support	
Anxiety	
Depression	
Other (please specify)	

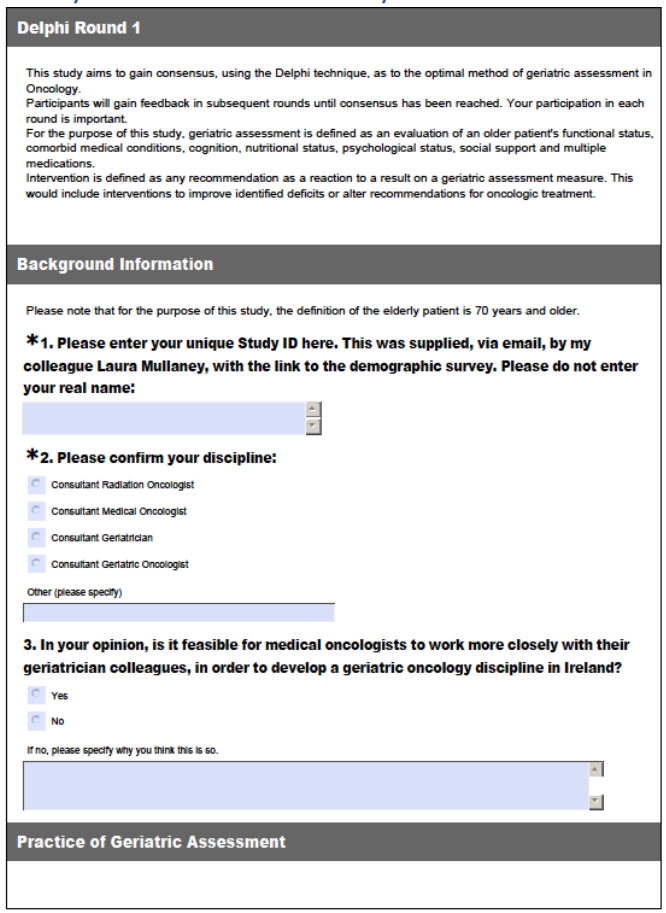
30. Should impairments in any of the following affect cancer treatment decisions, in your opinion?

	Yes	No	I don't know
Functional status	○	○	○
Physical performance status (eg gait speed, balance, strength)	○	○	○
Cognitive status	○	○	○
Co-morbidities	○	○	○
Polypharmacy	○	○	○
Nutritional status	○	○	○
Social support	○	○	○
Anxiety	○	○	○
Depression	○	○	○

For any domains that you've indicated should influence decisions, please indicate how:

Thank you for taking the time to participate in this study. Your contribution is greatly appreciated.

Appendix 4b: Study 1 Round 1 Survey Medical Oncologists



Delphi Round 1

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Intervention is defined as any recommendation as a reaction to a result on a geriatric assessment measure. This would include interventions to improve identified deficits or alter recommendations for oncologic treatment.

Background Information

Please note that for the purpose of this study, the definition of the elderly patient is 70 years and older.

***1. Please enter your unique Study ID here. This was supplied, via email, by my colleague Laura Mullaney, with the link to the demographic survey. Please do not enter your real name:**

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- Consultant Radiation Oncologist
- Consultant Medical Oncologist
- Consultant Geriatrician
- Consultant Geriatric Oncologist

Other (please specify)

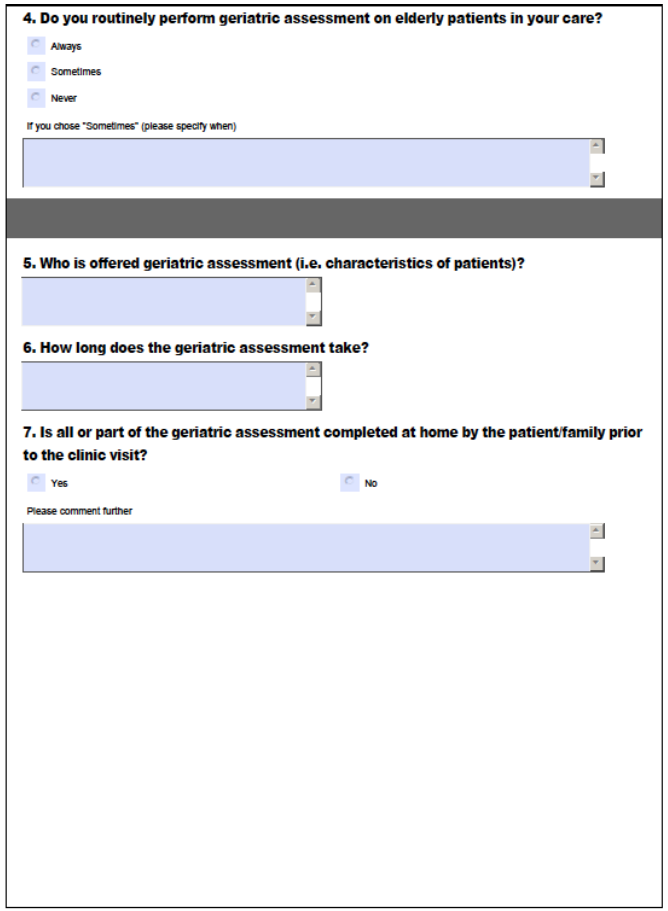
3. In your opinion, is it feasible for medical oncologists to work more closely with their geriatrician colleagues, in order to develop a geriatric oncology discipline in Ireland?

- Yes
- No

If no, please specify why you think this is so.

Practice of Geriatric Assessment

Page 1



4. Do you routinely perform geriatric assessment on elderly patients in your care?

- Always
- Sometimes
- Never

If you chose "Sometimes" (please specify when)

5. Who is offered geriatric assessment (i.e. characteristics of patients)?

6. How long does the geriatric assessment take?

7. Is all or part of the geriatric assessment completed at home by the patient/family prior to the clinic visit?

- Yes
- No

Please comment further

Page 2

8. What staff members participate in the interpretation of geriatric assessment? (Choose all that apply)

- Geriatric Oncologist
- Geriatrician
- Radiation Oncologist
- Medical Oncologist
- Palliative Care team
- Social worker
- Dietician
- Physiotherapist
- Occupational therapist
- Psychologist
- Psycho-oncology liaison nurse
- Pharmacist
- Nurse
- Nurse Practitioner

Other (please specify)

9. In your opinion, what are the educational needs required to implement geriatric assessment in your institution?

10. Do you use assessment results to identify patients at high risk for adverse outcomes in your practice?

- Yes
- No

11. Do you use a fit/vulnerable/frail model?

- Yes
- No
- I don't know what this is

12. How do you determine patients for each category of the model?

13. How do you use geriatric assessment to identify patients at high risk for adverse outcomes?

14. Do you recommend interventions based on geriatric assessment (please see definitions at the beginning of the survey)?

- Yes
- No

15. How do you currently estimate life expectancy in your elderly patient population?

16. How do you currently estimate life expectancy in your elderly patient population?

17. What are the potential barriers that you anticipate regarding implementation of geriatric assessment for older patients at your institution?

Process

18. In your opinion, is there an age cut-off that should be used to establish a standard for who should undergo geriatric assessment in Oncology?

- Yes
- No

19. What age?

- 65 and over
- 70 and over
- 75 and over
- 80 and over
- 85 and over

Why did you choose this age?

20. If you do not have an age cut-off, please explain why not?

21. In your opinion, what patient characteristics should be used to establish guidelines for who should undergo geriatric assessment in Oncology?

22. Please rate the importance of using geriatric assessment to help inform the following oncology treatment decisions:

	Not important 0	1	2	3	4	5	6	7	8	9	very important 10	I don't know
Screening for cancer												
Undergoing invasive diagnostic procedures for cancer												
Prior to chemotherapy (for curative intent)												
Prior to palliative chemotherapy												
During a course of chemotherapy												
Survivorship care (after completion of treatment)												
Chemotherapy dosing and schedule												

What other kinds of treatment decisions in oncology do you think geriatric assessment could help inform?

23. Please rate the importance of including the following team members for developing recommendations based on geriatric assessment results in an Oncology setting:

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Medical Oncologist											
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Physiotherapist											
Occupational therapist											
Psychologist											
Pharmacist											
Nurse											
Nurse practitioner											
Psycho-oncology liaison nurse											

You may add other important team members, comments and thoughts:

24. What is the ideal process for patients to complete geriatric assessment (e.g. mailed, web-based, ipads, in person)?

25. Rate the importance of the following domains to be included in geriatric assessment of oncology patients:

	Not Important 0	1	2	3	4	5	6	7	8	9	Very Important 10
Functional status	○	○	○	○	○	○	○	○	○	○	○
Objective physical performance (e.g. gait, speed, balance, strength)	○	○	○	○	○	○	○	○	○	○	○
Comorbidity	○	○	○	○	○	○	○	○	○	○	○
Medications	○	○	○	○	○	○	○	○	○	○	○
Nutrition	○	○	○	○	○	○	○	○	○	○	○
Social support	○	○	○	○	○	○	○	○	○	○	○
Psyhological status - Anxiety	○	○	○	○	○	○	○	○	○	○	○
Psychological status - Depression	○	○	○	○	○	○	○	○	○	○	○
Cognition	○	○	○	○	○	○	○	○	○	○	○

You may add comments of other domains that you believe are important in geriatric assessment:

26. What do you believe are the three most important domains and why?

Screening Tools and Interventions in Geriatric Assessment

27. Do you currently assess each of the following domains of geriatric assessment in clinical practice?

	Yes	No
Functional impairment	○	○
Physical performance impairment (eg gait speed, balance, strength)	○	○
Cognitive impairment	○	○
Co-morbidities	○	○
Polypharmacy	○	○
Nutritional impairment	○	○
Social support impairment	○	○
Anxiety	○	○
Depression	○	○

Please specify any other assessment that you use:

28. Please list any assessment tool(s) that you currently use in your clinical practice, to screen for the following:

Functional impairment	
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Cognitive impairment	
Co-morbidities	
Polypharmacy	
Nutritional impairment	
Social support impairment	
Anxiety	
Depression	
Other (please specify)	

29. Please list interventions, if any, that you would recommend for impairments in the following:

Functional status	
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Cognitive status	
Co-morbidities	
Polypharmacy	
Nutritional status	
Social support	
Anxiety	
Depression	
Other (please specify)	

30. Are there any other healthcare professionals who would be essential in developing interventions for the following:

Functional status	
Physical performance status (eg gait speed, balance, strength)	
Cognitive status	
Co-morbidities	
Polypharmacy	
Nutritional status	
Social support	
Anxiety	
Depression	
Other (please specify)	

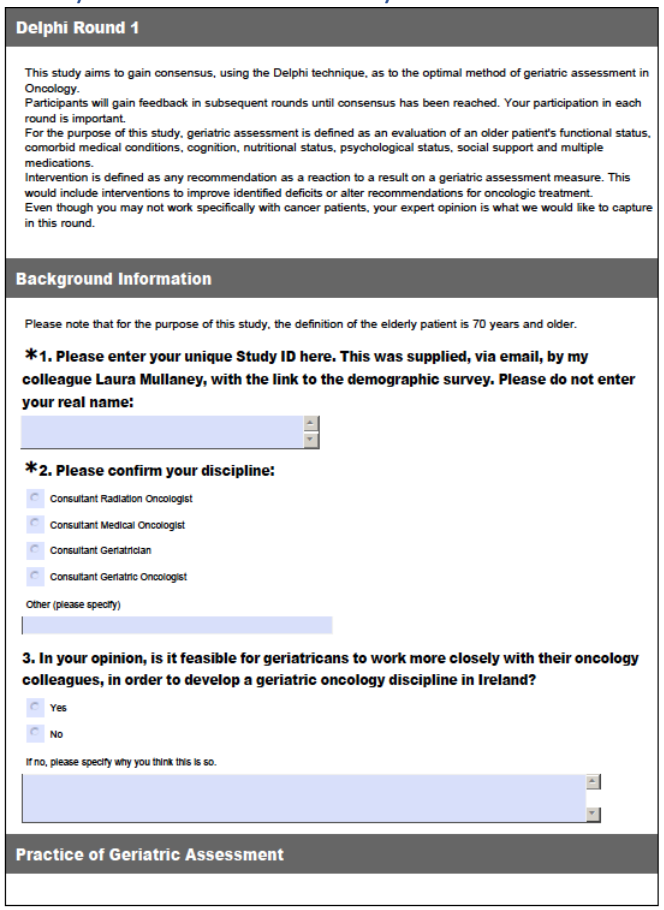
31. Should impairments in any of the following affect cancer treatment decisions, in your opinion?

	Yes	No	I don't know
Functional status	○	○	○
Physical performance status (eg gait speed, balance, strength)	○	○	○
Cognitive status	○	○	○
Co-morbidities	○	○	○
Polypharmacy	○	○	○
Nutritional status	○	○	○
Social support	○	○	○
Anxiety	○	○	○
Depression	○	○	○

For any domains that you've indicated should influence decisions, please indicate how:

Thank you for taking the time to participate in this study. Your contribution is greatly appreciated.

Appendix 4c: Study 1 Round 1 Survey Geriatricians



Delphi Round 1

This study aims to gain consensus, using the Delphi technique, as to the optimal method of geriatric assessment in Oncology.
Participants will gain feedback in subsequent rounds until consensus has been reached. Your participation in each round is important.
For the purpose of this study, geriatric assessment is defined as an evaluation of an older patient's functional status, comorbid medical conditions, cognition, nutritional status, psychological status, social support and multiple medications.
Intervention is defined as any recommendation as a reaction to a result on a geriatric assessment measure. This would include interventions to improve identified deficits or alter recommendations for oncologic treatment.
Even though you may not work specifically with cancer patients, your expert opinion is what we would like to capture in this round.

Background Information

Please note that for the purpose of this study, the definition of the elderly patient is 70 years and older.

***1. Please enter your unique Study ID here. This was supplied, via email, by my colleague Laura Mullaney, with the link to the demographic survey. Please do not enter your real name:**

***2. Please confirm your discipline:**

- Consultant Radiation Oncologist
- Consultant Medical Oncologist
- Consultant Geriatrician
- Consultant Geriatric Oncologist

Other (please specify)

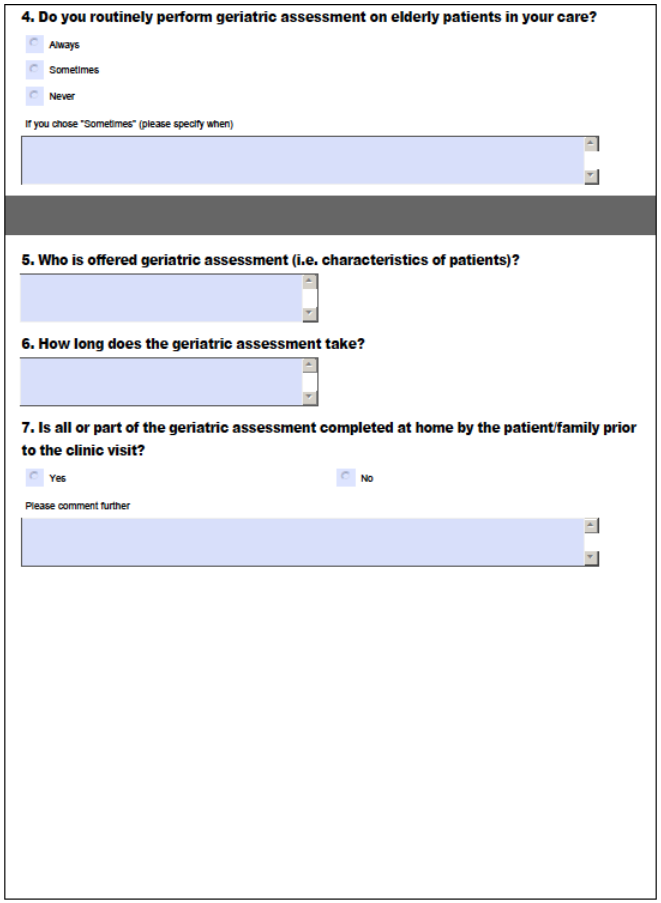
3. In your opinion, is it feasible for geriatricans to work more closely with their oncology colleagues, in order to develop a geriatric oncology discipline in Ireland?

- Yes
- No

If no, please specify why you think this is so.

Practice of Geriatric Assessment

Page 1



4. Do you routinely perform geriatric assessment on elderly patients in your care?

- Always
- Sometimes
- Never

If you chose "Sometimes" (please specify when)

5. Who is offered geriatric assessment (i.e. characteristics of patients)?

6. How long does the geriatric assessment take?

7. Is all or part of the geriatric assessment completed at home by the patient/family prior to the clinic visit?

- Yes
- No

Please comment further

Page 2

8. What staff members participate in the interpretation of geriatric assessment? (Choose all that apply)

- Geriatric Oncologist
- Geriatrician
- Radiation Oncologist
- Medical Oncologist
- Palliative Care team
- Social worker
- Dietician
- Physiotherapist
- Occupational therapist
- Psychologist
- Psycho-oncology liaison nurse
- Pharmacist
- Nurse
- Nurse Practitioner

Other (please specify)

9. In your opinion, what are the educational needs required to implement geriatric assessment in an oncology setting?

10. Do you use assessment results to identify patients at high risk for adverse outcomes in your practice?

- Yes
- No

11. Do you use a fit/vulnerable/frail model?

- Yes
- I don't know what this is
- No

12. How do you determine patients for each category of the model?

13. How do you use geriatric assessment to identify patients at high risk for adverse outcomes?

14. Do you recommend interventions based on geriatric assessment (please see definitions at the beginning of the survey)?

- Yes
- No

15. What are the barriers that you have encountered regarding implementation of geriatric assessment for patients at your institution?

Process

16. In your opinion, is there an age cut-off that should be used to establish a standard for who should undergo geriatric assessment in Oncology?

- Yes
- No

17. What age?

- 65 and over
- 70 and over
- 75 and over
- 80 and over
- 85 and over

Why did you choose this age?

18. If you do not have an age cut-off, please explain why not?

19. In your opinion, what patient characteristics should be used to establish guidelines for who should undergo geriatric assessment in Oncology?

20. Please rate the importance of using geriatric assessment to help inform the following oncology treatment decisions:

	Not Important 0	1	2	3	4	5	6	7	8	9	very Important 10	I don't know
Screening for cancer												
Undergoing invasive diagnostic procedures for cancer												
Prior to surgery for cancer (for curative intent)												
Prior to chemotherapy (for curative intent)												
Prior to radiotherapy (for curative intent)												
Prior to palliative chemotherapy												
Prior to palliative radiotherapy												
During a course of cancer treatment												
Survivorship care (after completion of treatment)												
Deciding on dose and schedule in chemotherapy												
Deciding on dose and fractionation in radiotherapy												

What other kinds of treatment decisions in oncology do you think geriatric assessment could help inform?

21. Please rate the importance of including the following team members for developing recommendations based on geriatric assessment results in an Oncology setting:

	Not Important 0	1	2	3	4	5	6	7	8	9	Very Important 10
Radiation Oncologist											
Medical Oncologist											
Geriatrician											
Palliative care team											
Social worker											
Dietician											
Physiotherapist											
Occupational therapist											
Psychologist											
Pharmacist											
Nurse											
Nurse practitioner											
Psycho-oncology liaison nurse											

You may add other important team members, comments and thoughts:

22. What is the ideal process for patients to complete geriatric assessment (e.g. mailed, web-based, ipads, in person)?

23. Rate the importance of the following domains to be included in geriatric assessment of oncology patients:

	Not important 0	1	2	3	4	5	6	7	8	9	Very important 10
Functional status	○	○	○	○	○	○	○	○	○	○	○
Objective physical performance (e.g. gait, speed, balance, strength)	○	○	○	○	○	○	○	○	○	○	○
Comorbidity	○	○	○	○	○	○	○	○	○	○	○
Medications	○	○	○	○	○	○	○	○	○	○	○
Nutrition	○	○	○	○	○	○	○	○	○	○	○
Social support	○	○	○	○	○	○	○	○	○	○	○
Psychological status - Anxiety	○	○	○	○	○	○	○	○	○	○	○
Psychological status - Depression	○	○	○	○	○	○	○	○	○	○	○
Cognition	○	○	○	○	○	○	○	○	○	○	○

You may add comments of other domains that you believe are important in geriatric assessment:

24. What do you believe are the three most important domains and why?

Screening Tools and Interventions in Geriatric Assessment

25. Do you currently assess each of the following domains of geriatric assessment in clinical practice?

	Yes	No
Functional impairment	○	○
Physical performance impairment (eg gait speed, balance, strength)	○	○
Cognitive impairment	○	○
Co-morbidities	○	○
Polypharmacy	○	○
Nutritional impairment	○	○
Social support impairment	○	○
Anxiety	○	○
Depression	○	○

Please specify any other assessment that you use:

26. Please list any assessment tool(s) that you currently use in your clinical practice, to screen for the following:

Functional impairment	
Physical performance impairment (eg gait speed, balance, strength)	
Cognitive impairment	
Co-morbidities	
Polypharmacy	
Nutritional impairment	
Social support impairment	
Anxiety	
Depression	
Other (please specify)	

27. Please list interventions, if any, that you would recommend for impairments in the following:

Functional status	
Physical performance status (eg gait speed, balance, strength)	
Cognitive status	
Co-morbidities	
Polypharmacy	
Nutritional status	
Social support	
Anxiety	
Depression	
Other (please specify)	

28. Are there any other healthcare professionals who would be essential in developing interventions for the following:

Functional status	
Physical performance status (eg gait speed, balance, strength)	
Cognitive status	
Co-morbidities	
Polypharmacy	
Nutritional status	
Social support	
Anxiety	
Depression	
Other (please specify)	

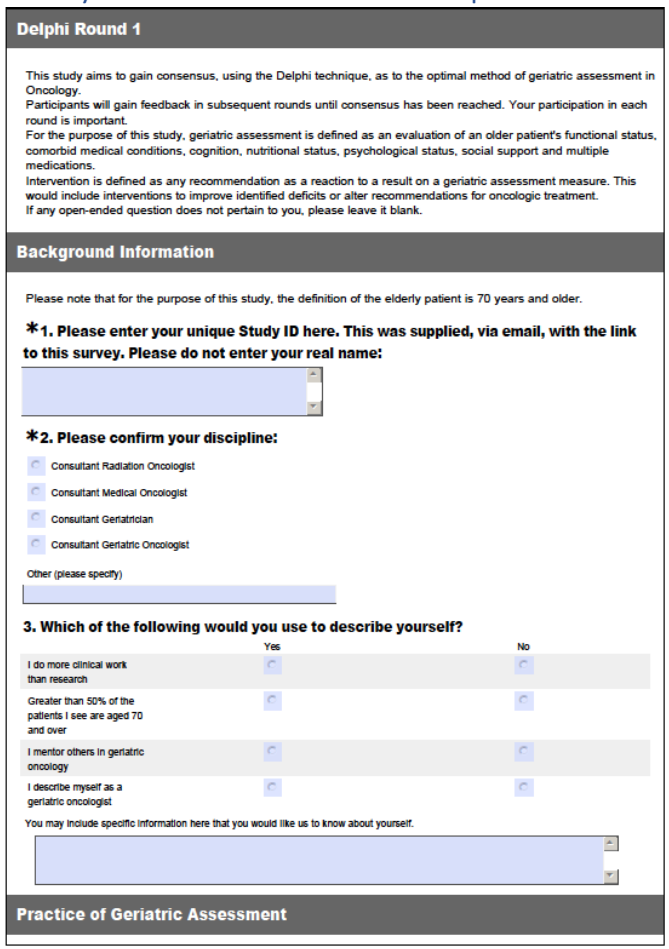
29. Should impairments in any of the following affect cancer treatment decisions, in your opinion?

	Yes	No	I don't know
Functional status	○	○	○
Physical performance status (eg gait speed, balance, strength)	○	○	○
Cognitive status	○	○	○
Co-morbidities	○	○	○
Polypharmacy	○	○	○
Nutritional status	○	○	○
Social support	○	○	○
Anxiety	○	○	○
Depression	○	○	○

For any domains that you've indicated should influence decisions, please indicate how:

Thank you for taking the time to participate in this study. Your contribution is greatly appreciated.

Appendix 4d: Study 1 Round 1 SIOG Group



Delphi Round 1

This study aims to gain consensus, using the Delphi technique, as to the optimal method of geriatric assessment in Oncology.
Participants will gain feedback in subsequent rounds until consensus has been reached. Your participation in each round is important.
For the purpose of this study, geriatric assessment is defined as an evaluation of an older patient's functional status, comorbid medical conditions, cognition, nutritional status, psychological status, social support and multiple medications.
Intervention is defined as any recommendation as a reaction to a result on a geriatric assessment measure. This would include interventions to improve identified deficits or alter recommendations for oncologic treatment.
If any open-ended question does not pertain to you, please leave it blank.

Background Information

Please note that for the purpose of this study, the definition of the elderly patient is 70 years and older.

***1. Please enter your unique Study ID here. This was supplied, via email, with the link to this survey. Please do not enter your real name:**

***2. Please confirm your discipline:**

- Consultant Radiation Oncologist
- Consultant Medical Oncologist
- Consultant Geriatrician
- Consultant Geriatric Oncologist

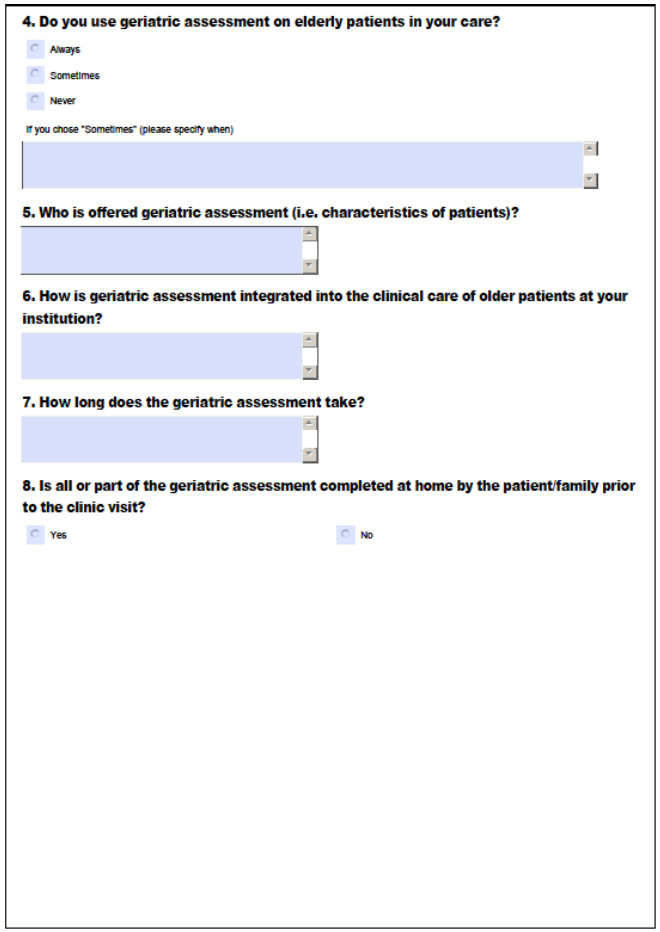
Other (please specify)

3. Which of the following would you use to describe yourself?

	Yes	No
I do more clinical work than research		
Greater than 50% of the patients I see are aged 70 and over		
I mentor others in geriatric oncology		
I describe myself as a geriatric oncologist		

You may include specific information here that you would like us to know about yourself.

Practice of Geriatric Assessment



4. Do you use geriatric assessment on elderly patients in your care?

- Always
- Sometimes
- Never

If you chose "Sometimes" (please specify when)

5. Who is offered geriatric assessment (i.e. characteristics of patients)?

6. How is geriatric assessment integrated into the clinical care of older patients at your institution?

7. How long does the geriatric assessment take?

8. Is all or part of the geriatric assessment completed at home by the patient/family prior to the clinic visit?

- Yes
- No

9. What staff members participate in the interpretation of geriatric assessment? (Choose all that apply)

- ☐ Geriatric Oncologist
- ☐ Geriatrician
- ☐ Radiation Oncologist
- ☐ Medical Oncologist
- ☐ Palliative Care team
- ☐ Social worker
- ☐ Dietician
- ☐ Physiotherapist
- ☐ Occupational therapist
- ☐ Psychologist
- ☐ Psycho-oncology liaison nurse
- ☐ Pharmacist
- ☐ Nurse
- ☐ Nurse Practitioner

Other (please specify)

10. Do you use assessment results to identify patients at high risk for adverse outcomes?

- ○ Yes
- ○ No

11. Do you use a fit/vulnerable/frail model?

- ○ Yes
- ○ I don't know what this is
- ○ No

12. How do you determine patients for each category of the model?

13. How do you use geriatric assessment to identify patients at high risk for adverse outcomes?

14. Do you recommend interventions based on geriatric assessment (please see definitions at the beginning of the survey)?

- ○ Yes
- ○ No

15. Who implements and monitors the geriatric assessment intervention (i.e. geriatric oncology team versus radiation/medical oncology vs geriatrician)?

16. Are there intervention recommendations regarding cancer-based treatments that you incorporate into clinical care after reviewing geriatric assessment results (e.g. modifications to chemotherapy/radiation dose, palliative care referral etc.)

- ○ Yes
- ○ No

Please list all of these

17. What are the barriers that you have experienced regarding geriatric assessment for older patients at your institution?

18. Why do you not use geriatric assessment in the clinical care of your older patients?

19. Do you think geriatric assessment would be helpful in the clinical care of your older patients?

- ○ Yes
- ○ No

Why or why not?

20. What do you believe are the barriers regarding geriatric assessment for older patients at your institution?

Process

21. Is there an age cut-off that should be used to establish a standard for who should get geriatric assessment?

- Yes
- No

22. What age?

- 65 and over
- 70 and over
- 75 and over
- 80 and over
- 85 and over

Why did you choose this age?

23. If you do not have an age cut-off, please explain why not?

24. What patient characteristics should be used to establish guidelines for who should get geriatric assessment?

25. Rate the importance of using geriatric assessment to help inform the following oncology treatment decisions:

	Not important 0	1	2	3	4	5	6	7	8	9	very important 10
Screening for cancer											
Undergoing invasive diagnostic procedures for cancer											
Prior to surgery for cancer (for curative intent)											
Prior to chemotherapy (for curative intent)											
Prior to radiotherapy (for curative intent)											
Prior to palliative chemotherapy											
Prior to palliative radiotherapy											
During a course of cancer treatment											
Survivorship care (after completion of treatment)											
Deciding on dose and schedule in chemotherapy											
Deciding on dose and fractionation in radiotherapy											

What other kinds of treatment decisions in oncology do you think geriatric assessment could help inform?

26. Which screening tools would be helpful in identifying patients in an oncology setting who would most benefit from geriatric assessment?

	Not helpful 0	1	2	3	4	5	6	7	8	9	Very helpful 10	Not aware of this
Vulnerable Elders Survey (VES-13)	○	○	○	○	○	○	○	○	○	○	○	○
G8	○	○	○	○	○	○	○	○	○	○	○	○
Groningen Frailty Index	○	○	○	○	○	○	○	○	○	○	○	○
Self rated health	○	○	○	○	○	○	○	○	○	○	○	○
Objective physical performance (i.e. Timed Up and Go or Short Physical Performance Battery)	○	○	○	○	○	○	○	○	○	○	○	○
Functional status (e.g. Activities of Daily Living or Instrumental Activities of Daily Living)	○	○	○	○	○	○	○	○	○	○	○	○
ECOG performance	○	○	○	○	○	○	○	○	○	○	○	○
Karnofsky performance	○	○	○	○	○	○	○	○	○	○	○	○
Cancer and Ageing Research Group chemotherapy toxicity score	○	○	○	○	○	○	○	○	○	○	○	○
CRASH score	○	○	○	○	○	○	○	○	○	○	○	○

Please add comments or other measures that you believe would be helpful:

27. Rate the importance of including the following team members for developing recommendations based on geriatric assessment results?

	Not important 0	1	2	3	4	5	6	7	8	9	Very important 10
Radiation Oncologist	○	○	○	○	○	○	○	○	○	○	○
Medical Oncologist	○	○	○	○	○	○	○	○	○	○	○
Geriatric Oncologist	○	○	○	○	○	○	○	○	○	○	○
Geriatrician	○	○	○	○	○	○	○	○	○	○	○
Palliative care team	○	○	○	○	○	○	○	○	○	○	○
Social worker	○	○	○	○	○	○	○	○	○	○	○
Dietician	○	○	○	○	○	○	○	○	○	○	○
Physiotherapist	○	○	○	○	○	○	○	○	○	○	○
Occupational therapist	○	○	○	○	○	○	○	○	○	○	○
Psychologist	○	○	○	○	○	○	○	○	○	○	○
Pharmacist	○	○	○	○	○	○	○	○	○	○	○
Nurse	○	○	○	○	○	○	○	○	○	○	○
Nurse practitioner	○	○	○	○	○	○	○	○	○	○	○
Psycho-oncology liaison nurse	○	○	○	○	○	○	○	○	○	○	○

You may add other important team members, comments and thoughts:

28. What is the ideal process for patients to complete geriatric assessment (e.g. mailed, web-based, ipads, in person)?

29. Rate the importance of the following domains to be included in geriatric assessment:

	Not Important 0	1	2	3	4	5	6	7	8	9	Very Important 10
Functional status	○	○	○	○	○	○	○	○	○	○	○
Objective physical performance (e.g. gait, speed, balance, strength)	○	○	○	○	○	○	○	○	○	○	○
Comorbidity	○	○	○	○	○	○	○	○	○	○	○
Medications	○	○	○	○	○	○	○	○	○	○	○
Nutrition	○	○	○	○	○	○	○	○	○	○	○
Social support	○	○	○	○	○	○	○	○	○	○	○
Psyhological status - Anxiety	○	○	○	○	○	○	○	○	○	○	○
Psychological status - Depression	○	○	○	○	○	○	○	○	○	○	○
Cognition	○	○	○	○	○	○	○	○	○	○	○

You may add comments of other domains that you believe are important in geriatric assessment:

30. What do you believe are the three most important domains and why?

Screening Tools and Interventions in Geriatric Assessment

31. Do you currently assess each of the following domains of geriatric assessment in clinical practice?

	Yes	No
Functional impairment	○	○
Physical performance impairment (eg gait speed, balance, strength)	○	○
Cognitive impairment	○	○
Co-morbidities	○	○
Polypharmacy	○	○
Nutritional impairment	○	○
Social support impairment	○	○
Anxiety	○	○
Depression	○	○

Please specify any other assessment that you use:

32. Please list any assessment tool(s) that you currently use in your clinical practice, to screen for the following:

Functional impairment	
Physical performance impairment (eg gait speed, balance, strength)	
Cognitive impairment	
Co-morbidities	
Polypharmacy	
Nutritional impairment	
Social support impairment	
Anxiety	
Depression	
Other (please specify)	

33. Please list interventions, if any, that you would recommend for impairments in the following:

Functional status	
Physical performance status (eg gait speed, balance, strength)	
Cognitive status	
Co-morbidities	
Polypharmacy	
Nutritional status	
Social support	
Anxiety	
Depression	
Other (please specify)	

34. Are there any other healthcare providers who would be essential in developing interventions for impairments in the following:

Functional status	
Physical performance status (eg gait speed, balance, strength)	
Cognitive status	
Co-morbidities	
Polypharmacy	
Nutritional status	
Social support	
Anxiety	
Depression	
Other (please specify)	

35. Should impairments in the following domains affect oncology decisions?

	Yes	No	I don't know
Functional status			
Physical performance status (eg gait speed, balance, strength)			
Cognitive status			
Co-morbidities			
Polypharmacy			
Nutritional status			
Social support			
Anxiety			
Depression			

36. How would you rate the evidence base, on a scale of 0 to 10 (where 0=weakest, 10=strongest) for interventions in older patients in geriatric oncology under the following domains:

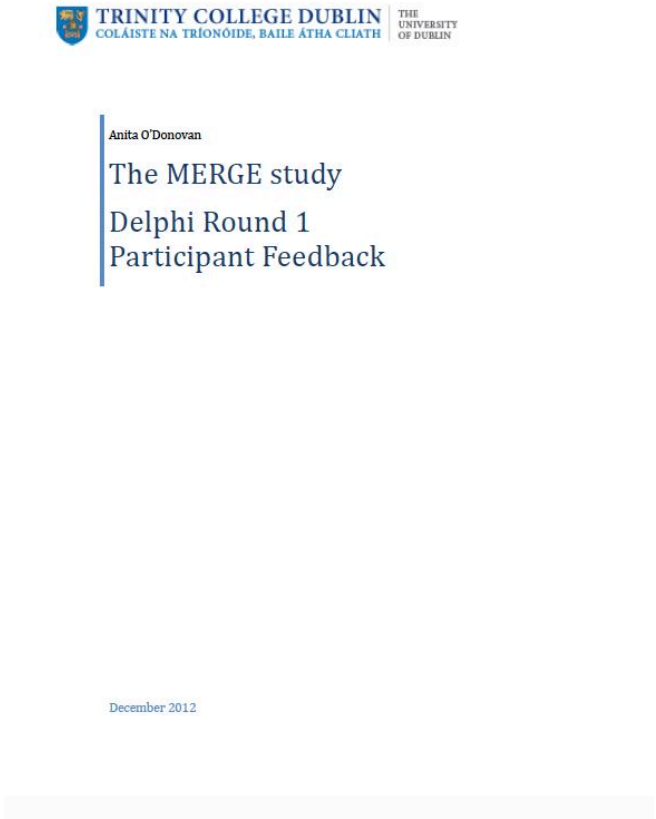
	0	1	2	3	4	5	6	7	8	9	10
Functional status											
Physical performance status (eg gait speed, balance, strength)											
Cognitive status											
Co-morbidities											
Polypharmacy											
Nutritional status											
Social support											
Anxiety											
Depression											

Please comment

End of Round 1

Thank you for taking the time to complete Round 1, your contribution is greatly appreciated.

Appendix 5: Study 1 Round 1 Feedback Report



TRINITY COLLEGE DUBLIN
COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH
THE UNIVERSITY OF DUBLIN

Anita O'Donovan

The MERGE study

Delphi Round 1
Participant Feedback

December 2012

The MERGE study: Delphi Round 1 Participant Feedback

Table of Contents

Introduction

This report contains both quantitative and qualitative feedback from the first Delphi round of the MERGE study. In keeping with Delphi tradition, it aims to be as inclusive and comprehensive as possible, and every participant's contribution is acknowledged. For your convenience, attempts are made to summarise certain aspects, with additional appendices containing the qualitative data from the open-ended questions in Round One, which are located at the end of the document. I would encourage each contributor to make reference to these appendices, in addition to the summarised sections. This is important for subsequent rounds, and will provide different perspectives on the many approaches that are taken to geriatric assessment.

In relation to the report itself, assumptions cannot be made about the practice of geriatric assessment in Ireland, or internationally, based on this Delphi survey. An expert panel, who are specialists in their field, has been chosen to inform this process, but it is not a random sample. It is a heterogeneous sample, which is desirable in order to ensure that the entire spectrum of opinion is determined. The purpose of this report is to give descriptive feedback to participants, it is not intended to be analytical.

The results of this collaborative process will be used to inform the design of a geriatric assessment methodology for Irish Radiation and Medical Oncology patients.

List of Abbreviations Used in This Document:

AD=Alzheimer's Disease

AMTS=Abbreviated Mental Test Score

ASA=American Society of Anaesthesiologists

CARST = Community Assessment of Risk Screening Tool

CCI=Charlson Comorbidity Index

CGA=Comprehensive Geriatric Assessment

CHS=Cardiovascular Health Study

CIRS-G=Cumulative Illness Rating Scale-Geriatric

GA=Geriatric Assessment

Ger=Geriatrician (Ireland)

ECOG = Eastern Cooperative Oncology Group

EMS=Elderly Mobility Scale

FIM/FAM=Functional Independence Measure and Functional Assessment Measure

GFI=Groningen Frailty Indicator

IQ Rge=Interquartile Range

MEAMS=Middlesex Elderly Assessment of Mental State

MDT=Multidisciplinary Team

mMOS-SS=modified Medical Outcomes Study – Social Support

MMSE=Minimental State Examination

MNA=Mini Nutritional Assessment

MO=Medical Oncology (Ireland)

MOCA=Montreal Cognitive Assessment

MUST=Malnutrition Universal Screening Tool

PD=Parkinson's Disease

PHN=Public Health Nurse

PS=Performance Status

PSP=Progressive Supranuclear Palsy

RBANS=Repeatable Battery for the Assessment of Neuropsychological Status

QMCI = Quick Mild Cognitive Impairment

RO=Radiation Oncology (Ireland)

SCS=Simplified Comorbidity Score

SIOG=International Society of Geriatric Oncology

SPPB=Short Physical Performance Battery

STOPP/START= Screening Tool of Older People's potentially inappropriate Prescriptions/ Screening Tool to Alert doctors to the Right Treatment

TUG=Timed Up and Go

VES=Vulnerable Elders Survey

VIP=Variable Indicative of Placement (risk)

Wrt=with respect to

Study Definitions

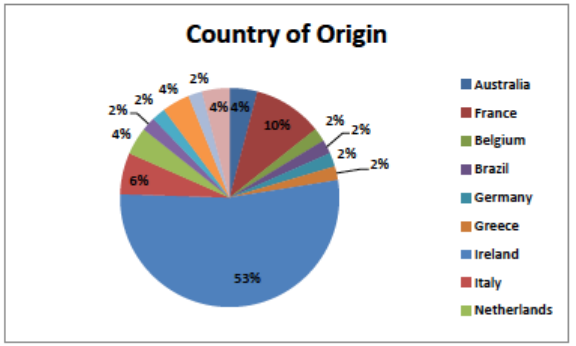
For the purpose of this study, geriatric assessment (GA) is defined as an evaluation of an older patient's functional status, comorbid medical conditions, cognition, nutritional status, psychological status, social support and multiple medications.
Intervention is defined as any recommendation as a reaction to a result on a geriatric assessment measure. This includes interventions to improve identified deficits or alter recommendations for oncology treatment.

Section 1: Demographics of the Study Group

Composition of the Expert Panel

There are 49 members on this expert panel, encompassing four disciplines: Medical Oncology (49%), Geriatric Medicine (29%), Radiation Oncology (18%) and Geriatric Oncology (6%).

Country of Origin:



International experts are grouped together for analysis, as they were selected due to a specific interest in Geriatric Oncology through research or clinical experience (or both). These international experts are collectively called the SIOG group, as they were identified through the International Society of Geriatric Oncology. The SIOG group consists of Medical Oncologists, Geriatricians and Geriatric Oncologists, and participants are mainly from Europe, as a parallel study is ongoing in the US.

For the purpose of data analysis, the national and international groups are categorised separately, where appropriate i.e. SIOG group **(SIOG)**, Irish Geriatricians **(Ger)**, Irish Radiation Oncologists **(RO)** and Irish Medical Oncologists **(MO)**.

Section 2: Background Information

Participants' rating of the current evidence-based knowledge in geriatric oncology

All respondents were asked to rate the current evidence base in geriatric oncology, on a ten-point Likert scale where 0=weakest, 10=strongest, as part of the initial demographic round.

Results indicate that most participants do *not* feel that there is a strong evidence base in this field at present, as indicated by a modal value of 5 (median=4, IQ rge=2).

Is Geriatric Oncology feasible in Ireland?

93% of Irish participants believe that Geriatric Oncology is feasible in Ireland. One participant stated:

"But very challenging because of an already extensive commitment to numerous MDTs and dwindling resources. (RO)"

Reasons given by those who don't think geriatric oncology is feasible are also related to time/resources:

"The resources at Consultant level are probably insufficient in both Geriatrics and Oncology to achieve this. (Ger)"

"It would be difficult because of lack of time/resources (both disciplines very stretched) and so many other services (surgical/radiation/medical oncology and palliative care to name just a few) need to be involved. However with complex planning it might be achievable. (RO)"

Do you use GA on elderly patients in your care?

All of the **SIOG** group perform GA on their patients (always or sometimes), as do the Irish Geriatrician group.

For those who answered "sometimes", specified reasons include clinical judgement, when radical treatment is proposed, as part of a research protocol, when there is evidence of comorbidities or cognitive impairment and when time allows. Please see Appendix 1 for detailed responses.

The majority of Irish Oncologists (Radiation and Medical) do not currently perform GA on their elderly patients (53%). 41% of participants stated that they "sometimes" perform GA, under specific conditions, such as obvious frailty, concerns about ability to give consent for treatment and for curative treatment.

How is GA integrated into the clinical care of older patients at your institution?

SIOG participants were asked to specify how GA is integrated into clinical practice in their institutions. As stated previously, these participants were identified through SIOG as having a special interest in geriatric oncology, through research and clinical experience.

Many different approaches are taken (please see Appendix 2 for further details). For some institutions, it is considered routine practice and the standard of care to offer all elderly patients CGA on initial consultation. Some use an initial screening tool, such as the G8 to identify patients who require full CGA. Geriatrician review is available upon request, or by provision of dedicated Oncology clinics at regular intervals in some centres. Nurse-led assessments are also used to provide the initial screening of patients, which is followed up, if required. Institutions participating in research perform full CGA routinely for elderly trial patients.

Stratification of Patients by Age

Participants were asked if there is an age cut-off that should be used to identify patients for GA. The majority of the SIOG group (57%) feel there should be an age cut-off (70 and over), while the majority of Irish Geriatricians feel that there shouldn't be (70%). This may reflect SIOG recommendations in the former group, as documented in the open-ended statements. Radiation and Medical Oncologists (Irish) were divided 50/50 on this response.

Group	65 and over	70 and over	75 and over	80 and over	85 and over
SIOG	6%	81%	13%	0.0%	0.0%
Ger	40.0%	0%	40.0%	20%	0%
RO	0%	67%	33%	0%	0%
MO	40.0%	20%	40.0%	0%	0%

The reasons for choosing age as a cut-off for GA include increased risk of medical and social problems, research protocols, convention, clinical experience and SIOG recommendations.

For those who feel there shouldn't be an age cut-off, many alluded to the heterogeneity of elderly patients, the need to exercise clinical judgement for each individual patient, and the importance of frailty assessment (see Appendix 3 for more detailed responses).

Section 3: Practice of Geriatric Assessment

Length of time for completion of GA

The length of time for GA varied considerably among respondents, from less than 10 minutes to >1 hour, and it was noted that this depends on the complexity of individual cases, as well as the extent of multidisciplinary involvement. The most commonly reported time was 20-30 minutes (21%).

Is all or part of the GA completed at home by the patient/family prior to the clinic visit?

79% of **all** participants answered no to this question. Some respondents use a combined approach, as follows:

- Family score cognition (we have developed a tool for caregivers/family to score cognition and it works) ADL, mood, behaviours and safety (Ger).
- For research, we use some caregiver completed forms on function, behaviour etc, but not in routine clinical practice (Ger)
- Ideally this would be done by the primary care team or PHN (Ger)
- Specialist nurses visit patients in the home to take a medication history, and perform routine geriatric bloods (Ger)
- Some of the out-patient assessment is done at home prior to clinic visit (Ger)
- This is generally done within the hospital by a multi-disciplinary team assessing numerous aspects of the patient's health (RO)
- At home by the GP or by the referring hospital Geriatrician - we are an outpatient radiotherapy unit (RO)
- Occupational therapy may visit the home to assess falls risk and safety (MO)

Staff members who participate in the interpretation of GA

Discipline	SIOG Respondents	Ger Respondents	RO Respondents	MO Respondents
Geriatric Oncologist	27%	0%	0%	0%
Geriatrician	59%	100%	75%	33%
Radiation Oncologist	0.0%	0%	25%	0%
Medical Oncologist	68%	10%	0%	83%
Palliative Care team	9%	40%	25%	33%
Social worker	23%	60%	75%	17%
Dietician	14%	80%	50%	17%
Physiotherapist	14%	90%	50%	33%
Occupational therapist	9%	90%	50%	33%
Psychologist	5%	0%	0%	0%
Psycho-oncology liaison nurse	0.0%	0%	25%	0%
Pharmacist	9%	20%	0%	0%
Nurse	50.0%	80%	50%	17%
Nurse Practitioner	18%	30%	25%	33%

***Values ≥ 60% are highlighted**

The importance of different disciplines in the process of GA interpretation varied between groups, as shown in the above table. Other disciplines that were identified by some respondents include the research team, a speech and language therapist, cancer care coordinator, surgeons and anaesthesists.

The education needs required to implement GA in Irish Oncology (Irish participants only)

This question was addressed to Irish participants only due to the current lack of a Geriatric Oncology discipline in Ireland. Identified needs include:

- Gerontology nurse training
- CGA education, including training on assessment of specific domains such as functional status, frailty, cognition (dementia vs. delirium), falls versus syncope and social support needs
- Formation of MDTs for GA
- Lectures/seminars on the principles of geriatric oncology

[Please see Appendix 4 for more detailed responses.]

