Modifiable Risk Factors for dementia, awareness of, and barriers to, brain health behaviours

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List of Abbreviations

AChE-I: Acetylcholinesterase inhibitor
AD: Alzheimer's Disease
ANOVA: Analysis of Variance
AOR: Adjusted odds ratio
ARHL: Age-related hearing loss
BMI: Body mass index
CAIDE: Cardiovascular Risk factors, Ageing, and Dementia
CI: Confidence interval
DALYs: Disability adjusted life years
DEIS: Delivering Equality of Opportunity in Schools
EU: European Union
FDA: Federal Drug Administration
FLBHIS: Five Lives Brain Health Ireland Survey
GDP: Gross Domestic Product
GDPR: General data Protection Regulation
iADRS: integrated Alzheimer's Disease rating Scale
IBM: International Business Machines
LBCHQ: Lifestyle Barriers for Cognitive Health Questionnaire
LMICs: Low and Middle Income Countries
MCI: Mild Cognitive Impairment
NIH: National Institutes of Health
OR: Odds Ratio
SBP: Systolic blood pressure
SES: Socioeconomic status
SPSS: Statistical Package for Social Sciences
TBI: Traumatic brain injury
TDR: Transdisciplinary research
WHO: World Health Organisation
YO: Years old

Abstract

Introduction:

Dementia is common and in many societies, underdiagnosed. The commonest cause of dementia globally is Alzheimer's disease. Dementia prevalence is increasing globally. It is estimated that the number of people living with dementia globally will increase from 57.4 million people in 2019 to 152.8 million in 2050. Whilst pharmacological agents for treating dementia are limited, recent years have seen an increasing focus on drug trials for Alzheimer's disease. As of January 2023, there were 141 agents in 187 clinical trials for Alzheimer's Disease. A handful of disease modifying agents are now at advanced stage of clinical development. In addition to disease modification, an increasing body of literature supports the potential for dementia prevention. It is now recognised that 12 modifiable risk factors account for 40% of dementias globally. The life-course model of brain health highlights that it is never too early and never too late to consider reducing one's dementia risk. Whilst evidence supports the benefits of so called 'brain health behaviours', the adoption of such habits is not widespread. Knowledge regarding dementia risk factors is variable and barriers to brain health behaviours numerous. In this context, the aims of this project were as follows: 1) to examine prevalence of modifiable risk factors for dementia amongst the study cohort, 2) to investigate awareness of specific modifiable risk factors for dementia, 3) to investigate whether exposure to dementia risk factors varies between groups, 4) to investigate whether awareness for modifiable risk factors varies between groups, 5) to assess barriers to risk reduction behaviours, 6) to investigate the distribution of barriers across sociodemographic factors.

Methods:

1. A cross-sectional survey was distributed online among an Irish non-patient population. Inclusion criteria comprised those aged ≥50 years old. Those who had a history of dementia, or who had worked in the healthcare sector were excluded. A pilot version of the survey was undertaken in January 2022 and the final survey was subsequently administered in February 2022.

2. The survey was adapted from the Lifestyle Barriers for Cognitive Health Questionnaire and captured the following information: 1) Sociodemographic factors; 2) Exposure to, as well as knowledge of modifiable risk factors for dementia; 3) Barriers to brain health behaviours; 4) Participants' perceptions regarding potential for dementia prevention, and risk reduction (Likert scale).
3. Analyses were conducted using StataMP 17.0 for Mac or IBM SPSS Statistics software for Windows (version 29). Frequency counts and percentages were used to show the sociodemographic characteristics and rates of exposure to modifiable risk. To investigate differences in awareness levels for modifiable risk factors across groups, 2-way mixed ANOVAs with Greenhouse-Geisser correction were performed. Binary logistic regression models were used to investigate the associations between exposure to modifiable risk factors for dementia, and sociodemographic factors. Binary logistic regression analyses were adjusted for potential confounding factors such as household income and educational attainment, as well as for sex and age depending on the predictor variable used in the model.
4. Z-tests with a Bonferroni correction for multiple comparisons were utilised to examine distribution of barriers between groups. A two-step cluster analysis was used to classify participants in distinct groups based on age, gender, education and household income. The distance measure was log-likelihood and the clustering criterion was Schwartz's Bayesian Criterion.

Results:

Sample characteristics: The study population comprised 551 participants (50.3% male; 49.6% female). Mean age was 59.7 years, with the majority of the sample ranging between 50-59 years of age (54.3%). 98.9% of respondents were of white ethnicity. Most participants were educated to secondary school level or higher (98.2%), were employed or self-employed (52.2%), and cohabited with one or more persons (74.4%).

Exposure to modifiable risk factors: Modifiable risk factors for dementia were prevalent with the commonest exposures as follows: being overweight (60.6%), having a lack of social engagement (54.9%), physical inactivity (42.7%), hypertension (36.7%), and self-assessed poor sleep quality (33.5%).

Impact of sociodemographic factors on exposure to modifiable risk factor exposure: Male gender was significantly associated with an increased likelihood to report multiple risk factors, namely excess alcohol consumption (AOR 3.127, CI 1.953 - 5.007), smoking (AOR 1.618, CI 1.065 - 2.457), diabetes (AOR 2.141, CI 1.097 - 4.176) and low mental stimulation (AOR 1.796, CI 1.171 - 2.754). With increasing age, participants were less likely to report multiple risk factors. Relative to the secondary school education group, participants educated to undergraduate and postgraduate level were significantly less likely to report smoking (AOR 0.468, CI 0.296-0.738; AOR 0.199, CI 0.076-0.520, respectively).

Awareness of modifiable risk factors for dementia: Across the total sample, head injury (90.9%, n = 500), low mental stimulation (85.3%, n = 469) and excess alcohol consumption (77.8%, n = 428) were the three most commonly recognised modifiable risk factors for dementia. Hearing impairment had the poorest recognition (34.7%, n = 191).

Impact of sociodemographic actors on awareness of modifiable risk factors for dementia: Awareness of low mental stimulation as a dementia risk factor was higher in the female group (p=.05). Two-way mixed ANOVA with Greenhouse-Geisser correction did not demonstrate a significant interaction effect between risk factors and age on awareness $F(21.49,5879.15) = 1.16$, $p = 0.279$. With regard to education, awareness was significantly greater in both university groups (undergraduate and postgraduate) relative to the secondary education group for multiple risk factors, namely diabetes, air pollution, sleep, diet, low social interaction, and low mental stimulation (p=.01). Awareness of hearing loss, hypertension, and depression were significantly greater in the university postgraduate group when compared to the secondary school group (p=.05).

Barrier prevalence: Various practical barriers, and lack of motivation were the most prevalently cited barriers across multiple risk factors. Practical barriers were most commonly reported, with at least one practical barrier reported by 84.2% of the study population ($n = 464$). One or more emotional barriers were reported by 83.5% of the population ($n = 460$), motivational barriers by 62.6% ($n = 345$), and social barriers by 48.8% ($n = 269$). Knowledge barriers were least commonly reported with 34.7% of participants reporting one or more knowledge barriers ($n = 191$).

Association between sociodemographic factors, risk factor exposure, and barriers to individual risk factors: Multiple individual effects were noted between sociodemographic factors and exposure to individual barriers. Cluster analysis revealed six clusters. Multiple risk factors disproportionately impact those of lower educational status (clusters A, C, and E). Secondary educated males (cluster E) were more likely to report exposure to excess alcohol when compared to other clusters, with the exception of university educated males (cluster F). They were also more likely to report smoking when compared to other clusters, with the exception of secondary educated females (cluster A). Secondary educated females (cluster A) were more likely to report poor sleep when compared to older males (cluster B), Secondary-educated, higher income (cluster C), and Uni-educated males (cluster F).

Discussion:

Modifiable risk factors for dementia were common among the study cohort. The distribution of exposure to modifiable risk factors for dementia was unequal across gender, age and education groups. Awareness levels vary considerably across risk factors, gender, and education level. A majority of the study cohort were unaware of the significance of certain risk factors. In this study, clusters defined by lower socio-economic status were disproportionately impacted by multiple risk factors, and several barriers were unequally distributed across socioeconomic groups. Our study highlights the individualised nature of risk factor profiles, and barriers to brain health behaviours, thereby underlining the utility of devising personalised risk reduction plans. These findings highlight the importance of individual risk profiling and tailoring interventions towards an individual's specific needs. Nonetheless, individualised assessment and primary prevention in the context of specialist brain health clinics is unlikely to be impactful on a population level in the short to medium term. Novel health promotion and risk reduction approaches must be prioritised with public health interventions, rooted in the sociocultural contexts of their intended recipients, targeting relevant barriers to risk reduction behaviours.

Lay Abstract:

Dementia is a common condition and is thought to affect more than 50 million people around the world. In the next 25 years, the number of people living with dementia will climb to more than 150 million. It is increasingly recognised that common lifestyle risk factors such as being overweight, and having high blood pressure increase dementia risk. 40% of dementia cases around the world could be prevented if 12 different risk factors were tackled effectively. Many people are unaware that dementia can be prevented. In many cases, barriers prevent people from engaging in healthy behaviours. In this research study we set out to answer the following questions: 1) How common are lifestyle risk factors for dementia, 2) Are people aware of particular risk factors, 3) How do factors such as age, gender, and education impact knowledge and exposure, 4) What barriers stop people engaging in healthy behaviours which would reduce dementia risk.

To answer the questions set out above, a survey was distributed online to a large group of people in early 2022. The survey contained many questions related to dementia risk factors and reasons why people might not be able to engage in healthy behaviours. A computer programme was used to perform different tests to answer our questions

551 people with an average age of 59.7 years, took part in the study. Most people were educated to secondary school level or higher (98.2%), and were employed or self-employed (52.2%). Dementia risk factors were common in people who completed the survey. Broadly speaking, risk factors were more common among men, older people, and people with lower levels of education. Some risk factors, such as head injury, and low mental stimulation, were recognised by a majority of those who took part whereas other risk factors such as hearing loss were recognised only by a minority. Practical barriers and lack of motivation were most commonly reported in the study. People of lower socioeconomic status were more likely to report having many risk factors.

Risk factors for dementia were common and often under-recognised in this study. Both having a risk factor, and being aware of risk factors, varied depending on people's sex, age, and education level. People of lower socio-economic status were more likely to report multiple risk factors. This study has emphasised the importance of developing individualised prevention plans to reduce people's dementia risk. Public-health campaigns should target those who are most at risk and should take into account relevant barriers.

Hypothesis and aims:

The principal hypothesis of this study is that modifiable risk factors for dementia are common and under-recognised. It was further hypothesised that barriers to brain health are likely to be numerous and individualised.

Aims:

1. To investigate the prevalence of modifiable risk factors for dementia in a non-patient population of Irish older adults.

2. To investigate awareness of modifiable risk factors for dementia.

3. To investigate whether exposure to dementia risk factors varies depending on factors such as age, gender, and education level.

4. To investigate whether awareness for modifiable risk factors varies depending on factors such as age, gender, and education level.

5. To assess barriers to risk reduction behaviours.

6. To investigate the distribution of barriers across sociodemographic factors.

Value of Research

This research is of considerable value in a national, and International context. Dementia prevention is a global public health imperative. If successful population based strategies targeting modifiable risk factors for dementia are to be devised, quantification of risk factor prevalence, and awareness are essential. This research has demonstrated that modifiable risk factors for dementia are prevalent in Ireland. Significantly, whilst modifiable risk factors are prevalent, knowledge and awareness of their import are not. Renewed efforts to increase awareness of individual dementia risk factors must be prioritised.

Hithertofore, a detailed exploration of barriers to brain health behaviours had been lacking. Herein, we demonstrate that barriers are complex and highly individualised. Collaborative development of personal prevention plans which account for individual risk factor profiles as well as barriers to brain health should be considered in the outpatient setting. From a broader public health perspective, the finding that cohorts of lower socio-economic status are disproportionately impacted by multiple risk factors will be central in targeting future public health messaging.

Outputs

Publications:

1. **Dukelow T**, Lawrence EG, Jacobson L, Vassilev P, Koychev I, Muhammed K, Kennelly SP. Modifiable risk factors for dementia, and awareness of brain health behaviors: Results from the Five Lives Brain Health Ireland Survey (FLBHIS). Front Psychol. 2023 Jan 12;13:1070259. doi: 10.3389/fpsyg.2022.1070259. PMID: 36710802; PMCID: PMC9879702.

2. **Dukelow T**, Vassilev P, Lawrence EG, Jacobson L, Koychev I, Muhammed K, Kennelly SP. Barriers to brain health behaviours: results from the Five Lives Brain Health Ireland Survey. Front Psychol. 2023 Aug 24;14:1101514. doi: 10.3389/fpsyg.2023.1101514. PMID: 37691817; PMCID: PMC10483831.

Presentations:

1. **Dukelow T**. Trinity College Dublin, Postgraduate Research (PGR) Day, 14/04/2023.

2. **Dukelow T.** Dementia Research Network of Ireland(DRNI); Research presented as part of online Brain health Webinar Series, 15/11/2024.

Awards:

3. Medal winner, Trinity College Dublin, Postgraduate Research (PGR) Day, 14/04/2023.

Chapter 1 - Dementia

1.1 Dementia

Dementia is an umbrella term encompassing several conditions, the hallmark of which is a progressive deterioration in cognition and function (McKhann et al., 2012). The condition is not newly recognised, and references to its existence can be traced back several hundred years.

The word dementia was first used by Saint Isidore in approximately 600AD in his book *Etymologies* (Yang et al., 2016). Published almost one millennium later, de Pratis' '*De cerebri morbis*' included a chapter on the subject (Roman C, 1999). The syndrome of post-stroke vascular dementia was subsequently described by Thomas Willis in his work *De Anima Brutorum* (Willis T, 1672). Advances in the fields of clinical medicine and neuropathology at the beginning of the 20th century saw correlation between the histological finding of senile plaques and the clinical syndrome of dementia. This disease, named after German psychiatrist and neuropathologist Alois Alzheimer, is now the commonest cause of dementia globally (Li et al., 2022).

1.2 Dementia epidemiology

Dementia is common and, in many societies, underdiagnosed (Gauthier et al., 2021). The aetiologies of dementia are multitudinous with Alzheimer's disease representing the commonest cause globally (Li et al., 2022). The last 3 decades have seen a significant increase in dementia prevalence globally. The number of people living with dementia has more than doubled between 1990 and 2016, increases largely attributable to population growth and ageing (GBD, 2016). Global dementia prevalence is projected to continue to increase. It is estimated that the number of people living with dementia globally will increase from 57.4 million people in 2019 to 152.8 million in 2050 (GBD, 2019). Although the rate of dementia incidence has been declining in recent years in some western societies (Wolters et al., 2020; Prince et al., 2016), global dementia prevalence is increasing (Nichols et al., 2022). In Ireland, there are approximately 65000 people living with dementia, a figure projected to increase to 141,200 by 2050 (Alzheimer Europe., 2019)

Gender differences in dementia epidemiology are prominent. Alzheimer's Disease is recognised to occur more commonly in women. A meta-analysis suggests an Alzheimer's Disease incidence of 7.02 per 1000 person years in men and 13.25 per 1000 person years in

women (Niu et al., 2016). Gender differences in dementia incidence are attributable in part to greater longevity in those of female sex. Age is the biggest risk factor for the development of AD and females live longer than males (Nebel et al., 2018).

Dementia accounts for a significant proportion of health and social care expenditure. The bulk of costs are borne by high income countries (Wimo et al., 2017). Spending related to dementia is increasing. By 2050 it is estimated that dementia-attributable spending globally will reach 1.6 trillion dollars (Velandia et al, 2022). Much of the cost associated with dementia relates to informal care (Wimo et al., 2018). The global contribution of informal carers is estimated to equate to more than 40 million full-time workers (Wimo et al., 2018). In Ireland, the estimated annual cost of dementia was exceeded €1.69 billion in 2010. Almost half of this cost was attributable to informal care (Connolly et al., 2014).

Dementia has assumed an increasingly prominent role in public health policy globally. The WHO Global action plan on the public health response to dementia seeks to improve the lives of people and families living with dementia, as well as decreasing the societal impact of the condition (WHO, 2017). Several major countries have dementia strategies attuned to takin early action to mitigate disease burden (Hampel et al., 2022). Many LMICs do not, however, have a national dementia plan (Vinay & Biller-Andorno, 2023).

1.3 Alzheimer's disease:

In 1906, German psychiatrist and neuropathologist Alois Alzheimer undertook a brain biopsy in a patient that he had diagnosed with 'presenile dementia'. The patient, Ms. Auguste Deter, had died after a 5-year history of progressive cognitive decline (Yang et al., 2016). Biopsy results demonstrated diffuse atrophy and 'particular changes in cortical cell clusters' (Soria-Lopez et al., 2019). Delineation of the molecular structure of the proteins in question was not achieved until many decades later, when, in the 1980s, beta-amyloid was isolated from the twisted beta-pleated sheet fibrils associated with Alzheimer's disease (Glenner & Wong, 1984). The same decade saw formalisation of dual clinical-pathologic diagnostic criteria (McKhann et al., 1984). Diagnostic criteria subsequently evolved to encompass the spectrum of disease as well as enshrining biomarkers as being central to defining the disease (Dubois et al., 2007; Dubois et al., 2010; Jack et al, 2018). Guidelines and diagnostic

criteria have been developed by 2 principal groups, namely the National Institute on Aging-Alzheimer's Association (NIA-AA) and the International Working Group (IWG). The NIA-AA criteria posits Alzheimer's Disease as a biological construct, irrespective of symptomatology (Jack et al., 2018), whereas the IWG recommends that the diagnosis of Alzheimer's disease only be imparted to those with coexistent biomarker positivity and an Alzheimer's disease phenotype (Dubois et al., 2021).

Since Glenner and Wong isolated a 'novel cerebrovascular amyloid protein' in the early 1980s (Glenner & Wong, 1984), considerable attention has been devoted to the Amyloid Hypothesis of Alzheimer's Disease pathogenesis. The amyloid hypothesis posits that pathological accumulation of Aβ is central to AD development (Selkoe & Hardy., 2016). In normal circumstances, Aβ undergoes proteolytic cleavage from the larger Amyloid Precursor Protein and is thereafter rapidly removed (Kametani & Hasegawa, 2018). It is thought that abnormal Aβ production may set in train a series of events, ultimately leading to neuronal loss through the accumulation of neurofibrillary tangles and amyloid plaques.

As discussed below, burgeoning evidence from a new generation of disease modifying drugs, lends support to the amyloid hypothesis. The tau hypothesis differs, positing the notion that abnormal phosphorylation of tau, a microtubule binding protein, ultimately precipitates aggregation of complex monomers and neurofibrillary tangles which may cause cell death (Liu et al., 2019). Competing and complementary hypotheses are numerous and a detailed explanation of each is beyond the scope of this work. They include the cholinergic, neurovascular, and inflammatory hypotheses (Liu et al., 2019).

1.4 Pharmacological management of dementia

Acetylcholinesterase inhibitors: The cholinergic hypothesis of Alzheimer's disease has long been mooted (Bartus et al., 1982). AChE-Is, through preventing the breakdown of acetylcholine at the synaptic cleft, contribute to ameliorating the cholinergic deficit. Tacrine was the first AChE-I, licensed for use in Alzheimer's Disease dementia in 1993. The drug was associated with significant hepatotoxicity and was ultimately with drawn from use (Girek & Szymański., 2019). Donepezil, rivastigmine and galantamine were subsequently introduced.

Donepezil perhaps the most commonly used AchE-I, was licensed for use in mild to moderate AD in 1996 (Rogers et al., 1996). Whilst generally well tolerated, gastrointestinal side effects occur commonly. Vagotonic effects on heart rate may also occur, precluding the use of donepezil in individuals with significant cardiac conduction disease (Pfizer Healthcare Ireland, 2022). In addition to oral preparations, transdermal formulations of rivastigmine and donepezil are available. None of these drugs exert large treatment effects (Birks J, 2006) but may confer symptomatic benefit in a proportion of recipients.

