

Diabetes and Brain Health

MD

2020

Dr Catherine Dolan

MB BCh BAO PGDip Clin Ed MRCPsych

Trinity College Dublin
School of Medicine

Declaration

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

I agree to deposit this thesis in the University's open access institutional repository or allow the Library to do so on my behalf, subject to Irish Copyright Legislation and Trinity College Library conditions of use and acknowledgement.

I consent to the examiners retaining a copy of the thesis beyond the examining period, should they so wish (EU GDPR May 2018).

To date, two publications have resulted from the work of this thesis, and I duly acknowledge the work of my co-authors: Dr Joanna McHugh, Dr Ronan Glynn, Sarah Griffin, Caroline Conroy, Dr Colm Loftus, Dr Philip Wiehe, Dr Marie-Louise Healy and Professor Brian Lawlor.

Summary

Type 2 diabetes mellitus (T2DM) is one of the most common non-communicable diseases in the world. In 2017 the International Diabetes Federation (IDF) estimated 425 million people to be living with diabetes globally, with numbers set to increase by almost half by 2045. Both type 1 diabetes (T1DM) and T2DM are linked with complications in various organs of the body. An association between diabetes and brain health complications, including dementia, is increasingly being recognised. Given the projected increase in prevalence globally of T2DM and dementia, identifying effective prevention strategies for both, in tandem with timely effective management of brain health complications of diabetes, is an important target. As a first step, we need to establish the level of awareness of the effects of diabetes on brain health among individuals with diabetes and the general public.

A narrative review of the literature found no validated survey instrument available to assess diabetes and brain health awareness. For this reason, a questionnaire was developed using Delphi methodology, for use in a pilot study among a sample of individuals with diabetes, nursing staff, and the general Irish population. Results of this pilot study, including Delphi and survey components, informed the research approach and design of the definitive survey measure used in the Diabetes and Brain Health (DBH) study.

With regard to the development of the definitive survey measure, a systematic review and a more extensive Delphi study were used to develop consensus on (i) potential brain-related complications of diabetes and, (ii) the common modifiable risk factors for T2DM and dementia. Thirteen studies, out of 9,709 abstracts that were identified in the literature review, were included in a qualitative synthesis of results. As this review identified mainly evidence from observational studies linking diabetes and brain health, a Delphi study was undertaken as a next step in establishing DBH questionnaire content validity. Of 46 international experts invited to take part in the Delphi study, there was a response rate of 32%. The expert panel reached agreement on memory problems, dementia and depression as brain health complications of diabetes. The panel also reached consensus on the following risk factors for T2DM shared with dementia: hypertension, obesity, physical inactivity and heavy alcohol consumption. A consensus was not reached on depression, cognitive inactivity, smoking and high cholesterol as T2DM risk factors shared with

dementia. Findings from the systematic review and the Delphi study informed development of the DBH questionnaire.

Following the development of the DBH questionnaire, it was administered by an interviewer to a sample of individuals with diabetes and members of the general population in Ireland, in a cross-sectional study. The study population consisted of an opportunistic sample of adults with diabetes recruited through the Diabetes Day Centre, St. James's Hospital, Dublin and attendees of two primary care practices, one in the urban Dublin area and one in the North-West of Ireland.

There were 502 adult respondents to the DBH questionnaire: 250 in the diabetes group (37% women, mean age 63 +/-14 years, 88% with T2DM) and 252 in the general population group (51% women, mean age 47 +/-17 years, 7% with T2DM).

Among the total group, levels of awareness of memory problems (47%), dementia (35%) and depression (63%) as complications of diabetes were low compared to awareness of kidney (84%) and eye damage (84%). Respondents were 1.5 times more likely to identify that individuals can modify their risk of developing T2DM, compared to being able to modify their risk of developing dementia.

Except for depression, respondents in the diabetes group attending St James's Hospital, were significantly more aware of brain health complications of diabetes, including memory problems and dementia, compared to the general population group.

These results point to a low level of awareness of the effects of diabetes on brain health among individuals with diabetes and the general population in Ireland. They would suggest a need to expand diabetes education programmes to promote awareness of the link between diabetes and brain health. Increased awareness of such complications among individuals with established diabetes may encourage those experiencing symptoms of depression or cognitive impairment to present to healthcare professionals for timely interventions that could potentially improve function and quality of life.

Further high-quality research identifying overlapping modifiable risk factors for T2DM and dementia is also necessary to guide shared public health preventative approaches to these conditions.

Acknowledgements

To my husband Colin, for his continued support throughout the work on this project and our daughter Éadaoin. To my parents, for their assistance and unwavering support.

To my local advisor and academic supervisor Professor Brian Lawlor, for his excellent and tireless supervision and guidance

To my co-supervisor Dr Ronan Glynn, for his advice and expertise, particularly in the area of public health and epidemiology.

To my co-authors on publications resulting from this thesis work: Dr Joanna McHugh, Sarah Griffin, Caroline Conroy, Irene Bruce, Dr Sabina Brennan, Dr Colm Loftus, Dr Philip Wiehe, Dr Marie-Louise Healy.

I thank Professor Leslie Daly, Centre for Support and Training in Analysis and Research (CSTAR), University College Dublin, for help with statistical analysis planning. I thank Ms Helen Clarke for help with systematic review methodology and Dr Sabina Brennan for help with questionnaire development. I thank Dr Niamh Phelan, Dr Margaret Loftus, Dr Katie Loftus, Dr Joe Hussey, Dr Silvia Bernabeu Diez, Dr Patrick Burke, Dr Imelda Sliney, Dr Cliona O'Rorke, Dr George Dennis and Ms Anne O'Connell for help with participant recruitment. I thank all participants involved in this study.

Publications resulting from this work

Peer Reviewed Publications

- I. *Brain complications of diabetes mellitus: a cross-sectional study of awareness among individuals with diabetes and the general population in Ireland.*

Dolan C, Glynn R, Griffin S, Conroy C, Loftus C, Wiehe PC, et al. Diabetic Medicine. 2018 Jul;35(7):871–9.

This paper outlines results of an observational, cross-sectional survey study exploring awareness of brain complications of diabetes among individuals with diabetes and the public.

Results of this survey study demonstrate poor awareness of brain health complications of diabetes among individuals with diabetes and general population in Ireland. Findings suggest a need for expansion of public awareness campaigns and diabetes education programmes to promote awareness of brain complications of diabetes as part of a life-course approach to dementia prevention.

- II. *Diabetes and brain health: implications for practice.*

Dolan C, McHugh J, Lawlor B. Irish Journal of Psychological Medicine. 2015 Nov; FirstView: 1–13.

This paper outlines results of a narrative literature review. This review addresses the prevalence and potential mechanisms linking depression and cognitive impairment with diabetes, as well as implications for detection and management. The potential for brain health protection among people with T2DM through enhanced awareness, health promotion and lifestyle modification is highlighted.

Abstract Publications

- I. *Brain health complications of diabetes mellitus: Awareness among individuals with diabetes and the general population in Ireland*

C. Dolan, R. Glynn, S. Griffin, G. McCarthy, B. Lawlor

(2018) *European Psychiatric Association (EPA) European Congress of Psychiatry, Nice, France*. European Psychiatry Volume 48, Supplement, March 2018, Page S134

- II. *A Delphi study to establish an expert consensus opinion on risk factors for type 2 diabetes, and potential complications of diabetes, including brain health associations*

C. Dolan, I. Bruce, B. Lawlor

(2017) *European Psychiatric Association (EPA) European Congress of Psychiatry, Florence, Italy*.

European Psychiatry Volume 41, Supplement, April 2017, Page S64

- III. *An exploration of diabetes brain health literacy among the general public, healthcare professionals and diabetic patients.*

C. Dolan, B. Lawlor, S. Brennan, I. Bruce

(2015) *European Psychiatric Association (EPA) European Congress of Psychiatry, Vienna, Austria*. European Psychiatry Volume 30, Supplement 1, 28–31 March 2015, Pages 1462a, 1462b, 1462c

Presentations resulting from this work

Oral Presentations

I. Diabetes and Brain Health

C. Dolan

Foundation of European Nurses in Diabetes (FEND), Annual European Conference, Lisbon, Portugal, 9th September 2017

II. Diabetes and Multi-Systems Impact: Diabetes and Brain Health

C. Dolan

Diabetes Ireland Conference & Exhibition (DICE), Croke Park, Dublin, 24th March 2017

MD Thesis Dr Catherine Dolan MB BCh BAO PGDip Clin Ed MRCPsych

Diabetes and Brain Health

Table of Contents

Declaration.....	ii
Summary.....	iii
Acknowledgements.....	v
Publications resulting from this work.....	vi
Presentations resulting from this work	viii
Table of Contents.....	ix
List of Tables	xiv
List of Figures.....	xv
Abbreviations.....	xvi
Chapter 1: Background	1
1.1 Introduction	1
1.2 Study aims and objectives.....	6
1.2.1. Overarching aims	6
1.2.2 Primary aim.....	6
1.2.3 Secondary aims	6
1.2.4 Objectives.....	6
Chapter 2: Diabetes and Brain Health: a Pilot Study.....	8
2.1 Introduction	8
2.2 Existing diabetes awareness measures: a narrative literature review.....	8
2.3 Pilot study methodology	9
2.3.1 Development of a diabetes and brain health awareness measure using a Delphi study.....	10
2.3.2 Pilot study participants and methods	11
2.3.3 Pilot study results	13
2.4 Discussion	18
2.4.1 Pilot study limitations.....	20

2.5 Conclusions	20
Chapter 3: Brain Health Complications of Diabetes	22
3.1 Relative risk of dementia in established diabetes: A systematic review.....	23
3.1.1 Methodology.....	23
3.1.2 Results	24
3.2 Diabetes, cognitive impairment and dementia: potential mechanisms of association	24
3.2.1 Cerebrovascular mechanisms	24
3.2.2 Non-cerebrovascular mechanisms.....	25
3.3 Relative risk of depression in established diabetes: a systematic review	26
3.3.1 Methodology.....	26
3.3.2 Results	26
3.4 Diabetes and depression: potential mechanisms of association.....	26
3.4.1 Shared mechanisms	27
3.4.2 Diabetes-related mechanisms	27
3.4.3 Depression-related mechanisms	28
3.5 Impact of cognitive impairment, dementia and depression on diabetes	29
3.6 Other brain health complications associated with diabetes.....	30
3.7 Discussion and conclusion	30
Chapter 4: Modifiable Risk Factors for T2DM shared with Dementia	32
4.1 Introduction	32
4.2 Common risk factors for T2DM and dementia: a systematic review	32
4.3 Discussion	37
4.4 Conclusion.....	38
Chapter 5: Diabetes and Brain Health: Development of a New Survey Instrument	39
5.1 Introduction	39
5.2 Delphi study methodology	39
5.2.1 Delphi questionnaire development	39

5.2.2 Data collection and analysis	40
5.2.3 Synthesis of information.....	41
5.2.4 Results	41
5.2.5 Discussion.....	44
5.2.6 Delphi study limitations.....	45
5.3 Other DBH questionnaire items	47
Chapter 6: Diabetes and Brain Health Study: Methods.....	49
6.1 Study type.....	49
6.2 Study population	49
6.3 Inclusion and exclusion criteria	49
6.4 Sample size calculation	50
6.5 Sampling technique: quota sampling	50
6.6 Field sites	51
6.7 Recruitment	52
6.7.1 Interviewer briefing and training.....	52
6.7.2 Participant information and consent.....	53
6.8 Data entry and data validation.....	53
6.9 Data analysis	53
6.10 Diabetes and Brain Health Study Results	54
6.10.1 Response rate.....	54
6.10.2 Socio-demographic and lifestyle factors	54
6.10.3 Contact with persons with dementia.....	56
6.10.4 Personal health indicators.....	56
6.10.5 Awareness of the complications of diabetes mellitus.....	58
6.10.6 Awareness of risk factors for dementia and T2DM among total group	59
6.10.7 Diabetes group: knowledge associations.....	60
6.11 Discussion	62
6.12 Conclusion.....	64

Chapter 7: Future Directions.....	65
7.1 Low levels of awareness of the link between diabetes and brain health.....	65
7.2 Shared risk factors for dementia and diabetes.....	65
7.3 Healthcare professionals: need for further studies to determine diabetes and brain health awareness.....	66
7.4 Implications for care and treatment of diabetes	66
7.5 Future studies	67
7.6 Conclusions	68
References.....	69
Appendices.....	83
Appendix 1: Older Adult General Health Questionnaire: Medicine for the Elderly Nursing Staff	83
Appendix 2: Older Adult General Health Questionnaire: Diabetes Day Centre	87
Appendix 3: Health Questionnaire: General Population.....	91
Appendix 4: Study protocol with search strategy: incident dementia and depression in adults with established diabetes	95
Appendix 5: Electronic search strategy: incident dementia and depression in adults with established diabetes.....	99
Appendix 6: PRISMA flow diagram: incident depression and dementia in adults with established diabetes	102
Appendix 7: Short listed studies with full text review: incident depression and dementia in adults with established diabetes	105
Appendix 8: Study protocol and search strategy: common modifiable risk factors for T2DM and dementia	108
Appendix 9: Electronic search strategy: modifiable risk factors for T2DM.....	112
Appendix 10: PRISMA flow diagram: modifiable risk factors for T2DM.....	125
Appendix 11: Short listed studies with full text review: modifiable risk factors for T2DM.....	133
Appendix 12: Delphi Questionnaire: Round 1.....	141
Appendix 13: Delphi Questionnaire: Round 2.....	149

Appendix 14: Diabetes and Brain Health (DBH) study participant information sheet	163
Appendix 15: Diabetes and Brain Health (DBH) questionnaire	167

List of Tables

Table 1.1. Differences in cognitive functioning between subjects with T2DM and controls without diabetes	3
Table 2.1. Pilot study: complications of diabetes and Parkinson's disease meeting consensus criteria.....	11
Table 2.2. Pilot study: respondent socio-demographic profile	13
Table 2.3. Pilot study: respondents' awareness of brain health complications of diabetes.	15
Table 2.4. Pilot study: respondents' awareness of non-brain health complications of diabetes	15
Table 2.5. Pilot study: respondents' awareness of Parkinson's disease complications	16
Table 2.6. Pilot study: nursing versus diabetes group awareness of brain health complications of diabetes	17
Table 2.7. Pilot study: nursing versus diabetes group awareness of non-brain health complications of diabetes	17
Table 5.1. Delphi study: Profile of invited expert panel participants	41
Table 5.2. Delphi study: Expert panel participant profile.....	42
Table 5.3. Delphi study: risk factors for T2DM meeting consensus criteria.....	42
Table 5.4. Delphi study: diabetes complications meeting consensus criteria.....	43
Table 6.1. DBH study: respondent socio-demographic profile	55
Table 6.2. DBH study: respondent health and diabetes profile	57
Table 6.3. DBH study: awareness of diabetes complications by subgroup* following adjustment for age and sex	59
Table 6.4. DBH study: awareness of dementia as a complication of diabetes among diabetes group respondents.....	61

List of Figures

Figure 6. 1. DBH study: percentage (%) awareness of diabetes complications	58
Figure 6. 2. DBH study: percentage (%) awareness of risk factors for dementia	60

Abbreviations

3DFE, 3 Dimensions of Care for Diabetes

ACCORD, Action to Control Cardiovascular Risk in Diabetes

AD, Alzheimer's disease

ADA, American Diabetes Association

AMNCH/SJH, Adelaide and Meath Hospital Dublin Incorporating the National Children's Hospital/St James's Hospital

AOR, adjusted odds ratio

BDNF, Brain-derived neurotrophic factor

BMI, Body mass index

BRAIN- diabetes, Border Region Area lifestyle Intervention study for healthy Neurocognitive ageing in Diabetes

CHITIN, Cross-Border Healthcare Intervention Trials in Ireland Network

CI, Confidence interval

CODEIRE, Cost Of Diabetes-ÉIRE

CSO, Central Statistics Office

CSTAR, Centre for Support and Training in Analysis and Research

DAWN, Diabetes, Attitudes, Wishes, and Needs

DBH, Diabetes Brain Health

DCC, Diabetes Day Centre

DKQ, Diabetes Knowledge Questionnaire

DKT, Diabetes Knowledge Test

FINGER, Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability

GP, General practitioner

HPA, hypothalamic-pituitary-adrenal

HR, Hazard ratio

HRS, Health and Retirement Study

HSE, Health Service Executive

HTTPS, Hyper Text Transfer Protocol Secure

IDF, International Diabetes Federation

IPAQ, International Physical Activity Questionnaire

MCI, Mild cognitive impairment

MMSE, Mini Mental State Examination

Montreal Cognitive Assessment, MoCA

NEIL, Neuro-Enhancement for Independent Lives

NICE, National Institute for Health and Care Excellence

OD, Odds ratio

PD, Parkinson's disease

PHQ, Patient Health Questionnaire

PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RCT, Randomised controlled trial

RR, Relative risk

SC, Social class

SPSS, Statistical Package for the Social Sciences

T1DM, Type 1 diabetes mellitus

T2DM, Type 2 diabetes mellitus

TCD, Trinity College Dublin

TIA, Transient ischaemic attack

TILDA, The Irish Longitudinal Study of Ageing

TLS, Transport Layer Security

TNF, Tumour necrosis factor

Chapter 1: Background

1.1 Introduction

Worldwide, the prevalence of diabetes mellitus has quadrupled in the past three decades and affects approximately 8.3% of adults, with this figure projected to increase by half over the next two decades [1-2]. In Ireland, it is estimated that there are up to 196,500 people living with diabetes in the 20-79 age group, representing a prevalence of 4.3% in the Irish adult population [3]. Over 90% of people with diabetes have type 2 diabetes (T2DM) [4]. A projected rise in the number of individuals with T2DM, by over half by 2045, is attributed to the rapidly rising number of people with a sedentary lifestyle and obesity, on the background of an ageing population [2]. It is also widely accepted that genetic susceptibility partly contributes to individual T2DM risk [5].

Of 425 million people estimated to be living with diabetes globally, one third are aged over 65 [3]. Given the global population aged 60 years and over is growing faster than all younger age groups, at a rate of 3% per year, diabetes is an increasing public health concern [6]. With regards to a rapidly ageing population, Ireland is no different, evidenced by a 19% increase in the Irish population aged 65 years plus from census data, 2011 to 2016 [7]. Data from The Irish Longitudinal Study of Ageing (TILDA) highlights the fact that a high proportion of the older population in Ireland have diabetes. TILDA figures show the prevalence of diagnosed T2DM among community-dwelling adults aged over 50 years to be 8.4%, and higher among men than women (10.3% versus 6.6%) [8]. Of further concern are findings from a 2015 study, also using data from TILDA, indicating the prevalence of pre-diabetes and undiagnosed diabetes among older adults in Ireland was 5.5% and 0.9%, respectively [9].

Compounding the care burden at an individual and healthcare resource level is the link between diabetes and complications in various organs of the body. Despite this burden, there is limited information on the prevalence of complications among adults in Ireland. A 2015 meta-analysis by Tracey et al. [10], including 15 studies, found the prevalence of diabetes complications ranged widely; 6.5- 25.2% retinopathy; 3.2- 32.0% neuropathy; and 2.5- 5.2% nephropathy. Stroke and transient ischaemic attack (TIA) were the only brain-related complications of diabetes addressed in studies included in this meta-analysis. Other

brain health complications of diabetes, including cognitive impairment, dementia, and depression, which are increasingly being recognised in the literature, were not included.

Both type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) are associated with brain-related complications [11]. However, for the purpose of this thesis, diabetes will refer to T2DM, given that it accounts for approximately 90% of cases of diabetes globally [4], thus the term diabetes will be used interchangeably with T2DM.

Brain health complications of diabetes, contributing to increased dementia prevalence, have the potential to increase the pressure on limited health resources globally, particularly among populations of ageing adults with complex mental and physical healthcare needs [12]. In a prospective cohort study with a ten year follow up period, older adults with T2DM were found to have double the rate of global cognitive decline over five years, compared to those without T2DM [13]. A 2012 meta-analysis found that having a diagnosis of diabetes was associated with a 1-2 fold increased risk for mild cognitive impairment (MCI), a 1.5 fold higher risk for Alzheimer's disease (AD), and a 2-3 fold increased risk of vascular dementia [14]. The magnitude of cognitive functioning deficits found in diabetes, as identified in a 2014 meta-analysis by Monette et al. [15], is outlined in **Table 1.1**. Findings highlight the majority of effect sizes were within the small range, with inconsistencies in the cognitive domains tested in cross-sectional case controlled studies included in the meta-analysis [15].

Table 1.1. Differences in cognitive functioning between subjects with T2DM and controls without diabetes (relevant studies adapted from a meta-analysis by Monette et al., 2014)

Reference	Methodology	Sample	Effect sizes (Cohen's <i>d</i> range)	Measured cognitive abilities ¹
Arvanitakis et al., 2004 [16]	Population, longitudinal, case-control	127 with diabetes, 697 in control group, >55 years old	-0.29 to 0.03	a,b,d,f,g,h,j,k,l,o,p,q,r, t,u, x
Christman et al., 2010 [17]	Population, case-control, cross-sectional	28 with diabetes, 150 in control group, ≥ 65 years old	-0.76 to -0.17	a,b,c,d,f,g,h,i,j,k,l,m,o,p,q,r,s, t,u, v, w,x
Cosway et al., 2001 [18]	Population, case-control, cross-sectional	38 with diabetes, 38 in control group, aged 40-75	-0.33 to 0.19	a,g,h,i,k,m,o,p,q,r,s,t,u,v,w
Espeland et al 2011 [19]	Population, case-control, longitudinal	179 women with diabetes, 1984 in control group, aged 65-80	-0.28 to 0.02	a,b,d,f,h,i,j,n,o,p,r,s,t,v,x
Gallacher et al., 2005 [20]	Population, case-control, cross-sectional	165 with diabetes, 1573 in control group, men aged 59-65	-0.19 to -0.15	a,h,j,k,m
McFall et al., 2010 [21]	Population, case-control, cross-sectional	41 with diabetes, 458 in control group, aged 53-90	-0.53 to -0.02	a,b,c,e,k,m,o,p,t
Mehrabian et al., 2012 [22]	Population, case-control, cross-sectional	37 with diabetes, 22 in control group, aged 45-65	-1.68 to -0.63	a,b,c,h,i,j,k,m
Nandipati et al., 2012 [23]	Population, case-control, cross-sectional	300 with diabetes, 2994 in control group, mean age approx.74 years	-0.51 to -0.18	a,b,c,f,h,j,k,m,o,p,q,t,u
Toro et al., 2009 [24]	Population, case-	27 with diabetes, 132 in	-0.43 to 0.10	a,b,c,k,m,o,p,q,t,u

Reference	Methodology	Sample	Effect sizes (Cohen's <i>d</i> range)	Measured cognitive abilities ¹
	control, longitudinal	control group, mean age 74.2 years		
Van den Berg et al., 2010 [25]	Case-control, longitudinal	68 with diabetes, 38 in control group, aged 56-80	-0.61 to 0.02	a,b,c,d,e,f,g,h,i,j,k,l,m,o,p,r,s,t,v,w,x
Van Elderen et al., 2010 [26]	Population, case-control, longitudinal	89 with diabetes, 438 in control group, aged 70-82	-0.32 to -0.20	a,b,e,k,m,o,p,t,w

¹Cognitive ability for the diabetes group versus the non-diabetes control group comparison, Average *d* (95% confidence intervals)

a General Cognitive Functioning -0.25 (-0.29, -0.22), b Attention -0.29 (-0.34, -0.24), c Divided Attention/Shifting -0.36 (-0.42, -0.31), d Focused Attention -0.15 (-0.21, -0.08), e Selective Attention -0.33 (-0.44, -0.22), f Working Memory -0.20 (-0.24, -0.15), g Non-Verbal Reasoning -0.29 (-0.41, -0.17), h Fluency -0.26 (-0.30, -0.22), i Verbal Phonemic Fluency -0.28 (-0.34, -0.21), j Verbal Semantic Fluency -0.25 (-0.29, -0.21), k Processing Speed -0.33 (-0.38, -0.29), l Oral Task Demands -0.14 (-0.24, -0.04), m Motor Task Demands -0.37 (-0.41, -0.32), n Motor Speed -0.30 (-0.38, -0.23), (o) Memory -0.20 (-0.28, -0.12), p Learning and Immediate Recall -0.21 (-0.25, -0.17), q Story Learning & Immediate Recall -0.18 [-0.23, -0.12], r Verbal Learning and Immediate Recall -0.27 (-0.34, -0.20), s Visual Learning and Immediate Recall -0.21 (-0.29, -0.13), t Delayed Recall -0.20 (-0.24, -0.15), u Story Delayed Recall -0.18 (-0.24, -0.12), v Verbal Delayed Recall -0.22 (-0.28, -0.15), w Visual Delayed Recall -0.26 (-0.39, -0.14), x Visuospatial/Visuoconstructional -0.18 (-0.25, -0.10) ^{*}All effect sizes are significant ($p < 0.05$)

Furthermore, the incidence and prevalence of clinically relevant depressive symptoms have been found to be up to 30% among individuals with diabetes, and the presence of diabetes doubled the odds of depression when compared to those without diabetes [27 -29].

Despite the projected increase in prevalence of diabetes in Ireland, the cost of the condition and associated complications, to the Irish state is unclear. However, the CODEIRE study, by Prof. John Nolan et al., remains the best available estimate. Results of this observational study (N = 701) over 12 months in 1999/2000 indicated that 6.4% of the Irish Healthcare budget was consumed by treating the condition [30]. Given dementia is a costly condition, with the global cost estimated to be about a trillion US dollars per year, and set to double by 2030 [12], a link between T2DM and brain health complications in a rapidly ageing population has the potential therefore to increase the cost of diabetes care to the Irish healthcare system. Findings of a 2018 national prevalence study in Ireland highlights an increasing burden of dementia in the Irish population as it ages, with an incidence of just under 7,700 new cases per year. This study also estimates the total number of people with dementia in Ireland ranges between approximately 39,000 and 55,000 [31].

In the context of evidence that having a diagnosis of diabetes increases an individual's risk of cognitive impairment and dementia, prevention or delay of such brain health complications in those with established diabetes is therefore an important target of a brain health approach to dementia prevention. Additionally, overlapping modifiable risk factors for T2DM and dementia potentially represent a target for shared public health preventative approaches for these conditions.

Firstly, gathering data on public and patient awareness of diabetes and brain health associations will enhance understanding of how these groups perceive the link and will help identify any gaps in awareness. There is limited information on this topic in the literature, although a recent cross-sectional study found less than 40% of a population based sample in Holland identified diabetes as a risk factor for dementia [32]. Such information could guide the expansion of diabetes education programmes to promote awareness of diabetes and brain health associations, as well as guide public awareness campaigns focused on a life course approach to dementia prevention.

1.2 Study aims and objectives

1.2.1. Overarching aims

This study seeks to identify gaps in awareness of the effects of diabetes on brain health among individuals with diabetes and the general population in Ireland. Such information may inform future diabetes education programmes, as well as public awareness campaigns relating to dementia prevention.

1.2.2 Primary aim

The primary aim of this study is to determine the level of awareness of the effects of diabetes on brain health among both a group of individuals with diabetes attending a specialist diabetes care service and a representative sample of the general population in Ireland.

1.2.3 Secondary aims

Secondary aims include

- (i) comparing levels of awareness of the effects of diabetes on brain health among the two study groups.
- (ii) identifying evidence for risk factors for T2DM that overlap with dementia that might inform shared public health preventative approaches to both conditions.

1.2.4 Objectives

The objectives of the study are to:

- (i) Conduct a pilot study, with Delphi and survey components, using a study-specific measure designed to determine levels of awareness of the relationship between diabetes and brain health among a sample of individuals with diabetes, nursing staff, and the general Irish population.
- (ii) Use results of this pilot study to inform the research approach and design of the definitive survey measure used in the Diabetes and Brain Health (DBH) study.
- (iii) Develop a measure for use in the DBH study to determine levels of awareness of the relationship between diabetes and brain health for use among a group of

individuals with diabetes attending a specialist diabetes care service and a sample of the general population in Ireland.

- (iv) Undertake a systematic review of the literature to identify risk factors for T2DM to ensure content in the measure are valid and to also potentially inform shared public health preventative approaches to T2DM and dementia by identifying overlapping modifiable risk factors.
- (v) Use this measure in an interviewer-administered cross-sectional survey study to assess awareness levels in the two study groups of:
 - I. Brain health complications of diabetes
 - II. Other complications of diabetes
 - III. Modifiable risk factors for T2DM overlapping with dementia
- (vi) In each group:

Investigate the relationship between diabetes and brain health awareness and the following:

- I. Sociodemographic factors
 - II. Lifestyle behaviours
 - III. Personal health indicators
 - IV. Personal/family experience of dementia
- (vii) Using results, extrapolate estimates of awareness of the effects of diabetes on brain health among:
 - I. Individuals with diabetes in Ireland
 - II. Members of the general population in Ireland
- (viii) Make recommendations, relevant to findings, for interventions, including education focused on the link between diabetes and brain health for individuals with diabetes and the public, as well as detection of brain health complications in those with established diabetes.

Chapter 2: Diabetes and Brain Health: a Pilot Study

2.1 Introduction

In 2014, prior to undertaking the definitive Diabetes and Brain Health (DBH) study, a pilot study to explore diabetes and brain health awareness was carried out among a sample of individuals with diabetes, members of the general population, and nursing staff. Firstly, a narrative literature review was performed to search for an appropriate awareness measure for use in the pilot study. The plan was to design a study-specific questionnaire if no suitable measurement tool was identified in the literature review. Outlined in this chapter, are the findings of the literature review, the methodology used to develop a study-specific questionnaire, and the results of the subsequent pilot study. Limitations of this pilot study are discussed, in addition to the influence of the pilot study and preliminary data gathered, on the definitive DBH study.