Fit/Vulnerable/Frail Criteria

52% of all participants stated that they use a fit/vulnerable/frail model to identify high risk elderly patients. 15% of respondents admitted that they are not aware of this model. The SIOG group were most likely to use such criteria.
Participants listed a variety of factors that are used to stratify patients into fit, vulnerable and frail categories, as follows (please see Appendix 5 for more detailed responses):

- Balducci's criteria was most commonly cited by the SIOG group.
  (i.e. the combination of selected risk factors from several components of a CGA, including age older than 85 years, dependence in one or more ADLs, the presence of three or more comorbid conditions, and the presence of one or more geriatric syndromes).
- Screening tools, such as the G8
- Care needs, function, cognition risk, comorbidities.
- Clinical judgement, as opposed to formal assessment tools
- VIP score

The use of GA to identify patients at high risk for adverse outcomes

Responses varied between participants as to how they use GA to identify patients at high risk for adverse outcomes, and include the following:

- Deficits in specific domains of CGA are used to indicate high risk patients, with different combinations being used, including functional, nutritional, cognitive impairment and comorbidities.
- Decisions on radical versus palliative treatment are based on PS and various other factors such as frailty, comorbidities, functional status, nutritional status etc.
- Many respondents employ screening tools to identify patients at high risk e.g. CRASH, CARST and VIP.
- Frailty measures are used to identify patients who require dose reductions
- MDT discussion, medications review and clinical experience are other suggested approaches.

[Please see Appendix 6 for more detailed responses.]

Do you recommend interventions based on GA?

The majority of disciplines recommend interventions based on GA. For the MO group, this was split 50/50. Details of such interventions are contained below.

Subgroup	Yes	No
SIOG	91%	9%
Ger	100%	0%
RO	67%	33%
MO	50%	50%

Potential barriers regarding implementation of GA

Participants were asked to address this question with regard to their own institution. Common themes in response to this question relate to time, education and available resources, as well as the lack of institutional support and integration of existing services. Staffing issues and motivation were identified as potential barriers to implementation of GA. Identification of deficits on specific CGA domains may require appropriate follow-up care in the community, which is sometimes difficult to access. Training with respect to the principles of GA and a dedicated geriatric service are deemed important. Please see Appendix 7 for more detailed responses.

Patient characteristics that should be used to establish guidelines for who should undergo GA in Oncology

According to the expert panel, patient characteristics that should be used to establish guidelines for those who should undergo GA include:

- Frailty
- Age
- Patients with poor performance on screening tools
- Functional impairment
- Poor PS
- Patients with a number of comorbidities
- Cognitive impairment
- Social isolation
- Polypharmacy

Please see Appendix 8 for further details.

The ideal process for patients to complete GA

The majority of participants (81%) feel GA should be completed by face-to-face interview. A minority (9%) feel a combination approach is feasible, while others suggest nurse-led assessments, as well as electronic-based and mailed methodologies.

The three most important domains

Below are the three most common combinations reported by all participants, in order of importance:

1. Functional status, comorbidities and cognition (19%)
2. Functional status, comorbidities and nutrition (17%)
3. Functional status, comorbidities and social support (7%)

Percentage of Respondents who assess each of the following GA domains in clinical practice

Domains	SIOG	Ger	RO	MO
Functional impairment	100%	100%	100%	100%
Physical performance impairment (e.g. gait speed, balance, strength)	57%	100%	33%	50%
Cognitive impairment	96%	100%	67%	88%
Comorbidities	96%	100%	100%	100%
Polypharmacy	91%	100%	83%	88%
Nutritional impairment	82%	100%	67%	71%
Social support impairment	86%	100%	83%	100%
Anxiety	63%	90%	67%	50%
Depression	95%	90%	50%	50%

Details of assessment tools used are contained below. However, not all participants specified which assessments they currently use.

Section 4: Assessment and Interventions

Assessment tool(s) currently used in clinical practice

The SIOG group and Irish geriatricians are more likely to use assessment tools in clinical practice, than the other groups. The different types of assessment used, and the percentage of all respondents who use them in clinical practice is detailed below. The most common assessment tools are highlighted. Please note that many participants use a combination of these, and response rate varied for each domain. Therefore, these figures are rough approximations, and will be explored further in subsequent rounds.

Functional impairment

Assessment Type	Percentage of Respondents
TUG	2%
ADL	22%
IADL	29%
ECOG/Karnofsky PS	24%
VES-13	4%
Barthel Index	4%
GFI	2%
FIM/FAM	2%
Patient History/Clinical Examination	8%

The majority of the expert panel employ ADL and IADL scales, usually in combination, to measure functional impairment. Performance status measures, such as ECOG and Karnofsky, are also commonly used.

Recommended Interventions for Functional Impairment

The majority of participants (31%) recommend physiotherapy/exercise intervention for functional impairments. Involvement of Occupational Therapists (16%) and nurses (4%) is also proposed, as well as further assessment in the form of a CGA (n=1). Homecare interventions including environment adaptations, PHN/OT home visits and a review of social support structure were identified as important by 12% of respondents.

Physical performance impairment

Assessment Type	Percentage of Respondents
TUG	27%
Gait speed	8%
Balance assessment e.g. BERG	14%
Grip strength	10%
CHS	2%
EMS	10%
SPPB	2%
Observation	2%

The Timed Up and Go test, as well as balance tests are commonly used, alone, or in combination, with a variety of other assessments, as detailed above.

Recommended Interventions for Physical Performance Impairment

Interventions for physical performance impairment are similar to those listed for functional impairments above.

Cognitive impairment

The MMSE is the most commonly used assessment method for cognitive impairment (53%). Other less commonly used tools include the AMTS, MiniCog, MOCA, Clock drawing test, Rivermead, Addenbrooks, QMCI, Pfeiffer questionnaire, fluency frontal assessment battery, MEAMS, CAMCOG, RBANS, delayed word recall and clinical judgement.

Recommended Interventions for Cognitive Impairment

Intervention	Percentage of Respondents
Psychologist/psychiatrist Review	10%
Geriatrician Referral	14%
Medication	16%
Advance Care Planning	4%
Home care intervention/day hospital	8%
Occupational Therapy	8%
Other	8%

Other interventions for cognitive impairment include referral to a memory clinic, dementia workup and lifestyle advice.

Comorbidities

The majority of participants use the Charlson Comorbidity Index (24%). Other methods include chart review/medical history (16%), CIRS-G (14%), with a minority using the ASA grade and SCS (both 2%).

Recommended Interventions for Comorbidities

Referral to organ specialists/other disciplines (such as physiotherapy) for optimisation and management of designated comorbidities is employed, as deemed appropriate.

Polypharmacy

Three participants use the STOPP START tool to address potentially inappropriate medication use. All other respondents use medical history/list of medications or pharmacy review.

Recommended Interventions for Polypharmacy

The majority of participants recommend review of medications, as above, with the cessation of inappropriate medication use. The patients' GP, pharmacist and geriatrician were identified as having a role to play in this intervention.

Nutritional impairment

The MNA (short and long forms) is the most commonly cited assessment for nutritional impairment (27%), followed by the MUST (16%), patient history in relation to weight loss and BMI (12%). One participant uses the Determine Index.

Recommended Interventions for Nutritional Impairment

Dietician referral is the most commonly used intervention for nutritional impairment.

Social support impairment

Patient and caregiver interview is employed to assess social support requirements. Some participants (n=4) use one of each of the following assessment tools: mMOS-SS, Socio-familiar Gijon Test, CARST and GFI.

Recommended Interventions for Social Support Impairment

Interventions for social support impairment may be broadly divided into two categories: Referral to a Social Worker (37%) and home support in the form of homecare teams, PHN support and daycare centre, if feasible and acceptable to the patient (27%).

Psychological Status: Anxiety and Depression

The GDS is the most commonly used assessment for depression (39%), while the HADS is used for assessment of both anxiety and depression by a minority of respondents. Other less commonly used tools include the Yesavage questionnaire, GFI, and patient history/interview.

Recommended Interventions for Anxiety and Depression

Interventions for anxiety and depression treatment includePsychiatrist/Psychologist/Cognitive Behavioural Therapy referral (33%) and medication (24%). Other interventions include Psycho-Oncology referral, cancer support services, social worker, palliative care and geriatrician referrals.

Other Assessments

Other assessment tools in use by participants include the G8, Distress thermometer, Burden scale, behaviour scale and safety score.

Respondents who specified that impairments in specified GA domains should affect Oncology decisions

Domain	SIOG	Ger	RO	MO
Functional status	100%	90%	100%	100%
Physical performance status (e.g. gait speed, balance, strength)	55%	70%	100%	100%
Cognitive status	95%	100%	100%	100 %
Comorbidities	95%	100%	100%	88%
Polypharmacy	86%	40%	50%	75 %
Nutritional status	82%	80 %	100 %	100%
Social support	86%	70%	100%	75%
Anxiety	55%	40%	50%	50%
Depression	91%	30 %	50 %	63%

Functional and cognitive status, as well as comorbidites, appear to be the most important domains, in terms of their ability to affect oncology decisions.

Section 5: Statistical Analysis

These Likert scales contain a ten point scale ranging in importance, where 0=not important and 10=very important. Statistical values are given below.

Please rate the importance of using GA to help inform the following oncology treatment decisions:

Oncology Treatment Decision	SIOG	Ger	RO	MO
Screening for Cancer	Median=6 Mode=9 IQ Rge=6.5 Frequency:19%	Median=5.5 Mode=7 IQ Rge=5.25 Frequency:30%	Median= 9 Mode=9 IQ Rge=6.5 Frequency:40%	Median= 5.5 Mode=5 IQ Rge=4.5 Frequency:25%
Undergoing invasive diagnostic procedures for cancer	Median= 8 Mode=6 IQ Rge=2.5 Frequency:24%	Median=8 Mode=10 IQ Rge=5.75 Frequency:40%	Median=9 Mode=9 IQ Rge=1.5 Frequency:40%	Median=7.5 Mode=7 IQ Rge=2.5 Frequency:25%
Prior to surgery for cancer (for curative intent)	Median= 9 Mode=10 IQ Rge=2.5 Frequency:34%	Median=9.5 Mode=10 IQ Rge=3 Frequency:50%	NA	NA
Prior to chemotherapy (for curative intent)	Median= 9 Mode=10 IQ Rge=2 Frequency:33%	Median=8.5 Mode=10 IQ Rge=3 Frequency:40%	NA	Median=9.5 Mode=10 IQ Rge=2 Frequency:50%
Prior to radiotherapy (for curative intent)	Median= 8 Mode=8 IQ Rge=5 Frequency:33%	Median=7.5 Mode=7 IQ Rge=3.5 Frequency:30%	Median= 9 Mode=9 IQ Rge=1.5 Frequency:60%	NA
Prior to palliative chemotherapy	Median= 9 Mode=10 IQ Rge=3 Frequency:33%	Median=7.5 Mode=10 IQ Rge=6.25 Frequency:30%	NA	Median=9.5 Mode=10 IQ Rge=2 Frequency:50%
Prior to palliative radiotherapy	Median= 8 Mode=8 IQ Rge=2.75 Frequency:20%	Median=7.5 Mode=10 IQ Rge=6.25 Frequency:30%	Median= 7 Mode=9 IQ Rge=5 Frequency:40%	NA
During a course of cancer treatment	Median= 7 Mode=7 IQ Rge=1 Frequency:40%	Median=7 Mode=0 IQ Rge=4.5 Frequency:20%	Median=7 Mode=7 IQ Rge=3.5 Frequency:40%	Median=5.5 Mode=2 IQ Rge=5.5 Frequency:25%

Survivorship care (after completion of treatment)	Median= 8 Mode=8 IQ Rge=3 Frequency:20%	Median=7 Mode=7 IQ Rge=3 Frequency:40%	Median=7 Mode=3 IQ Rge=6.5 Frequency:40%	Median=6.5 Mode=5 IQ Rge=3.75 Frequency:25%
Deciding on dose and schedule in chemotherapy	Median= 8 Mode=10 IQ Rge=3 Frequency:33%	Median=7 Mode=7 IQ Rge=6.5 Frequency:30%	NA	Median=8.5 Mode=8 IQ Rge=1 Frequency:38%
Deciding on dose and schedule in radiotherapy	Median= 8 Mode=8 IQ Rge=1 Frequency:35%	Median=7 Mode=7 IQ Rge=6 Frequency:30%	Median= 9 Mode=9 IQ Rge=2 Frequency:40%	NA

What other kinds of treatment decisions in oncology do you think GA could help inform?

- Risk/benefit of treatment, when to stop, or offer a more palliative approach
- Use of bisphosphonate therapy or not
- Need for inpatient rather than outpatient care
- Combined modality treatment.
- Intensity of follow-up. Referral to community supports.
- Oral versus IV chemo e.g. based on home support or mental test score etc. Aggressive e.g. curative liver resection versus palliative chemo in a potentially curable patient with metastatic disease-e.g. how aggressive can/should we be?
- Supportive care needs and carer support.

Please rate the importance of the following domains to be included in GA:

Domain	SIOG	Ger	RO	MO
Functional Status	Median=10 Mode=10 IQ Rge=1 Frequency:55%	Median=10 Mode=10 IQ Rge=0.25 Frequency:80%	Median=9.5 Mode=10 IQ Rge=2 Frequency:50%	Median=10 Mode=10 IQ Rge=0.75 Frequency:75%
Objective Physical Performance	Median=9 Mode=9 IQ Rge=2.25 Frequency:32%	Median=8.5 Mode=10 IQ Rge=3.25 Frequency:30%	Median=9 Mode=10 IQ Rge=2.25 Frequency:50%	Median=8 Mode=6 IQ Rge=3.5 Frequency:25%
Cognition	Median=8.5 Mode=8 IQ Rge=2 Frequency:36%	Median=10 Mode=10 IQ Rge=2 Frequency:60%	Median=9 Mode=10 IQ Rge=2.5 Frequency:50%	Median=10 Mode=10 IQ Rge=0.75 Frequency:75%
Comorbidity	Median=9.5 Mode=10 IQ Rge=1.25 Frequency:50%	Median=9 Mode=10 IQ Rge=2.25 Frequency:40%	Median=9.5 Mode=10 IQ Rge=2 Frequency:50%	Median=10 Mode=10 IQ Rge=1.75 Frequency:63%
Medications	Median=9.5 Mode=10 IQ Rge=2 Frequency:50%	Median=8 Mode=10 IQ Rge=3.25 Frequency:40%	Median=8 Mode=8 IQ Rge=3.25 Frequency:33%	Median=10 Mode=10 IQ Rge=2.75 Frequency63:%
Nutrition	Median=9 Mode=10 IQ Rge=2 Frequency:36%	Median=9 Mode=10 IQ Rge=3 Frequency:40%	Median=8 Mode=8 IQ Rge=1.75 Frequency:50%	Median=10 Mode=10 IQ Rge=2.5 Frequency:63%
Social Support	Median=9 Mode=10 IQ Rge=2 Frequency:32%	Median=7.5 Mode=10 IQ Rge= 4.5 Frequency:30%	Median=8 Mode=7 IQ Rge=3 Frequency:33%	Median=9.5 Mode=10 IQ Rge=3 Frequency50:%
Anxiety	Median=8 Mode=8 IQ Rge=2 Frequency:27%	Median=7 Mode=7 IQ Rge=4.5 Frequency:30%	Median=7.5 Mode=6 IQ Rge=4 Frequency=33%	Median=8 Mode=10 IQ Rge=4.5 Frequency:38%
Depression	Median=8 Mode=8 IQ Rge=2.25 Frequency:32%	Median=8 Mode=7 IQ Rge=3 Frequency:30%	Median=7 Mode=6 IQ Rge=4 Frequency:33%	Median=8 Mode=8 IQ Rge=.75 Frequency38:%

*Please note: Frequencies relate to modal values

Other domains that are important in GA:

- Sensory functions
- Bone density assessment (w DXA scan)
- Frailty
- IADLS including mobility. Distress thermometer, Pain scale. Social supports should also ask about existing supportive care services in the home, e.g. cleaning, nursing care etc.

Please rate the importance of including the following team members for developing recommendations based on GA results in an Oncology setting:

Discipline	SIOG	Ger	RO	MO
Radiation Oncologist	Median=7 Mode=5 IQ Rge= 4.5 Frequency: 24%	Median= 9.5 Mode=10 IQ Rge= 2 Frequency50: %	Median= 8.5 Mode=8 IQ Rge=1.5 Frequency:33 %	Median= 8.5 Mode=10 IQ Rge= 4.75 Frequency: 50%
Medical Oncologist	Median= 9 Mode=10 IQ Rge= 2 Frequency48%	Median=9.5 Mode=10 IQ Rge=2 Frequency:50%	Median=8.5 Mode=8 IQ Rge=2.25 Frequency:33%	Median=10 Mode=10 IQ Rge=1 Frequency:63 %
Geriatric Oncologist	Median= 10 Mode=10 IQ Rge= 2 Frequency62: %	No GO discipline in Ireland	No GO discipline in Ireland	No GO discipline in Ireland
Geriatrician	Median= 9 Mode=10 IQ Rge= 2 Frequency43:%	Median= 10 Mode=10 IQ Rge= 2 Frequency: 60%	Median= 9 Mode=9 IQ Rge=2.75 Frequency: 33%	Median= 10 Mode=10 IQ Rge= 1 Frequency: 63 %
Palliative Care Team	Median= 8 Mode=8 IQ Rge=2 Frequency:38 %	Median= 9.5 Mode=10 IQ Rge= 2 Frequency:50 %	Median= 9 Mode=8 IQ Rge=2 Frequency: 33%	Median= 8.5 Mode=10 IQ Rge= 3.75 Frequency: 38%
Social Worker	Median=8 Mode=8 IQ Rge=1 Frequency:50 %	Median= 7.5 Mode=10 IQ Rge= 6 Frequency:30 %	Median= 8 Mode=8 IQ Rge=4 Frequency:40 %	Median=10 Mode=10 IQ Rge= 1.75 Frequency: 63%
Dietician	Median= 8 Mode=8 IQ Rge=1.5 Frequency:52 %	Median= 7.5 Mode=7 IQ Rge=4.75 Frequency: 20%	Median= 7 Mode=7 IQ Rge=3.5 Frequency:40 %	Median=9.5 Mode=10 IQ Rge= 2 Frequency50: %
Physiotherapist	Median= 7 Mode=8 IQ Rge=2 Frequency:29 %	Median= 8 Mode=10 IQ Rge= 4.25 Frequency: 40%	Median= 7 Mode=7 IQ Rge=4 Frequency:40 %	Median= 9 Mode=10 IQ Rge= 2.75 Frequency: 38%
Occupational Therapist	Median= 6 Mode=6 IQ Rge=2.5 Frequency:29 %	Median= 8 Mode=10 IQ Rge= 3.5 Frequency: 40%	Median= 6 Mode=3 IQ Rge=5 Frequency:20 %	Median=8.5 Mode=10 IQ Rge= 3.75 Frequency: 38%

Psychologist	Median= 6 Mode=6 IQ Rge=3 Frequency: 29%	Median= 7 Mode=7 IQ Rge=4 Frequency:40 %	Median= 6 Mode=4 IQ Rge=4 Frequency:20 %	Median=9.5 Mode=10 IQ Rge= 4.25 Frequency: 50%
Pharmacist	Median= 7 Mode=8 IQ Rge=3 Frequency:24 %	Median= 7 Mode=7 IQ Rge=3.75 Frequency: 30%	Median= 5 Mode=3 IQ Rge=4.5 Frequency: 20%	Median=10 Mode=10 IQ Rge= 2 Frequency: 57 %
Nurse	Median= 8 Mode=8 IQ Rge=2.5 Frequency:29 %	Median= 7 Mode=7 IQ Rge=3.5 Frequency: 40%	Median= 8 Mode=8 IQ Rge=3.25 Frequency: 33%	Median= 10 Mode=10 IQ Rge= 1 Frequency:57 %
Nurse Practitioner	Median= 8 Mode=8 IQ Rge=3 Frequency:29 %	Median= 8 Mode=7 IQ Rge=3 Frequency: 40%	Median= 7.5 Mode=8 IQ Rge=3 Frequency:33 %	Median= 10 Mode=10 IQ Rge= 2 Frequency:63 %
Psychoncology Liaison Nurse	Median= 7 Mode=6 IQ Rge=2 Frequency:25 %	Median= 7 Mode=7 IQ Rge=4.25 Frequency: 40%	Median= 7 Mode=5 IQ Rge=3.5 Frequency:20 %	Median= 9 Mode=10 IQ Rge= 4.25 Frequency: 63%

*Please note: Frequencies relate to modal values

Other Team Members who are Important in GA:

- GP
- A spiritual care needs practitioner (e.g. priest, rabbi, imam, humanist etc. as appropriate
- Patient and family members

Which screening tools would be helpful in identifying patients in an oncology setting who would most benefit from GA?

This question was addressed to SIOG affiliated participants only, as many of these screening tools are specific to geriatric oncology.

Screening Tool	SIOG
VES-13	Median=6 Mode=5 IQ Rge= 4.5 Frequency:23%
G8	Median=7 Mode=7 IQ Rge= 1.75 Frequency:38%
GFI	Median=5 Mode=3 IQ Rge= 4 Frequency:14%
Self rated health	Median=5.5 Mode=5 IQ Rge= 4 Frequency:18%
Objective physical performance	Median=8 Mode=8 IQ Rge= 1.5 Frequency:33%
Functional Status	Median=8 Mode=8 IQ Rge= 3 Frequency:32%
ECOG PS	Median=6.5 Mode=10 IQ Rge= 5.25 Frequency:18%
Karnofsky PS	Median=5 Mode=3 IQ Rge= 5 Frequency:18%
Cancer and Ageing Research Group chemotherapy toxicity score	Median=6.5 Mode=7 IQ Rge= 5 Frequency:18%

CRASH Score	**Median=6** **Mode=6** **IQ Rge= 4** **Frequency: 20%**

How would you rate the evidence base, on a scale of 0 to 10 (where 0=weakest, 10=strongest) for interventions in older patients in geriatric oncology under the following domains:

This question was addressed to SIOG affiliated participants only, as it is specific to geriatric oncology.

Evidence Base	SIOG
Functional Status	**Median= 8.5** **Mode=10** **IQ Rge= 5** **Frequency:27 %**
Objective Physical Performance	**Median= 8** **Mode=8** **IQ Rge= 3.5** **Frequency:29 %**
Cognition	**Median= 7** **Mode=7** **IQ Rge= 2.5** **Frequency:23 %**
Comorbidity	**Median= 8** **Mode=8** **IQ Rge= 3.25** **Frequency: 23%**
Medications	**Median= 7** **Mode=8** **IQ Rge= 3.5** **Frequency:24 %**

Evidence Base	SIOG Respondents
Nutrition	**Median= 8** **Mode=8** **IQ Rge= 3.5** **Frequency:38 %**
Social Support	**Median= 7** **Mode=6** **IQ Rge= 3.5** **Frequency:19 %**
Anxiety	**Median= 6** **Mode=8** **IQ Rge= 3.5** **Frequency:24 %**
Depression	**Median= 8** **Mode=8** **IQ Rge= 4** **Frequency:23 %**

Author's Note

Thank you for your important contribution to this process. Your input is invaluable in the design of the Round 2 survey, and in the process as a whole. Please note that many of the above items may be included in Round 2, as an important aspect of a Delphi survey is assessment of stability between rounds, as well as the participant's right to change their minds, based on peer opinion. Round 1 is typically open-ended, compared to other rounds, in order to encompass all expert opinion. Please do not hesitate to contact me if you feel that your views are not contained within this report. A copy of your individual response has been submitted with this document for that purpose.

Further detailed qualitative analysis has been undertaken, using NVivo software. This is also available to study participants, upon request.

I look forward to your continued participation in this process, which will be duly acknowledged in the final report.

Best wishes,

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Trinity EngAGE

Trinity College Dublin Centre for Research in Ageing

Appendix 1: Do you use geriatric assessment on elderly patients in your care?

Respondents who specified "sometimes":

- Informally I do it almost every time an older patient is admitted. Formally I do it in some pre-operative evaluations. By formally I mean that I score the different domains using validated scales.
- When I see the need to.
- When active treatment is planned.
- Whilst routine screening for supportive care needs is meant to occur in all patients over the age of 70 years, there is not a 100% uptake.
- In the context of research studies.
- If the clinical presentation and the decisions are unclear.
- As per protocol within clinical trials (CTs) and some kind of assessment in daily practice.
- When I have time to do it, and also when I need to do therapeutic decisions.
- Patients with complex or multiple problems when assessing them for the first time.
- When there is evidence of multisystem disease, cognitive problems or impaired mobility.
- I provide a very busy integrated adult Internal Medicine and Geriatric Medicine service (with a major commitment to unselected on-call General Medicine, and basically when time allows, I endeavour to do a comprehensive geriatric assessment on my patients.

41% of Irish ROs and MOs stated that they "sometimes" perform GA, under the following conditions (specified by five of these respondents):

- I don't use a formal geriatric assessment, but I would enquire about ADLs, functional status, cognitive impairment, mobility. (RO)
- Realistically this is generally done by the referring team. Occasionally this is necessary when trying to decide whether curative radiotherapy is possible. (RO)
- If they are frail. (MO)
- When concerned about competence to provide consent, comply with treatment instructions etc. (MO)
- Patients deemed borderline suitable for cancer directed treatment on the basis of clinical examination (MO)

Appendix 2: How is geriatric assessment integrated into the clinical care of older patients at your institution?

- It is considered mandatory
- 3 patterns of care: - GA as a part of standard medical examination in my own clinics - multidisciplinary GA (MGA) led by a geriatrician once a week comprehensive GA at the geriatric hospital sometimes
- Mobile geriatric team
- Geriatric nurse looks for all patients in the hospital, and contacts them directly. She puts the results of CGA in the medical files and makes it available to treating physician. She also discusses the results on paper with a geriatrician and gives concrete geriatric advice, but the treating oncologist finally decides what will be done.
- Ad hoc basis
- CGA helps clinical decision making
- Not routinely integrated except at the geriatric ward
- Geriatrician in house x3/week
- Initial screening for new patients 70-75+ with G8, systematic referral to geriatrician if positive screening Clinical trials for elderly (adjuvant and metastatic, breast cancer mostly)
- We offer the assessment for all patients
- Multifactorial GA screening test is a self administered questionnaire with follow up phone call from a cancer care coordinator.
- In difficult decision process a consultation is requested
- A complete geriatric assessment within clinical trials or a screening assessment in daily practice
- We can ask the geriatricians to meet the patients when needed
- Colleagues call me to see their patients (Geriatrician)
- It is a part of the standard care
- It isn't integrated; I do it by myself. I have some scales at my outpatient clinic and I do it If I have time (almost never)
- Admin by staff before 1st visit for cancer treatment, based on individual study protocol, or in general geriatric care on 1st visit to clinic

- There is a Unit of Cancer in the Elderly, and every patient >= 70 years is offered geriatric assessment

Appendix 3: Is there an age cut-off that should be used to establish a standard for who should undergo GA in Oncology?

Rationale for choosing this age cut-off:

- Because the probability of having medical or social problems in addition to cancer becomes more important beyond 75 years. (SIOG)
- SIOG recommendations (SIOG)
- Most age-related problems start to occur after that age (SIOG)
- As defined by SIOG. (SIOG)
- Need to put a cut-off. (SIOG)
- It sticks to our programmes of clinical research specifically developed for patients 70+ (SIOG)
- 75+ may be alternatively considered (SIOG)
- 60 and over because this is the age that defines elderly in my country(SIOG)
- You do need a threshold of some sort and there is no right answer to this question. (SIOG)
- In my main tumour site (breast cancer) this is where evidence base tails off. (SIOG)
- Increasing number of patients with deficits. (SIOG)
- Most physiological changes and age-related problem occur after 70. (SIOG)
- Also I use under 70 age If the patients have comorbidity (SIOG)
- Because I think that the geriatric assessment should be applied to every older patient that I consider. (SIOG)
- That the age over 70 years is the limit between older patients and not older patients. (SIOG)
- Above 70 more comorbidities and more polypharmacy. (SIOG)
- If I was to choose an age - this is the age I would choose.(Ger)
- Most likely to yield appropriate population.(Ger)
- Usually this but there are frail younger people with complex needs who would also benefit... can't definitively give an age cut off.(Ger)
- International age of retirement and leaving middle age to old age. younger patients may be biologically older and should be able to access similar types of assessment through specialty services or rehab specialty.(Ger)
- This is current practice - however, this is purely convention and probably needs to change. A better standard would include a higher age and some criterion for frailty.(Ger)
- Most 69 year olds I see are fairly fit (MO)
- It is an age above which few patients are represented in clinical trials. I believe using an older cut off would potentially miss patients with significant impairment. (MO)
- Far fewer studies evaluating the benefit (or detriment) from treatment in this group (MO)
- Generally the elderly medicine teams may not see pts younger than 70 or 65 however we may have an elderly 63 years old that may benefit from the geriatricians and support service skill set. Realistically it probably should be set at 65-70 (MO)
- Pragmatism. This is the age in my country that the incidence of geriatric syndromes and other issues starts to rise steadily. Having said that if someone younger looks or sounds older I will assess them in the same way (MO)
- Above this age very few patients in clinical trials. We tend to extrapolate their treatment from clinical trials on younger patients which is not ideal. (RO)
- Chronological age is a poor predictor for life expectancy. Trials rarely include patients over 70 making decision making more difficult. (RO)
- Personal Clinical opinion (RO)

Rationale for <u>not</u> having an age cut-off:

- Inappropriate to deny patients good care due to age (SIOG)
- However, younger people may have true geriatric problems! (SIOG)
- 69 years old or 71 years old for example...which is the difference? (SIOG)
- The need for GA depends more on functional status and comorbidities than chronological age. (SIOG)
- Ageing is a highly individualized process. (SIOG)
- Not depending on the calendar age but on the physiologic age. (SIOG)

- Age does not do justice to the heterogeneity of the older population. (SIOG)
- There can be many patients who are 78 and biologically fitter and younger than a 58 year old who has chronic illness. (Ger)
- Because many 70+ year olds are very well, and some 60 year olds physically have very similar issues to frail older people, so as a geriatrician, have to reject a purely age based cut-off, although useful as a guide. (Ger)
- There may be patients who are biologically older than their chronological age suggests. (Ger)
- I believe that patients should have a CGA based on needs, not age. (Ger)
- Often younger patients have geriatric needs and often older pts have no geriatric needs i.e. have single system pathology. (Ger)
- Age related frailty is the main determinant of the need for geriatric assessment. This can occur as early as 50 or well into 90's. Below 50 years frailty is usually for reasons other than ageing and often geriatricians do not have the skill set to deal with those individuals (who often include learning disability, mental health problems, substance abuse disorders sufferers). The requirement for CGA should be needs based therefore. (Ger)
- I think it's difficult to select a specific chronological age but it is, of course more practical than trying to define a biological age. If I had to pick one age it would probably be 70 (RO)
- Should depend upon PS, cognition, functionality and comorbidity rather than age alone (RO)
- It depends on patients general condition whether the patient is mentally and physically fit enough at the time of consultation (RO)
- There is a general uncertainty as to the appropriate age cut-off and some clinical discretion should be used (MO)
- It's more based on functionality than absolute age (MO)
- Patient with co-morbidities aged 68 should be assessed, independent patient without e.g. aged 78 may not need it. (MO)

Appendix 4: Education Needs Required to Implement GA in Irish Oncology

- Gerontology nurse training a programme to educate regarding geriatric medicine(Ger)
- Very little, all you need is the right tools...easy to learn... (Ger)
- Cognitive impairment - dementia and delirium and overlap training, falls versus syncope differentiation and check list approach to multifactorial falls assessment; atypical presentations of older people (e.g. painless PE, perforation; systemic complaints with pneumonia rather than dyspnoea, etc); urinary retention/ incontinence; basics of Parkinson's disease; and overall medical care that I'm sure is part of oncology anyway. (Ger)
- Little integration of specialties in Ireland. Understanding of concept of frailty in non-cancer illnesses, role of family & social supports, rehabilitation - role and resources. (Ger)
- Probably very little really-providing the ward already has physiotherapy and occupational therapy staff members. (Ger)
- Need full MDT geriatric assessment. (Ger)
- Knowledge of frailty, cognitive impairment, functional disability, social needs of older people, sound, broad pharmacological knowledge. (Ger)
- Education wrt CGA. (Ger)
- An understanding of, and experience in, multi-disciplinary geriatric assessment. Ideally this would include some familiarity with a variety of assessment scales. (Ger)
- Better training and awareness of the issues elderly and infirm patients face in the form of, at least, lectures/seminars (RO)
- Some sort of training in the form of lectures/seminars to help highlight the most crucial aspects of an assessment would be the minimum I believe (RO)
- Training and review of skills by Geriatricians of other staff members (RO)
- Focused training regarding GA. (RO)
- Basic geriatric assessments can be performed by medical oncologists but are very crude tools. Complete geriatric assessments should preferably be performed by a multidisciplinary team under the supervision of a geriatrician.(MO)
- Education regarding the principles of geriatric oncology, the role of and means of

performing assessments, what tools are available and how they are interpreted, the potential benefits of a combined approach by geriatricians and oncologists in the management of older patients, the potential for assessments to impact treatment decisions and predict tolerance to therapy.(MO)

- Less so educational needs but more a dedicated structure e.g. Geriatric Oncology team, OPD, nurse i.e. an identified service. (MO)
- Not very much. (MO)
- Time factor. (MO)
- Resources need to take priority (MO)

Appendix 5: How do you determine patients for each category (fit/vulnerable/frail)?

- Discussion regarding their overall function and level of independence (MO)
- A la Balducci modified by toxicity risk criteria of Hurria and Extermann except do not use absolute age in any judgement (MO)
- Don't understand this (MO)
- Care needs, function, cognition risk (Ger)
- We rarely use frailty tools in clinical practice, but use our "gut feeling" based on all available information (Ger)
- General clinical judgement (Ger)
- We use VIP score on all pts admitted following a fall (Ger)
- Global clinical assessment. I don't use a frailty scale for the final decision but I often use assessment scales to help me inform the decision (Ger)
- Depending on the number of problems detected by GA (SIOG)
- According to Balducci classification (SIOG)
- No good established criteria available. we just describe and make recommendations for geriatric interventions (SIOG)
- Balducci's operative definition (SIOG)
- According to Balducci definition (SIOG)
- Published guidelines when exist (prostate and SIOG for example G8 (fit if screening > 14) (SIOG)
- The screening tool allows allocation to a category depending on a scoring system preformed by the cancer care coordinator (SIOG)
- Fit no major comorbidity, no cognitive impairment, no IADL / ADL impairment (SIOG)
- Fit: no ADL or only 1 IADL dependency, no severe comorbidity at CIRS-G, no geriatric syndromes. Vulnerable: no ADL dependency, intermediate comorbidity, no geriatric syndromes. Frail: ADL dependency, more than 2 grade 3 or a grade 4 CIRS-G comorbidity, geriatric syndromes. (In general, some minor differences depends on the protocol when in CTs) (SIOG)
- This done by the geriatricians (SIOG)
- G8 score for fit pts. Full CGA if abnormal G8 and CIRSG for frail vs. vulnerable pts. (SIOG)

- I use Balducci classification (SIOG)
- I use Balducci's criteria and Fried's criteria (SIOG)
- Above certain threshold points the patient belongs to category vulnerable or frail (SIOG)

Appendix 6: How do you use GA to Identify Patients at High Risk for Adverse Outcomes?

- If immobile, poor performance status and not independent I would be less inclined to offer them radical treatment or combined chemoradiation (RO)
- A poor performance status or presence of significant comorbidities may result in me delivering palliative (or no) treatment. Similarly an assessment that identifies that an elderly person is very fit for their age might lead us to treat them more "aggressively" (RO)
- A very basic, largely subjective, inclusion of age related comorbidity would be factored into an overall performance status (RO)
- All patients are assessed for ECOG PS. In selected patients I use MMSE to screen for cognitive impairment (MO)
- Not routinely done. The CRASH score and Hurria papers are referred to in selected patients but not routinely utilized in all patients (MO)
- Frail and poorer performance status patients may be dose-reduced to avoid serious toxicity (MO)
- We base geriatric assessment similar to all patients i.e. Performance status ECOG/KPS and review their psychosocial fitness for treatment in addition to their disease features and physiologic capability to withstand treatment. This assessment is done for all pts except this age group will obviously identify more adverse features (MO)
- If dependent in IADL, falls, malnourished, cognitively impaired, severe comorbidity (ASA grade IV), severe social isolation (MO)
- Use to supplement assessment of fitness for systemic therapy (MO)
- Those who clinically look frail or have multiple comorbidities or score lowly on Barthel score / MMSE etc.(Ger)
- To identify risk based on comorbidities, falls risk, cognitive decline .(Ger)
- We have a short screening tool that measures risk...called the Community Assessment of Risk Screening Tool (CARST) (Ger)
- Barthel score good for overall function (although flaws), combined with social supports available (i.e. if very dependent and lives alone, not good), cognitive ability (i.e. risk of doing something unsafe), previous adverse events, specific risks e.g. warfarin and falls, ongoing alcohol use, and the specific medical

condition severities.(Ger)

- Interdisciplinary assessment, MDT discussion, reassessment, collateral history on change. Scoring scales for personal & instrumental function, cognition, mood, frailty, balance.(Ger)
- I focus on factors like functional status including mobility, cognition, falls, urinary incontinence all of which can be good guides to likely adverse outcomes. (Ger)
- Review of premorbid diagnosis/functioning, cognitive assessment +/- Competency. Review of medications and compliance with same Physio assessment of balance/mobility (Berg/EMS/TUG) .(Ger)
- Patients are identified for falls risk, malnutrition risk, risk from impairment of judgement secondary to cognitive impairment, risk of elder abuse. Inpatients are assessed for pressure ulcer risk.(Ger)
- We use VIP score and all pts admitted following a fall.(Ger)
- Experience.(Ger)
- Identification of problems in the different domains of GA, identification of risk factors according to treatment options (SIOG)
- A combination of co morbidity and irreversible pathology in the CGA (SIOG)
- General impression of the CGA is integrated in the treatment plan. no strict cut-offs (does not exist)
- Based on a nomogram we developed locally (SIOG)
- Functional status and comorbidities (SIOG)
- We look for severe comorbidity and disability, as well as cognitive dysfunction (SIOG)
- Frailty items to correct upfront oncological decisions (SIOG)
- Identify frailty(SIOG)
- Our method has not been shown to be useful for this aim (SIOG)
- I do not use these routinely, but have several research projects validating this approach. (SIOG)
- CGA or shorter screening and fit/vulnerable/frail characterization (SIOG)
- Major comorbidity, cognitive impairment, IADL / ADL impairment (SIOG)
- MNA GDS15 (SIOG)
- I use ADL and IADL and comorbidity scales (SIOG)

- I consider that there is a high risk for adverse outcomes if there are two or more scales of the Comprehensive Geriatric Assessment in which there is a deficit. (SIOG)

Appendix 7: The Potential Barriers Regarding Implementation of GA

- We have no interactions with Geriatric specialists Time Organisation (RO)
- For clinicians, lack of training in caring for older patients, so therefore not familiar or comfortable with performing geriatric assessment (RO)
- Limited resources. Over-stretched geriatric teams. (RO)
- Time, resources, difficulty accessing appropriate disciplines (RO)
- Time and lack of familiarity (RO)
- Training and staff to do it (RO)
- Time (RO)
- No consultant geriatrician (MO)
- We do not have a dedicated geriatric service. Time pressure prevent implementation of complex geriatric assessment tools (MO)
- Time and staff resource limitations coupled with large volumes of older patients with cancer render comprehensive assessments difficult to implement. Underappreciation among the medical oncologists and geriatric services of the merits of integrating the specialities
- Lack of time and human resources (MO)
- Space, time constraints, resources e.g. OPD space, geriatricians willing to take on service, access to support services etc. (MO)
- As always want to do is the major hurdle. what to do and how to do can be more readily overcome by using one of the screening questionnaires (MO)
- Time (MO)
- Lack of staff and time, all medical staff already working many hours beyond scheduled hours and oncology clinics routinely overbooked; these assessments take time. Also, importantly, motivation of staff to undertake detailed assessments of patient needs is undermined by lack of available resources to address those needs, e.g. if a geriatric assessment identifies difficulties in ADLs and support needs, but staff e.g. MSWs routinely encounter difficulties already in accessing home care packages and other community supports then identifying needs which cannot be met may seem futile. (MO)
- Time. Resources - lack of full MDT support.(Ger)
- Time and personnel constraints traditional modes of isolated practice service organisation, consultant and AHP staffing levels (Ger)
- Time and trained staff (Ger)
- Geriatricians can only see a fraction of the older people in the community or in hospital, so this 5-10% get a great service, rest get nothing (Ger)
- Resources, slow integration of clinical care programmes, ageism (Ger)
- Lack of resources at medical and nursing level (Ger)
- The lack of understanding of the importance of MDT working. Maternity leave for physiotherapists and OT is not covered and there is a general assumption that a geriatrician alone can do a geriatric assessment (Ger)
- My institution is co-operative and sensitive to the needs of older patients. However the greatest barriers to effective assessment include lack of time, and lack of knowledge amongst more junior staff. (Ger)
- Lack of staff and time. Interface with community services (Ger)
- There are delays in formal assessments by multi-disciplinary team members because of resource issues (Ger)
- Takes a long time. Poor understanding of process by non geriatric medicine trained staff (SIOG)
- Lack of knowledge from colleagues lack of geriatric resources (SIOG)
- Time consuming (SIOG)
- (Finding the patients; we are currently very efficient in this). Motivate the oncologists to use the geriatric information and proposed geriatric interventions. Some are very interested, others really don't care. (SIOG)
- Time consuming (SIOG)
- Build a team and time to perform assessment (SIOG)
- Too little knowledge about the impact of functional status (SIOG)
- Collaboration with geriatricians already fully involved in the activity of their service (SIOG)
- Organisation demonstration of utility to convince presence of geriatrician limited to 2 days/week no specific trained nurse (SIOG)
- Time of application small team of geriatricians (SIOG)
- Perceived as being too difficult, not showing a measurable benefit and being too costly in terms of time and money (SIOG)

- Time: lack of validation (against relevant outcomes) in this group no exact cut-off levels for decisions defined, no qualified stuff available no reimbursement (SIOG)
- No educated staff, no geriatric oncology team (SIOG)
- Not enough geriatricians (SIOG)
- Lack of referral (SIOG)
- In geriatrics: none in geriatric oncology: hesitance from cancer specialists to solicit aid from geriatricians (SIOG)
- In X country, institutions are not recognising the needs for geriatric assessment; so I do it by myself because I believe in it, but we are far away to do it in an institutional form (SIOG)
- Time to implement in oncology care (SIOG)
- I am the only Medical Oncologist who performs Comprehensive Geriatric Assessment and not every elderly patient diagnosed with cancer is referred to me. (SIOG)
- Regular contact with geriatrician (SIOG)

Appendix 8: Patient Characteristics that should be used to Establish Guidelines for those who should Undergo GA in Oncology

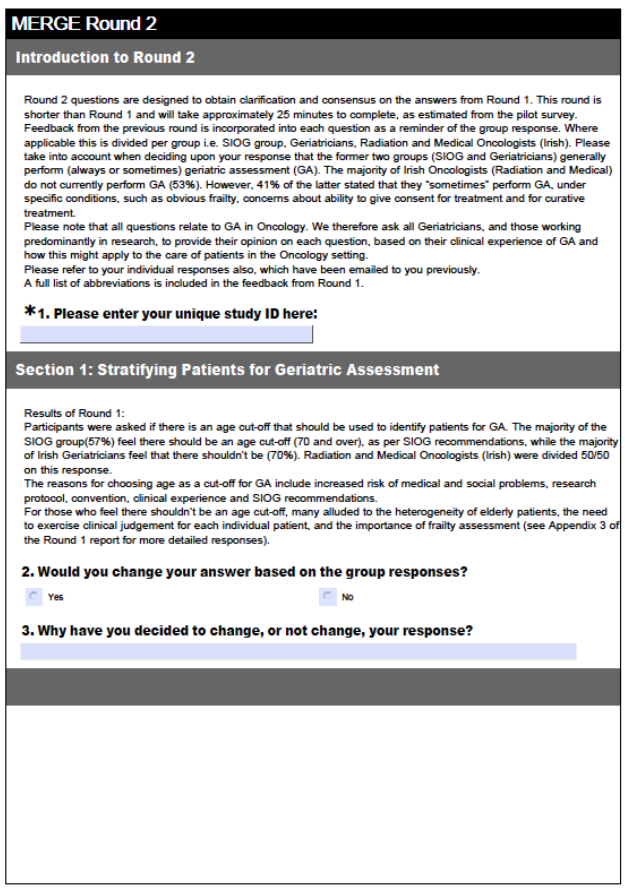
- Frailty in those under 70. (SIOG)
- I don't think we are able to define patient characteristics to date. A major concern is the tumour type and the treatment planned like complex surgery, sequential treatment, curative intent.....(SIOG)
- We do a short screening test in all, and only do CGA in the pts with bad screening test. (SIOG)
- No particular characteristics. (SIOG)
- For practical reasons I think an age limit is important. But disability and cognitive dysfunction as well as comorbidities (or clinical judgment indicating frailty) should also prompt a geriatric assessment. (SIOG)
- Type of treatment/approach they are candidates for. (SIOG)
- Comorbidities, functional status place where they live and importance of family and friends (social). (SIOG)
- Polypharmacy, frailty, cognitive impairment three or more comorbidities falls. (SIOG)
- Obvious frailty. (SIOG)
- Age above a certain level. (SIOG)
- Age, obvious functional impairment for those near age cut-off, short screening tools. (SIOG)
- Comorbidities. (SIOG)
- Comorbidities. (SIOG)
- I think every patient should get a short form of geriatric assessment. (SIOG)
- I think that age is the only factor. (SIOG)
- Difficult question. The point is to discover hidden shortcomings. Predefined characteristics can miss hidden features. (SIOG)
- History of significant illness - heart / chest / neurological / rheumatologic. Generally frail Multiple comorbidities Complex social difficulties. (Ger)
- Age and screening. (Ger)
- Screening tool. We use CARST risk assessment...(Ger)
- Frail, cognitive impairment, functionally dependent, concerns in community. (Ger)

- Age cut off. Oncology diagnosis, staging and prognosis. Presence of geriatric syndromes, social isolation, polypharmacy. (Ger)
- All elderly patients (e.g. >/= 70 years) and leave open the option for a needs related approach also (i.e. a frail younger adult with complex care-needs). (Ger)
- Any patient with multiple comorbidities. Any neurological disorder. The presence of Alzheimer's/vascular dementia Frailty of old age. (Ger)
- Frailty characteristics (e.g. Fried criteria); those identified as abnormal on a cognitive screen. (Ger)
- Identifications of geriatric syndromes. Although I appreciate debate using screening tools often can be helpful wrt guidance. (Ger)
- Performance in activities in daily living at personal, domestic and social participation levels. (Ger)
- Age and life expectancy. (RO)
- Level of independence i.e. reliance on family/friends/social services. Level of cognitive impairment. Performance status. (RO)
- PS, cognition, functionality and comorbidity. (RO)
- ECOG performance status, no and type of medical co morbidities, physical examination. (RO)
- Age and clinical observation of patient by Physician and Nursing staff. (RO)
- Comorbidities, suspected dementia. (MO)
- A brief screening tool would be useful: i.e. recent falls, social isolation, and comorbidites. (MO)
- Screening assessments should be used to determine need for full geriatric assessment with a focus on functional dependencies, cognition, mood and nutrition. (MO)
- Very difficult in such a diverse group of individuals. There are physiologically old 65yo patients and vigorous 80 year olds. How do you reflect that? (MO)
- Poor social circumstances e.g. poor housing, poor support, no family, suboptimal place home facilities. Multiple comorbidities e.g. cerebrovascular disease or neurological conditions e.g. dementia, Parkinson's. Older age where features may be subclinical but extra support helpful. (MO)
- 1. Age > 75 2. Age <75 but factors favouring premature ageing/frailty e.g. heavy cig/alcohol use, multiple comorbidity, social isolation all of which available from

standard history taking. (MO)

- Age as one part comorbidities social circumstances. (MO)

Appendix 6: Study 1 Round 2 Survey



MERGE Round 2

Introduction to Round 2

Round 2 questions are designed to obtain clarification and consensus on the answers from Round 1. This round is shorter than Round 1 and will take approximately 25 minutes to complete, as estimated from the pilot survey.
Feedback from the previous round is incorporated into each question as a reminder of the group response. Where applicable this is divided per group i.e. SIOG group, Geriatricians, Radiation and Medical Oncologists (Irish). Please take into account when deciding upon your response that the former two groups (SIOG and Geriatricians) generally perform (always or sometimes) geriatric assessment (GA). The majority of Irish Oncologists (Radiation and Medical) do not currently perform GA (53%). However, 41% of the latter stated that they "sometimes" perform GA, under specific conditions, such as obvious frailty, concerns about ability to give consent for treatment and for curative treatment.
Please note that all questions relate to GA in Oncology. We therefore ask all Geriatricians, and those working predominantly in research, to provide their opinion on each question, based on their clinical experience of GA and how this might apply to the care of patients in the Oncology setting.
Please refer to your individual responses also, which have been emailed to you previously.
A full list of abbreviations is included in the feedback from Round 1.