Memantine is an uncompetitive NMDA receptor antagonist which blocks excessive NMDA activity without interrupting normal activity, thereby potentially protecting against excitotoxicity (Tampi and van Dyck, 2007). Memantine dose titration is undertaken over a 4-week period to a maximum ongoing dose of 20mg. High quality evidence supports a small beneficial effect when memantine is administered in people with moderate to severe AD (McShane et al., 2019).

The aforementioned medicines are well-established and may provide transient symptomatic benefit. Until recently, however, the search for effective disease modifying agents had proven fruitless. Recent years have seen an increasing focus on dementia treatment and prevention. As of January 2023, there were 141 agents in 187 clinical trials for Alzheimer's Disease (AD) (Cummings et al., 2023). Aducanumab, a human monoclonal antibody which targets aggregated amyloid-beta, was granted accelerated approval by the FDA in 2021 (Wang, 2023). Early clinical studies suggested a slowing of decline as measured by the mini-mental state exam and Clinical Dementia Rating – Sum of Boxes (Sevigny et al., 2016). Despite two subsequent randomised phase-3 studies delivering apparently contradictory results (Budd Haeberlein S et al., 2022), aducanumab was controversially approved by the FDA in 2021 (Walsh S et al., 2021). In January of 2024, Biogen announced plans to discontinue the development and commercialisation of aducanumab (Biogen, 2024). Robust evidence supports the ability of subsequently developed monoclonal antibodies to reduce decline as assessed by cognitive and functional outcome measures. Donanemab, a humanised IgG1antibody to AB, was demonstrated in a Phase 2 study to reduce clinical decline, as measured by the iADRS, by 32% (Mintun et al., 2021). Slowing of clinical progression was further demonstrated in a recent large Phase 3 Study (Sims et al., 2023). A decision from the FDA with regard to approval is awaited. Lecanemab, a further IgG1

antibody, has also demonstrated promising efficacy signals with improvements seen in clinical and biomarker endpoints in Phase 2 (Swanson et al., 2021) and Phase 3 studies (van Dyck et al., 2023). The randomised, placebo-controlled CLARITY AD Study demonstrated a 27% reduction in cognitive decline over 18 months, as measured by the CDR Sum of boxes, when lecanemab was administered fortnightly (van Dyck et al., 2023).

Chapter 2 - Brain Health

2.1 The evolving concept of Brain Health

As pharmacotherapeutic options have evolved, the concepts of brain health and dementia prevention through risk factor assessment and modification have also assumed a more prominent place in scientific literature and global health policy (Livingston et al., 2020; WHO, 2017). It is now recognised that up to 40% of dementias globally are attributable to modifiable risk factors (Livingston et al., 2020). The life-course model of brain health underscores the principle that it is never too early and never too late to consider reducing one's dementia risk, with different risk factors impacting to various degrees depending on one's age. It is noteworthy that the use of the term brain health in medical literature has increased exponentially since 2011 (Chen et al., 2021). Multiple different definitions have proliferated. A 2021 concept analysis defined brain health as follows: "a life-long dynamic state of cognitive, emotional and motor domains underpinned by physiological processes. It is multidimensional and can be objectively measured and subjectively experienced. Brain health is influenced by eco-biopsychosocial determinants, resulting in a continuum of quality of life and wellness" (Chen et al., 2021).

Whilst the term brain health has attracted increased attention in recent years, the concept of dementia prevention is not new. The last decade has witnessed the establishment of multiple clinics designed to operationalise the primary prevention of Alzheimer's disease (Isaacson., 2017). Isaacson and colleagues have espoused the value of clinical precision medicine in delivering personalised prevention strategies to patients (Isaacson., 2017). Galvin, in setting out a framework for the prevention of Alzheimer's Disease, highlights the necessity for prevention initiatives to be multimodal as well as tailored to individual risk factor profiles (Galvin., 2017).

2.2 Modifiable Risk Factors for dementia

The Lancet International Commission on Dementia Prevention and Care, in a seminal 2017 work, set out that 35% of dementia globally is attributable to 9 modifiable risk factors, namely low levels of education in younger life, hypertension, obesity, hearing loss, depression, diabetes, physical inactivity, smoking and social isolation (Livingston et al.,

2017). These risk factors are of varying relevance at different point in the life course. In the face of evolving evidence, this work was updated in 2020 to include 3 further modifiable risk factors, namely alcohol excess, TBI, and air pollution. The resulting 12 risk factor life-course model of brain health is thought to account for 40% of dementia globally (Livingston et al., 2020).

2.2.1 Lower childhood education levels

Low levels of childhood education represent an established risk factor for the development of dementia in later life with multiple systematic reviews underscoring its impact (Valenzuela & Sachdev., 2005; Caamaño-Isorna et al., 2006; Xu et al., 2016; Meng & Darcy., 2012). Gains in intellectual capability related to levels of educational attainment may plateau in early adulthood (Kremen et al., 2019). It has been highlighted that inconsistencies in defining, measuring, and operationalising education may have implications for dementia risk reduction policy implementation (Maccora et al., 2020).

2.2.2 Hearing loss

The association between hearing loss in mid-life and increased dementia risk is well recognised. Prospective studies demonstrate a significant association between ARHL and the development of cognitive impairment and dementia (Loughrey et al., 2018). ACHIEVE, a multicentre, randomised trial, demonstrated a beneficial effect of a hearing intervention (audiological counselling, and the provision of hearing aids) in those at risk of cognitive decline (Lin et al., 2023).

2.2.3 Traumatic Brain Injury

TBI is a major cause of morbidity and mortality globally (Popescu et al., 2015). A recent systematic review and meta-analysis highlights that TBI is associated with an increased risk of dementia (OR = 1.81, 95%, CI = 1.53–2.14) (Gu et al., 2021). Mechanism of dementia pathogenesis after TBI are increasingly understood, with multiple potential pathways contributing to neurodegeneration (Graham & Sharp., 2019).

2.2.4 Hypertension

Current European guidelines suggest a blood pressure threshold of >140/90 for the diagnosis of hypertension (Mancia et al., 2023). Hypertension is of particular relevance in mid-life as a dementia risk factor. A recent large systematic review and meta-analysis highlighted moderate quality evidence indicating that mid-life hypertension was associated with a 1.19 to 1.55 fold excess risk of cognitive disorders (Ou et al., 2020). Aggressive blood pressure management is associated with a reduction in dementia risk. The SPRINT MIND investigators, in a large prospective multicentre study, demonstrated a reduction in dementia risk in ambulatory hypertensive adults who underwent intensive blood pressure management (SBP goal <120mmHg) as opposed to standard treatment (SBP goal <140mmHg) (7.2 vs 8.6 cases per 1000 person-years; hazard ratio [HR], 0.83; 95% CI, 0.67-1.04) (SPRINT MIND Investigators., 2019).

2.2.5 Alcohol Excess

The prevalence of alcohol use disorders is high, with large variation witnessed globally (Glantz et al., 2020). The relationship between alcohol consumption and dementia risk appears dose-responsive with all-cause dementia risk seemingly elevated when dose surpasses a particular threshold, namely 38 grams per day (Xu et al., 2017). The relationship does not appear linear. A prospective UK study with 23 years follow up highlighted an increased dementia risk in those who abstained from alcohol, as well as those who consumed >14 units per week (Sabia et al., 2018).

2.2.6 Obesity

Obesity, widely defined as a BMI >30 kg/m2, is increasingly prevalent. The age-standardized global prevalence of obesity increased from 4.6% in 1980 to 14.0% in 2019 (Boutari & Mantzoros., 2022). The economic cost of overweight and obesity is considerable, estimated at 2.19% of global GDP (Okunogbe et al., 2022). Evidence from systematic reviews and meta-analyses supports an association between mid-life obesity and increased risk of developing dementia (Pedditzi et al., 2016; Anstey et al., 2011; Albanese et al., 2017). Even

small amounts of intentional weight loss in those who are overweight or obese are associated with improvements in cognitive function (Veronese et al., 2016).

2.2.7 Smoking

Smoking remains prevalent and has a significant public health impact globally. In 2020 it was estimated that 1.18 billion people worldwide smoked regularly, with the epidemic of smoking shifting globally to LMICs (Dai et al., 2022). Smoking increases dementia risk (Zhong et al., 2015; Anstey et al., 2007; Peters et al., 2008). Long-term quitters (4 years or more) have been demonstrated to have a reduced risk of dementia over 8 years of follow up (Choi et al., 2018).

2.2.8 Depression

Depression increases dementia risk (Santabárbara et al, 2020). The relationship between depression and dementia is not, however, straightforward. Depressive symptoms can represent an early symptom of dementia, or potentially be triggered by the emergence of cognitive impairment. Furthermore, cognition can be impaired in the context of depression, manifesting as a so-called pseudo-dementia (Byers and Yaffe., 2011). In people with MCI and a history of depression, long term SSRI therapy was found to significantly delay progression to dementia (Bartels et al., 2017).

2.2.9 Social isolation

The prevalence of social isolation increased during the COVID-19 pandemic, with men and older people most significantly impacted (Murayama et al., 2021). A meta-analysis which including more than 2 million participants highlighted that poor social engagement indices were associated with increased dementia risk. In long-term cohort studies, good social engagement was a modestly protective factor in reducing dementia risk (Penninkilampi et al., 2018).

2.2.10 Physical Inactivity

Physical inactivity is prevalent (Guthold et al., 2018) and sedentary behaviour has been demonstrated to be significantly associated with higher incidence of all-cause dementia (Raichlen et al., 2023). Exercise is, in longitudinal observational studies, associated with reduced dementia risk (Livingston et al., 2017).

2.2.11 Air pollution

Pollution represents a major public health concern, particularly in LMICs (Fuller et al., 2022). Air pollution alone is recognised to cause over 6.5 million deaths annually (Fuller et al., 2022). Greater exposure to common pollutants, namely particulate matter, nitrogen dioxide, nitrous oxides, and carbon monoxide has been demonstrated to increase dementia risk (Peters et al., 2019). Neurotoxic effects of air pollution include oxidative stress and neuro-inflammation (Costa et al., 2014).

2.2.12 Diabetes

Diabetes is common and often goes undiagnosed. In 2021, it was estimated that almost one in two adults, approximately 240 million people, were unaware of their diabetes status (Ogurtsova et al, 2022). Diabetes is a recognised risk factor for dementia. A 2016 meta-analysis highlighted that, when compared to individuals who are not diabetic, people with type 2 diabetes are at 60% higher risk of developing dementia (Chatterjee et al., 2016). Intensive diabetic control has not been demonstrated to decrease dementia risk (Livingston et al., 2020).

2.2.13 Emerging Risk Factors

Sleep, and specifically sleep disturbance, has attracted attention as an emerging risk factor for dementia (Livingston et al., 2020). A 2018 meta-analysis highlighted that sleep disturbances may predict the risk of incident dementia (Shi et al., 2018). Multiple potential pathophysiological mechanisms have been postulated, including cardiovascular disease,

hypertension, glymphatic function, and inflammation (Lam et al, 2024). Among community dwelling older adults, sleep disturbance is associated with higher Amyloid Beta burden as assessed by PET scan (Spira et al., 2013).

Engaging in mentally stimulating activities is thought to impact dementia risk. Whilst the impact of education on cognitive ability may plateau in early adulthood(Kremen et al., 2019), mentally stimulating cognitive activity in later life may confer a reduced risk of developing cognitive impairment. Cognitively normal older people, for example, who undertake mentally stimulating activities, even in late life, have a diminished risk of incident MCI (Krell-Roesch et al., 2017). Furthermore, a longitudinal observational study undertaken in China highlighted reduced incident dementia in those undertaking mentally stimulating activities in later life such as reading, playing board or card games, and betting on horse races (Lee et al., 2018).

2.3 Brain Health Interventions

Multidomain interventions have been demonstrated to beneficially impact cognitive outcomes, particularly in those at higher risk of cognitive decline. The FINGER study, a large randomised controlled trial, highlighted the ability of a multidomain intervention to improve or maintain cognitive function in 'at-risk' older individuals, as defined by higher CAIDE scores and cognition at mean or lower than expected levels for age (Nagandu et al., 2015). Analyses from the Multidomain Alzheimer's Preventive Trial demonstrated the beneficial effect of a multidomain intervention with Omega-3 in a subgroup at high risk of dementia (Andrieu., et al 2017). The Prevention of Dementia by Intensive Vascular Care (preDIVA) study sought to ascertain whether a multidomain intervention targeting cardiovascular risk factors was effective in reducing dementia risk in community dwelling older adults. Whilst the intervention did not reduce the incidence of all-cause dementia in the study cohort, a subgroup analysis demonstrated the strongest impact of the intervention in hypertensive patients who were not taking antihypertensive medications (Moll van Charante et al., 2016)

2.4 Barriers to brain health behaviours

Whilst burgeoning evidence supports the potential for lifestyle modification to reduce dementia risk (Livingston et al., 2017; Livingston et al., 2020), behaviours conducive to health promotion are not prevalent among the general population. Whilst modifiable risk factors for dementia disproportionately impact those in LMICs, there is a dearth of research in these settings. Rates of physical inactivity are high in higher-income Western countries (Guthold et al., 2018). Perhaps relatedly, obesity is long recognised to have reached epidemic proportions in Europe (Berghöfer et al., 2008). Adherence to cardiovascular medicines such as antihypertensives is far from uniform (Naderi et al., 2012). Hearing aid use, a protective factor in terms of reducing dementia risk in the context of hearing impairment, varies widely across studies (Gimsing, 2008; Lupsakko et al., 2005; Smeeth et al., 2002). Whilst primary and secondary dementia prevention offers tangible benefits, the introduction of persistent behavioural change in mid- and late-life is challenging. The implementation of disease prevention is difficult, with numerous factors impacting its successful application (Fineberg, 2013).

Many factors are thought to impair adherence to brain health behaviours. Lack of knowledge has been cited as the 'main barrier' to behavioural change in the context of dementia risk reduction (Curran et al., 2021). Existing literature highlights numerous barriers, including organisational issues, financial reasons, lack of motivation, lack of time, health problems, and other factors (Heger et al., 2019; Curran et al., 2021; Van Asbroeck et al., 2021).

2.5 Brain Health Clinics

The landscape of dementia care is evolving apace. This decade has seen the advent of disease modifying therapies and, in parallel, an increased focus on brain health promotion through lifestyle risk factor modification. As set out in Section 2.1, efforts to operationalise brain health interventions in a clinical context are ongoing, albeit in a disparate fashion. The design and implementation of integrated services capable of risk assessment, communication, and delivery of individualised, multimodal treatment plans targeting measures of biological risk via disease modifying therapies, as well as targeting lifestyle risk

must represent a core priority at national and international level and are further discussed in Section 5.3.3 below.

Chapter 3 - Modifiable risk factors for dementia, and awareness of brain health behaviours: Results from the Five Lives Brain Health Ireland Survey (FLBHIS)

3.1 Introduction

Dementia is an umbrella term encompassing several conditions, the hallmark of which is a progressive deterioration in cognition and function (McKhann et al., 2012). Dementia is common and, in many societies, underdiagnosed (Gauthier et al., 2021). Although the rate of dementia incidence has been declining in recent years in some western societies (Wolters et al., 2020; Prince et al., 2016), global dementia prevalence is increasing (Nichols et al., 2022). Dementia accounts for a significant proportion of health and social care expenditure and this is projected to increase. By 2050 it is estimated that dementia-attributable spending globally will reach 1.6 trillion dollars (Velandia et al, 2022). Much of the cost associated with dementia relates to informal care (Wimo et al., 2018).

Recent years have seen an increasing focus on dementia treatment and prevention. As of January 2022, there were 143 agents in 172 clinical trials for Alzheimer's Disease (AD) (Cummings et al., 2022). Citing an urgent need for treatments, the FDA in January 2021 granted accelerated approval for aducanumab in the treatment of AD (FDA, 2021) but concerns over its real-world utility remain (Canevelli et al., 2021; Padovani et al., 2022).

As disease modification options remain elusive, the concepts of brain health and dementia prevention through risk factor control have assumed a more prominent place in scientific literature and global health policy (Livingston et al., 2020; WHO, 2017). The use of the term brain health in medical literature has increased exponentially since 2011 (Chen et al., 2021). A 2021 concept analysis defined brain health as follows: "a life-long dynamic state of cognitive, emotional and motor domains underpinned by physiological processes. It is multidimensional and can be objectively measured and subjectively experienced. Brain health is influenced by eco-biopsychosocial determinants, resulting in a continuum of quality of life and wellness" (Chen et al., 2021). It is now recognised that up to 40% of dementias globally are attributable to modifiable risk factors (Livingston et al., 2020). On a related note, the observed decline in incidence rate of dementia in Europe and North America over the past 25 years, has been attributed to improved treatment options and outcomes for cardiovascular disorders (Wolters et al., 2020). The life-course model for modifiable dementia risk factors highlights that it is never too early or too late in the life course to consider dementia prevention (Figure 1). Whilst brain health services designed to

operationalise primary and secondary dementia prevention measures are evolving, significant challenges remain in providing scalable programmes and equity of access (Altomare et al, 2021).

Whilst a weight of evidence supports the potential for risk factor modification in reducing dementia risk (Livingston et al., 2020), health-promoting behaviours are not prevalent among the general population. Whilst modifiable risk factors for dementia disproportionately impact those in low- and middle-income countries, there is a relative paucity of research in these settings. Conversely, rates of physical inactivity are high in higher-income Western countries (Guthold et al., 2018) and adherence to cardiovascular medicines such as antihypertensives is poor (Naderi et al., 2012). Hearing aid use, a protective factor in the context of hearing impairment, varies considerably across studies (Gimsing, 2008; Lupsakko et al., 2005; Smeeth et al., 2002). Thus, while primary and secondary dementia prevention offers a tangible route to reduce its disease burden, the introduction of persistent behavioural change in mid- and late-life remains a challenge (Fineberg, 2013).

Misconceptions regarding the nature of dementia and its risk factors are prevalent and a barrier to the implementation of prevention programmes. A recent systematic review of population-based surveys demonstrated that more than half of respondents in Europe and the United States believed that dementia was a part of normal ageing (Cations et al., 2018). Misconceptions regarding the pathologic nature of cognitive decline and the absence of treatment options have been recognised as contributing to the underdiagnosis of dementia (Bradford et al., 2009). Furthermore, a family history of dementia may skew perspectives and confer a sense of resignation to ‘one’s inevitable fate’ (Kim et al., 2016). Relatedly, knowledge surrounding dementia risk reduction behaviours is often lacking (Smith et al., 2014). The importance of cardiovascular risk factors, for example, is poorly understood while risk reduction strategies of limited or no evidence are often endorsed by the general public (Cations et al., 2018).