2.2 Existing diabetes awareness measures: a narrative literature review

On review of the literature, in advance of the pilot survey study, many diabetes knowledge and awareness assessment tools were identified. However, none include items that assess awareness of cognitive impairment, dementia, or depression as complications of diabetes. In this section I explore the domains included in a number of diabetes knowledge and awareness assessment tools identified, however the list of included tools is not exhaustive.

The Michigan Diabetes Research and Training Centre developed a diabetes-specific knowledge instrument in the 1980s; the Diabetes Knowledge Test (DKT), for use by diabetes educators and researchers [33]. Recognised experts in diabetes education and diabetes care identified key content domains and developed test items for DKT, with subsequent extensive evaluation. The DKT has been adapted for particular groups and interventions [34 - 35].

In 1998, Fitzgerald et al. published and validated The Brief Diabetes Knowledge Test (Brief DKT), including 23 items, to assess the knowledge of patients with both type 1 diabetes mellitus (T1DM) and T2DM [36]. The Brief DKT is a 14-item general test and a nine-item insulin-use subscale. Although this measure tests knowledge of vision, kidney,

and nerve problems as potential diabetes complications, it does not test knowledge of brain-related complications.

In 2016, Fitzgerald et al. reviewed the 1998 version of the DKT, finding that the content of the test had become outdated and in need of revision to reflect up-to-date diabetes care and education guidelines [37]. The authors developed, piloted, and validated a generic, brief diabetes knowledge questionnaire. This test is capable of measuring knowledge change following a diabetes education intervention and is suitable for people with both T1DM and T2DM. Despite updating the DKT, the revised version does not measure knowledge of brain health complications of diabetes.

A validated knowledge questionnaire, the ADKnowl, consisting of 23-item sets with a total of 104 items, was developed and tested in the UK [38]. Following a significant update in 2009 and again in 2011, the ADKnowl now includes 33 item-sets (138 items) [39].

Although more comprehensive than DKT, it requires a licence for use and is a resource-intensive tool for application in a clinical setting. The ADKnowl does not include items examining knowledge of brain health complications of diabetes.

In 2011, an Australian based research group developed a Diabetes Knowledge Questionnaire (DKQ) capable of measuring knowledge change following a diabetes education intervention [40]. This measure is suitable for use among people with T1DM or T2DM. It addresses knowledge of the following complications of diabetes: kidney damage, blindness, heart disease, foot ulcers. DKQ does not measure knowledge of brain health complications of diabetes, however.

As a narrative review of the literature did not reveal a suitable measurement tool, a questionnaire was designed, for use in a pilot study, to assess diabetes and brain health awareness among a sample of individuals with diabetes, nursing staff and members of the general population.

2.3 Pilot study methodology

This pilot study was a cross-sectional study conducted in 2014, using Delphi methods and survey methodology.

This study was reviewed and approved by the AMNCH/SJH Ethical and Research Committee, Dublin. Informed consent was obtained from all participants and the data

collected was kept confidential. As such, no personal identifiers were recorded on the questionnaires.

2.3.1 Development of a diabetes and brain health awareness measure using a Delphi study

To establish content validity of questionnaire items relating to brain health complications, as well as non-central nervous system complications of diabetes, the literature related to diabetes and brain health, as well as patient diabetes educational materials and disease management guidelines, was reviewed [41-42]. Evidence for an association between diabetes, cognitive impairment, dementia, and depression in the literature was mostly observational. Therefore, as a next step, a consensus study was undertaken using a modified Delphi technique [43]. The aim of this Delphi study was to establish a consensus on correct responses to questionnaire items relating to brain health complications of diabetes. The following eight individuals were invited to partake in the study and form a Delphi expert panel: two medicine for the elderly consultant physicians, a psychiatry for the elderly consultant physician, two medicine for the elderly clinical nurse specialists, two medicine for the elderly research fellows, and a psychiatry for the elderly research fellow. Among those invited to partake in the Delphi study, there was a 100% response rate. All participants were employed by the Department of Medicine for the Elderly, St James's Hospital, Dublin.

In the first round of a two-round Delphi study, panel members were asked to complete a questionnaire and answer 'yes/no' to indicate their agreement or disagreement with a list of diabetes complication items. Panel members were also asked to indicate their agreement or disagreement with a list of Parkinson's disease complications.

In keeping with the literature, consensus in a Delphi study is determined by the majority response being significantly large [44]. In this Delphi study, the criterion for consensus on complication items was set at 70% or more responses indicating agreement or disagreement in keeping with the diabetes literature [45].

In the first round, the percentage response to individual questionnaire items addressing complications of diabetes ranged from 75-100% agreement or disagreement. Feedback on questionnaire wording and suggestions for additional items was also welcomed. In the first round, participants suggested re-wording of the complication item 'vision problems' to 'eye disease', and the addition of 'TIA or mini-stroke' as a diabetes complication.

In the second round, a questionnaire incorporating aggregated results from the first round and participant feedback, was re-circulated to the panel. Participants were asked to review their responses in light of group opinion. Following the second round of the Delphi study, majority responses to complication items remained unchanged. Results informed the design of the measure used in the pilot study to assess awareness of diabetes and brain health (see Table 2.1). Expert panel responses to Parkinson's disease complication items are also reported in Table 2.1.

Table 2.1. Pilot study: complications of diabetes and Parkinson's disease meeting consensus criteria

Delphi study	Round 1		Round 2
	Group result (n=8)		Group result (n=8)
T2DM complication			
Kidney disease ¹	100% agreement	Eye disease ²	100% agreement
Vision problems ²	100% agreement		
Nerve damage ¹	100% agreement		
Memory loss ¹	75% agreement		
Dementia ¹	75% agreement		
Stroke ¹	75% agreement		
Foot ulcers and amputation ¹	100% agreement		
Depression ¹	87.5% agreement		
Heart disease ¹	75% agreement		
TIA or mini-stroke ³	-		75% agreement
Parkinson's disease complication			
Kidney disease ¹	100% disagreement	Eye disease ²	75% disagreement
Vision problems ²	75% disagreement		
Nerve damage ¹	100% disagreement		
Memory loss ¹	100% agreement		
Dementia ¹	100% agreement		
Stroke ¹	100% disagreement		
Foot ulcers and amputation ¹	100% disagreement		
Depression ¹	100% agreement		
Heart disease ¹	100% disagreement		
TIA or mini-stroke ³	-		100% disagreement

¹complication item reaching consensus agreement/disagreement in round 1.

² wording of questionnaire item changed on foot of expert panel group suggestion in round 1

³additional complication items suggested by expert group in round 1 reaching consensus agreement/disagreement in round 2

2.3.2 Pilot study participants and methods

Informed by the results of the Delphi study, a subsequently developed diabetes and brain health awareness measure included 'Yes/No' answer options to indicate a respondent's

agreement/disagreement with listed diabetes complications. The questionnaire also included specific items addressing respondent awareness of complications of a number of other medical conditions, including Parkinson's disease. This allowed for comparison of the level of respondent awareness of cognitive impairment, dementia, and depression as complications of Parkinson's disease, and awareness of cognitive impairment, dementia, and depression as complications of diabetes.

The questionnaire used in each subgroup differed slightly (**see Appendices 1 - 3**) and therefore basic demographic information gathered was group dependent.

Members of the Delphi study expert panel reviewed the awareness measure for face validity, readability, and clarity. Feedback was incorporated into the final draft of the awareness measure.

The study time period was from September to December 2014.

Diabetes group participants were individuals with diabetes attending the Diabetes Day Centre (DDC) in St. James's Hospital. The DDC provides an outpatient facility for diabetes education, clinical nutrition services, podiatry, eye and general support for patients and their families. All DDC attendees within the study period were afforded an opportunity to complete the questionnaire. The questionnaire was located in the outpatient waiting room, along with a study information sheet. A total of 77 diabetes outpatient attendees completed the questionnaire while attending the DDC during the study time period.

Nursing staff participants consisted of nurses employed by the Medicine for the Elderly Department in St. James's Hospital, Dublin. Hard copies of the questionnaire were distributed to relevant wards and nursing environments in the Department of Medicine for the Elderly, St. James's Hospital during the study time period. There were 96 nursing staff member respondents.

The third group consisted of a sample of the Irish general population, recruited via a Dublin based university website. A total of 227 adults completed the questionnaire disseminated to the general population via a survey invitation and a link posted on a Trinity College Dublin (TCD) website (www.tcd.ie/neuroscience/neil). This website provides information on the Neuro-Enhancement for Independent Lives (NEIL) project, TCD, which conducts research aimed at dementia prevention and cognitive enhancement.

However, the study presented in this thesis is not part of the NEIL project.

2.3.3 Pilot study results

The response rate in the nursing group (n=96) was estimated at less than 58%, calculated by taking into account the number of nursing staff employed by the Medicine for the Elderly Department in St James's Hospital. Response rate in the diabetes group and general population group could not be determined due to the "opt-in" design. However, the DDC electronic health records showed that approximately 1,156 patients (62% male, 38% aged over 65 years) attended DCC for a variety of clinics during the study time period. Therefore, 77 survey respondents represent approximately 7% of DDC attendees.

Data were entered into SPSS (version 22) and descriptive and inferential statistical analyses were performed. Basic demographic information relating to each group is outlined in **Table 2.2**.

Table 2.2. Pilot study: socio-demographic profile of respondents

	General population group*	Nursing group*	Diabetes group*
	N= 227	N= 96	N = 77
Age group [years] <i>Mean, standard deviation, range</i>	43 ± 14, 22-84		
Nursing Experience [years] <i>Mean, standard deviation, range</i>		14 ± 7, 2-30	
	% (n)	% (n)	% (n)
Diabetes duration [years] >20 10-20 5 -10 <5			26 (20) 34 (26) 18 (14) 22 (17)
Gender Women	63 (144)	92 (88)	20 (15)
Health professional status Yes	67 (152)	100 (96)	-
Personal disease burden Diabetes History of CVA Parkinson's disease	5 (12) 1 (3) 2 (4)	3 (3) 0 0	100 (77) 7 (5) 5 (4)

	General population group*	Nursing group*	Diabetes group*
	N= 227	N= 96	N = 77
Education Level Tertiary Secondary Primary	60 (136) 35 (80) 1 (3)		21 (16) 44 (34) 22 (17)
Nursing Grade Clinical Nurse Manager Clinical Nurse Specialist Senior Nurse Registered Practice Nurse		18 (17) 8 (8) 16 (15) 56 (54)	
Diabetes profile			
Diabetes type T2DM T1DM Unsure			69 (53) 27 (21) 4 (3)
Diabetes treatment Insulin dependent Non- insulin dependent			51 (39) 49 (38)
Received formal diabetes education Yes			62 (48)

*numerical discrepancies represent missing data

The likelihood of a sample bias within the general population group was considered high, given 67% of respondents identified themselves as health professionals, compared to figures from the National Skills Council Report in 2017 showing only 12.6% of national employment was made up of healthcare workers [46]. Furthermore, 60% of respondents were educated to tertiary level, compared to 42% of the general Irish population having third level education as per 2016 census figures [47] (**see Table 2.2**). Therefore, descriptive analysis was only performed on data from this group. Comparative analysis was performed between patient and nursing groups only.

Within-group analyses

Among the general population group, 7% correctly identified dementia as a complication of diabetes, compared to 15% of the nursing group and 35% of individuals with diabetes surveyed (**Table 2.3**). Approximately, two to three times as many respondents in each of the three subgroups identified depression as a complication of diabetes, compared to dementia as a complication of diabetes (**Table 2.3**).

Table 2.3. Pilot study: respondents' awareness of brain health complications of diabetes

	Total group	General population group	Nursing group	Diabetes group
	N = 400	N = 227	N= 96	N = 77
	% (n)	% (n)	% (n)	% (n)
Memory Loss	26 (104)	15 (34)	28 (27)	57 (43)
Memory Problems	25 (99)	12 (28)	24 (23)	62 (48)
Dementia	14 (57)	7 (16)	15 (14)	35 (27)
Depression	37 (147)	26 (60)	37 (35)	68 (52)
CVA ('stroke')	47 (187)	29 (66)	56 (54)	87 (67)

In contrast with low levels of awareness of brain health complications of diabetes among respondents, 61% of the general population group, 100% of the nursing group, and 97% of the group with diabetes correctly identified eye disease and 67% of the general population group, 100% of the nursing group and 97% of the diabetes group identified foot disease as a complication of diabetes (see **Table 2.4**).

Table 2.4. Pilot study: respondents' awareness of non-brain health complications of diabetes

	Total group	General population group	Nursing group	Diabetes group
	N = 400	N= 227	N= 96	N = 77
	% (n)	% (n)	% (n)	% (n)
Eye disease	76 (305)	61 (138)	100 (96)	97 (75)
Foot disease	81 (324)	67 (153)	100 (96)	97 (75)
Kidney problems	69 (274)	55 (124)	79 (76)	96 (74)
Neuropathy	70 (279)	58 (131)	80 (77)	92 (71)

Levels of awareness among respondents of memory loss, dementia, and depression as complications of Parkinson's disease are outlined in **Table 2.5**. Participants in the nursing group had the highest awareness rates of memory loss, dementia and depression as a complication of Parkinson's disease among all three groups.

Table 2.5. Pilot study: respondents' awareness of Parkinson's disease complications

	Total group N = 400	General population group N= 227	Nursing group N= 96	Diabetes group N = 77
Parkinson's disease complication	% (n)	% (n)	% (n)	% (n)
Memory Loss	59 (237)	56 (126)	73 (70)	53 (41)
Dementia	48 (190)	48 (110)	56 (54)	34 (26)
Depression	61 (244)	52 (117)	78 (75)	68 (52)

Between-group analyses

Using a chi-square test, the diabetes group was found to have a higher frequency of correct answers ($p < 0.001$) to each item addressing brain health complications of diabetes when compared to the nursing group (**see Table 2.6**). In addition, when compared to the nursing group, the diabetes group also had significantly ($p < 0.001$) higher levels of awareness of foot disease, kidney disease, neuropathy, and heart disease as complications of diabetes. However, there was no statistically significant difference in rates of awareness of eye disease as a diabetes complication between the groups (0.749) (**see Table 2.7**).

Table 2.6. Pilot study: nursing versus diabetes group awareness of brain health complications of diabetes

	Nursing group N= 96	Diabetes group N = 77	
Diabetes complication	% (n)	% (n)	Test Statistic (p value)¹
Memory loss	28 (27)	57 (43)	$\chi^2= 14.23 (<0.001)$
Memory problems	24 (23)	62 (48)	$\chi^2= 26.01 (<0.001)$
Dementia	15 (14)	35 (27)	$\chi^2= 9.912 (<0.001)$
Depression	37 (35)	68 (52)	$\chi^2= 16.50 (<0.001)$
CVA (“stroke”)	56 (54)	87 (67)	$\chi^2= 19.23 (<0.001)$
TIA (“mini-stroke”)	51 (49)	83 (64)	$\chi^2= 19.41 (<0.001)$

¹chi-square test statistic relates to a test for independence in a frequency table

Table 2.7. Pilot study: nursing versus diabetes group awareness of non-brain health complications of diabetes

	Nursing group N= 96	Diabetes group N = 77	
	% (n)	% (n)	Test Statistic (p value)¹
Eye disease	96 (92)	97 (75)	$\chi^2= 0.102 (0.749)$
Foot disease	79 (76)	97 (75)	$\chi^2= 12.802 (<0.001)$
Kidney problems	79 (76)	96 (74)	$\chi^2= 10.633 (<0.001)$
Neuropathy	80 (77)	92 (71)	$\chi^2= 4.977 (0.026)$
Heart disease	64 (61)	90 (69)	$\chi^2= 15.547 (<0.001)$

¹chi-square test statistic relates to a test for independence in a frequency table

Correlations between predictor and outcomes variables

A diabetes brain complication awareness composite score, composed of correct answers to the following diabetes complication items - memory loss, depression and dementia - was used for the purpose of correlation analysis. In the nursing group, using Spearman's correlation analysis, there were no significant correlations between years of nursing experience and median composite score ($p>0.05$).

In the diabetes group, the following variables did not significantly affect median composite score: delivery of a previous diabetes education intervention, use of insulin therapy, subtype of diabetes (T1DM versus T2DM), and diabetes disease duration ($p>0.05$).

2.4 Discussion

Overall, the results of this pilot study suggested limited awareness of an association between diabetes and brain health in members of the general population, nursing staff working with older adults, and in individuals with diabetes. Respondents in the diabetes group had higher levels of awareness of brain health complications of diabetes, compared to the general population and nursing group respondents. Surprisingly, rates of awareness of kidney disease, foot complications and heart disease were less amongst the nursing staff compared to diabetes group. This suggests that the diabetes patient participants were a self-selected group who participated because they were knowledgeable about the condition. However, only one-third of respondents in the diabetes subgroup were aware that dementia is a complication of diabetes. This finding suggests a need to expand diabetes education programmes to promote awareness of the link between diabetes and brain health. In a 2009 Irish study, awareness rates among patients attending diabetes outpatient clinics ($n = 258$) was 17.1% for stroke, compared to awareness rates of 87% in our pilot study, however the larger sample size used in the 2009 study may contribute to the discrepancy between findings. Other brain health complications, including depression and dementia were not included as questionnaire items [48].

In the general population group, a high percentage of respondents were from a healthcare background and had a high level of educational attainment. This profile likely limits generalisability of study findings given the general population in Ireland has much lower rates of third level educational attainment and lower rates of employment in the healthcare field [46-47]. Although, given the socio-demographic profile of respondents, a higher level of awareness of the associations between diabetes and brain health could be presumed.

However, although a potential sampling bias limits the generalisability of study findings, the general population group has the lowest level of awareness of dementia as a brain health complication of diabetes when compared to the other two groups. This finding suggests a need for public awareness campaigns related to dementia prevention to emphasise T2DM as a modifiable risk factor for dementia, as part of a life course approach to prevention.

In the nursing group, low levels of awareness of brain health complications of diabetes suggest gaps in nursing education related to diabetes. Furthermore, a lack of association found between more years of nursing practice and higher levels of awareness of diabetes brain health complication indicates that more time spent in a nursing career does not necessarily influence diabetes and brain health awareness. However, it must be acknowledged that nursing staff members in the group did not consist of diabetes specialists or primary care practice nurses, who would be expected to have greater awareness of diabetes-related complications than non-diabetes trained nursing staff.

Results also point to wider gaps in diabetes-related awareness among nursing respondents as levels of awareness of foot disease, kidney disease, neuropathy and heart disease as complications of diabetes, was higher in the diabetes group compared to the nursing group. Given the pivotal role healthcare professionals play in effective screening and management of chronic conditions such as diabetes, it is imperative then that nursing staff members have adequate awareness of diabetes complications. Despite the methodological limitations of this pilot study, the findings suggest that there is a need to expand diabetes-related education for nursing staff to include information on diabetes and brain health complications. To the best of my knowledge, there are no studies exploring awareness of brain health complications among medicine for the elderly nursing staff members in the literature to date. However, a 2013 study by Abduelkarem and El-Shareif in Libya found knowledge of chronic complications of diabetes was found to be lacking in a group (n=116) of general hospital nursing staff [49].

Findings of this pilot study also indicate that diabetes group and nursing group respondents had higher levels of awareness of memory loss and dementia as complications of Parkinson's disease, compared to memory loss and dementia as complications of diabetes. One potential explanation for this finding is that respondents may associate brain-related complications more readily with primary central nervous system conditions than with diabetes, as such conditions more frequently have visible disease manifestations; for

example, motor and speech abnormalities.

2.4.1 Pilot study limitations

A number of limitations, relating to design and methodology of both the Delphi and survey study components of this pilot study, were identified. Efforts were made to address these limitations in the definitive diabetes and brain health (DBH) study.

Limitations included a lack of a systematic review of the literature on the topic of diabetes and brain health undertaken in advance of this pilot study and a low number of Delphi study participants. Although the Delphi literature does not specify a criterion for the minimum number of expert panel members in a Delphi study, ensuring ‘high-quality’ panel members with adequate knowledge about the topic in question is suggested [44]. Furthermore, a number of relevant sociodemographic variables and duplication of diabetes complication items were omitted in the pilot study awareness measure. Limitations are also noted with regards to recruitment of nursing group and diabetes group participants for the survey component of the pilot study given participants were not actively informed about the study by the researcher other than by poster notifications in study sites. Additionally, a potential sampling bias associated with recruitment of the general population through a third level university website linked with NEIL project was also a limitation likely impacting on generalisability of the study findings. Another potential limitation is the generalisability of the findings in the diabetes group given a large cohort of individuals with diabetes in Ireland are managed in primary care. Thus, this study sample may be biased by having a higher level of exposure to diabetes-specific education opportunities compared to individuals with diabetes treated in primary care, potentially influencing their awareness of brain health complications.

2.5 Conclusions

Despite methodological flaws, this pilot study has a number of interesting findings. Of specific concern, is the low level of awareness of diabetes brain health complications among respondents. These findings, if replicated, would emphasise a need for expansion of diabetes specific education programmes, and dementia prevention public health campaigns, to promote awareness of the link between diabetes and brain health.

Specifically, results highlighting a low level of awareness of the effect of diabetes on the brain among nursing staff respondents, suggest a need to expand nursing education to

include a focus on diabetes and brain health. Healthcare professionals working with individuals with diabetes must be aware of the potential for brain health complications to promote timely detection and intervention, which may improve patient quality of life and function.

Findings and methodology used in this pilot study informed the development and design of the definitive DBH study. Limitations of this pilot study were considered in the development of the study protocol for the DBH study, and attempts were made to address them. Data gathered in the pilot study was also used to inform the design of the statistical analysis plan, including sample size calculation, for the DBH study.

Chapter 3: Brain Health Complications of Diabetes

Building on the questionnaire designed for use in the pilot study, a survey measure was developed for use in the definitive DBH study. Given the limitations of the pilot study mentioned in the previous chapter the research approach to the definitive study was considered and refined to address methodological flaws.

This chapter and Chapter 4 focus on findings of literature reviews which informed design of the DBH survey measure. To more comprehensively examine the literature on the topic of diabetes and brain health, a systematic literature review was undertaken exploring modifiable risk factors for T2DM overlapping with dementia. The strength of the evidence for the risk of brain health complications in those with established diabetes was assessed in this review. A narrative review of the literature also explored mechanisms potentially underlying the association between diabetes and brain health.

In Chapter 5 there is an outline of a subsequent Delphi study undertaken as part of the definitive DBH study. In this Delphi study a larger international panel, considered to be more broadly representative of individuals with knowledge in academic and clinical fields related to diabetes and brain health, were invited to take part. In an effort to decrease the likelihood of a response bias, questionnaire items were not duplicated and efforts were made to ensure the wording of items was unambiguous.

To address potential confounders for diabetes and brain health awareness in the definitive DBH study, broad socio-demographic and health-related information was collected. To improve the generalisability of study findings, the general population group was recruited from two primary care practices, one located in the urban Dublin area, and the second in the North- West of Ireland. Quota sampling by age and sex was also employed, with the distribution of age and sex determined according to 2016 Central Statistic Office (CSO), Ireland figures [7]. To further address selection bias issues inherent in the pilot study and enhance study response rate, interviewer led, face-to-face administering of the questionnaire was used in the definitive DBH study.

3.1 Relative risk of dementia in established diabetes: A systematic review

As aforementioned, there is a growing body of evidence linking diabetes to different stages of cognitive dysfunction and greater cognitive decline compared to controls without diabetes.

3.1.1 Methodology

The Cochrane Database of Systematic Reviews (all years), MEDLINE, and EMBASE (2013-2017) were searched to identify English-language systematic reviews and meta-analyses of both observational and interventional studies examining the associations between dementia and diabetes. Diabetes was selected as the exposure of interest when the outcome was incident dementia. References in articles identified were also searched (see systematic review protocol and electronic search strategy, in **Appendix 4** and **Appendix 5**, respectively, performed in accordance with PRISMA guidelines) [50]. Unpublished literature, including letters, conference abstracts, working papers, and dissertations were not included.

Systematic reviews or meta-analyses of prospective cohort and case-cohort studies, and randomised control trials (RCT), controlled trials, controlled before and after trials, with reporting on effect size, were eligible. If meta-analyses of prospective cohort studies and/or case-cohort studies were not available, meta-analyses, including case-control and/or cross-sectional studies, were examined. Participants were aged 18 years or over and recruited from non-specialised populations. Studies with reported risk estimates, including relative risk (RR) and hazard ratio (HR) with 95% confidence intervals (CI), based on the best available adjusted estimates from Cochrane reviews when available, or on the most recent and comprehensive meta-analysis, were eligible.

Duplicate publications were omitted. Screened publications were then short-listed against study criteria, with relevant exclusions made (see **Appendix 6**).

Relevant characteristics and results extracted from short-listed eligible studies included population characteristics, systematic review characteristics, exposure and outcome data, and measures of effect (see **Appendix 7**). For RCTs, the component assessment method of Cochrane was used, and quality scoring was not performed [51]. For systematic reviews and meta-analyses sourced in MEDLINE and EMBASE, the PRISMA checklist [50] was used for critical appraisal. A qualitative synthesis of the results of the most relevant short-listed studies is presented below.

3.1.2 Results

Of 673 relevant abstracts relating to diabetes as a risk factor for dementia retrieved in the systematic review, a qualitative synthesis draws results together of two of these studies, as outlined below.

A 2013 meta-analysis of 28 prospective cohort studies, exploring the risk of dementia in individuals with established diabetes, found pooled RR of developing all-type dementia was 1.73 (95% CI 1.65–1.82), Alzheimer's disease (AD) was 1.56 (95% CI 1.41–1.73), and vascular dementia was 2.27 (95% CI 1.94 –2.66) [52].

A 2017 Cochrane review, which assessed the effects of different strategies for managing T2DM on cognitive function and the incidence of dementia, included four studies. Diabetes medication treatment strategies were found to not differ in their effect on global cognitive functioning over 40-60 months. There was no comparison of the effect of treatment versus the usual treatment and/or no treatment of diabetes on dementia risk [53].

3.2 Diabetes, cognitive impairment and dementia: potential mechanisms of association

To explore the possible mechanisms linking cognitive impairment and dementia with diabetes, as well as the implications for detection and management, a narrative literature review was undertaken using the electronic databases PubMed and Cochrane Library. The search, in August 2015, was for human studies published in English, with no time limits using the search string: "type 2 diabetes mellitus OR diabetes mellitus OR diabetes AND (dementia OR cognitive impairment OR mild cognitive impairment OR cognition)". References of retrieved papers were manually searched. Results are outlined below.

3.2.1 Cerebrovascular mechanisms

Proposed cerebrovascular mechanisms linking diabetes with cognitive dysfunction include brain infarcts and white matter disease [54]. Chronic hyperglycaemia is associated with microvascular disease [55]. Evidence that microvascular diabetic complications such as diabetic retinopathy [56] and microalbuminuria [57] are predictive of increased risk of dementia in individuals with diabetes adds weight to this cerebrovascular mechanism theory. Imaging studies have observed an increase in white matter hyperintensities associated with ischaemic change among people with diabetes, compared with

normoglycaemic controls [58]. Furthermore, white matter ischaemic change severity has been shown to be independently predictive of cognitive decline in a longitudinal study among an elderly population [59].

3.2.2 Non-cerebrovascular mechanisms

Brain insulin resistance has received much attention in the literature in recent years as a potential causal mechanism of AD [60-61]. This theory is biologically plausible, as effective insulin action in the brain is required for a of neuronal synapses and facilitates learning and memory [62-63]. The metabolic syndrome has been found to be associated with an increased risk of conversion from MCI to all-cause dementia in individuals with pre-diabetes, which adds further credibility to the theory of systemic and brain insulin resistance [64]. Therapies targeting insulin resistance and impaired signalling both systemically and/or in the brain to slow down or prevent neurodegeneration, including AD, are currently being researched [65].

Cortical atrophy patterns akin to pre-clinical AD have also been discovered in imaging studies among individuals with diabetes, with atrophy of the hippocampus and surrounding medial temporal lobe structures, regions that are associated with learning and memory problems [54]. Neuroimaging studies have also indicated a loss of brain connectivity, mainly in frontotemporal areas, in patients with diabetes, which has been related to reduced information processing [11, 66]. There is a suggestion that diabetes accelerates neurodegeneration and longitudinal case studies have shown the rate of global brain atrophy in individuals with diabetes to be up to three times that of non-diabetic controls [26, 67]. Additionally, interactions between T2DM and genetic risk predict a more rapid decline in cognitive speed [68].

The possibility that cognitive decrements in diabetes might be a result of the premorbid cognitive status of diabetes-prone individuals, thus indicating reverse causality, has also been considered in the literature [69]. As such, further high-quality studies are needed to explore this theory.

Incomplete evidence from the literature does not disentangle all factors that may contribute to cognitive impairment in diabetes. However, it is likely that mechanisms accelerate one another with additive effects, on a background of the normal ageing process [70].

3.3 Relative risk of depression in established diabetes: a systematic review

Depression has a multifactorial aetiology, and although the precise underlying causal mechanisms remain poorly understood, it is widely accepted that a relationship exists between diabetes and depression.

3.3.1 Methodology

A systematic review of the literature to identify English-language systematic reviews and meta-analyses of both observational and interventional studies exploring the onset of depression in individuals with established diabetes was undertaken. The methodology was identical to that outlined in Section 3.1.1, except diabetes was selected as the exposure of interest when the outcome was incident depression.