***1. Please enter your unique study ID here:**

Section 1: Stratifying Patients for Geriatric Assessment

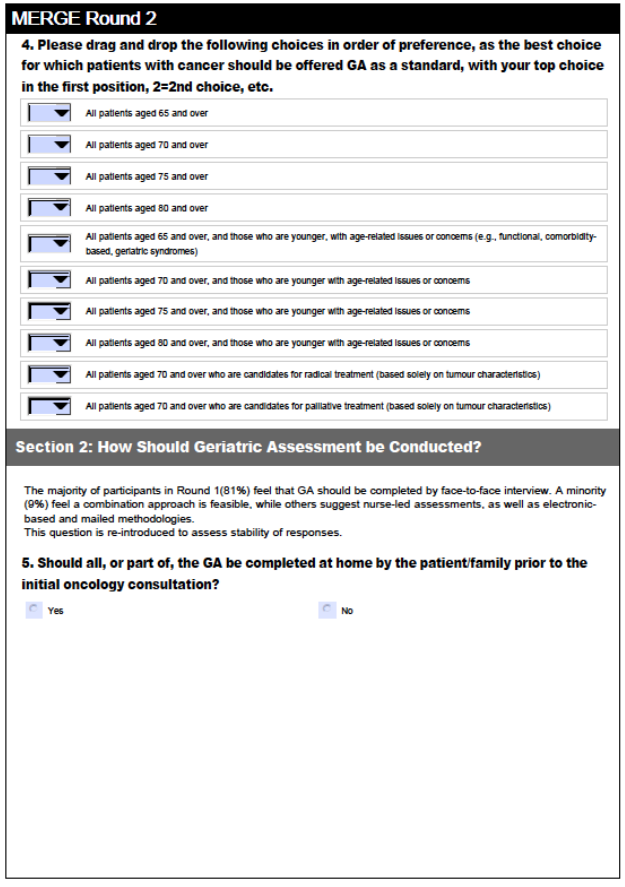
Results of Round 1:
Participants were asked if there is an age cut-off that should be used to identify patients for GA. The majority of the SIOG group(57%) feel there should be an age cut-off (70 and over), as per SIOG recommendations, while the majority of Irish Geriatricians feel that there shouldn't be (70%). Radiation and Medical Oncologists (Irish) were divided 50/50 on this response.
The reasons for choosing age as a cut-off for GA include increased risk of medical and social problems, research protocol, convention, clinical experience and SIOG recommendations.
For those who feel there shouldn't be an age cut-off, many alluded to the heterogeneity of elderly patients, the need to exercise clinical judgement for each individual patient, and the importance of frailty assessment (see Appendix 3 of the Round 1 report for more detailed responses).

2. Would you change your answer based on the group responses?

Yes No

3. Why have you decided to change, or not change, your response?

Page 1



MERGE Round 2

4. Please drag and drop the following choices in order of preference, as the best choice for which patients with cancer should be offered GA as a standard, with your top choice in the first position, 2=2nd choice, etc.

All patients aged 65 and over
All patients aged 70 and over
All patients aged 75 and over
All patients aged 80 and over
All patients aged 65 and over, and those who are younger, with age-related issues or concerns (e.g., functional, comorbidity-based, geriatric syndromes)
All patients aged 70 and over, and those who are younger with age-related issues or concerns
All patients aged 75 and over, and those who are younger with age-related issues or concerns
All patients aged 80 and over, and those who are younger with age-related issues or concerns
All patients aged 70 and over who are candidates for radical treatment (based solely on tumour characteristics)
All patients aged 70 and over who are candidates for palliative treatment (based solely on tumour characteristics)

Section 2: How Should Geriatric Assessment be Conducted?

The majority of participants in Round 1(81%) feel that GA should be completed by face-to-face interview. A minority (9%) feel a combination approach is feasible, while others suggest nurse-led assessments, as well as electronic-based and mailed methodologies.
This question is re-introduced to assess stability of responses.

5. Should all, or part of, the GA be completed at home by the patient/family prior to the initial oncology consultation?

Yes No

Page 2

MERGE Round 2

6. Do you think self-report GA items are feasible for any of the following domains of GA?

	Yes	No
Functional status	○	○
Objective physical performance status (i.e. gait speed, balance, strength)	○	○
Comorbidity	○	○
Cognitive status	○	○
Polypharmacy	○	○
Nutritional status	○	○
Social support status	○	○
Psychological status-anxiety	○	○
Psychological status-depression	○	○

If you said no to any of the above, please specify why you think self-report items are not feasible.

MERGE Round 2

7. Please rank the following from the least feasible to the most feasible in Oncology, with 0=least feasible, 10 = most feasible

	0=not feasible	1	2	3	4	5	6	7	8	9	10=most feasible
Send GA paper survey to patients to complete before first consultation	○	○	○	○	○	○	○	○	○	○	○
Send email with web-based link to patients to complete GA items prior to initial consultation	○	○	○	○	○	○	○	○	○	○	○
Ask patient (with the assistance of carer(s)) to complete GA items with pen and paper at clinic visit (in office)	○	○	○	○	○	○	○	○	○	○	○
Ask patient (with the assistance of a nurse) to complete GA items with pen and paper at clinic visit (in office)	○	○	○	○	○	○	○	○	○	○	○
Complete GA items through web-based program by computer at clinic visit (in office/waiting area)	○	○	○	○	○	○	○	○	○	○	○
Complete GA items through web-based program by touch pad at clinic visit (in office/waiting area)	○	○	○	○	○	○	○	○	○	○	○
Home-based assessment by the primary care team/Public Health Nurse/OT/homecare team	○	○	○	○	○	○	○	○	○	○	○

Please comment further

Section 3: Screening Tools

8. Do you think screening, with a shorter geriatric-based measure, should be instituted as standard practice in order to help determine who should undergo full GA in Oncology?

○ Yes ○ No

Please comment further

MERGE Round 2

9. Why/why not?

10. If you answered yes to the above question, please tick the answer you agree with the most below

- A specific screening measure should be recommended for all patients to identify those who should get a full GA.
- At this point, no specific screening measure should be recommended, and any screening measure could potentially be used
- NA

If you selected option A, please indicate which screening tool you would use.

11. Please drag and drop the following choices in order of preference, as the best choice of screening tool for use in Oncology, with your top choice in the first position, 2=2nd choice, etc.

You may skip this question if you are not familiar with the screening tools below.

- VES-13
- G8
- GFI
- Self rated health
- Objective physical performance
- Functional status
- ECOG PS
- Karnofsky PS
- Cancer and Ageing Research Group chemotherapy toxicity score
- CRASH score
- Abbreviated Comprehensive Geriatric Assessment (aCGA)

GA: Functional Status

The majority of the expert panel employ ADL and IADL scales, usually in combination, to measure functional

MERGE Round 2

impairment. Performance status measures, such as ECOG and Karnofsky, are also commonly used.

12. Drag and drop the following choices in order of preference, as the best choice of functional assessment method for older patients, with your top choice in the first position, 2=2nd choice, etc.

- ADL only
- IADL only
- ADL/IADL in combination
- KPS
- ECOG PS
- VES-13
- FIM/FAM
- Barthel Index
- Patient history/clinical examination

The majority of participants (31%) recommend physiotherapy/exercise intervention for functional impairments. Involvement of Occupational Therapists (16%) and nurses (4%) is also proposed, as well as further assessment in the form of a CGA (n=1). Homecare interventions including environment adaptations, PHN/OT home visits and a review of social support structure were identified as important by 12% of respondents.

13. Please rank the top 3 interventions for functional impairment, where 1=the best option, 2=2nd best etc:

- Physiotherapy referral
- Occupational Therapist referral
- Nurse intervention
- Public Health Nurse/ Homecare intervention/day hospital
- Exercise programme

14. Can any healthcare professional, with sufficient training, perform functional status assessment?

- Yes
- No

If you answered no, please specify who should complete the assessment.

MERGE Round 2

15. If there is anything further you would like to add in relation to functional assessment, please do so here.

GA: Objective Physical Performance Status

Results of Round 1 showed that the Timed Up and Go test, as well as balance tests are commonly used, alone, or in combination, with a variety of other assessments.

16. Please rank the top 3 assessment tools for physical performance impairment, in your opinion, where 1=best, 2=2nd best etc.

- TUG
- Gait speed
- Balance assessment e.g. Berg
- Grip strength
- EMS
- SPBB
- CHS criteria
- Observation

Interventions for physical performance impairment are similar to those listed for functional impairments above.

17. Please rank the top 3 interventions for physical performance impairment, where 1=the best option, 2=2nd best etc:

- Physiotherapy referral
- Occupational Therapist referral
- Nurse intervention
- Public Health Nurse/ Homecare intervention/day hospital
- Exercise programme

18. Can any healthcare professional, with sufficient training, perform physical performance status assessment?

Yes No

If you answered no, please specify who should complete the assessment.

MERGE Round 2

19. If there is anything further you would like to add in relation to physical performance assessment, please do so here.

GA: Cognitive Status

The MMSE is the most commonly used assessment method for cognitive impairment (53%). Other less commonly used tools include the AMTS, MiniCog, MOCA, Clock drawing test, Rivermead, Addenbrooks, QMCI, Pfeiffer questionnaire, fluency frontal assessment battery, MEAMS, CAMCOG, RBANS, delayed word recall and clinical judgement.

20. Please rank the top 3 assessment tools for cognitive status, in your opinion, where 1=best, 2=2nd best etc.

- MMSE
- AMTS
- MiniCog
- MOCA
- Clock drawing test
- Rivermead test
- Addenbrooks test
- QMCI
- Pfeiffer questionnaire
- Fluency frontal assessment battery
- MEAMS
- CAMCOG
- RBANS
- Delayed word recall
- Clinical judgement

Recommended interventions for cognitive impairment included: psychologist/psychiatrist review (10%), geriatrician referral (14%), medication (16%), advance care planning (4%), homecare interventions/day hospital (8%), OT (8%) and other (8%).
Other interventions for cognitive impairment include referral to a memory clinic, dementia workup and lifestyle advice.

MERGE Round 2

21. Please rank the top 3 interventions for cognitvie impairment, where 1=the best option, 2=2nd best etc:

- Psychologist/psychiatrist referral
- OT referral
- Geriatrician referral
- Medication
- Home care intervention
- Day hospital care
- Memory clinic referral
- Advance care planning

22. Can any healthcare professional, with sufficient training, perform cognitive assessment?

Yes No

If you answered no, please specify who should complete the assessment.

23. If there is anything further you would like to add in relation to cognitive assessment, please do so here.

GA: Co-morbidities

The majority of participants use the Charlson Comorbidity Index (24%). Other methods include chart review/medical history (16%), CIRS-G (14%), with a minority using the ASA grade and SCS (both 2%).

24. Please rank the top 3 assessment tools for co-morbidities, in your opinion, where 1=best, 2=2nd best etc.

- Charlson Comorbidity Index
- CIRS-G
- Chart review/medical history/list
- ASA grade
- SCS

MERGE Round 2

Referral to organ specialists/other disciplines (such as physiotherapy) for optimisation and management of designated comorbidities is employed, as deemed appropriate.

25. Please rank the top 3 interventions for co-morbidities where 1=the best option, 2=2nd best etc:

- Referral to specialists as deemed suitable for a given co-morbidity
- Medication
- Geriatrician referral

26. Can any healthcare professional, with sufficient training, perform co-morbidities assessment?

Yes No

If you answered no, please specify who should complete the assessment.

27. If there is anything further you would like to add in relation to co-morbidities assessment, please do so here.

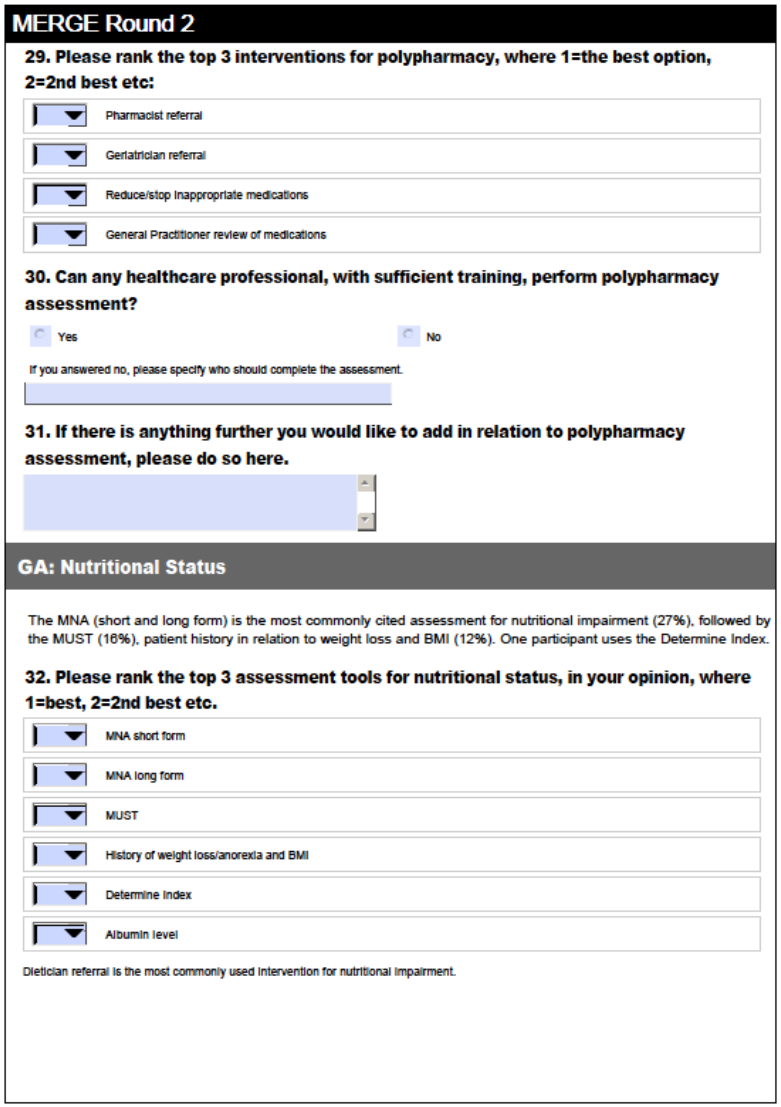
GA: Polypharmacy

Three participants use the STOPP START tool to address potentially inappropriate medication use. All other respondents use medical history/list of medications or pharmacy review.

28. Please rank the top 3 assessment tools for medications, in your opinion, where 1=best, 2=2nd best etc.

- STOPP START criteria
- BEERs criteria
- List of medications/medical history
- Pharmacist review

The majority of participants recommended review of medications with the cessation of inappropriate medication use. The patients' GP, pharmacist and geriatrician were identified as having a role to play in this intervention.



MERGE Round 2

29. Please rank the top 3 interventions for polypharmacy, where 1=the best option, 2=2nd best etc:

- Pharmacist referral
- Geriatrician referral
- Reduce/stop inappropriate medications
- General Practitioner review of medications

30. Can any healthcare professional, with sufficient training, perform polypharmacy assessment?

Yes No

If you answered no, please specify who should complete the assessment.

31. If there is anything further you would like to add in relation to polypharmacy assessment, please do so here.

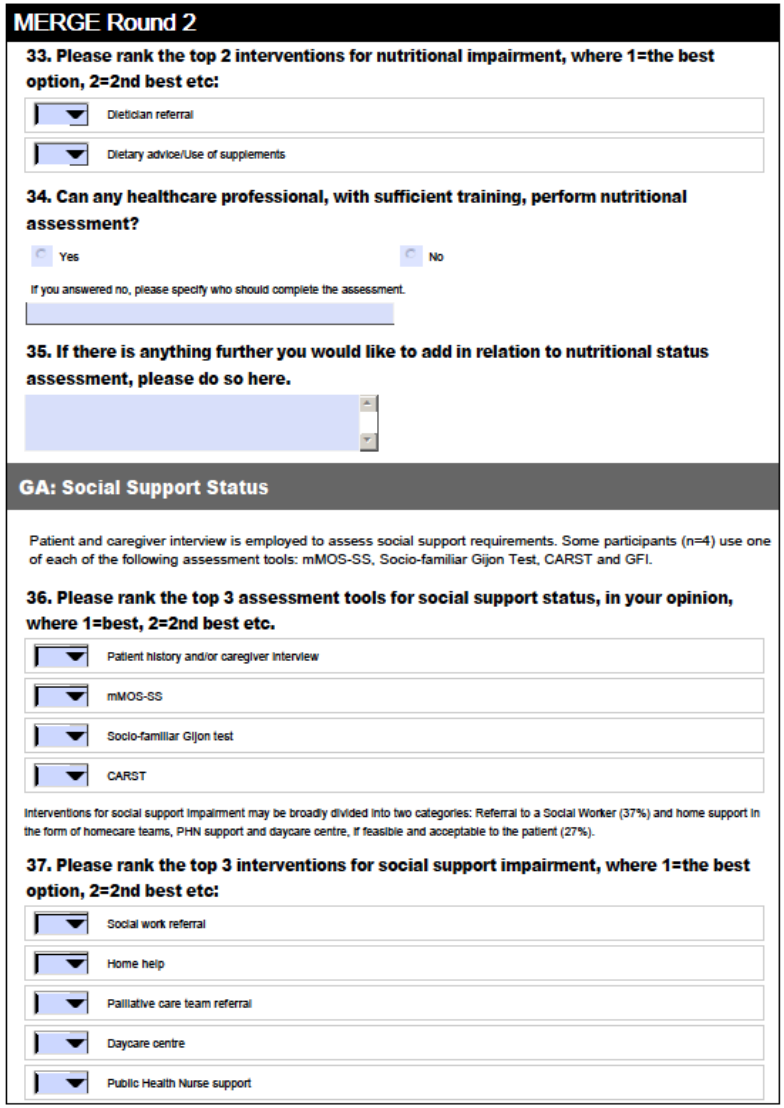
GA: Nutritional Status

The MNA (short and long form) is the most commonly cited assessment for nutritional impairment (27%), followed by the MUST (16%), patient history in relation to weight loss and BMI (12%). One participant uses the Determine Index.

32. Please rank the top 3 assessment tools for nutritional status, in your opinion, where 1=best, 2=2nd best etc.

- MNA short form
- MNA long form
- MUST
- History of weight loss/anorexia and BMI
- Determine Index
- Albumin level

Dietician referral is the most commonly used intervention for nutritional impairment.



MERGE Round 2

33. Please rank the top 2 interventions for nutritional impairment, where 1=the best option, 2=2nd best etc:

- Dietician referral
- Dietary advice/Use of supplements

34. Can any healthcare professional, with sufficient training, perform nutritional assessment?

Yes No

If you answered no, please specify who should complete the assessment.

35. If there is anything further you would like to add in relation to nutritional status assessment, please do so here.

GA: Social Support Status

Patient and caregiver interview is employed to assess social support requirements. Some participants (n=4) use one of each of the following assessment tools: mMOS-SS, Socio-familiar Gijon Test, CARST and GFI.

36. Please rank the top 3 assessment tools for social support status, in your opinion, where 1=best, 2=2nd best etc.

- Patient history and/or caregiver interview
- mMOS-SS
- Socio-familiar Gijon test
- CARST

Interventions for social support impairment may be broadly divided into two categories: Referral to a Social Worker (37%) and home support in the form of homecare teams, PHN support and daycare centre, if feasible and acceptable to the patient (27%).

37. Please rank the top 3 interventions for social support impairment, where 1=the best option, 2=2nd best etc:

- Social work referral
- Home help
- Palliative care team referral
- Daycare centre
- Public Health Nurse support

MERGE Round 2

38. Can any healthcare professional, with sufficient training, perform social support assessment?

Yes No

If you answered no, please specify who should complete the assessment.

39. If there is anything further you would like to add in relation to social support status assessment, please do so here.

GA: Psychological Status: Anxiety and Depression

The GDS is the most commonly used assessment for depression (39%), while the HADS is used for assessment of both anxiety and depression by a minority of respondents.

40. Please rank the top 3 assessment tools for anxiety, in your opinion, where 1=best, 2=2nd best etc.

- HADS
- Patient history/interview
- Distress thermometer

41. Please rank the top 3 assessment tools for depression, in your opinion, where 1=best, 2=2nd best etc.

- GDS-short form
- GDS-long form
- HADS
- Patient history/interview

Interventions for anxiety and depression treatment include Psychiatrist/Psychologist/CBT (33%) and medication (24%). Other interventions include Psycho-Oncology referral, cancer support services, social worker, palliative care and geriatrician referrals.

MERGE Round 2

42. Please rank the top 3 interventions for anxiety, where 1=the best option, 2=2nd best etc:

- Referral to a Psychiatrist/Psychologist/Cognitive Behavioural Therapy
- Psycho-Oncology liaison nurse referral
- Social work referral
- Palliative care team involvement
- Medication
- Geriatrician referral

43. Please rank the top 3 interventions for depression, where 1=the best option, 2=2nd best etc:

- Referral to a Psychiatrist/Psychologist/Cognitive Behavioural Therapy
- Psycho-Oncology liaison nurse referral
- Social work referral
- Palliative care team involvement
- Medication
- Geriatrician referral

44. Can any healthcare professional, with sufficient training, perform psychological assessment?

Yes No

If you answered no, please specify who should complete the assessment.

45. If there is anything further you would like to add in relation to psychological status assessment, please do so here.

Conclusion of Survey

MERGE Round 2

46. Please rate the importance of impairments in each of the following in terms of their ability to affect oncology decisions, in your opinion, where 0=not important, 10=very important.

	0=not important	1	2	3	4	5	6	7	8	9	10=very important
Functional status	○	○	○	○	○	○	○	○	○	○	○
Physical performance status	○	○	○	○	○	○	○	○	○	○	○
Cognitive status	○	○	○	○	○	○	○	○	○	○	○
Comorbidities	○	○	○	○	○	○	○	○	○	○	○
Polypharmacy	○	○	○	○	○	○	○	○	○	○	○
Nutritional status	○	○	○	○	○	○	○	○	○	○	○
Social support status	○	○	○	○	○	○	○	○	○	○	○
Psychological status - anxiety	○	○	○	○	○	○	○	○	○	○	○
Psychological status - depression	○	○	○	○	○	○	○	○	○	○	○

Thank you for completing Round 2. Your continued participation is greatly appreciated.

Appendix 7: Study 1 Round 2 Feedback Report

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Anita O'Donovan

The MERGE Study:

Round 2 Participant Feedback

April 2013

Contents

Introduction

This report contains feedback from the second Delphi round of the MERGE study. In keeping with Delphi tradition, it aims to be as inclusive and comprehensive as possible, and each participant's contribution is acknowledged. For your convenience, attempts are made to summarise certain aspects, with additional appendices containing the qualitative data from the open-ended questions in Round Two, which are located at the end of the document. I would encourage each contributor to make reference to these appendices, in addition to the summarised sections. This is important for Round 3, and will provide different perspectives on the many approaches that are taken to geriatric assessment in Oncology.

As stated previously, in relation to the report itself, assumptions cannot be made about the practice of geriatric oncology in Ireland, or internationally, based on this Delphi survey. The purpose of Round 2 was to present the items collected as part of the open-ended Round 1 process for each participant to score or rank. As a result of Round 2, areas of agreement and disagreement are clearly identified.

The results of this collaborative process will be used to inform the design of a geriatric assessment methodology for Irish Radiation and Medical Oncology patients.

Please note that this report is part of an overall Delphi process and may not be cited or reproduced without the author's permission.

Definitions of Stability and Consensus

Stability, or the degree of permanence of participants' vote distribution over successive rounds, reflects consensus. Changes of less than 15% offer a working definition of stability in the literature, when the responses obtained in two successive rounds are shown statistically to be not significantly different from each other(1). Group stability, rather than individual stability will be assessed in this study.

A predetermined threshold has been chosen for consensus, at an interquartile range of 2 or less units (on a scale of 0-10). The interquartile range is the measure of dispersion for the median and consists of the middle 50% of observations. Thus, an interquartile range of less than 2 means that more than 50% of all opinions fall within 2

points on the scale. It is widely accepted as an objective and rigorous method of defining consensus in Delphi studies(2, 3).

For nominal data, consensus is defined as 67% i.e. two-thirds majority.

If consensus is reached in Round 2, for any particular item, this will be reintroduced in Round 3 to determine stability between rounds. However, it will not be reintroduced in Round 4 if stability is confirmed. It is anticipated that some items may not reach consensus, and this is an important finding in itself.

This iterative process allows participants to reassess their initial judgements about the information provided in previous rounds. **As noted from Round 2 responses, some participants were unfamiliar with some of the items presented e.g. screening tools. In the event of this happening in Round 3, it is permissible to skip these questions, to avoid influencing the decision-making process.** Also, please note that a full list of abbreviations was given in the Round 1 feedback report, and is available for reference in Appendix 1.

Round 2 Data Analysis

Data analysis of Round 2 responses was performed using SPSS version 20. The statistical group response is presented using measures of central tendency (mean, median, mode) and dispersion (interquartile range). Where consensus has not been reached, boxplots are also provided to illustrate divergence of opinion. For the latter, participants may find it useful that outliers have been identified by Study ID.

Round 3

In the third round, each Delphi panellist will complete a questionnaire that includes the items and ratings summarized in the previous round and are asked to revise his/her judgments. This round gives Delphi panellists an opportunity to make further clarifications of both the information and their judgments of the relative importance of the items. This may seem repetitive to many participants, but it is an important feature of the Delphi technique. Thank you in advance for your patience.

Please see the link provided in your email for the Round 3 questionnaire.

Author's Note

Thank you for your important contribution in previous rounds. Your input is invaluable in the design of the Round 3 survey, and in the process as a whole.

Please do not hesitate to contact me if you feel that your views are not contained within this report. A copy of your individual response has been submitted with this document for that purpose.

I look forward to your continued participation in this process, which will be duly acknowledged in the final report.

Best wishes,

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MERGE Study Coordinator

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Trinity EngAGE

Trinity College Dublin Centre for Research in Ageing

Section 1: Stratifying Patients for Geriatric Assessment

Section 1: Stratifying Patients for Geriatric Assessment

When participants were asked if they would change their minds, based on the group responses, the majority of participants (82%) stated that they would **not** change their opinion. Some reasons given for this included personal opinion, clinical experience, the heterogeneity of older patients and poor correlation of chronological age with frailty. These are detailed in Appendix 2:

Eight participants (all Irish Oncologists or Geriatricians) stated that they would change their minds, citing the following reasons:

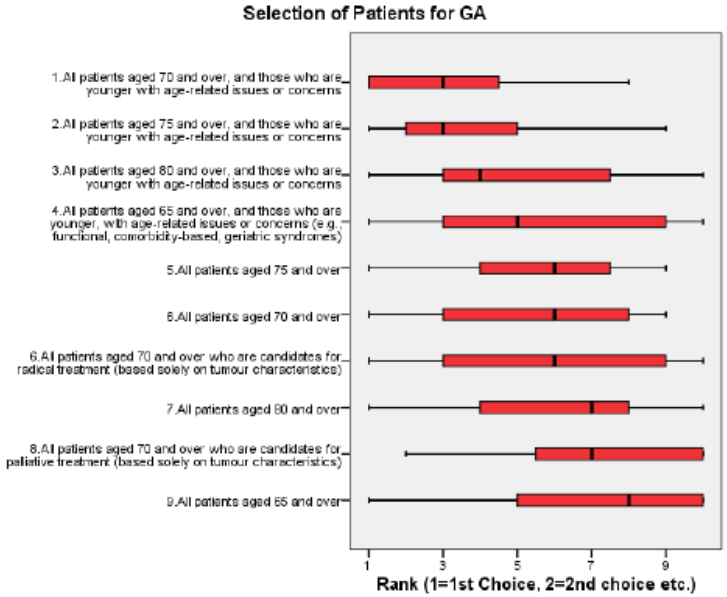
- SIOG recommendations
- Reasonable to select an age, though somewhat arbitrary, for the reasons stated above
- Geriatric assessment should be needs-related and not age-related.
- Moderately happy with consensus threshold of 70 yrs. Reflects improved mortality & lifespan and resource implications
- Recognise expertise of SIOG group
- I probably should be assessing patients more extensively from a geriatric assessment point of view
- Common guidelines are important

Patient Selection for GA

Consensus was not reached on a suitable age cut-off or stratification criteria for GA in Oncology. This item represents the most dissensus in the Delphi panel, and will be reintroduced in Round 3.

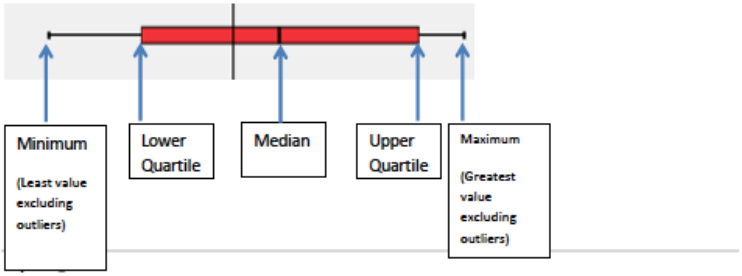
Table 1 Patient Selection for Geriatric Assessment (in order of preference: 1=first place etc.)

Rank	Mean Rank	Median	Mode	Interquartile Range	Consensus
1. All patients aged 70 and over, and those who are younger with age-related issues or concerns	3.16	3.00	1.00	{1.00, 5.00}	No
2. All patients aged 75 and over, and those who are younger with age-related issues or concerns	3.60	3.00	2.00	{2.00, 5.00}	No
3. All patients aged 80 and over, and those who are younger with age-related issues or concerns	5.00	4.00	3.00	{3.00, 8.00}	No
4. All patients aged 65 and over, and those who are younger, with age-related issues or concerns	5.37	5.00	9.00	{3.00, 9.00}	No
5. All patients aged 75 and over	5.65	6.00	6.00	{4.00, 8.00}	No
6. All patients aged 70 and over And All patients aged 70 and over who are candidates for radical treatment	5.72	6.00	8.00	{3.00, 8.00}	No
	5.72	6.00	9.00	{3.00, 9.00}	No
7. All patients aged 80 and over	6.19	7.00	7.00	{4.00, 8.00}	No
8. All patients aged 70 and over who are candidates for palliative treatment (based solely on tumour characteristics)	7.16	7.00	10.00	{5.00, 10.00}	No
9. All patients aged 65 and over	7.42	8.00	10.00	{5.00, 10.00}	No



Consensus wasn't achieved for any of the above options.

READING A BOX-AND-WHISKER PLOT



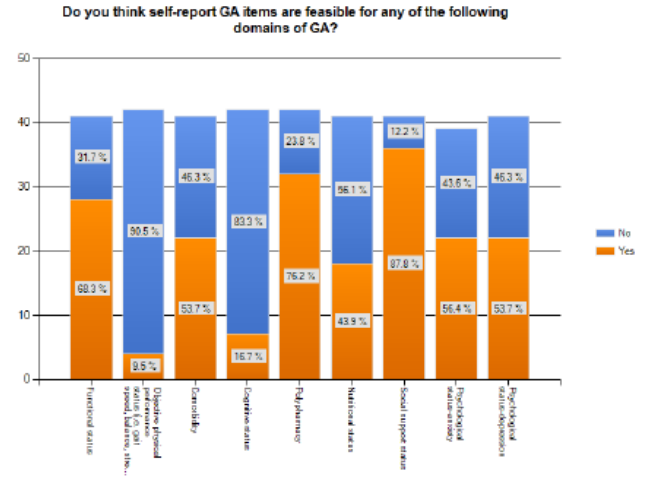
Section 2: How Should Geriatric Assessment be Conducted?

Section 2: How Should Geriatric Assessment be Conducted?

In Round 1, **the majority of participants (81%) felt that GA should be completed by face-to-face interview.**

This opinion changed slightly in Round 2. Thirty-four percent of participants (therefore at the 15% threshold for stability) now feel that completion of *all or part of* GA at home by the patient/family is desirable, while the remaining 66% feel that it isn't. This may represent different attitudes towards different assessment types, some of which participants feel are feasible by self-report methods (see below), and others which are not. This will be re-examined in Round 3 to gain clarity. The question will be rephrased to check if *partial* completion of self-report items is acceptable.

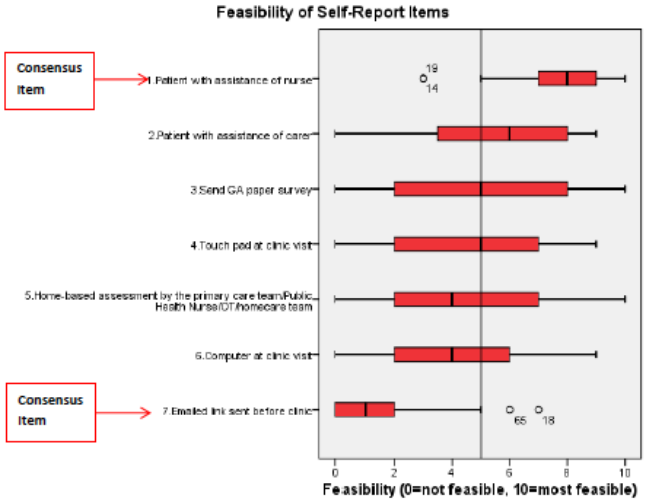
Self-Report Methods



Consensus was reached for items objective physical performance and cognitive status, with the majority of participants stating that self-report is not feasible for these assessments (91% and 83% respectively). Participants feel that self-report

is possible for functional status, polypharmacy and social support status however, reaching consensus at 68%, 76% and 88% respectively. Please see the above chart for other values.

For reasons specified for lack of feasibility of self-report items, please see Appendix 3. These may be summarised under the following categories: the need for medical competence to carry out these tests, the risk of subjectivity and inaccuracy when patients complete them, the impact of specific deficits on the ability to complete such measures e.g. cognitive deficits and the patients' own level of education. Participants also identified the need for objective measurement in some of the above domains, such as the timed up and go test, balance tests etc. Some participants expressed difficulties in interpreting this question. Please see the below chart and table for the self-report options that require evaluation in this study.



***Outliers are identified by participant ID**

Table 2 Feasibility of Self-Report Methods in Order of Preference (0=not feasible, 10=most feasible)

Rank		Mean Rank	Median	Mode	Interquartile Range	Consensus
1.	Ask patient (with the assistance of a nurse) to complete GA items with pen and paper at clinic visit (in office)	7.72	8.00	9.00	{7.00, 9.00}	Yes
2.	Ask patient (with the assistance of carer(s)) to complete GA items with pen and paper at clinic visit (in office)	6.93	7.00	5.00	{5.00, 9.00}	No
3.	Send GA paper survey to patients to complete before first consultation	5.12	5.00	9.00	{2.00, 8.00}	No
4.	Complete GA items through web-based program by touch pad at clinic visit (in office/waiting area)	4.67	5.00	2.00	{2.00, 7.00}	No
5.	Home-based assessment by the primary care team/Public Health Nurse/OT/homecare team	4.58	4.00	4.00	{2.00, 7.00}	No
6.	Complete GA items through web-based program by computer at clinic visit (in office/waiting area)	4.35	4.00	2.00	{2.00, 6.00}	No
7.	Send email with web-based link to patients to complete GA items prior to initial consultation	1.63	1.00	1.00	{0.00, 2.00}	Yes

Section 3: Screening Tools

Section 3: Screening Tools

Screening Tools

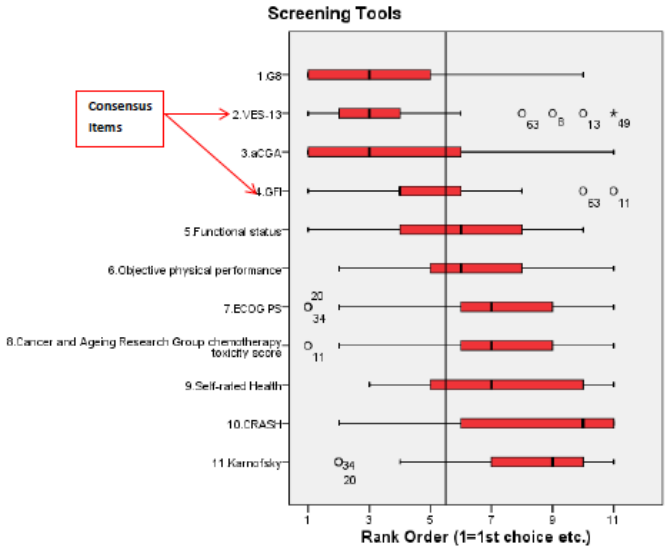
89% agreed that screening with a shorter geriatric-based measure should be instituted as standard practice, in order to help determine who should undergo full GA. However, a number of stipulations were given (please see Appendix 4).

53% of participants feel that no specific screening measure should be recommended, and that any measure could potentially be used. The remaining 37% of the panel recommend a specific measure to identify patients who could potentially benefit from full GA. Of these, four participants recommend the use of the G8 tool, while others recommend the use of the VES13 or G8 (n=1), ADL or IADL (n=1), the aCGA (n=1), SAOP (n=1) and the SHARE frailty instrument (n=1). Please see Appendix 4 for further comments.

In Round 3, clarity will be sought on whether or not participants are satisfied with their recommendations of using a short screening tool, given the current lack of discriminative power for the commonly recommended tools in Oncology, as articulated by many members of the expert panel and summarised in a recent systematic review(4).

Table 3 Best Choice of Screening Tool in Oncology (in order of preference: 1=1st place etc.)

Rank		Mean Rank	Median	Mode	Interquartile Range	Consensus
1.	G8	3.62	3.00	1.00	{1.00, 5.00}	No
2.	VES-13	3.62	3.00	2.00	{2.00, 4.00}	Yes
3.	aCGA	4.14	3.00	1.00	{1.00, 7.00}	No
4.	GFI	5.17	4.00	4.00	{4.00, 6.00}	Yes
5.	Functional Status	5.79	6.00	7.00	{3.50, 8.00}	No
6.	Objective Physical Performance	5.97	6.00	2.00	{4.50, 8.00}	No
7.	ECOG PS	6.86	7.00	7.00	{6.00, 9.00}	No
8.	Cancer and Ageing Research Group chemotherapy toxicity score	7.21	7.00	9.00	{5.50, 9.50}	No
9.	Self-rated Health	7.52	7.00	11.00	{5.00, 10.50}	No
10.	CRASH score	8.03	10.00	11.00	{5.50, 11.00}	No
11.	Karnofsky PS	8.07	9.00	8.00	{7.00, 10.00}	No



*Outliers are identified by participant ID

Section 4: Assessments and Interventions

Section 4: Assessments and Interventions

For your convenience, items are summarised separately by assessment and interventions. For each domain, participants were asked to rank their top 3 choices (or all choices in the case of functional assessment). Please refer to the definition of consensus in the introduction before reading this section.

Table 4 Assessment and Interventions (in order of preference: 1=1st place etc.)

Rank	Mean Ranking	Median	Mode	Interquartile Range	Consensus
Functional Status Assessment					
1. ADL/IADL in combination	1.74	1.00	1.00	{1.00, 2.00}	Yes
2. ADL only	4.24	4.00	4.00	{2.00, 6.00}	No
3. IADL only	4.55	4.00	3.00	{3.00, 5.25}	No
4. KPS	5.38	5.00	5.00	{4.00, 6.25}	No
5. Barthel Index	5.40	6.00	8.00	{3.00, 8.00}	No
6. ECOG PS	5.45	6.00	5.00	{4.00, 7.00}	No
7. VES-13	5.90	6.00	7.00	{4.00, 8.00}	No
8. Patient history/clinical examination	6.02	6.00	9.00	{3.00, 9.00}	No
9. FIM/FAM	6.31	7.00	7.00	{4.00, 8.25}	No
Functional Status Interventions					
1. Physiotherapy referral	1.79	1.00	1.00	{1.00, 3.00}	Yes
2. OT referral	2.50	2.00	2.00	{2.00, 3.00}	Yes
3. Public Health Nurse/ Homecare intervention/day hospital	3.05	3.00	4.00	{2.00, 4.00}	Yes
Physical Performance Impairment: Assessment					
1. TUG	1.64	1.00	1.00	{1.00, 2.00}	Yes
2. Gait Speed	2.75	2.00	2.00	{2.00, 3.75}	Yes
3. Balance tests	3.78	4.00	3.00	{3.00, 4.00}	Yes

Physical Performance Impairment: Interventions					
1. Physiotherapy Referral	1.17	1.00	1.00	{1.00, 1.00}	Yes
2. OT referral	2.93	3.00	2.00	{2.00, 4.00}	Yes
3. Public Health Nurse/ Homecare intervention/day hospital	3.38	4.00	4.00	{3.00, 4.00}	Yes
Cognitive Status: Assessment					
1. MMSE	1.14	1.00	1.00	{1.00, 1.00}	Yes
2. MiniCog And AMTS	3.94 3.94	4.00 4.00	4.00 4.00	{3.00, 5.00} {2.25, 4.75}	Yes No
3. Clock Drawing Test	4.42	5.00	5.00	{3.00, 5.00}	Yes
Cognitive Status: Interventions					
1. Geriatrician referral	1.67	1.00	1.00	{1.00, 2.00}	Yes
2. Psychologist/ psychiatrist referral	3.31	3.00	2.00	{2.00, 4.00}	Yes
3. Memory clinic referral	3.69	3.00	1.00	{1.00, 6.25}	No
Co-morbidities: Assessment					
1. Charlson Comorbidity Index	1.67	1.00	1.00	{1.00, 2.00}	Yes
2. CIRS-G	2.36	2.00	2.00	{2.00, 3.00}	Yes
3. Chart review/medical history/list	2.49	3.00	3.00	{2.00, 3.00}	Yes
Co-morbidities: Interventions					
1. Geriatrician Referral	1.55	1.00	1.00	{1.00, 2.00}	Yes
2. Referral to specialists as deemed suitable for a given co-morbidity	1.79	2.00	2.00	{1.00, 2.00}	Yes
3. Medication	2.67	3.00	3.00	{2.00,3.00}	Yes

Polypharmacy: Assessment					
1. List of Medications	2.00	2.00	1.00	{1.00, 3.00}	Yes
2. Pharmacist Review	2.21	2.00	2.00	{1.00, 3.00}	Yes
3. STOPP/START	2.37	3.00	3.00	{1.75, 3.00}	Yes
Polypharmacy: Interventions					
1. Geriatrician Referral	1.70	1.00	1.00	{1.00, 2.00}	Yes
2. Reduce/stop inappropriate medications	2.26	2.00	3.00	{1.00, 3.00}	Yes
3. Pharmacist referral	2.72	3.00	3.00	{2.00, 4.00}	Yes
Nutritional Status: Assessment					
1. MNA Short form	1.87	1.00	1.00	{1.00, 2.00}	Yes
2. MNA Long form	2.63	2.00	2.00	{1.25, 3.00}	Yes
3. History of weight loss/ anorexia/ BMI	2.87	3.00	4.00	{1.00, 4.00}	No
Nutritional Status: Interventions					
1. Dietician Referral	1.13	1.00	1.00	{1.00,1.00}	Yes
2. Dietary advice/ Use of supplements	1.88	2.00	2.00	{2.00, 2.00}	Yes
Social Support Status: Assessment					
1. Patient History/ caregiver interview	1.06	1.00	1.00	{1.00, 1.00}	Yes
2. mMOS-SS	2.03	2.00	2.00	{2.00, 2.00}	Yes
3. Socio-familiar Gijon Test	2.94	3.00	3.00	{3.00, 3.00}	Yes
Social Support: Interventions					
1. Social work referral	1.70	1.00	1.00	{1.00, 2.00}	Yes
2. Home help	2.81	3.00	2.00	{2.00, 4.00}	Yes
3. Public Health Nurse support	3.02	3.00	5.00	{2.00, 5.00}	No
Anxiety: Assessment					
1. Patient history/ Interview	1.64	2.00	2.00	{1.00, 2.00}	Yes
2. HADS	1.67	2.00	1.00	{1.00, 2.00}	Yes
3. Distress thermometer	2.69	3.00	3.00	{3.00, 3.00}	Yes

Anxiety: Interventions					
1. Referral to a Psychiatrist/ Psychologist /Cogntive Behavioural Therapy	1.39	1.00	1.00	{1.00, 2.00}	Yes
2. Psycho-Oncology liaison nurse referral	2.18	2.00	2.00	{2.00, 3.00}	Yes
3. Social work referral	4.25	4.00	4.00	{3.00, 5.00}	Yes
Depression: Assessment					
1. GDS Short form	1.75	1.00	1.00	{1.00, 2.00}	Yes
2. GDS Long form	2.55	2.50	2.00	{2.00, 3.00}	Yes
3. Patient history/ Interview	2.78	3.00	4.00	{1.25, 4.00}	No
4. HADS	2.92	3.00	4.00	{2.00, 4.00}	Yes
Depression: Interventions					
1. Referral to a Psychiatrist /Psychologist /Cognitive Behavioural Therapy	1.56	1.00	1.00	{1.00, 2.00}	Yes
2. Psycho-Oncology liaison nurse referral	2.63	2.00	2.00	{2.00, 3.00}	Yes
3. Medication	3.93	4.00	3.00	{3.00, 5.00}	Yes

Please see Appendix 5 for additional comments related to each domain.

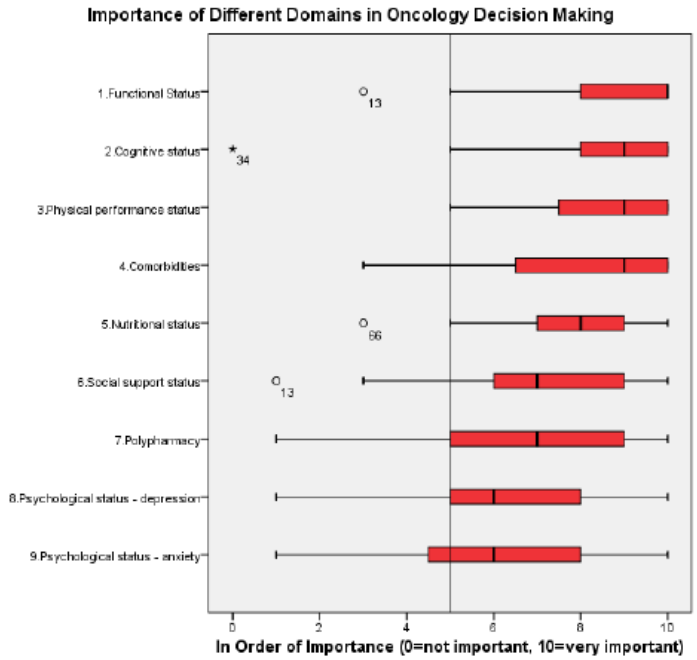
Importance of Each Domain in Oncology Decision-Making

Table 5 Importance of Each Domain in Oncology in Rank Order (1=1st place etc.)

Domain Rank	Average Rating*	Median	Mode	Interquartile Range	Consensus
1. Functional status	8.91	10.00	10.00	{8.00, 10.00}	Yes
2. Cognitive status	8.79	9.00	10.00	{8.00, 10.00}	Yes
3. Physical performance status	8.52	9.00	10.00	{7.25, 10.00}	No
4.Comorbidities	8.07	9.00	10.00	{6.25, 10.00}	No
6.Nutritional status	7.66	8.00	8.00	{7.00, 9.00}	Yes
7.Social support status	6.93	7.00	7.00	{6.00, 9.00}	No
5.Polypharmacy	6.82	7.00	9.00	{5.00, 9.00}	No
8.Psychological status - depression	6.48	6.00	6.00	{5.00, 8.00}	No
9.Psychological status - anxiety	6.02	6.00	6.00	{4.25, 8.00}	No

*In order of importance from highest to lowest

Panellists rated functional status as the most important domain in influencing oncology decisions, followed by cognitive and physical performance status.



***Outliers are identified by participant ID**

Section 5: Training Requirements for Assessment

Section 5: Training Requirements for Assessment

Table 6 Can any Healthcare Professional Perform this Assessment?

Domain	Any Healthcare Professional with Sufficient Training
Functional Status	Yes (98%)*
Objective Physical Performance	Yes (98%)*
Cognitive Status	Yes (80%)*
Comorbidity	Yes (73%)*
Polypharmacy	No (57%)
Nutritional Status	Yes (68%)*
Social Support Status	Yes (82%)*
Psychological Status	No (52%)

Consensus items *

Clear consensus exists for most items, apart from polypharmacy and psychological status. Some participants asked for clarification in relation to the definition of "sufficient training". To clarify this, it means staff are competent to carry out the designated assessment e.g. completion of ADL/IADL assessment for functional status, MMSE for cognitive status etc. For the former, it usually involves asking the patient a series of questions and noting their responses. On the other hand, cognitive assessment requires extra competency in the form of MMSE training, for example, which some institutions provide for their staff. It's difficult to define this further, as different institutions will have their own requirements as to who will ensure competency. Ideally, this should be endorsed by the Department of Geriatric Medicine in individual centres.