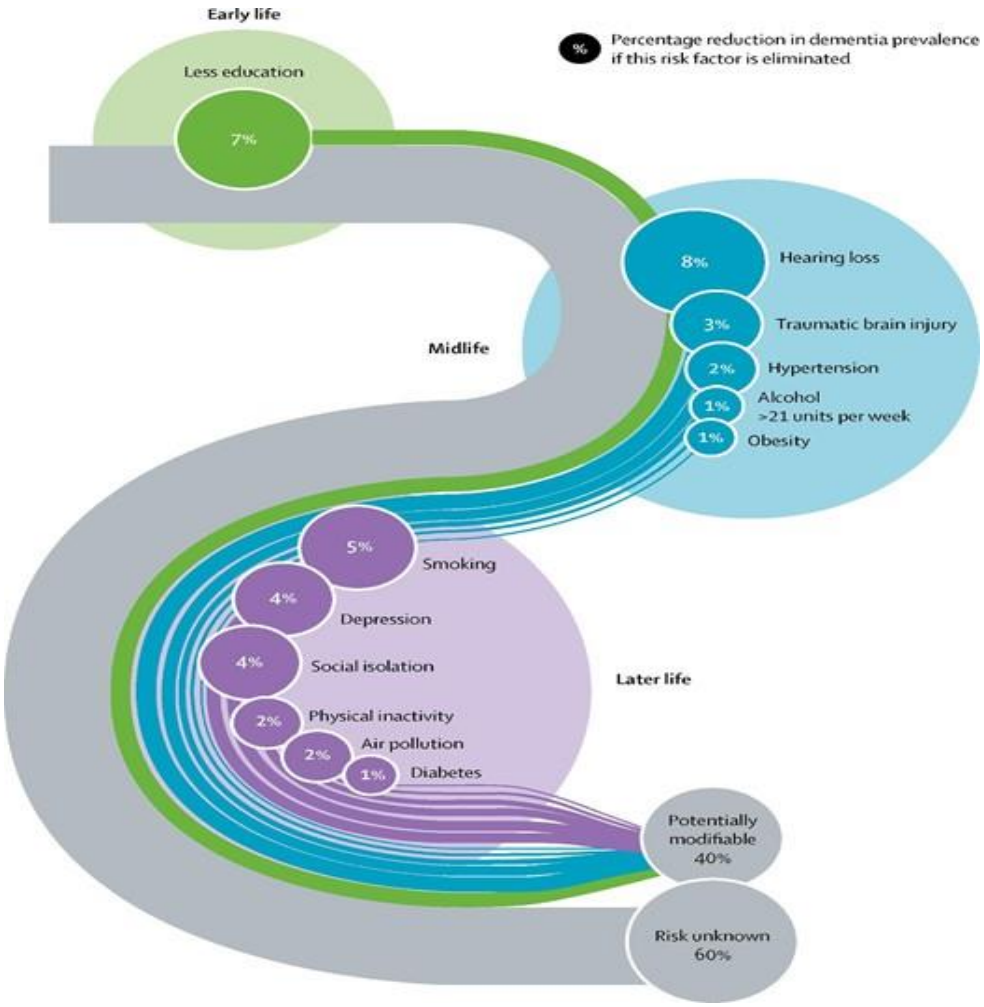

Figure 1: Population attributable fraction of potentially modifiable risk factors for dementia. Reprinted with permission from the Lancet, Vol. 396, Gill Livingston, Jonathan Huntley, Andrew Sommerlad, David Ames, Clive Ballard, Sube Banerjee, Carol Brayne, Alistair Burns, Jiska Cohen-Mansfield, Claudia Cooper, Sergi G. Costafreda, Amit Dias, Nick Fox, Laura N.

Modifiable risk factors are unequally distributed in the general population due to their dependence on sociodemographic, cultural, and economic factors (Deckers et al., 2019; Röhr et al., 2022). Personalisation of brain health interventions is thus critical and indeed individualised interventions are valued by patients (Curran et al., 2021). Such personalised preventative interventions are not a new phenomenon and have been provided in individual settings over the last decade (e.g., Seifan et al., 2015). A novel form of brain health service focused on delivering dementia risk profiling, risk communication, and risk reduction interventions has been proposed but equity of access, and indeed the widespread availability of such services, is not yet a reality (Milne et al., 2021). Better understanding of

barriers to lifestyle change specific to dementia risk is crucial if large-scale, effective brain health interventions are to be developed.

Many existing studies examining attitudes to brain health are limited by a failure to consider a range of pertinent risk factors and associated barriers to protective behaviours. In Ireland, self-reported knowledge of dementia is poor compared to other conditions, and almost half of the population are unaware that dementia risk is modifiable (Hickey, 2019). In this context, the current study aimed to explore exposure to and awareness of specific modifiable risk factors for dementia. As previous research has reported an unequal distribution of modifiable risk factors in the general population (Bobrow et al., 2021; LaPlume et al.,2022), we also aimed to investigate whether exposure to these risk factors is associated with demographic and socioeconomic factors, and to explore whether modifiable risk factor awareness varies between groups.

3.2 Methods

3.2.1 Study design and participants

The Five Lives Brain Health Ireland Survey (FLBHIS) is a cross-sectional survey that was distributed online among an Irish non-patient population. Participants were considered eligible for inclusion in this study if they were aged 50 years old and above, had no history of dementia diagnosis and had never worked in the healthcare sector. A pilot version of the survey was undertaken by 50 volunteers in January 2022. The survey was subsequently administered to a further 555 volunteers in February 2022. A Professional market research company, CDR Insights & Analytics Limited, was responsible for administration of the survey online to an existing market research panel. Consent was assumed when participants proceeded to complete and submit the survey.

Prior to commencement, this study was reviewed by The St. James' Hospital / Tallaght University Hospital Joint Research Ethics Committee who advised that, in keeping with local institutional and legislative requirements, formal approval was not necessary.

3.2.2 Measures

The FLBHIS was developed through an iterative process. Informed by current literature and expert opinion, a 100-question survey was devised (see Appendix 1). The survey was adapted from the Lifestyle Barriers for Cognitive Health Questionnaire (LBCHQ) (K. Muhammed 2021, personal communication, 2 September) to be suitable for an Irish population. Previously unpublished, the LBCHQ, is, at the time of writing, freely accessible online (Open Science Framework, 2021). The instrument has not been utilised, or to the author's knowledge, validated elsewhere. The survey instrument was chosen for its comprehensive nature, and robust grounding in theoretical models of behavioural change. Risk factors contained therein were derived from the 2020 Report of the Lancet Commission on Dementia Prevention, Intervention, and Care (Livingston et al., 2020). Additional items relating to other emerging modifiable risk factors for cognitive decline such as sleep issues (Spira et al., 2014) and mental stimulation (Krell-Roesch, 2019) were added to the survey. Barriers were derived and adapted from the behaviour change wheel, specifically from the COM-B model (Michie et al., 2011) (see section 4.2.1 for further details). The survey captured the following information: 1) Sociodemographic factors (gender, age, ethnicity, household income, level of education); 2) Exposure to, as well as knowledge of modifiable risk factors for dementia, namely diet, social interaction, exercise, hypertension, sleep, current low mood/depression, current smoking, alcohol consumption, cognitive stimulation, hearing impairment, diabetes, air pollution, and head injury. Awareness was measured on a Likert scale. Alcohol intake (>14 units per week), being overweight, smoking, low physical activity, sleep quality, depression/low mood, low social interaction, low mental stimulation and residing in an area with high air pollution were self-reported risk factors, whereas diabetes, hypertension and hearing impairment were defined as being diagnosed by a healthcare professional. With regard to being overweight, subject perception was utilised as opposed to BMI to minimise any potential impact of missing data; 3) Barriers to brain health behaviours (reported separately); 4) Participants' perceptions regarding potential for dementia prevention, and risk reduction (Likert scale).

3.2.3 Statistical Methods

All personal data was removed from the dataset prior to analyses. Analyses were conducted using StataMP 17.0 for Mac or IBM SPSS Statistics software for Windows (version 29). Frequency counts and percentages were used to show the sociodemographic characteristics and rates of exposure to modifiable risk factors for dementia among the sample. For all analyses, statistical significance was defined as $p<0.05$. To investigate differences in awareness levels for modifiable risk factors across groups, 2-way mixed ANOVAs with Greenhouse-Geisser correction were performed. Three 2-way mixed ANOVAs were undertaken with gender, age, and education as respective between-subject factors. Each ANOVA had 'risk factor' as a within-subject factor with 13 levels, each level representing one risk factor. The outcome measure for each ANOVA was awareness level measured by a Likert scale. Age was categorised into three groups, defined as 50-59 years old, 60-69 years old, and 70 years and above for the purpose of analysis. Due to small numbers in this group (n=3), those who responded that they would prefer not to disclose their gender were excluded from the dataset for analyses. Education was categorised into three groups for the purpose of analysis, defined as primary/secondary school, university undergraduate, and university postgraduate levels. Due to small numbers who had been educated to primary school level (n = 10), this group was combined with those who had been educated to secondary school level. Adjustment for post-hoc comparisons was undertaken using the Sidak correction. Binary logistic regression models were used to investigate the associations between exposure to modifiable risk factors for dementia, age, gender, and education presenting odds ratios (OR) and adjusted odds ratios (AOR) for the likelihood of reporting exposure to risk factors. Risk factor exposure variables that were measured on a Likert scale (social interaction, exposure to air pollution) were regenerated into binary variables for the purposes of analyses. Binary logistic regression analyses were adjusted for potential confounding factors such as household income and educational attainment, as well as for sex and age depending on the predictor variable used in the model.

3.3 Results

3.3.1 Sample characteristics

The study population ultimately comprised 551 participants. Of the 555 volunteers to whom the survey was originally administered, 3 participants were excluded as they did not disclose

their gender. One further participant was excluded due to an incomplete dataset. Table 1 outlines the sociodemographic characteristics of the sample. The study population comprised 551 participants with an almost equal proportion of male and female respondents (50.3% male; 49.6% female). Mean age was 59.7 years, with the majority of the sample ranging between 50-59 years of age (54.3%). 98.9% of respondents were of White ethnicity. Most participants were educated to secondary school level or higher (98.2%), were employed or self-employed (52.2%), and cohabited with one or more persons (74.4%).

Characteristic	**n (%)**
Age in years	
50-64	437 (79.3)
65 and above	114 (20.7)
Gender	
Male	277 (50.3)
Female	274 (49.7)
Educational attainment	
Primary school	10 (1.8)
Secondary school	282 (51.3)
Undergraduate degree	196 (35.6)
Postgraduate degree	62 (11.3)
Household income level	
Less than €20 000	104 (18.9)
€20 000 - €40 000	189 (34.4)
€40 000 - €60 000	91 (16.6)
€60 000 - €80 000	63 (11.5)
Above €80 000	48 (8.7)
Employment status	
Employed or self-employed	287 (52.2)
Unemployed	91 (16.6)

Retired	172 (31.3)
Home circumstances	
Living alone	141 (25.6)
Living with one other person	197 (35.8)
Living with more than one person	212 (38.6)

Table 1: Sociodemographic characteristics of the sample. Total sample (N = 551). Not all totals for each variable sum to 551 due to missing data. Previously published (Dukelow et al., 2023a).

3.3.2 Exposure to modifiable risk factors

Exposure to modifiable risk factors for dementia across the sample is illustrated in Table 2. Modifiable risk factors for dementia were prevalent among the study population, where the most commonly reported exposures were being overweight (60.6%), having a lack of social engagement (54.9%), physical inactivity (42.7%), hypertension (36.7%), and self-assessed poor sleep quality (33.5%). The least common risk factor was exposure to activities with risk of head injury (1.8%). The impact of gender, age and levels of education on exposure to modifiable risk factors are presented in Table 3 and summarised below.

Modifiable risk factor	**n (%)**
Overweight	333 (60.6)
Low social interaction	302 (54.9)
Low physical activity	215 (42.7)
Hypertension	202 (36.7)
Poor quality sleep	184 (33.5)
Alcohol consumption (14+ units/week)	119 (29.4)
Depression/low mood	154 (28.0)
Smoking (≥ 1 cigarette/week)	125 (22.7)
Low mental stimulation	116 (21.1)
Air pollution	83 (15.1)
Hearing impairment	69 (12.6)

Diabetes (Type I or II, diet or medication controlled)	45 (8.2)
Activities with risk of head injury	10 (1.8)

Table 2: Exposure to modifiable risk factors. Total sample (N = 551). Not all totals for each variable sum to 551 due to missing data. Previously published (Dukelow et al., 2023a).

3.3.4 Impact of gender on exposure to modifiable risk factors

Gender differences are presented in Table 3. Relative to females, male gender was significantly associated with an increased likelihood to report multiple risk factors, namely excess alcohol consumption (AOR 3.127, CI 1.953 - 5.007), smoking (AOR 1.618, CI 1.065 - 2.457), diabetes (AOR 2.141, CI 1.097 - 4.176) and low mental stimulation (AOR 1.796, CI 1.171 - 2.754). Males were also significantly less likely than females to report poor quality sleep (AOR 0.547, CI 0.379 - 0.789), and depression (AOR 0.678, CI 0.462 - 0.996).

3.3.5 Impact of age on exposure to modifiable risk factors

Age differences are presented in Table 3 as AOR change per year increase in age. With increasing age, participants were less likely to report poor quality sleep (AOR 0.967, CI 0.942 - 0.993), low mental stimulation (AOR 0.945, CI 0.915 - 0.976), smoking (AOR 0.94, CI 0.911 - 0.971), depression (AOR 0.959, CI 0.932 - 0.986), low social interaction (AOR 0.966, CI 0.943 - 0.990) and exposure to air pollution (AOR 0.956, CI 0.923 - 0.991). Increasing age was also significantly associated with an increased likelihood of reporting diagnosis of hypertension (AOR 1.033, CI 1.009 - 1.057) and hearing impairment (AOR 1.066, CI 1.032 - 1.100).

3.3.6 Impact of education on exposure to modifiable risk factors

Education differences are presented in Table 3. Relative to the secondary school education group, participants educated to undergraduate and postgraduate level were significantly less likely to report smoking (AOR 0.468, CI 0.296-0.738; AOR 0.199, CI 0.076-0.520, respectively). The undergraduate group were less likely to report depression (AOR 0.611, CI 0.401-0.930). Relative to the secondary school education group, participants educated to undergraduate and postgraduate level were significantly less likely to report exposure to low mental stimulation (AOR 0.573, CI 0.361-0.908; AOR 0.353, CI 0.152-0.818 respectively).

	Predictors													
	Age			**Gender**				**Education**						
Risk factor	AOR change per 1 year increase			Male			Female	University undergraduate			University postgraduate			Secondary school
	AOR	95% CI	P	AOR	95% CI	P	AOR	AOR	95% CI	P	AOR	95% CI	P	AOR
Hypertension	**1.033**	**1.009 - 1.057**	**0.008**	1.252	.876 - 1.788	0.217	1	0.94	.643 - 1.375	0.75	0.678	.373 - 1.233	0.203	1
Hearing loss	**1.066**	**1.032 - 1.100**	**<.001**	1.303	.764 - 2.222	0.331	1	0.748	.422 - 1.324	0.319	0.573	.227 - 1.444	0.237	1
Smoking	**0.94**	**.911 - .971**	**<.001**	**1.618**	**1.065 - 2.457**	**0.024**	1	**0.468**	**.296 - .738**	**0.001**	**0.199**	**.076 - .520**	**<.001**	1
Overweight	0.979	.956 - 1.002	0.077	0.822	.573 - 1.180	0.288	1	0.9	.612 - 1.323	0.593	0.667	.379 - 1.172	0.159	1
Lack of exercise	1.005	.980 - 1.029	0.717	1.043	.726 - 1.497	0.821	1	0.834	.566 - 1.228	0.357	0.577	.313 - 1.064	0.078	1
Depression	**0.959**	**.932 - .986**	**0.004**	**0.678**	**.462 - .996**	**0.048**	1	**0.611**	**.401 - .930**	**0.022**	0.631	.328 - 1.214	0.168	1
Diabetes	1.03	.992 - 1.070	0.124	**2.141**	**1.097 - 4.176**	**0.026**	1	1.312	.685 - 2.516	0.413	0.767	.252 - 2.336	0.641	1
social	**0.966**	**.943 - .990**	**0.005**	0.777	.539 - 1.122	0.178	1	1.213	.818 - 1.800	0.337	1.18	.652 - 2.136	0.584	1
Alcohol	0.993	.964 - 1.023	0.623	**3.127**	**1.953 - 5.007**	**<.001**	1	0.933	.577 - 1.507	0.776	0.509	.220 - 1.178	0.115	1
Head injury	1.025	.938 - 1.120	0.589	0.431	.106 - 1.750	0.239	1	0.098	.012 - .806	0.806	0.108	.010 - 1.215	0.072	1
Air pollution	**0.956**	**.923 - .991**	**0.013**	1.402	.870 - 2.260	0.165	1	1.123	.680 - 1.856	0.651	0.867	.383 - 1.964	0.733	1
Sleep problems	**0.967**	**.942 - .993**	**0.012**	**0.547**	**.379 - .789**	**0.001**	1	0.847	.571 - 1.256	0.409	0.789	.429 - 1.454	0.448	1
Low mental stimulation	**0.945**	**.915 - .976**	**<.001**	**1.796**	**1.171 - 2.754**	**0.007**	1	**0.573**	**.361 - .908**	**0.018**	**0.353**	**.152 - .818**	**0.015**	1

Table 3: Association between exposure to modifiable risk factors age, gender and education. Significant effects are reported in bold. Previously published (Dukelow et al., 2023a).

3.3.7 Awareness of modifiable risk factors for dementia

65.6% of participants believed that lifestyle improvements can decrease a person's risk of developing dementia. However, only 31.4% believed that dementia could be prevented with lifestyle modifications.

Awareness of modifiable risk factors by age, gender, and education is illustrated in Figures 2, 3, and 4 respectively. Across the total sample, head injury (90.9%, n = 500), low mental stimulation (85.3%, n = 469) and excess alcohol consumption (77.8%, n = 428) were the three most commonly recognised modifiable risk factors for dementia. Hearing impairment had the poorest recognition as a modifiable risk factor for dementia (34.7%, n = 191).

3.3.8 Awareness of modifiable risk factors by gender

Awareness of modifiable risk factors by gender is illustrated in Figure 2. Two-way mixed ANOVA with Greenhouse-Geisser correction demonstrated significant main effects of risk factor ($F(10.75,5888.82) = 134.88$, $p < .001$) but not gender ($F(1,548) = 0.48$, $p = 0.491$) on awareness, and the interaction effect between risk factors and gender on awareness was not significant ($F(10.75,5888.82) = 1.62$, $p = 0.09$). Awareness of low mental stimulation as a dementia risk factor was higher in the female group ($p = .05$).

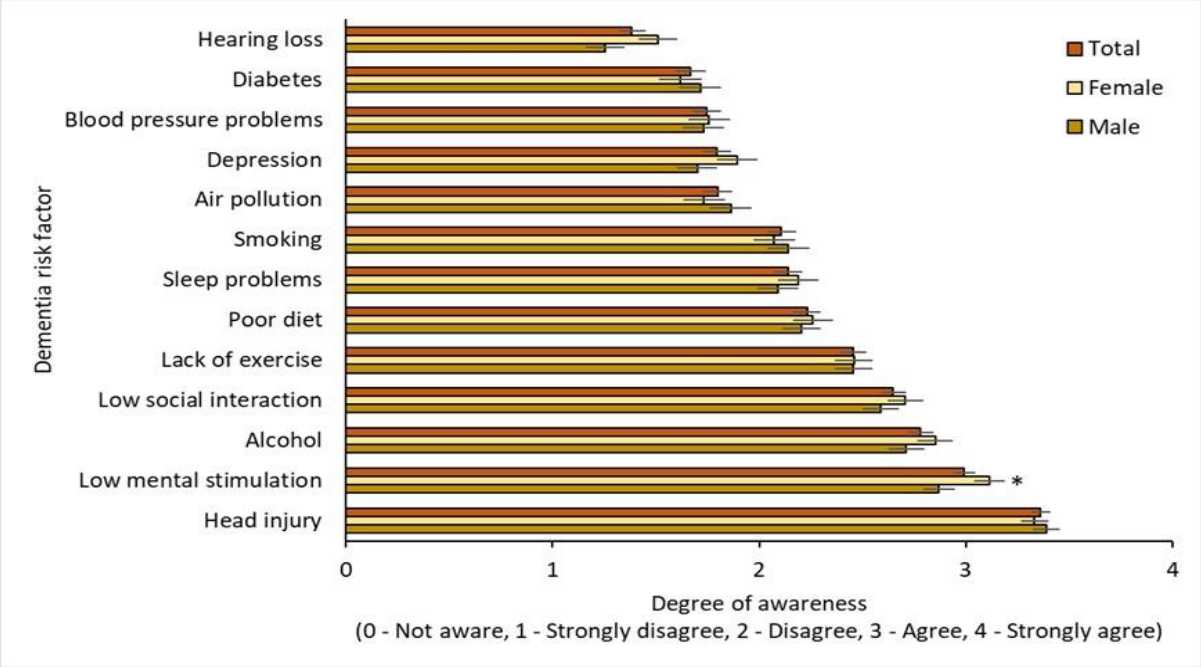

Figure 2: Awareness of modifiable risk factors by gender. * = sig. different from male group at .05 level. Previously published (Dukelow et al., 2023a).