3.3.2 Results

Of 695 relevant abstracts retrieved in the systematic review, results of one study relating to diabetes as a risk factor for depression is outlined below.

A 2013 meta-analysis of 16 longitudinal studies examined the relationship between clinical depression in those with established diabetes. It included 497,223 subjects and 42,633 cases of incident depression and mean follow-up was six years. The adjusted HR of depression in subjects with diabetes was 1.25 (95% CI 1.10 – 1.44) [28].

No Cochrane reviews investigating incident depression in adults with established diabetes were found.

3.4 Diabetes and depression: potential mechanisms of association

In order to investigate the potential mechanisms linking depression with diabetes, as well as implications for detection and management, a narrative review of the literature was performed using the electronic databases PubMed and Cochrane Library. The literature search performed in August 2015 was for human studies published in English, with no time limits using the search string: "type 2 diabetes mellitus OR diabetes mellitus OR diabetes AND (depression OR mental disorder OR emotional distress)". References of retrieved papers were manually searched. Results of this narrative literature review are outlined below.

3.4.1 Shared mechanisms

While factors on a psychosocial and biological level have been suggested as potential mechanisms for the link between diabetes and depression, the direction of the association currently remains unclear. A bidirectional link has been acknowledged in the literature, with depression also considered a risk factor for the onset of diabetes. Psychosocial factors such as adverse social and physical environments, more unhealthy diet, and lower physical activity patterns are, unsurprisingly, associated with both conditions [71-72]. Mutual factors such as poorer self-care in those with both diabetes and depression can serve to increase blood glucose further, which in turn may contribute to depressive symptoms and worsening diabetes self-management [73-74].

Depression, diabetes, and insulin resistance also share biological factors such as an adverse impact on the HPA axis and an association with the pro-inflammatory pathway, which raises systemic levels of cytokines, C-reactive protein and TNF- α , and which in turn may increase the risk of the other condition [75-76].

In imaging studies, reduced hippocampal volume has also been associated with both diabetes and untreated depression, suggesting impaired neurogenesis as a mutual risk factor [77]. A more widely recognised shared vascular risk profile is indicated by other imaging studies, which find evidence for an important subcortical component to depression comorbid with diabetes and structural alterations of the basal ganglia [78].

3.4.2 Diabetes-related mechanisms

One such psychological factor, which may influence the risk of depression among individuals with diabetes, is the "psychological stress" associated with the management of a complex chronic illness such as diabetes [79]. Findings from a 2011 meta-analysis by Nouwen and colleagues, add weight to this theory. Authors found individuals with either impaired glucose metabolism or undiagnosed T2DM, not to be at an increased risk for depression, when compared with people with normal glucose metabolism. However, those with known T2DM had a significantly higher risk of having depressive symptoms [80]. Results suggest receiving a diagnosis of T2DM, and the associated stress of managing a chronic illness, may confer a higher propensity to developing depression. Negative coping strategies are often a feature in patients diagnosed with diabetes, with a common perception among diagnosed individuals that diabetes will negatively affect their future [81].

Diabetes disease-specific factors have also been associated with the development of depression. Evidence exists for a higher rate of depression among insulin users when compared to non-insulin users [82-83]. A higher diabetes complication burden, including sexual dysfunction, peripheral neuropathy, and nephropathy has also been shown to predict the development of depression [84-85]. These associations may reflect the severity of the disease or an increased diabetes self-management burden.

Chronic hyperglycaemia contributing to oxidative stress and neural cell death in areas of the brain associated with affective regulation, including the hippocampus and frontal cortex, is another potential biological mechanism by which diabetes may precede depression. Support for this theory from animal studies includes findings suggesting apoptosis in the hippocampus and frontal cortex and reduced serum brain-derived neurotrophic factor (BDNF) in mice models with comorbid depression and diabetes [86]. Human imaging studies have also shown greater atrophy in temporal areas among individuals with diabetes, compared to non-diabetic controls [87]. These findings suggest a potential adverse impact on neurogenesis, which is associated with emotional and cognitive behaviour.

3.4.3 Depression-related mechanisms

Depression has been shown to impact adversely on compliance with medical treatment, whereby people with depression are more likely to be overweight, have increased propensity to a sedentary lifestyle, and choose behaviours like smoking and eating unhealthy diets, all factors which may contribute to increased risk of developing T2DM [88-90].

A meta-analysis of observational studies, controlled trials and unpublished data by Kan and colleagues, in 2013, found a small, but significant association between depression and insulin resistance, a prediabetes stage [91]. Biological theories underpinning this link include the effects of depression on the HPA axis increasing cortisol circulation and stimulating glucose production, lipolysis, and circulating free fatty acids, leading to decreased insulin secretion and sensitivity [92]. Activation of a systemic inflammatory response by psychological stress has also been linked with increased cytokine production, leading to insulin resistance [93]. There is conflicting evidence from the literature linking atypical antipsychotic and antidepressant use as a possible contributor to the development of diabetes, due to effects on weight gain and glycaemic control. However, a causal link is yet to be established [94-95].

3.5 Impact of cognitive impairment, dementia and depression on diabetes

Individuals with cognitive impairment comorbid with diabetes, as shown in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, have increased risk of complications, including severe hypoglycaemia [96]. Factors underlying this finding may include poorer diabetes control [97]. Evidence that worse diabetes control, manifested as hyperglycaemia, is linked with cognitive status comes from the Health and Retirement Study (HRS). Findings from this study indicate that participants with lower cognitive indices had higher glycated haemoglobin (HbA1c) levels than those with higher cognitive indices [98]. Worse diabetes self-management was demonstrated once again using data from the HRS in a 2012 cross-sectional observational study among 1,398 older individuals with diabetes [99]. Executive function abnormalities likely to contribute to deficits in complex self-care behaviours have been found among older adults with diabetes in a number of studies and involve problem-solving, planning, organisation, insight, reasoning, and attention [100].

Data from the literature suggests that depressive episodes diagnosed in those with diabetes are more long-lasting [101] and more likely recurrent [102], with less treatment response to antidepressants [103] when compared to individuals with depression only. Poorer scores on measures of self-care, medical appointment attendance, glycaemic control, quality of life and ability to perform activities of daily living, as well as increased rates of hospitalisation have been observed in individuals with diabetes and comorbid depression [102, 104].

Results from the Diabetes, Attitudes, Wishes and Needs (DAWN) study in 2001 found that diabetes-related distress was common amongst people with diabetes. Diabetes-related distress is a term used to describe the emotional burden of self-managing diabetes [105]. In the DAWN study, diabetes-related distress was found to impact adversely on diabetes self-management [106]. However, for the purpose of this thesis, the focus was on depression and not diabetes-related emotional distress.

In addition, diabetes and comorbid depression is associated with higher healthcare costs [107], increased mortality [108], and a higher incidence of diabetic complications [109]. Such diabetic complications include diabetic retinopathy, nephropathy, neuropathy, macrovascular complications, sexual dysfunction, and foot ulcers [110- 111].

3.6 Other brain health complications associated with diabetes

Brain health complications of diabetes are not limited to cognitive impairment, dementia and depression. A 2008 study by Li et al. has shown diabetes to be associated with a higher overall burden of anxiety symptoms when compared to healthy controls [83]. Anxiety symptoms, in particular, can overlap with symptoms of hypoglycaemia. Li et al. postulate that this overlap may have implications for diabetes self-care, as patients may under-treat themselves, resulting in an increased risk of hyperglycaemia and further complications.

Also, a cross-sectional study gathering data on psychiatric comorbidity in 19 countries among those with adult-onset diabetes (52,095 participants), found a 1.6 fold increased risk of intermittent explosive disorder, 2.6 fold increased risk of binge eating disorder, and 2.1 fold increased risk of bulimia nervosa following comorbidity adjustment [112]. Proposed linking mechanisms include disturbed glucose metabolism contributing to the onset and maintenance of binge eating disorder and bulimia nervosa [113]. Suggestions for the mechanisms of association between intermittent explosive disorder and diabetes include low levels of HDL-cholesterol and reduced serotonin functioning, which have been associated with aggression and diabetes [114].

Diabetes is also an independent risk factor for stroke disease. Individuals with diabetes, when compared to those without, have at least twice the risk for stroke following adjustment for demographic and other cardiovascular risk factors [115]. Diabetes duration has been shown to increase ischaemic stroke disease risk, and hyperglycaemia has been observed to worsen clinical outcomes, post stroke [116].

3.7 Discussion and conclusion

As identified in a systematic review of the literature, the evidence base exploring the association between diabetes and brain health complications consists mainly of observational studies. Furthermore, there is ambiguity in the literature regarding the direction of the association between T2DM and depression, which cannot be addressed by observational studies. However, while we await further high-quality interventional studies addressing knowledge gaps, there is epidemiological evidence to suggest that the brain should be added to the suite of end organs, such as heart, foot, eye, and kidney, which can be adversely affected in diabetes.

Results of this systematic review of the literature exploring diabetes and brain health

associations helped inform the development of a measure used in the definitive DBH study to explore awareness among patients and the public of the effects of diabetes on the brain.

Chapter 4: Modifiable Risk Factors for T2DM shared with Dementia

4.1 Introduction

Similarities exist between T2DM and dementia; both have multifactorial aetiologies, are associated with ageing, and have well-recognised lifestyle, cardiovascular, and psychosocial risk factors. A 2011 review of the literature estimates that seven modifiable risk factors - diabetes, hypertension in midlife, obesity in midlife, physical inactivity, smoking, depression, and cognitive inactivity - contribute to up to half of Alzheimer's disease (AD) cases, globally [117]. Based on a growing body of evidence, there is an increasing focus on prevention or delaying onset of dementia through addressing modifiable risk factors, while research aimed at finding a cure for dementia-causing diseases, such as AD, is ongoing.

Gathering data on public and patient awareness of modifiable risk factors for dementia, including cardio-metabolic and lifestyle factors, may help identify key modifiable risk areas warranting greater education at a population level. Shared public health preventive approaches to T2DM and dementia may also represent an opportunity to target common modifiable risk factors. For these reasons, questionnaire items, measuring levels of awareness of modifiable risk factors for T2DM overlapping with dementia, were included in the questionnaire used in the definitive DBH study.

4.2 Common risk factors for T2DM and dementia: a systematic review

To establish content validity of questionnaire items in the DBH awareness measure relating to common risk factors for T2DM and dementia, a systematic review of the literature was undertaken. This systematic review aimed to assess the strength of the evidence for hypertension, obesity, depression, physical inactivity, cognitive inactivity, smoking, high cholesterol, and heavy alcohol consumption, as modifiable risk factors for T2DM.

Hypertension, obesity, depression, physical inactivity, cognitive inactivity, and smoking as modifiable risk factors for T2DM were included in the search strategy, as they are considered modifiable risk factors for AD-dementia based on a 2011 review by Barnes and Yaffe [117]. Given that prospective cohort studies have identified a wide range of potential

cardiovascular and lifestyle risk factors for non-AD dementia, high cholesterol, and heavy alcohol consumption, as T2DM risk factors, were also included in the search strategy [118-120].

For each of the factors mentioned above, the Cochrane Database of Systematic Reviews (all years) and MEDLINE and EMBASE (2011-2016) was searched to identify English-language systematic reviews and meta-analyses of both observational and interventional studies for associations with diabetes. Searches were performed separately for each risk factor, with references in the articles identified also searched. The systematic review protocol and electronic search strategy, conducted in accordance with PRISMA protocol [50] are outlined in **Appendices 8 -9**. Unpublished literature, including letters, conference abstracts, working papers, and dissertations were not included.

Systematic reviews or meta-analyses of prospective cohort and case-cohort studies, and randomised control trials (RCT), controlled trials, controlled before and after trials, with reporting on effect size, were eligible. If meta-analyses of prospective cohort studies and/or case-cohort studies were not available, meta-analyses including case-control and/or cross-sectional studies were examined. Participants were aged 18 years or over and recruited from non-specialised populations, meaning mostly community-dwelling participants, and therefore findings were considered generalisable to general adult populations. Studies with reported risk estimates including relative risk (RR) and hazard ratio (HR) with 95% confidence intervals (CI), based on the best available adjusted estimates from Cochrane reviews when available, or on the most recent and comprehensive meta-analysis, were eligible.

Hypertension, obesity, depression, physical inactivity, cognitive inactivity, smoking, high cholesterol and heavy alcohol consumption were selected as exposures of interest when the outcome of interest was incident T2DM. RR or HR estimates for T2DM were used when available; otherwise, RR or HR estimates for diabetes (unspecified type) were used.

Duplicate publications were omitted. Screened publications were then short-listed against study criteria, and relevant exclusions made (**see Appendix 10**). Differences of opinion were resolved via the input of the wider research group.

Relevant characteristics and results extracted from shortlisted eligible studies included population characteristics, systematic review characteristics, exposure and outcome data and measures of effect (**see Appendix 11**). For RCTs, the component assessment method of

Cochrane was used, and quality scoring was not performed [51]. For systematic reviews and meta-analyses sourced in MEDLINE and EMBASE, the PRISMA checklist [50] was used for critical appraisal.

Of 8,341 abstracts retrieved in the systematic review, a qualitative synthesis draws results together from ten of these studies, relating to eight proposed common risk factors for T2DM and dementia, together in results outlined below.

Hypertension: a risk factor for T2DM

A 2015 meta-analysis retrieved in the systematic review identified 30 prospective cohort studies with at least one-year follow-up, including 285,664 participants and 17,388 incident T2DM events. The pooled RR of diabetes for a 20mm Hg higher than usual systolic blood pressure across these studies was 1.77 (95% CI 1.53 - 2.05). Authors also examined a cohort of 4.1 million adults, free of diabetes and cardiovascular disease, using UK electronic health records. Elevated blood pressure was associated with incident T2DM; for a 20mm Hg higher systolic blood pressure HR was 1.58 (95% CI 1.56 - 1.59) and for a 10 mm Hg higher diastolic blood pressure HR was 1.52 (95% CI 1.51 - 1.54) [121].

No Cochrane systematic reviews examining the impact of treatment or modification, of hypertensive indices on T2DM incidence, were retrieved.

Obesity: a risk factor for T2DM

Systematic review findings included a 2015 meta-analysis of nine prospective cohort studies that examined the effect of body mass index (BMI) on incident T2DM. There were 11,237 incident T2DM events among 117,878 participants and mean follow-up was approximately nine years. The pooled adjusted HR, for incident T2DM for adults who were overweight and obese, compared to normal weight, was 2.33 (95% CI 1.95 – 2.78) and 6.10 (95% CI 4.63 – 8.04), respectively [122].

A 2005 Cochrane review examining the effects of long-term non-pharmacological weight loss interventions for individuals with pre-diabetes identified nine RCTs with a total of 5,168 participants. The outcome of diabetes was examined in five studies. Effect size from pooled results was not reported, but the incidence of T2DM was significantly lower in the intervention groups versus the controls in three of these five studies [123].

Depression: a risk factor for T2DM

The systematic review retrieved a 2014 meta-analysis that included 16 longitudinal studies with approximately 205 participants examining the association between depression and incident diabetes. Follow-up time ranged from 3 -16 years with 9,833 incident cases of diabetes. Both RR and HR for incident diabetes associated with depressive symptoms were significant, at 1.67 (95% CI 1.30 – 2.15) and 1.45 (95% CI 1.12 – 1.87), respectively [124].

No systematic reviews of RCTs examining the impact of treatment or modification of depression on T2DM incidence were found upon searching the Cochrane library.

Physical inactivity: a risk factor for T2DM

A 2016 meta-analysis examines 28 prospective cohort studies exploring the impact of physical activity on incident T2DM (1,261,991 participants and 84,134 incident T2DM cases). Follow-up time ranged from 3-23 years. Authors found strong evidence for an inverse association between physical activity and risk of T2DM, with RR of 0.87 (95% CI 0.84 -0.89) for every ten metabolic equivalents of task (MET) hours/week of physical activity [125].

A 2008 Cochrane review identified ten RCTs assessing the effects of exercise or exercise and diet on preventing T2DM. Exercise plus diet interventions (eight studies) in people with impaired glucose tolerance or the metabolic syndrome reduced the risk of diabetes when compared with standard recommendations (RR 0.63; 95% CI 0.49 - 0.79). However, no statistical effects on diabetes incidence were observed when comparing exercise only interventions (one study) with standard recommendations, or with diet only interventions [126].

Cognitive inactivity: a risk factor for T2DM

The systematic review did not reveal any meta-analyses including relevant studies with a prospective cohort design only. Therefore, a meta-analysis including case-control studies, in addition to cohort studies, was included in the qualitative analysis. This 2011 meta-analysis examined 23 case-control and cohort studies investigating the association between socioeconomic position (measured by education level, occupation, and income) and T2DM incidence. There was strong evidence for an inverse association between low educational

level, occupation and income and risk of T2DM, compared with high levels of these determinants (RR 1.41; 95% CI 1.28 -1.51) [127].

No Cochrane reviews investigating the association between cognitive inactivity and the risk of diabetes were retrieved.

Smoking: a risk factor for T2DM

A 2015 meta-analysis was retrieved in systematic review of the literature, which included 88 prospective cohort studies investigating the association between smoking and T2DM incidence. There were almost six million participants and the median follow-up was nine years (295,446 incident cases). Compared with never smoking, there was strong evidence for an association between risk of T2DM and current smoking (RR 1.37; 95% CI 1.33 – 1.42), former smoking (RR 1.14; 95% CI 1.10 – 1.18) and passive smoking (RR 1.22; 95% CI 1.10 – 1.35). The risk of diabetes was greater for heavy smokers, defined as over 20 cigarettes/day, (RR 1.57), than for lighter smokers (RR 1.21), compared with never smokers [128].

No Cochrane reviews investigating the association between smoking and the risk of diabetes were retrieved.

High cholesterol: a risk factor for T2DM

A 2014 meta-analysis of five longitudinal cohort studies exploring the risk of incident T2DM in relation to cholesterol intake included five studies, with a total of 203,903 participants and 7,589 incident cases of T2DM. Mean follow-up duration was 9-14 years. Compared with the lowest category of dietary cholesterol consumption, the highest category had a significantly higher association with T2DM risk (RR 1.25; 95% CI 1.16-1.36) [129].

No Cochrane reviews which included clinical trials examining the effects of dyslipidemia treatment on diabetes incidence were retrieved.

Heavy alcohol consumption: a risk factor for T2DM

As per systematic review findings, a 2015 meta-analysis examined the relationship between alcohol consumption and new-onset diabetes in 38 observational cohort studies with 1,902,605 participants and 125,956 incident T2DM cases. Relative to abstainers (current non-drinkers and never drinkers), the risk of T2DM increased at intake more than 63g/day.

Peak risk reduction was present between 10-14g/day, at an 18% decrease in hazards. However, stratification of data revealed that reductions in risk among moderate drinkers may apply to women only and may be absent in study populations from the Asian region [130].

No Cochrane reviews that included clinical trials examining the effects of interventions to reduce alcohol use on diabetes incidence were retrieved.

4.3 Discussion

Evidence, mostly observational, that the following modifiable risk factors for dementia; hypertension, obesity, depression, physical inactivity, obesity, high cholesterol consumption, and heavy alcohol consumption, are also risk factors for T2DM, is highlighted in this systematic review.

However, there were no studies found in this systematic review of the literature that explored the impact of cognitive inactivity on the risk of developing T2DM. Cognitive inactivity, defined as a lack of stimulating mental activity in relation to the concept of 'brain reserve' is an accepted risk factor for AD [117, 131]. 'Brain reserve' refers to the capacity of the brain to tolerate disease-related pathology such as AD, without developing clear clinical signs [131]. This review of the literature identified evidence that a low socioeconomic position is related to an increased risk of T2DM in a meta-analysis including case-control studies [127]. However, low socioeconomic status is not considered an acceptable proxy measure for cognitive inactivity as it does not capture the effect of a lack of stimulating mental activity on T2DM risk. Therefore, the association between incident T2DM and cognitive inactivity remains unclear.

Evidence was identified from RCTs that interventions addressing weight loss and physical inactivity, respectively, reduce the incidence of T2DM. However, design and methodological features of these trials limit generalisation of results to the general population [123, 126]. Specifically, trials included in a Cochrane systematic review exploring the impact of weight-loss interventions on incident diabetes include individuals with pre-diabetes, who were not necessarily overweight or obese at baseline [123]. Furthermore, retrieved in the Cochrane review of RCTs assessing the effect of physical activity on preventing T2DM, was a systematic review that includes only one study. This study compares exercise only interventions with standard recommendations or with diet only interventions, with no statistical effects on diabetes incidence found. The other eight

studies included in this Cochrane review assess the impact of exercise plus diet interventions on preventing T2DM [126].

Despite attempts to perform a comprehensive literature search according to PRISMA protocol [50], journals were not hand searched nor were attempts made to identify unpublished studies. Only studies in MEDLINE, EMBASE, and the Cochrane Database were included; other databases, such as PsychINFO, were not included. Moreover, the search was limited to articles published in English and there was a time frame on the MEDLINE and EMBASE search. As such, some studies may have been missed.

4.4 Conclusion

As highlighted in this systematic review of the literature, there is limited evidence from interventional studies for a number of modifiable risk factors for T2DM that overlap with dementia. For this reason, a Delphi study was undertaken as a next step in establishing DBH questionnaire content validity.

Chapter 5: Diabetes and Brain Health: Development of a New Survey Instrument

5.1 Introduction

A Delphi study was undertaken as a next step in establishing the content validity of questionnaire items for use in the definitive DBH survey measure. The Delphi study aimed to establish consensus among an expert panel on a number of (i) risk factors for T2DM and, (ii) complications of diabetes.

An electronic Delphi method was considered the best approach to reach international experts, as face-to-face contact with geographically dispersed diabetes and brain health specialists in different fields was unachievable [43, 44]. Limitations of the pilot study addressed in design of this Delphi study are outlined in Chapter 3.

5.2 Delphi study methodology

5.2.1 Delphi questionnaire development

The Delphi process traditionally begins with an open-ended questionnaire to elicit specific information about a content area from the Delphi experts. However, an acceptable and common modification is to use a structured questionnaire in the first round, based on an extensive review of the literature [44].

Using a modified Delphi study design, a questionnaire was developed for use in the first round. Items included in this questionnaire were based on findings of literature reviews, undertaken as part of this study, exploring associations between diabetes and brain health, in addition to diabetes disease management guidelines [132-133].

Questionnaire items relating to the following modifiable risk factors for T2DM, overlapping with dementia were included in the first round questionnaire: high blood pressure, obesity, depression, physical inactivity, not keeping the mind active (included as 'cognitive inactivity' in an earlier systematic review), smoking, high cholesterol, and heavy alcohol consumption. 'Poor level of engagement in social/leisure activities' was also included as a questionnaire item. A number of non-modifiable risk factors for T2DM were also included in the first round of the Delphi study. Participants were asked to rate their level of agreement with each item.

To avoid acquiescence response bias [134], ‘Frequent exposure to strong sunlight’ was included in the first round questionnaire as a potential T2DM risk factor. Of note, authors were aware at the time of inclusion that this is not an evidence-based risk factor for T2DM.

The following items addressing brain health and non-brain related complications of diabetes, were included in the first round Delphi study questionnaire; memory problems, depression, dementia, kidney damage, damage to the back of the eye, nerve damage, stroke, leg ulcers, and breathing problems.

To reduce an acquiescence effect [134], ‘Multiple sclerosis’ and ‘lung cancer’ were included as potential diabetes complications.

5.2.2 Data collection and analysis

The second step was group member identification. There is no consensus in the Delphi literature on the number of expert panellists, and no exact criterion concerning the selection of Delphi panellists. However, it is proposed that eligible individuals must have somewhat related backgrounds and experiences concerning the topic in question [45]. The quality of the experts on the panel is considered more important than the number of panellists [45].

Internationally recognised professionals with involvement in research, academic, and clinical practice, related to diabetes and dementia epidemiology and prevention, were invited to participate as an expert panel in this Delphi study, through email.

A link to the first round of the Delphi study was included in the invitation email. Participants were asked to rate their level of agreement with each diabetes complication item and T2DM risk factors in the electronic questionnaire using a five-point Likert scale (from strongly agree to strongly disagree). Participants were invited to comment on the phrasing of the questionnaire items and to suggest additional items for inclusion, or omission, in the next round of the study. In the second round, participants were provided with an updated questionnaire incorporating rephrased and additional items, in addition to aggregated results from the first round. Participants were asked to revise or qualify their responses, following consideration of group opinion. They were also asked to indicate in the first round of the Delphi study if they were willing to be identified as Delphi study panellists in future publications relating to the study.

A maximum of two email reminders was sent to invited panellist who did not reply by completing the questionnaire in each round.

5.2.3 Synthesis of information

In keeping with the literature, consensus in a Delphi study is determined by the majority response being significantly large [45]. In this Delphi study, a consensus criterion for provisional acceptance was set at $\geq 70\%$ agreement ('agree' plus 'strongly agree') or disagreement ('disagree' plus 'strongly disagree') between respondents on questionnaire items in keeping with accepted Delphi methodology [45]. Additional domains identified by experts during the study were included or omitted if they were listed by $\geq 15\%$ of respondents, a prevalence agreed upon by the wider research group to avoid omission of potentially relevant additional items in the context of the expert group having heterogeneous clinical and research backgrounds.

5.2.4 Results

In the first round of the Delphi study, of 46 experts invited to participate via email, 14 experts (32% response rate) took part. The time frame of the Delphi study was from June to July 2016. The profile of the expert panel invited is outlined in **Table 5.1**.

Table 5.1. Delphi study: Profile of invited expert panel participants

Professional expertise	
Geriatric medicine	5
Public health/epidemiology	6
Endocrinology/diabetology	15
Academic primary care	7
Diabetes education	3
Neuroscience	1
Neurology	4
Psychiatry	5
Total	46

Of the 14 initial participants, 13 completed both rounds of the Delphi study (93% response rate). The profile of the expert panel is outlined in **Table 5.2**.

Table 5.2. Delphi study: Expert panel participant profile

Professional expertise	Round 1 (n)	Round 2 (n)
Geriatric medicine	5	5
Public health/epidemiology	2	2
Endocrinology/diabetology	2	2
Academic primary care	1	1
Diabetes education	1	1
Neuroscience	1	1
Neurology	1	1
Psychiatry	1	-
Total	14	13

T2DM modifiable risk factor items meeting consensus criteria in the first round included obesity, physical inactivity, and heavy alcohol consumption. In the second round, high blood pressure (85% agreement) met consensus criteria as a risk factor for T2DM, as did poor social engagement (70% agreement). Depression (62% agreement), smoking (69% agreement), and high cholesterol (54% agreement) did not meet consensus criteria. Cognitive inactivity, phrased as ‘not keeping mind active’, did not reach group consensus as a risk factor for T2DM in the first round of the Delphi study and was omitted in the second round. Results are outlined in **Table 5.3**.

Table 5.3. Delphi study: risk factors for T2DM meeting consensus criteria

	Risk Factor	Round 1 (n=14)	Round 2 (n=13)
1	Physical inactivity ¹	100% agreement	Omitted 70% disagreement 54% agreement 69% agreement 62% agreement 85% agreement
2	Obesity ¹	100% agreement	
3	Family history of diabetes ¹	100% agreement	
4	Ageing ¹	93% agreement	
5	Heavy alcohol consumption ¹	85% agreement	
6	Exposure to strong sunlight ¹	86% disagreement	
7	Not keeping mind active	72% disagreement	
8	Poor social engagement	43% disagreement	
9	High Cholesterol	57% disagreement	
10	Smoking	50% disagreement	
11	Depression	50% disagreement	
12	High blood pressure	54% disagreement	

	Risk Factor	Round 1 (n=14)	Round 2 (n=13)
13	Unhealthy diet ²		100% agreement
14	Abnormal fasting blood sugar levels ²		100% agreement
15	History of cardiovascular disease ²		92% agreement
16	History of gestational diabetes ²		85% agreement
17	Certain race or ethnicity ²		85% agreement
18	Lower than normal birth weight ²		46% agreement

¹ risk factor items reaching consensus agreement/disagreement in round 1.

²additional complication items suggested by >15% expert group in round 1 and included in round 2

Suggestions by the expert panel in the first round included re-phrasing of the question regarding T2DM risk factors, from ‘X is a risk factor for T2DM’ to ‘T2DM is more common in individuals with/who have X...’. Additionally, on foot of respondents’ suggestions, the proposed T2DM risk factor ‘not keeping mind active’ (proxy for cognitive inactivity) was omitted in the second round.

Five of six additional modifiable and non-modifiable T2DM risk factors suggested by respondents for inclusion in the second round, met consensus criteria; ethnicity, gestational diabetes, unhealthy diet, abnormal fasting blood sugar, and history of cardiovascular disease (see **Table 5.4**).

Table 5.4. Delphi study: diabetes complications meeting consensus criteria

Complication	Round 1 (n=14)	Round 2 (n=13)
Kidney damage ¹	100% agreement	
Damage to the back of the eye ¹	100% agreement	
Nerve damage ¹	100% agreement	
Memory problems ¹	92% agreement	
Lung cancer ¹	92% disagreement	
Dementia ¹	92% agreement	
Stroke ¹	92% agreement	
Leg ulcers ¹	85% agreement	92% agreement
Depression	72% agreement	
Multiple sclerosis ¹	100% disagreement	
Breathing problems	57% agreement	Omitted

Complication	Round 1 (n=14)	Round 2 (n=13)
Pneumonia ²		77% agreement
Cardiovascular disease ²		100% agreement
Erectile dysfunction ²		92% agreement
Problems with attention and concentration ²		92% agreement
Cataracts ²		85% agreement

¹complication items reaching consensus agreement/disagreement in round 1.