Please see Appendix 6 for further comments in relation to the above.

Appendices

Appendix 1: List of Abbreviations Used in This Document:

AD=Alzheimer's Disease

AMTS=Abbreviated Mental Test Score

ASA=American Society of Anaesthesiologists

CARST = Community Assessment of Risk Screening Tool

CCI=Charlson Comorbidity Index

CGA=Comprehensive Geriatric Assessment

CHS=Cardiovascular Health Study

CIRS-G=Cumulative Illness Rating Scale-Geriatric

GA=Geriatric Assessment

Ger=Geriatrician (Ireland)

ECOG = Eastern Cooperative Oncology Group

EMS=Elderly Mobility Scale

FIM/FAM=Functional Independence Measure and Functional Assessment Measure

GFI=Groningen Frailty Indicator

IQ Rge=Interquartile Range

MEAMS=Middlesex Elderly Assessment of Mental State

MDT=Multidisciplinary Team

mMOS-SS=modified Medical Outcomes Study – Social Support

MMSE=Minimental State Examination

MNA=Mini Nutritional Assessment

MO=Medical Oncology (Ireland)

MOCA=Montreal Cognitive Assessment

MUST=Malnutrition Universal Screening Tool

PD=Parkinson's Disease

PHN=Public Health Nurse

PS=Performance Status

PSP=Progressive Supranuclear Palsy

RBANS=Repeatable Battery for the Assessment of Neuropsychological Status

QMCI = Quick Mild Cognitive Impairment

RO=Radiation Oncology (Ireland)

SCS=Simplified Comorbidity Score

SIOG=International Society of Geriatric Oncology

SPPB=Short Physical Performance Battery

STOPP/START= Screening Tool of Older People's potentially inappropriate Prescriptions/ Screening Tool to Alert doctors to the Right Treatment

TUG=Timed Up and Go

VES=Vulnerable Elders Survey

VIP=Variable Indicative of Placement (risk)

Appendix 2: Stratifying Patients for Geriatric Assessment

- I believe age alone is too simplistic.
- I am being asked for my views, therefore changing them on basis of group not appropriate.
- The age cut-off reflects the age at which all patients should be assessed as there is a reasonable probability of positives. This does not preclude examining younger patients.
- For keeping things consistent and ease of making and implementing guidelines it should be clear.
- Based on my experience 70yo seems to be better due to heterogeneity of elderly.
- I believe biological age is relative.
- Because we need a pragmatic answer: refusing to determine an effective limit jeopardizes any attempt of organization, research, guidelines, and progress.
- The comments about the heterogeneity of older patients emphasise my previous belief. However, I do recognise that if there is an age cut off then there may be more patients who do have a GA.
- Because there are better ways to identify need for GA than chronological age.
- While the majority of frail elderly will be identified, it will miss younger old with geriatric syndromes.
- If this is a global directive then you need a practical cut-off. There is nothing to stop you using the GA in younger patients where necessary and the skills learnt in the over 70's will be easily applied to younger patients.
- Some 60 plus year old patients have very similar problems to a 72 year old.
- I believe frailty is more important than chronological age when assessing need for comprehensive geriatric assessment. Simple screening questions will identify those at risk as quickly (and much more accurately) as a date of birth.
- Need for a specific age cut-off for practical reasons and common language.
- In general no problems in the less than 70 years group.
- As the tools are not well established in younger patients and the number of patients identified very low.
- Because I have my personal opinion and it doesn´t depend on the rest of participants.

- I still believe that the elderly are a very heterogenous group and that chronological age is not the same as biological age.
- There has been no evidence presented that would change my opinion.
- I think we have to start somewhere, and for practical purposes a cut-off is important.

Appendix 3: Reasons for Lack of Feasibility of Self-Report Methodology

- Patients not having insight into certain areas.
- Objective evaluation is just that. Cognitive status requires objective assessment and collaborative history.
- Require review and assessment by clinical staff.
- Medical competences needed, validity of the evaluation.
- Patients might find it difficult if they are cognitively impaired and might not appreciate what is polypharmacy.
- I think doing GA in a clinic setting likely to be associated with greater rates of completion of assessment.
- Physical performance assessments by definition are objective, not subjective, cognitive status self-determined is prone to inaccuracies in responses, patients often need to be specifically asked about certain medications which are not reported when asked what medications are taken (e.g. OTC, herbal medications).
- If using objective measures like timed up and go these need observation. Although self-report can be used for cognitive issues there is probably better value in e.g. minicog.
- This will depend on the cognitive status of the person, insight and executive functions. Sorry these questions are much too simplistic to just give blanket yes/no answers. I seriously can't just give yes/no..SHOULD is the wrong verb, can is better. We do this routinely in a memory clinic but it is problematic...
- Validated screening questionnaire tools are in place for many/all of the domains for completion by patient or NOK. These are useful adjuncts to, but should not replace, some degree of assessment of each domain at patient-doctor/nurse/therapist person to person review. GA requires flexibility to pursue a domain of suspicion that cannot be replaced by questionnaire.
- Home assessment functionality and not held by health team can be ineffective.
- More objective medically assessed measures may be needed here rather than subjective. Also hard for patient/family to quantify.
- Objectivity is an issue and these points require assessment - patients can have fixed unrealistic ideas.

- Patients and carers may not recognise subtle deficits in these areas. Lack of awareness plus/minus denial.
- Hard to accurately self-measure. Others like comorbidity & polypharmacy may produce suboptimal results.
- Too much subjectivity and the risk is that it is not self-completed but completed by family.
- Re. physical performance - self report would likely be subjective rather than objective. For cognitive status -maybe limited insight. Polypharmacy - patients can report on the number and names of medications, but wouldn't necessarily have the knowledge about side effect profile, necessity to be on those medications etc. Nutritional status - basic numbers (weight / height / BMI can be self-assessed - but may not be an in depth assessment of nutritional status. Re. Anxiety and depression - patients could complete a HADS score (or similar) - but important to assess by professional as well.
- Significance and severity of comorbid disease too difficult for patients and relatives to self-report; objective parameters obviously need objective measurement.
- I would be doubtful of the ability of patients to objectively assess themselves reliably.
- Elderly patients are often not aware of the problems and relatives might not always recognise/understand them.
- Cognitive assessment really needs someone else to assess this domain.
- Objective physical performances should be that, objective. Co-morbidity assessments probably best done as a medical history.
- Objective measures need to be objectively validated. Patients tend to over-report their functional status. Cognitive function cannot be tested subjectively, as patients with dementia often lack insight. Nutritional status in part needs to be based on objective measurements for accuracy.
- If patient is cognitively normal, used to filling in forms and with good insight then self-report for many domains may be adequate. However as these are hard to assess prior to actually meeting the patient I'd prefer to go with objective assessment, collateral validation for the initial meeting at least. It may still be worth sending a form to be filled in prior to interview but answers needed to be

taken with a pinch of salt. The consequences of being deemed too frail for curative treatment are significant, the ultimate decision should be based on a face to face meeting with a clinician.

- Need for specific tools to measure the relative item.
- Functional status is better determined as performance task so is tinetti for falls and balance. Comorbidity is a physician's task and cognitive status can't be determined by self-assessment if the patients are suffering from dementia.
- Please note this question is open to interpretation. I am taking self-report to mean literally that, i.e. not "at home "assessment but self-report performed in a clinical setting with help where needed and as a once off. Re the "nos". By definition Objective physical performance cannot be self-reported as it is objective, Simple experience of history taking from patients of all ages has made me realise that patients often forget comorbidities and medications unless in a structured interview - and sometimes only remember surgery after a scar is found on examination. Cognitive status requires performance of some measure, by definition a cognitively-impaired patient may not be able to navigate this. Nutritional status requires evaluation by an experienced professional as it takes into account objective measures such as serum protein, and also because cognitively impaired patients may need help with food recall questionnaires.
- I think that some self-reports tools might be useful but can't replace at all an objective assessment led by health professionals (physicians, or other). They can help collect data, they save time but they cannot be used alone.
- These factors require explanation and interpretation.
- Because of the educational level of our patients.
- Because neither the patient nor his/her family, are accustomed to this language or these items, and perhaps, the final results could be different form the results if the scales were registered by a medical team.
- Likely to be too subjective.
- A patient cannot administer a TUG or perform a balance test such as BERG. People invariably forget comorbidities and some time needs to be spent ascertaining how significant a reported comorbidity is. Formal cognitive testing needs to be performed if there is a suggestion of CI.

- Not objective enough. To complete a co-morbidity assessment requires some training.

Appendix 4: Comments on Screening Tools

Respondents who agreed that screening with a shorter geriatric-based measure should be instituted as standard practice, in order to help determine who should undergo full GA:

- Not sure of the types. We use ECOG but this is not a geriatric assessment.
- I don't have one in mind and there would probably need to be one devised.
- Not tested in oncology patients but perhaps the Share Frailty instrument(5). Validated in a very large cohort of community dwelling people. Web based calculator. Brief. trichotomizes categories into - frail/pre-frail/not frail.
- Needs to include frailty / function and to be well validated.
- Don't know. I would defer to my geriatric medicine colleagues on this question.
- Many different screening tools and many different clinical settings so can capture too many or too little. Combination of simple screening tool with clinical judgement is best.
- GFI, MNA currently used. TUG should be next part of the screening program.
- I think that, at the moment, this screening tool has not been designed. They have been used the G8, the VES-13 questionnaire, the GFI, the Barber test... but they are not as good as necessary to be a substitute of the GA.
- I'm not familiar with any particular screening tools.
- If validated by research
- But resources need to be available to direct patients to appropriate service if deficits found which is the limiting factor at present
- We use screening tools to determine who needs more comprehensive assessment...
- To meet reduced resources-i.e. select out those most in need.
- Yes - and if so I might revise opinion as to whether it should be done as standard for say all over 70 year olds.
- Careful selection of tool necessary.
- A 5 to 10 min max assessment.

- Full GA on all is impractical.
- A simple ADL scale would be much more informative at detecting frailty.
- Saving time and personnel. No specific screening tool generally accepted at the moment.
- But I think that, at the moment, it doesn´t exist the ideal screening tool.
- If it was simple to complete it might be very helpful.
- Assuming the assessment tool is verified.
- Evidence is that it does not work

Rationale:

- 30% are fit and you don't need to waste time on them.
- If validated, it could save a lot of clinic time.
- Might enable focus scarce resource to those most in need.
- I think the assessment we use has to be practical for situation in Ireland which generally is very large Oncology clinics with relatively short times for GA.
- These are good easy to apply tools which can identify those most likely to benefit from full CGA.
- Pragmatism. There are insufficient resources to perform CGA on all so try and pick those most likely to benefit.
- It will help pick out the most appropriate patient to go a GA on.
- It will be a start to recognising the problem and developing initiatives that are applicable to everyday practice. Oncology could promote research on developing a comprehensive validated tool with good sensitivity and reasonable specificity across multiple domains. Some domains e.g. co-morbidity are amenable to questionnaire format; others require direct observation/assessment by a healthcare professional e.g. timed up and go or grip strength. Any format for this patient group will have to rely on a mix of low & high technology & direct & indirect assessment.
- Lessen the potentially vast workload of full screens for all patients.
- CGA for all patients simply not workable in context of current resources.

- It overlooks potential deficits that can/should be addressed. If the GA is not too long it can assess important deficits in multiple domains but still be usable.
- Due to heterogeneity of patients and duration of full CGA w need to screen patients who need full CGA.
- Time constraints. Should be specific to each patient based upon Consultant assessment.
- It is not rocket science, question of time...
- To prospectively see if it works.
- Would have concerns that non-evidenced-based tool may miss vulnerable clients.
- This type of assessment would help formalise the assessment of the pts appropriateness for treatment.
- Could be a useful tool to reduce the need for full assessments.
- Fit patients do not need a full GA.
- Provided there is an evidence base, it would be logical to screen, rather than do in-depth assessments. This is the philosophy behind the InterRAI suite of tools.
- Mostly for allocation of resources to the patients who need it most.
- Frailty measures are well validated in predicting outcome.
- Saving time and personnel. No specific screening tool generally accepted at the moment.
- If full GA can be avoided, this will help in reducing costs (time and personnel).
- It provides a first impression about time frame, instruments needed etc.
- A first step of screening would be very helpful. However, the perfect screening tool has not been developed yet!
- None of the currently available screening tools have sufficient discriminative power (lancet oncology 2012)(4).
- At the moment, it doesn´t exist the ideal screening tool.
- MDT working benefits patients.
- Quicker. The challenge is which tool and what to do with results.

Appendix 5: Additional Comments Related to Each Assessment Type

Functional Assessment

- Can't say that one is better than the other in 13, depends on what the issue is e.g. if Diabetes, nurse, if falls PT, if cognition/safety in home OT.
- An oncology functional assessment via ECOG or KPS is limited (i.e. fit for treatment or not) and may not meet the global needs of the patient
- It should be brief 5 to 10 minutes. I am not familiar at all with 2 of the above assessment tools and somewhat familiar with another 3.
- FIM/FAM excellent but very long. Barthel very well used and often already available but not a great tool.
- There seems to be a move to performing tests like TUG for screening and this also gives assessment of frailty. In my opinion the assessment is important but the subsequent intervention is more important. You need to decide why you are are assessing.... is it to help the patient or guide therapy decisions? (or both)
- Timed Up & Go test for screening seems very useful.
- I think it is also very important to include another tools such as gait speed, test get up and go, test SPPB.

Physical Performance Assessment

- An oncology functional assessment via ECOG or KPS is limited (i.e. fit for treatment or not) and may not meet the global needs of the patient.
- TUG can be used by any healthcare professional whereas EMS more specific to the patient.
- I am not familiar with all of the tests mentioned above. I get a feeling that this test may be met with resistance from oncologists possibly due to unfamiliarity with the test and what to do with the results.
- While any professional can be trained to do this, involvement of physiotherapy would be beneficial.
- I don't know what the abbreviations to most of Q16 mean (please see Appendix 1).

Cognitive Assessment

- Really hard to be cut and dried, I honestly find this thing too cut and dried with no room for comments, sorry if I am fussy.
- I do not like & have difficulty answering q 21 & 22. Level of assessment & appropriate intervention should reflect on the individual patient in front of you with all listed tests/interventions having merit in particular circumstances. Which of any you use/rank may reflect referral bias in your centre of work. A HCP trained in cognition can decide what test is most appropriate based on the individual circumstance & in a decision on intervention is usually based on MDT input.
- Need to use a well-known and used tool so MMSE probably best here overall.
- Any professional can be trained to do a screening cognitive assessment. If the screening test is failed then referral to a memory clinic or dementia service is required.

Comorbidity Assessment

- Elderly patients may have multiple problems that a geriatrician may be able to manage rather than separate OPDs for respiratory then cardiology etc.
- I think that it requires an experienced clinician to know whether the list of co-morbidities has a significant impact on that particular patient. There are some patients who have a formidable list of co-morbidities and yet would be able to tolerate further intervention and vice versa.
- CIRS-G gives severity as well as presence but takes a lot of practice to be able to do quickly without having to refer to the guide!
- There is no appropriate tool to assess comorbidity. CIRS-G, Charlson were developed for prognostic purpose not for clinical practice

Polypharmacy Assessment

- This is probably more difficult to train all disciplines as so specialised.
- A tool such as STOPP START useful and easy to apply, but not specifically relevant or validated in an oncology setting
- This can be a contentious area with trained HCPs being slow to d/c meds in other specialists' areas. STOPP/START is validated across different care settings but doesn't account for prognosis in its decision process which is also crucial when addressing polypharmacy.
- Non-elderly GP but elderly geriatrician with GP to manage meds
- GPs often reluctant to stop medication of no value in patients current state e.g. statin therapy in metastatic lung cancer
- GPs are very well positioned here as they usually know the pt well and for a long time
- Wouldn't it be nice if all our patients could see a pharmacist? Medicines being such an important part of disease management and geriatric assessment.
- I am not familiar with items in Q28
- unfamiliar with question 28

Nutritional Status Assessment

If there is anything further you would like to add in relation to nutritional status assessment, please do so here.

- Nutritional tools useful, but realistically a dietician assessment to assess status would be ideal should resources allow
- Concern if other HCPs - accurate calorie counting, appropriate supplementation/advice & use of enteral feeding
- Being pragmatic anorexia weight loss and BMI will prove sufficient in the majority. you can make it too complex
- Only familiar with 2 of the assessment tools in que 32
- Nutritional status using a tool is very straightforward

- SALT assessment may also be indicated
- Interesting that in my opinion the dietician almost has a special role.... we receive such little training in dietary assessment as medics that I am not sure we could adequately perform an assessment, let alone recommend an intervention (apart from saying eat little and often!)

Social Support Status

- Whilst we are opining on each section here, do not forget if you use every one of these tests you will have a very comprehensive GA that cannot be routinely undertaken in all patients
- There is an ambiguity to these questions in terms of what is sufficient training.
- Not familiar with any of the tools here - usually history is fine for this
- Not familiar with the social support tools
- I think this also requires specialist knowledge to assess and then arrange intervention..... I agree, the social worker and home nursing/ geriatric assessment teams are both required.

Psychological Status

- With regards to interventions, access to different disciplines may affect order of list
- Only vaguely familiar with the above assessment tools
- I haven't answered some of these questions as I find it difficult to rank the best interventions in a general question. for some patients they will need referral to psychiatrist, some to social worker, some I might start on an anti-depressant. Different solutions for different patients.
- Some of the above options e.g. psycho-oncology nurse not available in my service
- Assessment probably anyone can do.... but intervention requires specialist skills in this domain.
- I am not very familiar with items in Q40

Appendix 6: Who Can Perform Assessments?

Cognitive Assessment

- People with appropriate training and experience Geriatrician, Psychiatrist, OT, CNS
- Geriatrician
- Probably any healthcare professional can fill out a form by asking questions. Requires clinical experience to determine whether an MMSE score of say 22/30 is significant cognitive impairment or not.
- Requires special knowledge about cognitive dysfunction
- Geriatrician, neurologist, psychologist
- Neuropsychologist trained in geriatrics
- Screening can be done by a healthcare professional but the interpretation and diagnosis should be done by a professional

Comorbidity Assessment

- Doctor
- Geriatrician/gerontology nurse
- Staff with medical training f ex doctors, nurses
- Requires specific knowledge. Should be performed by physicians
- An experienced doctor or nurse is required.
- Physician
- Geriatrician
- This also requires interpretation

Polypharmacy

- Should understand why they take medication
- Need medical or pharmacy training

- Pharmacist or doctor
- Sufficient training is the key, anyone can do just about anything with "sufficient training"
- Nurses, pharmacists or doctors
- Knowledge in internal medicine
- The top 3 professionals in question 29
- Pharmacist, Geriatrician, Experienced physician looking after older patients
- Very difficult beyond doctors and nurses
- Geriatrician/clinical pharmacist/GP
- Doctor, Pharmacist
- Junior doctors or non-medical specialists not appropriate
- Requires extensive knowledge
- A suitably trained doctor. Sometimes a potentially inappropriate medication may be justified (it usually isn't) and only a physician can make that judgement
- A physician
- Oncologist, geriatrician
- Cannot be independent of current cancer diagnosis and proposed anti-cancer therapy
- Pharmacist with geriatric skills

Nutritional Status

- Nurse ,doctor or dietician
- I think dietician essential for this
- Possibly so - but my answer may highlight my own lack of expertise in nutritional assessment!
- Ideally a dietician
- Dietician
- CNS, Dietician
- Dietician
- Dietician
- Dietician
- Nutritionist

Social Support Status

- Legal and social competences needed
- Discharge liaison nurse or social worker
- Social worker ideally should do
- Social worker, PHN required to navigate current bureaucracy to access services
- Social worker

Psychological Status

- Specific competences needed
- Psych liaison nurse or doctor
- Needs to be someone trained
- Nurse or psychologist or doctors
- Trained staff - Geriatrician, Psychiatrist, Psychologist, CNS
- Skill in psychological issues assessment
- Sufficient training is difficult for this
- Geriatrician
- It really depends on the psychological status of the patient. I think that most healthcare professionals anyway are tuned into assessing patient's psychological well-being. I think that if there are concerns then the patients should be referred to the relevant specialist.
- Psychiatry/clinical nurse specialist/psychologist
- Doctors/psychiatrists, trained nurses, psychologists
- Requires skills and sensitivity
- Neuropsychologist with geriatric training
- Doctor specialized in this issue

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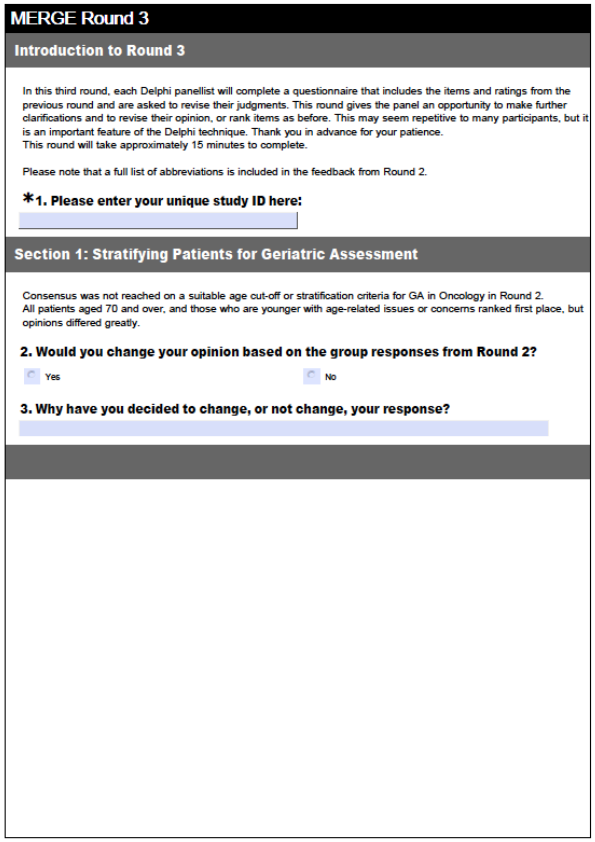
Appendix 8: Study 1 Round 3 Survey



MERGE Round 3

Introduction to Round 3

In this third round, each Delphi panellist will complete a questionnaire that includes the items and ratings from the previous round and are asked to revise their judgments. This round gives the panel an opportunity to make further clarifications and to revise their opinion, or rank items as before. This may seem repetitive to many participants, but it is an important feature of the Delphi technique. Thank you in advance for your patience.
This round will take approximately 15 minutes to complete.

Please note that a full list of abbreviations is included in the feedback from Round 2.

*1. Please enter your unique study ID here:

Section 1: Stratifying Patients for Geriatric Assessment

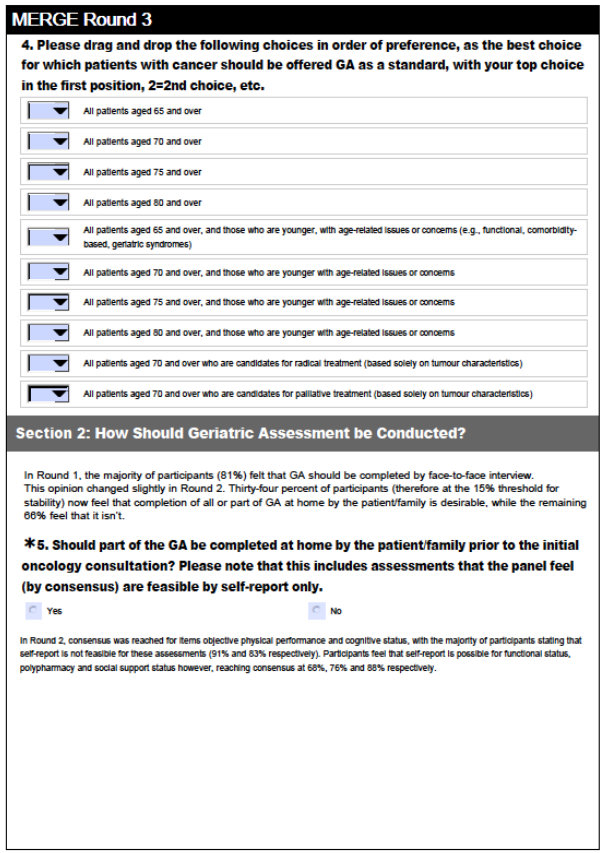
Consensus was not reached on a suitable age cut-off or stratification criteria for GA in Oncology in Round 2.
All patients aged 70 and over, and those who are younger with age-related issues or concerns ranked first place, but opinions differed greatly.

2. Would you change your opinion based on the group responses from Round 2?

Yes No

3. Why have you decided to change, or not change, your response?

Page 1



MERGE Round 3

4. Please drag and drop the following choices in order of preference, as the best choice for which patients with cancer should be offered GA as a standard, with your top choice in the first position, 2=2nd choice, etc.

All patients aged 65 and over

All patients aged 70 and over

All patients aged 75 and over

All patients aged 80 and over

All patients aged 65 and over, and those who are younger, with age-related issues or concerns (e.g., functional, comorbidity-based, geriatric syndromes)

All patients aged 70 and over, and those who are younger with age-related issues or concerns

All patients aged 75 and over, and those who are younger with age-related issues or concerns

All patients aged 80 and over, and those who are younger with age-related issues or concerns

All patients aged 70 and over who are candidates for radical treatment (based solely on tumour characteristics)

All patients aged 70 and over who are candidates for palliative treatment (based solely on tumour characteristics)

Section 2: How Should Geriatric Assessment be Conducted?

In Round 1, the majority of participants (81%) felt that GA should be completed by face-to-face interview.
This opinion changed slightly in Round 2. Thirty-four percent of participants (therefore at the 15% threshold for stability) now feel that completion of all or part of GA at home by the patient/family is desirable, while the remaining 66% feel that it isn't.

*5. Should part of the GA be completed at home by the patient/family prior to the initial oncology consultation? Please note that this includes assessments that the panel feel (by consensus) are feasible by self-report only.

Yes No

In Round 2, consensus was reached for items objective physical performance and cognitive status, with the majority of participants stating that self-report is not feasible for these assessments (91% and 83% respectively). Participants feel that self-report is possible for functional status, polypharmacy and social support status however, reaching consensus at 68%, 76% and 88% respectively.

Page 2

MERGE Round 3

6. Do you think self-report GA items are feasible for any of the following domains of GA?

	Yes	No
Functional status	○	○
Objective physical performance status (i.e. gait speed, balance, strength)	○	○
Comorbidity	○	○
Cognitive status	○	○
Polypharmacy	○	○
Nutritional status	○	○
Social support status	○	○
Psychological status-anxiety	○	○
Psychological status-depression	○	○

If you said no to any of the above, please specify why you think self-report items are not feasible.

In the previous round "Ask patient (with the assistance of a nurse) to complete GA items with pen and paper at clinic visit (in office)" ranked first place as the most feasible option, followed by: 2. Ask patient (with the assistance of carer(s)) to complete GA items with pen and paper at clinic visit (in office) and 3. Send GA paper survey to patients to complete before first consultation

MERGE Round 3

7. Please rank the following from the least feasible to the most feasible in Oncology, with 0=least feasible, 10 = most feasible

	0=not feasible	1	2	3	4	5	6	7	8	9	10=most feasible
Send GA paper survey to patients to complete before first consultation	○	○	○	○	○	○	○	○	○	○	○
Send email with web-based link to patients to complete GA items prior to initial consultation	○	○	○	○	○	○	○	○	○	○	○
Ask patient (with the assistance of carer(s)) to complete GA items with pen and paper at clinic visit (in office)	○	○	○	○	○	○	○	○	○	○	○
Ask patient (with the assistance of a nurse) to complete GA items with pen and paper at clinic visit (in office)	○	○	○	○	○	○	○	○	○	○	○
Complete GA items through web-based program by computer at clinic visit (in office/waiting area)	○	○	○	○	○	○	○	○	○	○	○
Complete GA items through web-based program by touch pad at clinic visit (in office/waiting area)	○	○	○	○	○	○	○	○	○	○	○
Home-based assessment by the primary care team/Public Health Nurse/OT/homecare team	○	○	○	○	○	○	○	○	○	○	○

Please comment further

Section 3: Screening Tools

In Round 2, 89% agreed that screening with a shorter geriatric-based measure should be instituted as standard practice, in order to help determine who should undergo full GA.
53% of participants feel that no specific screening measure should be recommended, and that any measure could potentially be used. The remaining 37% of the panel recommend a specific measure to identify patients who could potentially benefit from full GA.
Please do not attempt to answer Q11 if you are unfamiliar with the screening tools listed.

MERGE Round 3

8. Do you think screening, with a shorter geriatric-based measure, should be instituted as standard practice in order to help determine who should undergo full GA in Oncology?

- Yes
- No

Please comment further

9. Why/why not?

10. If you answered yes to the above question, please tick the answer you agree with the most below

- A specific screening measure should be recommended for all patients to identify those who should get a full GA.
- At this point, no specific screening measure should be recommended, and any screening measure could potentially be used
- NA

If you selected option A, please indicate which screening tool you would use.

MERGE Round 3

11. Please drag and drop the following choices in order of preference, as the best choice of screening tool for use in Oncology, with your top choice in the first position, 2=2nd choice, etc.

You may skip this question if you are not familiar with the screening tools below.

- VES-13
- G8
- GFI
- Self rated health
- Objective physical performance
- Functional status
- ECOG PS
- Karnofsky PS
- Cancer and Ageing Research Group chemotherapy toxicity score
- CRASH score
- Abbreviated Comprehensive Geriatric Assessment (aCGA)

Section 4: Assessment, Interventions and Training

Consensus has been achieved for most of the assessments and interventions in Round 2. These questions have been re-introduced to assess stability.

GA: Functional Status

MERGE Round 3

12. Drag and drop the following choices in order of preference, as the best choice of functional assessment method for older patients, with your top choice in the first position, 2=2nd choice, etc.

- ADL only
- IADL only
- ADL/IADL in combination
- KPS
- ECOG PS
- VES-13
- FIM/FAM
- Barthel Index
- Patient history/clinical examination

13. Please rank the top 3 interventions for functional impairment, where 1=the best option, 2=2nd best etc:

- Physiotherapy referral
- Occupational Therapist referral
- Nurse intervention
- Public Health Nurse/ Homecare intervention/day hospital
- Exercise programme

14. Can any healthcare professional, with sufficient training, perform functional status assessment?

Yes No

If you answered no, please specify who should complete the assessment.

15. If there is anything further you would like to add in relation to functional assessment, please do so here.

GA: Objective Physical Performance Status

MERGE Round 3

16. Please rank the top 3 assessment tools for physical performance impairment, in your opinion, where 1=best, 2=2nd best etc.

- TUG
- Gait speed
- Balance assessment e.g. Berg
- Grip strength
- EMS
- SPBB
- CHS criteria
- Observation

17. Please rank the top 3 interventions for physical performance impairment, where 1=the best option, 2=2nd best etc:

- Physiotherapy referral
- Occupational Therapist referral
- Nurse intervention
- Public Health Nurse/ Homecare intervention/day hospital
- Exercise programme

18. Can any healthcare professional, with sufficient training, perform physical performance status assessment?

Yes No

If you answered no, please specify who should complete the assessment.

19. If there is anything further you would like to add in relation to physical performance assessment, please do so here.

GA: Cognitive Status

MERGE Round 3

20. Please rank the top 3 assessment tools for cognitive status, in your opinion, where 1=best, 2=2nd best etc.

- MMSE
- AMTS
- MiniCog
- MOCA
- Clock drawing test
- Rivermead test
- Addenbrooks test
- QMCI
- Pfeiffer questionnaire
- Fluency frontal assessment battery
- MEAMS
- CAMCOG
- RBANS
- Delayed word recall
- Clinical judgement

21. Please rank the top 3 interventions for cognitvie impairment, where 1=the best option, 2=2nd best etc:

- Psychologist/psychiatrist referral
- OT referral
- Geriatrician referral
- Medication
- Home care intervention
- Day hospital care
- Memory clinic referral
- Advance care planning

MERGE Round 3

22. Can any healthcare professional, with sufficient training, perform cognitive assessment?

Yes No

If you answered no, please specify who should complete the assessment.

23. If there is anything further you would like to add in relation to cognitive assessment, please do so here.

GA: Co-morbidities

24. Please rank the top 3 assessment tools for co-morbidities, in your opinion, where 1=best, 2=2nd best etc.

- Charlson Comorbidity Index
- CIRS-G
- Chart review/medical history/list
- ASA grade
- SCS

25. Please rank the top 3 interventions for co-morbidities where 1=the best option, 2=2nd best etc:

- Referral to specialists as deemed suitable for a given co-morbidity
- Medication
- Geriatrician referral

26. Can any healthcare professional, with sufficient training, perform co-morbidities assessment?

Yes No

If you answered no, please specify who should complete the assessment.

27. If there is anything further you would like to add in relation to co-morbidities assessment, please do so here.

MERGE Round 3

GA: Polypharmacy

28. Please rank the top 3 assessment tools for medications, in your opinion, where 1=best, 2=2nd best etc.

- STOPP START criteria
- BEERs criteria
- List of medications/medical history
- Pharmacist review

29. Please rank the top 3 interventions for polypharmacy, where 1=the best option, 2=2nd best etc:

- Pharmacist referral
- Geriatrician referral
- Reduce/stop inappropriate medications
- General Practitioner review of medications

30. Can any healthcare professional, with sufficient training, perform polypharmacy assessment?

Yes No

If you answered no, please specify who should complete the assessment.

31. If there is anything further you would like to add in relation to polypharmacy assessment, please do so here.

GA: Nutritional Status

MERGE Round 3

32. Please rank the top 3 assessment tools for nutritional status, in your opinion, where 1=best, 2=2nd best etc.

- MNA short form
- MNA long form
- MUST
- History of weight loss/anorexia and BMI
- Determine index
- Albumin level

33. Please rank the top 2 interventions for nutritional impairment, where 1=the best option, 2=2nd best etc:

- Dietician referral
- Dietary advice/Use of supplements

34. Can any healthcare professional, with sufficient training, perform nutritional assessment?

Yes No

If you answered no, please specify who should complete the assessment.

35. If there is anything further you would like to add in relation to nutritional status assessment, please do so here.

GA: Social Support Status

36. Please rank the top 3 assessment tools for social support status, in your opinion, where 1=best, 2=2nd best etc.

- Patient history and/or caregiver interview
- mMOS-SS
- Socio-familiar Gijon test
- CARST

MERGE Round 3

37. Please rank the top 3 interventions for social support impairment, where 1=the best option, 2=2nd best etc:

- Social work referral
- Home help
- Palliative care team referral
- Daycare centre
- Public Health Nurse support

38. Can any healthcare professional, with sufficient training, perform social support assessment?

Yes No

If you answered no, please specify who should complete the assessment.

39. If there is anything further you would like to add in relation to social support status assessment, please do so here.

GA: Psychological Status: Anxiety and Depression

40. Please rank the top 3 assessment tools for anxiety, in your opinion, where 1=best, 2=2nd best etc.

- HADS
- Patient history/interview
- Distress thermometer

41. Please rank the top 3 assessment tools for depression, in your opinion, where 1=best, 2=2nd best etc.

- GDS-short form
- GDS-long form
- HADS
- Patient history/interview

MERGE Round 3

42. Please rank the top 3 interventions for anxiety, where 1=the best option, 2=2nd best etc:

- Referral to a Psychiatrist/Psychologist/Cognitive Behavioural Therapy
- Psycho-Oncology liaison nurse referral
- Social work referral
- Palliative care team involvement
- Medication
- Geriatrician referral

43. Please rank the top 3 interventions for depression, where 1=the best option, 2=2nd best etc:

- Referral to a Psychiatrist/Psychologist/Cognitive Behavioural Therapy
- Psycho-Oncology liaison nurse referral
- Social work referral
- Palliative care team involvement
- Medication
- Geriatrician referral

44. Can any healthcare professional, with sufficient training, perform psychological assessment?

Yes No

If you answered no, please specify who should complete the assessment.

45. If there is anything further you would like to add in relation to psychological status assessment, please do so here.

Conclusion of Survey

MERGE Round 3

46. Please rate the importance of impairments in each of the following in terms of their ability to affect oncology decisions, in your opinion, where 0=not important, 10=very important.

	0=not important	1	2	3	4	5	6	7	8	9	10=very important
Functional status	○	○	○	○	○	○	○	○	○	○	○
Physical performance status	○	○	○	○	○	○	○	○	○	○	○
Cognitive status	○	○	○	○	○	○	○	○	○	○	○
Comorbidities	○	○	○	○	○	○	○	○	○	○	○
Polypharmacy	○	○	○	○	○	○	○	○	○	○	○
Nutritional status	○	○	○	○	○	○	○	○	○	○	○
Social support status	○	○	○	○	○	○	○	○	○	○	○
Psychological status - anxiety	○	○	○	○	○	○	○	○	○	○	○
Psychological status - depression	○	○	○	○	○	○	○	○	○	○	○

Thank you for completing Round 3. Your continued participation as part of the expert panel for this Delphi study is greatly appreciated.

Appendix 9: Study 1 Round 3 Feedback Report

TRINITY COLLEGE DUBLIN | THE UNIVERSITY OF DUBLIN
COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH

Anita O'Donovan

The MERGE Study: Round 3 Participant Feedback

June 2013

Contents

Introduction

This report contains feedback from the third Delphi round of the MERGE study. In keeping with Delphi tradition, it aims to be as inclusive and comprehensive as possible, and each participant's contribution is acknowledged. For your convenience, attempts are made to summarise certain aspects, with additional appendices containing the qualitative data from the open-ended questions in Round Three, which are located at the end of the document. I would encourage each contributor to make reference to these appendices, in addition to the summarised sections. This is important for the final round, and will provide different perspectives on the many approaches that are taken to Geriatric Assessment in Oncology.

Please note that this report is part of an overall Delphi process and may not be cited or reproduced without the author's permission.

Definitions of Stability and Consensus

Stability, or the degree of permanence of participants' vote distribution over successive rounds, reflects consensus. Changes of less than 15% offer a working definition of stability in the literature, when the responses obtained in two successive rounds are shown statistically to be not significantly different from each other(1). Group stability, rather than individual stability will be assessed in this study.

A predetermined threshold had previously been chosen for consensus, at an interquartile range of 2 or less units (on a scale of 0-10). The interquartile range is the measure of dispersion for the median and consists of the middle 50% of observations. Thus, an interquartile range of less than 2 means that more than 50% of all opinions fall within 2 points on the scale. It is widely accepted as an objective and rigorous method of defining consensus in Delphi studies(2, 3). However, as some respondents have indicated that they only ranked their top five (or less) options, as directed for certain items, the definition of consensus has been revised to an interquartile range of 1 or less for those items only, in keeping with the literature. Round 2 data has been reclassified to highlight this important change. This will not affect the overall number of rounds and Round 4 will be the final round.

For nominal data, consensus is defined as 67% i.e. two-thirds majority.

Please note that a full list of abbreviations was given in the Round 1 feedback report, and is available for reference in Appendix 1.

Round 3 Data Analysis

Data analysis of Round 3 responses was performed using SPSS version 20. The statistical group response is presented using measures of central tendency (mean, median, mode) and dispersion (interquartile range). Where consensus has not been reached, boxplots are also provided to illustrate divergence of opinion. For the latter, participants may find it useful that outliers have been identified by Study ID.

Round 4

In the fourth and final round, each Delphi panellist will complete a questionnaire that includes some of the items and ratings summarized in the previous rounds and are asked to revise his/her judgments. This round gives Delphi panellists an opportunity to make final clarifications of both the information and their judgments of the relative importance of the items.

Please see the link provided in your email for the Round 4 questionnaire.

Author's Note

Thank you for your important contribution in previous rounds. I am delighted to report that attrition between rounds has been minimal, with none occurring between rounds 2 and 3. Your input is invaluable in the design of a model of care for older patients in Oncology.

Please do not hesitate to contact me if you feel that your views are not contained within this report. A copy of your individual response has been submitted with this document for that purpose.

The results of this study will be presented at the upcoming SIOG conference, in Copenhagen in October (24th-26th). Please see Appendix 7 for the submitted abstract, with results up to Round 3. For further details of the scientific programme click here. The final report will acknowledge participants who have given consent to being named as part of the expert panel.

Best wishes,

Anita O'Donovan,

MERGE Study Coordinator and SIOG National Representative

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Trinity EngAGE

Centre for Research in Ageing

Section 1: Stratifying Patients for Geriatric Assessment

Section 1: Stratifying Patients for Geriatric Assessment

When participants were asked if they would change their minds, based on the Round 2 group responses, the majority of participants (83%) stated that they would **not** change their opinion. Some reasons given for this included personal opinion, clinical experience, the heterogeneity of older patients and poor correlation of chronological age with frailty, similar to Round 2. Please see Appendix 2.

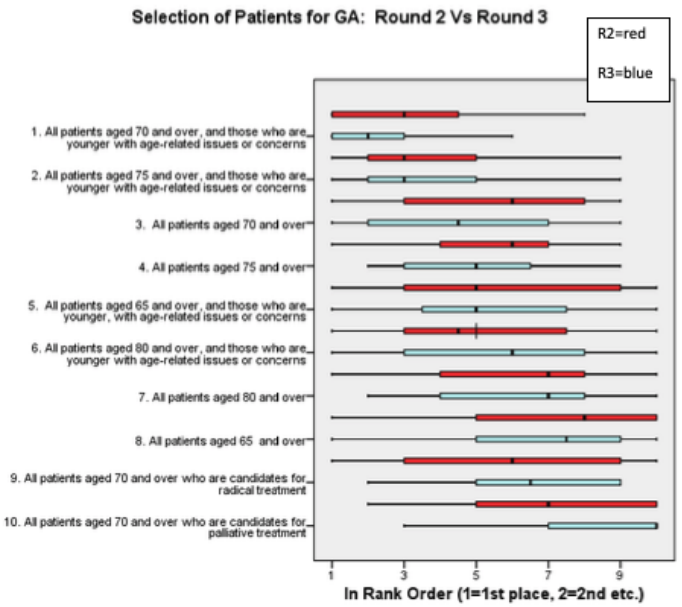
As in Round 2, seven participants (all Irish Oncologists or Geriatricians) stated that they would change their minds, citing the following reasons:

- Important to have common guidelines
- I had ranked my choices as 2,1 for the groups top two choices, 1,2 respectively, therefore I am happy to accept the group's choice as it is not really significantly different to my own choice, but I do counsel that dropping from 75 to 70 creates a huge amount of additional work and 70 nowadays is not that old- as time goes on, the threshold for "elderly" keeps rising.....
- Guidelines are probably important
- Other doctors' opinions and thoughts influence my decision. This is why we have multidisciplinary meetings so that doctors from other specialities can give opinions on their area of expertise
- Sounds reasonable
- Influenced by others valuation of screening instruments in particular
- Depending on resource issues-ideally greater than 65 but could be over 70 with co morbidities if trying to reduce numbers

None of the SIOG participants changed their minds in Round 3.

Patient Selection for GA

Consensus was not reached on a suitable age cut-off or stratification criteria for GA in Oncology. There was a higher level of consensus in Round 3 for the option "All patients aged 70 and over, and those who are younger with age-related issues or concerns". The SIOG group and Irish participants were analysed independently. Only Irish Medical Oncologists were found to be able to achieve consensus within their group for the above age cutoff as first choice. Again, this item represents the most dissensus in the Delphi panel, and only the top three ranking items will be reintroduced in Round 4. Please see Table 1 below for a summary of Round 2 and 3 responses.



Consensus wasn't achieved for any of the above options.

Table 1 Patient Selection for Geriatric Assessment (in order of preference in Round 3: 1=first place etc.)

Rank	Mean Rank	Median	Mode	Interquartile Range	Consensus
1. All patients aged 70 and over, and those who are younger with age-related issues or concerns	**R2:** 3.16 **R3:** 2.68	3.00 2.00	1.00 1.00	{1.00, 5.00} {1.00, 3.50}	**No** **(Greater agreement in R3)**
2. All patients aged 75 and over, and those who are younger with age-related issues or concerns	**R2:** 3.60 **R3:**3.51	3.00 3.00	2.00 2.00	{2.00, 5.00} {2.00, 5.00}	**No** **(No change between rounds)**
3. All patients aged 70 and over	**R2:** 5.72 **R3:** 4.63	6.00 4.00	8.00 1.00	{3.00, 8.00} {2.00, 7.00}	**No** **(Considerable change in rank between rounds)**
4. All patients aged 75 and over	**R2:** 5.65 **R3:** 4.93	6.00 5.00	6.00 3.00	{4.00, 8.00} {3.00, 6.50}	**No** **(Greater agreement in R3)**
5. All patients aged 65 and over, and those who are younger, with age-related issues or concerns	**R2:** 5.37 **R3:** 5.27	5.00 5.00	9.00 5.00	{3.00, 9.00} {3.50, 7.50}	**No** **(Greater agreement in R3)**
6. All patients aged 80 and over, and those who are younger with age-related issues or concerns	**R2:** 5.00 **R3:** 5.71	4.00 6.00	3.00 8.00	{3.00, 8.00} {3.00, 8.00}	**No** **(Considerable change in rank between rounds)**
7. All patients aged 80 and over	**R2:** 6.19 **R3:** 6.29	7.00 7.00	7.00 8.00	{4.00, 8.00} {4.00, 8.00}	**No** **(No change in rank between rounds)**
8. All patients aged 65 and over	**R2:** 7.42 **R3:** 6.73	8.00 7.00	10.00 8.00	{5.00, 10.00} {5.00, 9.00}	**No** **(Greater agreement in R3)**
9. All patients aged 70 and over who are candidates for radical treatment (based solely on tumour characteristics)	**R2:** 5.72 **R3:** 6.76	6.00 7.00	9.00 9.00	{3.00, 9.00} {5.00, 9.00}	**No** **(Greater agreement in R3)**
10. All patients aged 70 and over who are candidates for palliative treatment (based solely on tumour characteristics)	**R2:** 7.16 **R3:** 8.49	7.00 10.00	10.00 10.00	{5.00, 10.00} {7.00, 10.00}	**No** **(Greater agreement in R3)**

SECTION 2: HOW SHOULD GERIATRIC ASSESSMENT BE CONDUCTED?

Section 2: How Should Geriatric Assessment be Conducted?

In **Round 1**, the majority of participants (81%) felt that GA should be completed by face-to-face interview.

This opinion changed slightly in **Round 2**. Thirty-four percent of participants (therefore at the 15% threshold for stability) felt that completion of *all or part of* GA at home by the patient/family is desirable, while the remaining **66%** feel that it isn't. This may represent different attitudes towards different assessment types, some of which participants feel are feasible by self-report methods (see below), and others which are not.

Using expert panel guidance, this was re-examined in **Round 3** to gain clarity, and the question was rephrased as follows:

"Should part of the GA be completed at home by the patient/family prior to the initial oncology consultation? Please note that this includes assessments that the panel feel (by consensus) are feasible by self-report only."

Sixty-six percent of participants now feel that this option **is** feasible (the reverse of Round 2). This represents borderline consensus, even though this is in opposition to rounds 1 and 2, and will be reintroduced in the final round. The SIOG group was divided 50/50 on this response.

Self-Report Methods

	Is Self-report possible for this domain?	
Domain	**Round 2**	**Round 3**
Functional status	68% Yes*	85% Yes*
Objective physical performance status (i.e. gait speed, balance, strength)	91% No*	93% No*
Comorbidity	54% Yes	54% No
Cognitive status	83% No*	93% No*
Polypharmacy	76% Yes*	83% Yes*
Nutritional status	56% No	59% No
Social support status	88% Yes*	90% Yes*
Psychological status-anxiety	56% Yes	61% Yes
Psychological status-depression	54% Yes	50%

* Consensus items are marked with an asterix.

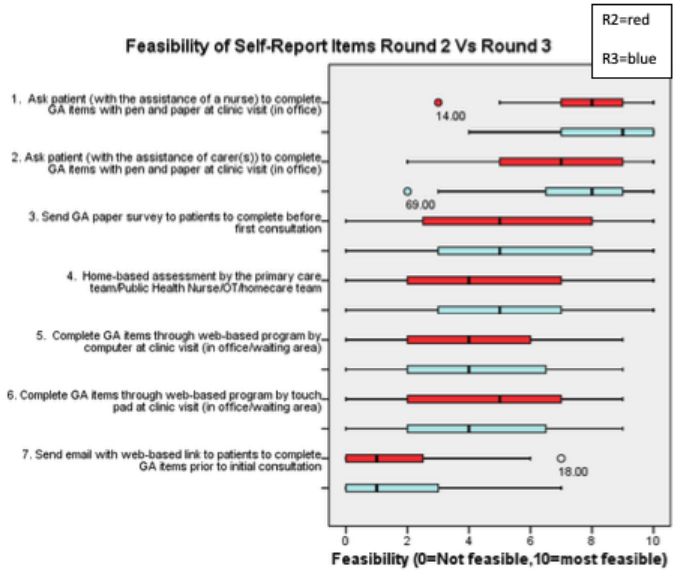
In **Round 2**, consensus was reached for items objective physical performance and cognitive status, with the majority of participants stating that self-report is **not** feasible for these assessments (91% and 83% respectively). Participants feel that self-report is possible for functional status, polypharmacy and social support status however, reaching consensus at 68%, 76% and 88% respectively.