3.3.9 Awareness of modifiable risk factors by age

Awareness of modifiable risk factors by age is illustrated in Figure 3. Two-way mixed ANOVA with Greenhouse-Geisser correction revealed a significant main effect of risk factor ($F(10.75,5879.15) = 93.71$, $p < .001$) but not age ($F(2.547) = 0.94$, $p = 0.393$) and did not demonstrate a significant interaction effect between risk factors and age on awareness $F(21.49,5879.15) = 1.16$, $p = 0.279$.

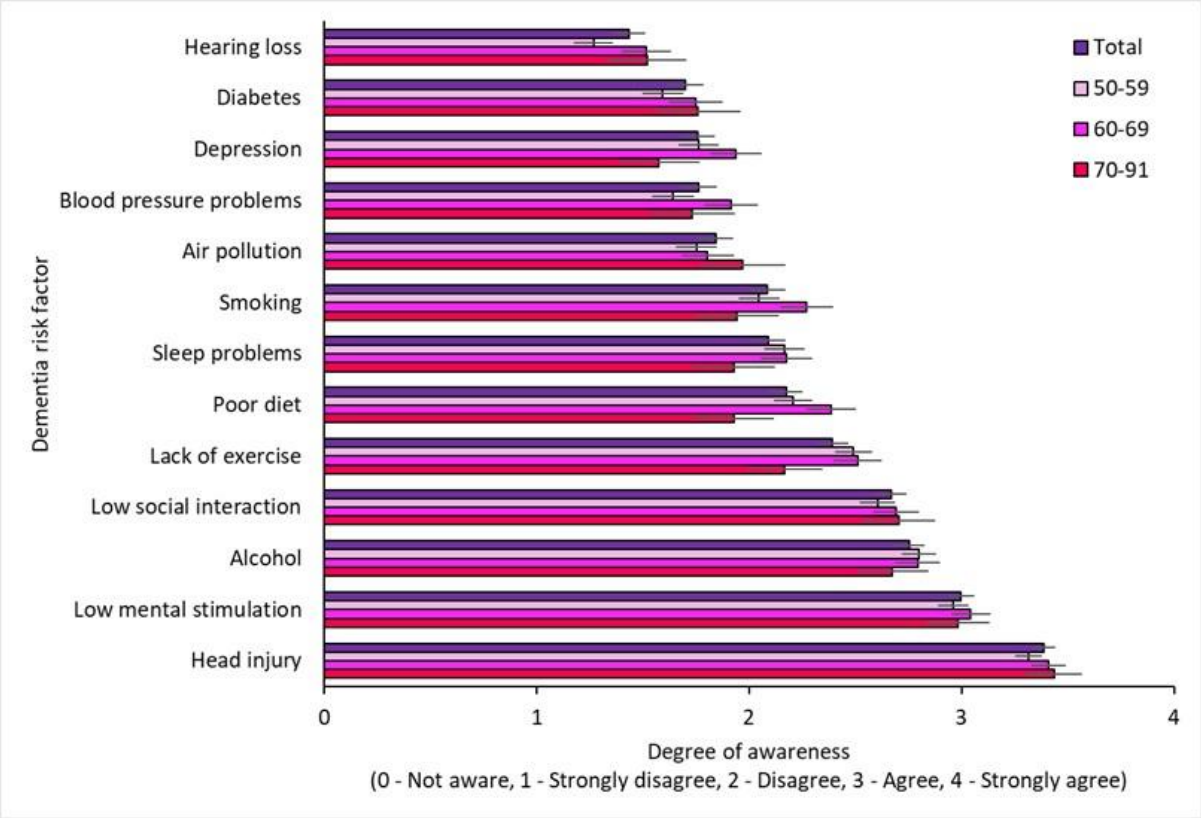

Figure 3: Awareness of modifiable risk factors by age. Previously published (Dukelow et al., 2023a).

3.3.10 Awareness of modifiable risk factors by education levels

Awareness of modifiable risk factors by education level is illustrated in Figure 4. Two-way mixed ANOVA with Greenhouse-Geisser correction revealed a significant main effect of risk factor ($F(10.75,5881.99) = 82.69$, $p < .001$) and main effect of education ($F(2,547) = 11.99$, $p < .001$). The interaction effect between risk factors and educational level on awareness was not significant ($F(21.51,5881.99) = 1.42$, $p = .09$). Awareness was significantly greater in both university groups (undergraduate and postgraduate) relative to the secondary education

group for multiple risk factors, namely diabetes, air pollution, sleep, diet, low social interaction, and low mental stimulation (p=.01). Awareness of hearing loss, hypertension, and depression were significantly greater in the university postgraduate group when compared to the secondary school group (p=.05). Awareness of depression was greater in the postgraduate university group when compared to the undergraduate and secondary school groups (p=.05).

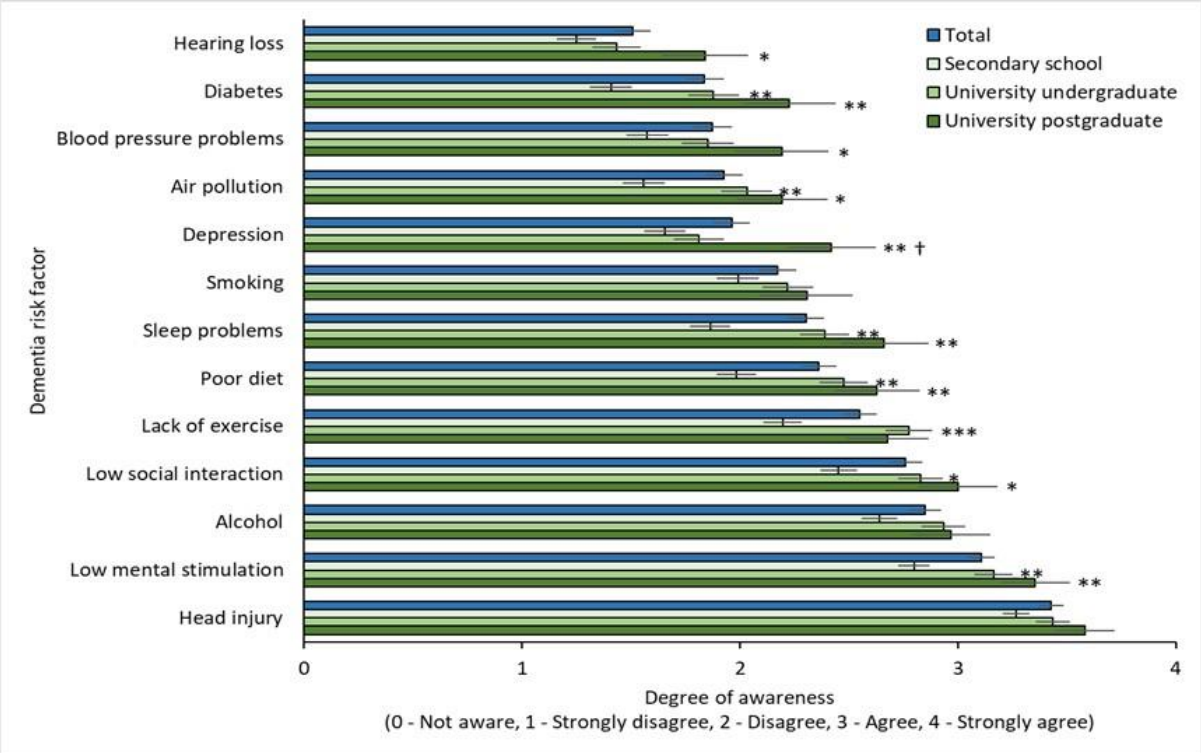

Figure 4: Awareness of modifiable risk factors by education. * = sig. different from secondary school group at .05 level; ** = sig. different from secondary school group at .01 level; *** = sig. different from secondary school group at .001 level; † = sig. different from university undergraduate group at .05 level. Previously published (Dukelow et al., 2023a).

3.4 Discussion

In this study, we investigated the exposure to modifiable risk factors for dementia and their associations with gender, age, and education in an Irish sample of adults aged 50 and above. We assessed participants' perception regarding the potential for dementia prevention, and risk reduction, as well as awareness levels of individual risk factors. Our findings demonstrate that the distribution of exposure to modifiable risk factors for dementia is

unequal across gender, age and education groups, and that awareness levels vary across risk factors, gender, and education level. These findings highlight that focus surrounding dementia prevention should shift towards individual risk profiling and should be tailored towards an individual's specific needs.

Dementia has long been labelled a public health crisis (White, 1988). Dementia represents a public health priority for WHO member states, with cross-sectoral responses set out in the Global action plan on the public health response to dementia 2017-2025 (WHO, 2017). The Global status report on the public health response to dementia highlights an urgent need to raise public awareness, and improve understanding of dementia, as well as the potential for risk reduction (WHO, 2021).Our finding that a significant proportion of respondents felt that dementia cannot be prevented is in line with a global survey commissioned by Alzheimer's Disease International (ADI) that demonstrated that two thirds of the general public, and 62% of healthcare practitioners believe that dementia is part of normal ageing (ADI, 2019). Only 31.4% of people we surveyed believed that dementia could be prevented via lifestyle modifications. Despite this, 65.6% of participants believed that lifestyle improvements could decrease a person's risk of developing dementia. This apparent disassociation between the concepts of prevention and risk reduction in the minds of participants perhaps speaks to a lack of reach or clarity in public health messaging on the subject. Ireland's dementia awareness campaign, whilst impactful, has not been effective in increasing knowledge that dementia risk is modifiable (Hickey, 2019). Terminology is likely to be of particular importance in such contexts. It has been speculated that the term 'risk reduction' may be a source of ambiguity with 'prevention' representing a more tangible and actionable concept (Hodes et al 2019).

In addition to a lack of awareness that dementia could be prevented via lifestyle modifications, knowledge of individual risk factors varied among the study group. High levels of awareness for certain risk factors may relate to the study population being relatively highly educated. 98.2% of survey respondents had attained at least secondary school level education as compared to 62% of older adults in a nationally representative Irish longitudinal study (Barrett et al., 2011). Our results are in line with a recent Dutch study of community dwelling older adults which found that individuals with lower levels of

educational attainment were less likely to agree that dementia risk reduction is possible (Heger et al., 2019). In our study, participants educated to undergraduate university level or higher were significantly more aware of diabetes, air pollution, sleep, diet, low social interaction, and low mental stimulation as risk factors for dementia. Being educated to a post-graduate level was associated with additional awareness of the role of hearing loss, hypertension, and depression as compared to the secondary school group. This suggests a need to promote wider public awareness of these risk factors, especially considering that hearing loss is one of the most impactful mid-life risk factors for dementia with a population attributable fraction of 8% (Livingston et al., 2020). On the other hand, major depression is considered the fourth leading cause of morbidity globally according to the World Health Organisation (WHO, 2008). Awareness of certain risk factors (air pollution, diabetes, hypertension, alcohol consumption) was broadly congruent with existing literature (Cations et al., 2018) and highlights the necessity to devise effective strategies to influence public perception. Dementia risk reduction campaigns are not a global phenomenon, with only 28 of 62 Global Dementia Observatory countries reporting having run such a campaign. The majority of campaigns were conducted in high income countries (WHO, 2021). Only eight low- and middle-income countries report having run dementia risk reduction campaigns (WHO, 2021), despite these nations being disproportionately impacted by modifiable risk factors and thus potentially having the greatest potential for dementia risk reduction (Livingston et al., 2020). Increasing dementia prevalence and the projected increase in costs associated with the disease make effective awareness campaigns encompassing dementia prevention a global imperative.

Modifiable risk factors for dementia were prevalent among study participants. More than half of those surveyed described themselves as being impacted by low social interaction, a well-established dementia risk factor (Penninkilampi et al., 2018). Conversely, high social engagement and large social networks are associated with better late-life cognitive function (Evans et al., 2019). Social engagement has been significantly impacted by the Covid-19 pandemic and its associated public health restrictions (Hwang et al., 2020) which raises the potential impact of this factor over the next decade. Loneliness and social isolation have been prevalent among older adults during the Covid-19 pandemic (Su et al., 2022) and mental and physical health have been negatively impacted over this period (Sepúlveda-

Loyola et., 2020). Fear of Covid-19 is prevalent amongst older adults (Agrawal et al., 2021). The promotion of social engagement as a means of dementia risk reduction is likely to prove challenging in this context.

Cardiovascular risk factors were prevalent amongst the study population (Table 2). Individual cardiovascular risk factors have been demonstrated to increase dementia risk (Livingston et al., 2020), and higher composite cardiovascular risk is associated with both vascular and AD dementia (Song et al., 2021). The role of brain vasculature in the pathogenesis of AD is increasingly recognised (Sweeney et al., 2018). Vascular risk factors have been demonstrated to potentially enhance neurodegeneration in individuals with preclinical AD (Bos et al., 2019). With regard to specific cardiovascular risk factors, 36.7% of study participants described a history of hypertension. Data from a large longitudinal Irish study suggests comparable hypertension prevalence but low levels of hypertension awareness, treatment, and control (Murphy et al, 2016). The number of adults with hypertension globally was predicted to increase by about 60% to a total of 1.56 billion by 2025 (Kearney et al., 2005). Whilst hypertensive awareness is improving (Burnier et al., 2019), multiple studies have demonstrated poor adherence to antihypertensive medications (Algabanni et al., 2020; Vrijens et al., 2008;). It has been speculated that lack of a 'pay for performance' remuneration system may contribute to poor treatment and control in an Irish context (Murphy et al, 2016). We have demonstrated a substantial lack of awareness of hypertension as a risk factor for dementia (52.0% of those surveyed). It is plausible that this lack of knowledge may impact antihypertensive adherence.

Age profile and gender were independently associated with exposure to a variety of risk factors. Male gender, for example, was significantly associated with an increased likelihood to report multiple risk factors, namely excess alcohol consumption, smoking, diabetes, and low mental stimulation. Males were also significantly less likely than females to report poor quality sleep, and depression. This gender disparity, and spectrum of exposure across the age-range studied, highlights the need to avoid a 'one size fits all' approach when it comes to dementia prevention. The concept of personalised primary and secondary prevention plans, tailored to an individual's risk factor profile is central to proposed and evolving brain health services (Altomare et al., 2021).

This study is not without its limitations. This study comprises a population-based survey, distributed via a market research company to an existing online survey panel. This approach introduces the potential for selection bias. Furthermore, the degree to which these results are generalisable in a global context is unclear. Ireland is a wealthy, Western European nation with high levels of educational attainment (OECD, 2021). As highlighted, our study population appears highly educated with 98.2% having attained at least secondary school level education as compared to 62% of older adults in a nationally representative longitudinal study (Barrett et al., 2011). Online administration of the survey arguably represents a weakness as it further excludes individuals with low levels of education who may be lacking in technological literacy or do not have access to a digital device. Absence of laboratory investigations precluded computation of individualised dementia risk scores.

Strengths of the study include the detailed and robust survey design. The questionnaire comprised multiple questions, addressing both established and emerging risk factors. This study highlights ongoing knowledge deficits among the general public with regard to dementia risk factors and the potential for dementia prevention. Exposure to modifiable risk factors for dementia is considerable among this population of older adults. Individualised assessment and primary prevention in the context of specialist brain health clinics is unlikely to be impactful on a population level in the short to medium term. Novel health promotion and risk reduction approaches must be prioritised.

Chapter 4 - Barriers to brain health behaviours: results from the Five Lives Brain Health Ireland Survey

4.1 Introduction

The number of people living with dementia globally is increasing. Estimated dementia prevalence is projected to increase from 57·4 million cases globally in 2019 to 152·8 million cases in 2050 (GBD 2019 Dementia Forecasting Collaborators, 2022). Negative stereotypes of the condition predominate (Low and Purwaningrum, 2020), and dementia has been cited as one of the most feared conditions amongst members of the public (MetLife Foundation, 2011; Kessler et al., 2012). Dementia research funding is increasing, with spending doubling in many Western countries between 2011 and 2016 (Pickett and Brayne, 2019). The importance of research into dementia prevention, and risk reduction is emphasised in the WHO's Global action plan on the public health response to dementia 2017–2025 (WHO, 2017).

Burgeoning evidence supports the potential for dementia prevention globally. The Lancet Dementia Commission identified 12 modifiable risk factors which account for 40% of dementias globally (Livingston et al., 2020). The population attributable fraction for modifiable dementia risk factors is higher in low-and middle-income countries where certain risk factors are more prevalent (Livingston et al., 2020). Less childhood education, smoking, hypertension, obesity, and diabetes are, for example, more prevalent in China, India, and certain Latin American countries as compared to high income countries (Mukadam et al., 2019). Whilst improvements in cardiovascular risk reduction in particular may account for falling dementia incidence in Western Society (Larson et al., 2013; Wolters et al., 2020), these trends have not been replicated in Low-and Middle-Income Countries (LMICs; Li et al., 2007; Wu et al., 2018).

It is recognised that cognition exists on a spectrum encompassing normal cognition, subjective cognitive decline, mild cognitive impairment (MCI), and dementia (Knopman et al., 2015). People with MCI have cognitive impairment beyond that expected for age and education but remain functionally unimpaired (Petersen et al., 1999, 2021). The entities of subjective cognitive decline and MCI have represented opportune stages at which to intervene from a risk reduction perspective. Specific risk reduction strategies for those with MCI, as well as normal cognition, are set out in the World Health Organisation Risk Reduction of Cognitive decline and dementia guidelines (World Health Organization, 2019).

In clinical settings, such risk reduction is increasingly addressed in a personalised and protocolised fashion. Evolving brain health services are likely in time to fulfil a number of roles, including risk profiling, risk communication, and risk reduction (Altomare et al., 2021). Furthermore, large scale, multidomain interventions have demonstrated the potential to benefit cognition in those at risk of dementia (Kivipelto et al., 2018). Particular efforts are ongoing to harmonise lifestyle intervention studies based on the FINGER study globally (Kivipelto et al., 2020). Such 'high risk' prevention strategies may however have limited impact at population level (Rose, 2001). Whilst secondary prevention in those with, or indeed seeking, a diagnosis is important, shifting the focus to encompass primary prevention in the general population is vital if dividends are to be seen at a population level (Milne et al., 2021). Population based strategies are radical and may confer a large benefit (Rose, 2001). Increasing awareness of modifiable risk factors for dementia represents a core function of dementia awareness campaigns (WHO, 2017). Indeed, lack of knowledge has been cited as the main barrier to behavioural change in dementia risk reduction (Curran et al., 2021). Barriers to engaging in risk reduction behaviours are numerous and diverse. In addition to lack of knowledge, existing research suggests that barriers might include lack of motivation, lack of time, organisational issues, financial reasons, health problems, and other factors (Heger et al., 2019; Curran et al., 2021; Van Asbroeck et al., 2021). In this context, whether risk reduction strategies are implemented on an individual or population level, it is uncertain if increasing awareness of dementia risk factors alone will be sufficient to engender behavioural change. Addressing barriers to dementia risk reduction is thus essential.

As illustrated elsewhere in this thesis, modifiable risk factors for dementia remain prevalent in Ireland (Dukelow et al., 2023). A detailed examination of barriers to risk reduction behaviours in an Irish context has heretofore been lacking. More broadly, many existing studies examining barriers to brain health behaviours consider barriers generically, failing to examine how they might vary across different modifiable risk factors for dementia. In this context, this study aimed to undertake a detailed assessment of barriers to individual risk reduction behaviours. As existing research suggests that barriers to brain health behaviours may vary across sociodemographic factors (Heger et al., 2019; Van Asbroeck et al., 2021),

we sought to investigate the distribution of barriers across factors such as age, gender, educational status, and household income.