²additional complication items suggested by >15% expert group in round 1 and included in round 2

Of proposed diabetes complications, 14 out of a total of 15 items met consensus criteria including brain health complications; memory problems, dementia, and stroke. On foot of respondents' suggestions, proposed diabetes complication 'breathing problems', was omitted and replaced by 'pneumonia' in the second round of the Delphi study.

All four additional diabetes complications proposed by experts in the first round - cardiovascular disease, erectile dysfunction, problems with concentration and attention, and cataracts - met consensus criteria in the second round of the Delphi study.

5.2.5 Discussion

Results of this Delphi study, along with systematic review findings, helped inform the design of the awareness measure used in the definitive DBH study by helping to establish content validity of items relating to brain health complications of diabetes, and modifiable risk factors for T2DM overlapping with dementia.

Consensus agreement was not reached in the Delphi study on a number of proposed risk factors for T2DM. These risk factors include depression, smoking, and high cholesterol. One possible explanation for this finding is limited evidence from intervention studies linking these risk factors with incident T2DM, as highlighted in the systematic review of diabetes and brain health literature. Another reason may be that the complex nature of the relationship between cardio-metabolic, psychosocial and lifestyle risk factors, and incident T2DM, influenced participant responses in the Delphi study. Adding weight to this theory, is a suggestion from an expert panel member to re-phrase the question stem in the first round of the Delphi study from, 'X is a risk factor for T2DM' to 'T2DM is more common in individuals with X...', in the second round of the Delphi study. As the participant pointed out, in light of mainly epidemiological evidence in the literature, to date, we cannot

confidently say that addressing a certain risk factor would lead to a lower disease incidence because of a change in that specific factor.

Views on depression as a risk factor for T2DM, expressed by participants, highlights variability in awareness and understanding of this association. One participant commented, *‘Evidence is very clear from cohort studies of people with depression that the incidence of diabetes is increased...’* while another participant commented *‘With respect to depression: I would say that depression is more common in patients with T2DM, not the other way around’*. Such comments reflect ambiguity in the literature regarding the direction, as well as the magnitude, of the association between diabetes and depression.

Despite observational evidence for smoking as a risk factor for T2DM, this factor narrowly missed expert panel consensus [128]. This finding suggests uncertainty among panellists about whether there is a direct causal association between smoking and T2DM. An unhealthy lifestyle associated with smoking is one possible explanation for the link; however, further high-quality intervention studies are required to determine causality.

There was less ambiguity among Delphi study participants with regards to reaching consensus on diabetes complication items. Dementia and depression both met expert panel agreement as diabetes complications. Once again, a comment by an expert panel member acknowledged the potential bidirectional link between depression and diabetes; *‘depression probably is associated with diabetes most likely through reduced physical activity’*. This comment further highlights the complexity of the linkage between the two conditions, which share a number of common risk factors and biological mechanisms [91- 92].

Given the DBH study aimed to determine diabetes and brain health awareness among respondents, not all diabetes risk factor and complication items reaching consensus in the Delphi study were included in the final DBH questionnaire. Similarly, a number of items not meeting consensus criteria as T2DM modifiable risk factors in the Delphi study were included in final DBH questionnaire given supportive, albeit limited evidence found in the systematic literature review undertaken as part of this study.

5.2.6 Delphi study limitations

This Delphi study has a number of limitations. These include ambiguous wording of a number of questionnaire items. Cognitive inactivity, defined as a lack of stimulating mental activity, is a recognised risk factor for AD dementia in relation to the concept of ‘brain

reserve' [131]. In this Delphi study, participants highlighted ambiguity with regards to the interpretation of, 'not keeping mind active', as a risk factor for T2DM. This item was used as a proxy for cognitive inactivity. As a result, this item was omitted in the second round of the Delphi study. However, an earlier systematic review of the literature highlighted a lack of studies exploring evidence for an association between cognitive inactivity and incident T2DM, as well as variability in the use of proxy measures for cognitive inactivity in the literature. Therefore, it is unlikely that an alternative wording of this item would have resulted in the expert panel reaching agreement on cognitive inactivity as a risk factor for T2DM.

It is also unclear in the literature whether dyslipidaemia or specific components (e.g. low HDL, high LDL, total cholesterol, hypertriglyceridaemia) are associated with T2DM risk. 'High cholesterol' was the T2DM risk factor item included in the Delphi questionnaire based on the weight of existing evidence for high cholesterol being a risk factor for both T2DM and dementia [118, 129]. It is possible that participants may have been more likely to reach consensus agreement if the term 'dyslipidaemia' was included as a risk factor for T2DM instead.

There are a number of generic methodological issues raised in the literature with regards to reliability, validity, and credibility of the Delphi research method. Such issues include a lack of accountability and arrival at a diluted version of best opinion [135 - 136]. However, in this Delphi study, we endeavoured to ensure expert panel membership was of high quality by inviting individuals with extensive clinical and research experience in the area of diabetes and brain health. Although the number of participants was low (32% response rate), the Delphi literature emphasises the quality of the panellist is considered more important than the quantity [45]. It is suggested that researchers using the Delphi method should use the minimally sufficient number of panellists, and panellists should be representative with regards to expertise on the topic in question [45]. As acknowledged in the Delphi literature, the information obtained in a Delphi study 'is only as good as the experts who participated on the panel' [137] and this Delphi study had a non-homogenous group of participants, with international experts from different clinical and research backgrounds. Therefore, the low number of panellists in this Delphi study with limited participation of invited experts with clinical backgrounds in diabetes care may have influenced the results. However, given a systematic review of the literature highlights limited interventional evidence exploring the association between diabetes and brain health, it is unlikely that a greater number of Delphi participants would significantly affect results.

5.3 Other DBH questionnaire items

A review of specific indicators used in The Irish Longitudinal Study of Ageing (TILDA) [138], the Healthy Ireland Survey [139], American Society of Aging Brain Health Poll [140], the Irish Health Survey conducted by the Central Statistics Office [141] and Dementia Friendly Ireland Study [142] informed other standard questions for the DBH questionnaire.

The questionnaire included the following domains:

- a. Sociodemographic factors: sex, age group, relationship status, nationality, area of residence (urban/rural), employment status, social class, educational attainment.
- b. Personal health indicators: subjective height and weight (BMI), personal illness burden
- c. Awareness of potential complications of diabetes including brain health complications
- d. Awareness of risk factors for dementia
- e. Awareness of risk factors for T2DM
- f. Subjective specific illness awareness, personal/family experience of diabetes and/or dementia
- g. Lifestyle-related factors: social participation, smoking, alcohol, levels of physical activity

Social class

Social class was captured in the questionnaire rather than socio-economic status, akin to Healthy Ireland Study [139]. SLÁN 2007, a survey of lifestyle, attitudes, and nutrition in Ireland [143] used the CSO96 social class classification, which was also adopted for this study.

The CSO96 classification uses 6 categories:

- professional workers (social class 1);
- managerial and technical (social class 2);
- non-manual (social class 3);
- skilled manual (social class 4);
- semi-skilled (social class 5);

- unskilled (social class 6).

For the purpose of this analysis, these six categories were regrouped into three social classes (SC), SC 1-2, SC 3-4, and SC 5-6.

In cases where there was not enough information available to assign a social class classification to a participant, he or she was assigned to an 'unclassified' group.

Physical activity level

International Physical Activity Questionnaire (IPAQ) scoring was as per official IPAQ scoring protocol [144]. Categorical and continuous scores were recorded.

Questionnaire testing

Before producing the final version of the DBH questionnaire, face validity was established following review by a group of experienced endocrinology specialists in St James's Hospital, Dublin. This included rephrasing of a number of questionnaire stems and items.

Pilot testing of the questionnaire was subsequently undertaken among a group of individuals with diabetes attending a secondary care diabetes day service in St. James's Hospital, Dublin (Diabetes Day Centre) and attendees of a general practice primary care clinic, Dublin 12. Piloting the questionnaire in this way further tested face validity. Appropriate revisions were made to the questionnaire thereafter, taking participant comments and interviewer experience, regarding administering the survey, into account. This included the addition of 'drop-down' and multiple-choice options to the web-based survey software to allow for the recording of numerous diabetes complications and/or health conditions where appropriate.

Chapter 6: Diabetes and Brain Health Study: Methods

6.1 Study type

The DBH study was an observational, cross-sectional survey study, among a sample of adults with diabetes and the general population in Ireland.

Ethical approval was secured for this study from the St. James's Hospital/AMNCH Research Ethics Committee, on 6th July 2016. REC Reference: 2016-07 Chairman's Action.

6.2 Study population

This study involved surveys of two distinct groups:

- (i) A group of individuals with diabetes attending a secondary care diabetes day service in St. James's Hospital, Dublin.
- (ii) Members of the Irish general population, represented by attendees of two general practice (GP) primary care clinics located in (i) the Dublin urban area and (ii) the North West of Ireland, a mixed urban-rural catchment area.

Previous studies looking at large primary care attendee populations have found the characteristics to be comparable with the Irish adult general population according to census data [145].

6.3 Inclusion and exclusion criteria

Inclusion criteria for all study sites required:

- Adult attendees of each study site, aged 18 years or older, who agree to complete the study questionnaire
- Adult attendees of the specialist diabetes centre who have a doctor's diagnosis of diabetes
- In the primary care study sites, all adult GP attendees were eligible for inclusion in the study according to proportional quota sampling methods, as outlined in this text.

Exclusion criteria for all study sites included:

- Limited English language proficiency precluding completion of the questionnaire
- Individuals under 18 years of age
- Individuals with incomplete questionnaires including demographic data only
- Self-reported diagnosis of dementia.

6.4 Sample size calculation

Statistical advice was sought from the Centre for Support and Training in Analysis and Research (CSTAR), University College Dublin, in devising a statistical analysis plan, including sampling strategy and data analysis.

Sample size calculation was based on unpublished results of aforementioned diabetes and brain health awareness pilot study, undertaken in 2014, the results of which found that approximately 7% of the general population (N = 227), and 35% of individuals with diabetes (N = 77) surveyed, correctly identified dementia as a complication of diabetes. The sample size for the present study was based on a requirement that the 95% confidence interval precision is at least 6% for estimates of proportions correctly identifying dementia as a complication. Based on the pilot study figures, the sample size was driven by the 35% level observed in individuals with diabetes. A sample size of 250 would give a 6% precision for a 35% estimate. Assuming equal sample sizes, the precision of an estimate in the other group of around 7% would be much less than the 6%. The total sample size of 500 (completed and valid questionnaires), i.e. 250 in each group, gives a power of approximately 99% to detect a 7% vs 35% difference between groups of awareness of dementia as a complication of diabetes.

6.5 Sampling technique: quota sampling

Proportional quota sampling was used in this study. Proportional quota sampling is a type of non-probability sampling, which was used to ensure the sample in both study groups is similar to the target population. GP attendees, representative of the general population in Ireland, were selected using quota sampling. Quotas were set by age and sex, with the distribution of age and sex determined according to 2016 Central Statistics Office (CSO), Ireland figures [7].

Distribution of gender across the general population, according to the 2016 CSO figures, is 49.4% male [7]. Therefore, 50% of male participants were recruited in the GP attendee group. For recruitment purposes and in accordance with 2016 CSO data, the GP attendee population was divided into three age groups; 18 to 44 years, 45-64 years, 65 plus years. Using 2016 CSO figures, approximately 44% of the Irish population are estimated to be aged 45 or older, and, as such, this figure was set as an age quota for the GP attendee study group. Age and sex quotas for GP attendee participants were in place for both urban and rural study populations.

Data analysis, post study, allowed for the calculation of representation of individuals with diabetes among the GP attendee group.

Quota sampling was set by diabetes type only among the diabetes group participants recruited from a diabetes secondary care centre. The quota was set at 10% T1DM, given this is the estimated percentage of the population of people in Ireland with diabetes living with T1DM [9].

6.6 Field sites

The DBH study utilised an interviewer-administered study specific questionnaire (**Appendix 15**). Steps undertaken to develop this diabetes and brain health awareness measure are outlined in the previous chapter of this thesis. Interviews were conducted on a face-to-face basis with participants in the following locations to administer the questionnaire.

- Field site 1: Diabetes Day Centre (DDC), St. James's Hospital, Dublin 8
- Field site 2: An urban primary care practice, Sundrive Medical Practice, Dublin 12
- Field site 3: A mixed urban-rural primary care practice in the North West of Ireland: Loftus Medical Practice, Boyle, Co Roscommon

St James's Hospital catchment area has a relatively deprived and elderly population and serves as an acute care setting for a local Dublin city catchment area of 270,000 adults [146-147]. Dublin 12, where the urban general practice study site was located is also an area with a high level of social deprivation with 27% of residents in the local area primary educated only and an age dependency ratio of up to 31% [148]. Boyle electoral area in County Roscommon, where the mixed urban-rural general practice study site was located

is considered a disadvantaged area with 25% of the population primary school educated only, and an age dependency ratio of 41% within the area [148].

6.7 Recruitment

At each site, the interviewer approached consecutive attendees. If the attendee was not eligible, declined participation, or quota has already been filled, the next attendee was invited to participate.

Fieldwork was conducted between December 2016 and February 2017.

6.7.1 Interviewer briefing and training

A research assistant was recruited as a study interviewer from a group of postgraduate students who successfully completed a Public Health Masters Degree programme run by University College Dublin.

The author, CD, held an introductory session with the interviewer, and comprehensive instructions on all aspects of the project were provided.

Topics covered during this introductory session included:

- Background of the study
- Questionnaire items
- Recruitment procedure
- Maximising survey response
- Sampling and use of quotas
- Qualtrics software usage
- Social class coding
- Ethical considerations
- Project administration

The interviewer was provided with detailed written instruction on all aspects of the project and a handheld electronic device to administer the questionnaire and enter data using Qualtrics software (www.qualtrics.com). Qualtrics is a web-based survey instrument used to conduct survey research, evaluations, and other data collection activities.

The interviewer had ongoing access to telephone support and face-to-face progress meetings with the author, CD, throughout the fieldwork period.

6.7.2 Participant information and consent

Brief written information, including an outline of the project, its aims, and consent details (**Appendix 14**) was offered to potential participants by the interviewer. Study information stressed the greater benefit to the broader community of an individual's participation. One of the initial questionnaire items requested that the respondent give consent to take part in the study. Participants were required to confirm they have read and understood the study description and that they are 18 years of age or older, in order to proceed.

It was presumed that participants might obtain knowledge about diabetes and dementia that they might not have before participating in the survey. Therefore, the interviewer highlighted to participants where they may get further information on diabetes and brain health on completion of the survey.

The maximum privacy option of the Qualtrics software was employed. Qualtrics maintains a log of accesses by customers to its system. Qualtrics uses Transport Layer Security (TLS) encryption (also known as HTTPS) for all transmitted data. All data were collected anonymously in accordance with the Data Protection Act 2003 [149]. Names, addresses or date of birth were not collected, and participants consented to analysis of data provided for research purposes.

6.8 Data entry and data validation

Interviewer entered respondents' responses directly to a purpose-built online survey instrument at www.qualtrics.com. Data was exported to, cleaned, and analysed in Statistical Package for the Social Sciences (SPSS) version 24. The variables of interest examined were sex, age group, educational attainment, marital status, social class, and experience of knowing someone living with dementia, as well as personal health indicators, including diabetes-related factors.

6.9 Data analysis

Descriptive analysis of the data was undertaken, and results presented in this thesis include frequency counts, ranges, means, and standard deviation.

Multivariable logistic regression was chosen as an appropriate statistical method to conduct a predictive analysis to explain the relationship between the dependent dichotomous variable (awareness of dementia as complication of T2DM - Yes or No) and multiple nominal and ordinal independent variables (sex, age, education, marital status, social class, diabetes duration, diabetes pharmacological treatment, diabetes complication burden and participation in formal diabetes education). Of respondents in the diabetes group, 4 of the 250 did not provide complete data, and these were excluded from the logistic regression analysis.

The significance of the covariates was assessed by the p-values (<0.05), odds ratios (OR), and 95% confidence intervals (CI) for associations between the predictor variables and the outcomes of interest. Non-probability quota sampling allowed for the calculation of target population-level estimates of awareness of the link between diabetes and brain health.

6.10 Diabetes and Brain Health Study Results

6.10.1 Response rate

The DBH study had 502 respondents, with an overall response rate of 87%. The response rate in the diabetes group attending St James's Hospital was 94%. Response rates were 89% and 74% in the urban and mixed urban-rural GP attendee groups, respectively.

6.10.2 Socio-demographic and lifestyle factors

Among the total group, over half (56%) of respondents were men, and the mean age of respondents was 55 (± 17) years (see **Table 6.1**).

Compared to the GP attendee group, respondents in the diabetes group were significantly more likely to be men ($p = 0.003$), older ($p < 0.001$), and to have a lower level of education ($p < 0.001$) (see **Table 6.1**).

Table 6.1. DBH study: respondent socio-demographic profile

	Total group	Diabetes group	GP attendee group	Between group difference
	N = 502	N = 250	N = 252	p value
Age group [years] <i>Mean ± standard deviation, range</i>	55 ± 17, 18-90	63 ± 14, 20-90 ³	47 ± 17, 18 -90	<0.001
	% (n)	% (n)	% (n)	p value
Age group [years]				
18-44	40 (150)	10 (24) ¹	50 (126)	
45 to 64	38 (188)	43 (106)	33 (82)	
≥ 65	33 (163)	48 (119)	18 (44)	0.001
Gender				
Women	44 (223)	37 (94)	51 (129)	
Men	56 (279)	62 (156)	49 (123)	0.003
Nationality				
Non-Irish	15 (73)	12 (30)	17 (43)	
Irish	86 (429)	88 (220)	83 (209)	0.108
Education Level				
Tertiary	41 (204)	29 (73) ¹	52 (131) ¹	
Secondary	36 (179)	35 (86)	37 (93)	
Primary	23 (117)	36 (90)	11 (27)	<0.001
Marital status				
Single/divorced	39 (193)	39 (97) ¹	38 (96) ²	
Married/civil partnership	61 (306)	61 (152) ⁴	62 (154)	0.899
Social Class				
High (SC1 & SC2)	34 (170)	29 (73) ¹	39 (97)	
Middle (SC3 & SC4)	34 (168)	38 (94)	29 (74)	
Low (SC5 & SC6)	27 (136)	28 (70)	26 (66)	
Unclassified	5 (27)	5 (12)	6 (15)	0.102
Contact with person with dementia	62 (277)	58 (118) ³	65 (159) ⁴	0.088
Contact type				
Family/partner	55 (151)	56 (66)	54 (85)	
Other	45 (126)	21 (52)	47 (74)	0.683

¹missing subgroup data n = 1

²missing subgroup data n = 2

³missing subgroup data n = 45

⁴missing subgroup data n = 9

Significantly, more GP attendee respondents, compared to diabetes group respondents, self-reported engagement in high levels of physical activity (20% and 13%, respectively, $p = 0.027$), classified using the International Physical Activity Questionnaire (IPAQ) criteria [144]. Additionally, a higher proportion of GP attendee respondents compared to diabetes group respondents self-reported being a healthy weight (49% and 16%, $p < 0.0001$), defined as having a BMI in the range 18.5 to 24.9. Significantly, more GP attendee

respondents, compared to diabetes group respondents, smoked tobacco (28% and 13%, $p < 0.0001$) and drank alcohol (75% and 65%, $p = 0.017$).

6.10.3 Contact with persons with dementia

Over half of the total group has contact with an individual with dementia (62%), who is a family member or a partner in the majority of cases (55%) (see **Table 6.1**).

6.10.4 Personal health indicators

Compared with GP attendee respondents, diabetes group respondents were significantly more likely to report that they had been diagnosed with high cholesterol ($p < 0.001$), hypertension ($p < 0.001$) and heart problems ($p < 0.001$) (see **Table 6.2**). Among diabetes group respondents, 88% have a diagnosis of T2DM, with a mean duration of diagnosis of 14 (± 10) years, and 44% have experienced diabetes-related complications. Among GP attendee respondents, 7% have a diagnosis of diabetes, diagnosed for a mean duration of 10 (± 8) years; 29% have experienced diabetes-related complications (see **Table 6.2**).

Table 6.2. DBH study: respondent health and diabetes profile

	Total group N = 502	Diabetes group N = 250	GP attendee group N = 252	Between group difference
Diagnosis	% (n)	% (n)	% (n)	p-value
Diabetes	53 (267)	100 (250)	7 (17) ¹	<0.001
High cholesterol	41 (205)	57 (141) ¹	25 (64)	<0.001
Hypertension	43 (217)	63 (156) ¹	24 (61)	<0.001
Depression	14 (72)	16 (41) ¹	12 (31)	0.227
Heart problems	21 (105)	33 (81) ²	10 (24)	<0.001
CVA/TIA	2 (12)	4 (9) ¹	1 (3)	0.076
Memory problems	6 (30)	8 (20) ¹	4 (10)	0.055
	Total group N= 267	Diabetes group N= 250	GP attendee group with diabetes N = 17	Between group Difference p-value
DIABETES PROFILE				
Duration of Diabetes [years] <i>Mean ± standard deviation, range</i>	13 ± 10, 0-62	14 ± 10, 0-62 ²	10 yrs ± 8, 1- 27	0.424
	% (n)	% (n)	% (n)	% (n)
Glucose lowering drugs	94 (249)	94 (235) ¹	82 (14)	0.05
Diabetes formal education	33 (87)	33 (81) ¹	35 (6)	0.814
Diabetes complications	43 (112)	44 (107) ²	29 (5)	0.709

¹missing subgroup data n = 1, ²missing subgroup data n = 2

6.10.5 Awareness of the complications of diabetes mellitus

Fig. 6.1 demonstrates respondent awareness of complications associated with diabetes.

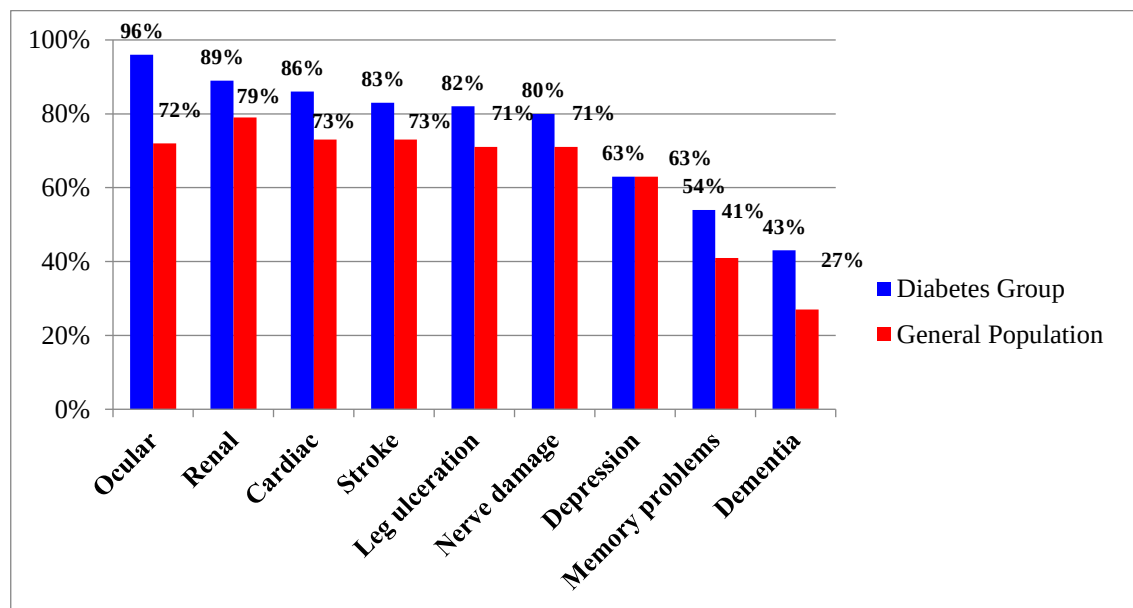


Figure 6.1. DBH study: percentage (%) awareness of diabetes complications among diabetes group (n= 250) and GP attendee (General Population) (n=252) group

Among the total study group, there was poor awareness of dementia (35%) and memory problems (47%) as potential complications of diabetes. The most commonly identified potential brain health complication of diabetes was stroke (78%), and 63% of the total respondent group identified depression as a diabetes brain health complication. In contrast, respondents have higher levels of awareness of other organ complications of diabetes, including, eye damage (84%), kidney damage (84%), heart disease (80%), leg ulcers (77%), and nerve damage (76%).

When adjustments were made for age and gender, diabetes group respondents were significantly more likely to correctly identify all diabetes complications listed in the questionnaire ($p < 0.05$), except for depression, compared with GP attendee respondents (see Table 6.3).

Table 6.3. DBH study: awareness of diabetes complications by subgroup* following adjustment for age and sex

N=501	Adjusted odds ratio (AOR)	95% confidence interval (95% CI)	p-value
Complication			
Ocular			
GP attendee group	1		
Diabetes group	7.024	3.44 – 14.35	<0.001
Renal			
GP attendee group	1		
Diabetes group	2.157	1.23 – 3.79	0.007
Cardiac			
GP attendee group	1		
Diabetes group	2.707	1.62 – 4.52	<0.001
CVA			
GP attendee group	1		
Diabetes group	1.846	1.13 – 3.01	0.014
Leg ulceration			
GP attendee group	1		
Diabetes group	2.599	1.59 – 4.25	<0.001
Nerve damage			
GP attendee group	1		
Diabetes group	2.694	1.66 – 4.37	<0.001
Depression			
GP attendee group	1		
Diabetes group	1.111	0.74 - 1.68	0.616
Memory problems			
GP attendee group	1		
Diabetes group	1.899	1.26 – 2.85	0.002
Dementia			
GP attendee group	1		
Diabetes group	1.850	1.21 – 2.82	0.004

*diabetes group versus GP attendee group

6.10.6 Awareness of risk factors for dementia and T2DM among total group

Across the group as a whole, just over half (54%) of respondents were aware that the risk of dementia is modifiable, with respondents having a greater awareness of the non-

modifiable, compared to modifiable, risk factors for dementia. Approximately, nine in every ten respondents correctly identified increasing age (94%) and family history of dementia (87%) as risk factors for dementia. However, less than half of respondents were aware that diabetes is a risk factor for dementia (43%). The most commonly recognised modifiable risk factors for dementia were physical inactivity (70%) and depression (67%), with obesity recognised by only 43% of respondents (see Fig. 6.2).

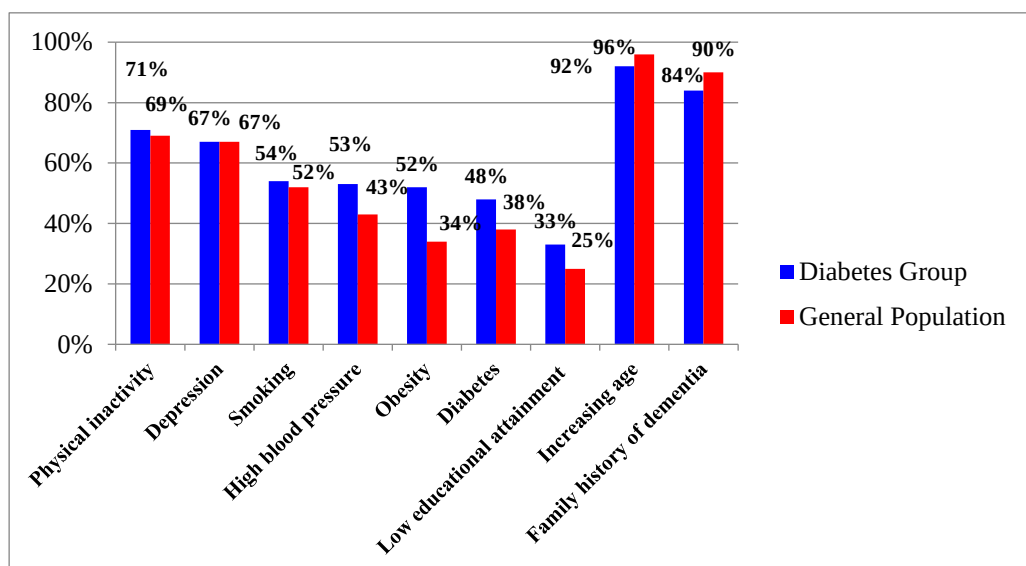


Figure 6.2. DBH study: percentage (%) awareness of risk factors for dementia among diabetes group (n= 250) and GP attendee (General Population) (n=252) group

Among the total respondent group, 88% were aware that the risk of T2DM is modifiable. The majority of respondents correctly identified increasing age (70%) and family history of diabetes (87%) as risk factors for T2DM. The most commonly recognised modifiable risk factors for T2DM were unhealthy diet (97%), obesity (95%), and physical inactivity (92%).

6.10.7 Diabetes group: knowledge associations

Within the diabetes group, those with a longer duration of diabetes were significantly more likely than those with shorter disease duration, to have an awareness that dementia is a brain health complication of diabetes (adjusted odds ratio (AOR) 1.03, $p=0.029$), however given the low AOR this result is unlikely to be clinically significant. Additionally, those who have not received a formal diabetes educational intervention were significantly less likely to correctly identify dementia as a diabetes complication (AOR 0.49, $p=0.018$) (see Table 6.4).