Consensus was strengthened in **Round 3** for all of the Round 2 consensus items, as indicated in the above table. No new items achieved consensus. Subset analysis showed that these results represent the views of the SIOG group as well as the entire expert panel. Please see the above chart for other values.

This question will not be reintroduced in Round 4 as stability between rounds has been demonstrated.

For reasons specified for lack of feasibility of self-report items, please see Appendix 3. These may be summarised under the following categories: the need for medical competence to carry out these tests, the risk of subjectivity and inaccuracy when patients complete them, the impact of specific deficits on the ability to complete such measures e.g. cognitive deficits and the patients' own level of education. Participants also identified the need for objective measurement in some of the above domains, such as the timed up and go test, balance tests etc.

Please see the below chart and table for the self-report options that have not yet reached consensus in this study. Only the top 3 options will be presented in Round 4.



***Outliers are identified by participant ID**

Table 2 Feasibility of Self-Report Methods in Order of Preference (0=not feasible, 10=most feasible)

Rank		Mean Rank	Median	Mode	Interquartile Range	Consensus
1.	Ask patient (with the assistance of a nurse) to complete GA items with pen and paper at clinic visit (in office)	R2:7.72 R3:8.29	8.00 9.00	9.00 10.00	{7.00, 9.00} {7.00, 10.00}	Yes No
2.	Ask patient (with the assistance of carer(s)) to complete GA items with pen and paper at clinic visit (in office)	R2:6.93 R3:7.56	7.00 8.00	5.00 8.00	{5.00, 9.00} {6.50, 9.00}	No No
3.	Send GA paper survey to patients to complete before first consultation	R2:5.12 R3:5.27	5.00 5.00	9.00 3.00	{2.00, 8.00} {3.00, 8.00}	No No
4.	Home-based assessment by the primary care team/Public Health Nurse/OT/homecare team	R2:4.58 R3:4.83	4.00 5.00	4.00 7.00	{2.00, 7.00} {2.50, 7.00}	No
5.	Complete GA items through web-based program by computer at clinic visit (in office/waiting area)	R2:4.35 R3:4.32	4.00 4.00	2.00 4.00	{2.00, 6.00} {2.00, 6.50}	No No
6.	Complete GA items through web-based program by touch pad at clinic visit (in office/waiting area)	R2:4.67 R3:4.29	5.00 4.00	2.00 6.00	{2.00, 7.00} {2.00, 6.50}	No No
7.	Send email with web-based link to patients to complete GA items prior to initial consultation	R2:1.63 R3:1.93	1.00 1.00	1.00 0.00	{0.00, 2.00} {0.00, 3.00}	Yes No

Please find additional comments regarding feasibility below. Many of these relate to the perceived lack of digital literacy skills among older patients.

- We have had the patient and carer fill out assessment without problems for some years now

- Paper based surveys are less desirable due to problems with time taken to analyse, transfer information etc. Computer based solutions are the most appropriate if resources allow this
- I think most elderly people don't deal with e-mail or the web. I think this or having to fill out a form before attending clinic would increase stress. Touchpad at clinic would be good if member of staff could help but probably not feasible in resource limited world. I think primary care could perhaps do but not sure they have resources
- A nurse guiding the patient through the questions in a non-leading manner at the clinic is the best method. It is known that this is best from clinical trials
- Staff shortages and computer/space shortages render these modalities difficult to adapt- though not an insurmountable challenge.
- PHN do not have time for this and currently some areas have no PHN at all. No touch pads available
- Public health nurse assessment / primary care team would take too long
- As this is not exclusive like your ranking tool for the age groups I think you must mean score, not rank. I have not ranked them but scored them therefore. Why have you not got an option for the patient to complete using technology but with assistance? - that would be the most feasible of all. That age group are MORE likely to need a nurse or carer with technology than with pen and paper. (*Unfortunately, I cannot introduce new items at this stage AOD*) Therefore as I do not think technology without assistance is very feasible I have not ranked it highly but I would have ranked it highest of all if there was assistance with it.
- I've marked down nurse and primary care team as both require human resources
- I am happy to revise my top three order to fit in with majority: I had group's 1,2,3 as my order 3,1,2 so I have no great objection to changing. However, use of a nurse to help involves a resource need, whereas the other two options don't....
- Web-based program would be difficult to use in the majority of people aged 80 years and older, as well as in cognitively-impaired patients Home-based assessment would be fanstastic but totally unrealistic nowadays! We can pragmatically count on available resources: patients, carers and nurses

- Elderly patients often do not have computer skills, especially if they are demented
- I think that the own doctor is the best person to control the answers given by the patient.

SECTION 3: SCREENING TOOLS

Section 3: Screening Tools

In **Round 2**, 89% agreed that screening with a shorter geriatric-based measure should be instituted as standard practice, in order to help determine who should undergo full GA. This increased to 93% in **Round 3**. However, a number of stipulations were given (please see Appendix 4).

In **Round 2**, 53% of participants felt that no specific screening measure should be recommended, and that any measure could potentially be used. The remaining 37% of the panel recommended a specific measure to identify patients who could potentially benefit from full GA. Of these, four participants recommend the use of the G8 tool, while others recommend the use of the VES13 or G8 (n=1), ADL or IADL (n=1), the aCGA (n=1), SAOP (n=1) and the SHARE frailty instrument (n=1). Please see Appendix 4 for further comments.

In **Round 3**, clarity was sought on whether or not participants were satisfied with their recommendations of using a short screening tool, given the current lack of discriminative power for the commonly recommended tools in Oncology, as articulated by many members of the expert panel and summarised in a recent systematic review(5). Forty-nine percent of participants (a decrease of 4%) now feel that no specific screening measure should be recommended, and that any measure can potentially be used. Equally, the remaining 49% of the panel recommend a specific measure to identify patients who could potentially benefit from full GA. Of these, 15 participants elaborated on their choice of screening tool, as follows:

- A specific screening measure should be recommended for all patients to identify those who should get a full GA. VES13 or G8 ?
- aCGA
- Don't know
- aCGA
- Although not high sensitivity, consider the G-8 would be most applicable

instrument

- G8
- One that both geriatricians and oncologists agree on as there is no currently available screening measure based on evidence for oncology patients
- Again, I would refer back to my answer in Round 2 - SHARE-frailty instrument
- Unknown
- I am not certain which the best screening measure would be - but do feel that a standard approach would be appropriate
- G8
- G8
- I can't answer question 11 as I think none of the proposed tools are appropriate
- I don't think we should be too prescriptive for just one tool as there is no one tool which covers all relevant domains, but I would suggest that any patient who has a functional problem identified on Barthel Index, or frailty on a validated tool (e.g. SHARE) or cognitive impairment on a screening cognitive test eg MMSE, is flagged up for GA.
- I think that none of the screening tools that have been used at the moment, is as good as necessary to substitute the CGA, but perhaps, the best tools are VES-13, G8 and GFI.

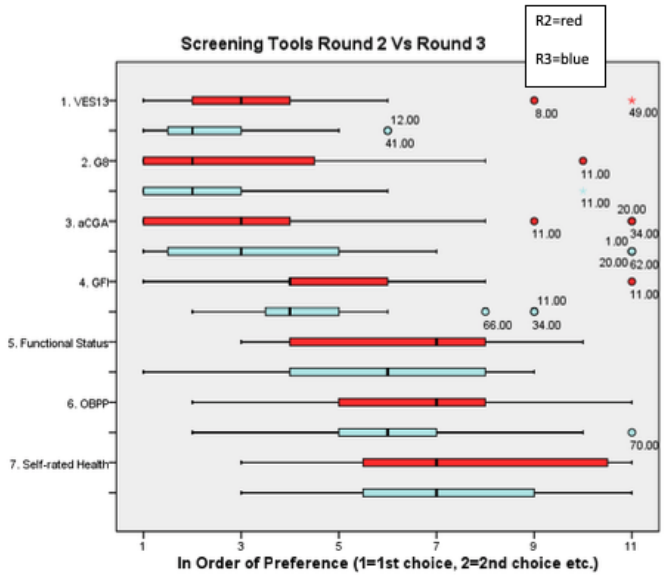
Six participants chose not to answer this question. Please see Appendix 4 for further comments.

Table 3 Best Choice of Screening Tool in Oncology (in order of preference: 1=1st place etc.)

Rank	Mean Rank	Median	Mode	Interquartile Range	Consensus
1. VES-13	**R2:**3.62	3.00	2.00	{2.00, 4.00}	**No**
	R3:2.73	2.00	2.00	{1.75, 3.25}	**No (this represents a change in rank from 2nd to 1st place)**
2. G8	**R2:**3.62	3.00	1.00	{1.00, 5.00}	**No**
	R3:2.92	2.00	1.00	{1.00, 4.00}	**No (this represents a change in rank from 1st to 2nd place)**
3. aCGA	**R2:**4.14	3.00	1.00	{1.00, 7.00}	**No**
	R3:3.69	3.00	1.00	{1.00, 4.50}	**No**
4. GFI	**R2:**5.17	4.00	4.00	{4.00, 6.00}	**No**
	R3:4.92	5.00	5.00	{3.75, 6.00}	**No**
5. Functional Status	**R2:**5.79	6.00	7.00	{3.50, 8.00}	**No**
	R3:5.81	6.00	4.00	{4.00, 8.00}	**No**
6. Objective Physical Performance	**R2:**5.97	6.00	2.00	{4.50, 8.00}	**No**
	R3:5.92	6.00	6.00	{4.00, 7.00}	**No**
7. Self-rated Health	**R2:**7.52	7.00	11.00	{5.00, 10.50}	**No**
	R3:7.12	7.00	7.00	{5.00, 9.00}	**No**
8. ECOG PS	**R2:**6.86	7.00	7.00	{6.00, 9.00}	**No**
	R3:7.15	8.00	8.00	{6.00, 9.00}	**No**
9. Cancer and Ageing Research Group chemotherapy toxicity score	**R2:**7.21	7.00	9.00	{5.50, 9.50}	**No**
	R3:8.12	9.00	10.00	{7.00, 10.00}	**No**
10. Karnofsky PS	**R2:**8.07	9.00	8.00	{7.00, 10.00}	**No**
	R3:8.69	9.00	9.00	{8.00, 10.00}	**No**
11. CRASH score	**R2:**8.03	10.00	11.00	{5.50, 11.00}	**No**
	R3:8.92	10.00	11.00	{6.00, 11.00}	**No**

The VES-13 was ranked highest, however it did not achieve consensus in this round.

On further analysis, there is consensus among SIOG experts in Round 3 in relation to its place as the first choice of screening tool, with a slightly higher mean ranking (2.53) and an interquartile range of {2.00, 3.00}.



***Outliers are identified by participant ID**

Only the top 7 items are presented in the above boxplot. The top 3 ranked screening tools will be used in Round 4.

SECTION 4: ASSESSMENTS AND INTERVENTIONS

Section 4: Assessments and Interventions

For your convenience, items are summarised separately by assessment and interventions.

Table 4 Assessment and Interventions (in order of preference: 1=1st place etc.)

Rank	Mean Rank	Median	Mode	Interquartile Range	Consensus
Functional Status Assessment					
1. ADL/IADL in combination	R2:1.74 R3:1.86	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	Yes Yes
2. ADL only	R2:4.24 R3:4.31	4.00 4.00	4.00 3.00	{2.00, 6.00} {3.00, 5.75}	No No
3. IADL only	R2:4.55 R3:4.36	4.00 4.00	3.00 4.00	{3.00, 5.25} {3.00, 5.75}	No No
4. Barthel Index	R2:5.40 R3:5.08	6.00 4.00	8.00 4.00	{3.00, 8.00} {2.25, 8.00}	No No
5. VES-13	R2:5.90 R3:5.33	6.00 6.00	7.00 7.00	{4.00, 8.00} {3.00, 7.00}	No No
6. Patient history/clinical examination	R2:6.02 R3:5.55	6.00 6.00	9.00 9.00	{3.00, 9.00} {2.00, 9.00}	No No
7. KPS	R2:5.38 R3:5.72	5.00 5.50	5.00 5.00	{4.00, 6.25} {5.00, 7.00}	No No
8. ECOG PS	R2:5.45 R3:6.03	6.00 6.00	5.00 6.00	{4.00, 7.00} {4.25, 8.00}	No No
9. FIM/FAM	R2:6.31 R3:6.81	7.00 8.00	7.00 8.00	{4.00, 8.25} {4.50, 8.75}	No
Functional Status Interventions					
1. Physiotherapy referral	R2:1.79 R3:1.82	1.00 2.00	1.00 1.00	{1.00, 3.00} {1.00, 2.25}	No No, but borderline
2. OT referral	R2:2.50 R3:2.42	2.00 2.00	2.00 2.00	{2.00, 3.00} {2.00, 3.00}	Yes yes
3. Public Health Nurse/ Homecare intervention/day hospital	R2:3.05 R3:3.08	3.00 3.00	4.00 1.00	{2.00, 4.00} {1.75, 4.25}	No No

Physical Performance Impairment: Assessment					
1. TUG	**R2:**1.64 **R3:**1.94	1.00 2.00	1.00 1.00	{1.00, 2.00} {1.00, 3.00}	**Yes** **No**
2. Gait Speed	**R2:**2.75 **R3:**2.63	2.00 2.00	2.00 2.00	{2.00, 3.75} {2.00, 3.00}	**No** **Yes**
3. Grip Strength	**R2:**3.89 **R3:**3.54	4.00 3.00	4.00 3.00	{3.00, 5.00} {2.00, 5.00}	**No** **No**
4. Balance tests	**R2:**3.78 **R3:**3.91	4.00 4.00	3.00 4.00	{3.00, 4.00} {3.00, 5.00}	**Yes** **No**
Physical Performance Impairment: Interventions					
1. Physiotherapy Referral	**R2:**1.17 **R3:**1.24	1.00 1.00	1.00 1.00	{1.00, 1.00} {1.00, 1.00}	**Yes** **Yes**
2. OT referral	**R2:**2.93 **R3:**2.68	3.00 3.00	2.00 2.00	{2.00, 4.00} {2.00, 3.00}	**No** **Yes**
3. Public Health Nurse/ Homecare intervention/day hospital	**R2:**3.38 **R3:**3.34	4.00 3.00	4.00 5.00	{3.00, 4.00} {2.00, 5.00}	**Yes** **No**
Cognitive Status: Assessment					
1. MMSE	**R2:**1.14 **R3:**1.55	1.00 1.00	1.00 1.00	{1.00, 1.00} {1.00, 2.00}	**Yes** **Yes**
2. MiniCog	**R2:**3.94 **R3:**3.97	4.00 4.00	4.00 4.00	{3.00, 5.00} {3.00, 5.00}	**No** **No**
3. MOCA	**R2:**4.75 **R3:**4.00	5.00 4.00	5.00 5.00	{4.00, 5.75} {3.00, 5.00}	**No** **No**
4. AMTS	**R2:**3.94 **R3:**4.52	4.00 4.00	4.00 4.00	{2.25, 4.75} {2.50, 4.50}	**No** **No**
Cognitive Status: Interventions					
1. Geriatrician referral	**R2:**1.67 **R3:**1.97	1.00 1.50	1.00 1.00	{1.00, 2.00} {1.00, 3.00}	**Yes** **No**
2. Psychologist/ Old Age Psychiatrist referral	**R2:**3.31 **R3:**3.24	3.00 3.00	2.00 2.00	{2.00, 4.00} {2.00, 4.00}	**No** **No**
3. Memory clinic referral	**R2:**3.69 **R3:**3.26	3.00 2.50	1.00 1.00	{1.00, 6.25} {1.00, 4.50}	**No** **No**
Co-morbidities: Assessment					
1. Charlson Comorbidity Index	**R2:**1.67 **R3:**1.53	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	**Yes** **Yes**
2. CIRS-G	**R2:**2.36 **R3:**2.19	2.00 2.00	2.00 2.00	{2.00, 3.00} {2.00, 3.00}	**Yes** **Yes**

3. Chart review/medical history/list	**R2:**2.49 **R3:**2.66	3.00 3.00	3.00 3.00	{2.00, 3.00} {2.00, 3.00}	**Yes** **Yes**
Co-morbidities: Interventions					
1. Geriatrician Referral	**R2:**1.55 **R3:**1.43	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	**Yes** **Yes**
2. Referral to specialists as deemed suitable for a given co-morbidity	**R2:**1.79 **R3:**1.95	2.00 2.00	2.00 2.00	{1.00, 2.00} {1.00, 2.00}	**Yes** **Yes**
3. Medication	**R2:**2.67 **R3:**2.62	3.00 3.00	3.00 3.00	{2.00,3.00} {2.00,3.00}	**Yes** **Yes**
Polypharmacy: Assessment					
1. List of Medications	**R2:**2.00 **R3:**2.03	2.00 2.00	1.00 1.00	{1.00, 3.00} {1.00, 3.00}	**No** **No**
2. Pharmacist Review	**R2:**2.21 **R3:**2.12	2.00 2.00	2.00 2.00	{1.00, 3.00} {1.00, 2.50}	**No** **No**
3. STOPP/START	**R2:**2.37 **R3:**2.36	3.00 3.00	3.00 3.00	{1.75, 3.00} {2.00,3.00}	**No** **Yes**
Polypharmacy: Interventions					
1. Geriatrician Referral	**R2:**1.70 **R3:**1.54	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	**Yes** **Yes**
2. Reduce/stop inappropriate medications	**R2:**2.26 **R3:**2.13	2.00 2.00	3.00 1.00	{1.00, 3.00} {1.00, 3.00}	**No** **No**
3. Pharmacist referral	**R2:**2.72 **R3:**2.86	3.00 3.00	3.00 3.00	{2.00, 4.00} {2.00, 4.00}	**No** **No**
Nutritional Status: Assessment					
1. MNA Short form	**R2:**1.87 **R3:**2.00	1.00 2.00	1.00 1.00	{1.00, 2.00} {1.00, 3.00}	**Yes** **No**
2. MNA Long form	**R2:**2.63 **R3:**2.38	2.00 2.00	2.00 2.00	{1.25, 3.00} {2.00, 3.00}	**No** **Yes**
3. History of weight loss/ anorexia/ BMI	**R2:**2.87 **R3:**2.81	3.00 3.00	4.00 3.00	{1.00, 4.00} {2.00, 4.00}	**No** **No**
Nutritional Status: Interventions					
1. Dietician Referral	**R2:**1.13 **R3:**1.11	1.00 1.00	1.00 1.00	{1.00,1.00} {1.00,1.00}	**Yes** **Yes**
2. Dietary advice/ Use of supplements	**R2:**1.88 **R3:**1.89	2.00 2.00	2.00 2.00	{2.00, 2.00} {2.00, 2.00}	**Yes** **Yes**

Social Support Status: Assessment					
1. Patient History/ caregiver interview	**R2:**1.06 **R3:**1.27	1.00 1.00	1.00 1.00	{1.00, 1.00} {1.00, 1.00}	**Yes** **Yes**
2. mMOS-SS	**R2:**2.03 **R3:**2.04	2.00 2.00	2.00 2.00	{2.00, 2.00} {2.00, 2.00}	**Yes** **Yes**
3. Socio-familiar Gijon Test	**R2:**2.94 **R3:**2.85	3.00 3.00	3.00 3.00	{3.00, 3.00} {3.00, 3.00}	**Yes** **Yes**
Social Support: Interventions					
1. Social work referral	**R2:**1.70 **R3:**1.57	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	**Yes** **Yes**
2. Home help	**R2:**2.81 **R3:**2.76	3.00 2.00	2.00 2.00	{2.00, 4.00} {2.00, 4.00}	**No** **No**
3. Public Health Nurse support	**R2:**3.02 **R3:**3.43	3.00 3.00	5.00 5.00	{2.00, 5.00} {2.00, 5.00}	**No** **No**
Anxiety: Assessment					
1. Patient history/ Interview	**R2:**1.64 **R3:**1.62	2.00 2.00	2.00 1.00	{1.00, 2.00} {1.00, 2.00}	**Yes** **Yes**
2. HADS	**R2:**1.67 **R3:**1.71	2.00 2.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	**Yes** **Yes**
3. Distress thermometer	**R2:**2.69 **R3:**2.68	3.00 3.00	3.00 3.00	{3.00, 3.00} {2.00, 3.00}	**Yes** **Yes**
Anxiety: Interventions					
1. Referral to a Psychiatrist/ Psychologist /Cogntive Behavioural Therapy	**R2:**1.39 **R3:**1.63	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	**Yes** **Yes**
2. Psycho-Oncology liaison nurse referral	**R2:**2.18 **R3:**2.08	2.00 2.00	2.00 2.00	{2.00, 3.00} {2.00, 2.00}	**Yes** **Yes**
3. Social work referral	**R2:**4.25 **R3:**3.95	4.00 4.00	4.00 4.00	{3.00, 5.00} {3.00, 5.00}	**Yes** **No**
Depression: Assessment					
1. GDS Short form	**R2:**1.75 **R3:**1.86	1.00 2.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	**Yes** **Yes**
2. GDS Long form	**R2:**2.55 **R3:**2.60	2.50 3.00	2.00 3.00	{2.00, 3.00} {2.00, 3.00}	**Yes** **Yes**
3. Patient history/ Interview	**R2:**2.78 **R3:**2.69	3.00 3.00	4.00 4.00	{1.25, 4.00} {1.00, 4.00}	**No** **No**
4. HADS	**R2:**2.92 **R3:**2.86	3.00 3.00	4.00 3.00	{2.00, 4.00} {2.00, 4.00}	**No** **No**

Depression: Interventions					
1. Referral to a Psychiatrist /Psychologist /Cognitive Behavioural Therapy	**R2:**1.56 **R3:**1.50	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	**Yes** **Yes**
2. Psycho-Oncology liaison nurse referral	**R2:**2.63 **R3:**2.34	2.00 2.00	2.00 2.00	{2.00, 3.00} {2.00, 3.00}	**Yes** **Yes**
3. Medication	**R2:**3.93 **R3:**4.16	4.00 5.00	3.00 5.00	{3.00, 5.00} {3.00, 5.00}	**No** **No**
4. Palliative Care Team Involvement	**R2:** **R3:**4.18	4.50	5.00	{3.00, 5.00}	**No**

There was a change in the definition of consensus in Round 3 for ranked items, from an interquartile range of 2, to an interquartile range of 1. This resulted in some minor changes. Consensus was met for the following tools in Round 3: functional status (ADL/IADL), cognition (MMSE) physical performance (gait speed – 2nd choice), comorbidity (Charlson score), nutrition (MNA), social support status (patient history/caregiver interview)and depression (Geriatric Depression Scale).

In Round 3, first choice GA-driven interventions to address impaired domains that met consensus included: 1) physiotherapy, occupational therapy for impaired function and physical performance; 2) geriatrician referral for comorbidity and polypharmacy assessment; 3) dietician consult for poor nutrition; 4) social work consult for poor social support and 5) Referral to a Psychiatrist/Psychologist/Cognitive Behavioural Therapy for psychological assessment.

Some of these items will be represented in Round 4 to assess stability and to gain consensus.

Psychiatrist will be changed to Old Age Psychiatrist in the Cognitive Assessment section in Round 4, as pointed out by one panelist:

> *"Can you change psychiatrist to old age psychiatrist, or include them as an extra option in that answer as older people with cognitive impairment are seen by POA, not psychiatrists."*

Thank you for highlighting this, and apologies for any offence caused.

Please see Appendix 5 for additional comments related to each domain.

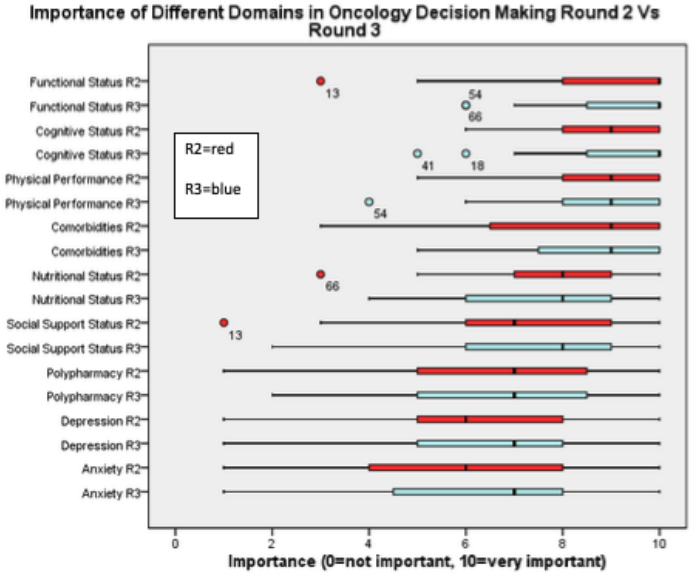
Importance of Each Domain in Oncology Decision-Making

Table 5 Importance of Each Domain in Oncology in Rank Order (1=1st place etc.)

Domain Rank	Average Rating*	Median	Mode	Interquartile Range	Consensus
1. Functional status	**R2:**8.91	10.00	10.00	{8.00, 10.00}	Yes
	R3:9.23	10.00	10.00	{8.25, 10.00}	Yes
2. Cognitive status	**R2:**8.79	9.00	10.00	{8.00, 10.00}	Yes
	R3:8.98	9.50	10.00	{8.00, 10.00}	Yes
3. Physical performance status	**R2:**8.52	9.00	10.00	{7.25, 10.00}	No
	R3:8.70	9.00	10.00	{8.00, 10.00}	Yes
4.Comorbidities	**R2:**8.07	9.00	10.00	{6.25, 10.00}	No
	R3:8.60	9.00	10.00	{7.25, 10.00}	No
5.Nutritional status	**R2:**7.66	8.00	8.00	{7.00, 9.00}	Yes
	R3:7.75	8.00	6.00	{6.00, 9.00}	No
6.Social support status	**R2:**6.93	7.00	7.00	{6.00, 9.00}	No
	R3:7.03	8.00	8.00	{6.00, 9.00}	No
7.Polypharmacy	**R2:**6.82	7.00	9.00	{5.00, 9.00}	No
	R3:6.88	7.50	8.00	{5.00, 9.00}	
8.Psychological status - depression	**R2:**6.48	6.00	6.00	{5.00, 8.00}	No
	R3:6.30	7.00	7.00	{5.00, 8.00}	No
9.Psychological status - anxiety	**R2:**6.02	6.00	6.00	{4.25, 8.00}	No
	R3:6.13	7.00	8.00	{4.00, 8.00}	No

***In order of importance from highest to lowest**

In **Round 2**, panellists rated functional status as the most important domain in influencing oncology decisions, followed by cognitive and physical performance status. This was reinforced in **Round 3**, with objective physical performance now reaching consensus as the third most important domain.



***Outliers are identified by participant ID**

SECTION 5: TRAINING REQUIREMENTS FOR ASSESSMENT

Section 5: Training Requirements for Assessment

Table 6 Can any Healthcare Professional Perform this Assessment?

Domain	Round 2	Round 3
Functional Status	Yes (98%)*	Yes (93%)*
Objective Physical Performance	Yes (98%)*	Yes (88%)*
Cognitive Status	Yes (80%)*	Yes (73%)*
Comorbidity	Yes (73%)*	Yes (68%)*
Polypharmacy	No (57%)	No (53%)
Nutritional Status	Yes (68%)*	Yes (65%)
Social Support Status	Yes (82%)*	Yes (85%)*
Psychological Status	No (52%)	Yes (53%)

Consensus items *

In **Round 2**, clear consensus existed for most items, apart from polypharmacy and psychological status. Some participants asked for clarification in relation to the definition of "sufficient training", which was provided. In **Round 3**, stability was maintained for all items, but nutritional status does not meet consensus at 65%, compared to 68% in Round 2. Only this domain will be represented in Round 4.

Please see Appendix 6 for further comments in relation to the above.

APPENDICES

Appendix 1: List of Abbreviations Used in This Document

AD=Alzheimer's Disease

AMTS=Abbreviated Mental Test Score

ASA=American Society of Anaesthesiologists

CARST = Community Assessment of Risk Screening Tool

CCI=Charlson Comorbidity Index

CGA=Comprehensive Geriatric Assessment

CHS=Cardiovascular Health Study

CIRS-G=Cumulative Illness Rating Scale-Geriatric

GA=Geriatric Assessment

Ger=Geriatrician (Ireland)

ECOG = Eastern Cooperative Oncology Group

EMS=Elderly Mobility Scale

FIM/FAM=Functional Independence Measure and Functional Assessment Measure

GFI=Groningen Frailty Indicator

IQ Rge=Interquartile Range

MEAMS=Middlesex Elderly Assessment of Mental State

MDT=Multidisciplinary Team

mMOS-SS=modified Medical Outcomes Study – Social Support

MMSE=Minimental State Examination

MNA=Mini Nutritional Assessment

MO=Medical Oncology (Ireland)

MOCA=Montreal Cognitive Assessment

MUST=Malnutrition Universal Screening Tool

PD=Parkinson's Disease

PHN=Public Health Nurse

PS=Performance Status

PSP=Progressive Supranuclear Palsy

RBANS=Repeatable Battery for the Assessment of Neuropsychological Status

QMCI = Quick Mild Cognitive Impairment

RO=Radiation Oncology (Ireland)

SCS=Simplified Comorbidity Score

SIOG=International Society of Geriatric Oncology

SPPB=Short Physical Performance Battery

STOPP/START= Screening Tool of Older People's potentially inappropriate Prescriptions/ Screening Tool to Alert doctors to the Right Treatment

TUG=Timed Up and Go

VES=Vulnerable Elders Survey

VIP=Variable Indicative of Placement (risk)

Appendix 2: Stratifying Patients for Geriatric Assessment

- I am happy with my responses
- Agree with above
- I feel that being very restrictive would limit access for patients who need this intervention
- I believe that I know and understand the evidence and my views are evidence based
- I feel strongly about my first response
- Depending on resource issues-ideally greater than 65 but could be over 70 with co morbidities if trying to reduce numbers
- I think it is pragmatic to choose an age above which the incidence of issues is high enough for a routine policy, but this should not preclude the younger patients being assessed. To some degree the choice of age should reflect local patterns of age related problems.
- It was the first ranked option as per Q1
- Can't remember my initial response but this seems reasonable statement
- I agree with the above mentioned criteria
- Agree with the first place ranking, of 70+ or younger with age-related issues
- Changed my opinion in round 2
- It remains arbitrary
- No convincing reason to do so
- Happy with original answer
- Consistency with international guidelines, life expectancy and threshold for recent clinical trials

- There was no consensus among participants stating that the matter is subjective
- It was my 1st choice
- I agree with the majority
- From my practice, patients aged 75 and over, and those who are younger with age-related issues are those who need a GA
- I agree with the comment above
- Patients in 70-75 range can unexpectedly demonstrate shortcomings in tests, relevant for outcome of treatment
- Chronological age is definitely a poor parameter to define a cut-off for offering CGA
- Because I have my own opinion.
- 70 is a pragmatic cut-off

Appendix 3: Reasons for Lack of Feasibility of Self-Report Methodology

- Medical competences needed; validity of the evaluation
- Items I have listed "no" - think these would be difficult for patient/family to objectively assess
- Insight may be poor for these areas, objective measurement better
- Some need clinical input and others are best addressed with a clinician present to reassure or support the findings i.e. cognition or depression
- Both need objectivity and a degree of medical expertise
- May require objective assessment to prevent underreporting
- Objective measures require an independent observer
- These require external assessment as problems with cognition will affect all other reporting and people may underplay physical disabilities
- Self-assessment can be impaired when the items were placed above which consider that the Self-Reported are not feasible. My account is due to the fact that such evaluations require a trained and that the self can bring reported misinterpretation and loses sensitivity
- I think they are objective rather than subjective assessments
- Because it may not be objective and accurate
- Objective physical performance probably would not be truly objective especially if the patient really wanted treatment but was physically not able for it. I find that patients are unreliable when it comes to co morbidities , some patients are knowledgeable , others are quite clearly not, hence self-assessment in this regard would not be accurate, a cognitively impaired patient cannot self-report accurately his / her cognitive status , nutritional status I don't think would be accurately assessed by self-reporting and similarly for depression and anxiety

- Knowledge of comorbidity is poor. Testing cognitive function by cognitive impaired is not possible. Anxiety and depression are sensitive issues and should be accompanied by a therapeutic talk.
- As before, physical performance assessments by definition are objective, not subjective, cognitive status self-determined is prone to inaccuracies in responses, patients often need to be specifically asked about certain medications which are not reported when asked what medications are taken (e.g. OTC, herbal medications).
- As per round 2 feedback
- Requires medical knowledge or interpretation
- Cognitive status cannot be self-assessed and depression is a medical diagnosis.
- Reliability in reporting, self-awareness, poor understanding
- They require specialised training
- As before. Patients / family in the majority of cases are unlikely to have the objectivity or training to give an accurate assessment.
- No extensive assessment, trouble in understanding questions by patient, increased subjectivity and under (comorbidity) or over (psychological issues) statements
- Complex instruments used for assessment
- Objective measurements should be objective, while cognitive status requires insight. Medical records need to be assessed for comorbidity
- Comorbidity - Health literacy is a problem in patients and I whist it is possible to self assess this the results may not be reliable. Cognitive function - needs to be done by someone else - ditto for objective physical performance tests
- Objective assessment more valuable
- Objective cannot be self-report!

- Objective physical performance status - is objective, therefore by definition not self-report. Co-morbidity - will require collateral from notes/ GP notes as patient's are often unaware of past diagnoses Cognitive status - can be self-administered (iPad etc) but still requires some sort of objective measure. Polypharmacy - patients often don't know what they're taking Nutritional status - most patients will report that its fine.
- Comorbidity needs more than box ticking and patients often misunderstand diagnoses, so form could be filled in at home but would need healthcare worker to qualify / fill in the blanks etc.
- In fact, all items require an objective assessment. Self-reports can facilitate the collection of data but they must be objectively verified
- Patients cannot evaluate themselves on all domains
- Because it is necessary a special training to be sure that the final answers are objective answers and perhaps I would not be sure that the patient has answered by an objective way.
- The criteria of what amounts to a co-morbidity are quite strict: and need seem trained input.

Appendix 4: Comments on Screening Tools

- Evidence for this is very poor
- If resource limitations
- Because of the high incidence of elderly patients with cancer, it is virtually impossible to accomplish the complete evaluation in all patients
- Saves time
- There is a need to be pragmatic - not all older patients will require a full GA. Screening will help identify those most likely to benefit
- More feasible than wider screening for all
- More efficient than screening everybody
- Just a way to talk about same information
- But I don't think that we can use tools developed and validated outside the oncology field, because frailty for cancer treatment is not the same that the frailty concept studied in gerontology.the tool should be designed specificallty for an oncology purpose.
- We need to select one tool, all use it.

Why/Why not?

- Help to standardise practice, would also allow research collaboration between institutions.
- May enable scarce resources to be directe4d to the more appropriate candidates
- Pragmatism. It is too time and resource consuming to do it on everyone
- Standardizing assessment has to be beneficial for patients in the longer term
- I think a shorter tool which is validated is a more practical approach given time constraints at clinic and all the paperwork that needs to be done
- Saves time
- Yes because this will help to determine if the patient will benefit or not from oncological treatment. provided it is done in a timely manner and from an oncological treatment point of view
- It helps to address topics of CGA
- Here is a need to be pragmatic - not all older patients will require a full GA. Screening will help identify those most likely to benefit
- My comments from round 2 apply.
- No tool has sufficient discriminative power
- To indicate which patients would benefit from CGA
- It is not rocket science! Question of time

and logistics.

- To save time and personnel.
- For feasibility
- A long, full CGA is impractical.
- Heterogeneity of elderly patients
- We are looking for an efficient tool that can identify healthy older people who can be treated with similar options used in younger adults
- Will help exclude 30% of older patients without functional/cognitive difficulties
- I think we should be encouraging objective tools, even if not proven specifically in oncology setting, as they are well validated for identifying frail / vulnerable older adults in general and these tools help non-specialists to quickly screen for potential problems and so not refer highly functioning older people unnecessarily
- To help physicians in order to screen witch patients would benefit most from complete CGA. As aging population increases and resources are the same, we have little time to do all things at clinical practice
- Time AND money saving
- 30% are fit and you don't need to waste time on them
- Reduce the numbers for full assessment
- But it is necessary to find the best screening tool. At the moment, I think that

none of the screening tools are as good to substitute the CGA.

- We need to start routinely using these tools to work out what is useful/practical

Appendix 5: Additional Comments Related to Each Assessment Type

Functional Assessment

- In our service we utilize tests: Time up and go, and Hand GRIP
- Question 12 really should be a combination of the options , ECOG or KPS are part of the history and physical exam , and really ECOG = KPS except ECOG score is easier to use and remember
- Functional assessment is a critical step, because functional status must be considered as an important outcome of cancer treatment plan
- Please note that the Barthel Index is a measurement tool for ADL, so we have been asked to compare generic ADL assessment with a specific ADL tool, which might be affecting the results – i.e. I chose Barthel as number one as it is important to use validated tools, but I also agree with ADL assessment being important, so which one do I choose to reflect my opinion.....

Objective Physical Performance Assessment

- Screening tests often evaluated the risk of falling but not physical abilities as a whole domain. Clinical examination, POMA test provide accurate data on physical capacities of an older patient
- Please reconsider gait speed as a useful measure of physical performance - what is the evidence to support this????? I am concerned that some respondents were not familiar with other excellent tools e.g. EMS and SPPB and chose a term they understood, without knowing the actual value of this parameter versus these tools. I do not feel comfortable recommending gait speed as an assessment here! *(This recent systematic review summarises the evidence base to date, which the panel may find useful(6). Also, its prognostic value in Oncology, along with the SPPB, have been demonstrated in a recent study of older women with gynaecological cancer(7). I would also invite the panel to comment further here. AOD)*

Cognitive Assessment

- My answers to Q21-22 in Round 2 still hold around assessment selection appropriate to the individual patient. I am not familiar with QMCI or Pfeiffer questionnaire so ranked these last.
- All these tests should be weighed by a geriatrician's opinion. None of them should be used by oncologists without training in geriatrics.
- I have only ranked the first 4 with which I am familiar but there is an automatic ranking once I have filled those. I am not an expert in psychogeriatric assessment so I do not know enough to rank all these.
- Can you change psychiatrist to old age psychiatrist, or include them as an extra option in that answer as older people with cognitive impairment are seen by POA, not psychiatrists.

Comorbidity Assessment

- A scale that "grades" the impact of the co-morbid condition as opposed to just a list is useful when assessing a patients suitability for treatment
- There is no appropriate tool to assess comorbidity in clinical practice. CIRS-G provides a systematic approach that helps not to forget one or another organ system

Polypharmacy Assessment

- While tool are helpful, interpretation with GP or Geriatrician ideal

Nutritional Status Assessment

No other comments

Social Support Status

- Legal and social competences needed
- Not familiar with social support tools listed in 36 so have left blank
- Takes significant time
- There are a range of interventions. I don't think you can rank them. It depends on the issue. All are relevant.

- Social assessment is a key step because social precariousness may limit cancer treatment plan and cancer treatment may cause institutionalisation of older patients with social difficulties
- There are not enough social workers so more practical to refer to PHN first

Psychological Status

- Mood has been associated with treatment tolerance and it is often under-evaluated in older people
- Palliative care will rank differently depending on the disease status. It might rank 1st for a patient whose depression was due to a terminal diagnosis and be entirely inappropriate for a depressed patient having treatment with curative intent, therefore I found this v hard to answer and it will be v difficult to interpret

Appendix 6: Who Can Perform Assessments?

Functional Assessment

- They can but not enough time
- Geriatrician, physiotherapy and nurse
- Occupational therapist, physiotherapist, nurse
- Not competent to answer questions 12 and 13

Objective Physical Performance Assessment

- Requires optimal training and time
- Geriatrician , physiotherapist, nurse
- MDT
- Physical therapist, psychomotor therapist

Cognitive Assessment

- This requires time and skills to be done well though
- Geriatrician , nurse with specific training
- This is complex and I think only certain professionals are capable of doing this well
- Psychologist, nurse, doctor, OT
- OT Neurologist
- Geriatrician/psychiatrist/CPN
- Depends on the complexity of the assessment tool
- Neuropsychologist trained in geriatrics, geriatrician

Comorbidity Assessment

- Physician or clinical nurse specialist
- Nurse, geriatrician
- Only certain professionals can capable of doing this
- Geriatrician, GP or general physician
- Doctor with geriatric training / experience
- Physician
- Geriatrician, advanced practice nurse

- Geriatrician, gerontology nurse, GP
- Needs medical education

Polypharmacy

- Think person should have some sort of medical/pharmacy training
- Doctor or pharmacist
- Physician or pharmacist
- Nurse, geriatrician
- It needs to be pharmacist or doctor
- Only certain professionals capable of this
- See above
- Sometimes difficult to stop medications without speaking to person/ team who commenced them
- Skill in internal medicine required
- Physician
- This is indeed best done by a pharmacist
- Pharmacist
- Physician or ANP only
- Should understand why they take medication
- Persons with pharmaceutical education, Doctor, Pharmacist

Nutritional Status

- Nurse, doctor or dietician
- Inadequate time and training
- Dietician only proper professional capeable ofthis
- Dietician
- Dietician
- Dietician
- Need time to do properly
- Ideally a dietician should perform it and intervene at the same time.
- Nutritional screening can be performed by any healthcare professional, but an accurate assessment requires dietician skills

Social Support Status

- No time or sufficient training
- It needs to be someone who can assess home situation
- Social worker or public health nurse
- Social worker well informed on geriatric aspects

Psychological Status

- Specific competences needed
- Nurse or doctor
- Not enough time or training
- Nurse, geriatrician, psychologist
- Needs properly trained professionals
- Psychologist with geriatric training
- Specific clinical training necessary
- Oncology or psych professional
- Doctor, Psychiatrist, Psychologist, Nurse

Appendix 7 SIOG Abstract Copenhagen 2013

Geriatric Assessment for Older Adults with Cancer: An International Delphi Study

O'Donovan, A.[1], Mohile, S.[2] and Leech, M.[1]

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Introduction:
Despite the evidence demonstrating the benefits of Geriatric Assessment (GA), its adoption in Oncology has not been widespread. Given the increasing older population in Ireland, there is a growing impetus for the development of a model of care for GA in Oncology, informed by national stakeholders and an international expert panel.

Objective:
To obtain consensus on the optimal model of care for GA in Oncology to inform the implementation of Geriatric Oncology in Ireland.

Methods:
This study uses a structured iterative process, the Delphi technique, to gain consensus. All Irish Consultant Radiation and Medical Oncologists and Geriatricians were invited to participate in this study. An international expert panel, with expertise in geriatric oncology and active SIOG membership, or active researchers in the field of geriatric oncology, were also invited to participate. The first round (R1) was an open round seeking the panel's opinion on GA in Oncology. R1 comprised 49 members, encompassing four disciplines: Radiation Oncology (n=9), Medical Oncology (n=7), Geriatric Medicine (n=10) and SIOG-affiliated (n=24). R1 responses were used in the design of subsequent rounds where participants were asked to rank order preference for GA tools and interventions. A predetermined threshold for consensus has been chosen, at an interquartile range of 1 or less units (scale of 0-5,) or 2 (scale of 1-10). For nominal data, consensus is defined as two-thirds majority.

Results:
Forty-nine participants completed R1 and 44 completed R2 and R3. The majority of SIOG affiliated members use GA in the care of their patients (n=13 always, n=9 sometimes). All of the Irish geriatrician participants employ GA. Ninety-three percent of Irish participants believe that Geriatric Oncology is feasible in Ireland.
No consensus has been reached on a suitable age cut-off to select patients for GA. The SIOG affiliated group was also found to be unable to achieve consensus within their group. The majority (93%) of the panel felt that a screening tool should be employed to identify patients for GA (R3). VES-13 achieved consensus among the SIOG group as the first choice of screening tool.
All geriatric domains were deemed important for a full GA. Consensus was met for the following tools in R3: functional status (ADL/IADL), cognition (MMSE) physical performance (gait speed), comorbidity (Charlson score), nutrition (MNA), social support status (patient history/caregiver interview)and depression (Geriatric Depression Scale). In R3, first choice GA-driven interventions to address impaired domains that met consensus included: 1) physiotherapy, occupational therapy for impaired function and physical performance; 2) geriatrician referral for comorbidity and polypharmacy assessment; 3) dietician consult for poor nutrition; 4) social work consult for poor social support; 5) Referral to an Old Age Psychiatrist/Psychologist/Cognitive Behavioural Therapy for psychological assessment.

Conclusions:
This Delphi investigation of geriatric oncology experts provides some consensus on assessments and interventions that could be considered standard of care for older cancer patients in Oncology. Final results will be presented at the meeting.

Conflict of Interest: None
Key words: Geriatric Assessment
Acknowledgements: Members of the expert panel who contributed to this study and whose input was invaluable

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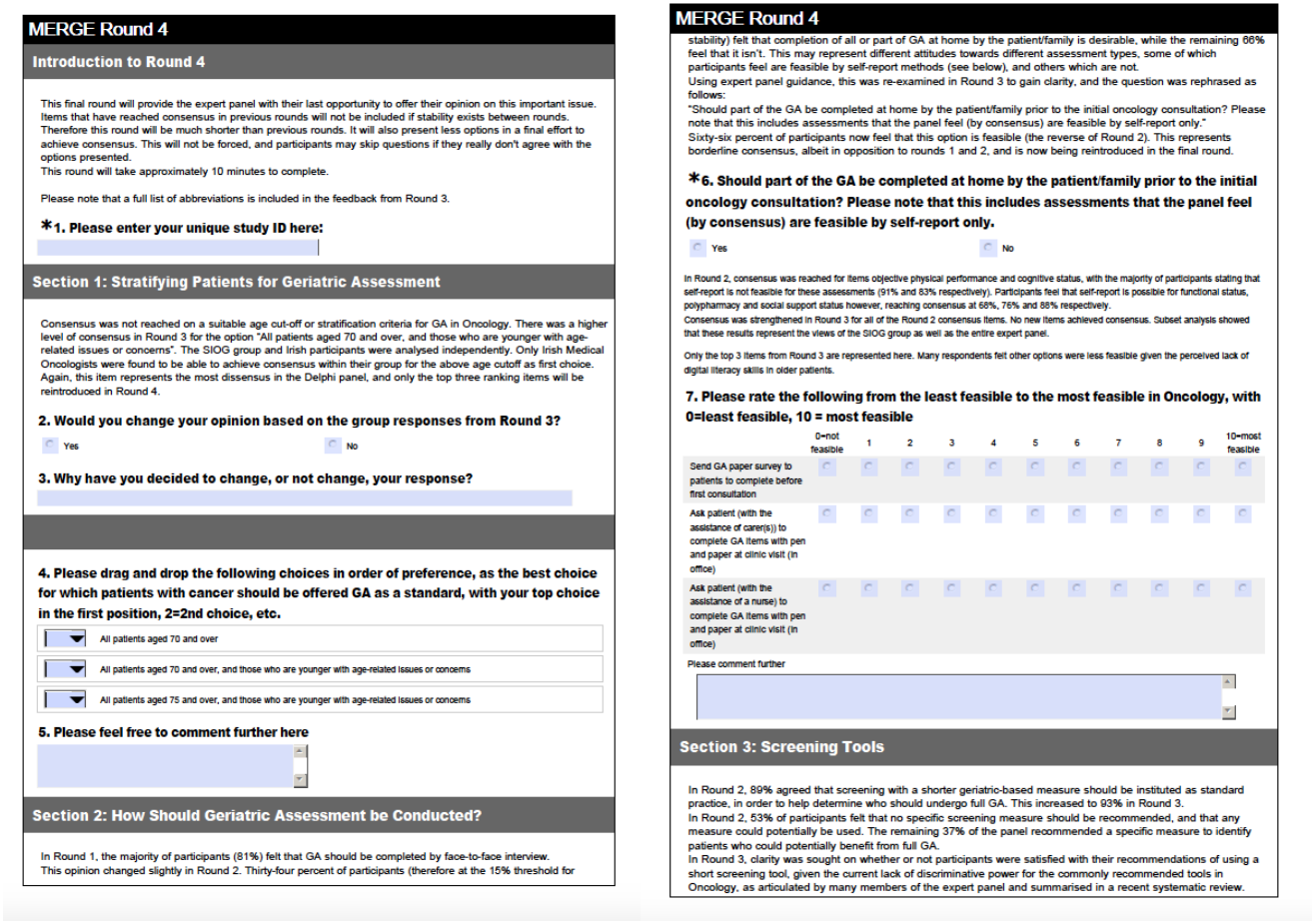
Appendix 10: Study 1 Round 4 Survey



MERGE Round 4

Introduction to Round 4

This final round will provide the expert panel with their last opportunity to offer their opinion on this important issue. Items that have reached consensus in previous rounds will not be included if stability exists between rounds. Therefore this round will be much shorter than previous rounds. It will also present less options in a final effort to achieve consensus. This will not be forced, and participants may skip questions if they really don't agree with the options presented.
This round will take approximately 10 minutes to complete.