4.2 Methods

4.2.1. Study design and participants

The Five Lives Brain Health Ireland Survey (FLBHIS) is a cross-sectional survey that was distributed online amongst an Irish non-patient population. The FLBHIS was developed through an iterative process. Informed by current literature and expert opinion, a 100-question survey was devised (see Appendix 1). The survey was adapted from the Lifestyle Barriers for Cognitive Health Questionnaire (K. Muhammed 2021, personal communication, 2 September) to be suitable for an Irish population. Risk factors were derived from the 2020 report of the Lancet Commission on Dementia prevention, intervention, and care (Livingston et al., 2020). Additional items relating to other modifiable risk factors for cognitive decline such as sleep issues (Spira et al., 2014) and mental stimulation (Krell-Roesch et al., 2019) were also added to the survey. The barriers used in our study were derived and adapted from the behaviour change wheel, specifically from the COM-B model (Michie et al., 2011). At the heart of this model are three essential conditions, namely capability, opportunity, and motivation. From this model, five subcategory barriers were derived specifically to cover the risk factors for brain health. Conditions were developed and subcategories defined as follows: capability (emotional factors, practical factors, and lack of knowledge), opportunity (social factors), and motivation (lack of motivation). Subcategories related to capability differ from those set out by Michie who distinguished between physical and psychological capability (Michie et al., 2011). Questions were constructed in order to elicit information related to each subcategory. Examples of questions/statements related to smoking and its associated barriers, for example, include the following: '*I want to stop smoking but I have not got the willpower to stop on my own*' (motivation-lack of motivation); '*I do not think I could stop smoking due to the social life I have*' (opportunity-social); and '*Stress and pressures from work or personal life mean I cannot quit smoking'* (capability-emotional). This approach allowed the main sources of behaviour to be captured at a higher level whilst allowing more granular sub-categorisation where possible.

Inclusion criteria comprised people aged over 50. Participants were excluded if they had a diagnosis of dementia, or had worked in the healthcare sector. A pilot version of the survey

was undertaken in January 2022 ($n = 50$). The survey pilot revealed a tendency for respondents to 'straight-line' answers, potentially indicating respondent satisficing (Reuning and Plutzer, 2020) or indeed respondent fatigue related to repetitive questions in the original survey design. Phraseology and number of questions were modified accordingly. The modified survey was subsequently administered to a further 555 volunteers in February 2022. A professional market research company, CDR Insights & Analytics Limited, was responsible for administration of the survey online to an existing market research panel. Choice of sample size was guided by logistical constraints and review of comparable literature (Heger et al., 2019). With regard to the sampling technique, a 1:1 male to female gender split was pre-specified in order to approximately reflect the Irish population. No upper age-limit was pre-determined.

Prior to commencement, this study was reviewed by The St. James' Hospital/Tallaght University Hospital Joint Research Ethics Committee who advised that, in keeping with local institutional and legislative requirements, formal approval was not necessary.

4.2.2 Measures

The survey captured the following information: (1) Sociodemographic factors (gender, age, ethnicity, household income and level of education); (2) Barriers to brain health behaviours; (3) Exposure to, as well as knowledge of modifiable risk factors for dementia, namely diet, social interaction, exercise, hypertension, sleep, current low mood/depression, current smoking, alcohol consumption, cognitive stimulation, hearing impairment, diabetes, air pollution and head injury; (4) Participants' perceptions regarding potential for dementia prevention and risk reduction.

Alcohol intake (>14 units per week), being overweight, smoking, low physical activity, sleep quality, depression/low mood, low social interaction, low mental stimulation and residing in an area with high air pollution were self-reported risk factors, whereas diabetes, hypertension and hearing impairment were defined as being diagnosed by a healthcare professional.

4.2.3 Statistical analysis

All personal data were removed from the dataset prior to receipt by the research team. Analyses were conducted using IBM SPSS Statistics software. Frequency counts and percentages were used to show rates of exposure to modifiable risk factors for dementia

amongst the sample. For reporting and analysis purposes, barriers were broadly classified as relating to lack of knowledge, lack of motivation, emotional factors, social factors and practical factors. Frequency counts and percentages were used to illustrate prevalence of barriers relevant to individual risk factors. For all analyses, statistical significance was defined as $p < 0.05$.

Z-tests with a Bonferroni correction for multiple comparisons were utilised to examine distribution of barriers between groups. Significant differences were confirmed using chi-square tests. Age was categorised into two groups, defined as 50–64 years old, and 65 years and above for the purpose of analysis. Household income was categorised into two groups, defined as ≤€40,000 per year, and > €40,000 per year. Due to small numbers in this group ($n = 3$), those who responded that they would prefer not to disclose their gender were excluded from the dataset for analyses. Due to small numbers who had been educated to primary school level ($n = 10$), this group was combined with those who had been educated to secondary school level for the purpose of analysis. People who chose not to disclose their household income ($n = 55$) were excluded from analyses including the household income variable. Due to low numbers which precluded Z-tests, blood pressure, hearing impairment, diabetes and head injury were excluded from the analysis of sociodemographic factors as predictors of barrier prevalence.

A two-step cluster analysis was used to classify participants in distinct groups based on age, gender, education and household income. The distance measure was log-likelihood and the clustering criterion was Schwartz's Bayesian Criterion. Initially, the automatic clustering algorithm of SPSS produced three clusters based on these settings but the cluster quality was classified as 'Fair' (average Silhouette measure of cohesion and separation = 0.4). To improve the cluster quality, the number of clusters was increased manually by a factor of 1 until reaching the lowest number of clusters for which a 'Good' cluster quality was achieved.

The percentages of people reporting barriers to alcohol use represent a fraction of those exposed to greater than 14 units of alcohol per week. For the barriers to preventing all other risk factors, the percentages refer to the fraction of people who reported exposure to the respective risk factor.

4.3 Results

4.3.1 Sample characteristics

The study population ultimately comprised 551 participants. Of the 555 volunteers to whom the survey was originally administered, three participants were excluded as they did not disclose their gender. One further participant was excluded due to an incomplete dataset. Table 1 outlines the sociodemographic characteristics of the sample. The study population comprised 551 participants with an almost equal proportion of male and female respondents (50.3% male; 49.6% female). Mean age was 59.7 years, with the majority of the sample ranging between 50 and 59 years of age (54.3%). 98.9% of respondents were of White ethnicity. Most participants were educated to secondary school level or higher (98.2%), were employed or self-employed (52.2%), and cohabited with one or more persons (74.4%).

4.3.2 Risk factor exposure and barrier prevalence for individual risk factors

Table 2 below outlines exposure to modifiable risk factors, as well as the prevalence of different barriers across individual risk factors. Various practical barriers, and lack of motivation were the most prevalently cited barriers across multiple risk factors. Lack of motivation was the most prevalent barrier to consuming a healthy diet (64%, $n = 213$), physical activity (77.7%, $n = 167$), smoking cessation (68%, $n = 85$), and moderation of alcohol intake (56.3%, $n = 67$). Practical factors were the most prevalent barriers to addressing low mood (56.5%, $n = 87$), air pollution (30.1%, $n = 58$), hearing impairment (63.8%, $n = 44$), diabetes (11.1%, $n = 5$), and head injury (80%, $n = 8$). Emotional factors were the most prevalent barriers to engaging in mentally stimulating activity (56.9%, $n = 66$), social activity (54.9%, $n = 302$), and good sleep (70.1%, $n = 129$). Lack of knowledge was the most prevalent barrier to hypertension control (14.4%, $n = 29$).

Characteristic	n (%)
Age in years	
50-64	437 (79.3)
65 and above	114 (20.7)
Gender	
Male	277 (50.3)
Female	274 (49.7)
Educational attainment	
Primary school	10 (1.8)
Secondary school	282 (51.3)
Undergraduate degree	196 (35.6)
Postgraduate degree	62 (11.3)
Household income level	
Less than €20 000	104 (18.9)
€20 000 - €40 000	189 (34.4)
€40 000 - €60 000	91 (16.6)
€60 000 - €80 000	63 (11.5)
Above €80 000	48 (8.7)
Employment status	
Employed or self-employed	287 (52.2)
Unemployed	91 (16.6)
Retired	172 (31.3)
Home circumstances	
Living alone	141 (25.6)
Living with one other person	197 (35.8)
Living with more than one person	212 (38.6)

Table 1: Sociodemographic characteristics of the sample. Note. Total sample (N=551). Not all totals for each variable sum to 551 due to missing data. Previously published (Dukelow et al., 2023b).

4.3.4 Risk factor exposure and barrier prevalence for individual risk factors

Table 4 below outlines exposure to modifiable risk factors, as well as the prevalence of different barriers across individual risk factors. Various practical barriers, and lack of motivation were the most prevalently cited barriers across multiple risk factors. Lack of motivation was the most prevalent barrier to consuming a healthy diet (64%, $n = 213$), physical activity (77.7%, $n = 167$), smoking cessation (68%, $n = 85$), and moderation of alcohol intake (56.3%, $n = 67$). Practical factors were the most prevalent barriers to addressing low mood (56.5%, $n = 87$), air pollution (30.1%, $n = 58$), hearing impairment (63.8%, $n = 44$), diabetes (11.1%, $n = 5$), and head injury (80%, $n = 8$). Emotional factors were the most prevalent barriers to engaging in mentally stimulating activity (56.9%, $n = 66$), social activity (54.9%, $n = 302$), and good sleep (70.1%, $n = 129$). Lack of knowledge was the most prevalent barrier to hypertension control (14.4%, $n = 29$).

4.3.5 Overall barrier prevalence

Figure 5 below illustrates the proportion of participants reporting at least one barrier of each subtype. Practical barriers were most commonly reported, with at least one practical barrier reported by 84.2% of the study population ($n = 464$). One or more emotional barriers were reported by 83.5% of the population ($n = 460$), motivational barriers by 62.6% ($n = 345$), and social barriers by 48.8% ($n = 269$). Knowledge barriers were least commonly reported with 34.7% of participants reporting one or more knowledge barriers ($n = 191$).

4.3.6 Effect of gender on exposure to barriers

Table 5 below illustrates the effect of gender on exposure to barriers. Females were significantly more likely to report stress from their work and personal life [$\chi^2(1) = 5.72$, $p = 0.017$], and people they live with [$\chi^2(1) = 9.03$, $p = 0.003$] as barriers to consuming a healthy diet. Males were more likely to report not having many friends [$\chi^2(1) = 6.46$, $p = 0.011$], and living too far away [$\chi^2(1) = 5.18$, $p = 0.023$] as barriers to engaging in social activity. Females were more likely to report the gym being too expensive as a barrier to engaging in physical activity [$\chi^2(1) = 3.87$, $p = 0.049$] Male participants were more likely to report caffeine intake [$\chi^2(1) = 4.77$, $p = 0.029$], work commitments [$\chi^2(1) = 9.97$, $p = 0.002$] and residing in a noisy area [$\chi^2(1) = 12.12$, $p < 0.001$] as barriers to sleep. Males were also more likely to report work related stress as a barrier to treating low mood and depression

[$\chi^2(1) = 3.89$, $p = 0.049$]. Female participants were more likely to report that alcohol helped them to cope with stress [$\chi^2(1) = 4.51$, $p = 0.034$]. Male participants were more likely to report a lack of close friends as being a barrier to engaging in mentally stimulating activity [$\chi^2(1) = 5.56$, $p = 0.018$].

4.3.7 Effect of age on exposure to barriers

Table 6 below illustrates the effect of age on exposure to barriers. Younger participants were more likely to report stress from their work or personal life as being a barrier to consuming a healthy diet [$\chi^2(1) = 17.08$, $p < 0.001$]. Younger participants were more likely to report multiple barriers to engaging in social activity, namely not having many friends [$\chi^2(1) = 4.09$, $p = 0.04$], being unable to afford the cost [$\chi^2(1) = 15.92$, $p < 0.001$], being stressed by meeting others [$\chi^2(1) = 4.79$, $p = 0.03$], and not having enough time [$\chi^2(1) = 4.16$, $p = 0.04$]. With regard to physical activity, younger participants were more likely to report home commitments as being a barrier [$\chi^2(1) = 7.71$, $p = 0.006$]. Younger participants were more likely to report stress as being a barrier to sleep [$\chi^2(1) = 8.29$, $p = 0.004$], whereas older participants were more likely to be unable to identify a specific barrier [$\chi^2(1) = 3.88$, $p = 0.049$]. Younger participants were more likely to identify work related stress as being a potential cause of low mood and depression [$\chi^2(1) = 5.91$, $p = 0.015$]. Younger participants were more likely to report not having the willpower to stop [$\chi^2(1) = 13.46$, $p < 0.001$], and stress from work or personal life [$\chi^2(1) = 4.15$, $p = 0.04$] as barriers to smoking cessation. No statistically significant differences between age groups were noted for barriers pertaining to alcohol consumption, mentally stimulating activity and air pollution.

			Lack of motivation	Emotional	Social	Practical	Lack of knowledge		
Risk factor	**Exposed (% total)**	**Exposed (n total)**	**Barriers (% from exposed to risk factor)**						
Unhealthy diet	60.4%	333	I have no motivation	Healthy foods do not satisfy my appetite	Stress from work / personal life	Healthy foods take too long to prepare	Healthy foods cost too much	Not like the taste of healthy foods	I am unsure about what a healthy diet is	people I live with
		%	64.0%	42.6%	37.5%	31.8%	31.2%	26.7%	26.4%	21.9%
		n	213	142	125	106	104	89	88	73
Low social interaction	54.8%	302	do not socialise much as I like being by myself	worried about COVID-19	not many friends	no access to facilities to meet	live too far away	cannot afford the costs	stress meeting others	not enough time
		%	54.9%	49.7%	49.0%	47.0%	46.4%	39.4%	35.1%	24.5%
		n	302	150	148	142	140	119	106	74
Low physical activity	39.0%	215	no drive to do it	gym too expensive	no access to facilities	physical disability	home commitments	work commitments		
		%	77.7%	45.1%	34.4%	33.0%	30.2%	22.3%		
		n	167	97	74	71	65	48		
Hypertension	36.7%	202	would not know how to change my lifestyle	would not be able to get health support	would be worried of the outcome of checking BP					
		%	14.4%	9.9%	3.0%					
		n	29	20	6					
Poor quality sleep	33.4%	184	too stressed	do not know why	family commitments	caffeine intake	work commitments	noisy area		
		%	70.1%	64.7%	18.5%	17.4%	12.0%	10.9%		
		n	129	119	34	32	22	20		
Low mood and depression	27.9%	154	life at home	financial worries	health worries	worried about asking others	bad previous experiences with health professionals	work related stress	not know how to access services	
		%	56.5%	49.4%	48.7%	37.0%	33.8%	25.9%	23.4%	
		n	87	76	75	57	52	40	36	
Smoking	22.7%	125	not have the willpower to stop	stress from work or personal life	other people I live with continue to smoke	social life I have				
		%	68.0%	46.4%	42.4%	24.8%				
		n	85	58	53	31				
Alcohol consumption	21.6%	119	not feeling I need to reduce alcohol consumption	alcohol helps me cope with stress	people around me continue to drink	social life I have				
		%	56.3%	35.3%	20.2%	16.8%				
		n	67	42	24	20				
Low mental stimulation	21.1%	116	not entertaining	no close friends	lack of time	financial means				
		%	56.9%	42.2%	36.2%	34.5%				

		n	66	49	42	40	
Air pollution	15.1%	83	Could afford to change the area I live or work in				
		%	30.1%				
		n	58				
Hearing impairment	12.5%	69	too high cost	worried perception of hearing aid	worried about assessment outcome	too busy for assessment	not know how to do assessment
		%	63.8%	20.3%	10.1%	8.7%	2.9%
		n	44	14	7	6	2
Diabetes	8.2%	45	forget to take medication	no time to monitor sugar levels	sugar levels not well controlled	worried if problem found	not know how to seek advice
		%	11.1%	11.1%	11.1%	6.7%	4.4%
		n	5	5	5	3	2
Activities with risk of head injury	1.8%	10	Activities that increase the risk of head injury are part of my life	I enjoy taking part in contact sports too much to stop doing them			
		%	80.0%	70.0%			
		n	8	7			

Table 4: Risk factor exposure and barrier prevalence for individual risk factors. Figures in red indicate small sample sizes excluded from further analyses. Previously published (Dukelow et al., 2023b).

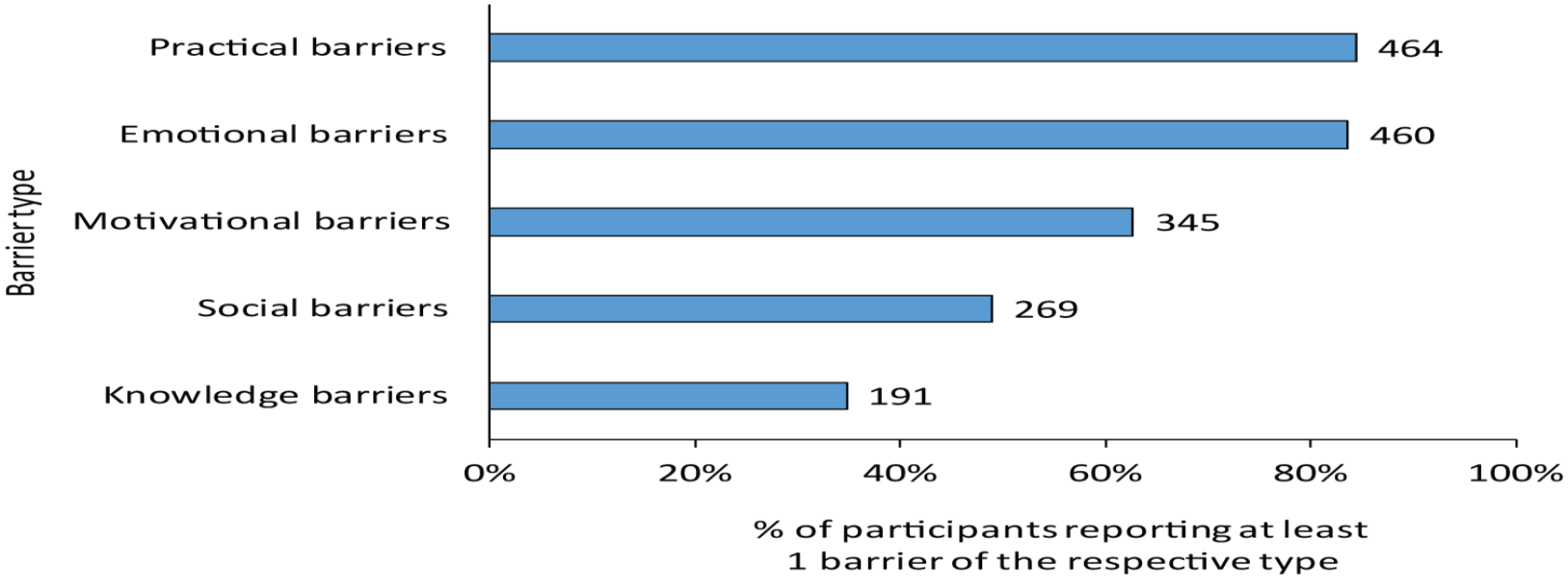

Figure 5: Percentage of participants reporting at least one barriers of each respective type. Previously published (Dukelow et al., 2023b).