Table 6.4. DBH study: awareness of dementia as a complication of diabetes among diabetes group respondents

n = 246	Adjusted odds ratio (AOR)	95% confidence interval (95% CI)	p value
Demographic variable			
Age	0.99	0.97 – 1.02	0.627
Gender			
Men	1		
Women	1.45	0.81 – 2.59	0.212
Nationality			
Non-Irish	1		
Irish	1.06	0.44 – 2.53	0.899
Education Level			
Tertiary	1		
Secondary	0.82	0.41 – 1.67	
Primary	1.18	0.54 – 2.59	0.582
Marital status			
Single/divorced	1		
Married/civil partnership	1.08	0.61 – 1.90	0.789
Social Class			
High (SC1 & SC2)	1		
Middle (SC3 & SC4)	0.77	0.38 – 1.58	
Low (SC5 & SC6)	1.34	0.62 – 2.91	
Unclassified	1.13	0.30 – 4.30	0.486
Diabetes duration [years]	1.03	1.00 – 1.07	0.029
Diabetes pharmacological treatment			
Yes	1		
No	0.61	0.15-2.44	0.487
Diabetes formal education			
Yes	1		
No	0.49	0.27-0.89	0.018
Diabetes complications			
Yes	1		0.842

n = 246	Adjusted odds ratio (AOR)	95% confidence interval (95% CI)	p value
Demographic variable			
No	0.94	0.54 – 1.66	

6.11 Discussion

The aim of the DBH study was to gather data on levels of awareness of the effects of diabetes on brain health among individuals attending a secondary care diabetes service and from the general public, as represented by GP attendees.

Results point to low levels of awareness among patients and the public that dementia and memory problems (35% and 47%, respectively) are brain health complications of diabetes. Greater respondent awareness of other organ complications of diabetes, such as eye, kidneys, and lower limb (84%, 84% and 77%, respectively), a result reflected in both subgroups, suggests a lack of focus on brain health complications in current diabetes-related education in Ireland.

Respondents in the diabetes group have a significantly greater awareness of dementia, memory problems, and stroke as potential diabetes complications, compared to GP attendee respondents. These findings echo those of the pilot study, undertaken as part of this body of work. Respondents in the diabetes group are older and less educated compared to the GP attendee group. Over two-thirds of the diabetes group respondents have low educational attainment, in keeping with evidence demonstrating a strong association between lower levels of education and poorer health outcomes [150]. Despite this socio-demographic profile, diabetes group respondents have a higher level of diabetes and brain health awareness. One possible explanation for this finding is that respondents attending a secondary care diabetes service may have more frequent contact with healthcare professionals with associated formal and informal health education opportunities. Adding weight to this theory are findings that respondents in the diabetes group with a longer duration of diabetes, and those who received a formal diabetes educational intervention, were more likely to correctly identify dementia as a diabetes complication. However, another possible explanation is that this study was inadequately powered to allow for the determination of an association between, awareness of the link between diabetes and brain health, and educational attainment.

Another interesting finding is that there is a low level of awareness among participants that there are steps that can be taken to potentially reduce their risk of developing dementia. Despite the existence of a brain health-focused Irish National Dementia Strategy and associated dementia education campaign [151], respondents in this study were 1.5 times less likely to identify dementia risk as having a modifiable component, when compared to T2DM risk. DBH study findings highlight poor recognition of cardio-metabolic risk factors for dementia such as diabetes (43%), hypertension (48%), and smoking (53%), compared to non-modifiable dementia risk factors, including increasing age (94%) and family history of dementia (87%). These findings indicate a need for diabetes-related and public education programmes to focus on the association between modifiable risk factors and later dementia risk, which may encourage the adoption of healthy lifestyle behaviours.

DBH study results are in keeping with the findings of a 2016 national survey in Ireland, Dementia Friendly Ireland, which found that less than half (46%) of 1,217 respondents believe that there are things they can do to reduce their risk of dementia [142]. An Alzheimer's Australia study had similar findings, with only 51% of Australians aware that dementia risk reduction was possible [152]. Such results suggest a lack of translation of a growing body of evidence, bringing the role of modifiable risk factors, which exacerbate or reduce one's risk of developing dementia in later life, into public awareness.

There is evidence that intensive diabetes education, along with case management by a care manager, can improve glycaemic control and quality of life among individuals with diabetes and end-stage kidney disease, and reduce presentations to health services for the treatment of diabetes complications [153]. This highlights the benefits of educational interventions for individuals with diabetes, and adds further impetus to the need to raise awareness of the effect of diabetes on the brain, by expanding formal diabetes education programmes. Reinforcement, with education of the links between diabetes and brain health provided at additional points of contacts with health professionals, is also likely to be helpful. This demands that health professionals are aware of the association between diabetes and brain health. Results of a pilot study undertaken as part of this thesis found low levels of awareness of a link between diabetes and brain health among a relatively small sample of nursing staff members (N=96) in a large urban hospital in Ireland. Given that this study had a number of limitations, further studies, with a larger number of subjects and across different healthcare professional groups, are needed to confirm this preliminary finding.

Limitations of the DBH study include the significant difference in age and gender between respondents in the diabetes and GP attendee groups. However, the age difference was a result of quota sampling by age and gender, used to ensure the GP attendee group was representative of the Irish population who are aged over 18 years. Furthermore, the diabetes group was representative of attendees of a diabetes secondary care service in Ireland and, as the prevalence of diabetes is consistently higher in males compared to females, it was not surprising that it was an older group with more males [8].

6.12 Conclusion

There are no other published studies that examine awareness of diabetes and brain health among individuals with diabetes and the public. The results of this study thus highlight the lack of awareness of the association between diabetes and brain health among individuals attending a specialist diabetes service, and amongst members of the general public. These findings point to the need to develop diabetes-specific education programmes on this topic, as well as public awareness campaigns that emphasise diabetes as a potentially modifiable risk factor for dementia prevention.

Chapter 7: Future Directions

This thesis has highlighted a number of findings that have direct implications for diabetes education and awareness and for the potential to prevent dementia in this at-risk population.

7.1 Low levels of awareness of the link between diabetes and brain health

There is a low level of awareness of the link between diabetes and brain health in the general public and those with diabetes. The immediate implications for these findings, therefore, are that there is a clear need for raising public awareness about the association between diabetes and depression and cognitive impairment, and to ensure that brain health is included in the diabetes education programmes for people with diabetes. Interestingly, Irish people are more aware that there is potential to reduce the risk of developing diabetes, compared to dementia. This represents a gap in awareness about addressing modifiable risk factors for dementia in Ireland, and it underscores the importance of taking a brain health advice approach, as emphasised in the Understand Together Campaign, the Irish Dementia Awareness Campaign [154].

7.2 Shared risk factors for dementia and diabetes

Risk reduction messages for diabetes, as well as other chronic illnesses such as ischaemic heart disease and stroke, potentially apply to dementia. In a 2015 paper exploring a population health approach to dementia prevention, the authors proposed that economies of scale might be gained through the cross-promotion of public health messages and policies, providing opportunities for resource sharing between health promotion agencies [155]. However, there was limited evidence found in the systematic review of the literature in this study for a number of modifiable risk factors for T2DM overlapping with dementia e.g. obesity, physical inactivity, hypertension, and heavy alcohol consumption. Further high-quality interventional trials are necessary to guide shared public health preventative approaches to T2DM and dementia as overlapping risk factors represent an opportunity for shared public health approaches.

The Irish National Dementia Strategy [151] suggests the 2008 Department for Health Policy Frameworks for the Management of Chronic Disease, which includes diabetes

[156], should guide dementia prevention strategies in Ireland. However, dementia is not currently a listed illness included in the HSE chronic disease management programme in Ireland.

7.3 Healthcare professionals: need for further studies to determine diabetes and brain health awareness

Preliminary findings from the pilot study, suggesting that the nursing profession have low levels of awareness of the brain health effects of diabetes, need further replication but is likely to be borne out in larger studies. Nursing staff members who participated in the pilot study worked with older adults in a large urban Irish hospital. Future studies, using larger numbers and more robust sampling methods should thus aim to replicate these findings in this and other healthcare professional groups. These studies should also explore specific knowledge gaps and awareness of the links between diabetes and brain health e.g. the relationship between poor glycaemic control and the increased rate of brain health complications. Establishing gaps in diabetes and brain health awareness among staff providing clinical care for individuals with diabetes will guide the development of diabetes-related education and training programmes for healthcare professionals. It will also be important to establish whether there is awareness or implementation of best practice guidelines regarding screening of older adults for depression and cognitive decline.

7.4 Implications for care and treatment of diabetes

The findings of this thesis also have implications for the care and treatment of diabetes. As older adults with T2DM are a group at higher risk of brain health diabetes complications, an annual review may represent a significant opportunity to integrate mental and cognitive health screening and treatment, into multidisciplinary team diabetes care [132]. Early detection of diabetes brain health complications may provide an opportunity for the introduction of timely measures to optimise support for diabetes self-management and appropriately adjust diabetes treatment regimes. Such action has the potential to minimise further complication risk [102, 104, 157].

International best practice guidelines, specifically for older adults with T2DM, recommend baseline and yearly screening for both cognitive impairment and depression [132-133].

The 9-item Patient Health Questionnaire (PHQ-9) or 5-item Geriatric Depression Scale is recommended to screen for changes in mood status [132-133, 158].

For assessment of cognitive impairment, the use of the Montreal Cognitive Assessment (MoCA), the MiniCog and the Mini-Mental State Examination (MMSE) screening tools are recommended [132-133].

However, international best practice recommendations are not reflected in current national diabetes primary care guidelines in Ireland, which do not include advice on screening for brain health complications of diabetes [159]. Future revisions of diabetes care guidelines in Ireland should, therefore, be expanded to include advice on screening and management of brain health complications of diabetes.

7.5 Future studies

Given the interdependence of health behaviour risk factors, results of interventional trials exploring the effectiveness of multicomponent risk reduction strategies for cognitive impairment in older groups with T2DM may have the potential to prevent cognitive decline. One such trial aiming to examine the acceptability and feasibility of a lifestyle modification intervention in older adults in Ireland with T2DM is the BRAIN-diabetes trial. This study, due to commence in mid-2019, is funded by the Cross-Border Healthcare Intervention Trials in Ireland Network (CHITIN) and supported by the European Union's INTERREG VA Programme. Planned interventions in this trial are modelled on an intensive multi-component lifestyle intervention included in a dementia prevention study in Finland; the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) [160]. Results of the FINGER study show a significant between-group difference in the change of cognitive test score per year at 0.022 (95% CI 0.002–0.042), favouring the intervention group. The BRAIN-diabetes trial will adapt the FINGER intervention for use among a high-risk group of older participants with T2DM in Ireland. The intensive intervention programme will include nutrition, exercise, cognitive stimulation, and intensive vascular risk factor control. Results of this study may inform and guide further development of dementia prevention and education strategies in Ireland.

7.6 Conclusions

It is clear from the findings of these studies that there is still much work to be done in raising awareness among individuals with diabetes and the public about the links between diabetes and brain health.

The gaps in diabetes and brain health awareness highlighted in these studies mean that there needs to be an expansion of diabetes education programmes to include awareness of the link between diabetes and brain health. Public awareness campaigns relating to dementia prevention must emphasise the role of modifiable risk factors, particularly T2DM, physical inactivity, and obesity as part of a life-course approach to dementia prevention. Given that T2DM and dementia have a number of common modifiable risk factors, cross-promotion of public health messages for these conditions may represent a useful opportunity to address awareness deficits highlighted in the DBH study. However, given the limited evidence from the literature with regards to modifiable risk factors for T2DM that may overlap with dementia, further high-quality interventional trials are necessary to guide shared public health preventative approaches to T2DM and dementia.

In parallel with diabetes-specific and public education campaigns with a focus on the link between diabetes and brain health, it is vital that healthcare professionals working with individuals with diabetes become more aware of the association so that detection and multicomponent intervention approaches can be introduced in this at-risk population, in order to address both depression and cognitive decline.

References

1. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Res Clin Pract.* 2014 Feb;103(2):137–49.
2. International Diabetes Federation. *IDF diabetes atlas.* Brussels: International Diabetes Federation; 2015.
3. International Diabetes Federation. *IDF diabetes atlas.* Brussels: International Diabetes Federation; 2017.
4. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nature Reviews Endocrinology.* 2018 Feb;14(2):88–98
5. Grarup N, Sandholt CH, Hansen T, Pedersen O. Genetic susceptibility to type 2 diabetes and obesity: from genome-wide association studies to rare variants and beyond. *Diabetologia.* 2014 Aug;57(8):1528–41
6. World Population Prospects: The 2017 Revision | Multimedia Library - United Nations Department of Economic and Social Affairs [Internet]. [cited 2019 Nov 30]. Available from: <https://www.un.org/development/desa/publications/world-population-prospects-the-2017-revision.html>
7. Census of Population 2016 - Profile 3 An Age Profile of Ireland - CSO - Central Statistics Office [Internet]. [cited 2019 Nov 30]. Available from: <https://www.cso.ie/en/releasesandpublications/ep/p-cp3oy/cp3/>
8. Tracey ML, McHugh SM, Buckley CM, Canavan RJ, Fitzgerald AP, Kearney PM. The prevalence of Type 2 diabetes and related complications in a nationally representative sample of adults aged 50 and over in the Republic of Ireland. *Diabet Med.* 2016 Apr;33(4):441–5.
9. Leahy S, O' Halloran AM, O' Leary N, Healy M, McCormack M, Kenny RA, et al. Prevalence and correlates of diagnosed and undiagnosed type 2 diabetes mellitus and pre-diabetes in older adults: Findings from the Irish Longitudinal Study on Ageing (TILDA). *Diabetes Research and Clinical Practice.* 2015 Dec;110(3):241–9.
10. Tracey ML, Gilmartin M, O'Neill K, Fitzgerald AP, McHugh SM, Buckley CM, et al. Epidemiology of diabetes and complications among adults in the Republic of Ireland 1998-2015: a systematic review and meta-analysis. *BMC Public Health* [Internet]. 2015 Dec [cited 2016 Nov 27];16(1). Available from:

<http://www.biomedcentral.com/1471-2458/16/132>

11. Biessels GJ, Reijmer YD. Brain Changes Underlying Cognitive Dysfunction in Diabetes: What Can We Learn From MRI? *Diabetes*. 2014 Jul 1;63(7):2244–52.
12. World Alzheimer Report 2018 - The state of the art of dementia research: New frontiers. *NEW FRONTIERS*. :48.
13. Tilvis RS, Kähönen-Väre MH, Jolkkonen J, Valvanne J, Pitkala KH, Strandberg TE. Predictors of cognitive decline and mortality of aged people over a 10-year period. *J Gerontol A Biol Sci Med Sci*. 2004 Mar;59(3):268–74.
14. Cheng G, Huang C, Deng H, Wang H. Diabetes as a risk factor for dementia and mild cognitive impairment: a meta-analysis of longitudinal studies: *Diabetes and cognitive function*. *Internal Medicine Journal*. 2012 May;42(5):484–91.
15. Monette M.C.E., Baird A., Jackson D.L. A Meta-Analysis of Cognitive Functioning in Nondemented Adults with Type 2 Diabetes Mellitus. *Can J Diabetes*. 2014;38(6):401–8.
16. Arvanitakis Z, Wilson RS, Bienias JL, Evans DA, Bennett DA. Diabetes mellitus and risk of Alzheimer disease and decline in cognitive function. *Arch Neurol*. 2004 May;61(5):661–6.
17. Christman AL, Vannorsdall TD, Pearlson GD, Hill-Briggs F, Schretlen DJ. Cranial Volume, Mild Cognitive Deficits, and Functional Limitations Associated with Diabetes in a Community Sample. *Arch Clin Neuropsychol*. 2010 Feb;25(1):49–59.
18. Cosway R, Strachan MWJ, Dougall A, Frier BM, Deary IJ. Cognitive function and information processing in type 2 diabetes. *Diabetic Medicine*. 2001;18(10):803–810.
19. Espeland MA, Miller ME, Goveas JS, Hogan PE, Coker LH, Williamson J, et al. Cognitive Function and Fine Motor Speed in Older Women with Diabetes Mellitus: Results from the Women’s Health Initiative Study of Cognitive Aging. *J Womens Health (Larchmt)*. 2011 Oct;20(10):1435–43.
20. Gallacher JEJ, Pickering J, Elwood PC, Bayer AJ, Yarnell JW, Ben-Shlomo Y. Glucoregulation has greater impact on cognitive performance than macro-vascular disease in men with type 2 diabetes: data from the Caerphilly study. *Eur J Epidemiol*. 2005;20(9):761–8.
21. McFall GP, Geall BP, Fischer AL, Dolcos S, Dixon RA. Testing covariates of Type 2 diabetes-cognition associations in older adults: moderating or mediating effects? *Neuropsychology*. 2010 Sep;24(5):547–62.
22. Mehrabian S, Raycheva M, Gateva A, Todorova G, Angelova P, Traykova M, et al. Cognitive dysfunction profile and arterial stiffness in type 2 diabetes. *J Neurol Sci*.

- 2012 Nov 15;322(1–2):152–6.
23. Nandipati S, Luo X, Schimming C, Grossman HT, Sano M. Cognition in Non-Demented Diabetic Older Adults. *Curr Aging Sci.* 2012 Jul;5(2):131–5.
 24. Toro P, Schönknecht P, Schröder J. Type II Diabetes in Mild Cognitive Impairment and Alzheimer’s Disease: Results from a Prospective Population-Based Study in Germany. *Journal of Alzheimer’s Disease.* 2009 Apr 15;16(4):687–91.
 25. van den Berg E, Reijmer YD, de Bresser J, Kessels RPC, Kappelle LJ, Biessels GJ. A 4 year follow-up study of cognitive functioning in patients with type 2 diabetes mellitus. *Diabetologia.* 2010 Jan;53(1):58–65.
 26. van Elderen SGC, de Roos A, de Craen AJM, Westendorp RGJ, Blauw GJ, Jukema JW, et al. Progression of brain atrophy and cognitive decline in diabetes mellitus: A 3-year follow-up. *Neurology.* 2010 Sep 13;75(11):997–1002.
 27. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The Prevalence of Comorbid Depression in Adults With Diabetes A meta-analysis. *Dia Care.* 2001 Jun 1;24(6):1069–78
 28. Rotella, F., Mannucci, E., 2013. Depression as a risk factor for diabetes: a meta-analysis of longitudinal studies. *J Clin Psychiatry* 74, 31–37.
 29. Ali, S., Stone, M.A., Peters, J.L., Davies, M.J., Khunti, K., 2006. The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. *Diabetic Medicine* 23, 1165–73.
 30. Nolan JJ, O’Halloran D, McKenna TJ, Firth R, Redmond S. The cost of treating type 2 diabetes (CODEIRE). *Ir Med J.* 2006 Dec;99(10):307–10
 31. Pierse T, Shea EO, Carney P. Estimates of the prevalence, incidence and severity of dementia in Ireland. *Irish Journal of Psychological Medicine.* 2018 Jul;1–9.
 32. Heger I, Deckers K, van Boxtel M, de Vugt M, Hajema K, Verhey F, et al. Dementia awareness and risk perception in middle-aged and older individuals: baseline results of the MijBreincoach survey on the association between lifestyle and brain health. *BMC Public Health.* 2019 Jun 3;19(1):678.
 33. Hess GE, Davis WK. The Validation of a Diabetes Patient Knowledge Test. *Diabetes Care.* 1983 Nov 1;6(6):591–6.
 34. Garcia AA, Villagomez ET, Brown SA, Kouzekanani K, Hanis CL. The Starr County Diabetes Education Study: Development of the Spanish-language diabetes knowledge questionnaire. *Diabetes Care.* 2001 Jan 1;24(1):16–21.
 35. Persell SD, Keating NL, Landrum MB, Landon BE, Ayanian JZ, Borbas C, et al. Relationship of diabetes-specific knowledge to self-management activities,

- ambulatory preventive care, and metabolic outcomes. *Prev Med.* 2004 Oct;39(4):746–52.
36. Fitzgerald JT, Funnell MM, Hess GE, Barr PA, Anderson RM, Hiss RG, et al. The Reliability and Validity of a Brief Diabetes Knowledge Test. *Diabetes Care.* 1998 May 1;21(5):706–10.
 37. Fitzgerald JT, Funnell MM, Anderson RM, Nwankwo R, Stansfield RB, Piatt GA. Validation of the Revised Brief Diabetes Knowledge Test (DKT2). *Diabetes Educ.* 2016;42(2):178–87.
 38. Speight J, Bradley C. The ADKnowl: identifying knowledge deficits in diabetes care. *Diabet Med.* 2001 Aug;18(8):626–33.
 39. Audit of Diabetes Knowledge (ADKnowl) | Health Psychology Research [Internet]. [cited 2019 Dec 2]. Available from: <https://www.healthpsychologyresearch.com/find-a-questionnaire/audit-diabetes-knowledge-1>
 40. Eigenmann C, Skinner T, Colagiuri R. Development and validation of a diabetes knowledge questionnaire. *Practical Diabetes International.* 2011;28(4):166–170d.
 41. American Diabetes Association. Standards of medical care in diabetes--2014. *Diabetes Care.* 2014 Jan;37 Suppl 1:S14-80
 42. International Diabetes Federation Guideline Development Group. Global guideline for type 2 diabetes. *Diabetes Res Clin Pract.* 2014 Apr;104(1):1–52.
 43. Turoff M, Linstone HA. The Delphi Method: Techniques and Applications. :618.
 44. Gupta UG, Clarke RE. Theory and applications of the Delphi technique: A bibliography (1975–1994). *Technological Forecasting and Social Change.* 1996 Oct 1;53(2):185–211.
 45. Hsu C-C, Sandford BA. The Delphi Technique: Making Sense Of Consensus. 12(10):8.
 46. McNaboe J, Shally C, Burke N, Wowczko I, Guerin S. A Report by the Skills and Labour Market Research Unit (SLMRU) in SOLAS on behalf of the National Skills Council December 2017. 2017;138.
 47. Level of Education - CSO - Central Statistics Office [Internet]. [cited 2019 Nov 30]. Available from: <https://www.cso.ie/en/releasesandpublications/ep/p-cp10esil/p10esil/le/>
 48. O’Sullivan EP, Bhargava A, O’Callaghan M, Buckley U, De Faoite T, Moynihan K, et al. Awareness of diabetes complications in an Irish population. *Ir J Med Sci.* 2009 Mar 4;178(4):401.
 49. Journal of Diabetes Nursing- Issue: 29-02-2016, Vol 20, No 2 - article: Assessment of diabetes knowledge in trained and untrained ward nurses before and after

- intensive specialist support - DOTN [Internet]. [cited 2019 Dec 1]. Available from: <https://www.diabetesonthenet.com/journals/issue/348/article-details/assessment-of-diabetes-knowledge-in-trained-and-untrained-ward-nurses-before-and-after-intensive-specialist-support>
50. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009 Jul 21;6(7):e1000097.
 51. Higgins JP, Green S. *Cochrane Handbook for Systematic Reviews of Interventions* : Cochrane Book Series. :674.
 52. Gudala K, Bansal D, Schifano F, Bhansali A. Diabetes mellitus and risk of dementia: A meta-analysis of prospective observational studies. *J Diabetes Investig.* 2013 Nov 27;4(6):640–50
 53. Areosa Sastre A, Vernooij RW, González-Colaço Harmand M, Martínez G. Effect of the treatment of Type 2 diabetes mellitus on the development of cognitive impairment and dementia. *Cochrane Database Syst Rev.* 2017 15;6:CD003804.
 54. Moran C, Phan TG, Chen J, Blizzard L, Beare R, Venn A, et al. Brain Atrophy in Type 2 Diabetes Regional distribution and influence on cognition. *Dia Care.* 2013 Dec 1;36(12):4036–42.
 55. McCrimmon RJ, Ryan CM, Frier BM. Diabetes and cognitive dysfunction. *The Lancet.* 2012;379(9833):2291–2299.
 56. Bruce DG, Davis WA, Starkstein SE, Davis TM. Mid-life predictors of cognitive impairment and dementia in type 2 diabetes mellitus: the Fremantle Diabetes Study. *J Alzheimers Dis.* 2014;42 Suppl 3:S63-70.
 57. Bruce DG, Davis WA, Casey GP, Starkstein SE, Clarnette RM, Almeida OP, et al. Predictors of Cognitive Decline in Older Individuals With Diabetes. *Diabetes Care.* 2008 Nov;31(11):2103–7.
 58. Harten B van, Leeuw F-E de, Weinstein HC, Scheltens P, Biessels GJ. Brain Imaging in Patients With Diabetes A systematic review. *Dia Care.* 2006 Nov 1;29(11):2539–48.
 59. Verdelho A, Madureira S, Moleiro C, Ferro JM, Santos CO, Erkinjuntti T, et al. White matter changes and diabetes predict cognitive decline in the elderly: the LADIS study. *Neurology.* 2010 Jul 13;75(2):160–7.
 60. Talbot K, Wang H-Y, Kazi H, Han L-Y, Bakshi KP, Stucky A, et al. Demonstrated brain insulin resistance in Alzheimer’s disease patients is associated with IGF-1 resistance, IRS-1 dysregulation, and cognitive decline. *The Journal of clinical investigation.* 2012;122(4):1316.