Please note that a full list of abbreviations is included in the feedback from Round 3.

***1. Please enter your unique study ID here:**

Section 1: Stratifying Patients for Geriatric Assessment

Consensus was not reached on a suitable age cut-off or stratification criteria for GA in Oncology. There was a higher level of consensus in Round 3 for the option "All patients aged 70 and over, and those who are younger with age-related issues or concerns". The SIOG group and Irish participants were analysed independently. Only Irish Medical Oncologists were found to be able to achieve consensus within their group for the above age cutoff as first choice. Again, this item represents the most dissensus in the Delphi panel, and only the top three ranking items will be reintroduced in Round 4.

2. Would you change your opinion based on the group responses from Round 3?

Yes No

3. Why have you decided to change, or not change, your response?

4. Please drag and drop the following choices in order of preference, as the best choice for which patients with cancer should be offered GA as a standard, with your top choice in the first position, 2=2nd choice, etc.

All patients aged 70 and over

All patients aged 70 and over, and those who are younger with age-related issues or concerns

All patients aged 75 and over, and those who are younger with age-related issues or concerns

5. Please feel free to comment further here

Section 2: How Should Geriatric Assessment be Conducted?

In Round 1, the majority of participants (81%) felt that GA should be completed by face-to-face interview.
This opinion changed slightly in Round 2. Thirty-four percent of participants (therefore at the 15% threshold for

MERGE Round 4

stability) felt that completion of all or part of GA at home by the patient/family is desirable, while the remaining 66% feel that it isn't. This may represent different attitudes towards different assessment types, some of which participants feel are feasible by self-report methods (see below), and others which are not.
Using expert panel guidance, this was re-examined in Round 3 to gain clarity, and the question was rephrased as follows:
"Should part of the GA be completed at home by the patient/family prior to the initial oncology consultation? Please note that this includes assessments that the panel feel (by consensus) are feasible by self-report only."
Sixty-six percent of participants now feel that this option is feasible (the reverse of Round 2). This represents borderline consensus, albeit in opposition to rounds 1 and 2, and is now being reintroduced in the final round.

***6. Should part of the GA be completed at home by the patient/family prior to the initial oncology consultation? Please note that this includes assessments that the panel feel (by consensus) are feasible by self-report only.**

Yes No

In Round 2, consensus was reached for items objective physical performance and cognitive status, with the majority of participants stating that self-report is not feasible for these assessments (91% and 83% respectively). Participants feel that self-report is possible for functional status, polypharmacy and social support status however, reaching consensus at 68%, 76% and 88% respectively.
Consensus was strengthened in Round 3 for all of the Round 2 consensus items. No new items achieved consensus. Subset analysis showed that these results represent the views of the SIOG group as well as the entire expert panel.

Only the top 3 items from Round 3 are represented here. Many respondents felt other options were less feasible given the perceived lack of digital literacy skills in older patients.

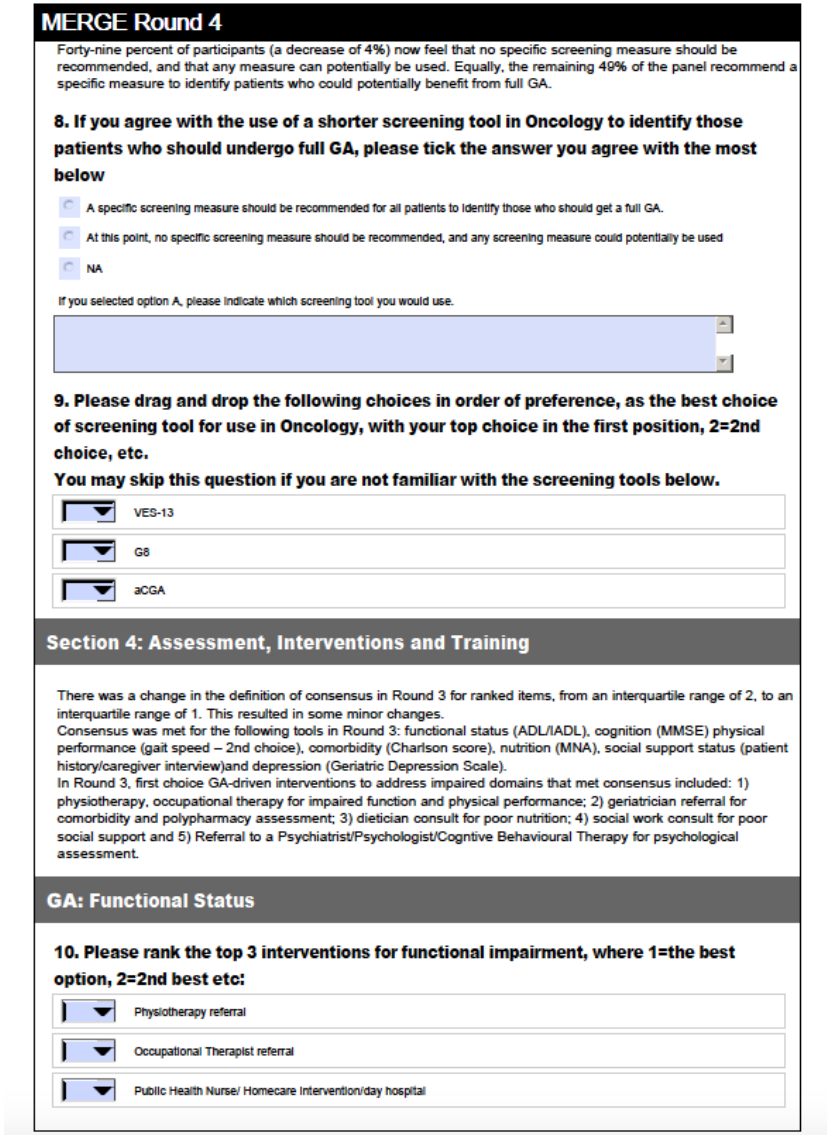
7. Please rate the following from the least feasible to the most feasible in Oncology, with 0=least feasible, 10 = most feasible

	0=not feasible	1	2	3	4	5	6	7	8	9	10=most feasible
Send GA paper survey to patients to complete before first consultation											
Ask patient (with the assistance of carer(s)) to complete GA items with pen and paper at clinic visit (in office)											
Ask patient (with the assistance of a nurse) to complete GA items with pen and paper at clinic visit (in office)											

Please comment further

Section 3: Screening Tools

In Round 2, 89% agreed that screening with a shorter geriatric-based measure should be instituted as standard practice, in order to help determine who should undergo full GA. This increased to 93% in Round 3.
In Round 2, 53% of participants felt that no specific screening measure should be recommended, and that any measure could potentially be used. The remaining 37% of the panel recommended a specific measure to identify patients who could potentially benefit from full GA.
In Round 3, clarity was sought on whether or not participants were satisfied with their recommendations of using a short screening tool, given the current lack of discriminative power for the commonly recommended tools in Oncology, as articulated by many members of the expert panel and summarised in a recent systematic review.



MERGE Round 4

Forty-nine percent of participants (a decrease of 4%) now feel that no specific screening measure should be recommended, and that any measure can potentially be used. Equally, the remaining 49% of the panel recommend a specific measure to identify patients who could potentially benefit from full GA.

8. If you agree with the use of a shorter screening tool in Oncology to identify those patients who should undergo full GA, please tick the answer you agree with the most below

- A specific screening measure should be recommended for all patients to identify those who should get a full GA.
- At this point, no specific screening measure should be recommended, and any screening measure could potentially be used
- NA

If you selected option A, please indicate which screening tool you would use.

9. Please drag and drop the following choices in order of preference, as the best choice of screening tool for use in Oncology, with your top choice in the first position, 2=2nd choice, etc.

You may skip this question if you are not familiar with the screening tools below.

1. VES-13
2. G8
3. aCGA

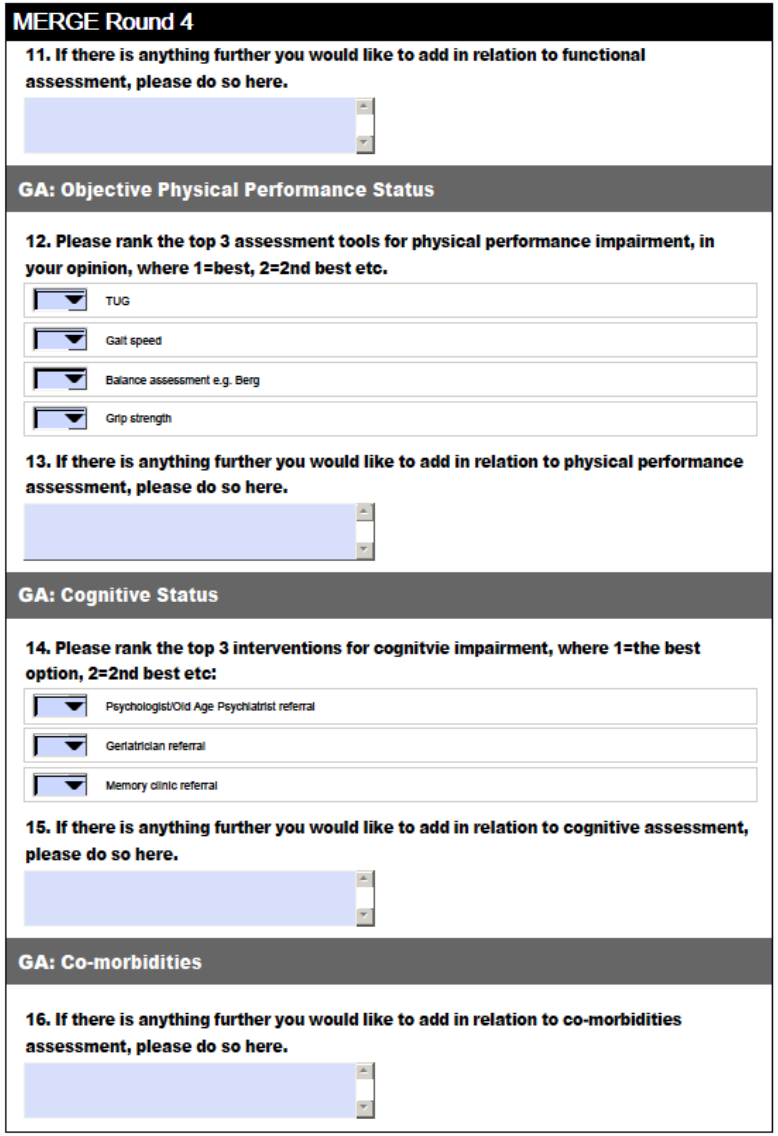
Section 4: Assessment, Interventions and Training

There was a change in the definition of consensus in Round 3 for ranked items, from an interquartile range of 2, to an interquartile range of 1. This resulted in some minor changes.
Consensus was met for the following tools in Round 3: functional status (ADL/IADL), cognition (MMSE) physical performance (gait speed – 2nd choice), comorbidity (Charlson score), nutrition (MNA), social support status (patient history/caregiver interview)and depression (Geriatric Depression Scale).
In Round 3, first choice GA-driven interventions to address impaired domains that met consensus included: 1) physiotherapy, occupational therapy for impaired function and physical performance; 2) geriatrician referral for comorbidity and polypharmacy assessment; 3) dietician consult for poor nutrition; 4) social work consult for poor social support and 5) Referral to a Psychiatrist/Psychologist/Cogntive Behavioural Therapy for psychological assessment.

GA: Functional Status

10. Please rank the top 3 interventions for functional impairment, where 1=the best option, 2=2nd best etc:

1. Physiotherapy referral
2. Occupational Therapist referral
3. Public Health Nurse/ Homecare intervention/day hospital



MERGE Round 4

11. If there is anything further you would like to add in relation to functional assessment, please do so here.

GA: Objective Physical Performance Status

12. Please rank the top 3 assessment tools for physical performance impairment, in your opinion, where 1=best, 2=2nd best etc.

1. TUG
2. Gait speed
3. Balance assessment e.g. Berg
4. Grip strength

13. If there is anything further you would like to add in relation to physical performance assessment, please do so here.

GA: Cognitive Status

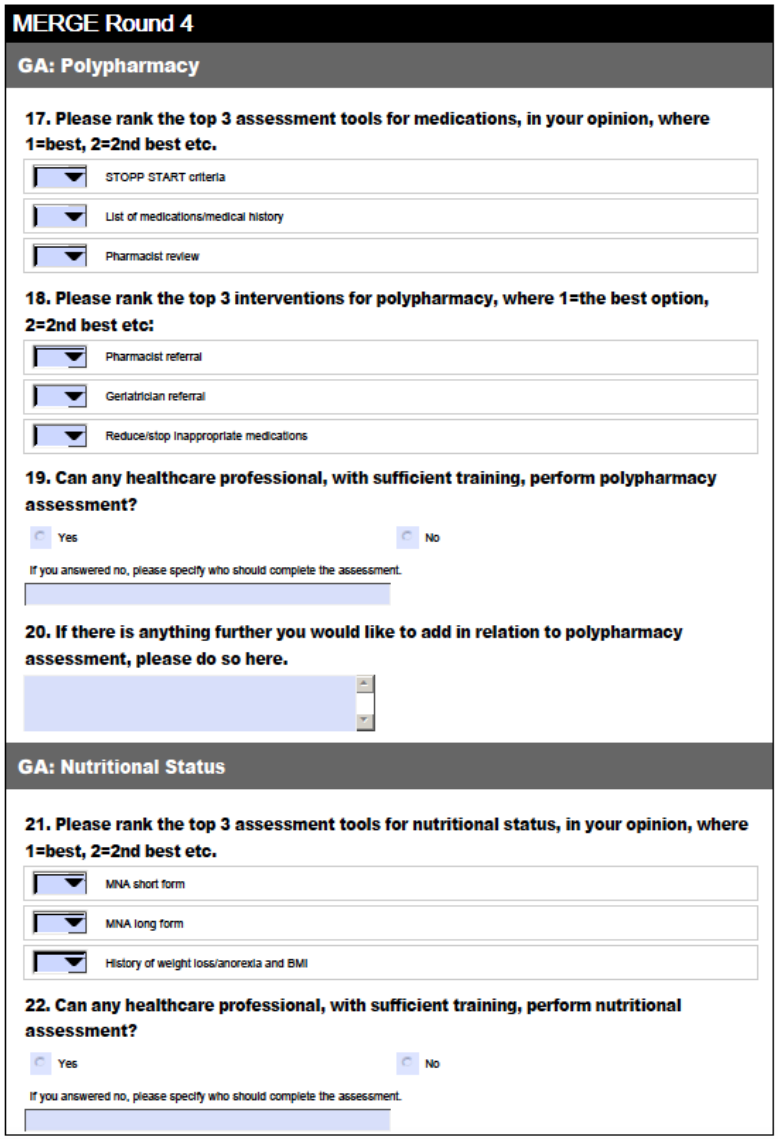
14. Please rank the top 3 interventions for cognitvie impairment, where 1=the best option, 2=2nd best etc:

1. Psychologist/Old Age Psychiatrist referral
2. Geriatrician referral
3. Memory clinic referral

15. If there is anything further you would like to add in relation to cognitive assessment, please do so here.

GA: Co-morbidities

16. If there is anything further you would like to add in relation to co-morbidities assessment, please do so here.



MERGE Round 4

GA: Polypharmacy

17. Please rank the top 3 assessment tools for medications, in your opinion, where 1=best, 2=2nd best etc.

- STOPP START criteria
- List of medications/medical history
- Pharmacist review

18. Please rank the top 3 interventions for polypharmacy, where 1=the best option, 2=2nd best etc:

- Pharmacist referral
- Geriatrician referral
- Reduce/stop inappropriate medications

19. Can any healthcare professional, with sufficient training, perform polypharmacy assessment?

Yes No

If you answered no, please specify who should complete the assessment.

20. If there is anything further you would like to add in relation to polypharmacy assessment, please do so here.

GA: Nutritional Status

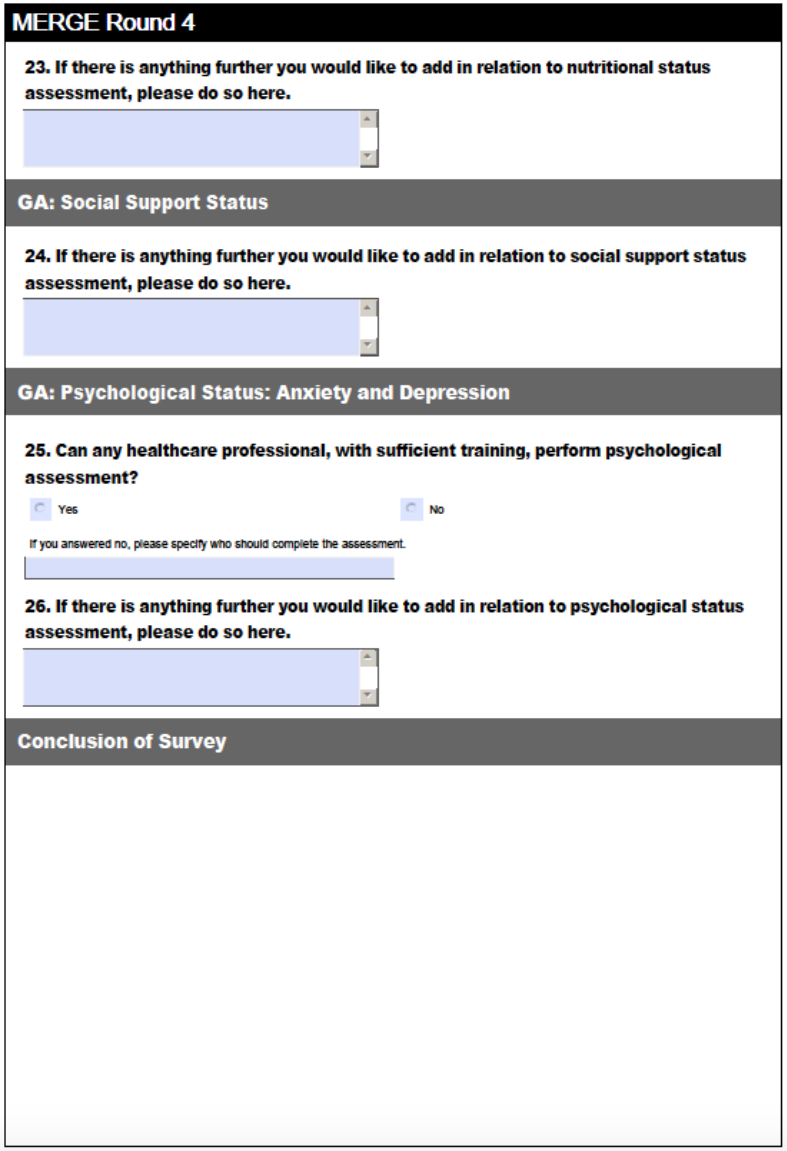
21. Please rank the top 3 assessment tools for nutritional status, in your opinion, where 1=best, 2=2nd best etc.

- MNA short form
- MNA long form
- History of weight loss/anorexia and BMI

22. Can any healthcare professional, with sufficient training, perform nutritional assessment?

Yes No

If you answered no, please specify who should complete the assessment.



MERGE Round 4

23. If there is anything further you would like to add in relation to nutritional status assessment, please do so here.

GA: Social Support Status

24. If there is anything further you would like to add in relation to social support status assessment, please do so here.

GA: Psychological Status: Anxiety and Depression

25. Can any healthcare professional, with sufficient training, perform psychological assessment?

Yes No

If you answered no, please specify who should complete the assessment.

26. If there is anything further you would like to add in relation to psychological status assessment, please do so here.

Conclusion of Survey

MERGE Round 4

27. Please rate the importance of impairments in each of the following in terms of their ability to affect oncology decisions, in your opinion, where 0=not important, 10=very important.

	0=not important	1	2	3	4	5	6	7	8	9	10=very important
Functional status	○	○	○	○	○	○	○	○	○	○	○
Physical performance status	○	○	○	○	○	○	○	○	○	○	○
Cognitive status	○	○	○	○	○	○	○	○	○	○	○
Comorbidities	○	○	○	○	○	○	○	○	○	○	○
Polypharmacy	○	○	○	○	○	○	○	○	○	○	○
Nutritional status	○	○	○	○	○	○	○	○	○	○	○
Social support status	○	○	○	○	○	○	○	○	○	○	○
Psychological status - anxiety	○	○	○	○	○	○	○	○	○	○	○
Psychological status - depression	○	○	○	○	○	○	○	○	○	○	○

Thank you for completing the study. Your participation as part of the expert panel for this Delphi study is greatly appreciated.

Appendix 11: Study 1 Round 4 Feedback Report

TRINITY COLLEGE DUBLIN
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THE UNIVERSITY OF DUBLIN

Anita O'Donovan

The MERGE Study: Round 4 Participant Feedback

June 2013

Contents

Introduction

This report contains feedback from the final round of the MERGE study. In keeping with Delphi tradition, it aims to be as inclusive and comprehensive as possible, and each participant's contribution is acknowledged. For your convenience, attempts are made to summarise certain aspects, with additional appendices containing the qualitative data from the open-ended questions in Round Four, which are located at the end of the document. Please note that this report is part of an overall Delphi process and may not be cited or reproduced without the author's permission.

Definitions of Stability and Consensus

Stability, or the degree of permanence of participants' vote distribution over successive rounds, reflects consensus. Changes of less than 15% offer a working definition of stability in the literature, when the responses obtained in two successive rounds are shown statistically to be not significantly different from each other(1). Group stability, rather than individual stability will be assessed in this study.

A predetermined threshold had previously been chosen for consensus, at an interquartile range of 2 or less units (on a scale of 0-10). The interquartile range is the measure of dispersion for the median and consists of the middle 50% of observations. Thus, an interquartile range of less than 2 means that more than 50% of all opinions fall within 2 points on the scale. It is widely accepted as an objective and rigorous method of defining consensus in Delphi studies(2, 3). However, as some respondents have indicated that they only ranked their top five (or less) options, as directed for certain items, the definition of consensus has been revised to an interquartile range of 1 or less for those items only, in keeping with the literature. Round 2 data has been reclassified to highlight this important change. This will not affect the overall number of rounds and Round 4 will be the final round.

For nominal data, consensus is defined as 67% i.e. two-thirds majority.

Please note that a full list of abbreviations was given in the Round 1 feedback report, and is available for reference in Appendix 1.

Round 4 Data Analysis

Data analysis of Round 4 responses was performed using SPSS version 20. The statistical group response is presented using measures of central tendency (mean, median, mode) and dispersion (interquartile range). Where consensus has not been reached, boxplots are also provided to illustrate divergence of opinion. For the latter, participants may find it useful that outliers have been identified by Study ID.

Author's Note

Thank you for your important contribution to this consensus-seeking process. I am delighted to report that attrition between rounds has been minimal, with none occurring between rounds 2 and 3, and only 4 between rounds 3 and 4. Your input has been invaluable in the design of a model of care for older patients in Oncology.

Please do not hesitate to contact me if you feel that your views are not contained within this report.

The results of this study will be presented at the upcoming SIOG conference, in Copenhagen in October (24th-26th). Please see Appendix 7 for the submitted abstract, with results up to Round 3. The final report will acknowledge participants who have given consent to being named as part of the expert panel.

Best wishes,

Anita O'Donovan,
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odonova4@tcd.ie
(01)8963149.

Section 1: Stratifying Patients for Geriatric Assessment

Section 1: Stratifying Patients for Geriatric Assessment

When participants were asked if they would change their minds, based on the Round 3 group responses, the majority of participants (73%) stated that they would **not** change their opinion. This is lower than Round 3, where 83% of participants stated that they would not change their minds, and may be a result of the forcing of consensus on certain items.
Of those that said they would change their minds based on Round 4 responses, 5 were geriatricians, 4 were SIOG participants and one Radiation Oncologist.
Reasons given by those who changed their minds included:

- Interesting what the group has to say
- It may well mean that geriatric assessment would be offered to more patients if there was an age cut off. There would be the option of deciding that a biological young older person may need just a very abbreviated GA.
- I think it is a reasonable blend of pragmatism (pick a cutoff with a reasonable probability of finding problems) and practicality (do not do it too soon so wasting resources). The exact age you pick is less important than picking an age: I would go for 75 but would not care about 70. 80 is too old.
- This age 65 will ensure more of the 'younger' elderly patients be included
- With compression of morbidity towards the end of life, it makes sense to raise the age
- Overall agree with summary of main areas, would make minor changes in age cut off etc. as agree with others comment-i.e. 70 not so 'old' and increased work generated by screening all between 70 and 575
- To achieve consensus
- Average between upper limit of age for haematologists (65) and for oncologists (70)

Some reasons given in Rounds 3 and 4 for not changing included personal opinion, clinical experience, the heterogeneity of older patients and poor correlation of chronological age with frailty, similar to Round 2. Please see Appendix 2 for Round 4 responses.

Patient Selection for GA

Consensus was finally reached in Round 4 on a suitable age cut-off or stratification criteria for GA in Oncology. This item represented the most dissensus in the Delphi panel, and only the top three ranking items were reintroduced in Round 4. The number one choice in the final round was: "All patients aged 70 and over, and those who are younger with age-related issues or concerns"

Table 1 Patient Selection for Geriatric Assessment (in order of preference in Round 3: 1=first place etc.)

Rank	Mean Rank	Median	Mode	Interquartile Range	Consensus
1.All patients aged 70 and over, and those who are younger with age-related issues or concerns	**R2**: 3.16	3.00	1.00	(1.00, 5.00)	**No**
	R3: 2.68	2.00	1.00	(1.00, 3.50)	**No**
	R4: 1.28	1.00	1.00	(1.00, 2.00)	**Yes**
2.All patients aged 75 and over, and those who are younger with age-related issues or concerns	**R2:** 3.60	3.00	2.00	(2.00, 5.00)	**No**
	R3:3.51	3.00	2.00	(2.00, 5.00)	**No**
	R4: 2.10	2.00	2.00	(1.00, 3.00)	**No**
3.All patients aged 70 and over	**R2:** 5.72	6.00	8.00	(3.00, 8.00)	**No**
	R3: 4.63	4.00	1.00	(2.00, 7.00)	**No**
	R4: 2.62	3.00	3.00	(2.00, 3.00)	**No**

Section 2: How Should Geriatric Assessment be Conducted?

Section 2: How Should Geriatric Assessment be Conducted?

In **Round 1**, the majority of participants (81%) felt that GA should be completed by face-to-face interview.

This opinion changed slightly in **Round 2**. Thirty-four percent of participants (therefore at the 15% threshold for stability) felt that completion of *all or part of* GA at home by the patient/family is desirable, while the remaining **66%** feel that it isn't. This may represent different attitudes towards different assessment types, some of which participants feel are feasible by self-report methods (see below), and others which are not.

Using expert panel guidance, this was re-examined in **Round 3** to gain clarity, and the question was rephrased as follows:

"Should part of the GA be completed at home by the patient/family prior to the initial oncology consultation? Please note that this includes assessments that the panel feel (by consensus) are feasible by self-report only."

In Round 3, sixty-six percent of participants felt that this option was feasible (the reverse of Round 2). This represented borderline consensus, even though this is in opposition to rounds 1 and 2, and was reintroduced in the final round.

In Round 4, 83% of participants felt that completion of part of the GA at home by the patient/family prior to an Oncology consultation is feasible, therefore representing clear consensus on this item.

Self-Report Methods

For reasons specified for lack of feasibility of self-report items, please see Appendix 3. These may be summarised under the following categories: the need for medical competence to carry out these tests, the risk of subjectivity and inaccuracy when patients complete them, the impact of specific deficits on the ability to complete such measures e.g. cognitive deficits and the patients' own level of education. Participants also identified the need for objective measurement in some of the above domains, such as the timed up and go test, balance tests etc. Only the top 3 options were presented in Round 4.

Only 32 participants chose to answer this question in Round 4, with eight participants choosing not to respond. This may reflect dissatisfaction with the options presented, which affected overall ability to achieve consensus on this item.

Table 2 Feasibility of Self-Report Methods in Order of Preference (0=not feasible, 10=most feasible)

Rank	Mean Rank	Median	Mode	Interquartile Range	Consensus
1.Ask patient (with the assistance of a nurse) to complete GA items with pen and paper at clinic visit (in office)	R2:7.72	8.00	9.00	(7.00, 9.00)	Yes
	R3:8.29	9.00	10.00	(7.00, 10.00)	No
	R4: 6.69	7.50	8.00	(4.75, 8.00)	No
2.Ask patient (with the assistance of carer(s)) to complete GA items with pen and paper at clinic visit (in office)	R2:6.93	7.00	5.00	(5.00, 9.00)	No
	R3:7.56	8.00	8.00	(6.50, 9.00)	No
	R4: 6.91	8.00	8.00	(6.25, 8.00)	No
3.Send GA paper survey to patients to complete before first consultation	R2:5.12	5.00	9.00	(2.00, 8.00)	No
	R3:5.27	5.00	3.00	(3.00, 8.00)	No
	R4:5.19	5.00	5.00	(4.00, 7.00)	No

SECTION 3: SCREENING TOOLS

Section 3: Screening Tools

In **Round 2**, 89% agreed that screening with a shorter geriatric-based measure should be instituted as standard practice, in order to help determine who should undergo full GA. This increased to 93% in **Round 3**. However, a number of stipulations were given (please see Appendix 4).

In **Round 2**, 53% of participants felt that no specific screening measure should be recommended, and that any measure could potentially be used. The remaining 37% of the panel recommended a specific measure to identify patients who could potentially benefit from full GA. Of these, four participants recommend the use of the G8 tool, while others recommend the use of the VES13 or G8 (n=1), ADL or IADL (n=1), the aCGA (n=1), SAOP (n=1) and the SHARE frailty instrument (n=1).

In **Round 3**, clarity was sought on whether or not participants were satisfied with their recommendations of using a short screening tool, given the current lack of discriminative power for the commonly recommended tools in Oncology, as articulated by many members of the expert panel and summarised in a recent systematic review(5). Forty-nine percent of participants (a decrease of 4%) felt that no specific screening measure should be recommended, and that any measure can potentially be used. Equally, the remaining 49% of the panel recommend a specific measure to identify patients who could potentially benefit from full GA. Six participants chose not to answer this question.

In **Round 4**, this question was further explored. Fifty percent of participants (an increase of 1%) felt that no specific screening measure should be recommended, and that any measure can potentially be used. Forty percent of the panel recommend a specific measure to identify patients who could potentially benefit from full GA. Of these, four recommended the G8, two the abbreviated CGA, and the remainder varied as documented below. Four participants chose not to answer this question.

Best Choice of Screening Tool in Oncology (in order of preference: 1=1st place etc.)

Rank	Mean Rank	Median	Mode	Interquartile Range	Consensus
1. aCGA	**R2:**4.14	3.00	1.00	{1.00, 7.00}	**No**
	R2: 3.44	2.50	1.00	{1.00, 4.50}	**No**
	R3:3.69	3.00	1.00	{1.00, 4.50}	**No**
	R3:4.06	3.00	1.00	{1.50, 6.00}	**No**
	R4:1.96	2.00	1.00	{1.00, 3.00}	**No**
	R4: 2.00	2.00	2.00	{1.00, 3.00}	**No**
2. G8	**R2:**3.62	3.00	1.00	{1.00, 5.00}	**No**
	R2: 2.50	2.00	1.00	{1.00, 3.00}	**Yes**
	R3:2.92	2.00	1.00	{1.00, 4.00}	**No**
	R3: 2.47	2.00	1.00	{1.00, 3.00}	**Yes**
	R4:2.00	2.00	1.00	{1.00, 3.00}	**No**
	R4: 1.88	1.50	1.00	{1.00, 3.00}	**No**
3. VES-13	**R2:**3.62	3.00	2.00	{2.00, 4.00}	**No**
	R2: 3.17	2.50	2.00	{2.00, 4.00}	**Yes**
	R3:2.73	2.00	2.00	{1.75, 3.25}	**No**
	R3: 2.53	2.00	2.00	{2.00, 3.00}	**Yes**
	R4: 2.04	2.00	2.00	{1.00, 3.00}	**No**
	R4: 2.13	2.00	2.00	{2.00, 3.00}	**No**

The aCGA was ranked highest, however it did not achieve consensus in this round. VES-13 ranked highest in Round 3, but again did not achieve consensus. Seventeen participants chose not to answer this question, with only 23 respondents to this item. This highlights a lack of consensus on the use of a particular screening tool in Oncology by the expert panel.

On further analysis, there is consensus among SIOG experts in Round 3 in relation to its place as the first choice of screening tool, with a slightly higher mean ranking (2.53) and an interquartile range of {2.00, 3.00}.

Section 4: Assessments and Interventions

Section 4: Assessments and Interventions

For your convenience, items are summarised separately by assessment and interventions.

Table 3 Assessment and Interventions (in order of preference: 1=1st place etc.)

Functional Status Assessment					
Rank	**Mean Rank**	**Median**	**Mode**	**Interquartile Range**	**Consensus**
1. ADL/IADL in combination	**R2:**1.74 **R3:**1.86	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	Yes Yes
2. ADL only	**R2:**4.24 **R3:**4.31	4.00 4.00	4.00 3.00	{2.00, 6.00} {3.00, 5.75}	No No
3. IADL only	**R2:**4.55 **R3:**4.36	4.00 4.00	3.00 4.00	{3.00, 5.25} {3.00, 5.75}	No No
4. Barthel Index	**R2:**5.40 **R3:**5.08	6.00 4.00	8.00 4.00	{3.00, 8.00} {2.25, 8.00}	No No
5. VES-13	**R2:**5.90 **R3:**5.33	6.00 6.00	7.00 7.00	{4.00, 8.00} {3.00, 7.00}	No No
6. Patient history/clinical examination	**R2:**6.02 **R3:**5.55	6.00 6.00	9.00 9.00	{3.00, 9.00} {2.00, 9.00}	No No
7. KPS	**R2:**5.38 **R3:**5.72	5.00 5.50	5.00 5.00	{4.00, 6.25} {5.00, 7.00}	No No
8. ECOG PS	**R2:**5.45 **R3:**6.03	6.00 6.00	5.00 6.00	{4.00, 7.00} {4.25, 8.00}	No No
9. FIM/FAM	**R2:**6.31 **R3:**6.81	7.00 8.00	7.00 8.00	{4.00, 8.25} {4.50, 8.75}	No
Functional Status Interventions					
1. Physiotherapy referral	**R2:**1.79 **R3:**1.82 **R4:** 1.59	1.00 2.00 1.00	1.00 1.00 1.00	{1.00, 3.00} {1.00, 2.25} {1.00, 2.00}	No No Yes
2. OT referral	**R2:**2.50 **R3:**2.42 **R4:**1.95	2.00 2.00 2.00	2.00 2.00 2.00	{2.00, 3.00} {2.00, 3.00} {2.00, 2.00}	Yes Yes Yes
3. Public Health Nurse/ Homecare intervention/day hospital	**R2:**3.05 **R3:**3.08 **R4:**2.46	3.00 3.00 3.00	4.00 1.00 3.00	{2.00, 4.00} {1.75, 4.25} {2.00, 3.00}	No No Yes
Physical Performance Impairment: Assessment					
1. TUG	**R2:**1.64 **R3:**1.94 **R4:**1.67	1.00 2.00 1.00	1.00 1.00 1.00	{1.00, 2.00} {1.00, 3.00} {1.00, 2.00}	Yes No Yes
2. Gait Speed	**R2:**2.75 **R3:**2.63 **R4:**2.09	2.00 2.00 2.00	2.00 2.00 2.00	{2.00, 3.75} {2.00, 3.00} {1.00, 3.00}	No Yes No
3. Grip Strength	**R2:**3.89 **R3:**3.54 **R4:** 2.94	4.00 3.00 3.00	4.00 3.00 3.00	{3.00, 5.00} {2.00, 5.00} {2.00, 4.00}	No No No
1. Balance tests	**R2:**3.78 **R3:**3.91 **R4:** 3.30	4.00 4.00 4.00	3.00 4.00 4.00	{3.00, 4.00} {3.00, 5.00} {3.00, 4.00}	Yes No Yes
Physical Performance Impairment: Interventions					
1. Physiotherapy Referral	**R2:**1.17 **R3:**1.24	1.00 1.00	1.00 1.00	{1.00, 1.00} {1.00, 1.00}	Yes Yes
2. OT referral	**R2:**2.93 **R3:**2.68	3.00 3.00	2.00 2.00	{2.00, 4.00} {2.00, 3.00}	No Yes
3. Public Health Nurse/ Homecare intervention/day hospital	**R2:**3.38 **R3:**3.34	4.00 3.00	4.00 5.00	{3.00, 4.00} {2.00, 5.00}	Yes No
Cognitive Status: Assessment					
1. MMSE	**R2:**1.14 **R3:**1.55	1.00 1.00	1.00 1.00	{1.00, 1.00} {1.00, 2.00}	Yes Yes
2. MiniCog	**R2:**3.94 **R3:**3.97	4.00 4.00	4.00 4.00	{3.00, 5.00} {3.00, 5.00}	No No
3. MOCA	**R2:**4.75 **R3:**4.00	5.00 4.00	5.00 5.00	{4.00, 5.75} {3.00, 5.00}	No No
1. AMTS	**R2:**3.94 **R3:**4.52	4.00 4.00	4.00 4.00	{2.25, 4.75} {2.50, 4.50}	No No
Cognitive Status: Interventions					
1. Geriatrician referral	**R2:**1.67 **R3:**1.97	1.00 1.50	1.00 1.00	{1.00, 2.00} {1.00, 3.00}	Yes No

	R4:1.46	1.00	1.00	{1.00, 2.00}	Yes
2. Psychologist/ Old Age Psychiatrist referral	**R2:**3.31 **R3:**3.24 **R4:** 2.32	3.00 3.00 2.00	2.00 2.00 3.00	{2.00, 4.00} {2.00, 4.00} {2.00, 3.00}	No No Yes
3. Memory clinic referral	**R2:**3.69 **R3:**3.26 **R4:**2.22	3.00 2.50 2.00	1.00 1.00 2.00	{1.00, 6.25} {1.00, 4.50} {2.00, 3.00}	No No Yes
Co-morbidities: Assessment					
1. Charlson Comorbidity Index	**R2:**1.67 **R3:**1.53	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	Yes Yes
2. CIRS-G	**R2:**2.36 **R3:**2.19	2.00 2.00	2.00 2.00	{2.00, 3.00} {2.00, 3.00}	Yes Yes
3. Chart review/medical history/list	**R2:**2.49 **R3:**2.66	3.00 3.00	3.00 3.00	{2.00, 3.00} {2.00, 3.00}	Yes Yes
Co-morbidities: Interventions					
1. Geriatrician Referral	**R2:**1.55 **R3:**1.43	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	Yes Yes
2. Referral to specialists as deemed suitable for a given co-morbidity	**R2:**1.79 **R3:**1.95	2.00 2.00	2.00 2.00	{1.00, 2.00} {1.00, 2.00}	Yes Yes
3. Medication	**R2:**2.67 **R3:**2.62	3.00 3.00	3.00 3.00	{2.00,3.00} {2.00,3.00}	Yes Yes
Polypharmacy: Assessment					
1. List of Medications	**R2:**2.00 **R3:**2.03 **R4:**1.95	2.00 2.00 2.00	1.00 1.00 1.00	{1.00, 3.00} {1.00, 3.00} {1.00, 3.00}	No No No
2. Pharmacist Review	**R2:**2.21 **R3:**2.12 **R4:**2.00	2.00 2.00 2.00	2.00 2.00 1.00	{1.00, 3.00} {1.00, 2.50} {1.00, 3.00}	No No No
3. STOPP/START	**R2:**2.37 **R3:**2.36 **R4:**2.05	3.00 3.00 2.00	3.00 3.00 2.00	{1.75, 3.00} {2.00,3.00} {1.00,3.00}	No Yes No

Polypharmacy: Interventions					
1. Geriatrician Referral	**R2:**1.70 **R3:**1.54 **R4:**1.51	1.00 1.00 1.00	1.00 1.00 1.00	{1.00, 2.00} {1.00, 2.00} {1.00, 2.00}	Yes Yes Yes
2. Reduce/stop inappropriate medications	**R2:**2.26 **R3:**2.13 **R4:**2.15	2.00 2.00 2.00	3.00 1.00 3.00	{1.00, 3.00} {1.00, 3.00} {1.00, 3.00}	No No No
3. Pharmacist referral	**R2:**2.72 **R3:**2.86 **R4:**2.33	3.00 3.00 2.00	3.00 3.00 3.00	{2.00, 4.00} {2.00, 4.00} {2.00, 3.00}	No No Yes
Nutritional Status: Assessment					
1. MNA Short form	**R2:**1.87 **R3:**2.00 **R4:**1.50	1.00 2.00 1.00	1.00 1.00 1.00	{1.00, 2.00} {1.00, 3.00} {1.00, 2.00}	Yes No Yes
2. MNA Long form	**R2:**2.63 **R3:**2.38 **R4:**2.13	2.00 2.00 2.00	2.00 2.00 2.00	{1.25, 3.00} {2.00, 3.00} {2.00, 3.00}	No Yes Yes
3. History of weight loss/anorexia/BMI	**R2:**2.87 **R3:**2.81 **R4:**2.38	3.00 3.00 3.00	4.00 3.00 3.00	{1.00, 4.00} {2.00, 4.00} {2.00, 3.00}	No No Yes
Nutritional Status: Interventions					
1. Dietician Referral	**R2:**1.13 **R3:**1.11	1.00 1.00	1.00 1.00	{1.00,1.00} {1.00,1.00}	Yes Yes
2. Dietary advice/ Use of supplements	**R2:**1.88 **R3:**1.89	2.00 2.00	2.00 2.00	{2.00, 2.00} {2.00, 2.00}	Yes Yes
Social Support Status: Assessment					
1. Patient History/ caregiver interview	**R2:**1.06 **R3:**1.27	1.00 1.00	1.00 1.00	{1.00, 1.00} {1.00, 1.00}	Yes Yes
2. mMOS-SS	**R2:**2.03 **R3:**2.04	2.00 2.00	2.00 2.00	{2.00, 2.00} {2.00, 2.00}	Yes Yes
3. Socio-familiar Gijon Test	**R2:**2.94 **R3:**2.85	3.00 3.00	3.00 3.00	{3.00, 3.00} {3.00, 3.00}	Yes Yes

Social Support: Interventions					
1. Social work referral	**R2:**1.70 **R3:**1.57	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	Yes Yes
2. Home help	**R2:**2.81 **R3:**2.76	3.00 2.00	2.00 2.00	{2.00, 4.00} {2.00, 4.00}	No No
3. Public Health Nurse support	**R2:**3.02 **R3:**3.43	3.00 3.00	5.00 5.00	{2.00, 5.00} {2.00, 5.00}	No No
Anxiety: Assessment					
1. Patient history/ Interview	**R2:**1.64 **R3:**1.62	2.00 2.00	2.00 1.00	{1.00, 2.00} {1.00, 2.00}	Yes Yes
2. HADS	**R2:**1.67 **R3:**1.71	2.00 2.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	Yes Yes
3. Distress thermometer	**R2:**2.69 **R3:**2.68	3.00 3.00	3.00 3.00	{3.00, 3.00} {2.00, 3.00}	Yes Yes
Anxiety: Interventions					
1. Referral to a Psychiatrist/Psychologist /Cognitive Behavioural Therapy	**R2:**1.39 **R3:**1.63	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	Yes Yes
2. Psycho-Oncology liaison nurse referral	**R2:**2.18 **R3:**2.08	2.00 2.00	2.00 2.00	{2.00, 3.00} {2.00, 2.00}	Yes Yes
3. Social work referral	**R2:**4.25 **R3:**3.95	4.00 4.00	4.00 4.00	{3.00, 5.00} {3.00, 5.00}	Yes No
Depression: Assessment					
1. GDS Short form	**R2:**1.75 **R3:**1.86	1.00 2.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	Yes Yes
2. GDS Long form	**R2:**2.55 **R3:**2.60	2.50 3.00	2.00 3.00	{2.00, 3.00} {2.00, 3.00}	Yes Yes
3. Patient history/ Interview	**R2:**2.78 **R3:**2.69	3.00 3.00	4.00 4.00	{1.25, 4.00} {1.00, 4.00}	No No
4. HADS	**R2:**2.92 **R3:**2.86	3.00 3.00	4.00 3.00	{2.00, 4.00} {2.00, 4.00}	No No
Depression: Interventions					
1. Referral to a Psychiatrist/Psychologist /Cognitive Behavioural Therapy	**R2:**1.56 **R3:**1.50	1.00 1.00	1.00 1.00	{1.00, 2.00} {1.00, 2.00}	Yes Yes
2. Psycho-Oncology liaison nurse referral	**R2:**2.63 **R3:**2.34	2.00 2.00	2.00 2.00	{2.00, 3.00} {2.00, 3.00}	Yes Yes
3. Medication	**R2:**3.93 **R3:**4.16	4.00 5.00	3.00 5.00	{3.00, 5.00} {3.00, 5.00}	No No
1. Palliative Care Team Involvement	**R2:** **R3:**4.18	 4.50	 5.00	 {3.00, 5.00}	 No

There was a change in the definition of consensus in Round 3 for ranked items, from an interquartile range of 2, to an interquartile range of 1. This resulted in some minor changes. Consensus was met for the following tools in Round 3: functional status (ADL/IADL), cognition (MMSE) physical performance (gait speed – 2nd choice), comorbidity (Charlson score), nutrition (MNA), social support status (patient history/caregiver interview)and depression (Geriatric Depression Scale).

In Round 3, first choice GA-driven interventions to address impaired domains that met consensus included: 1) physiotherapy, occupational therapy for impaired function and physical performance; 2) geriatrician referral for comorbidity and polypharmacy assessment; 3) dietician consult for poor nutrition; 4) social work consult for poor social support and 5) Referral to a Psychiatrist/Psychologist/Cognitive Behavioural Therapy for psychological assessment.

Some of these items will be represented in Round 4 to assess stability and to gain consensus. Psychiatrist will be changed to Old Age Psychiatrist in the Cognitive Assessment section in Round 4, as pointed out by one panelist:

> *"Can you change psychiatrist to old age psychiatrist, or include them as an extra option in that answer as older people with cognitive impairment are seen by POA, not psychiatrists."*

Thank you for highlighting this, and apologies for any offence caused.

Please see Appendix 5 for additional comments related to each domain.

Importance of Each Domain in Oncology Decision-Making

Domain and Rank	Round	Mean Rank	Median	Interquartile Range	Consensus {R4:W=0.427, 8df, p<0.001}
1. Functional status	R2:	8.91	10.00	{8.00, 10.00}	Yes
	R3:	9.23	10.00	{8.25, 10.00}	Yes
	R4:	9.31	10.00	{9.00, 10.00}	Yes
2. Objective physical performance status	R2:	8.52	9.00	{7.25, 10.00}	No
	R3:	8.70	9.00	{8.00, 10.00}	Yes
	R4:	8.82	9.00	{8.00, 10.00}	Yes
3.Comorbidities	R2:	8.07	9.00	{6.25, 10.00}	No
	R3:	8.60	9.00	{7.25, 10.00}	No
	R4:	8.74	9.00	{8.00, 10.00}	Yes
4. Cognitive status	R2:	8.79	9.00	{8.00, 10.00}	Yes
	R3:	8.98	9.50	{8.00, 10.00}	Yes
	R4:	8.54	9.00	{8.00, 10.00}	Yes
5.Nutritional status	R2:	7.66	8.00	{7.00, 9.00}	Yes
	R3:	7.75	8.00	{6.00, 9.00}	No
	R4:	7.59	8.00	{6.00, 9.00}	No
6.Social support status	R2:	6.93	7.00	{6.00, 9.00}	No
	R3:	7.03	8.00	{6.00, 9.00}	No
	R4:	7.38	8.00	{6.00, 9.00}	No
7.Polypharmacy	R2:	6.82	7.00	{5.00, 9.00}	No
	R3:	6.88	7.50	{5.00, 9.00}	No
	R4:	6.77	7.00	{5.00, 9.00}	No
8.Psychological status - depression	R2:	6.48	6.00	{5.00, 8.00}	No
	R3:	6.30	7.00	{5.00, 8.00}	No
	R4:	6.54	7.00	{5.00, 9.00}	No
9.Psychological status - anxiety	R2:	6.02	6.00	{4.25, 8.00}	No
	R3:	6.13	7.00	{4.00, 8.00}	No
	R4:	6.03	6.00	{5.00, 8.00}	No

Table 4 Importance of Each Domain in Oncology in Rank Order (1=1st place etc.)