			Lack of motivation	Emotional	Social	Practical	Lack of knowledge		
Risk factor	**Exposed (%)**	**Exposed (n)**	**Barriers (% from exposed to risk factor)**						
Unhealthy diet	60.4%	333	I have no motivation	Healthy foods do not satisfy my appetite	Stress from work / personal life	Healthy foods take too long to prepare	Healthy foods cost too much	Not like the taste of healthy foods	I am unsure about what a healthy diet is	people I live with
	male	160	61.3%	43.1%	***31.3%**	31.3%	33.8%	29.4%	28.8%	****15.0%**
	female	173	66.5%	42.2%	***43.4%**	32.4%	28.9%	24.3%	24.3%	****28.3%**
Low social interaction	54.8%	302	do not socialise much as I like being by myself	worried about COVID-19	not many friends	no access to facilities to meet	live too far away	cannot afford the costs	stress meeting others	not enough time
	male	147	53.1%	46.3%	***55.1%**	46.3%	***53.1%**	36.1%	35.4%	23.1%
	female	155	56.8%	52.9%	***43.2%**	47.7%	***40.0%**	42.6%	34.8%	25.8%
Low physical activity	39.0%	215	no drive to do it	gym too expensive	no access to facilities	physical disability	home commitments	work commitments		
	male	109	73.4%	***38.5%**	31.2%	33.9%	26.6%	22.9%		
	female	106	82.1%	***51.9%**	37.7%	32.1%	34.0%	21.7%		
Poor quality sleep	33.4%	184	too stressed	do not know why	family commitments	caffeine intake	work commitments	noisy area		
	male	72	72.2%	58.3%	18.1%	***25.0%**	****20.8%**	*****20.8%**		
	female	112	68.8%	68.8%	18.8%	***12.5%**	****6.3%**	*****4.5%**		
Low mood and depression	27.9%	154	life at home	financial worries	health worries	worried about asking others	bad previous experiences with health professionals	work related stress	not know how to access services	
	male	64	59.0%	50.8%	52.5%	37.7%	31.1%	***34.4%**	23.0%	
	female	90	54.8%	48.8%	46.4%	36.9%	35.7%	***20.2%**	23.8%	
Smoking	22.7%	125	not have the willpower to stop	stress from work or personal life	other people I live with continue to smoke	social life I have				
	male	70	64.3%	44.3%	40.0%	28.6%				
	female	55	72.7%	49.1%	45.5%	20.0%				
Alcohol consumption	21.6%	119	not feeling I need to reduce alcohol consumption	alcohol helps me cope with stress	people around me continue to drink	social life I have				
	male	85	56.5%	***29.4%**	20.0%	17.6%				
	female	34	55.9%	***50.0%**	20.6%	14.7%				
Low mental stimulation	21.1%	116	not entertaining	no close friends	lack of time	financial means				
	male	68	63.2%	***51.5%**	35.3%	32.4%				
	female	48	47.9%	***29.2%**	37.5%	37.5%				
Air pollution	15.1%	83	Could afford to change the area I live or work in							
	male	46	30.4%							
	female	37	29.7%							

Table 5: Effect of gender on exposure to barriers. Numbers in bold show significant group differences. **Sig. different at $p < 0.01$, ***Sig. different at $p < 0.001$. NB, missing risk factors are due to low n which makes Z-tests not applicable. Previously published (Dukelow et al., 2023b).

			Lack of motivation	Emotional	Social	Practical	Lack of knowledge		
Risk factor	**Exposed (%)**	**Exposed (n)**	**Barriers (% from exposed to risk factor)**						
Unhealthy diet	60.4%	333	I have no motivation	Healthy foods do not satisfy my appetite	Stress from work / personal life	Healthy foods take too long to prepare	Healthy foods cost too much	Not like the taste of healthy foods	I am unsure about what a healthy diet is	people I live with
	50-64 y.o.	278	65.1%	42.1%	***42.4%	31.7%	31.3%	29.1%	24.5%	21.9%
	65+ y.o.	55	58.2%	45.5%	***12.7%	32.7%	30.9%	31.5%	36.4%	21.8%
Low social interaction	54.8%	302	do not socialise much as I like being by myself	worried about COVID-19	not many friends	no access to facilities to meet	live too far away	cannot afford the costs	stress meeting others	not enough time
	50-64 y.o.	248	56.8%	48.0%	*52.0%	46.4%	44.4%	***44.8%	*37.9%	*27.0%
	> 65 y.o.	54	47.8%	57.4%	*35.2%	50.0%	55.6%	***14.8%	*22.2%	*13.0%
Low physical activity	39.0%	215	no drive to do it	gym too expensive	no access to facilities	physical disability	home commitments	work commitments		
	50-64 y.o.	170	80.0%	47.6%	34.7%	32.9%	**34.7%	24.7%		
	> 65 y.o.	45	68.9%	35.6%	33.3%	33.3%	**13.3%	13.3%		
Poor quality sleep	33.4%	184	too stressed	do not know why	family commitments	caffeine intake	work commitments	noisy area		
	50-64 y.o.	158	***74.1%	*63.3%	19.0%	19.0%	12.7%	12.0%		
	> 65 y.o.	26	***46.2%	*73.1%	15.4%	7.7%	7.7%	3.8%		
Low mood and depression	27.9%	154	life at home	financial worries	health worries	worried about asking others	bad previous experiences with health professionals	work related stress	not know how to access services	
	50-64 y.o.	139	56.2%	52.3%	48.5%	36.9%	35.4%	***29.2%	23.8%	
	> 65 y.o.	15	60.0%	26.7%	53.3%	40.0%	20.0%	***0%	20.0%	
Smoking	22.7%	125	not have the willpower to stop	stress from work or personal life	other people I live with continue to smoke	social life I have				
	50-64 y.o.	112	***73.2%	*49.1%	43.8%	25.0%				
	> 65 y.o.	13	***23.1%	*23.1%	30.8%	23.1%				
Alcohol consumption	21.6%	119	not feeling I need to reduce alcohol cons.	alcohol helps me cope with stress	people around me continue to drink	social life I have				
	50-64 y.o.	99	54.5%	38.4%	19.2%	16.2%				
	> 65 y.o.	20	65.0%	20.0%	25.0%	20.0%				
Low mental stimulation	21.1%	116	not entertaining	no close friends	lack of time	financial means				
	50-64 y.o.	102	55.9%	40.2%	36.3%	34.3%				
	> 65 y.o.	14	64.3%	57.1%	35.7%	35.7%				
Air pollution	15.1%	83	Could afford to change area I live or work in							
	50-64 y.o.	73	31.5%							
	> 65 y.o.	10	20%							

Table 6: Effect of age on exposure to barriers. Previously published (Dukelow et al., 2023b). Numbers in bold show significant group differences. *Sig. different at $p < 0.05$, **Sig. different at $p < 0.01$, ***Sig. different at $p < 0.001$. NB, missing risk factors are due to low n which makes Z-tests not applicable.

			Lack of motivation	Emotional	Social	Practical	Lack of knowledge		
Risk factor	**Exposed (%)**	**Exposed (n)**	**Barriers (% from exposed to risk factor)**						
Unhealthy diet	60.4%	333	I have no motivation	Healthy foods do not satisfy my appetite	Stress from work / personal life	Healthy foods take too long to prepare	Healthy foods cost too much	Not like the taste of healthy foods	I am unsure about what a healthy diet is	people I live with
	≤ €40000/year	179	***68.2%**	40.8%	36.9%	30.7%	35.8%	26.8%	30.2%	22.3%
	> €40000/year	118	***56.8%**	45.8%	39.8%	33.9%	27.1%	28.0%	22.0%	23.7%
Low social interaction	54.8%	302	do not socialise much as I like being by myself	worried about COVID-19	not many friends	no access to facilities to meet	live too far away	cannot afford the costs	stress meeting others	not enough time
	≤ €40000/year	178	****60.8%**	48.3%	46.6%	48.9%	40.4%	42.7%	40.4%	***18.5%**
	> €40000/year	99	****49.0%**	48.5%	50.5%	44.4%	52.5%	33.3%	29.3%	***30.3%**
Low physical activity	39.0%	215	no drive to do it	gym too expensive	no access to facilities	physical disability	home commitments	work commitments		
	≤ €40000/year	122	78.7%	48.4%	36.1%	37.7%	****23.0%**	****14.8%**		
	> €40000/year	71	76.1%	42.3%	31.0%	25.4%	****45.1%**	****38.0%**		
Poor quality sleep	33.4%	184	too stressed	do not know why	family commitments	caffeine intake	work commitments	noisy area		
	≤ €40000/year	115	73.0%	60.9%	21.7%	20.0%	****6.1%**	13.0%		
	> €40000/year	50	68.0%	72.0%	16.0%	18.0%	****28.0%**	10.0%		
Low mood and depression	27.9%	154	life at home	financial worries	health worries	worried about asking others	bad previous experiences with health professionals	work related stress	not know how to access services	
	≤ €40000/year	105	****65.1%**	***56.4%**	52.5%	34.2%	32.9%	****15.4%**	22.2%	
	> €40000/year	41	****37.5%**	***37.2%**	45.6%	44.9%	37.7%	****47.7%**	24.6%	
Smoking	22.7%	125	not have the willpower to stop	stress from work or personal life	other people I live with continue to smoke	social life I have				
	≤ €40000/year	80	68.8%	46.3%	41.3%	22.5%				
	> €40000/year	38	71.1%	50.0%	50.0%	34.2%				
Alcohol consumption	21.6%	119	not feeling I need to reduce alcohol consumption	alcohol helps me cope with stress	people around me continue to drink	social life I have				
	≤ €40000/year	60	51.7%	40.0%	20.0%	15.0%				
	> €40000/year	51	58.8%	27.5%	21.6%	21.6%				
Low mental stimulation	21.1%	116	not entertaining	no close friends	lack of time	financial means				
	≤ €40000/year	66	60.6%	45.5%	30.3%	39.4%				
	> €40000/year	36	63.9%	33.3%	38.9%	22.2%				
Air pollution	15.1%	83	Could afford to change the area I live or work in							
	≤ €40000/year	43	20.9%							
	> €40000/year	33	39.4%							

Table 7: Effect of income on exposure to modifiable risk factors. Numbers in bold show significant group differences. *Sig. different at $p < 0.05$, **Sig. different at $p < 0.01$, ***Sig. different at $p < 0.001$. NB, missing risk factors are due to low n which makes Z-tests not applicable. Previously published (Dukelow et al., 2023b).

			Lack of motivation	Emotional	Social	Practical	Lack of knowledge		
Risk factor	**Exposed (%)**	**Exposed (n)**	**Barriers (% from exposed to risk factor)**						
Unhealthy diet	60.4%	333	I have no motivation	Healthy foods do not satisfy my appetite	Stress from work / personal life	Healthy foods take too long to prepare	Healthy foods cost too much	Not like the taste of healthy foods	I am unsure about what a healthy diet is	people I live with
	Secondary school	180	63.3%	46.1%	36.1%	28.9%	33.3%	28.9%	27.8%	24.4%
	University	153	64.7%	38.6%	39.2%	35.3%	28.8%	24.2%	24.8%	19.0%
Low social interaction	54.8%	302	do not socialise much as I like being by myself	worried about COVID-19	not many friends	no access to facilities to meet	live too far away	cannot afford the costs	stress meeting others	not enough time
	Secondary school	153	52.4%	53.6%	45.8%	44.4%	42.5%	43.8%	37.3%	23.5%
	University	149	57.8%	45.6%	52.3%	49.7%	50.3%	34.9%	32.9%	25.5%
Low physical activity	39.0%	215	no drive to do it	gym too expensive	no access to facilities	physical disability	home commitments	work commitments		
	Secondary school	126	73.8%	46.8%	34.9%	****39.7%**	*****21.4%**	****15.9%**		
	University	89	83.1%	42.7%	33.7%	****23.6%**	*****42.7%**	****31.5%**		
Poor quality sleep	33.4%	184	too stressed	do not know why	family commitments	caffeine intake	work commitments	noisy area		
	Secondary school	103	68.9%	68.0%	16.5%	16.5%	12.6%	10.7%		
	University	81	71.6%	60.5%	21.0%	18.5%	11.1%	11.1%		
Low mood and depression	27.9%	154	life at home	financial worries	health worries	worried about asking others	bad previous experiences with health professionals	work related stress	not know how to access services	
	Secondary school	94	63.0%	50.0%	52.0%	39.0%	****23.0%**	19.0%	***28.0%**	
	University	60	63.0%	62.0%	39.0%	35.0%	****44.0%**	33.0%	***13.0%**	
Smoking	22.7%	125	not have the willpower to stop	stress from work or personal life	people I live with continue to smoke	social life I have				
	Secondary school	85	68.2%	42.4%	36.5%	25.9%				
	University	40	67.5%	55.0%	55.0%	22.5%				
Alcohol consumption	21.6%	119	not feeling I need to reduce alcohol cons.	alcohol helps me cope with stress	people around me continue to drink	social life I have				
	Secondary school	71	57.7%	39.4%	18.3%	15.5%				
	University	48	54.2%	29.2%	22.9%	18.8%				
Low mental stimulation	21.1%	116	not entertaining	no close friends	lack of time	financial means				
	Secondary school	74	58.1%	47.3%	36.5%	39.2%				
	University	42	54.8%	33.3%	35.7%	26.2%				
Air pollution	15.1%	83	Could afford to change a rea I live or work in							
	Secondary school	42	26.2%							
	University	41	34.1%							

Table 8: Effect of education on exposure to modifiable risk factors (Dukelow et al, 2023b). Numbers in bold show significant group differences. *Sig. different at $p < 0.05$, **Sig. different at $p < 0.01$, ***Sig. different at $p < 0.001$. NB, missing risk factors are due to low n which makes Z-tests not applicable.

4.3.8 Effect of household income on exposure to barriers

Table 7, above, illustrates the effect of household income on exposure to barriers. No statistically significant differences between income groups were noted for barriers pertaining to smoking, alcohol consumption, low mental stimulation, or air pollution. Participants with lower household income were more likely to report lack of motivation as a barrier to consuming a healthy diet [$\chi^2(1) = 3.98$, $p = 0.046$]. With regard to engaging in social activity, participants with lower household income were more likely to report liking being by oneself [$\chi^2(1) = 6.69$, $p = 0.01$] whereas those with higher household income were more likely to report not having enough time [$\chi^2(1) = 4.24$, $p = 0.04$]. Participants with greater household income were more likely to report home commitments [$\chi^2(1) = 10.25$, $p = 0.001$] and work commitments [$\chi^2(1) = 13.59$, $p < 0.001$] as barriers to undertaking physical activity. Work commitments were also more commonly reported as a barrier to sleep by participants with greater household income [$\chi^2(1) = 13.36$, $p < 0.001$]. With regard to low mood and depression, life at home [$\chi^2(1) = 9.12$, $p = 0.002$], and financial worries [$\chi^2(1) = 4.32$, $p = 0.04$] were more commonly reported as barriers by those with lower household income. Work-related stress was more commonly reported by those with greater household income as a potential cause of low mood and depression [$\chi^2(1) = 16.53$, $p < 0.001$].

4.3.9 Effect of education on exposure to barriers

Table 8 illustrates the effect of education on exposure to barriers. No statistically significant differences between education groups were noted for barriers pertaining to healthy diet, sleep, smoking, alcohol consumption, low social interaction, air pollution, or engaging in mentally stimulating activity. Participants with higher levels of educational attainment were more likely to report home [$\chi^2(1) = 11.19$, $p < 0.001$] and work [$\chi^2(1) = 7.31$, $p = 0.007$] commitments as barriers to engaging in physical activity whereas physical disability was more likely to impact those educated to secondary school level [$\chi^2(1) = 6.10$, $p = 0.013$]. With regard to low mood and depression, those educated to secondary school level were less likely to know how to access services [$\chi^2(1) = 4.75$, $p = 0.03$]. Distrust of healthcare professionals or previous bad experiences were, on the other hand, more likely to impact those of higher educational attainment [$\chi^2(1) = 7.48$, $p = 0.006$].

4.3.10 Cluster analysis

Cluster analysis revealed six clusters (average Silhouette measure of cohesion and separation = 0.6). Figure 6 shows the cluster size and the demographic variable distribution within each cluster. The colour grading reflects the overall predictor importance (age: 1.00; education = 0.79; gender = 0.68; household income = 0.40). The cluster label is based on the top two most important predictors within each cluster. The cluster descriptions mention all demographic characteristics of the cluster that are significantly more prevalent (i.e., characterise >50% of participants in the cluster). Appendix 2 shows the *z*-tests assessing the significance of this prevalence.

Figure 6: Cluster Analysis. Previously published (Dukelow et al., 2023b). Two-step cluster analysis output and cluster composition. The cluster labels and descriptions are based on the relative contribution of variables within each cluster. *indicates a significant difference from 50/50 distribution

Cluster 1 comprised younger females (aged 50–64), who had been educated to secondary school level and had a household income of less than €40,000 (16.4%, *n* = 81); cluster 2 comprised older adults (aged 65–91) who were more likely to be male, educated to high school level, and to have a household income of < €40,000 (20.6%, *n* = 102); cluster 3 comprised secondary school educated, younger adults with high household income, who

were more likely to be male (12.9%, *n* = 64); cluster 4 comprised university educated younger females, who were more likely to have low household income (18.6%, *n* = 92); cluster 5 comprised secondary school educated, younger males with low household income (12.5%, *n* = 62); cluster 6 comprised university educated younger males, who were more likely have high household income (19%, *n* = 94). Table 9 below shows the number and proportion of participants within each cluster that have reported being exposed to any of the dementia risk factors. Table 10 shows the significant differences between clusters in the prevalence of each risk factor (with p-values not corrected for multiple comparisons). Several statistically significant differences were detected. Multiple risk factors disproportionately impact those of lower educational status (clusters A, C, and E). Secondary educated males (cluster E) were more likely to report exposure to excess alcohol when compared to other clusters, with the exception of university educated males (cluster F). They were also more likely to report smoking when compared to other clusters, with the exception of secondary educated females (cluster A). Secondary educated females (cluster A) were more likely to report poor sleep when compared to older males (cluster B), Secondary-educated, higher income (cluster C), and Uni-educated males (cluster F).