61. Thambisetty M, Metter EJ, Yang A, Dolan H, Marano C, Zonderman AB, et al. Glucose Intolerance, Insulin Resistance, and Pathological Features of Alzheimer Disease in the Baltimore Longitudinal Study of Aging. *JAMA Neurology*. 2013 Sep 1;70(9):1167.
62. Zhao W-Q, Townsend M. Insulin resistance and amyloidogenesis as common molecular foundation for type 2 diabetes and Alzheimer's disease. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*. 2009 May;1792(5):482–96.
63. Chiu S-L, Chen C-M, Cline HT. Insulin receptor signaling regulates synapse number, dendritic plasticity, and circuit function in vivo. *Neuron*. 2008 Jun 12;58(5):708–19.
64. Cooper C., Sommerlad A., Lyketsos C.G., Livingston G. Modifiable predictors of dementia in mild cognitive impairment: A systematic review and meta-analysis. *Am J Psychiatry*. 2015;172(4):323–34
65. Verdile G, Fuller SJ, Martins RN. The role of type 2 diabetes in neurodegeneration. *Neurobiology of Disease* [Internet]. [cited 2015 May 12]; Available from: <http://www.sciencedirect.com/science/article/pii/S0969996115001552>
66. Biessels GJ, Deary IJ, Ryan CM. Cognition and diabetes: a lifespan perspective. *The Lancet Neurology*. 2008 Feb;7(2):184–90.
67. Kooistra M, Geerlings MI, Mali WPTM, Vincken KL, van der Graaf Y, Biessels GJ. Diabetes mellitus and progression of vascular brain lesions and brain atrophy in patients with symptomatic atherosclerotic disease. The SMART-MR study. *Journal of the Neurological Sciences*. 2013 Sep 15;332(1–2):69–74.
68. McFall GP, Wiebe SA, Vergote D, Anstey KJ, Dixon RA. Alzheimer's genetic risk intensifies neurocognitive slowing associated with diabetes in non-demented older adults. *Alzheimer's Dement* 2015;1:395–402
69. Bruce DG. Type 2 diabetes and cognitive function: many questions, few answers. *The Lancet Neurology*. 2015 Mar;14(3):241–2.
70. Luchsinger JA. Type 2 diabetes and cognitive impairment: linking mechanisms. *J Alzheimers Dis*. 2012 Jan 1;30(0):S185–98.
71. Harris MD. Psychosocial aspects of diabetes with an emphasis on depression. *Curr Diab Rep*. 2003 Feb;3(1):49–55.
72. Holt P. Blood glucose monitoring in diabetes. *Nurs Stand*. 2014 Mar 5;28(27):52–8.
73. Holt RIG, de Groot M, Golden SH. Diabetes and Depression. *Curr Diab Rep*. 2014 Jun;14(6):491
74. Champaneri S, Wand GS, Malhotra SS, Casagrande SS, Golden SH. Biological basis

- of depression in adults with diabetes. *Curr Diab Rep*. 2010 Dec;10(6):396–405.
75. Dantzer R, O'Connor JC, Freund GG, Johnson RW, Kelley KW. From inflammation to sickness and depression: when the immune system subjugates the brain. *Nat Rev Neurosci*. 2008 Jan;9(1):46–56.
 76. Shoelson SE, Lee J, Goldfine AB. Inflammation and insulin resistance. *J Clin Invest*. 2006 Jul;116(7):1793–801.
 77. Elcombe EL, Lagopoulos J, Duffy SL, Lewis SJG, Norrie L, Hickie IB, et al. Hippocampal volume in older adults at risk of cognitive decline: the role of sleep, vascular risk, and depression. *J Alzheimers Dis*. 2015;44(4):1279–90
 78. Kumar A, Gupta R, Thomas A, Ajilore O, Hellemann G. Focal subcortical biophysical abnormalities in patients diagnosed with type 2 diabetes and depression. *Arch Gen Psychiatry*. 2009 Mar;66(3):324–30.
 79. Musselman DL, Betan E, Larsen H, Phillips LS. Relationship of depression to diabetes types 1 and 2: epidemiology, biology, and treatment. *Biological Psychiatry*. 2003 Aug 1;54(3):317–29.
 80. Nouwen A, Nefs G, Caramlau I, Connock M, Winkley K, Lloyd CE, et al. Prevalence of Depression in Individuals With Impaired Glucose Metabolism or Undiagnosed Diabetes A systematic review and meta-analysis of the European Depression in Diabetes (EDID) Research Consortium. *Dia Care*. 2011 Mar 1;34(3):752–62.
 81. Walker RJ, Smalls BL, Hernandez-Tejada MA, Campbell JA, Davis KS, Egede LE. Effect of diabetes fatalism on medication adherence and self-care behaviors in adults with diabetes. *Gen Hosp Psychiatry*. 2012 Dec;34(6):598–603.
 82. Hermanns, N., Kulzer, B., Krichbaum, M., Kubiak, T., Haak, T., 2005. Affective and anxiety disorders in a German sample of diabetic patients: prevalence, comorbidity and risk factors. *Diabetic Medicine* 22, 293–300.
 83. Li C, Ford ES, Strine TW, Mokdad AH. Prevalence of depression among U.S. adults with diabetes: findings from the 2006 behavioral risk factor surveillance system. *Diabetes Care*. 2008 Jan;31(1):105–7.
 84. van Steenbergen-Weijenburg KM, van Puffelen AL, Horn EK, Nuyen J, van Dam PS, van Benthem TB, et al. More co-morbid depression in patients with Type 2 diabetes with multiple complications. An observational study at a specialized outpatient clinic. *Diabet Med*. 2011 Jan;28(1):86–9.
 85. de Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ. Association of depression and diabetes complications: a meta-analysis. *Psychosom Med*. 2001

- Aug;63(4):619–30.
86. Chen C, Wang Y, Zhang J, Ma L, Gu J, Ho G. Contribution of neural cell death to depressive phenotypes of streptozotocin-induced diabetic mice. *Dis Model Mech*. 2014 Jun;7(6):723–30
 87. Novak V, Zhao P, Manor B, Sejdić E, Alsop D, Abduljalil A, et al. Adhesion Molecules, Altered Vasoreactivity, and Brain Atrophy in Type 2 Diabetes. *Diabetes Care*. 2011 Nov;34(11):2438–41.
 88. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med*. 2000 Jul 24;160(14):2101–7.
 89. Bonnet F, Irving K, Terra J-L, Nony P, Berthezène F, Moulin P. Anxiety and depression are associated with unhealthy lifestyle in patients at risk of cardiovascular disease. *Atherosclerosis*. 2005 Feb;178(2):339–44.
 90. Luppino FS, de Wit LM, Bouvy PF, et al. Overweight, obesity, and depression: A systematic review and meta-analysis of longitudinal studies. *Arch Gen Psychiatry*. 2010 Mar 1;67(3):220–9.
 91. Kan C, Silva N, Golden SH, Rajala U, Timonen M, Stahl D, et al. A Systematic Review and Meta-analysis of the Association Between Depression and Insulin Resistance. *Diabetes Care*. 2013 Feb;36(2):480–9.
 92. Brown ES, Varghese FP, McEwen BS. Association of depression with medical illness: does cortisol play a role? *Biol Psychiatry*. 2004 Jan 1;55(1):1–9.
 93. Howren MB, Lamkin DM, Suls J. Associations of depression with C-reactive protein, IL-1, and IL-6: a meta-analysis. *Psychosom Med*. 2009 Feb;71(2):171–86.
 94. Abitbol R, Rej S, Segal M, Looper KJ. Diabetes mellitus onset in geriatric patients: does long-term atypical antipsychotic exposure increase risk? *Psychogeriatrics*. 2015 Mar;15(1):43–50.
 95. Azevedo Da Silva M, Dugravot A, Balkau B, Roussel R, Fumeron F, Elbaz A, et al. Antidepressant medication use and trajectories of fasting plasma glucose, glycated haemoglobin, β -cell function and insulin sensitivity: a 9-year longitudinal study of the D.E.S.I.R. cohort. *Int J Epidemiol*. 2015 Aug 4;
 96. Punthakee Z, Miller ME, Launer LJ, Williamson JD, Lazar RM, Cukierman-Yaffee T, et al. Poor cognitive function and risk of severe hypoglycemia in type 2 diabetes: post hoc epidemiologic analysis of the ACCORD trial. *Diabetes Care*. 2012 Apr;35(4):787–93.
 97. Munshi M, Capelson R, Grande L, Lin S, Hayes M, Milberg W, et al. Cognitive

- Dysfunction Is Associated With Poor Diabetes Control in Older Adults. *Diabetes Care*. 2006 Aug;29(8):1794–9.
98. Okura T, Heisler M, Langa KM. The Association of Cognitive Function and Social Support with Glycemic Control in Adults with Diabetes. *J Am Geriatr Soc*. 2009 Oct;57(10):1816–24.
 99. Feil DG, Zhu CW, Sultzer DL. The relationship between cognitive impairment and diabetes self-management in a population-based community sample of older adults with Type 2 diabetes. *J Behav Med*. 2012 Apr;35(2):190–9.
 100. Smith MA, Else JE, Paul L, Foster JK, Walker M, Wesnes KA, et al. Functional Living in Older Adults With Type 2 Diabetes: Executive Functioning, Dual Task Performance, and the Impact on Postural Stability and Motor Control. *J Aging Health*. 2014 Aug;26(5):841–59.
 101. Peyrot M, Rubin RR. Persistence of depressive symptoms in diabetic adults. *Diabetes Care*. 1999 Mar;22(3):448–52.
 102. Lustman PJ, Griffith LS, Clouse RE. Depression in Adults With Diabetes: Results of 5-yr Follow-Up Study. *Dia Care*. 1988 Sep 1;11(8):605–12.
 103. Lustman PJ, Clouse RE. Depression in diabetic patients: the relationship between mood and glycemic control. *J Diabetes Complicat*. 2005 Apr;19(2):113–22.
 104. Gonzalez JS, Peyrot M, McCarl LA, Collins EM, Serpa L, Mimiaga MJ, et al. Depression and Diabetes Treatment Nonadherence: A Meta-Analysis. *Diabetes Care*. 2008 Dec;31(12):2398–403.
 105. Chew B-H, Vos R, Mohd-Sidik S, Rutten GEHM. Diabetes-Related Distress, Depression and Distress-Depression among Adults with Type 2 Diabetes Mellitus in Malaysia. *PLOS ONE*. 2016 Mar 22;11(3):e0152095.
 106. Peyrot, M., Rubin, R.R., Lauritzen, T., Snoek, F.J., Matthews, D.R., Skovlund, S.E., 2005. Psychosocial problems and barriers to improved diabetes management: results of the Cross-National Diabetes Attitudes, Wishes and Needs (DAWN) Study. *Diabet. Med*. 22, 1379–1385
 107. Hutter N, Schnurr A, Baumeister H. Healthcare costs in patients with diabetes mellitus and comorbid mental disorders—a systematic review. *Diabetologia*. 2010 Aug 11;53(12):2470–9.
 108. Egede LE, Nietert PJ, Zheng D. Depression and All-Cause and Coronary Heart Disease Mortality Among Adults With and Without Diabetes. *Dia Care*. 2005 Jun 1;28(6):1339–45.
 109. Egede LE, Ellis C. Diabetes and depression: global perspectives. *Diabetes Res Clin*

- Pract. 2010 Mar;87(3):302–12.
110. de Groot M, Doyle T, Kushnick M, Shubrook J, Merrill J, Rabideau E, et al. Can Lifestyle Interventions Do More than Reduce Diabetes Risk? Treating Depression in Adults with Type 2 Diabetes with Exercise and Cognitive Behavioral Therapy. *Curr Diab Rep.* 2012 Apr;12(2):157–66.
 111. Williams LH, Rutter CM, Katon WJ, Reiber GE, Ciechanowski P, Heckbert SR, et al. Depression and incident diabetic foot ulcers: a prospective cohort study. *Am J Med.* 2010 Aug;123(8):748-754.e3.
 112. de Jonge P, Alonso J, Stein DJ, Kiejna A, Aguilar-Gaxiola S, Viana MC, et al. Associations between DSM-IV mental disorders and diabetes mellitus: a role for impulse control disorders and depression. *Diabetologia.* 2014 Apr;57(4):699–709.
 113. Raevuori A, Suokas J, Haukka J, Gissler M, Linna M, Grainger M, et al. Highly increased risk of type 2 diabetes in patients with binge eating disorder and bulimia nervosa. *Int J Eat Disord.* 2015 Sep;48(6):555–62.
 114. Buydens-Branchey L, Branchey M, Hudson J, Fergusson P. Low HDL cholesterol, aggression and altered central serotonergic activity. *Psychiatry Res.* 2000 Mar 6;93(2):93–102.
 115. Banerjee C, Moon YP, Paik MC, Rundek T, Mora-McLaughlin C, Vieira JR, et al. Duration of Diabetes and Risk of Ischemic Stroke: The Northern Manhattan Study. *Stroke.* 2012 May;43(5):1212–7.
 116. Kothari V, Stevens RJ, Adler AI, Stratton IM, Manley SE, Neil HA, et al. UKPDS 60: risk of stroke in type 2 diabetes estimated by the UK Prospective Diabetes Study risk engine. *Stroke.* 2002 Jul;33(7):1776–81.
 117. Barnes DE, Yaffe K. The Projected Impact of Risk Factor Reduction on Alzheimer's Disease Prevalence. *Lancet Neurol.* 2011 Sep;10(9):819–28.
 118. Solomon A, Kivipelto M, Wolozin B, Zhou J, Whitmer RA. Midlife serum cholesterol and increased risk of Alzheimer's and vascular dementia three decades later. *Dement Geriatr Cogn Disord.* 2009;28(1):75–80
 119. Ruitenberg A, van Swieten JC, Witteman JC, Mehta KM, van Duijn CM, Hofman A, et al. Alcohol consumption and risk of dementia: the Rotterdam Study. *The Lancet.* 2002 Jan 26;359(9303):281–6.
 120. Langballe EM, Ask H, Holmen J, Stordal E, Saltvedt I, Selbæk G, et al. Alcohol consumption and risk of dementia up to 27 years later in a large, population-based sample: the HUNT study, Norway. *Eur J Epidemiol.* 2015 Sep;30(9):1049–56
 121. Emdin CA, Anderson SG, Woodward M, Rahimi K. Usual Blood Pressure and Risk

- of New-Onset Diabetes: Evidence From 4.1 Million Adults and a Meta-Analysis of Prospective Studies. *Journal Of The American College Of Cardiology*. 2015 Oct 6;66(14):1552–62.
122. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of Type 2 Diabetes – a meta-analysis of 9 prospective cohort studies. *International Journal of Behavioral Nutrition and Physical Activity*. 2015 Dec 1;12:147.
 123. Norris SL, Zhang X, Avenell A, Gregg E, Schmid CH, Lau J. Long-term non-pharmacological weight loss interventions for adults with prediabetes. In: *Cochrane Database of Systematic Reviews* [Internet]. John Wiley & Sons, Ltd; 2005 [cited 2017 Oct 4]. Available from:
<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005270/abstract>
 124. Hasan SS, Clavarino AM, Mamun AA, Kairuz T. Incidence and risk of diabetes mellitus associated with depressive symptoms in adults: Evidence from longitudinal studies. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. 2014 Apr;8(2):82–7.
 125. Smith AD, Crippa A, Woodcock J, Brage S. Physical activity and incident T2DM mellitus: a systematic review and dose–response meta-analysis of prospective cohort studies. *Diabetologia*. 2016 Dec 1;59(12):2527–45
 126. Orozco LJ, Buchleitner AM, Gimenez-Perez G, Roqué I Figuls M, Richter B, Mauricio D. Exercise or exercise and diet for preventing T2DM mellitus. *Cochrane Database Syst Rev*. 2008 Jul 16;(3):CD003054.
 127. Agardh E, Allebeck P, Hallqvist J, Moradi T, Sidorchuk A. T2DM incidence and socio-economic position: a systematic review and meta-analysis. *Int J Epidemiol*. 2011 Jun;40(3):804–18.
 128. Pan A, Wang Y, Talaei M, Hu FB, Wu T. Relation of active, passive, and quitting smoking with incident type 2 diabetes: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol*. 2015 Dec;3(12):958–67.
 129. Tajima R, Kodama S, Hirata M, Horikawa C, Fujihara K, Yachi Y, et al. High cholesterol intake is associated with elevated risk of T2DM mellitus - a meta-analysis. *Clinical Nutrition (Edinburgh, Scotland)*. 2014 Dec;33(6):946–50.
 130. Knott C, Bell S, Britton A. Alcohol Consumption and the Risk of Type 2 Diabetes: A Systematic Review and Dose-Response Meta-analysis of More Than 1.9 Million Individuals From 38 Observational Studies. *Diabetes Care*. 2015 Sep 1;38(9):1804–

- 12.
131. Fratiglioni L, Wang H-X. Brain reserve hypothesis in dementia. *J Alzheimers Dis*. 2007 Aug;12(1):11–22.
132. International Diabetes Federation, Sinclair A, Dunning T, Colagiuri S. Managing older people with type 2 diabetes: global guideline. 2013.
133. Association AD. 12. Older Adults: Standards of Medical Care in Diabetes—2019. *Diabetes Care*. 2019 Jan 1;42(Supplement 1):S139–47.
134. Hinz A, Michalski D, Schwarz R, Herzberg PY. The acquiescence effect in responding to a questionnaire. *Psychosoc Med [Internet]*. 2007 Jun 20 [cited 2018 Jun 12];4. Available from:
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2736523/>
135. Sandelowski M. The problem of rigor in qualitative research. *ANS Adv Nurs Sci*. 1986 Apr;8(3):27–37.
136. Powell C. The Delphi technique: myths and realities. *J Adv Nurs*. 2003 Feb;41(4):376–82.
137. Yousuf MI. Using Experts’ Opinions Through Delphi Technique. 12(4):8.
138. Whelan BJ, Savva GM. Design and Methodology of The Irish Longitudinal Study on Ageing. *J Am Geriatr Soc*. 2013 May 1;61:S265–8
139. Health ID of. Healthy Ireland - a framework for improved health and wellbeing 2013 - 2025. [Internet]. 2013 [cited 2019 Dec 2]. Available from:
http://www.thehealthwell.info/node/463174?&content=resource&member=6841&catalogue=none&collection=none&tokens_complete=true
140. American Society on Ageing and MetLife Foundation. Attitudes and Awareness of Brain Health Poll. [Internet].2006 [cited 2019 Dec 2]. Available from:
<http://www.paulnussbaum.com/metlifedoc.pdf>.
141. Irish Health Survey - CSO - Central Statistics Office [Internet]. [cited 2019 Dec 1]. Available from: <https://www.cso.ie/en/statistics/health/irishhealthsurvey/>
142. Glynn RW, Shelley E, Lawlor BA. Public knowledge and understanding of dementia—evidence from a national survey in Ireland. *Age Ageing*. 2017 Sep 1;46(5):865–9.
143. Morgan K, McGee H, Watson D, Perry I, Barry M. SLAN 2007: Survey of Lifestyle, Attitudes & Nutrition in Ireland: Main Report. :159.
144. Craig C, Marshall A, Sjöström M, Bauman A, Booth M, Ainsworth B, et al. International Physical Activity Questionnaire: 12-Country Reliability and Validity. *Medicine & Science in Sports & Exercise*. 2003 Aug 1;35(8):1381–95.

145. Kearney PM, Harrington JM, Mc Carthy VJ, Fitzgerald AP, Perry IJ. Cohort Profile: The Cork and Kerry Diabetes and Heart Disease Study. *International Journal of Epidemiology*. 2013 Oct 1;42(5):1253–62.
146. Cournane S, Dalton A, Byrne D, Conway R, O’Riordan D, Coveney S, et al. Social deprivation, population dependency ratio and an extended hospital episode — Insights from acute medicine. *European Journal of Internal Medicine*. 2015 Nov;26(9):714–9.
147. Walsh JB, Coakley D, Murphy C, Coakley JD, Boyle E, Johnson H. Demographic profile of the elderly population in Dublin accident and emergency hospital catchment areas. *Irish Medical Journal*. 2004 Mar;97(3):84–6.
148. Deprivation Indices [Internet]. [cited 2019 Dec 1]. Available from: <https://maps.pobal.ie/WebApps/DeprivationIndices/index.html>
149. Data Protection (Amendment) Act 2003, Ireland [Internet].c2003. [Cited 2019 Dec 1]. Available from <http://www.irishstatutebook.ie/eli/2003/act/6/enacted/en/html>.
150. van der Heide I, Wang J, Droomers M, Spreeuwenberg P, Rademakers J, Uiters E. The relationship between health, education, and health literacy: results from the Dutch Adult Literacy and Life Skills Survey. *J Health Commun*. 2013;18 Suppl 1:172–84.
151. The Irish National Dementia Strategy. [Internet]. Ireland: Department of Health; 2014. [cited 2019 Dec 2] Available at: <http://health.gov.ie/wp-content/uploads/2014/12/30115-National-Dementia-Strategy-Eng.pdf>.
152. Smith BJ, Ali S, Quach H. Public knowledge and beliefs about dementia risk reduction: a national survey of Australians. *BMC Public Health* 2014;Jun 28;14:661.
153. McMurray SD, Johnson G, Davis S, McDougall K. Diabetes education and care management significantly improve patient outcomes in the dialysis unit. *Am J Kidney Dis*. 2002 Sep;40(3):566–75.
154. Understand Together Campaign [Internet]. Dementia. 2019. [cited 2019 Dec 2] Available at: <http://www.understandtogether.ie/understand-together-campaign/>.
155. Travers C, Lie D, Martin-Khan M. Dementia and the population health approach: promise, pitfalls and progress. An Australian perspective. *Reviews in Clinical Gerontology*. 2015 Feb;25(1):60–71.
156. Ireland. Health Services Executive. Clinical Strategy and Programmes Division. [Internet]. [cited 2019 Dec 2] Available at: <https://www.hse.ie/eng/about/who/cspd/icp/chronic-disease/>.
157. Schmitz N, Deschênes SS, Burns RJ, Danna SM, Franco OH, Ikram MA, et al.

- Cardiometabolic dysregulation and cognitive decline: potential role of depressive symptoms. *Br J Psychiatry*. 2018 Feb;212(2):96–102.
158. Overview | Type 2 diabetes in adults: management | Guidance | NICE [Internet]. [cited 2019 Dec 2]. Available from: <https://www.nice.org.uk/guidance/ng2>
159. Harkins DV. A Practical Guide to Integrated Type 2 Diabetes Care. *Diabetes Care*. 2016;77.
160. Ngandu T, Lehtisalo J, Solomon A, Levälahti E, Ahtiluoto S, Antikainen R, et al. A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. *The Lancet*. 2015 Jun 6;385(9984):2255–63.

Appendices

Appendix 1: Older Adult General Health Questionnaire: Medicine for the Elderly Nursing Staff

onnaire: Medicine for the Elderly Nursing Staff

Older Adult General Health Questionnaire: Medicine for the Elderly Nursing Staff

This questionnaire is designed to assess your general knowledge about complications of conditions which are common in older adults.

The questionnaire should take no longer than 2 minutes to complete. Your responses to this questionnaire are anonymous, and all data will be treated in the strictest confidence.

Responses to this questionnaire will be analysed in order to inform us on the current knowledge level of healthcare professionals on medical conditions common among older adults and their complications.

We hope the results of this survey will guide us in developing appropriate educational material to address any knowledge gaps we discover in the course of this research project.

Please return your completed survey to box marked "General Health Survey Return Box" situated in the ward nursing office.

Thank you for taking part in this survey.

Older Adult General Health Questionnaire: Medicine for the Elderly Nursing Staff

1. Below are a list of diseases that are more common in older people.

For each disease please tick the box under the complication that you think is associated with the disease. If you think that a particular disease can have more than one complication then please tick every complication that applies for that disease.

If you think that none of the complications apply for the disease then leave all of the boxes blank for that disease.

	Memory problems	Foot ulcers and amputations	Kidney disease	Stroke
Arthritis (osteoarthritis)	☐	☐	☐	☐
Diabetes	☐	☐	☐	☐
Osteoporosis	☐	☐	☐	☐
Parkinson's disease	☐	☐	☐	☐
Respiratory (airways) disease	☐	☐	☐	☐
Thyroid disease	☐	☐	☐	☐
Kidney & bladder infections	☐	☐	☐	☐

2. Below are a list of diseases that are more common in older people.

For each disease please tick the box under the complication that you think is associated with the disease. If you think that a particular disease can have more than one complication then please tick every complication that applies for that disease.

If you think that none of the complications apply for the disease then leave all of the boxes blank for that disease.

	Depression	Vision problems	Memory loss	Nerve damage in hands and feet
Arthritis (osteoarthritis)	☐	☐	☐	☐
Diabetes	☐	☐	☐	☐
Osteoporosis	☐	☐	☐	☐
Parkinson's disease	☐	☐	☐	☐
Respiratory (airways) disease	☐	☐	☐	☐
Thyroid disease	☐	☐	☐	☐
Kidney & bladder infections	☐	☐	☐	☐
Stroke	☐	☐	☐	☐

3. Below are a list of diseases that are more common in older people.

For each disease please tick the box under the complication that you think is associated with the disease. If you think that a particular disease can have more than one complication then please tick every complication that applies for that disease.

If you think that none of the complications apply for the disease then leave all of the boxes blank for that disease.

	Vision problems		Dementia	Heart disease	TIA or "mini-stroke"
Depression	☐	☐	☐	☐	☐
Diabetes	☐	☐	☐	☐	☐
Parkinson's disease	☐	☐	☐	☐	☐
Osteoporosis	☐	☐	☐	☐	☐
Pneumonia	☐	☐	☐	☐	☐
Thyroid disease	☐	☐	☐	☐	☐
Kidney and bladder infections	☐	☐	☐	☐	☐

4. What is your occupation

- ☐ Nursing Student
- ☐ Registered Staff Nurse
- ☐ Senior Staff Nurse
- ☐ Clinical Nurse Specialist
- ☐ Clinical Nurse Manager

Other (please specify)

5. For roughly how many years have you been practising as a nurse?

6. Are you male or female?

- ☐ Male
- ☐ Female

7. Do you have diabetes?

☐ Yes

☐ No

8. Do you have a partner or family member with diabetes?

☐ Yes

☐ No

9. Do you have any of the other medical illness (other than diabetes) mentioned in the above questions? If the answer is yes please specify which medical conditions in the box below.

10. Do you have a partner or family member with any of the medical illness (other than diabetes) mentioned below? If the answer is yes please specify which medical conditions in the box below.

Appendix 2: Older Adult General Health Questionnaire: Diabetes Day Centre

Older Adult General Health Questionnaire: Diabetes Day Centre

Older Adult General Health Questionnaire: Diabetes Day Care Centre

This questionnaire is designed to assess the knowledge of diabetic patients about complications of medical conditions which are common in older adults.

The questionnaire should take no longer than 2 minutes to complete. Your responses to this questionnaire are anonymous, and all data will be treated in the strictest confidence. Responses to this questionnaire will be reviewed in order to inform us on the current knowledge level of patients attending the Diabetes Day Centre on medical conditions common among older adults and their complications.

We hope the results of this survey will guide us in developing appropriate educational strategies to address any knowledge gaps we discover in the course of this research project.

Thank you for taking part in this survey.

1. Below are a list of potential complications of diabetes and of Parkinson's disease.

For each disease please tick the box under the complication that you think is associated with the disease. If you think that a particular disease can have more than one complication please tick every complication that applies for that disease.

If you think that none of the complications apply for the disease then leave all of the boxes blank for that disease.

	Memory problems	Foot ulcers and amputations	Kidney disease	Stroke
Diabetes	☐	☐	☐	☐
Parkinson's disease	☐	☐	☐	☐

2. Below are a list of potential complications of diabetes and of Parkinson's disease.

For each disease please tick the box under the complication that you think is associated with the disease. If you think that a particular disease can have more than one complication please tick every complication that applies for that disease.

If you think that none of the complications apply for the disease then leave all of the boxes blank for that disease.

	Depression	Vision problems	Memory loss	Nerve damage in hands and feet
Diabetes	☐	☐	☐	☐
Parkinson's disease	☐	☐	☐	☐

3. Below are a list of potential complications of diabetes and of Parkinson's disease.

For each disease please tick the box under the complication that you think is associated with the disease. If you think that a particular disease can have more than one complication please tick every complication that applies for that disease.

If you think that none of the complications apply for the disease then leave all of the boxes blank for that disease.

	Vision problems	Dementia	Heart disease	TIA or "mini-stroke"
Diabetes	☐	☐	☐	☐
Parkinson's disease	☐	☐	☐	☐

4. What type of diabetes do you have?

- ☐ Type 1 diabetes
- ☐ Type 2 diabetes
- ☐ I do not have diabetes
- ☐ Don't know

Other (please specify)

5. How far did you go in school?

- ☐ Some primary (not complete)
- ☐ Primary or equivalent
- ☐ Some secondary (not complete)
- ☐ Secondary or equivalent
- ☐ Diploma/certificate
- ☐ Primary Degree
- ☐ Postgraduate/higher degree
- ☐ None

6. What treatment do you receive for diabetes?

- ☐ Lifestyle (diet, exercise, weight control)
- ☐ Tablets to reduce blood sugar
- ☐ Insulin injections
- ☐ Injections to reduce blood sugar other than insulin e.g. Victoza, Byetta
- ☐ Insulin pump

Other (please specify)

7. What are the names of tablets, insulin or other injections you are taking to treat your diabetes?

8. Have you had formal diabetes education sessions with trained diabetes staff e.g. nursing staff or diabetes educator?

☐

Yes

☐

No

Appendix 3: Health Questionnaire: General Population

Health Questionnaire - take the test!

Health Questionnaire- take the test!

This questionnaire is designed to assess the general public's knowledge about complications of medical conditions which are common in older adults.
The questionnaire should take no longer than 5 minutes to complete.
Your responses to this questionnaire are anonymous, and all data will be treated in the strictest confidence.
The data from this questionnaire will only be used by Neuro-Enhancement for Independent Lives (NEIL) researchers to inform the development of educational materials and interventions. Responses to this questionnaire will be analysed in order to inform us on the general public's current level of knowledge about medical conditions common among older adults and their complications. We hope the results of this survey will guide us in developing appropriate educational material to address any knowledge gaps we discover in the course of this research project.

In order to progress through the survey, please use the following navigation links:

Click the 'next button' to continue to the next page
Click the 'previous' button to return to the previous page
Click 'exit the survey early' button if you need to exit the survey
Click the 'submit' button to submit your survey

***1. Before completing this questionnaire, please tick the box below to indicate that you have read and understand the information above, and consent for the information you provide to be used to inform development of educational materials and interventions.**

☐ Before completing this questionnaire, please tick the box below to indicate that you have read and understand the information above, and consent for the information you provide to be used by Neuro-Enhancement for Independent Lives (NEIL) researchers for development of educational materials and interventions. I consent to the information I provide in this questionnaire being used to inform the development of materials related to the NEIL project.

Health Questionnaire- take the test!

2. Below are a list of diseases that are more common in older people.

For each disease please tick the box under the complication that you think is associated with the disease.

If you think that a particular disease can have more than one complication then please tick every complication that applies for that disease.

If you think that none of the complications apply for the disease then leave all of the boxes blank for that disease.

	Memory Problems	Foot Ulcers and Amputations	Kidney Disease	Stroke
Arthritis (Osteoarthritis)	☐	☐	☐	☐
Diabetes	☐	☐	☐	☐
Osteoporosis	☐	☐	☐	☐
Parkinson's Disease	☐	☐	☐	☐
Respiratory Disease	☐	☐	☐	☐
Thyroid Disease	☐	☐	☐	☐
Kidney and Bladder Infections	☐	☐	☐	☐

Health Questionnaire - take the test!

3. Below are a list of diseases that are more common in older people.

For each disease please tick the box under the complication that you think is associated with the disease.

If you think that a particular disease can have more than one complication then please tick every complication that applies for that disease.

If you think that none of the complications apply for the disease then leave all of the boxes blank for that disease.

	Depression	Vision Problems	Memory Loss	Nerve Damage In Hands and Feet
Diabetes	☐	☐	☐	☐
Cardiovascular Problems (Blood Pressure and Heart Disease)	☐	☐	☐	☐
Osteoporosis	☐	☐	☐	☐
Parkinson's Disease	☐	☐	☐	☐
Hearing Loss	☐	☐	☐	☐
Stroke	☐	☐	☐	☐
Thyroid Disease	☐	☐	☐	☐

4. Below are a list of diseases that are more common in older people.

For each disease please tick the box under the complication that you think is associated with the disease.

If you think that a particular disease can have more than one complication then please tick every complication that applies for that disease.

If you think that none of the complications apply for the disease then leave all of the boxes blank for that disease.

	Eye Disease	Dementia	Heart Disease	Transient Ischaemic Attack (TIA) or "Mini-stroke"
Osteoporosis	☐	☐	☐	☐
Pneumonia	☐	☐	☐	☐
Thyroid Disease	☐	☐	☐	☐
Diabetes	☐	☐	☐	☐
Parkinson's Disease	☐	☐	☐	☐
Kidney and Bladder Infections	☐	☐	☐	☐
Depression	☐	☐	☐	☐

Some background information

Health Questionnaire - take the test!

5. Please indicate if you, your partner or a family member have been diagnosed with any of the following conditions

	I have the condition	My child, partner, parent or sibling has this condition
Arthritis (Osteoarthritis)	☐	☐
Cardiovascular Problems (Blood Pressure and Heart Disease)	☐	☐
Depression	☐	☐
Hearing Loss	☐	☐
History of Stroke	☐	☐
Kidney and Bladder Infections	☐	☐
Osteoporosis	☐	☐
Parkinson's Disease	☐	☐
Pneumonia	☐	☐
Respiratory Disease	☐	☐
Thyroid Disease	☐	☐
Type 2 Diabetes	☐	☐
Type 1 Diabetes	☐	☐

6. What is the highest level of education you have completed?

- ☐ Some primary (not complete)
- ☐ Primary or equivalent
- ☐ Some secondary (not complete)
- ☐ Secondary or equivalent
- ☐ Diploma/certificate
- ☐ Primary degree
- ☐ Postgraduate/higher degree
- ☐ None

7. Are you male or female?

- ☐ Male
- ☐ Female

8. What age are you currently?

Health Questionnaire - take the test!