***In order of importance from highest to lowest**

Overall, panellists rated functional status (subjective and objective measures) as the most important domain in influencing oncology decisions, followed by comorbidities and cognition. Other domains did not reach consensus in relation to overall importance.

Section 5: Training Requirements for Assessment

Section 5: Training Requirements for Assessment

Table 5 Can any Healthcare Professional Perform this Assessment?

Domain	Round 2	Round 3	Round 4
Functional Status	Yes (98%)*	Yes (93%)*	NA
Objective Physical Performance	Yes (98%)*	Yes (88%)*	NA
Cognitive Status	Yes (80%)*	Yes (73%)*	NA
Comorbidity	Yes (73%)*	Yes (68%)*	NA
Polypharmacy	No (57%)	No (53%)	No (56%)
Nutritional Status	Yes (68%)*	Yes (65%)	Yes (82%)*
Social Support Status	Yes (82%)*	Yes (85%)*	NA
Psychological Status	No (52%)	Yes (53%)	Yes (56%)

NA: Consensus and stability was reached in previous rounds

Consensus items *

In **Round 2**, clear consensus existed for most items, apart from polypharmacy and psychological status. Some participants asked for clarification in relation to the definition of "sufficient training", which was provided.

In **Round 3**, stability was maintained for all items, but nutritional status, polypharmacy and psychological status did not meet consensus and were therefore reintroduced in Round 4. In **Round 4**, only nutritional status achieved consensus from the panel that anyone with sufficient training can assess this domain.

Please see Appendix 6 for further comments in relation to the above.

APPENDICES

Appendix 1: List of Abbreviations Used in This Document

AD=Alzheimer's Disease

AMTS=Abbreviated Mental Test Score

ASA=American Society of Anaesthesiologists

CARST = Community Assessment of Risk Screening Tool

CCI=Charlson Comorbidity Index

CGA=Comprehensive Geriatric Assessment

CHS=Cardiovascular Health Study

CIRS-G=Cumulative Illness Rating Scale-Geriatric

GA=Geriatric Assessment

Ger=Geriatrician (Ireland)

ECOG = Eastern Cooperative Oncology Group

EMS=Elderly Mobility Scale

FIM/FAM=Functional Independence Measure and Functional Assessment Measure

GFI=Groningen Frailty Indicator

IQ Rge=Interquartile Range

MEAMS=Middlesex Elderly Assessment of Mental State

MDT=Multidisciplinary Team

mMOS-SS=modified Medical Outcomes Study – Social Support

MMSE=Minimental State Examination

MNA=Mini Nutritional Assessment

MO=Medical Oncology (Ireland)

MOCA=Montreal Cognitive Assessment

MUST=Malnutrition Universal Screening Tool

PD=Parkinson's Disease

PHN=Public Health Nurse

PS=Performance Status

PSP=Progressive Supranuclear Palsy

RBANS=Repeatable Battery for the Assessment of Neuropsychological Status

QMCI = Quick Mild Cognitive Impairment

RO=Radiation Oncology (Ireland)

SCS=Simplified Comorbidity Score

SIOG=International Society of Geriatric Oncology

SPPB=Short Physical Performance Battery

STOPP/START= Screening Tool of Older People's potentially inappropriate Prescriptions/ Screening Tool to Alert doctors to the Right Treatment

TUG=Timed Up and Go

VES=Vulnerable Elders Survey

VIP=Variable Indicative of Placement (risk)

Appendix 2: Stratifying Patients for Geriatric Assessment

- 70 vs 75 is no big deal. I dont like having an absolute cutoff so all over 70 is a poor choice as it encourages people not to think about doing it in younger patients
- Agree with other commentator that screening all over 70 generates a lot of probably unnecessary clinical work
- Pragmatically, this may become an issue of available resources for performing full GA. I still prefer 70 over 75 as cancers such a lung cancer (as opposed to breast or prostate cancer) more often occur in physiologically "old" than chronologically old.
- This is my clinical practice

Appendix 3: Reasons for Lack of Feasibility of Self-Report Methodology

- Nurse assistance would be preferable but staff shortages may mean assistance of carer more feasible
- To ensure compliance it should be done with a nurse. Often oncology patients are seen without family present at the initial consultation and then arrange to meet with family subsequently. Especially elderly patients are often unwell at time of cancer diagnosis and are often inpatients at time of consultation
- Most reliable picture would be gained from the patient / nurse in the office combination. Have ranked this as less feasible though on the basis of resource difficulties. I would have concerns as to how accurate the information would be if the GA paper survey was completed at home before the first consultation.
- I think that the interview must be made face to face, as it is the best method to be sure about the results of the Comprehensive Geriatric Assessment.
- We have routinely done options 2 and 3 without issue. we had relatively low adherence to 1st option.
- I think it is difficult enough for people to bring a list of medication they are on and people often forget something basic like this. I think GA paper survey could even put people off attending clinic as maybe afraid as "homework" not done
- Only certain assessments can be done this way such as functional staus using who performance score , polypharmacy , and social support
- Availability of a nurse as opposed to a carer would depend on resources
- Completion of a self-questionnaire with or without assistance saves time. But all items need to be checked in a face-to-face interview.
- the latter option seems most feasible for success
- It still remains an issue as to who will analyse and record these paper surveys. Nursing staff assistance / data management support is by no means a given in the current economic climate
- Nurse would be optimal as would have most medical knowledge but should happen before meeting the doctor so that info is available and so as not to delay the clinic visit (ie cant be done while seeing the doctor). patient may make errors if doing it at home on their own
- Need for specific staff

Appendix 4: Comments on Screening Tools

None

Appendix 5: Additional Comments Related to Each Assessment Type

Functional Assessment

- the difference between 1 and 2 is not so clear in our health care system.
- occupational therapist referral is very difficult to access in a timely manner , decisions re oncology treatment often need to take place quickly. public health nurse or home intervention is even more unlikely to happen in a timeframe to be of any use
- the best intervention depends on the patient
- Ideally all three so hard to separate

Objective Physical Performance Assessment

- Not familiar with all these
- Unfamiliar with these
- No opinion
- Do not use these
- I would have preferred observation or POMA test.

Cognitive Assessment

- 3 items are quite equal to me: depends on local availability
- The best answer to q14 depends on patient severity (mild cognitive imairment best seen in memory clinic, more severe cases best seen by geraitrician or Old Age Psych) and access issues (memory clinics can have long waiting times, oncology patients can't wait for prolonged period before deciding on treatment
- Have put geriatrician assessment ahead of OAP as individuals with cognitve impairment and cancer may require a physician's approach

Comorbidity Assessment

- Important to assess severity in addition to number of comorbidities
- The best approach to measuring comorbidity is to identify and to describe individual conditions, then to determine their respective influence on the other conditions. Charlson index, CIRS-G measure the risk for mortality and comorbidity burden.
- Again severity and access to specialist opinion will influence best response

Polypharmacy Assessment

- A simple assessment (without stopping medication) could be done by a non-mdeic with appropriate training
- Questions above are difficult to rank - the correct way of addressing polypharmacy I would have thought would be list medications / medical history and then apply STOPP / START criteria. Re. Q. 18 - in some cases there would be a necessity to reduce / stop medications whilst waiting for a Geriatrician review. The questions do not necessarily lend themselves to a "best" and "less best" order. I have ranked 18+ 19 in the order in which I think that polypharmacy should be addressed.
- Pharmacist desirable but difficult to fund
- Not sure what STOPP START is
- Pharmacist may know the drugs but not understand prognosis of patient

Nutritional Status Assessment

No other comments

Social Support Status

No other comments

Psychological Status

- Assessment from any healthcare professional based on specific instruments

Appendix 6: Who Can Perform Assessments?

Polypharmacy

- I feel that a doctor should decide which drugs should be stopped
- Requires specific knowledge
- physician or pharmacist
- Doctor or pharmacist
- Doctor - Geriatrician or others (including GP) with experience and expertise working with older people.
- Doctor, pharmacist
- No, Not ANY healthcare professional
- geriatrician , Dr , Pharmacist
- physician, pharmacist
- pharmacist
- Skilled medical doctor usually but not invariably a geriatrician
- geriatrician, clinical pharmacist, gero-oncologist
- an oncologist or geriatrician
- medically or pharmacy trained professionals
- doctor or ANP
- geriatrician
- geriatrician ,pharmacist, nurse
- A simple assessment (without stopping medication) could be done by a non-medic with appropriate training
- Questions above are difficult to rank - the correct way of addressing polypharmacy I would have thought would be list medications / medical history and then apply STOPP / START criteria. Re. Q. 18 - in some cases there would be a necessity to reduce / stop medications whilst waiting for a Geriatrician review. The questions do not necessarily lend themselves to a "best" and "less best" order. I have ranked 18+ 19 in the order in which I think that polypharmacy should be addressed.

Nutritional Status

- Dietician should do this
- Dietician/CNS
- Don't have time to do it, more appropriate for dietician
- Not familiar enough with these to comment
- Ideally a dietician should assess and intervene
- Dietician
- If we talk about nutritional screening, otherwise this requires dietician skills
- Dietician (though screening tests by non dieticians can be used first)
- Dietician

Social Support Status

No other comments

Psychological Status

- Psychologists should do this
- Geriatrician, psychologist, psychiatrist
- Psychologist
- Psychologist
- Don't' have time to do such an assessment
- Questions depend really on what is sufficient training.
- Psychiatrist, Psychologist, Geriatrician , Dr
- Psychologist with geriatric training
- Skilled doctor or psychologist
- Psychologist/psychiatrist
- Psychologist/psychiatrist
- Doctor
- It must be perfomed by Psychologist, Geriatrician

Appendix 7 SIOG Abstract Copenhagen 2013

Geriatric Assessment for Older Adults with Cancer: An International Delphi Study

O'Donovan, A.[1], Mohile, S.[2] and Leech, M.[1]

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Department of Geriatric Oncology, James P. Wilmot Cancer Centre, University of Rochester, NY.

Introduction:
Despite the evidence demonstrating the benefits of Geriatric Assessment (GA), its adoption in Oncology has not been widespread. Given the increasing older population in Ireland, there is a growing impetus for the development of a model of care for GA in Oncology, informed by national stakeholders and an international expert panel.

Objective:
To obtain consensus on the optimal model of care for GA in Oncology to inform the implementation of Geriatric Oncology in Ireland.

Methods:
This study uses a structured iterative process, the Delphi technique, to gain consensus. All Irish Consultant Radiation and Medical Oncologists and Geriatricians were invited to participate in this study. An international expert panel, with expertise in geriatric oncology and active SIOG membership, or active researchers in the field of geriatric oncology, were also invited to participate. The first round (R1) was an open round seeking the panel's opinion on GA in Oncology. R1 comprised 49 members, encompassing four disciplines: Radiation Oncology (n=9), Medical Oncology (n=7), Geriatric Medicine (n=10) and SIOG-affiliated (n=24). R1 responses were used in the design of subsequent rounds where participants were asked to rank order preference for GA tools and interventions. A predetermined threshold for consensus has been chosen, at an interquartile range of 1 or less units (scale of 0-5,) or 2 (scale of 1-10). For nominal data, consensus is defined as two-thirds majority.

Results:
Forty-nine participants completed R1 and 44 completed R2 and R3. The majority of SIOG affiliated members use GA in the care of their patients (n=13 always, n=9 sometimes). All of the Irish geriatrician participants employ GA. Ninety-three percent of Irish participants believe that Geriatric Oncology is feasible in Ireland.
No consensus has been reached on a suitable age cut-off to select patients for GA. The SIOG affiliated group was also found to be unable to achieve consensus within their group. The majority (93%) of the panel felt that a screening tool should be employed to identify patients for GA (R3). VES-13 achieved consensus among the SIOG group as the first choice of screening tool.
All geriatric domains were deemed important for a full GA. Consensus was met for the following tools in R3: functional status (ADL/IADL), cognition (MMSE) physical performance (gait speed), comorbidity (Charlson score), nutrition (MNA), social support status (patient history/caregiver interview)and depression (Geriatric Depression Scale). In R3, first choice GA-driven interventions to address impaired domains that met consensus included: 1) physiotherapy, occupational therapy for impaired function and physical performance; 2) geriatrician referral for comorbidity and polypharmacy assessment; 3) dietician consult for poor nutrition; 4) social work consult for poor social support; 5) Referral to an Old Age Psychiatrist/Psychologist/Cognitive Behavioural Therapy for psychological assessment.

Conclusions:
This Delphi investigation of geriatric oncology experts provides some consensus on assessments and interventions that could be considered standard of care for older cancer patients in Oncology. Final results will be presented at the meeting.

Conflict of Interest: None
Key words: Geriatric Assessment
Acknowledgements: Members of the expert panel who contributed to this study and whose input was invaluable

Appendix 12: Copy of Patient Assessment Details

MANAGING THE ELDERLY IN RADIOTHERAPY USING GERIATRIC ASSESSMENT (MERGE) CRF

Eligibility verification (screening form enclosed):

Verification that consent form has been signed (consent form enclosed and copy given to patient):

Permission to contact GP granted?

Date of assessment:

Indicate whether Baseline/Followup (please circle one)

Participant's identification checked:

Study ID:

Gender:

Length of assessment (time assessment from commencement of clinic to end of assessment procedure):

SELF-COMPLETED FORMS:

ADL ☐

IADL ☐

Falls ☐

GDS ☐

EORTC QLQ-C30 ☐

Social support status ☐

Completed fully: ☐

Help required: ☐

Also indicate how much of each was completed fully, with or without help, or any difficulties in completion

SOCIODEMOGRAPHICS

Age:

Communication Aspects:

Eyesight

Hearing

Nationality:

Highest level of education achieved (please circle):

- First level
- Second level
- Third level basic degree/diploma
- Advanced: Masters/PhD

Marital status:

- Married
- Long term, committed significant other
- Divorced
- Separated
- Single
- Widowed
- Other (please specify)

Household Composition:

- Lives alone
- With spouse/partner
- With child
- Other (please specify)

Employment Status:

- Full-time
- Part-time
- Retired
- Unemployed
- Disabled/medical leave
- Other (please specify)

TUMOUR CHARACTERISTICS

Diagnosis:

Stage and grade:

PROPOSED TREATMENT:

Please outline proposed treatment regime

Surgery:

Radiotherapy Dose and Px:

Chemotherapy Yes/No

Chemo regime:

Hormone therapy (please specify):

Other, please specify:

RELEVANT MEDICAL HISTORY

ACTIVITIES OF DAILY LIVING

Activities	Independence (1 point) No supervision, direction or personal assistance	Dependence (0 points) With supervision, direction, personal assistance or total care
Bathing ___ points	**(1 POINT)** Bathes self completely or needs help in bathing only a single part of the body such as the back or disabled extremity.	**(0 POINTS)** Needs help with bathing more than one part of the body, getting in or out of the tub or shower. Requires total bathing.
Dressing ___ points	**(1 POINT)** Gets clothes from closets and drawers and puts on clothes and outer garments complete with fasteners. May have help tying shoes.	**(0 POINTS)** Needs help with dressing self or needs to be completely dressed.
Toileting ___ points	**(1 POINT)** Goes to toilet, gets on and off, arranges clothes, cleans genital area without help.	**(0 POINTS)** Needs help transferring to the toilet, cleaning self or uses bedpan or commode.
Transferring __ points	**(1 POINT)** Moves in and out of bed or chair unassisted. Mechanical transferring aides are acceptable.	**(0 POINTS)** Needs help in moving from bed to chair or requires a complete transfer.
Continence ___ points	**(1 POINT)** Exercises complete self control over urination and defecation.	**(0 POINTS)** Is partially or totally incontinent of bowel or bladder.
Feeding ___ points	**(1 POINT)** Gets food from plate into mouth without help. Preparation of food may be done by another person.	**(0 POINTS)** Needs partial or total help with feeding or requires parenteral feeding.
Total ADL Score		

INSTRUMENTAL ACTIVITIES OF DAILY LIVING (IADL)

Domains	Score
ABILITY TO USE TELEPHONE	
Has never used the telephone	N/A
◆ Operates telephone on own initiative, looks up and dials numbers, etc.	1
◆ Dials a few well known-numbers	1
◆ Answers telephone but does not dial	1
◆ Does not use telephone at all	0
SHOPPING	
Has never done the shopping	N/A
◆ Takes care of all shopping needs independently	1
◆ Shops independently for small purchases	0
◆ Needs to be accompanied on any shopping trip	0
◆ Completely unable to shop	0
FOOD PREPARATION	
Has never done the food preparation	N/A
◆ Plans, prepares and serves adequate meals independently	1
◆ Prepares adequate meals if supplied with ingredients	0
◆ Heats, serves, and prepares meals but does not maintain adequate diet	0
◆ Needs to have meals prepared and served	0
HOUSEKEEPING	
Has never done the housekeeping	N/A
◆ Maintains house alone or with occasional assistance (e.g. "heavy work domestic help")	1
◆ Performs light daily tasks such as dish-washing, bed-making	1
◆ Performs light daily tasks but cannot maintain acceptable level of cleanliness	1
◆ Needs help with all home maintenance tasks	1
◆ Does not participate in any housekeeping tasks	0

Instrumental Activities of Daily Living (IADL)	
Domains	**Score**
LAUNDRY Has never done the laundry ◆ Does personal laundry completely ◆ Launders small items-rinses socks, stocking, etc. ◆ All laundry must be done by others	N/A 1 1 0
MODE OF TRANSPORTATION Has never travelled independently ◆ Travels independently on public transportation or drives own car ◆ Arranges own travel via taxi, but does not otherwise use public transportation ◆ Travels on public transportation when accompanied by other ◆ Travel limited to taxi or automobile with assistance of another ◆ Does not travel at all	N/A 1 1 1 0 0
RESPONSIBILITY FOR OWN MEDICATION Does not take tablets currently ◆ Is responsible for taking medication in correct dosages at correct time ◆ Takes responsibility if medication is prepared in advance in separate dosage ◆ Is not capable of dispensing own medication	N/A 1 0 0
ABILITY TO HANDLE FINANCES Never handled the finances ◆ Manages financial matters independently (budgets, writes checks, pays rent, bills, goes to the bank), collects and keeps track of income ◆ Manages day to day purchases, but needs help with banking, major purchases, etc. ◆ Incapable of handling money	N/A 1 1 0
Total domains which are assessable (0-8) **Domains in which patient is dependent (0-8)**	....

FALLS

INSTRUCTIONS: PLEASE TICK ONE RESPONSE FOR EACH QUESTION

1. IN THE PAST YEAR, HAVE YOU FALLEN DOWN?

(Select only one)

☐Yes
☐No
☐Don't know

2. IN THE PAST YEAR, HOW MANY TIMES HAVE YOU FALLEN DOWN?

☐Don't know

3. IN THAT FALL OR ANY OF THOSE FALLS, DID YOU HURT YOURSELF BADLY ENOUGH TO GET MEDICAL HELP?

(Select only one)

☐Yes
☐No
☐Don't know

4. DID YOU TALK TO A DOCTOR OR OTHER MEDICAL PROFESSIONAL ABOUT THAT FALL OR ANY OF THOSE FALLS?

(Select only one)

☐Yes
☐No
☐Don't know

5. DID THE HEALTH CARE PROVIDER TALK WITH YOU TO UNDERSTAND WHY YOU FELL?

(Select only one)

☐Yes
☐No
☐Don't know

6. DID THE HEALTH CARE PROVIDER TALK WITH YOU ABOUT HOW TO PREVENT FUTURE FALLS?

(Select only one)

☐Yes
☐No
☐Don't know

FALLS – FOLLOW-UP

INSTRUCTIONS: PLEASE TICK ONE RESPONSE FOR EACH QUESTION

Today's date:

1. SINCE THE BEGINNING OF RADIOTHERAPY, HAVE YOU FALLEN DOWN?

(Select only one)

☐Yes
☐No
☐Don't know

If the patient answered yes to question one, please complete the rest of this form.

2. IN THE FEW MONTHS (SINCE THE BEGINNING OF RADIOTHERAPY), HOW MANY TIMES HAVE YOU FALLEN DOWN?

☐Don't know

3. IN THAT FALL OR ANY OF THOSE FALLS, DID YOU HURT YOURSELF BADLY ENOUGH TO GET MEDICAL HELP?

(Select only one)

☐Yes
☐No
☐Don't know

4. DID YOU TALK TO A DOCTOR OR OTHER MEDICAL PROFESSIONAL ABOUT THAT FALL OR ANY OF THOSE FALLS?

(Select only one)

☐Yes
☐No
☐Don't know

5. DID THE HEALTH CARE PROVIDER TALK WITH YOU TO UNDERSTAND WHY YOU FELL?

(Select only one)

☐Yes
☐No
☐Don't know

TIMED UP AND GO TEST

Measures mobility in people who are able to walk on their own (assistive device permitted)

Date_____

Time to Complete _____seconds

Equipment: Chair with arms (approx. height 44cm, arm height 65cm), tape measure, tape, stopwatch

Instructions:

The person may wear their usual footwear and can use any assistive device they normally use.

1. Begin the test when the patient is sitting correctly (hips all of the way back to the back of the seat) in a chair with arm rests. The chair should be stable and positioned such that it will not move when the patient moves from sitting to standing. The patient is allowed to use the arm rests during the sit to stand and stand to sit movements.

2. Place a piece of tape or other marker on the floor 3 metres away from the chair so that it is easily seen by the patient.

3. Instructions: "On the word "GO", you will stand up, walk to the line on the floor, turn around and walk back to the chair and sit down. Walk at your regular pace."

4. Start the timing on the word "GO" and stop the timing when the patient is back seated again correctly in the chair with their back resting against the back of the chair.

5. The subject wears their regular footwear, may use any gait aid they normally use during ambulation, but may not be assisted by another person. There is no time limit. They may stop and rest (but not sit down) if they need to.

6. If a patient seems unsteady, walk beside them but do not offer support unless necessary, in which case the test is null and void.

The person should be given 1 practice trial (that is not timed) and then 3 actual trials. The times from the three actual trials are averaged.

Predictive Results

Seconds Rating

<10 Freely mobile

<20 Mostly independent

20-29 Variable mobility

>20 Impaired mobility

>13.5s High falls risk

Source: Podsiadlo, D., Richardson, S. The timed 'Up and Go' Test: a Test of Basic Functional Mobility for Frail Elderly Persons. Journal of American Geriatric Society. 1991; 39:142-148

POLYPHARMACY: LIST OF MEDICATIONS
1.
2.
3.
4.
5.
6.
7.
8.
9.
10.

>5 = POLYPHARMACY

POLYPHARMACY IS DEFINED AS THE REGULAR USE OF FIVE OR MORE MEDICINES (EXCLUDING FOOD SUPPLEMENTS AND ALTERNATIVE MEDICATIONS).

NUTRITION: MINI NUTRITIONAL ASSESSMENT (SHORT FORM)

INSTRUCTIONS: PLEASE TICK ONE RESPONSE FOR EACH QUESTION

Today's date:

Tools: weighing scales and height chart, tape measure.

SCREENING

A. HAS FOOD INTAKE DECLINED OVER THE PAST 3 MONTHS DUE TO LOSS OF APPETITE, DIGESTIVE PROBLEMS, CHEWING OR SWALLOWING DIFFICULTIES?

(Select only one)

0 = severe decrease in food intake
1 = moderate decrease in food intake
2 = no decrease in food intake

☐

B. WEIGHT LOSS DURING THE LAST 3 MONTHS

(Select only one)

0 = weight loss greater than 3 kg (6.6 lbs)
1 = does not know
2 = weight loss between 1 and 3 kg (2.2 and 6.6 lbs)
3 = no weight loss

☐

C. MOBILITY

(Select only one)

0 = bed or chair bound
1 = able to get out of bed / chair but does not go out
2 = goes out

☐

D. HAS SUFFERED PSYCHOLOGICAL STRESS OR ACUTE DISEASE IN THE PAST 3 MONTHS?

(Select only one)

0 = yes
2 = no

☐

E. NEUROPSYCHOLOGICAL PROBLEMS

(Select only one)

0 = severe dementia or depression (as defined by MMSE/GDS score)
1 = mild dementia or depression
2 = no psychological problems

☐

F1. BODY MASS INDEX (BMI) (WEIGHT IN KG) / (HEIGHT IN M2)

(Select only one)

0 = BMI less than 19
1 = BMI 19 to less than 21
2 = BMI 21 to less than 23
3 = BMI 23 or greater

☐

F2. CALF CIRCUMFERENCE (CC) IN CM

(Select only one)

0 = CC less than 31
3 = CC 31 or greater

☐

Screening score:
(max. 14 points)

12-14 points: Normal nutritional status
8-11 points: At risk of malnutrition
0-7 points: Malnourished

References:

Vellas B, Villars H, Abellan G, et al. *Overview of the MNA® - Its History and Challenges.* J Nutr Health Aging 2006;10:456-465.

Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. *Screening for Undernutrition in Geriatric Practice: Developing the Short-Form Mini Nutritional Assessment (MNA-SF).* J. Geront 2001;56A: M366-377.

Guigoz Y. *The Mini-Nutritional Assessment (MNA®) Review of the Literature - What does it tell us?* J Nutr Health Aging 2006; 10:466-487.

Kaiser MJ, Bauer JM, Ramsch C, et al. *Validation of the Mini Nutritional Assessment Short-Form (MNA®-SF): A practical tool for identification of nutritional status.* J Nutr Health Aging 2009; 13:782-788.

G8 GERIATRIC ASSESSMENT SCREENING TOOL

Notes: This screening tool includes 7 items of the Mini Nutritional Assessment (see above) and the age of the patient.
Score: Total score by adding up coded answers.

G8 Screening tool			
	Items	**Possible answers**	**Score**
A	Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?	**0**: severe reduction in food intake **1**: moderate reduction in food intake **2**: normal food intake	.....
B	Weight loss during the last 3 months?	**0**: weight loss >3kg **1**: does not know **2**: weight loss between 1 and 3 kg **3**: no weight loss	.....
C	Mobility	**0**: bed or chair bound **1**: able to get out of bed/chair but does not go out **2**: goes out	.....
E	Neuropsychological problems	**0**: severe dementia or depression **1**: mild dementia or depression **2**: no psychological problems	.....
F	Body Mass Index (weight in kg/height in m2)	**0**: BMI less than 19 **1**: BMI 19 to less than 21 **2**: BMI 21 to less than 23 **3**: BMI 23 or greater	.....
H	Takes more than 3 medications per day	**0**: yes **1**: no	.....
P	In comparison with other people of the same age, how does the patient consider his/her health status?	**0**: not as good **0,5**: does not know **1**: as good **2**: better	.....
	Age	**0**: >85 **1**: 80-85 **2**: <80	.....
	Total score (0-17)		.....

Ref.: P. Soubeyran et al. Validation of a screening test for elderly patients in oncology. JCO. Vol 26, 15S, 200

Mini-Mental State Examination (MMSE)

Process

In order to complete the assessment, the nurse will require the following equipment:

- The screening tool (MMSE)
- A watch
- A pencil

To gain the patient's confidence, consent and co-operation and to ensure confidentiality, the Nurse must introduce her or himself to the patient and family/carer in a friendly manner. Ensure the examination is carried out in private

Impairments (eg visual or hearing deficits) can impair orientation and impede other cognitive functions. Assess the patient's ability to hear and understand by asking "**do you have any trouble with your memory"** and "**may I ask you some questions about your memory"? (<u>These questions are not scored</u>)**. If the patient requires hearing or visual aids, provide these before starting. Make a note at the end of the form if aids are required

To promote the patient's confidence and allay fear of failure, questions and answers should be sympathetic and direct. Use short sentences or questions containing a single point

If the patient cannot answer a question, the examiner should move to the next question. Incorrect responses should not be pointed out or corrected. This approach avoids having the patient respond emotionally to the failure which can worsen cognitive performance

Assessment. The MMSE has 5 sections

- Orientation
- Registration
- Attention and Calculation
- Memory
- Language and Praxis

Orientation: To assess cognitive function relating to time and place Allocate a score of 1 to each correct response -Maximum score of 10

Ask day of the week, accept exact answer only

Ask today's date, accept exact answer only

Ask month of the year, accept exact answer only

Ask the year, accept exact answer only

Ask the season of the year. If it is near the start of a particular season, accept either

Ask what floor we are on, accept exact answer only

Ask the name of the hospital, accept exact answer only

Ask what city, accept exact answer only

Ask what county we are in, accept exact answer only

Ask what country we are in, accept exact answer only

Registration: To assess cognitive function relating to the ability to register, retain and recall information as well as the level of alertness

Allocate a score of 1 for each word repeated at one attempt: Maximum score of 3

Name **three** common objects e.g. ball, flag, tree. Say them slowly at approximately one second intervals. Ask the patient to repeat them and also to remember them because you are going to ask them again in a few minutes. Score one point for each correct reply on first attempt. If the patient did not repeat all three, repeat until they are learned or up to a maximum of 5 times.
For repeated use – **apple, penny, table**

Attention and Calculation: To assess cognitive function relating to the ability to maintain attention and mental calculation abilities
Allocate a score of 1 for each correct answer: Maximum score of 5.

Ask the examinee to subtract 7 from 100 and keep subtracting from what's left until you tell them to stop. Once the examinee starts, do not interrupt, allow him/her to proceed until **five** subtractions have been made. If the examinee stops before five subtractions have been made, say "***keep going"***. Score one point for each correct answer. An answer is considered correct if it is exactly 7 less than the previous answer regardless of whether that previous answer was correct

Ask the examinee to spell the word WORLD forward then backward. You may help the patient to spell world correctly and then ask the patient to spell it backwards. Score one point for each correct placement, only the backward spelling is scored, with one point for each correct placement.

When scoring, use <u>only</u> the highest score achieved for serial sevens or WORLD backwards for calculating the total MMSE score

Memory: To assess function relating to registration or recalling what has been learned before
Allocate a score of 1 to each correct answer: Maximum score of 3 points

Ask the patient "What were the three objects that I asked you to remember?" These are the three objects used in the Registration stage. Do not prompt or give hints. Score 1 point for each correct response, regardless of order

Language and Praxis: To assess cognitive function relating to expressive and receptive language ability and praxis i.e. the ability to direct and co-ordinate movements: Maximum score of 9 points.

To assess cognitive function relating to communication and naming, show a watch, ask what is this called and score 1 point for the correct answer. Do not accept clock, time etc.

Show a pencil, ask what is this called and score 1 point for correct answer. Do not accept pen.

Ask the patient to repeat the phrase **"No ifs ands or buts"** ensure the plural **"s"** is said clearly. Score 1 point for a correct repetition based on the first attempt, it must be exact.

To assess cognitive function relating to the ability to read and understand a simple sentence. Hand the patient the paper with CLOSE YOUR EYES written on it. Ask the patient to read the words on the page and then do what it says. If the patient just reads and does not then close their eyes, you may repeat "read the words on this page and then do what it says". Score 1 point only if the patient closes their eyes, the patient does not have to read the words aloud.

Ask the patient to write a short sentence. Score 1 point. The sentence should contain a subject and a verb, (eg I like this hospital) ignore any spelling errors.

3 Stage Command – ask if the examinee is right or left handed, alternate right/left hand in the statement. Take a piece of paper, hold it in front of the examinee and say the following – "take this paper in your right/left hand, fold the paper in half once with both hands and put the paper down on the floor". Score 1 point for each instruction correctly followed. (Max 3 points).

Ask the patient to copy the drawing that appears on the reverse of the page. Score 1 point for correctly copied diagram. The patient must have drawn a 4 sided figure between the two 5 sided figures.

Assessment Scores

Patients who score 24-30 are considered "above conventional range for significant cognitive impairment".

Patients who score below 24 should be referred to the medical team for further assessment and follow up

Records

The assessment and score must be documented in the patient's medical and nursing notes

In the event that the patient is assessed as having any degree of cognitive impairment i.e. achieved a score below 24, appropriate care plan/plans must be developed with the patient and family/carer if appropriate and a referral made to the relevant medical team

Audit of compliance to protocol will be undertaken in six months (December, 2013) and results will be fed back to staff.

Materials:
Paper, pencil, watch

References:

Cunningham, C. Archibald, C. (2006) Supporting people with dementia in acute hospital settings. Nursing Standard 20 (43): 51-55

Folstein, M.F. Folstein, S.E. McHugh, P.R. Fanjiang, G. (2001) Mini-Mental State Examination. User's Guide. Psychological Assessment Resources Inc

Folstein, M.F. Folstein, S.E. McHugh, P.R. (1975) Mini mental state: a practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research 12: 189-198

Health Service Executive (2012) National Clinical Programme for Older People. Model of Care for Specialist Geriatric Services. Health Service Executive, Dublin

APPENDIX 1

Mini Mental State Examination (Adapted)

Name.....MRN.....Date:
.....

Orientation to Time
What is the day of the week? ..... 1 ...
What is today's date?. ..... 1 ...
What is the month of the year? ..... 1 ...
What is the year? ..... 1 ...
What is the season? ..... 1 ...

Orientation To Place
What floor of the building are we on? ..... 1 ...
Name the building we are in? ..... 1 ...
What city are we in? ..... 1 ...
What county are we in? ..... 1 ...
What country are we in? ..... 1 ...

Registration
I am now going to say three words, please listen carefully because I am going to ask you to repeat them, here they are

Ball ..... 1 ...
Flag ..... 1 ...
Tree ..... 1 ...

The first repetition determines the score (0-3) but keep saying them (up to 5 times) until the patient can repeat them.

Now keep these words in mind, I am going to ask you to say them again in a few minutes

Attention and Calculation
Beginning at 100 subtract 7, then keep subtracting until I tell you to stop
(93) ..... 1 ...
(86) ..... 1 ...
(79) ..... 1 ...
(72) ..... 1 ...
(65) ..... 1 ...

Spell WORLD forward , then backward
Correct forward spelling if incorrect but only score backward spelling
"D" ..... 1 ...
"L" ..... 1 ...
"R" ..... 1 ...
"O" ..... 1 ...
"W" ..... 1 ...

NB – Administer both serial 7s and "world" backwards and use the highest score

Recall
What were the three words I asked you to repeat earlier? (Do not offer any hints)

"ball" ..... 1 ...
"flag" ..... 1 ...
"tree" ..... 1 ..

Name: ..... MRN: ..... Date: .....

Examiner: ..... **Title: .....**

Close your eyes

Name: ..... **MRN:** ..... **Date:** .....

Examiner: ..... **Title:** .....

Naming
What is this (point to a pencil) ..... 1...
What is this (point to a watch) ..... 1...

Repetition
Ask the patient to repeat the sentence "**no ifs, ands, or buts".**

Correct repetition ..... 1 ..

Comprehension
Give the patient a piece of paper and say "**take this paper in your right /left hand, fold it in half, and put it on the floor"**

Take in right/left hand ..... 1...
Fold in half ..... 1...
Put on the floor ..... 1...

Reading
Please read this and do what it says (show the paper with "close your eyes")

Close your eyes ..... 1...

Writing
Using the space provided ask the patient to

"**please write a short sentence for me"** ..... 1...

Score one point if the sentence is comprehensible and contains a subject and a verb.

Drawing
Show the patient the intersecting pentagon and ask

"please copy this design" ..... 1..

Score one point if the drawing consists of two 5-sided figures that intersect to form a 4-sided figure

Total score = ...

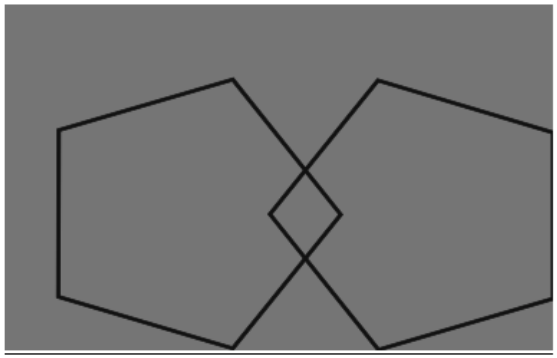
Comments:-

Name: ..... **MRN:** ..... **Date:** .....

Examiner: ..... **Title:** .....

Write a short sentence in the box below

Please copy the drawing



Name: ..... **MRN:** ..... **Date:** .....

Examiner: ..... **Title:** .....

CHARLSON COMORBIDITY INDEX (AGE ADJUSTED)

1. Indication

Assess whether a patient will live long enough to benefit from a specific

screening measure or medical intervention

2. Scoring: Comorbidity Component (Apply points specified)

COMORBIDITIES	PRESENT	POINTS
1. Myocardial infarction		**1**
2. Congestive heart failure		**1**
3. Peripheral vascular disease		**1**
4. Cerebrovascular disease		**1**
5. Dementia		**1**
6. COPD		**1**
7. Connective tissue disease		**1**
8. Peptic ulcer disease		**1**
9. Diabetes mellitus (without end-organ damage)		**1**
10. Diabetes mellitus (with end-organ damage)		**2**
11. Moderate to severe chronic kidney disease (renal failure)		**2**
12. Hemiplegia		**2**
13. Leukemia		**2**
14. Malignant lymphoma		**2**
15. Solid tumor		**2 points, 6 points if metastatic**
16. Moderate/severe liver disease		**1 point mild, 3 points if moderate to severe**
17. AIDS		**6**
Total points (0-37)		

3. Scoring: Age

1. Age <40 years: 0 points

2. Age 41-50 years: 1 points

3. Age 51-60 years: 2 points

4. Age 61-70 years: 3 points

5. Age 71-80 years: 4 points

KEY: (adapted from Charlson et al, 1987, and Extermann 2000)

Myocardial infarction: History of medically documented (ECG and enzyme changes) myocardial infarction

Congestive heart failure: Symptomatic (exertional or paroxysmal nocturnal dyspnoea) CHF with response to specific treatment.

Peripheral vascular disease: Intermittent claudication, peripheral arterial bypass for insufficiency, gangrene, acute arterial insufficiency, untreated aneurysm (>6 cm)
Cerebrovascular disease (except hemiplegia): History of TIA, or CVA with no or minor sequelae

Dementia: Chronic cognitive deficit

Chronic pulmonary disease: Symptomatic dyspnoea (with moderate activity) due to chronic respiratory conditions (including asthma)

Connective tissue disease: SLE, polymyositis, mixed CTD, polymyalgia rheumatica, moderate to severe RA.

Ulcerative disease: Patients who have required treatment for PUD, including those who have bled from ulcers.

Mild liver disease: Cirrhosis without PHT, chronic hepatitis

Diabetes (without complications): Diabetes with medication

Diabetes with end organ damage: Retinopathy, neuropathy, nephropathy

Hemiplegia (or paraplegia): Hemiplegia or paraplegia

Moderate or severe renal disease: Creatinine >3 mg/dl (265 mmol/l), dialysis, transplantation, uremic syndrome. According to International Society for Geriatric Oncology serum creatinine alone is insufficient as a means of evaluating renal function, and creatinine clearance should at least be calculated in every patient (Cockcroft-Gault equations) *

2nd solid tumour (non-metastatic): Initially treated in the last 5 years. Exclude non-melanomatous skin cancers and in situ cervical carcinoma.

Leukaemia: CML, CLL, AML, ALL, PV

Lymphoma, MM: Non-Hodgkin's lymphoma (NHL), Hodgkin's, Waldenstroem, multiple myeloma

Moderate or severe liver disease: Cirrhosis with PHT +/- variceal bleeding

2nd metastatic solid tumour: Self-explanatory

AIDS: AIDS and AIDS-related complex, Suggested: as defined in latest definition

Abbreviations:

CHF, congestive heart failure; TIA, transient ischemic attack; CVA, cerebro-vascular accident; SLE, systemic lupus erythematosus; CTD, connective tissue disease; RA, rheumatoid arthritis; PUD, peptic ulcer disease; PHT, portal hypertension; CML, chronic myeloid leukaemia; CLL, chronic lymphoid leukaemia; AML, acute myeloid leukaemia; ALL, acute lymphoblastic leukaemia; PV, polycythemia vera.

Ref.: Charlson et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. 1987. J. Chronic Dis. 40, pp. 373–383.

* Launay-Vacher V, et al; International Society of Geriatric Oncology. Renal insufficiency in elderly cancer patients: International Society of Geriatric Oncology clinical practice recommendations. Ann Oncol. 2007 Aug;18(8):1314-21

Gold (1994) J Clin Epidemiol 47: 1245–51

Participant Study ID:

GERIATRIC DEPRESSION SCALE (SHORT FORM)

Instructions: Choose the best answer for how you felt over the past week. Note: when asking the patient to complete the form, provide the self-rated form (included on the following page).

No.	Question	Answer	Score
1.	Are you basically satisfied with your life?	YES / ***NO***	
2.	Have you dropped many of your activities and interests?	***YES*** / NO	
3.	Do you feel that your life is empty?	***YES*** / NO	
4.	Do you often get bored?	***YES*** / NO	
5.	Are you in good spirits most of the time?	YES / ***NO***	
6.	Are you afraid that something bad is going to happen to you?	***YES*** / NO	
7.	Do you feel happy most of the time?	YES / ***NO***	
8.	Do you often feel helpless?	***YES*** / NO	
9.	Do you prefer to stay at home, rather than going out and doing new things?	***YES*** / NO	
10.	Do you feel you have more problems with memory than most people?	***YES*** / NO	
11.	Do you think it is wonderful to be alive?	YES / ***NO***	
12.	Do you feel pretty worthless the way you are now?	***YES*** / NO	
13.	Do you feel full of energy?	YES / ***NO***	
14.	Do you feel that your situation is hopeless?	***YES*** / NO	
15.	Do you think that most people are better off than you are?	***YES*** / NO	
		TOTAL	

(Sheikh & Yesavage, 1986)

Scoring:

Answers indicating depression are in bold and italicized; score one point for each one selected. A score of 0 to 5 is normal. A score greater than 5 suggests depression.

References:

Brink TL, Yesavage JA, Lum O, Heersema P, Adey MB, Rose TL: Screening tests for geriatric depression. *Clinical Gerontologist 1:* 37-44, 1982.

Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey MB, Leirer VO: Development and validation of a geriatric depression screening scale: A preliminary report. *Journal of Psychiatric Research 17:* 37-49, 1983.

Sheikh JI, Yesavage JA: Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. Clinical Gerontology : A Guide to Assessment and Intervention 165-173, NY: The Haworth Press, 1986.

Sheikh JI, Yesavage JA, Brooks JO, III, Friedman LF, Gratzinger P, Hill RD, Zadeik A, Crook T: Proposed factor structure of the Geriatric Depression Scale. *International Psychogeriatrics 3:* 23-28, 1991.

***Instructions*: Choose the best answer for how you felt over the past week.**

No.	Question	Answer	Score
1.	Are you basically satisfied with your life?	YES / NO	
2.	Have you dropped many of your activities and interests?	YES / NO	
3.	Do you feel that your life is empty?	YES / NO	
4.	Do you often get bored?	YES / NO	
5.	Are you in good spirits most of the time?	YES / NO	
6.	Are you afraid that something bad is going to happen to you?	YES / NO	
7.	Do you feel happy most of the time?	YES / NO	
8.	Do you often feel helpless?	YES / NO	
9.	Do you prefer to stay at home, rather than going out and doing new things?	YES / NO	
10.	Do you feel you have more problems with memory than most people?	YES / NO	
11.	Do you think it is wonderful to be alive?	YES / NO	
12.	Do you feel pretty worthless the way you are now?	YES / NO	
13.	Do you feel full of energy?	YES / NO	
14.	Do you feel that your situation is hopeless?	YES / NO	
15.	Do you think that most people are better off than you are?	YES / NO	
		TOTAL	

(Sheikh & Yesavage, 1986)

SOCIAL SUPPORT STATUS

Structured interview

1. Do you live alone, or with family?
2. If living with family members, please specify who with?
3. Do you require assistance with housework, dressing and other daily activities? If so, do you have somebody you can rely on to do this?
4. Do you engage in frequent social activities outside the home?
5. Do you have somebody to drive you to treatment every day?

EORTC QLQ-C30 (VERSION 3)

EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your first initial: |___|
Your birth date (Day, Month, Year): |__|__||__|__||__|__|__|
Today's date (Day, Month, Year): |__|__||__|__||__|__|__|

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:	Not at All	A Little	Quite a Bit	Very Much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4

During the past week:	Not at All	A Little	Quite a Bit	Very Much
16. Have you been constipated?	1	2	3	4
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you:

29. How would you rate your overall health during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

BALDUCCI FRAILTY CRITERIA

Category	Criteria
Fit	No functional dependence in ADLs/IADLs No comorbidities No geriatric syndromes
Vulnerable	Dependence in one or more IADLs but not ADLs Comorbidities present but not severe or life threatening Mild memory disorder and/or mild depression but no other significant geriatric symdromes
Frail	Age >85 years Dependence in one or more ADLs Any significant geriatric syndromes 3 or more grade 3 comorbidities or one grade 4 comorbidity (with limitation of daily life)

Geriatric Syndromes:

- Depression
- Dementia
- Delirium
- Falls
- Osteoporosis
- Incontinence
- Failure to thrive
- Neglect or abuse

CLINICAL FRAILTY SCALE

Clinical Frailty Scale*

1 **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 **Well** – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 **Managing Well** – People whose **medical problems are well controlled**, but are **not regularly active** beyond routine walking.

4 **Vulnerable** – While **not dependent** on others for daily help, often **symptoms limit activities**. A common complaint is being "slowed up", and/or being tired during the day.

5 **Mildly Frail** – These people often have **more evident slowing**, and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 **Moderately Frail** – People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **Severely Frail – Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 **Very Severely Frail** – Completely dependent, approaching the end of life. Typically they could not recover even from a minor illness.

9. **Terminally Ill** - Approaching the end of life. This category applies to people with a **life expectancy <6 months**, who are **not otherwise evidently frail**.

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging: Revised. 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

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DALHOUSIE UNIVERSITY
Inspiring Minds

TOXICITY CTC AE 4.03

Baseline

During Treatment:

Week 1:

Week 2:

Week 3:

Week 4:

Week 5:

Week 6:

Week 7:

Followup:

DURING TREATMENT

Please record weekly (dated) with toxicity above:

Rate of (one or more fractions) unplanned radiotherapy interruptions

Rate of radiotherapy incompletion (one or more fraction less than the prescribed radiation dose)

Radiotherapy/chemotherapy dose reduction during a course of treatment

Chemotherapy withdrawal

Hospital admission (not elective) rate

Radiotherapy- related adverse event (CTC Grade 3+)

SUMMARY OF ASSESSMENT AND RECOMMENDATIONS FOR RADIATION ONCOLOGIST:

Date sent (please specify if via email etc.):

Summary Guide:

DOMAIN	TOOL	SCORE SIGNIFYING IMPAIRMENT
Physical function	➢ ADL ➢ IADL ➢ Falls history	➢ Any ADL or IADL impairment* ➢ Any history of falls
Objective physical performance	➢ TUG	➢ <10s Freely mobile ➢ <20s Mostly independent ➢ 20-29s Variable mobility ➢ >20s Impaired mobility ➢ 13.5s threshold for increased falls risk
Comorbidity	➢ Charlson Comorbidity Index	➢ Dependent on type of comorbidity and cancer type-evaluated on a case-by-case basis
Nutrition	➢ MNA	➢ At risk of malnutrition (8-11 points) ➢ Malnourished (0-7 points)
Social support	➢ Patient history/caregiver interview	➢ Any deficit noted
Polypharmacy	➢ Number of total medications	➢ ≥5 medications
Psychological Status	➢ GDS ➢ Patient history/interview	➢ 10-19 mildly depressed ➢ 20-30 severely depressed
Cognition	➢ MMSE	➢ 24-30=normal ➢ 18-23=mild cognitive decline ➢ 0-17=severe cognitive decline
Screening	➢ G8	➢ ≤ 14

* Related to the cutoff for activities of daily living (ADLs) and instrumental ADLs (IADLs) in determining dependency in functional status, Luciani et al[1] rated patients as having some form of functional dependence if the number of preserved ADLs, IADLs, or both was five or fewer. This cutoff is correct for ADLs, **because the loss of just one of six ADLs defines a patient as frail,** whereas for IADLs, the same cutoff seems inadequate. Actually, National Comprehensive Cancer Network guidelines recommend assessing IADLs in every elderly patient with cancer before defining oncologic treatment. Patients who are dependent in at least one IADL should receive individualized treatment with cautious dosing and precautions, and if possible, an attempt should be made to reverse the problem.[2] Furthermore, a distinction according to sex must be made. In fact, only five of eight IADLs are detectable in older men. **Consequently, the cutoff should be seven or fewer for women and four or fewer for men.**

RADIATION ONCOLOGIST RECOMMENDATIONS/ACTION AND INTERVENTIONS

Recommendations/action:

Interventions:

Rad Onc completed Factors Affecting Treatment Decision date (please enclose):

Any other comments:

Date of Followup assessment (and decision regret scale Rad Onc):

Patient informed re: followup:

RANDOMISATION ARM

CONTROL/TREATMENT

Randomisation date:

Reminders added to diary:

Patient starting RT:

Patient finishing RT:

Appendix 13: Summary Assessment Template Sent to Radiation Oncologists

Summary of Assessment and Recommendations for Radiation Oncologist:

Date sent (please specify if via email/in person etc.):

This is the summary of the assessment performed for _____ on _____. Please find reference table on the last page for threshold levels for each domain assessed.