		Secondary-educated females		Older males		Secondary-educated, higher income		Uni-educated females		Secondary-educated males		Uni-educated males	
		Count	Column N %	Count	Column N %	Count	Column N %	Count	Column N %	Count	Column N %	Count	Column N %
Diabetes	Present	4	4.9%	11	10.8%	7	10.9%	6	6.5%	4	6.5%	11	11.7%
	Total	81	100.0%	102	100.0%	64	100.0%	92	100.0%	62	100.0%	94	100.0%
Low physical activity	Present	32	42.7%	40	45.5%	26	41.3%	38	46.3%	28	48.3%	29	34.5%
	Total	75	100.0%	88	100.0%	63	100.0%	82	100.0%	58	100.0%	84	100.0%
Sleep problems	Present	40	49.4%	26	25.5%	18	28.1%	33	35.9%	23	37.1%	25	26.6%
	Total	81	100.0%	102	100.0%	64	100.0%	92	100.0%	62	100.0%	94	100.0%
Activities with risk of head injury	Present	0	0.0%	2	2.0%	0	0.0%	3	3.3%	1	1.6%	4	4.3%
	Total	81	100.0%	102	100.0%	64	100.0%	92	100.0%	62	100.0%	94	100.0%
Hearing problems	Present	10	12.3%	19	18.6%	8	12.5%	8	8.7%	9	14.5%	9	9.6%
	Total	81	100.0%	102	100.0%	64	100.0%	92	100.0%	62	100.0%	94	100.0%
High blood pressure	Present	25	30.9%	50	49.0%	25	39.1%	30	32.6%	26	41.9%	31	33.0%
	Total	81	100.0%	102	100.0%	64	100.0%	92	100.0%	62	100.0%	94	100.0%
Overweight	Present	56	71.8%	48	49.5%	45	72.6%	58	63.0%	32	53.3%	58	63.0%
	Total	78	100.0%	97	100.0%	62	100.0%	92	100.0%	60	100.0%	92	100.0%
Smoking	Present	26	32.1%	13	12.7%	17	26.6%	16	17.4%	27	43.5%	19	20.2%
	Total	81	100.0%	102	100.0%	64	100.0%	92	100.0%	62	100.0%	94	100.0%
Social isolation	Present	48	59.3%	50	49.0%	31	48.4%	58	63.0%	36	58.1%	54	57.4%
	Total	81	100.0%	102	100.0%	64	100.0%	92	100.0%	62	100.0%	94	100.0%
Low mental stimulation	Present	18	22.2%	11	10.8%	15	23.4%	18	19.6%	22	35.5%	18	19.1%
	Total	81	100.0%	102	100.0%	64	100.0%	92	100.0%	62	100.0%	94	100.0%
Air pollution	Present	10	12.3%	8	7.8%	13	20.3%	16	17.4%	13	21.0%	16	17.0%
	Total	81	100.0%	102	100.0%	64	100.0%	92	100.0%	62	100.0%	94	100.0%
Alcohol	Present	10	19.6%	19	27.1%	17	28.8%	13	21.3%	27	50.9%	25	38.5%
	Total	51	100.0%	70	100.0%	59	100.0%	61	100.0%	53	100.0%	65	100.0%
Low mood/ depression	Present	36	44.4%	15	14.7%	20	31.3%	31	33.7%	24	38.7%	20	21.3%
	Total	81	100.0%	102	100.0%	64	100.0%	92	100.0%	62	100.0%	94	100.0%

Table 9: number and proportion of participants within each cluster that have reported being exposed to any of the dementia risk factors (Dukelow et al 2023b)

Risk factor	Cluster					
	Secondary-educated females	Older males	Secondary-educated, higher income	Uni-educated females	Secondary-educated males	Uni-educated males
	(A)	(B)	(C)	(D)	(E)	(F)
Air pollution			B(0.019)	B(0.044)	B(0.015)	
Alcohol					A(0.001) B(0.007) C(0.017) D(0.001)	A(0.028) D(0.036)
Low mood/ depression	B(0.000) F(0.001)		B(0.011)	B(0.002)	B(0.000) F(0.018)	
Diabetes						
Low physical activity						
Sleep problems	B(0.001) C(0.009) F(0.002)					
Activities with risk of head injury	.		.			
Hearing problems		D(0.046)				
High blood pressure		A(0.013) D(0.020) F(0.023)				
Overweight	B(0.003) E(0.025)		B(0.004) E(0.028)			
Smoking	B(0.001) D(0.024)		B(0.024)		B(0.000) C(0.046) D(0.000) F(0.002)	
Social isolation				B(0.050)		
Low mental stimulation	B(0.035)		B(0.029)		B(0.000) D(0.027) F(0.022)	

Table 10: significant differences between clusters in the prevalence of each risk factor (with p-values not corrected for multiple comparisons). Previously published (Dukelow et al., 2023b). When a risk factor is more prevalent within a cluster, the letter shows which other clusters have lower prevalence and the number in brackets shows the value of p of the difference

4.4 Discussion

In this study, we investigated barriers to lifestyle change to improve brain health in an Irish sample of adults aged 50 and above. Detailed subtyping of barriers, as well as examination of differences according to age, gender, education and income were undertaken, highlighting the diverse nature of barriers to brain health behaviours. Awareness of, and exposure to, modifiable risk factors for dementia, in addition to their associations with gender, age, and education were examined elsewhere and demonstrate a lack of awareness amongst our study population that dementia could be prevented through lifestyle modifications (Dukelow et al., 2023a). Increasing knowledge in this regard has been identified as a potential priority in Ireland's National Dementia public awareness campaign (Hickey, 2019). Effective dementia risk reduction approaches are likely to encompass individual and population focused approaches. In clinical contexts, it is anticipated that evolving memory clinics and dedicated brain health services will fulfil a significant role in dementia risk assessment, communication and delivery of personalised prevention (Frisoni et al., 2023). Our study highlights the individualised nature of risk factor profiles, and barriers to brain health behaviours, thereby underlining the utility of devising personalised risk reduction plans. Beyond secondary prevention, shifting the focus to encompass primary prevention in the general population is vital if dividends are to be seen at a population level (Milne et al., 2021). As well as increasing awareness of modifiable risk factors, we posit the argument that, in order to optimise their impact, public health interventions, rooted in the sociocultural contexts of their intended recipients, should target relevant barriers to risk reduction behaviours. It is recognised that homogeneous public health messages might not be persuasive to heterogeneous audiences (Wakefield et al., 2010). The heterogeneity of barriers to brain health behaviours revealed in this study further highlights that messaging may be irrelevant if it fails to take into account the gender, age, educational status, and income of its target audience. These points are further developed below.

In this study, clusters defined by lower socio-economic status (SES; as indicated by lower education and household income, namely clusters A and E) were disproportionately impacted by multiple risk factors, and several barriers were unequally distributed across socioeconomic groups. SES is a latent construct, comprising measures of income, education

and occupation, or some combination of these factors (Baker, 2014). In a global context, income inequality has increased in most high-income countries, and in some middle-income countries since 1990 (United Nations Department of Economic and Social Affairs, 2020). Lower SES is associated with a 2.1-year reduction in life expectancy (Stringhini et al., 2017), and in its own right has been recognised as a barrier to healthy behaviour at mid-life (Kelly et al., 2016). Those of lower SES have a higher risk of dementia, a difference which is explained in part by modifiable risk factors (Deckers et al., 2019). From a dementia perspective, it is known that individuals with higher household income may benefit from earlier diagnosis (Petersen et al., 2021). In our study, those of lower household income were more likely to report lack of motivation as a barrier to consuming a healthy diet. Liking being by oneself was more likely to represent a barrier to social activity in those with lower household income. Home and work commitments, on the other hand, were more likely to represent a barrier to physical activity in those with higher household income. It has been suggested that effective public health programmes must take the needs of those with lower SES into account when designing interventions for dementia prevention at individual and societal level (Deckers et al., 2019). We further postulate that large scale interventions targeted at those of lower SES should be tailored to account for the barriers to risk reduction behaviours which disproportionately impact this cohort. Public health interventions, if they do not account for sociocultural contexts, may paradoxically serve to worsen health inequalities (Stephens et al., 2012). Behaviour change interventions for low-income groups have, however, demonstrated positive effects on physical activity, smoking, and healthy eating (Bull et al., 2014), all of which represent modifiable risk factors for dementia. Specific behavioural change techniques and delivery/context components may significantly increase the effectiveness of interventions targeting healthy eating and physical activity in low-income groups (Bull et al., 2018). The investigation of interventions targeting the broader spectrum of modifiable risk factors for dementia in lower SES cohorts, and clarification of individual components conferring effectiveness, represent priorities in the field of brain health research.

Educational status is significantly associated with awareness of multiple modifiable risk factors for dementia (Dukelow et al., 2023). In the context of dementia, education has long been thought to impact cognitive reserve, reducing susceptibility to age-related changes and Alzheimer's Disease (AD) pathology (Stern, 2012). Higher educational status appears to

impact dementia risk indirectly through its relationship with higher wealth and better lifestyle (Deckers et al., 2019). Lower educational attainment in women, however, is independently associated with an increased risk of dementia-related death (Russ et al., 2013). In our study, individuals of lower educational status were more likely to report a physical disability as a barrier to engaging in physical activity. This cohort were also more likely to report lack of knowledge with regard to accessing services as a barrier to treatment of low mood and depression. Individuals educated to undergraduate level or higher were more likely to report a range of practical barriers. Education is thought to impact health via multiple potential pathways (Cohen and Syme, 2013). Whilst the relationship between education and health behaviours such as smoking, alcohol consumption, and exercise is explained in part by differences in health knowledge, most effects remain after differences in knowledge are controlled for (Kenkel, 1991). Amongst other factors, attending university education is associated with a range of preventative health behaviours (Folta et al., 2009). More broadly speaking, as opposed to relating to quantity, health benefits may relate to the delivery of quality education (Cohen and Syme, 2013). The relationship between educational status, exposure to modifiable risk factors, and broader health outcomes has profound policy implications. Educational inequality has long been a theme in Irish educational discourse (Jeffers and Lillis, 2021). A policy central to tackling educational disadvantage in an Irish context is 'Delivering Equality of Opportunity in Schools' (DEIS). Whilst DEIS has demonstrated consistent success in improving academic outcomes across all grade levels (Kavanagh et al., 2017), considerable disparities persist. The consistent prioritisation of educational equity in national policy may ultimately have unintended benefits on health outcomes, potentially impacting dementia risk.

Our study highlighted multiple gender differences across barriers to brain health behaviours. Gender based inequalities related to dementia are widespread (Andrew and Tierney, 2018; Bartlett et al., 2018). Globally, females are disproportionately impacted by dementia. Dementia incidence rates are higher amongst women, with a particular divergence in incidence after the age of 80 (Beam et al., 2018). Disability adjusted life years (DALYs) due to dementia are approximately 60% higher amongst women than men (WHO, 2022). In our study, certain barriers disproportionately impacted female participants. Females were more likely to report particular emotional factors as being barriers to consuming a healthy diet and reducing alcohol intake. The disproportionate impact of stress

in these contexts is broadly in keeping with previous work highlighting a tendency for women to relate stress to family and health-related events more frequently than men (Matud, 2004). Females were less likely to report practical factors as barriers to getting a good night's sleep. At a population health level, designing risk reduction strategies to target gender-specific differences in reported barriers may confer additional impact. Previously, gender has been neglected in many National Dementia Strategies (Bartlett et al., 2018). Despite dementia's disproportionate impact on those of female gender, it has been suggested that women's focused dementia research is underfunded. Only 12% of the $2.398 billion 2019 National Institutes of Health (NIH) Alzheimer's disease budget went to women-focused research (Baird et al., 2021). Gender-sensitive public health practise is a necessity, and recent years have seen delineation of implementation strategies at European level (Oertelt-Prigione et al., 2017). Successful examples of gender-sensitive public health interventions can be identified (Gaston et al., 2007; Folta et al., 2009), and may provide a basis for addressing gender-specific differences in brain health behaviours and associated barriers. The StrongWomen—Healthy Hearts programme for example has demonstrated efficacy in reducing cardiovascular disease risk in sedentary midlife and older women who were overweight or obese (Folta et al., 2009), and may provide a template for gender specific dementia risk reduction interventions.

Lack of motivation was the most often cited barrier across multiple cardiovascular risk factors (healthy diet, physical activity, smoking and alcohol excess). Cardiovascular risk factors were prevalent amongst the study population (Table 2). Whilst mortality related to stroke (Soto et al., 2021), and coronary heart disease (Marasigan et al., 2020) in Ireland are falling, the prevalence of some cardiovascular risk factors is increasing (Marasigan et al., 2020) and globally the burden of cardiovascular disease attributable to modifiable risk factors continues to increase (Roth et al., 2020). Burgeoning evidence supports a link between individual cardiovascular risk factors and Alzheimer's disease dementia (Takeda et al., 2020). Whilst improvements in cardiovascular risk factor control may account for falling dementia prevalence in high-income countries, we demonstrate that cardiovascular risk factors remain prevalent in Ireland. Engaging and motivating those disinclined to participate may be hard to achieve via a public health campaign. In this context, the high prevalence of lack of motivation as a barrier to cardiovascular risk factor control in our study is concerning. Many social psychological models applied in a health behaviour context assume

a degree of intrinsic motivation (Hardcastle et al., 2015). Whilst campaigns with mass media components aimed at increasing physical activity have yielded short-term increases, such increases are mainly in highly motivated individuals (Wakefield et al., 2010).

We have stressed the importance of tailored health communication in dementia risk reduction interventions. Tailored health communication may demonstrate increased personal relevance, thereby increasing intent to engage in behavioural change (Bol et al., 2020). Tailored health messaging aside, the authors advocate for the design, implementation, and evaluation of preventive, personalised medicine interventions targeting modifiable risk factors for dementia, and their associated barriers. Ideally, such studies would incorporate measures of genetic, and pathological risk which confer a far higher relative risk than the lifestyle factors discussed herein (Frisoni et al., 2023). The optimal means of evaluating such complex interventions is unclear and may no longer comprise traditional gold standard study designs such as randomised, controlled trials (Garton et al., 2022). Garton et al. (2022) highlight that complex interventions require complex evaluations, underlining the potential role of a non-standard research methodology, namely transdisciplinary research (TDR), in this context. Whilst definitions of TDR vary, common characteristics include, amongst others, transcending disciplinary boundaries through a focus on theoretical unity of knowledge; the inclusion of societal actors as process participants; a focus on specific, complex, societally relevant issues; and working in a transformative manner (Lawrence et al., 2022). TDR can influence scientific productivity and capacity, increasing academic output (Grigorovich et al., 2019). As well as impacting prespecified 'traditional' patient outcomes, TDR may have broader social impacts which are difficult to capture through traditional techniques such as assessing policy outcomes (Grigorovich et al., 2019). TDR may represent a promising means to tackle the 'wicked problem' (Rittel and Webber, 1973) of increasing dementia incidence.

This study is not without its limitations. The study design introduces the potential for selection bias as participants were members of an existing market research panel. Our study population was highly educated, perhaps limiting the degree to which our results are generalisable in a global context. Our exploration of barriers is systematic, and comparatively exhaustive, based as it is on the Behaviour Change Wheel and under-pinning COM-B model (Michie et al., 2011). It is, however, limited by the use of explicit questions and absence of free text responses which might have revealed novel barriers unanticipated

by the research team. We thus cannot be sure that certain barriers for each risk factor were not missed. Patient and public involvement in survey design would have further strengthened this study.

Our study's principal strength comprises its robust and comprehensive design. Existing literature highlights a multitude of barriers to dementia risk reduction behaviours. Lack of knowledge has been highlighted as the main barrier to behavioural change (Curran et al., 2021). Two studies utilising an identical survey instrument in different populations (Heger et al., 2019; Van Asbroeck et al., 2021) highlight lack of knowledge, and lack of motivation as the two most prevalent barriers. Other factors cited included lack of time, difficulty organising, financial reasons, health problems, and 'other reasons'. Our work is differentiated by the survey construction, and risk factor-specific nature of the barriers contained therein. The results are likely to be useful in guiding public health messaging and intervention design. A range of barriers were explored across multiple risk reduction behaviours. The heterogeneity of barriers to brain health behaviours revealed in this study highlights the necessity to tailor public health interventions to their target population, taking into account the gender, age, educational status, and income of recipients. Our study serves to add weight to one of the stated goals of the WHO Global action plan on the public health response to dementia 2017–2025, namely the need to organise national and local public health and awareness campaigns that are community and culture specific (WHO., 2017).

Chapter 5 - Strengths, Limitations, and Future Directions

5.1 Strengths

Strengths of the study include the detailed and robust survey design. The survey instrument (Appendix 1) is differentiated by its detail. Multiple questions are explored pertaining to a range of risk factors. Risk factors addressed are not confined to those traditionally regarded as impacting dementia risk. Emerging risk factor, namely sleep, and metal stimulation were also explored. Robust methodology, whereby a pilot survey was undertaken, and the instrument refined thereafter, also represents a strength of this study.

Categorisation and classification of barriers was systematic. Utilisation of an established behaviour-change framework, the behaviour change wheel, and central COM-B model (Michie et al., 2011) facilitated the delineation of detailed barrier subtypes. This is a particular strength of the study. Detailed questions were constructed which were specific to individual risk factors. The grounding of questions into the categories of capability, opportunity, and motivation may, in time, facilitate the design of effective interventions.

This study was differentiated by its comparatively large sample size. As discussed below, the sample was highly educated. Nonetheless, the demographic profile was such that individuals of lower socio-economic status were captured. This study thereby serves to highlight the disproportionate impact of modifiable risk factors for dementia in this cohort. This is a strength which may guide public health interventions in an Irish context.

5.2 Weaknesses

This study is not without weaknesses. The study design introduces an inherent risk of selection bias. The survey was distributed by a market research company to an existing panel of participants. Whilst such panels may be constructed to mirror the general population, and set sociodemographic quotas/criteria can be established at the outset, demographic differences may exist. Furthermore, those accessing a survey online may have more ready access to technology, and be more-technologically literate than those who do not partake. It is noteworthy that the study cohort were disproportionately educated. As previously highlighted, 98.2% of survey respondents had attained at least secondary school

level education as compared to 62% of older adults in a nationally representative Irish longitudinal study (Barrett et al., 2011).

This study targeted individuals aged over 50. When viewed in the context of a life-course model of brain health (Livingston et al, 2020), the failure to include those aged <50 is arguably a weakness. The life-course model of Brain Health highlights that it is never too early and never too late to consider reducing one's dementia risk(Livingston et al, 2020). It is recognised that specific risk factors exert a particular impact in early life. Study design was such that these risk factors, and associated barriers were not explored. This study also excluded those who had a diagnosis of dementia. Some might construe this as a weakness. The evidence for modifiable risk factor modification in those living with dementia is not strong. Nonetheless, inclusion of those living with dementia in research which seeks to quantify risk factors for cognitive decline, and barriers to adherence to brain health behaviours, is merited.

As set out in section 4.1, there is much to commend the survey design. Nonetheless, the survey instrument is not without weakness. A potential limitation comprises the use of explicit questions. The inclusion of free-text responses may have facilitated the capture of individual or novel barriers which had not been anticipated by the research team. Although the classification of barriers was systematic and grounded in an established behaviour-change model, it cannot be guaranteed that certain barriers were not omitted. This study assessed a range of modifiable risk factors for dementia. The inclusion of further novel and emerging risk factors may have further strengthened study design. Patient and public involvement in survey design would have further strengthened this study.

5.3 Future Directions

This study serves to highlight research, public health, and clinical imperatives in the field of brain health and dementia prevention . Future directions in these contexts are briefly discussed hereunder.

5.3.1 Research priorities

High risk groups merit further investigation. In this research we highlight that those of lower SES are disproportionately impacted by multiple modifiable risk factors for dementia. Whilst

our exploration of barriers was detailed, it was not exhaustive. Detailed engagement, including but not limited to expanded surveys, interviews, and focus groups is essential if a comprehensive understanding of barriers to brain health behaviours is to be gained in this cohort.

Those of female gender represent a further high risk cohort. Alzheimer's Disease is recognised to occur more commonly in women with a previous meta-analysis suggesting an Alzheimer's Disease incidence of 7.02 per 1000 person years in men and 13.25 per 1000 person years in women (Niu et al., 2016). In the first instance, inclusion of further novel modifiable risk/protective factors in future work should be considered. Qualitative approaches in this cohort, as well as expanding inclusion criteria to include females of all ages may prove to be fruitful approaches.

Previous studies of dementia risk reduction approaches have demonstrated the efficacy of multimodal interventions in high risk cohorts (Section 2.3 above). Those living with MCI represent a particularly high risk cohort, with an annual conversion rate to dementia of approximately 5-10% (Mitchell and Shiri-Feshki, 2009). Initial exploration of knowledge, and barriers surrounding modifiable dementia risk factors in this cohort, with subsequent longitudinal exploration of personalised interventions is a current focus of the author's Research Group.

5.3.2 Public Health priorities

Dementia risk reduction campaigns are far from ubiquitous globally and the majority are conducted in high income countries (WHO, 2021). Increasing dementia incidence in LMICs highlights the pressing imperative to implement effective campaigns worldwide. This is in keeping with one of the stated aims of the WHO Global action plan on the public health response to dementia 2017 - 2025 , namely the development, delivery, and promotion of evidence-based, sociodemographically attuned, and culturally sensitive interventions (WHO 2017). This research, through highlighting the individualised nature of risk factor profiles, and barriers to brain health behaviours, underscores the necessity for public health interventions to be rooted in the sociocultural contexts of their intended recipients (Dukelow et al., 2023b).

We highlight an apparent disconnect between the concepts of dementia risk reduction and dementia prevention. It is instructive that only 31.4% of people we surveyed believed that dementia could be prevented via lifestyle modifications. Despite this, 65.6% of participants believed that lifestyle improvements could decrease a person's risk of developing dementia. Clarity of communication and emphasis on the potential for prevention should be central to future public health messaging in this area.

5.3.3 Clinical priorities

As highlighted in Section 2.3 above, the design and implementation of integrated services capable of risk assessment, communication, and delivery of individualised, multimodal treatment plans targeting measures of biological as well as lifestyle risk must represent a core priority at national and international level. The European task force for Brain Health Services has recently articulated such a vision with, outlining the proposed structure and function of second generation memory clinics or Brain Health Services. The cornerstone functions are envisaged to comprise the following: (i) risk stratification and assessment of risk factors including brain pathology, (ii) communication of assessed risk (iii) risk reduction with multi-domain interventions, and (iv) cognitive enhancement (Frisoni et al., 2023). Funding and support for such services is essential if Integrated Brain Health Services are to be delivered.