9. If you are a health professional or work in an associated field or are involved in health research then please tick yes below

☐ Yes

☐ No

Appendix 4: Study protocol with search strategy: incident dementia and depression in adults with established diabetes

Aim

Examine evidence among the general population for:

- I. Incident depression and dementia in adults with established diabetes.

A. Rationale for the study

The strength of the association between established diabetes and incident depression and dementia, respectively, remains unclear.

B. Objective

The objective of this study is to assess the effect of a primary diagnosis of diabetes on incident depression and dementia among adults, through review of evidence from systematic reviews and meta-analyses of observational and interventional studies.

C. Primary research questions

- I. Does evidence exist in the literature for a higher incidence of depression and dementia, respectively, in adults with established diabetes?

D. Criteria for considering studies for this review

Inclusion criteria:

Articles will be considered for inclusion in systematic review if:

- I. The authors reported risk estimates; RR or HR with 95% CI from a meta-analysis or systematic review of incident depression and dementia, respectively, in individuals with established diabetes from (i) prospective cohort and/or case-cohort studies among non-specialised populations without diabetes at baseline or (ii) studies with RCT, controlled clinical trial, controlled before and after trial.
 - II. Studies were published in English between 2011- 2016
1. Participants:
 - I. Persons ≥ 18 years
 - II. General population sample
 2. Exposure/intervention:
 - I. Studies exploring complications of diabetes must include incidence of depression and dementia, respectively in adults with established diabetes
 - II. For intervention studies, one of the stated goals of the intervention is incidence of depression or dementia in adults with established diabetes
 3. Outcomes:

- I. T2DM incidence
- II. Incidence of depression or dementia in adults with established diabetes

Exclusion criteria:

- I. Specialised study populations e.g. pregnant women, children
- II. Letters, abstracts, conference proceedings, dissertations.
- III. Studies not conducted in humans

E. Search strategies for identification of studies

The systematic review will be performed in accordance with the PRISMA guidelines [2].

1. Databases:

The following electronic databases will be searched:

- Cochrane Library
- MEDLINE
- EMBASE

The titles and abstracts obtained from searches of electronic databases will be examined, and potentially relevant full-text articles will be requested. One researcher will screen the Medline, EMBASE and Cochrane review titles and abstracts. There will be English language restrictions on our searches and a time frame 2011- 2016 for MEDLINE and EMBASE searches. Conference proceedings and abstracts will not be included because there is insufficient detail available in these to evaluate the intervention and the quality of the study. Dissertations will be excluded, as these are difficult to locate in full text, and will likely yield few additional reports. If meta-analysis of prospective cohort studies and/or case-cohort studies are not available meta-analysis of case-control and/or cross-sectional studies will be examined.

2. Electronic search strategies

Example 1 (Publications in MEDLINE in English):

- I. Searches were performed separately for incident depression or dementia among individuals with established diabetes
- II. For diabetes as a risk factor for depression and dementia; where possible, searches identified publications with titles or abstracts containing terms related to each specific complication e.g. dementia related term plus a diabetes-related term plus a term indicative of systematic review or meta-analysis.
- III. Limit of English language and limits of 2011 – 2016 were placed on date of publication, in MEDLINE and EMBASE (not in Cochrane Library search).
- IV. In Cochrane Library search all randomised controlled trials examining the impact of established diabetes on incident depression and dementia, were included with no limits.

F. Methods of the review

1. Trials selection

Reviewer CD will identify potentially relevant studies by reviewing titles and abstracts retrieved from electronic searches. For studies identified as potentially relevant, the full text article will be retrieved. Reviewer CD will review potential studies to see if they fulfil inclusion criteria. There will be no blinding of the reviewer to study author and affiliation. If there is ambiguity, the reviewer

will discuss study with the wider research group to achieve consensus. Studies excluded at this point or thereafter will be recorded in the bibliographic database, noting the reason for exclusion.

Other search strategies

The reference lists of all relevant review studies included in the review will be searched. Additional key words of relevance may be identified during any of the electronic or other searches. If this is the case, electronic search strategies will be modified to incorporate these terms.

2. Quality assessment

For randomised controlled trials, the component assessment method of Cochrane will be used, and quality scoring will not be performed. During Cochrane review, internal validity of included studies is examined for potential selection, attrition, and detection bias. If studies are found to be of poor quality a sensitivity analysis is undertaken to compare results between studies with potential bias and those without [1].

For systematic reviews and meta-analyses sourced in MEDLINE and EMBASE, PRISMA [2] checklist will be used for critical appraisal.

The applicability of each study will be noted with respect to population, exposure, outcome and setting.

3. Data abstraction process

For studies that fulfill inclusion criteria, one reviewer will abstract the relevant data. Reviewer will attempt to contact the authors for missing data if clarification of the data presented is required.

Data to be extracted

- a. Population characteristics
 - number
 - age
 - sex
- b. For RCT intervention
 - country
 - type of health care setting
 - community-based
 - in-patient, out-patient
 - mode of delivery of the intervention
- c. Study design characteristics
 - study design: systematic review, meta-analysis, RCT, non-randomised trial, observational study with concurrent comparison group, pre vs post
 - sample size
 - follow-up interval
 - date of publication
- d. Quality Assessment of systematic review (PRISMA)
 - Reporting of background
 - Reporting of search strategy
 - Reporting of methods
 - Reporting of risk of bias in individual studies
 - Reporting of results
 - Reporting of discussion
- e. Outcomes
 - Reporting on effect size (RR or HR with 95% CI) of established diabetes on incident depression and dementia in a meta-analysis of (i) prospective cohort and/or case-cohort studies; or (ii) studies with RCT, controlled clinical trial, controlled before and after trial.

Reference List

1. Higgins JPT, Green SE. *Cochrane Handbook for Systematic Reviews of Interventions*. [Version 5.1.0 [updated March 2011]]. 2011. The Cochrane Collaboration 2012.
2. The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PloS Med*. 2009; 6:e1000097

Appendix 5: Electronic search strategy: incident dementia and depression in adults with established diabetes

(a) Diabetes: relative risk for dementia

DATABASE	MEDLINE via EBSCO
Date	June 2016
Strategy	#5 AND #9 AND #14
#5 = #1 OR #2 OR #3 OR #4 (634,804)	type 2 diabet* or type II diabet* or type 1 diabet* or type I diabet* or diabet& or diabetes (634,804) or (MM "Diabetes Mellitus, Type 2") (88,209) or MM "Diabetes Mellitus, Type 1") (55,804) or MM "Diabetes Mellitus") (74,032)
#9 = #6 OR #7 OR #8 (191,182)	systematic review* or meta-analysis or metaanalysis (185,382) or (MH "Review Literature as Topic+") (15,992) or (MH "Meta-Analysis as Topic+") (9,459)
#14 = #10 OR #11 OR #12 OR #13 (421,602)	Dementia or alzheimer* or alzheimer* disease or AD or vascular dementia (421,602) Or (MH "dementia") (43,436) Or (MH "Alzheimer disease") (80,049) OR (MH "or dementia, vascular (4,451)
#15 = #5 AND #9 AND #14	376
#15 Limiters - English Language	367
#15 Limiters - Date of Publication: 20110101-20161231; English Language	219

DATABASE	EMBASE via Elsevier
Date	June 2016
Strategy	#6 AND #10 AND #15
#6 = #1 OR #2 OR #3 OR #4 OR #5	'type 2 diabet*' OR 'type ii diabet*' OR 'type 1 diabet*' OR 'type i diabet*' OR 'diabet*' OR 'diabetes' (1066091) or "Diabetes Mellitus, Type 2"/exp (205282) or "Diabetes Mellitus, Type 1"/exp (101666) or "impaired glucose tolerance"/exp (25449) or "Diabetes Mellitus "/exp/mj (456107)
#10= #7 OR #8 OR #9 (316307)	"systematic review" or "meta-analysis" or metaanalysis (316307) or "Systematic review (topic)"/exp (21222) or "Systematic review "/exp (150479)
#15= #11 OR #12 OR #13 OR #14 (449608)	Dementia or alzheimer* or 'alzheimer* disease' or AD or 'vascular dementia' (418994) Or 'dementia'/exp/mj (184981) Or 'alzheimer disease'/exp (162715) OR 'multiinfarct dementia'/exp (10670)
#16 = #6 AND #10 AND #15	727
#16 Limiters - English Language	708
#16 Limiters - Date of Publication: 2011-2016; English Language	453

DATABASE	Cochrane Library
Date	June 2016
Strategy	#5 AND #10
#5 = #1 OR #2 OR #3 OR #4 (47267)	MeSH descriptor: [Diabetes Mellitus] explode all trees (21170) OR MeSH descriptor: [Diabetes Mellitus, Type 2] (11937) OR MeSH descriptor: [Diabetes Mellitus, Type 1] (3832) OR "diabetes":ti,ab,kw (Word variations have been searched) (45672)
#10 = #6 OR #7 OR #8 OR #9 (9695)	MeSH descriptor: [dementia] explode all trees (4677) OR MeSH descriptor: [Alzheimer disease] explode all trees (2588) OR MeSH descriptor: [dementia, vascular] explode all trees (317) OR "dementia":ti,ab,kw (Word variations have been searched) (7993)
#5 AND #10*	247 Of these Cochrane reviews = 1 Other reviews = 1 Trials = 238 Method studies = 5 Technological assessments = 1 Economic evaluations = 1

*No limits on search employed

(ii) Diabetes: relative risk for depression

DATABASE	MEDLINE via EBSCO
Date	June 2016
Strategy	#6 AND #10 AND #14
#5 = #1 OR #2 OR #3 OR #4 (634,804)	type 2 diabet* or type II diabet* or type 1 diabet* or type I diabet* or diabet& or diabetes (634,804) or (MM "Diabetes Mellitus, Type 2") (88,209) or MM "Diabetes Mellitus, Type 1" (55,804) or MM "Diabetes Mellitus") (74,032)
#9 = #6 OR #7 OR #8 (191,182)	systematic review* or meta-analysis or metaanalysis (185,382) or (MH "Review Literature as Topic+") (15,992) or (MH "Meta-Analysis as Topic+") (9,459)
#14 = #10 OR #11 OR #12 OR #13	Depression* or depressive or major depression or affective disorder or depress* N2 symptom* (398,005) or (MM "Depression") (58,706) or (MH "Depressive disorder") 67,023 or (MH "Depressive disorder, Major") (24,908)
#15 = #5 AND #9 AND #14	355
#15 Limiters - English Language	343
#15 Limiters - Date of Publication: 20110101-20161231; English Language	209

DATABASE	EMBASE via Elsevier
Date	June 2016
Strategy	#6 AND #10 AND #15
Diabetes #6 = #1 OR #2 OR #3 OR #4 OR #5	'type 2 diabet*' OR 'type ii diabet*' OR 'type 1 diabet*' OR 'type i diabet*' OR 'diabet*' OR 'diabetes' (1066091) or "Diabetes Mellitus, Type 2"/exp (205282) or "Diabetes Mellitus, Type 1"/exp (101666) or "impaired glucose tolerance"/exp (25449) or "Diabetes Mellitus "/exp/mj (456107)
Systematic Rv/Meta-analysis #10= #7 OR #8 OR #9 (316307)	"systematic review" or "meta-analysis" or metaanalysis (316307) or "Systematic review (topic)"/exp (21222) or "Systematic review "/exp (150479)
#14= #11 OR #12 OR #13 (4348342)	Depression* or depressive or major depression or affective disorder or (depress* Near/2 symptom*) (261653) or "Depression"/mj (133395) or "major depression"/exp (52701)
#15 = #6 AND #10 AND #14	753
#15 Limiters - English Language	739
#15 Limiters - Date of Publication: 2011-2016; English Language	446

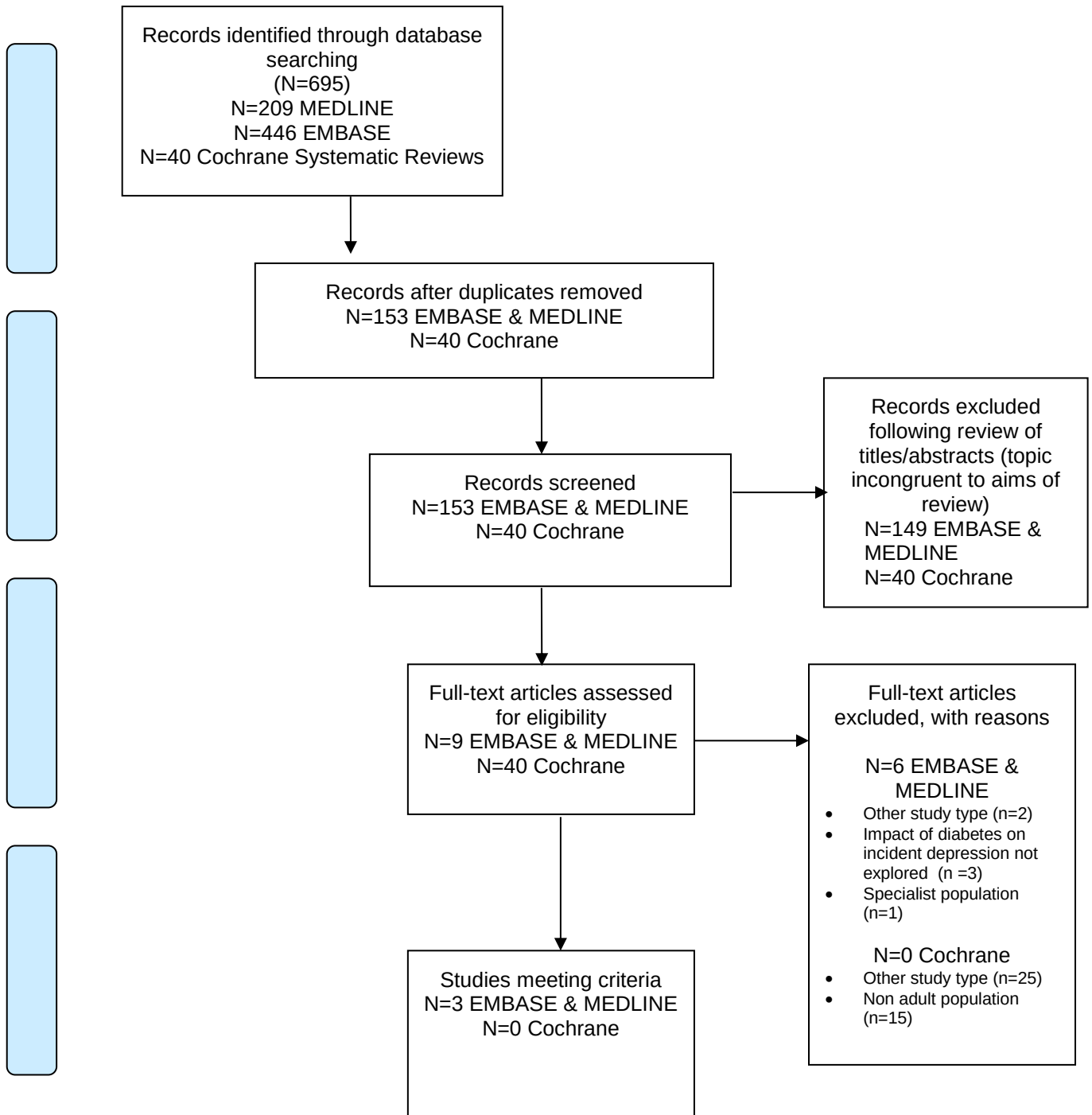
DATABASE	Cochrane Library
Date	June 2016
Strategy	#5 AND #10
#5 = #1 OR #2 OR #3 OR #4 (47267)	MeSH descriptor: [Diabetes Mellitus] explode all trees (21170) OR MeSH descriptor: [Diabetes Mellitus, Type 2] (11937) OR MeSH descriptor: [Diabetes Mellitus, Type 1] (3832) OR "diabetes":ti,ab,kw (Word variations have been searched) (45672)
#10 = #6 OR #7 OR #8 OR #9 (51198)	MeSH descriptor: [Depressive Disorder] explode all trees (9121) OR MeSH descriptor: [Depression] explode all trees (7487) OR "depression":ti,ab,kw (Word variations have been searched) (47099) OR "depressive":ti,ab,kw (Word variations have been searched) (9121)
#5 AND #10*	1380 Of these Cochrane reviews = 40 Other reviews = 11 Trials = 1312 Method studies = 7 Technological assessments= 1 Economic evaluations = 9

*No limits on search employed

Appendix 6: PRISMA flow diagram: incident depression and dementia in adults with established diabetes

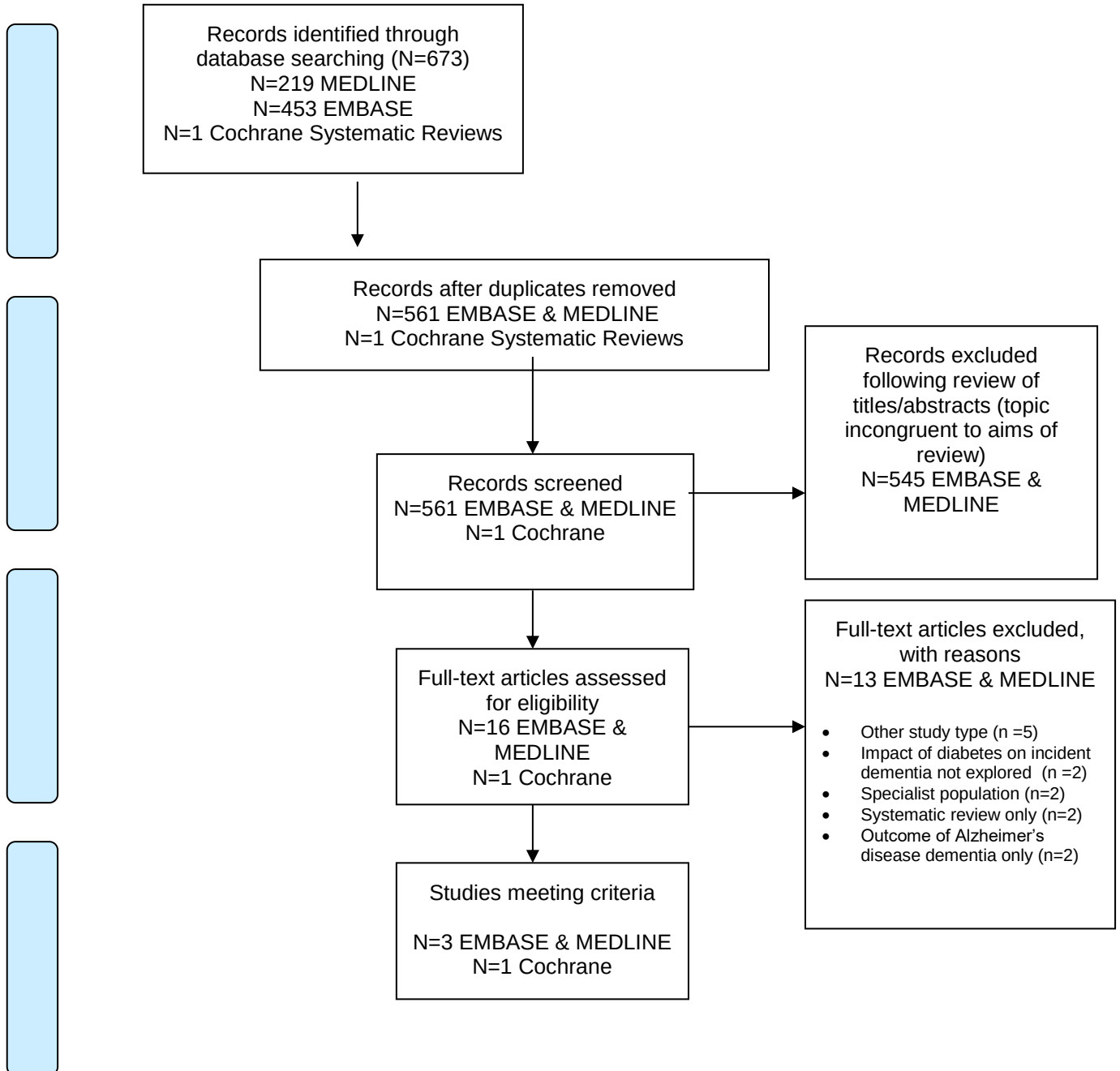


PRISMA Flow Diagram: Diabetes as a risk factor for depression





PRISMA Flow Diagram: Diabetes as a risk factor for dementia



Appendix 7: Short listed studies with full text review: incident depression and dementia in adults with established diabetes

i) Diabetes as a risk factor for dementia

Meta-analysis of prospective cohort studies

	Study (Author, year)	Study design characteristics	Population characteristics	Systematic review/review characteristics	Incident dementia as outcome measured	Exposure characteristics	Statistical Findings	Inclusion in qualitative synthesis
1	Chatterjee¹ (2016)	A meta-analysis of data from longitudinal studies to estimate the sex-specific relationship between women and men with diabetes with incident dementia.	General Adult population: 48% female, mean age 43-83 years	14 studies included, 2,310,330 individuals and 102,174 dementia case patients were included. Mean study duration 2 - 35 years.	Yes	Measured or self report diabetes	Diabetes was associated with increased risk of any dementia in both sexes; women: pooled RR 1.68 [95% CI 1.64-1.71] and men; pooled RR 1.61 [95% CI 1.42-1.83]	No: study by Gudala et al had larger number of participants
2	Cheng (2012) [13]	A meta-analysis of longitudinal studies examining the association of diabetes with the onset of dementia	General adult population	19 studies included, 6184 subjects with diabetes and 38 530 subjects without diabetes were included respectively. Study duration range 2 – 13 years.	Yes	Unclear	Results showed that subjects with diabetes had higher risk for AD RR:1.46, 95% (CI: 1.20–1.77), VD (RR: 2.48, 95% CI: 2.08–2.96), any dementia (RR: 1.51, 95% CI: 1.31–1.74) and MCI (RR: 1.21, 95% CI: 1.02–1.45) than those without	No: study by Gudala et al had larger number of participants
3	Gudala (2015) [30]	A meta-analysis of prospective observational studies examining risk of dementia in individuals with diabetes mellitus	General adult population	28 studies included -1,148,041 participants. Follow up 2-30 years, 15, 039 incident cases of all type dementia	Yes	Both T2DM and T2DM– self report/registry based/antidiabetic med use	Pooled RR of developing any type dementia (n = 20 studies) was 1.73 (1.65–1.82), AD (n = 20) was 1.56 (1.41–1.73) and VaD (n = 13) was 2.27 (1.94–2.66,) in patients with diabetes mellitus.	Included in qualitative synthesis

References

1. Chatterjee S, Peters SAE, Woodward M, Arango SM, Batty GD, Beckett N, et al. Type 2 Diabetes as a Risk Factor for Dementia in Women Compared With Men: A Pooled Analysis of 2.3 Million People Comprising More Than 100,000 Cases of Dementia. Diabetes Care. 2015 Dec 17;dc151588.

The Cochrane Database of Systematic Reviews

	Study (Author, year)	Population characteristics	Systematic review/review characteristics	Cognition outcome measured	Intervention characteristics	Statistical findings	Inclusion in qualitative synthesis
1	Areosa Sastre (2017) [31]	Two larger studies had a total of 13,934 participants and two smaller studies had approx 150 participants in each.	7 RCTs – data from cognition included in 4 studies only – 40-60 months follow up	Yes – baseline and follow up	Compared two or more different treatments for T2DM: 2 studies compared intensive versus standard glycaemic control and 2 compared different pharmacological treatments	No high quality evidence that diabetes medication strategies ediffer in their effect on global cognitive functioning over time.	Yes

ii) Diabetes as a risk factor for depression

Meta-analysis of prospective cohort studies

	Study (Author, year)	Study design characteristics	Population characteristics	Systematic review/review characteristics	Incident depression as outcome measured	Exposure characteristics	Statistical Findings	Inclusion in qualitative synthesis
1	Hasan¹ (2013)	A systematic review and meta-analysis of longitudinal studies examining the reciprocal relationship between depression and T2DM	General adult population. Female ranging from 48% - 100%.	9 studies included in analysis. Follow up range 2 – 10 years.	Yes	Laboratory test/self report/medical records	RR of incident depression in diabetes was 1.23 (95% CI: 1.15 – 1.31)	No
2	Tong² (2016)	A meta-analysis of prospective cohort studies to investigate the risk of depressive symptoms among individuals with impaired glucose metabolism (IGM), newly diagnosed diabetes (NDM), and previously diagnosed diabetes (PDM), compared with those with normal glucose metabolism (NGM)	General adult population	5 prospective cohort studies were included in the analyses, with a total of 18,051 participants.	Yes (depressive disorder or depressive symptoms)	Previously diagnosed or undiagnosed/untreated diabetes or its pre-diabetic stage - Studies unable to differentiate NDM and PDM were not included in the analysis of PDM versus NGM or NDM versus NGM.	People with IGM (RR = 1.08, 95 % CI 0.84–1.38) and NDM (RR = 1.07, 95 % CI 0.74–1.55) were not associated with risk of developing depressive symptoms. Patients with PDM were associated with a modest increased risk of depressive symptoms (RR = 1.29, 95 % CI 1.03–1.63)	No
3	Rotella & Mannucci (2013) [28]	A meta-analysis of longitudinal studies assessing the risk of incident depression in subjects with or without	General adult population	16 studies included in the meta-analysis, 497,223 subjects, with a	Yes	Laboratory test/self report/medical records/anti-diabetic medication use	Unadjusted and adjusted risk [95% CI] for depression in diabetic subjects of	Yes

	Study (Author, year)	Study design characteristics	Population characteristics	Systematic review/review characteristics	Incident depression as outcome measured	Exposure characteristics	Statistical Findings	Inclusion in qualitative synthesis
		diabetes		mean follow-up of 5.8 years. 42,633 cases of incident depression			of 1.29 [1.18–1.40] and 1.25 [1.10–1.44] respectively.	

References

1. Hasan SS, Clavarino AM, Mamun AA, Doi SAR, Kairuz T. Population impact of depression either as a risk factor or consequence of type 2 diabetes in adults: a meta-analysis of longitudinal studies. *Asian Journal Of Psychiatry*. 2013 Dec;6(6):460–72.
2. Tong A, Wang X, Li F, Xu F, Li Q, Zhang F. Risk of depressive symptoms associated with impaired glucose metabolism, newly diagnosed diabetes, and previously diagnosed diabetes: a meta-analysis of prospective cohort studies. *Acta Diabetologica*. 2016 Aug;53(4):589–98.

Appendix 8: Study protocol and search strategy: common modifiable risk factors for T2DM and dementia

Aim

Examine evidence among adults for the effect of a number of modifiable lifestyle risk factors, shared with dementia, on incident type 2 diabetes mellitus (T2DM).

C. Rationale for the study

Structured lifestyle interventions can reduce T2DM incidence among at risk adult populations but debate remains about the strength of the association between a number of individual modifiable risk factors common to dementia, and incident T2DM. Similarly, the strength of the association between established diabetes and incident depression and dementia, respectively, remains unclear.

D. Objective

The objective of this study is to (i) assess the effect of a number of modifiable lifestyle factors common to dementia on T2DM incidence among adults, through review of evidence from systematic reviews and meta-analyses of observational and interventional studies.

C. Primary research questions

- II. Does evidence exist in the literature for higher incidence of T2DM in adults with the following modifiable risk factors; hypertension, obesity, depression, physical inactivity, cognitive inactivity, smoking, heavy alcohol use and high cholesterol, respectively.

D. Criteria for considering studies for this review

Inclusion criteria:

Articles will be considered for inclusion in systematic review if:

- a. The authors reported risk estimates; relative risk (RR) or hazard ratio (HR) with 95% confidence intervals (CI) from a meta-analysis or systematic review of T2DM by risk factor status from (i) prospective cohort studies among non-specialised populations without diabetes at baseline or (ii) a studies with randomised clinical trial, controlled clinical trial, controlled before and after trial with reporting on effect size (RR or HR with 95% confidence intervals).
- b. randomised clinical trial (RCT), controlled clinical trial, controlled before and after trial with reporting on effect size
- c. Epidemiological studies were published in English between 2011- 2016. No time limitations on systematic reviews of RCT in Cochrane Library.

4. Participants:

- a. Persons ≥ 18 years
- b. general population sample

5. Exposure/intervention

- a. Studies exploring modifiable risk factors for T2DM must include one of hypertension, obesity, depression, physical inactivity, cognitive inactivity, smoking, heavy alcohol use or, high cholesterol.
- b. For intervention studies, one of the stated goals of the intervention is intentional reduction of T2DM incidence
- c. The intervention focuses primarily on adults based in the community rather than specialised populations e.g. pregnant women, children.

6. Outcomes:

- a. T2DM incidence

Exclusion criteria:

- IV. Specialised study populations e.g. pregnant women, children
- V. Letters, abstracts, conference proceedings, dissertations.
- VI. Studies not conducted in humans

E. Search strategies for identification of studies

The systematic review will be performed in accordance with the PRISMA guidelines [1].