This patient has been randomised to the treatment arm.

MERGE Study AOD July 2014 Patient Summary Report for Consultants

Domain	**Physical Function**	**Domain**	**Objective Physical Performance**
Tool	ADL/IADL/Falls history	**Tool**	Timed Up and Go test
Score	ADL= IADL= Unintended fall in last 6 months=	**Score**	
Deficit identified	Yes/No	**Deficit identified**	Yes/No
Nature of deficit		**Nature of deficit**	
Recommendations		**Recommendations**	
Domain	Comorbidity	**Domain**	Cognition
Tool	Charlson Comorbidity Index	**Tool**	MMSE
Score		**Score**	
Deficit identified	Yes/No	**Deficit identified**	Yes/No
Nature of deficit		**Nature of deficit**	
Recommendations		**Recommendations**	
Domain	Nutritional Status	**Domain**	Polypharmacy
Tool	MNA	**Tool**	List of Medications
Score		**Score**	
Deficit identified	Yes/No	**Deficit identified**	Yes/No
Nature of deficit		**Nature of deficit**	
Recommendations		**Recommendations**	
Domain	Depression	**Domain**	Social Support
Tool	GDS	**Tool**	Structured Interview
Score		**Score**	
Deficit identified	Yes/No	**Deficit identified**	Yes/No
Nature of deficit		**Nature of deficit**	
Recommendations		**Recommendations**	

Domain	Quality of Life	Domain	Screening tool
Tool	EORTC QLQ-C30	Tool	G8
Score		Score	
Deficit identified	Yes/No	Deficit identified	Yes/No
Nature of deficit		Nature of deficit	
Recommendations		Recommendations	

Summary of Recommendations:

Recommended referrals/action:

Follow-up Assessment scheduled:

Consultant signature:

_____

MERGE Study AOD July 2014 Patient Summary Report for Consultants

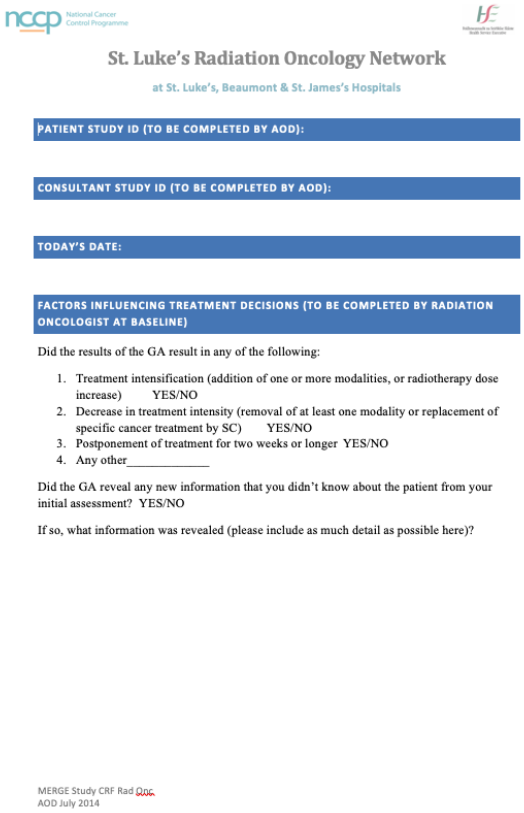
Summary Guide:

DOMAIN	TOOL	SCORE SIGNIFYING IMPAIRMENT
Physical function	➢ ADL ➢ IADL ➢ Falls history	➢ Any ADL or IADL impairment* ➢ Any history of falls
Objective physical performance	➢ TUG	➢ <10s Freely mobile ➢ <20s Mostly independent ➢ 20-29s Variable mobility ➢ >20s Impaired mobility ➢ 13.5s threshold for increased falls risk
Comorbidity	➢ Charlson Comorbidity Index	➢ Dependent on type of comorbidity and cancer type-evaluated on a case-by-case basis
Nutrition	➢ MNA	➢ At risk of malnutrition (8-11 points) ➢ Malnourished (0-7 points)
Social support	➢ Patient history/caregiver interview	➢ Any deficit noted
Polypharmacy	➢ Number of total medications	➢ ≥5 medications
Psychological Status	➢ GDS ➢ Patient history/interview	➢ 10-19 mildly depressed ➢ 20-30 severely depressed
Cognition	➢ MMSE	➢ 24-30=normal ➢ 18-23=mild cognitive decline ➢ 0-17=severe cognitive decline

Screening	➢ G8	➢ ≤ 14

* Related to the cutoff for activities of daily living (ADLs) and instrumental ADLs (IADLs) in determining dependency in functional status, Luciani et al[1] rated patients as having some form of functional dependence if the number of preserved ADLs, IADLs, or both was five or fewer. This cutoff is correct for ADLs, **because the loss of just one of six ADLs defines a patient as frail,** whereas for IADLs, the same cutoff seems inadequate. Actually, National Comprehensive Cancer Network guidelines recommend assessing IADLs in every elderly patient with cancer before defining oncologic treatment. Patients who are dependent in at least one IADL should receive individualized treatment with cautious dosing and precautions, and if possible, an attempt should be made to reverse the problem.[2] Furthermore, a distinction according to sex must be made. In fact, only five of eight IADLs are detectable in older men. **Consequently, the cutoff should be seven or fewer for women and four or fewer for men.**

Appendix 14: Impact on Treatment Decision – Radiation Oncologist



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at St. Luke's, Beaumont & St. James's Hospitals

PATIENT STUDY ID (TO BE COMPLETED BY AOD):

CONSULTANT STUDY ID (TO BE COMPLETED BY AOD):

TODAY'S DATE:

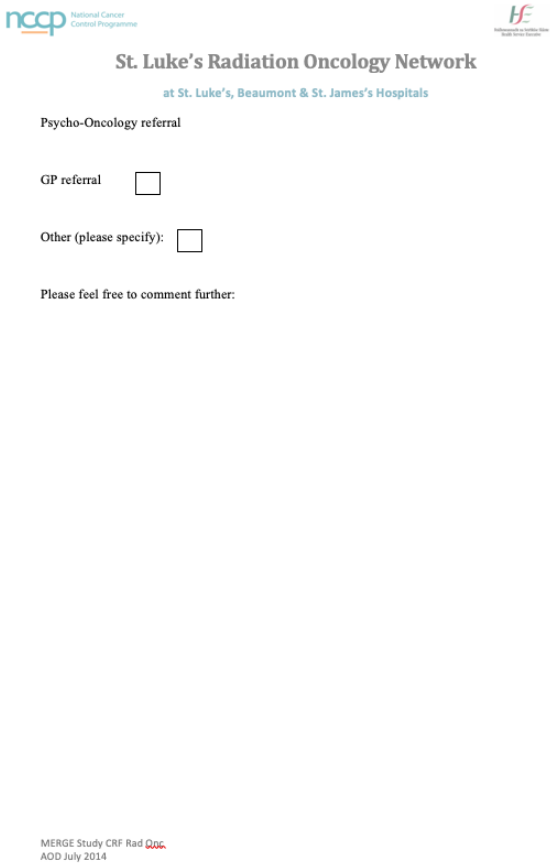
FACTORS INFLUENCING TREATMENT DECISIONS (TO BE COMPLETED BY RADIATION ONCOLOGIST AT BASELINE)

Did the results of the GA result in any of the following:

1. Treatment intensification (addition of one or more modalities, or radiotherapy dose increase) YES/NO
2. Decrease in treatment intensity (removal of at least one modality or replacement of specific cancer treatment by SC) YES/NO
3. Postponement of treatment for two weeks or longer YES/NO
4. Any other_____

Did the GA reveal any new information that you didn't know about the patient from your initial assessment? YES/NO

If so, what information was revealed (please include as much detail as possible here)?



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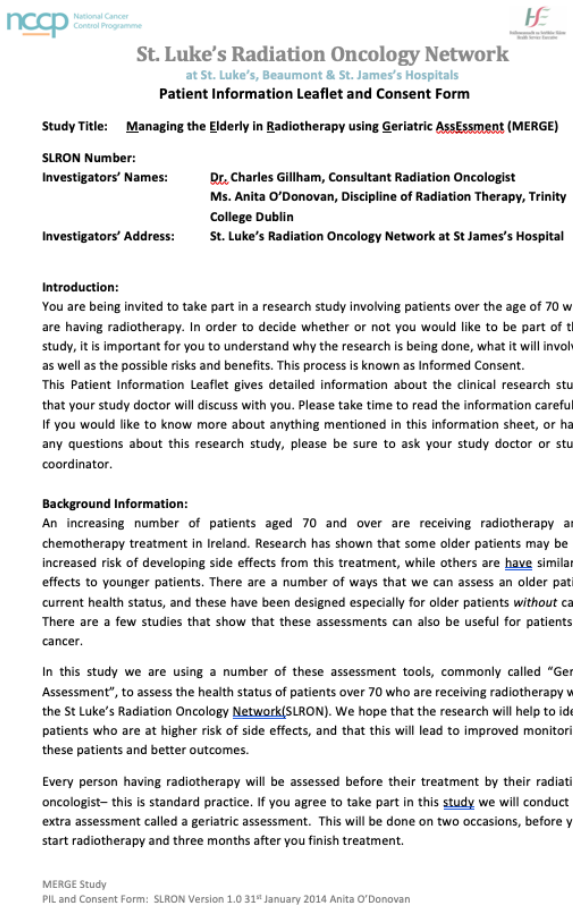
Psycho-Oncology referral

GP referral ☐

Other (please specify): ☐

Please feel free to comment further:

Appendix 15a: Participant Information Leaflet (Patient)



St. Luke's Radiation Oncology Network
at St. Luke's, Beaumont & St. James's Hospitals
Patient Information Leaflet and Consent Form

Study Title: Managing the Elderly in Radiotherapy using Geriatric AssEssment (MERGE)

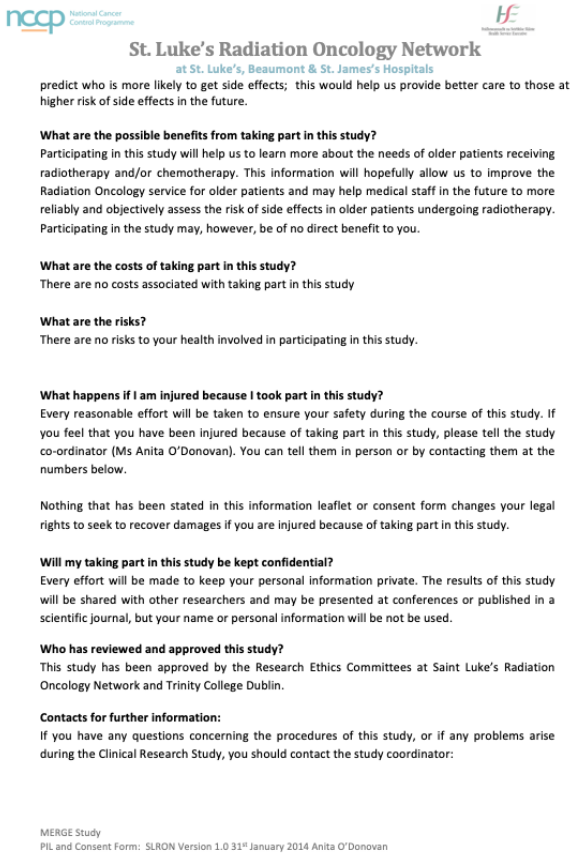
SLRON Number:
Investigators' Names: Dr. Charles Gillham, Consultant Radiation Oncologist
Ms. Anita O'Donovan, Discipline of Radiation Therapy, Trinity College Dublin
Investigators' Address: St. Luke's Radiation Oncology Network at St James's Hospital

Introduction:
You are being invited to take part in a research study involving patients over the age of 70 who are having radiotherapy. In order to decide whether or not you would like to be part of this study, it is important for you to understand why the research is being done, what it will involve, as well as the possible risks and benefits. This process is known as Informed Consent.
This Patient Information Leaflet gives detailed information about the clinical research study that your study doctor will discuss with you. Please take time to read the information carefully. If you would like to know more about anything mentioned in this information sheet, or have any questions about this research study, please be sure to ask your study doctor or study coordinator.

Background Information:
An increasing number of patients aged 70 and over are receiving radiotherapy and/or chemotherapy treatment in Ireland. Research has shown that some older patients may be at an increased risk of developing side effects from this treatment, while others are have similar side effects to younger patients. There are a number of ways that we can assess an older patient's current health status, and these have been designed especially for older patients *without* cancer. There are a few studies that show that these assessments can also be useful for patients *with* cancer.

In this study we are using a number of these assessment tools, commonly called "Geriatric Assessment", to assess the health status of patients over 70 who are receiving radiotherapy within the St Luke's Radiation Oncology Network(SLRON). We hope that the research will help to identify patients who are at higher risk of side effects, and that this will lead to improved monitoring of these patients and better outcomes.

Every person having radiotherapy will be assessed before their treatment by their radiation oncologist– this is standard practice. If you agree to take part in this study we will conduct an extra assessment called a geriatric assessment. This will be done on two occasions, before you start radiotherapy and three months after you finish treatment.



St. Luke's Radiation Oncology Network
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predict who is more likely to get side effects; this would help us provide better care to those at higher risk of side effects in the future.

What are the possible benefits from taking part in this study?
Participating in this study will help us to learn more about the needs of older patients receiving radiotherapy and/or chemotherapy. This information will hopefully allow us to improve the Radiation Oncology service for older patients and may help medical staff in the future to more reliably and objectively assess the risk of side effects in older patients undergoing radiotherapy. Participating in the study may, however, be of no direct benefit to you.

What are the costs of taking part in this study?
There are no costs associated with taking part in this study

What are the risks?
There are no risks to your health involved in participating in this study.

What happens if I am injured because I took part in this study?
Every reasonable effort will be taken to ensure your safety during the course of this study. If you feel that you have been injured because of taking part in this study, please tell the study co-ordinator (Ms Anita O'Donovan). You can tell them in person or by contacting them at the numbers below.

Nothing that has been stated in this information leaflet or consent form changes your legal rights to seek to recover damages if you are injured because of taking part in this study.

Will my taking part in this study be kept confidential?
Every effort will be made to keep your personal information private. The results of this study will be shared with other researchers and may be presented at conferences or published in a scientific journal, but your name or personal information will be not be used.

Who has reviewed and approved this study?
This study has been approved by the Research Ethics Committees at Saint Luke's Radiation Oncology Network and Trinity College Dublin.

Contacts for further information:
If you have any questions concerning the procedures of this study, or if any problems arise during the Clinical Research Study, you should contact the study coordinator:

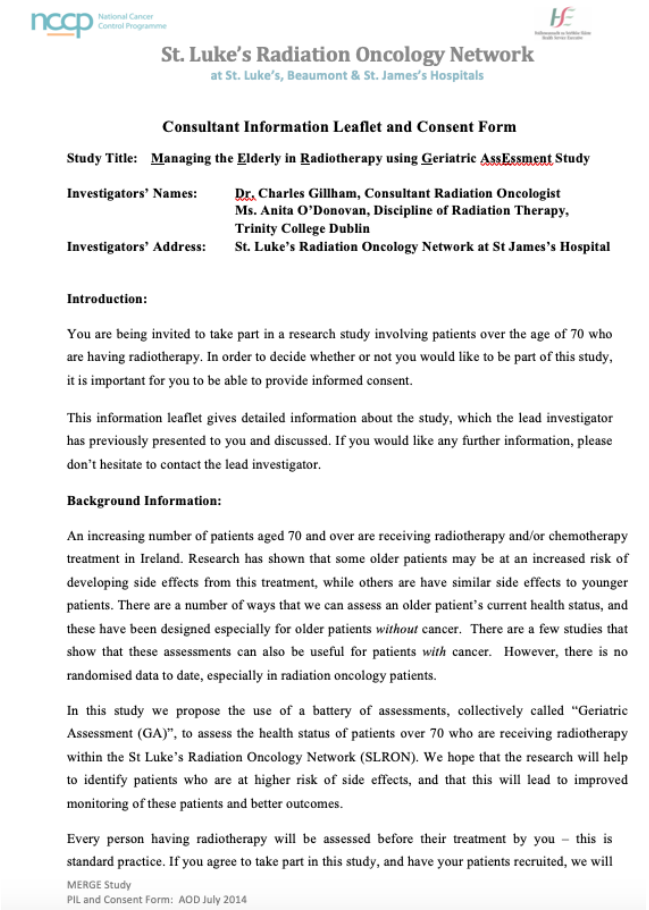
National Cancer Control Programme

St. Luke's Radiation Oncology Network
at St. Luke's, Beaumont & St. James's Hospitals

Study Coordinator: Ms Anita O'Donovan Telephone: 01 896 3149

For questions about your rights or if you wish to make a complaint whilst taking part in this study, call the Corporate Services Officer on 01 4065000 and your complaint will be dealt with promptly.

Appendix 15b: Participant Information Leaflet (Radiation Oncologist)



St. Luke's Radiation Oncology Network
at St. Luke's, Beaumont & St. James's Hospitals

Consultant Information Leaflet and Consent Form

Study Title: Managing the Elderly in Radiotherapy using Geriatric AssEssment Study

Investigators' Names: Dr. Charles Gillham, Consultant Radiation Oncologist
Ms. Anita O'Donovan, Discipline of Radiation Therapy, Trinity College Dublin

Investigators' Address: St. Luke's Radiation Oncology Network at St James's Hospital

Introduction:

You are being invited to take part in a research study involving patients over the age of 70 who are having radiotherapy. In order to decide whether or not you would like to be part of this study, it is important for you to be able to provide informed consent.

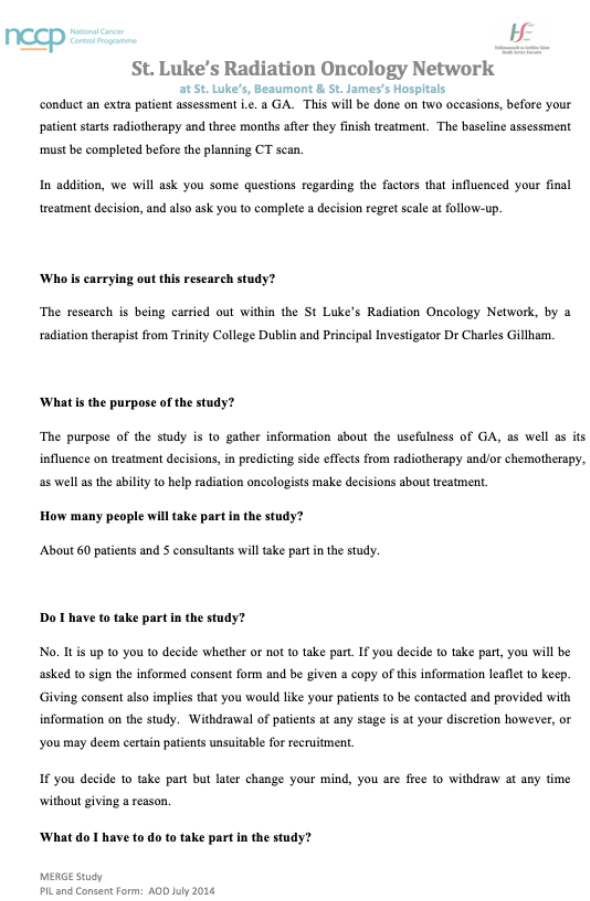
This information leaflet gives detailed information about the study, which the lead investigator has previously presented to you and discussed. If you would like any further information, please don't hesitate to contact the lead investigator.

Background Information:

An increasing number of patients aged 70 and over are receiving radiotherapy and/or chemotherapy treatment in Ireland. Research has shown that some older patients may be at an increased risk of developing side effects from this treatment, while others are have similar side effects to younger patients. There are a number of ways that we can assess an older patient's current health status, and these have been designed especially for older patients *without* cancer. There are a few studies that show that these assessments can also be useful for patients *with* cancer. However, there is no randomised data to date, especially in radiation oncology patients.

In this study we propose the use of a battery of assessments, collectively called "Geriatric Assessment (GA)", to assess the health status of patients over 70 who are receiving radiotherapy within the St Luke's Radiation Oncology Network (SLRON). We hope that the research will help to identify patients who are at higher risk of side effects, and that this will lead to improved monitoring of these patients and better outcomes.

Every person having radiotherapy will be assessed before their treatment by you – this is standard practice. If you agree to take part in this study, and have your patients recruited, we will



St. Luke's Radiation Oncology Network
at St. Luke's, Beaumont & St. James's Hospitals

conduct an extra patient assessment i.e. a GA. This will be done on two occasions, before your patient starts radiotherapy and three months after they finish treatment. The baseline assessment must be completed before the planning CT scan.

In addition, we will ask you some questions regarding the factors that influenced your final treatment decision, and also ask you to complete a decision regret scale at follow-up.

Who is carrying out this research study?

The research is being carried out within the St Luke's Radiation Oncology Network, by a radiation therapist from Trinity College Dublin and Principal Investigator Dr Charles Gillham.

What is the purpose of the study?

The purpose of the study is to gather information about the usefulness of GA, as well as its influence on treatment decisions, in predicting side effects from radiotherapy and/or chemotherapy, as well as the ability to help radiation oncologists make decisions about treatment.

How many people will take part in the study?

About 60 patients and 5 consultants will take part in the study.

Do I have to take part in the study?

No. It is up to you to decide whether or not to take part. If you decide to take part, you will be asked to sign the informed consent form and be given a copy of this information leaflet to keep. Giving consent also implies that you would like your patients to be contacted and provided with information on the study. Withdrawal of patients at any stage is at your discretion however, or you may deem certain patients unsuitable for recruitment.

If you decide to take part but later change your mind, you are free to withdraw at any time without giving a reason.

What do I have to do to take part in the study?

MERGE Study
PIL and Consent Form: AOD July 2014

If you decide to participate in our study, a radiation therapist will ask you questions during the initial stages of a patient's consultation process regarding the factors that influenced your treatment decision. You will be provided with the results of a GA procedure in order to inform this process.

You will also be asked to complete a decision regret scale at a patient's 3 month follow-up regarding the treatment decision, and whether or not you felt it was an appropriate choice of treatment plan.

Your patients will undergo GA at baseline and at 3 months follow-up.

What are the possible benefits from taking part in this study?

Participating in this study will help us to learn more about the needs of older patients receiving radiotherapy and/or chemotherapy, and the influence of GA on treatment decisions. This information will hopefully allow us to improve the radiation oncology service for older patients and may help medical staff in the future to more reliably and objectively assess the risk of side effects in older patients undergoing radiotherapy. Participating in the study may, however, be of no direct benefit to you.

What are the costs of taking part in this study?

There are no costs associated with taking part in this study

What are the risks?

There are no risks to your health involved in participating in this study.

What happens if I am injured because I took part in this study?

Every reasonable effort will be taken to ensure your safety and that of your patients during the course of this study. If you feel that you, or your patient, have been injured because of taking part in this study, please inform the study co-ordinator (Ms. Anita O'Donovan). You can do so in person or by contacting them at the numbers below.

Nothing that has been stated in this information leaflet or consent form changes your legal rights to seek to recover damages if you are injured because of taking part in this study.

St. Luke's Radiation Oncology Network
at St. Luke's, Beaumont & St. James's Hospitals

Will my taking part in this study be kept confidential?

Every effort will be made to keep your personal information private. The results of this study will be shared with other researchers and may be presented at conferences or published in a scientific journal, but your name or personal information will be not be used.

Who has reviewed and approved this study?

This study has been approved by the Research Ethics Committees at Saint Luke's Radiation Oncology Network and Trinity College Dublin.

Contacts for further information:

If you have any questions concerning the procedures of this study, or if any problems arise during the Clinical Research Study, you should contact the study coordinator:

Study Co-Ordinator: Ms. Anita O'Donovan **Telephone:** (01) 896 3149

Email: anita.odonovan@tcd.ie

MERGE Study
PIL and Consent Form: AOD July 2014

Appendix 16a: Consent Form (Patient)

St. Luke's Radiation Oncology Network
at St. Luke's, Beaumont & St. James's Hospitals

Informed Consent Form

Managing the Elderly in Radiotherapy using Geriatric AssEssment (MERGE)

Study Coordinator: Ms Anita O'Donovan
Hospital Name: Saint Luke's Radiation Oncology Network

Please initial boxes

1. I confirm that I have been given a copy of all 4 pages of the Patient Information Leaflet and Consent Form. I have read the Patient Information and Consent form or it has been read to me - or I have both read the Patient Information Leaflet and Consent form and also had it read to me. This information was explained to me and my questions were answered. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my medical care or legal rights being affected. ☐
3. I understand that relevant parts of my medical records may be seen by the SLH Research Ethics Committee and all organisations as listed in this consent form provided they agree not to disclose my name. ☐
4. I understand that data relating to me collected during this study will be processed and analysed as required by this research study and according to the Data Protection Act. ☐
5. I give my consent for the scans and information collected during this study to be used in future studies. ☐
6. I agree to take part in this study. ☐

St. Luke's Radiation Oncology Network
at St. Luke's, Beaumont & St. James's Hospitals

Name of Patient (Please Print)	Signature of Patient	Date
Name of Witness (Please Print) (IF APPLICABLE)	Signature of Witness	Date
Name of Investigator (Please Print)	Signature of Investigator	Date

MERGE Study
PIL and Consent Form: SLRON Version 1.0 31st January 2014 Anita O'Donovan

Appendix 16b: Consent Form (Radiation Oncologist)

St. Luke's Radiation Oncology Network
at St. Luke's, Beaumont & St. James's Hospitals

Consultant Informed Consent Form

Title: Managing the Elderly in Radiotherapy using Geriatric AssEssment (MERGE)

Investigators' Names: **Dr. Charles Gillham, Consultant Radiation Oncologist**
Ms. Anita O'Donovan, Discipline of Radiation Therapy, Trinity College Dublin
Investigators' Address: **St. Luke's Radiation Oncology Network at St James's Hospital**

BACKGROUND:

In this study, patients over the age of 70 will undergo an assessment called Geriatric Assessment, which will take approximately one hour in total. The information received from this assessment will be given to radiation oncologists as part of this study, who will be asked to provide information on how treatment decisions were made. Patient confidentiality will be ensured at all times.

DECLARATION:

I have read the study protocol for this project and I understand the contents. I have had the opportunity to ask questions and all my questions have been answered to my satisfaction. I freely and voluntarily agree to be part of this research study, though without prejudice to my legal and ethical rights. I understand that I may withdraw from the study at any time and I have received a copy of this agreement.

PARTICIPANT'S NAME: ……..

CONTACT DETAILS: ……..

PARTICIPANT'S SIGNATURE:……..

Date:……..

St. Luke's Radiation Oncology Network
at St. Luke's, Beaumont & St. James's Hospitals

Statement of investigator's responsibility: I have explained the nature and purpose of this research study, the procedures to be undertaken and any risks that may be involved. I have offered to answer any questions and fully answered such questions. I believe that the participant understands my explanation and has freely given informed consent.

INVESTIGATOR'S SIGNATURE:…… Date:……

MERGE Study
PIL and Consent Form: AOD July 2014

Appendix 17: TCD Ethical Approval MERGE Study

COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH

Dámh na nEolaíochtaí Slainte,
Foirgneamh na Ceimice
Colaiste na Tríonóide,
Baile Átha Cliath 2, Éire.

TRINITY COLLEGE DUBLIN

Faculty of Health Sciences,
Chemistry Building,
Trinity College,
Dublin 2, Ireland.
T:- +353 (0)1 8964255

Ms.Anita O'Donovan,
Discipline of Radiation Therapy,
Trinity Centre for Health Sciences,
St.James's Hospital
Dublin 8.

9th May

Re: Managing the Elderly in Radiotherapy using Geriatric AssEssment (MERGE)

Dear Applicant (s),

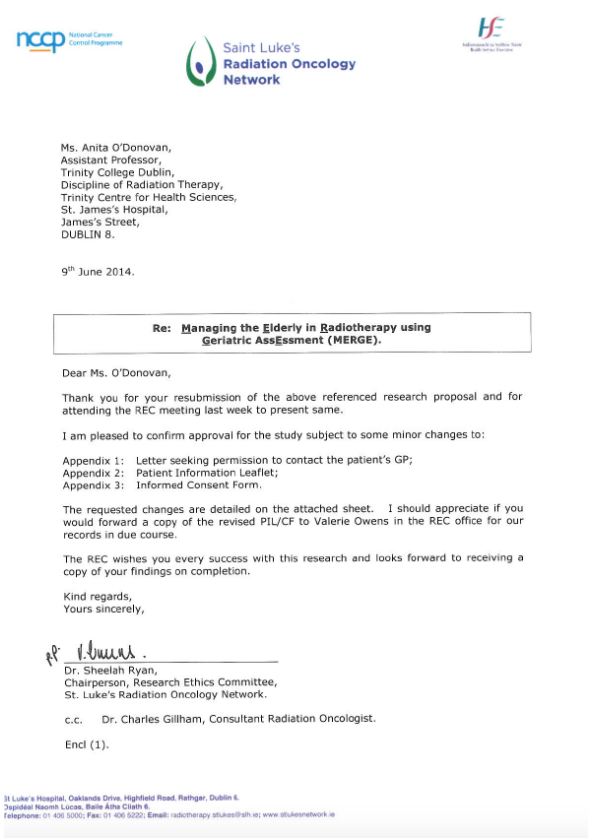
Further to a meeting of the Faculty of Health Sciences Ethics Committee held in February 2014, we are pleased to inform you that the above project has been approved without further audit.

Yours sincerely,

pp. Sonya mc Connon

Dr. Ruth Pilkington
Chairperson
Faculty Research Ethics Committee

Appendix 18: SLRON Ethical Approval MERGE Study



ncgp National Cancer Control Programme

Saint Luke's Radiation Oncology Network

Ms. Anita O'Donovan,
Assistant Professor,
Trinity College Dublin,
Discipline of Radiation Therapy,
Trinity Centre for Health Sciences,
St. James's Hospital,
James's Street,
DUBLIN 8.

9th June 2014.

Re: Managing the Elderly in Radiotherapy using Geriatric AssEssment (MERGE).

Dear Ms. O'Donovan,

Thank you for your resubmission of the above referenced research proposal and for attending the REC meeting last week to present same.

I am pleased to confirm approval for the study subject to some minor changes to:

Appendix 1: Letter seeking permission to contact the patient's GP;
Appendix 2: Patient Information Leaflet;
Appendix 3: Informed Consent Form.

The requested changes are detailed on the attached sheet. I should appreciate if you would forward a copy of the revised PIL/CF to Valerie Owens in the REC office for our records in due course.

The REC wishes you every success with this research and looks forward to receiving a copy of your findings on completion.

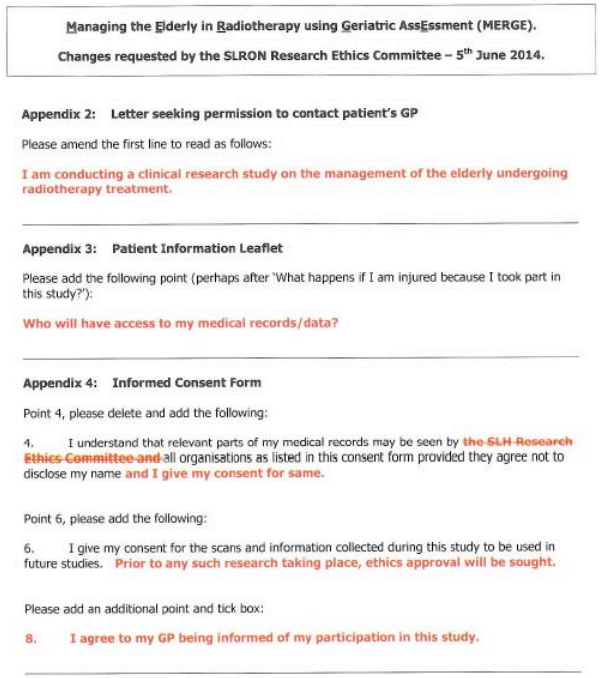
Kind regards,
Yours sincerely,

Dr. Sheelah Ryan,
Chairperson, Research Ethics Committee,
St. Luke's Radiation Oncology Network.

c.c. Dr. Charles Gillham, Consultant Radiation Oncologist.

Encl (1).

St Luke's Hospital, Oaklands Drive, Highfield Road, Rathgar, Dublin 6.
Ospidéal Naomh Lúcas, Baile Átha Cliath 6.
Telephone: 01 406 5000; Fax: 01 406 5020; Email: radiotherapy.stukes@slh.ie; www.stukesnetwork.ie



Managing the Elderly in Radiotherapy using Geriatric AssEssment (MERGE).

Changes requested by the SLRON Research Ethics Committee – 5th June 2014.

Appendix 2: Letter seeking permission to contact patient's GP

Please amend the first line to read as follows:

I am conducting a clinical research study on the management of the elderly undergoing radiotherapy treatment.

Appendix 3: Patient Information Leaflet

Please add the following point (perhaps after 'What happens if I am injured because I took part in this study?'):

Who will have access to my medical records/data?

Appendix 4: Informed Consent Form

Point 4, please delete and add the following:

4. I understand that relevant parts of my medical records may be seen by ~~the SLH Research Ethics Committee and~~ all organisations as listed in this consent form provided they agree not to disclose my name and I give my consent for same.

Point 6, please add the following:

6. I give my consent for the scans and information collected during this study to be used in future studies. Prior to any such research taking place, ethics approval will be sought.

Please add an additional point and tick box:

8. I agree to my GP being informed of my participation in this study.

Appendix 19: QIC Table for GEE analysis and correlation matrix selection in Chapter 5

Variable	Correlation Matrix	p	QIC	QIC_u
ADLs	Exchangeable	5	7812.285	7806.105
	Unstructured	5	7812.182	7805.999
	Independent	5	7811.242	7805.082
	Autoregressive	5	7812.178	7805.945
	Stationary	5	7812.914	7806.658
	Non-stationary	5	7812.622	7806.356
IADLs	Exchangeable	5	7563.508	7555.859
	Unstructured	5	7563.380	7555.766
	Independent	5	7563.241	7555.644
	Autoregressive	5	7564.001	7556.101
	Stationary	5	7564.441	7556.205
	Non-stationary	5	7564.453	7556.205
History of falls	Exchangeable	5	17795.637	17791.738
	Unstructured	5	17795.577	17791.689
	Independent	5	17795.361	17791.467
	Autoregressive	5	17795.621	17791.622
	Stationary	5	17795.676	17791.626
	Non-stationary	5	17795.677	17791.626
TUG	Exchangeable	5	1914046.722	1914048.371
	Unstructured	5	1914045.593	1914047.266
	Independent	5	1914044.478	1914046.134
	Autoregressive	5	1914445.459	1914446.906
	Stationary	5	1914446.167	1914447.622
	Non-stationary	5	1914465.424	1914466.905
Chronic conditions	Exchangeable	5	7013.879	7004.671
	Unstructured	5	7724.566	7714.369
	Independent	5	6970.481	6960.847
	Autoregressive	5	6440.925	6431.702
	Stationary	5	5531.202	5520.903
	Non-stationary	5	5548.294	5537.953
Social connectedness	Exchangeable	5	13241.744	13228.488
	Unstructured	5	13237.187	13223.996
	Independent	5	13175.580	13162.133
	Autoregressive	5	13185.139	13170.047
	Stationary	5	-	-
	Non-stationary	5	-	-
Polypharmacy	Exchangeable	5	17207.951	17196.840
	Unstructured	5	17206.967	17195.925
	Independent	5	17205.895	17194.698
	Autoregressive	5	17210.910	17199.367
	Stationary	5	17298.194	17277.569
	Non-stationary	5	17298.025	17277.418
Depression	Exchangeable	5	9250.699	9245.199
	Unstructured	5	9250.408	9244.941
	Independent	5	9241.537	9235.850
	Autoregressive	5	9260.330	9253.542
	Stationary	5	9266.697	9259.702
	Non-stationary	5	9266.159	9259.165
Cognition	Exchangeable	5	3744.180	3736.408
	Unstructured	5	3743.942	3736.078
	Independent	5	3743.320	3735.429
	Autoregressive	5	3744.458	3735.955
	Stationary	5	3744.669	3735.842
	Non-stationary	5	3744.792	3735.966
Quality of Life	Exchangeable	5	378372.831	378363.788
	Unstructured	5	377883.089	377874.130
	Independent	5	376428.489	376418.681
	Autoregressive	5	377482.584	377470.008
	Stationary	5	380240.116	380202.297
	Non-stationary	5	379612.807	379573.881

Note: lowest QIC is highlighted in bold
- indicates convergence not achieved

Appendix 20: Generalised Estimating Equations Methodology

Unlike a standard regression, a GEE model requires a number of specifications to be made at the analysis stage. The first of these is to specify the dependent variable distribution i.e. normal, inverse normal, binomial, Poisson, negative binomial and Gamma distributions. For many of the dichotomous variables created in the current study, a binomial function was chosen, for example.

The second option to be chosen for GEE analysis is the link function i.e. the transformation (if any) of the dependent variable. This is determined by the distribution of the dependent variable under investigation. The basic link function is the identity link function, which involves no transformation of the dependent variable, and this is reserved for normally distributed data. The logit link is used for binary variables, while the Poisson link function is usually used for count data.

The next option in the GEE methodology involves choosing the correct working correlation structure, as follows:

1. Independent: This is considered the simplest correlation structure. It assumes all measurements are independent.

2. Exchangeable: Assumes that the correlations between the dependent variables at different points in time in a cluster or subject are all the same. For studies that involve more than two measurements on a subject over time, the exchangeability assumption is considered too limiting (31).

3. Autoregressive (AR1): This structure assumes correlations to be exponentially related to the time between measures and is appropriate for longitudinal repeated measures data i.e. more than two timepoints.

4. Unstructured: This structure is considered the most complicated and assumes a saturated free specification of correlation coefficients with no constraints and is appropriate for longitudinal repeated measures data.

5. Stationary: Assumes constant correlations within equal time intervals only.

6. Nonstationary: Assumes non-constant correlations within equal time intervals only.

7. Fixed: This is a special case, used in cases when the correlations among subjects are already known, usually from a previous large study. The matrix then includes exact specifications of correlations. This was not used for the current study.

Choosing the correct time interval between measurements is important as it may affect the correlation structure (32). This is more of a concern where time intervals are unequally spaced. For the current study, a time interval of two years between each wave was assumed. Please see table below for a summary of the characteristics allowed for each correlation structure, which has an influence on GEE model selection. Panels are considered to be balanced if each has the same number of observations, which is unlikely in longitudinal data analysis, and all models allow unbalanced structures. Panels are considered equally spaced if the time intervals between observations is approximately constant. Gaps are allowed in most correlation structures, however some do not allow for missing observations. It is possible to override these requirements in Stata, using the "force" function. However, this wasn't used in the current analysis, as other options were available. An exchangeable correlation structure wasn't chosen as it's not considered valid for more than two observations on the same individual, as detailed above.

Correlation	Characteristics allowed		
	Unbalanced	Unequal spacing	Gaps
Independent	Yes	Yes	Yes
Exchangeable	Yes	Yes	Yes
Autoregressive k	Yes (*)	No	No
Unstructured	Yes	Yes	Yes
Stationary k	Yes (*)	No	No
Nonstationary k	Yes (*)	No	No
Fixed	Yes	Yes	Yes

*All panels must have k+1 observations

Correlation structures and characteristics allowed

Interpretation of Tables 5.6 and 5.7

Logit link:
The odds ratio of reporting a positive/worse outcome at follow-up vs baseline in the cancer group is exp(estimate) times the odds ratio of having an event at follow-up vs baseline in the control group. Exp(estimate) = (odds follow-up cancer group/odds baseline cancer group)/(odds follow-up group/odds baseline control group). For covariates, interpretation is similar, comparing the listed category with reference category (sex, education) or the effect of one unit increase in age.

Log link:
Ratio of expected number of positive items and number of chronic conditions respectively at follow-up vs baseline in the cancer group is exp(estimate) times the same ratio in the control group. Exp(estimate) = (average number follow-up cancer group/average number baseline cancer group)/ (average number follow-up control group/average number baseline control group). For covariates, interpretation is similar, comparing the listed category with reference category (sex, education) or the effect of one unit increase in age

Appendix 21: Benjamini-Hochberg False Discovery Rate Calculations (Chapter 5)

false discovery rate	0.25

Variables	↓ P-values ↓	Rank	Benjamini-Hochberg significance	Benjamini-Hochberg P-value
T0 polyph	0.001	**1**	**significant**	0.003676471
wave 1 chronic	0.001	**1**	**significant**	0.003676471
wave 1 age	0.001	**1**	**significant**	0.003676471
wave1 polyph	0.001	**1**	**significant**	0.003676471
long age	0.001	**1**	**significant**	0.003676471
Multiv GEE ADL	0.001	**1**	**significant**	0.003676471
Multiv GEE IADL	0.001	**1**	**significant**	0.003676471
Multiv GEE TUG	0.001	**1**	**significant**	0.003676471
Multiv GEE falls	0.001	**1**	**significant**	0.003676471
Multiv GEE chronic	0.001	**1**	**significant**	0.003676471
Multiv GEE social	0.001	**1**	**significant**	0.003676471
Multiv GEE polyph	0.001	**1**	**significant**	0.003676471
Multiv GEE depression	0.001	**1**	**significant**	0.003676471
Multiv GEE cognition	0.001	**1**	**significant**	0.003676471
Multiv GEE QoL	0.001	**1**	**significant**	0.003676471
Univ GEE polyph	0.002	2	**significant**	0.007352941
long sex	0.003	3	**significant**	0.011029412
wave 1 falls	0.005	4	**significant**	0.014705882
wave 1 sex	0.02	5	**not significant**	0.018382353
Univ GEE chronic	0.02	5	**not significant**	0.018382353
wave 1 ADL	0.03	6	**not significant**	0.022058824
T2 QoL	0.03	6	**not significant**	0.022058824
T0 falls	0.07	7	**not significant**	0.025735294
wave 1 QoL	0.08	8	**not significant**	0.029411765
T1 chronic	0.08	8	**not significant**	0.029411765
T0 cognition	0.09	9	**not significant**	0.033088235

wave 1 IADL	0.1	10	**not significant**	0.036764706
T2 chronic	0.1	10	**not significant**	0.036764706
T0 IADL	0.12	11	**not significant**	0.040441176
wave 1 marital status	0.13	12	**not significant**	0.044117647
T1 cognition	0.14	13	**not significant**	0.047794118
T2 IADL	0.14	13	**not significant**	0.047794118
T1 TUG	0.15	14	**not significant**	0.051470588
T2 social	0.16	15	**not significant**	0.055147059
T2 depression	0.19	16	**not significant**	0.058823529
T0 depression	0.2	17	**not significant**	0.0625
T1 falls	0.23	18	**not significant**	0.066176471
T1 polyph	0.24	19	**not significant**	0.069852941
long education	0.27	20	**not significant**	0.073529412
T2 polyph	0.27	20	**not significant**	0.073529412
T2 ADL	0.28	21	**not significant**	0.077205882
T0 TUG	0.29	22	**not significant**	0.080882353
Univ GEE social	0.29	22	**not significant**	0.080882353
T1 ADL	0.31	23	**not significant**	0.084558824
T1 social	0.34	24	**not significant**	0.088235294
Univ GEE depression	0.35	25	**not significant**	0.091911765
wave 1 cognition	0.36	26	**not significant**	0.095588235
Univ GEE IADL	0.4	27	**not significant**	0.099264706
T2 cognition	0.42	28	**not significant**	0.102941176
Univ GEE cognition	0.43	29	**not significant**	0.106617647
T0 chronic	0.44	30	**not significant**	0.110294118
T0 QoL	0.44	30	**not significant**	0.110294118
wave 1 social	0.45	31	**not significant**	0.113970588
Univ GEE QoL	0.48	32	**not significant**	0.117647059
wave 1 TUG	0.53	33	**not significant**	0.121323529
T2 TUG	0.53	33	**not significant**	0.121323529
long marital status	0.58	34	**not significant**	0.125
Univ GEE TUG	0.61	35	**not significant**	0.128676471
wave 1 education	0.62	36	**not significant**	0.132352941
T0 social	0.65	37	**not significant**	0.136029412
Univ GEE ADL	0.66	38	**not significant**	0.139705882

T1 IADL	0.68	39	**not significant**	0.143382353
T1 QoL	0.69	40	**not significant**	0.147058824
wave 1 depression	0.71	41	**not significant**	0.150735294
T2 falls	0.72	42	**not significant**	0.154411765
T1 depression	0.83	43	**not significant**	0.158088235
Univ GEE falls	0.9	44	**not significant**	0.161764706
T0 ADL	0.96	45	**not significant**	0.165441176

Appendix 22: Benjamini-Hochberg False Discovery Rate Calculations (Chapter 6)

false discovery rate	0.25			
Variables	**↓ P-values**	**Rank**	**Benjamini-Hochberg significance**	**Benjamini-Hochberg P-value**
cs age	0.001	**1**	**significant**	0.009259259
Frwghtloss	0.001	**1**	**significant**	0.009259259
Frslowtug	0.001	**1**	**significant**	0.009259259
FI	0.001	**1**	**significant**	0.009259259
Morley Resist	0.001	**1**	**significant**	0.009259259
Morley ambulation	0.001	**1**	**significant**	0.009259259
Morley weight loss	0.001	**1**	**significant**	0.009259259
Morley FRAIL scale	0.001	**1**	**significant**	0.009259259
CS Regression FI	0.001	**1**	**significant**	0.009259259
CS Regression Morley	0.001	**1**	**significant**	0.009259259
Long age	0.001	**1**	**significant**	0.009259259
long regression Fried	0.001	**1**	**significant**	0.009259259
long regression FI	0.001	**1**	**significant**	0.009259259
long regression Morley	0.001	**1**	**significant**	0.009259259
Fried	0.005	**2**	**significant**	0.018518519
Morley illness	0.005	2	**significant**	0.018518519
Frlowact	0.018	3	**significant**	0.027777778
cs sex	0.02	4	**significant**	0.037037037
Long sex	0.03	5	**significant**	0.046296296
CS Regression Fried	0.05	6	**significant**	0.055555556
Frlowgrip	0.08	7	**not significant**	0.064814815
cs marital status	0.13	8	**not significant**	0.074074074
Long edu	0.36	9	**not significant**	0.083333333
Morley fatigue	0.52	10	**not significant**	0.092592593
Long marital status	0.6	11	**not significant**	0.101851852
cs education	0.62	12	**not significant**	0.111111111
Frexhaust	0.76	13	**not significant**	0.12037037

Appendix 23: Prevalence of frailty for those aged ≥65 and <65

Operationalisation	Group	Cancer group proportion % [95% CI]	Control group proportion % [95% CI]	Difference between both groups (p value)
Fried	**Prefrail**	44.46 [36.92,52.27]	43.86 [41.50,46.25]	0.75
	Frail	10.21 [6.30,16.12]	8.63 [7.26,10.22]	
Frailty Index	**Prefrail**	41.06 [35.28,47.11]	37.19 [35.45,38.97]	<0.001**
	Frail	32.95 [27.32,39.11)	23.58 [22.01,25.22]	
Morley	**Prefrail**	32.99 [27.44,39.07]	27.49 [25.86,29.19]	0.006
	Frail	7.83 [4.99,12.09]	4.49 [3.76,5.38]	

Prevalence of frailty for all three measures and participants aged ≥65 (adjusted for age, sex and education)

Operationalisation	Group	Cancer group proportion % [95% CI]	Control group proportion % [95% CI]	Difference between both groups (p value)
Fried	**Prefrail**	34.61 [27.07,43.00]	26.90 [25.32,28.55]	0.09
	Frail	2.72 [1.00,7.17]	1.98 [1.52,2.58]	
Frailty Index	**Prefrail**	28.49 [22.71,35.07]	23.92 [22.64,25.24]	0.01
	Frail	11.71 [7.95,16.91]	7.38 [6.61,8.22]	
Morley	**Prefrail**	26.18 [20.55,32.71]	17.90 [16.76,19.10]	0.0003
	Frail	4.75[2.47,8.95]	2.05[1.64,2.54]	

Prevalence of frailty for all three measures and participants aged<65 (adjusted for age, sex and education