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Appendix One

Survey Instrument

*signifies questions altered from original instrument.

Page 1

Q1: What is your age (in years)?

- [1]

Q2: What is your gender

- [1] Male
- [2] Female
- [3] Prefer not to say

Page 2 - Logic : Q1 : 1 Age less Than 50

RUN ACTIONS ONLY IF **Q1_1 < 50**

Terminate respondent using code **Q1term2**

Page 4 - Logic : Q2 equals 3 - Gender not stated

RUN ACTIONS ONLY IF **Q2 = 3**

Terminate respondent using code **Gender not given**

Page 5

Q4: What is the highest level of formal education you have completed?*

- [1] Primary school
- [2] Secondary school
- [3] Undergraduate university degree
- [4] Post graduate university degree

Q3: What is your current employment status?

- [1] Employed or self employed
- [2] Unemployed
- [3] Retired

Page 6

Settings:

Skip logic: **(Q3 = 2 OR Q3 = 3)**

Q50: In which of the following sectors do you work?*

- [1] Education
- [2] Financial services
- [3] Government and public service
- [4] Law
- [5] Manufacturing
- [6] Healthcare
- [7] Retail
- [8] Other sectors

Page 7 - Logic : Q50 equals 6 Healthcare

RUN ACTIONS ONLY IF **Q50 = 6**

Terminate respondent using code **Q50term1**

Page 8

Q5: What is your weight (in kg or stones)?

Settings:

Require a response: **No**

Skip and auto-answer if one response: **Yes**

Instructions: Please select only one type of answer

- [1] Kg

- [2] Stone

Q6: What is your height (in cm or feet/inches)?

Settings:

Require a response: **No**

Skip and auto-answer if one response: **Yes**

Instructions: Please select only one type of answer

- [1] In cm
- [2] In feet/inches

Page 9

Q7: How would you describe your ethnicity?*

- [1] White
- [2] Mixed or multiple ethnic groups
- [3] Asian
- [4] Black, African, or Carribean
- [5] Irish traveller
- [6] Prefer not to say

Page 10

Q8: What is your annual household income level?*

- [1] Less than €20 000
- [2] €20 000 - €40 000
- [3] €40 000 - €60 000
- [4] €60 000 - €80 000
- [5] Above €80 000
- [6] Prefer not to say or do not know

Q9: What best describes your home circumstances?

- [1] Live alone
- [2] Live with only one person (partner, child, family or friend)
- [3] Live with more than one person (children, family or friends)

Page 11 : Comparison to other diseases

Q61: In this section, we would like to understand your view about future health risks*

Settings:

Min Count: **1**

Instructions: Which of these diseases are you most concerned about developing in the future? Tick all that apply*

- [1] Cancer
- [2] Stroke
- [3] Dementia
- [4] Heart disease
- [5] Other or none of the above

Page 12

Q49: Which of these diseases do you believe can be prevented with lifestyle modifications (doing more exercise, eating healthy foods, quitting smoking, etc)?*

Instructions: Tick the ones you believe can be prevented with lifestyle modifications, or select Don’t know

- [1] Cancer
- [2] Stroke
- [3] Heart Disease
- [4] Dementia
- [5] Don’t know

Page 13

Q10: Have you seen a healthcare professional about memory worries?

- [1] YES
- [2] NO

Page 14

Q11: Which of the following healthcare professionals have you seen for memory worries? (Please tick all that apply)*

Settings:

Show logic: **(Q10 HAS [1])**

Min Count: **1**

- [1] General practitioner ONLY
- [2] Neurologist
- [3] Psychiatrist
- [4] Geriatrician

Q12: Have you been given a diagnosis by a healthcare professional of any of the following: (Please tick all that apply)

Settings:

Show logic: **(Q10 HAS [1])**

Min Count: **1**

- [1] Subjective Cognitive Impairment
- [2] Mild Cognitive Impairment
- [3] Dementia
- [4] Depression
- [5] Anxiety
- [6] None of these

Page 15

Q62: Please indicate your level of agreement with this statement

Settings:

Mobile smart: **Yes**

Rows:

- [1] Lifestyle improvements can decrease a person's risk of developing dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 16

Q13: In this section, we want to understand your attitudes regarding memory loss and dementia

Settings:

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] If necessary, I could make significant and sustained changes to my lifestyle
- [2] I am currently worried about my memory
- [3] I am worried I might have dementia

Columns:

- [1] Strongly agree

- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 17 - Logic : Q12 equals 3

RUN ACTIONS ONLY IF **Q12_= 3**

Terminate respondent using code **Dementia diagnosed**

Page 18

Q18: I have been told by a healthcare professional that I have high blood pressure

- [1] YES
- [2] NO

Page 19

Q20: Please indicate your level of agreement with this statement

Settings:

Mobile smart: **Yes**

Rows:

- [1] Having well controlled blood pressure is important in terms of reducing a person's future risk of dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

- [5] Don't know

Page 20

Q19: In this section, we want to understand what are the barriers for you to maintain an optimal blood pressure

Settings:

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] If I had to make lifestyle changes to improve my blood pressure, I would know how to do this
- [2] If I had to make lifestyle changes to improve my blood pressure, I would be able to obtain assistance to do so (for example, I could easily access a healthcare professional)
- [3] I would not get my blood pressure checked as I would be too worried about the outcome

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 21

Q23: I have been told by a healthcare professional that I have a hearing impairment

- [1] YES

- [2] NO

Page 22

Q57: Please indicate your level of agreement with this statement

Settings:

Mobile smart: **Yes**

Rows:

- [1] Correcting hearing difficulties may reduce the risk of future memory decline and dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 23

Q24: In this section, we want to understand your attitudes regarding the treatment of potential hearing problems

Settings:

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] If I wanted to have my hearing assessed I would know how to arrange this
- [2] If I had hearing difficulties, I would be too busy to arrange a hearing assessment

- [3] If I had hearing difficulties, I would not undertake a hearing assessment as I would be too worried about the outcome*

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 24

Q24_CLONE

Settings:

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] If I required a hearing aid, the cost (approximately €2 000) would put me off*
- [2] If I required a hearing aid, I would be worried what people would think of me

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 25

Q25: I smoke at least 1 cigarette per week

- [1] YES
- [2] NO

Page 26

Q26: Please indicate your level of agreement with this statement

Settings:

Skip logic: **0**

Mobile smart: **Yes**

Rows:

- [1] Quitting smoking may reduce the risk of future memory decline and dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 27

Q27: In this section, we want to understand your attitudes to smoking

Settings:

Skip logic: **Q25 = 2**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I want to stop smoking but I haven't got the willpower to stop on my own
- [2] I don't think I could stop smoking when other people I live with continue to smoke
- [3] I don't think I could stop smoking due to the social life I have
- [4] Stress and pressures from work or personal life mean I cannot quit smoking

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 28

Q28: Based on my current weight, I would consider myself overweight

- [1] YES
- [2] NO

Page 29

Q58: Please indicate your level of agreement with this statement

Settings:

Mobile smart: **Yes**

Rows:

- [1] A healthy diet may reduce the risk of future memory decline and dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 30

Q29: In this section, we want to understand what are the barriers for you to have a healthy diet

Settings:

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I want to have a healthier diet but I do not have the motivation to do so
- [2] I want to have a healthier diet but I am unsure of what a healthy diet consists of*
- [3] The taste of healthy foods stops me from eating them regularly
- [4] Healthy foods do not satisfy my appetite and this stops me from eating them regularly

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 31

Q56

Settings:

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] Healthy meals cost too much for me to eat them regularly
- [2] Healthy meals take too long to prepare for me to eat them regularly
- [3] The person or people I live with do not enjoy healthy foods and this stops me from eating them regularly
- [4] Stress and pressures from my work or personal life cause me to eat less healthy meals

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 32

Q30: Each week, I do on average:
- At least 2 and a half hours of moderate intensity activity (such as brisk walking or cycling)
- Or at least 75 minutes of vigorous intensity activity (such as running)

- [1] YES
- [2] NO

Page 33

Q30bis: Please indicate your level of agreement with this statement

Settings:

Mobile smart: **Yes**

Rows:

- [1] Physical activity and exercise may reduce the risk of future memory decline and dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 34

Q40: In this section, we want to understand what are the potential barriers for you to complete regular exercise

Settings:

Skip logic: **Q30 = 1**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I do not exercise regularly as I do not have access to facilities or guidance on exercise
- [2] I do not exercise regularly as it is too expensive to join a gym or fitness centre
- [3] I do not exercise regularly as I have a physical disability which impairs my abilities to do this

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 35

Q31

Settings:

Skip logic: **Q30 = 1**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I want to exercise more but I do not have the drive to do it regularly
- [2] Work commitments mean I do not have enough time to exercise
- [3] Home commitments mean I do not have enough time to exercise*

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 36

Q31_CLONE

Settings:

Skip logic: **Q30 = 2**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] Moderate exercise has a positive impact on the mood*
- [2] Moderate exercise has a positive impact on the quality of sleep*

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 37

Q32: The following types of exercise would be most appealing to me (tick all that apply)*

Settings:

Skip logic: **(Q30 == 1)**

Min Count: **1**

- [1] Gentle walk
- [2] Brisk walk
- [3] Running
- [4] Cycling
- [5] Yoga
- [6] Swimming

Page 38

Q33: I currently have low mood or depression

- [1] YES
- [2] NO

Q59: Please indicate your level of agreement with this statement

Settings:

Mobile smart: **Yes**

Rows:

- [1] Mood difficulties like depression may contribute to future risk of memory decline and dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 39

Q34: In this section, we want to understand your attitudes to low mood and depression

Settings:

Skip logic: **Q33 = 1**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] If I had low mood or depression, I would know how to access services to help
- [2] If I had low mood or depression, I would be worried about asking others for help because of what they might think
- [3] If I had low mood or depression, I would not seek help from healthcare professionals due to previous bad experiences or lack of trust in their services

Columns:

- [1] Strongly agree

- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 40

Q34_CLONE

Settings:

Skip logic: **Q33 = 1**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] If I had low mood or depression, this would mainly relate to life at home
- [2] If I had low mood or depression, this would mainly relate to work stress
- [3] If I had low mood or depression, this would mainly relate to financial worries
- [4] If I had low mood or depression, this would mainly relate to worries about my health*

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 41

Q34_CLONE2: In this section, we want to understand your attitudes to low mood and depression

Settings:

Skip logic: **Q33 = 2**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I know how to access services to help with low mood or depression
- [2] I am worried about asking others for help because of what they may think
- [3] I do not seek help from healthcare professionals due to previous bad experiences or lack of trust in their services

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 42

Q34_CLONE3

Settings:

Skip logic: **Q33 = 2**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] My low mood or depression mainly relates to life at home
- [2] My low mood or depression mainly relates to work related stress
- [3] My low mood or depression mainly relates to financial worries
- [4] My low mood or depression mainly relates to worries about my health

Columns:

- [1] Strongly agree
- [2] Agree

- [3] Disagree
- [4] Strongly disagree

Page 43

Q35: I have diabetes (Type I or II, diet or medication controlled)

- [1] YES
- [2] NO

Q51: Please indicate your level of agreement with this statement

Settings:

Mobile smart: **Yes**

Rows:

- [1] Having good blood sugar control may reduce the risk of future memory decline and dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 44

Q36: In this section, we want to understand the barriers you may have to adequately manage your diabetes

Settings:

Skip logic: **Q35 = 2**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] My sugar levels are normally very well controlled
- [2] I know how to seek assessment and advice for diabetes
- [3] I often forget to take my diabetes medication at the correct time

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 45

Q36_CLONE: In this section, we want to understand the barriers you may have to adequately manage your diabetes

Settings:

Skip logic: **Q35 = 2**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I am often too busy or do not have the time to monitor my sugar levels as often as I should
- [2] I am too worried to get my sugar levels checked in case a problem is found

Columns:

- [1] Strongly agree
- [2] Agree

- [3] Disagree
- [4] Strongly disagree

Page 46

Q59_CLONE: Please indicate your level of agreement with this statement

Settings:

Mobile smart: **Yes**

Rows:

- [1] Increased social interactions may reduce the risk of future memory decline and dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 47

Q37: In this section, we want to understand the barriers you may have to social engagement and interaction

Settings:

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I do not socialise much, as I like being by myself and enjoy my own company
- [2] I do not have access to facilities like social clubs or social events to meet and see other people
- [3] I do not have many friends or family to socialise with
- [4] I don't have enough time to socialise regularly with friends or family

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 48

Q37_CLONE

Settings:

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I live too far away from friends or family to socialise with them on a regular basis
- [2] I do not socialise often as I have stress / anxiety around meeting others
- [3] I do not socialise with friends or family because I cannot afford the costs of going out and meeting people
- [4] I do not socialise as much anymore because I am worried about COVID-19*

Columns:

- [1] Strongly agree
- [2] Agree

- [3] Disagree
- [4] Strongly disagree

Page 49

Q38: I drink alcohol (even if occasionally)

- [1] YES
- [2] NO

Q52: Please indicate your level of agreement with this statement

Settings:

Mobile smart: **Yes**

Rows:

- [1] Excessive consumption of alcohol may increase the risk of future memory decline and dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 50

Q39_CLONE_2: On average, I drink more than 14 units of alcohol per week (1 unit is the equivalent of half a pint of beer or a small glass of wine)

Settings:

Skip logic: **(Q38 == 2)**

- [1] YES
- [2] NO

Page 51

Q39: In this section, we want to understand your attitudes to alcohol consumption

Settings:

Skip logic: **Q38 = 2**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I don't want to reduce my alcohol intake as I do not feel there is a need
- [2] I don't think I can reduce my alcohol intake due to stress from work or personal reasons and I feel alcohol helps me deal with this
- [3] I want to reduce my alcohol intake, however, I don't feel I can reduce it when the people I live with continue to drink alcohol
- [4] I don't feel I can reduce my alcohol intake due to the social life I have

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 52

Q41: I take part in activities that increase the risk of head injury, such as boxing or rugby

- [1] YES
- [2] NO

Q53: Please indicate your level of agreement with this statement

Settings:

Mobile smart: **Yes**

Rows:

- [1] Significant or repetitive head injuries may increase the risk of future memory decline and dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 53

Q42: In this section, we want to understand the barriers you may have to reducing the risk of head injury

Settings:

Skip logic: **Q41 = 2**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I enjoy taking part in contact sports or other activities too much to stop doing them
- [2] Activities that increase the risk of head injury are part of my life

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 54

Q43: Please indicate your level of agreement with this statement

Settings:

Mobile smart: **Yes**

Rows:

- [1] Prolonged exposure to poor air quality and pollution may increase the risk of future memory decline and dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 55

Q44: Please rate your level of agreement with this statement

Settings:

Skip logic: **Q43 = 2**

Mobile smart: **Yes**

Rows:

- [1] I live or work in an area with a relatively high level of air pollution
- [2] If I wanted to, I could afford to change the area I live or work in to reduce the amount of air pollution I am exposed to

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 56

[RADIO] Q45: Generally, I am able to get a good night's sleep every night.*

- [1] YES
- [2] NO

[SIMPLE_GRID][RADIO] Q54: Please indicate your level of agreement with this statement*

Settings:

Mobile smart: **Yes**

Rows:

- [1] Poor sleep may increase the risk of future memory decline and dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 57

Q46_CLONE: In this section, we want to understand the barriers you may have to getting a good night's sleep*

Settings:

Skip logic: **Q45 = 1**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I don't often get a good night's sleep because I am too stressed/find it difficult to unwind
- [2] I don't often get a good night's sleep because of family commitments
- [3] I don't often get a good night's sleep because of work commitments

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 58

Q46

Settings:

Skip logic: **Q45 = 1**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I don't often get a good night's sleep because I live in a noisy area
- [2] I don't often get a good night's sleep because of my caffeine intake
- [3] I don't often get a good night's sleep and I don't know why

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Page 59

Q47: I often take part in mentally stimulating activities, such as reading, crossword puzzles, chess, learning a new language or playing an instrument*

- [1] YES
- [2] NO

Q55: Please indicate your level of agreement with this statement

Settings:

Mobile smart: **Yes**

Rows:

- [1] A lack of engagement in mentally stimulating activities may increase the risk of memory decline and dementia

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree
- [5] Don't know

Page 60

Q48: In this section, we want to understand the barriers you may have to engage in mentally stimulating activities*

Settings:

Skip logic: **Q47 = 1**

Mobile smart: **Yes**

Instructions: Please rate your level of agreement with each statement

Rows:

- [1] I don't often have the time to engage in mentally stimulating activities
- [2] I don't find mentally stimulating activities entertaining
- [3] I don't engage in mentally stimulating activities as I do not have the financial means to do so
- [4] I don't take part in mentally stimulating activities because I don't have any close family members or friends to do them with

Columns:

- [1] Strongly agree
- [2] Agree
- [3] Disagree
- [4] Strongly disagree

Appendix 2

Prevalent demographic characteristics of the cluster – associated *z*-tests

Older males:

age: z-statistic 10.100; Significance level P < 0.0001; 95% CI of observed proportion 96.45% to 100.00%

education: z-statistic 0.788; Significance level P = 0.4308; 95% CI of observed proportion 43.75% to 63.82%

gender: z-statistic 3.171; Significance level P = 0.0015; 95% CI of observed proportion 55.64% to 74.82%

Income: z-statistic 1.394; Significance level P = 0.1634; 95% CI of observed proportion 46.72% to 66.67%

Uni educated males:

age: z-statistic 9.695; Significance level P < 0.0001; 95% CI of observed proportion 96.15% to 100.00%

education: z-statistic 9.695; Significance level P < 0.0001; 95% CI of observed proportion 96.15% to 100.00%

gender: z-statistic 9.695; Significance level P < 0.0001; 95% CI of observed proportion 96.15% to 100.00%

Income: z-statistic 1.648; Significance level P = 0.0993; 95% CI of observed proportion 47.87% to 68.58%

Uni-educated females:

age: z-statistic 9.592; Significance level P < 0.0001; 95% CI of observed proportion 96.07% to 100.00%

education: z-statistic 9.592; Significance level P < 0.0001; 95% CI of observed proportion 96.07% to 100.00%

gender: z-statistic 9.592; Significance level P < 0.0001; 95% CI of observed proportion 96.07% to 100.00%

Income: z-statistic 1.458; Significance level P = 0.1449; 95% CI of observed proportion 46.85% to 67.84%

Secondary-educated females:

age: z-statistic 9.000; Significance level P < 0.0001; 95% CI of observed proportion 95.55% to 100.00%

education: z-statistic 9.000; Significance level P < 0.0001; 95% CI of observed proportion 95.55% to 100.00%

gender: z-statistic 9.000; Significance level P < 0.0001; 95% CI of observed proportion 95.55% to 100.00%

Income: z-statistic 9.000; Significance level P < 0.0001; 95% CI of observed proportion 95.55% to 100.00%

Secondary-educated higher-income:

age: z-statistic 8.000; Significance level P < 0.0001; 95% CI of observed proportion 94.40% to 100.00%

education: z-statistic 8.000; Significance level P < 0.0001; 95% CI of observed proportion 94.40% to 100.00%

gender: z-statistic 0.992; Significance level P = 0.3212; 95% CI of observed proportion 43.23% to 68.58%

Income: z-statistic 8.000; Significance level P < 0.0001; 95% CI of observed proportion 94.40% to 100.00%

Secondary-educated males:

age: z-statistic 7.874; Significance level P < 0.0001; 95% CI of observed proportion 94.22% to 100.00%

education: z-statistic 7.874; Significance level P < 0.0001; 95% CI of observed proportion 94.22% to 100.00%

gender: z-statistic 7.874; Significance level P < 0.0001; 95% CI of observed proportion 94.22% to 100.00%

Income: z-statistic 7.874; Significance level P < 0.0001; 95% CI of observed proportion 94.22% to 100.00%