1. Databases:

The following electronic databases will be searched:

- Cochrane Library
- MEDLINE
- EMBASE

The titles and abstracts obtained from searches of electronic databases will be examined, and potentially relevant full-text articles will be requested. One researcher will screen the Medline, EMBASE and Cochrane review titles and abstracts. There will be English language restrictions on our searches and a time frame 2011- 2016 for MEDLINE and EMBASE searches. Conference proceedings and abstracts will not be included because there is insufficient detail available in these to evaluate the intervention and the quality of the study. Dissertations will be excluded, as these are difficult to locate in full text, and will likely yield few additional reports. If meta-analysis of prospective cohort studies is not available, meta-analysis of case-control and/or cross-sectional studies will be examined.

2. Other search strategies

The reference lists of all relevant review studies included in the review will be searched. Additional key words of relevance may be identified during any of the electronic or other searches. If this is the case, electronic search strategies will be modified to incorporate these terms.

4. Search strategies

Example 1 (Publications in MEDLINE in English):

- a. Searches were performed separately for each modifiable risk factor of interest;

- hypertension, obesity, depression, physical inactivity, cognitive inactivity, smoking, heavy alcohol use, high cholesterol.
- b. For each of these risk factors, we searched the Cochrane Database of Systematic Reviews, MEDLINE and EMBASE to identify English-language systematic reviews and meta-analyses pertaining to exposure and outcome of interest.
- c. For modifiable risk factors for T2DM: where possible, searches identified publications with titles or abstracts containing terms related to each specific modifiable risk factor e.g. alcohol-related term, plus a diabetes-related term plus a term indicative of systematic review or meta-analysis.
- d. Limit of English language and limits of 2011 – 2016 were placed on date of publication, in MEDLINE and EMBASE (not in Cochrane Library search).
- e. In Cochrane Library search, all randomised controlled trials examining the impact of (i) modifiable risk factor modification on T2DM incidence were selected with no limits.

F. Methods of the review

Trials selection

Reviewer CD will identify potentially relevant studies by reviewing titles and abstracts retrieved from electronic searches. For studies identified as potentially relevant, the full text article will be retrieved. Reviewer CD will review potential studies to see if they fulfil inclusion criteria. There will be no blinding of the reviewer to study author and affiliation. If ambiguity, the reviewer will discuss study with the wider research group to achieve consensus. Studies excluded at this point or thereafter will be recorded in the bibliographic database, noting the reason for exclusion.

Quality assessment

For randomised controlled trials, the component assessment method of Cochrane will be used, and quality scoring will not be performed. During Cochrane review process internal validity of included studies is examined for potential selection, attrition, and detection bias. If studies are found to be of poor quality a sensitivity analysis is undertaken to compare results between studies with potential bias and those without [2].

For systematic reviews and meta-analyses sourced in MEDLINE and EMBASE, PRISMA [1] checklist will be used for critical appraisal and to gauge quality.

The applicability of each study will be noted with respect to population, exposure, outcome and setting.

Data abstraction process

For studies that fulfil inclusion criteria, one reviewer will abstract the relevant data using a standardised template in an Excel database.

Reviewer will attempt to contact the authors for missing data if clarification of the data presented is required.

Data to be extracted

- a. Population characteristics
 - number
 - age
 - sex
- b. For RCT intervention
 - country
 - type of health care setting

- community-based
- in-patient, out-patient
- mode of delivery of the intervention
- c. Exposure characteristics
 - risk factor(s) addressed
- d. Study design characteristics
 - study design: systematic review, meta-analysis, RCT, non-randomised trial, observational study with concurrent comparison group, pre vs post
 - sample size
 - follow-up interval
 - date of publication
- e. Quality Assessment of systematic review (PRISMA)
 - Reporting of background
 - Reporting of search strategy
 - Reporting of methods
 - Reporting of risk of bias in individual studies
 - Reporting of results
 - Reporting of discussion
- f. Outcomes

Reporting on effect size (RR or HR with 95% CI) of named risk factor on incident T2DM in a meta-analysis of (i) prospective cohort studies; or (ii) studies with randomised clinical trial, controlled clinical trial, controlled before and after trial

References

1. Higgins JPT, Green SE. *Cochrane Handbook for Systematic Reviews of Interventions*. [Version 5.1.0 [updated March 2011]]. 2011. The Cochrane Collaboration 2012.
2. The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PloS Med*. 2009; 6:e1000097

Appendix 9: Electronic search strategy: modifiable risk factors for T2DM

Risk factors for T2DM

i) Hypertension: Relative risk for T2DM

Search Strategy

DATABASE	MEDLINE via EBSCO
Date:	June 2106
Strategy	#6 AND #10 AND #14
#6 = #1 OR #2 OR #3 OR #4 OR #5 (216,768)	type 2 diabet* or type II diabet* or glucose intoleran* or prediabet* or pre diabet* or impair* N2 glucose or insulin resist* (193,623) or (MM "Diabetes Mellitus, Type 2") (88,209) or (MH "Glucose Intolerance") (7,558) or (MH "Prediabetic State") (5,283) or (MH "Insulin Resistance") (48,709)
#10 = #7 OR #8 OR #9 (191,182)	systematic review* or meta-analysis or metaanalysis (185,382) or (MH "Review Literature as Topic+") (9,459) or (MH "Meta-Analysis as Topic+") (15,992)
#14 = #11 OR #12 OR #13 (510,304)	hypertension or hypertensive (470,214) or blood pressure N2 (raised or rise or elevated or systolic or diastolic) (75,327) or (MM "Hypertension") (157,902)
#15 = #6 AND #10 AND #14	604
#15 Limiters - English Language	562
#15 Limiters - Date of Publication: 20110101-20161231; English Language	322

DATABASE	EMBASE via Elsevier
Date:	June 2016
Strategy	#6 AND #10 AND #13
#6 = #1 OR #2 OR #3 OR #4 OR #5 (320658)	"type 2 diabet*" or "type II diabet*" or "glucose intoleran*" or prediabet* or "pre diabet*" or (impair* NEAR/2 glucose) or "insulin resist*" (299286) or "non insulin dependent diabetes mellitus"/exp/mj (114,465) or "glucose intolerance"/exp (15202) or "impaired glucose tolerance"/exp (25437) or "Insulin Resistance"/exp (105156)
#10= #7 OR #8 OR #9 (316307)	"systematic review" or "meta-analysis" or metaanalysis (316307) or "Systematic review (topic)"/exp (21222) or "Systematic review "/exp (150479)
#13 = #11 OR #12 (1164991)	'hypertension' OR 'hypertensive' OR 'blood pressure' OR 'elevated blood pressure' OR ('blood pressure' NEAR/2 (raised OR rise OR elevated OR systolic OR diastolic)) (1164991) OR "hypertension"/mj (205877)
#14 = #6 AND #10 AND #13	2436
#14 LIMITERS ENGLISH LANGUAGE	2386
#14 LIMITERS ENGLISH LANGUAGE and Years 2011 – 2016	1437

DATABASE	Cochrane Library
Date:	
Strategy	#4 AND #7
	Search
#4 = #1 OR #2 OR #3 (12747)	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees (11939) OR MeSH descriptor: [Glucose Intolerance] explode all trees (618) OR "prediabetes":ti,ab,kw (Word variations have been searched) (605)
#7 = #5 OR #6 (65578)	MeSH descriptor: [Hypertension] explode all trees OR "blood pressure" : ti,ab,kw (15810) OR "blood pressure":ti,ab,kw (Word variations have been searched) (62026)
#4 AND #7*	2642 Of these Cochrane reviews = 25 Other reviews = 50 Trials = 2523 Tehnological assessments =1 Economic evaluations = 43

*No limits on search employed

ii) Obesity: Relative risk for T2DM

Search Strategy

DATABASE	MEDLINE via EBSCO
Date:	
Strategy	#6 AND #10 AND #16
#6 = #1 OR #2 OR #3 OR #4 OR #5 (216,768)	type 2 diabet* or type II diabet* or glucose intoleran* or prediabet* or pre diabet* or impair* N2 glucose or insulin resist* (193,623) or (MH "Diabetes Mellitus, Type 2") (88,209) or (MH "Glucose Intolerance") (7,558) or (MH "Prediabetic State") (5,283) or (MH "Insulin Resistance") (48,709)
#10 = #7 OR #8 OR #9 (191,182)	systematic review* or meta-analysis or metaanalysis (185,382) or (MH "Review Literature as Topic+") (9,459) or (MH "Meta-Analysis as Topic+") (15,992)
#16 = #11 OR #12 OR #13 OR #14 OR #15 (482,663)	obesity or overweight or body fat or body mass index or BMI or weight loss (482,614) or MM obesity (107,420) Or MH body mass index (105,085) Or MH weight loss (30,592) Or MH weight reduction programs (1,320)
#17= #6 AND #10 AND #16	1,405
#17 Limiters - English Language	1361
#17 Limiters - Date of Publication: 20110101-20161231; English Language	855

DATABASE	EMBASE via Elsevier
Date:	June 2016
Strategy	#6 AND #10 AND #16
#6 = #1 OR #2 OR #3 OR #4 OR #5 (320658)	"type 2 diabet*" or "type II diabet*" or "glucose intoleran*" or prediabet* or "pre diabet*" or (impair* Near/2 glucose) or "insulin resist*" (299286) or "non insulin dependent diabetes mellitus"/exp/mj (114,465) or "glucose intolerance"/exp (15202) or "impaired glucose tolerance"/exp (25437) or "Insulin Resistance"/exp (105156)
#10= #7 OR #8 OR #9 (316307)	"systematic review" or "meta-analysis" or metaanalysis (316307) or "Systematic review (topic)/exp (21222) or "Systematic review "/exp (150479)
#16= #11 OR #12 OR #13 OR #14 OR #15 (863599)	obesity or overweight or "body fat" or "body mass index" or BMI or "weight loss" or "weight reduction program*" (760058) or "Obesity"/mj (162076) or "Body mass"/exp (311635) or "Weight reduction"/exp (145914) or "Weight loss Program"/exp (1137)
#17= #6 AND #10 AND #16	3938
#17 Limiters - English Language	3851
#17 Limiters - Date of Publication: 20110101-20161231; English Language	2526

DATABASE	Cochrane Library
Date:	
Strategy	#4 AND #8
	Search
#4 = #1 OR #2 OR #3 (12747)	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees (11939) OR MeSH descriptor: [Glucose Intolerance] explode all trees (618) OR "prediabetes":ti,ab,kw (Word variations have been searched) (605)
#8 = #5 OR #6 OR #7 (14956)	MeSH descriptor: [Obesity] explode all trees (10708) OR MeSH descriptor: [Body Weight Changes] explode all trees (6777) OR MeSH descriptor: [Overweight] explode all trees (11832)
#4 AND #8*	1952 Of these Cochrane reviews = 11 Other reviews = 59 Trials = 1845 Technological assessments = 3 Economic evaluations = 34

*No limits on search employed

iii) Depression: Relative risk for T2DM

Search Strategy

DATABASE	MEDLINE via EBSCO
Date:	
Strategy	#6 AND #10 AND #15
#6 = #1 OR #2 OR #3 OR #4 OR #5 (216,768)	type 2 diabet* or type II diabet* or glucose intoleran* or prediabet* or pre diabet* or impair* N2 glucose or insulin resist* (193,623) or (MM "Diabetes Mellitus, Type 2") (88,209) or (MH "Glucose Intolerance") (7,558) or (MH "Prediabetic State") (5,283) or (MH "Insulin Resistance") (48,709)
#10 = #7 OR #8 OR #9 (191,182)	systematic review* or meta-analysis or metaanalysis (185,382) or (MH "Review Literature as Topic+") (9,459) or (MH "Meta-Analysis as Topic+") (15,992)
#15 = #11 OR #12 OR #13 OR #14	Depression* or depressive or major depression or affective disorder or depress* N2 symptom* (397,876) or (MM "Depression") (58,646) or (MH "Depressive disorder") (67,003) or (MH "Depressive disorder, Major") (24,883)
#16 = #6 AND #10 AND #15	117
#16 Limiters - English Language	112
#16 Limiters - Date of Publication: 20110101-20161231; English Language	68

DATABASE	EMBASE via Elsevier
Date:	June 2016
Strategy	#6 AND #10 AND #14
Type 2 diabetes #6 = #1 OR #2 OR #3 OR #4 OR #5 (320658)	"type 2 diabet*" or "type II diabet*" or "glucose intoleran*" or prediabet* or "pre diabet*" or (impair* Near/2 glucose) or "insulin resist*" (299286) or "non insulin dependent diabetes mellitus"/exp/mj (114,465) or "glucose intolerance"/exp (15202) or "impaired glucose tolerance"/exp (25437) or "Insulin Resistance"/exp (105156)
Systematic Rv/Meta-analysis #10= #7 OR #8 OR #9 (316307)	"systematic review" or "meta-analysis" or metaanalysis (316307) or "Systematic review (topic)"/exp (21222) or "Systematic review "/exp (150479)
#14= #11 OR #12 OR #13 (348122)	Depression* or depressive or major depression or affective disorder or (depress* Near/2 symptom*) (261454) or "Depression"/mj (133359) or "major depression"/exp (52670)
#15 = #6 AND #10 AND #14	227
#15 Limiters - English Language	224
#15 Limiters - Date of Publication: 20110101-20161231; English Language	135

DATABASE	Cochrane Library
Date:	
Strategy	#4 AND #9
	Search
#4 = #1 OR #2 OR #3 (12747)	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees (11939) OR MeSH descriptor: [Glucose Intolerance] explode all trees (618) OR "prediabetes":ti,ab,kw (Word variations have been searched) (605)
#9 = #5 OR #6 OR #7 OR #8 (51198)	MeSH descriptor: [Depressive Disorder] explode all trees (9121) OR MeSH descriptor: [Depression] explode all trees (7487) OR "depression":ti,ab,kw (Word variations have been searched) (47099) OR "depressive":ti,ab,kw (Word variations have been searched) (18828)
#4 AND #9*	559 Of these Cochrane reviews = 14 Other reviews = 7 Trials = 535 Economic evaluations = 3

*No limits on search employed

iv) **Physical inactivity:** Relative risk for T2DM

Search Strategy

DATABASE	MEDLINE via EBSCO
Date:	
Strategy	#6 AND #10 AND #15
#6 = #1 OR #2 OR #3 OR #4 OR #5 (216,768)	type 2 diabet* or type II diabet* or glucose intoleran* or prediabet* or pre diabet* or impair* N2 glucose or insulin resist* (193,623) or (MH "Diabetes Mellitus, Type 2") (88,209) or (MH "Glucose Intolerance") (7,558) or (MH "Prediabetic State") (5,283) or (MH "Insulin Resistance") (48,709)
#10 = #7 OR #8 OR #9 (191,182)	systematic review* or meta-analysis or metaanalysis (185,382) or (MH "Review Literature as Topic+") (9,459) or (MH "Meta-Analysis as Topic+") (15,992)
#15 = #11 OR #12 OR #13 OR #14 (478,087)	Physical activit* or exercise* or prediabet* or exercise, physical or physical fitness or fit* N2 physical (408,216) or (MH "Physical fitness") (25,049) or (MH "Exercise") (86,942) or (MH "motor activity") (90,804)
#16 = #6 AND #10 AND #15	582
#16 Limiters - English Language	562
#16 Limiters - Date of Publication: 20110101-20161231; English Language	342

DATABASE	EMBASE via Elsevier
Date:	June 2016
Strategy	#6 AND #10 AND #15
#6 = #1 OR #2 OR #3 OR #4 OR #5 (320658)	"type 2 diabet*" or "type II diabet*" or "glucose intoleran*" or prediabet* or "pre diabet*" or (impair* Near/2 glucose) or "insulin resist*" (299286) or "non insulin dependent diabetes mellitus"/exp/mj (114,465) or "glucose intolerance"/exp (15202) or "impaired glucose tolerance"/exp (25437) or "Insulin Resistance"/exp (105156)
#10= #7 OR #8 OR #9 (316307)	"systematic review" or "meta-analysis" or metaanalysis (316307) or "Systematic review (topic)/exp (21222) or "Systematic review "/exp (150479)
#15= #11OR #12 OR #13 OR #14 (518831)	Physical activit* or exercise* or physical fitness or (fit* NEAR/2 physical) (44082) or "fitness"/exp (35632) or "fitness"/exp/mj (15094) or 'motor activity'/exp (468573)
#16 = #6 AND #10 AND #15	122
#16 Limiters - English Language	119
#16 Limiters - Date of Publication: 2011-2016; English Language	83

DATABASE	Cochrane Library
Date:	
Strategy	#4 AND #8
	Search
#4 = #1 OR #2 OR #3 (12747)	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees (11939) OR MeSH descriptor: [Glucose Intolerance] explode all trees (618) OR "prediabetes":ti,ab,kw (Word variations have been searched) (605)
#8 = #5 OR #6 OR #7 (24223)	MeSH descriptor: [Exercise] explode all trees (20039) OR MeSH descriptor: [Motor Activity] explode all trees (22022) OR MeSH descriptor: [Physical Fitness] explode all trees (2766)
#4 AND #8*	1135 Of these Cochrane reviews = 15 Other reviews = 43 Trials = 1056 Technological assessments = 4 Economic evaluations = 17

*No limits on search employed

v) **Cognitive inactivity***: Relative risk for T2DM

Search Strategy

DATABASE	MEDLINE via EBSCO
Date:	
Strategy	#6 AND #10 AND #15
#6 = #1 OR #2 OR #3 OR #4 OR #5 (216,768)	type 2 diabet* or type II diabet* or glucose intoleran* or prediabet* or pre diabet* or impair* N2 glucose or insulin resist* (193,623) or (MH "Diabetes Mellitus, Type 2") (88,209) or (MH "Glucose Intolerance") (7,558) or (MH "Prediabetic State") (5,283) or (MH "Insulin Resistance") (48,709)
#10 = #7 OR #8 OR #9 (191,182)	systematic review* or meta-analysis or metaanalysis (185,382) or (MH "Review Literature as Topic+") (9,459) or (MH "Meta-Analysis as Topic+") (15,992)
#15 = #11 OR #12 OR #13 OR #14 (163,424)	Cognitive activity or cognitive inactivity or cognit* N2 reserve* or brain N2 reserve* or education* N2 level or attainment or mental fitness or occupation or leisure activit* or socioeconomic status or social network 124,692 or (MH "Cognitive reserve") (342) or (MH "Education") (19,554) or (MH "Intelligence") (21,897)
#16 = #6 AND #10 AND #15	48
#16 Limiters - English Language	48
#16 Limiters - Date of Publication: 20110101-20161231; English Language	34

*Of note 'Cognitive reserve' is a latent construct that cannot be directly measured, and assessment therefore relies on proxy indicators.

MesH 'Cognitive Reserve' *search terms for cognitive inactivity based on study *Aging, Brain Disease, and Reserve: Implications for Delirium* Am J of Geriatr Psychiatry. Jones et al., 2010

DATABASE	EMBASE via Elsevier
Date:	June 2016
Strategy	#1 AND #2 AND #3
Type 2 diabetes	"type 2 diabet*" or "type II diabet*" or "glucose intoleran*" or prediabet* or "pre diabet*" or (impair* NEAR/2 glucose) or "insulin resist*" (299286) or "non insulin dependent diabetes mellitus"/exp/mj (114,465) or "glucose intolerance"/exp (15202) or "impaired glucose tolerance"/exp (25437) or "Insulin Resistance"/exp (105156)
Systematic Rv/Meta-analysis	"systematic review" or "meta-analysis" or metaanalysis (316307) or "Systematic review (topic)"/exp (21222) or "Systematic review "/exp (150479)
#10= #7 OR #8 OR #9 (316307)	
#15= #11 OR #12 OR #13 OR #14 (575037)	'cognitive reserve' OR 'cognitive activity' OR 'cognitive inactivity' OR (cognit* NEAR/2 reserve*) OR (brain NEAR/2 reserve*) OR (education* NEAR/2 level) OR

	attainment OR 'mental fitness' OR occupation OR 'leisure activit*' OR 'socioeconomic status' OR 'social network status' OR 'social network' (179812) or 'cognitive reserve'/exp/mj (518) or 'education'/de (375313) or 'Intelligence'/exp (51709)
#16 = #6 AND #10 AND #15	141
#16 Limiters - English Language	139
#16 Limiters - Date of Publication: 2011-2016; English Language	100

DATABASE	Cochrane Library
Date:	
Strategy	#4 AND #9
	Search
#4 = #1 OR #2 OR #3 (12747)	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees (11939) OR MeSH descriptor: [Glucose Intolerance] explode all trees (618) OR "prediabetes":ti,ab,kw (Word variations have been searched) (605)
#9 = #5 OR #6 OR #7 OR #8	MeSH descriptor: [Cognitive reserve] explode all trees (8) OR mental fitness:ti,ab,kw (Word variations have been searched) (444) OR MeSH descriptor: [Education] explode all trees (24613) OR MeSH descriptor: [Intelligence] explode all trees (5065)
#4 AND #9*	922 Of these Cochrane reviews = 9 Other reviews = 42 Trials = 837 Technological assessments = 8 Economic evaluations = 26

*No limits on search employed

vi) **Smoking:** Relative risk for T2DM

Search Strategy

DATABASE	MEDLINE via EBSCO
Date:	
Strategy	#6 AND #10 AND #14
#6 = #1 OR #2 OR #3 OR #4 OR #5 (216,768)	type 2 diabet* or type II diabet* or glucose intoleran* or prediabet* or pre diabet* or impair* N2 glucose or insulin resist* (193,623) or (MH "Diabetes Mellitus, Type 2") (88,209) or (MH "Glucose Intolerance") (7,558) or (MH "Prediabetic State") (5,283) or (MH "Insulin Resistance") (48,709)
#10 = #7 OR #8 OR #9 (191,182)	systematic review* or meta-analysis or metaanalysis (185,382) or (MH "Review Literature as Topic+") (9,459) or (MH "Meta-Analysis as Topic+") (15,992)
#14 = #11 OR #12 OR #13 (32,413)	Smok* or tobacco or smoking cessation or smok* N2 cigar* 332,413 or (MH "smoking") 71,792 or (MH "smoking cessation") 24,684
#15= #6 AND #10 AND #14	156
#15 Limiters - English Language	151
#15 Limiters - Date of Publication: 20110101-20161231; English Language	96

DATABASE	EMBASE via Elsevier
Date:	June 2016
Strategy	#6 AND #10 AND #14
#6 = #1 OR #2 OR #3 OR #4 OR #5 (320658)	"type 2 diabet*" or "type II diabet*" or "glucose intoleran*" or prediabet* or "pre diabet*" or (impair* Near/2 glucose) or "insulin resist*" (299286) or "non insulin dependent diabetes mellitus"/exp/mj (114,465) or "glucose intolerance"/exp (15202) or "impaired glucose tolerance"/exp (25437) or "Insulin Resistance"/exp (105156)
#10= #7 OR #8 OR #9 (316307)	"systematic review" or "meta-analysis" or metaanalysis (316307) or "Systematic review (topic)"/exp (21222) or "Systematic review "/exp (150479)
#14= #11 OR #12 OR #13 (496149)	smok* OR tobacco OR 'smoking cessation' OR 'smok* near/2 cigar*' (496034) or 'smoking'/exp/mj (86094) or 'smoking cessation'/exp (49631)
#15 = #6 AND #10 AND #14	524
#15 Limiters - English Language	516
#15 Limiters - Date of Publication: 2011-2016; English Language	348

DATABASE	Cochrane Library
Date:	
Strategy	#4 AND #8
	Search
#4 = #1 OR #2 OR #3 (12747)	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees (11939) OR MeSH descriptor: [Glucose Intolerance] explode all trees (618) OR "prediabetes":ti,ab,kw (Word variations have been searched) (605)
#8 = #5 OR #6 OR #7 (8265)	MeSH descriptor: [Smoking] explode all trees (6417) OR MeSH descriptor: [Smoking Cessation] explode all trees (3963) OR MeSH descriptor: [Tobacco Use Cessation] explode all trees (4050)
#4 AND #8*	105 Of these Cochrane reviews = 0 Other reviews = 4 Trials = 98 Economic evaluations = 3

*No limits on search employed

vii) Heavy Alcohol Use: Relative risk for T2DM

Search Strategy

DATABASE	MEDLINE via EBSCO
Date:	
Strategy	#6 AND #10 AND #15
#6 = #1 OR #2 OR #3 OR #4 OR #5 (216,768)	type 2 diabet* or type II diabet* or glucose intoleran* or prediabet* or pre diabet* or impair* N2 glucose or insulin resist* (193,623) or (MM "Diabetes Mellitus, Type 2") (88,209) or (MH "Glucose Intolerance") (7,558) or (MH "Prediabetic State") (5,283) or (MH "Insulin Resistance") (48,709)
#10 = #7 OR #8 OR #9 (191,182)	systematic review* or meta-analysis or metaanalysis (185,382) or (MH "Review Literature as Topic+") (9,459) or (MH "Meta-Analysis as Topic+") (15,992)
#11 = #6 AND #10	4,656
#15 = #12 OR #13 OR #14 (795,708)	Alcohol* or ethanol or alcohol* N2 intoxi* or drink* or alcohol* N2 intoxi* or drink* or consumption or alcohol miuse (795,708) or MH Ethanol (81,605) or MH Alcoholic beverages (6,525)
#15 = #11 AND #15	340
#15 Limiters - English Language	331
#15 Date of Publication: 20110101-20161231; English Language	227

DATABASE	EMBASE via Elsevier
Date:	June 2016
Strategy	#6 AND #10 AND #12
#6 = #1 OR #2 OR #3 OR #4 OR #5 (320658)	"type 2 diabet*" or "type II diabet*" or "glucose intoleran*" or prediabet* or "pre diabet*" or (impair* Near/2 glucose) or "insulin resist*" (299286) or "non insulin dependent diabetes mellitus"/exp/mj (114,465) or "glucose intolerance"/exp (15202) or "impaired glucose tolerance"/exp (25437) or "Insulin Resistance"/exp (105156)
#10= #7 OR #8 OR #9 (316307)	"systematic review" or "meta-analysis" or metaanalysis (316307) or "Systematic review (topic)"/exp (21222) or "Systematic review "/exp (150479)
#12= #10 OR #11 (1061523)	alcohol* OR ethanol OR (alcohol* NEAR/2 intoxi*) OR drink* OR consumption OR 'alcohol misuse' (1061523) or 'alcohol'/exp/mj (103235)
#13 = #6 AND #10 AND #12	740
#13 Limiters - English Language	726
#13 Limiters - Date of Publication: 2011-2016; English Language	508

DATABASE	Cochrane Library
Date:	
Strategy	#4 AND #9
	Search
#4 = #1 OR #2 OR #3 (12747)	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees (11939) OR MeSH descriptor: [Glucose Intolerance] explode all trees (618) OR "prediabetes":ti,ab,kw (Word variations have been searched) (605)
#9 = #5 OR #6 OR #7 OR #8	MeSH descriptor: [Alcohol Drinking] explode all trees (3108) OR MeSH descriptor: [Binge Drinking] explode all trees (95) OR MeSH descriptor: [Alcoholism] explode all trees (2798) OR MeSH descriptor: [Ethanol] explode all trees (4048)
#4 AND #9*	50 Of these Cochrane reviews = 0 Trials = 50

*No limits on search employed

viii) High cholesterol: Relative risk for T2DM

Search Strategy

DATABASE	MEDLINE via EBSCO
Date:	
Strategy	#6 AND #10 AND #14
#6 = #1 OR #2 OR #3 OR #4 OR #5 (216,768)	type 2 diabet* or type II diabet* or glucose intoleran* or prediabet* or pre diabet* or impair* N2 glucose or insulin resist* (193,623) or (MH "Diabetes Mellitus, Type 2") (88,209) or (MH "Glucose Intolerance") (7,558) or (MH "Prediabetic State") (5,283) or (MH "Insulin Resistance") (48,709)
#10 = #7 OR #8 OR #9 (191,182)	systematic review* or meta-analysis or metaanalysis (185,382) or (MH "Review Literature as Topic+") (9,459) or (MH "Meta-Analysis as Topic+") (15,992)
#14 = #11 OR #12 OR #13 (680,701)	Hypercholesterolemia or Hypercholesterolaemia or cholesterol level* N3 high or raised or elevated (641,372) or (MH "cholesterol") (45,767) or (MH "hypercholesterolemia") (24,302)
#15= #6 AND #10 AND #14	284
#15 Limiters - English Language	273
#15 Limiters - Date of Publication: 20110101-20161231; English Language	173

DATABASE	EMBASE via Elsevier
Date:	June 2016
Strategy	#6 AND #10 AND #14
#6 = #1 OR #2 OR #3 OR #4 OR #5 (320658)	"type 2 diabet*" or "type II diabet*" or "glucose intoleran*" or prediabet* or "pre diabet*" or (impair* Near/2 glucose) or "insulin resist*" (299286) or "non insulin dependent diabetes mellitus"/exp/mj (114,465) or "glucose intolerance"/exp (15202) or "impaired glucose tolerance"/exp (25437) or "Insulin Resistance"/exp (105156)
#10= #7 OR #8 OR #9 (316307)	"systematic review" or "meta-analysis" or metaanalysis (316307) or "Systematic review (topic)"/exp (21222) or "Systematic review "/exp (150479)
#14= #11 OR #12 OR #13 (1061023)	Hypercholesterolemia or Hypercholesterolaemia or cholesterol level* N3 high or raised or elevated (795712) or 'cholesterol'/exp (279149) or 'hypercholesterolemia'/exp/mj (26337)
#15 = #6 AND #10 AND #14	1568
#15 Limiters - English Language	1531
#15 Limiters - Date of Publication: 2011-2016; English Language	1007

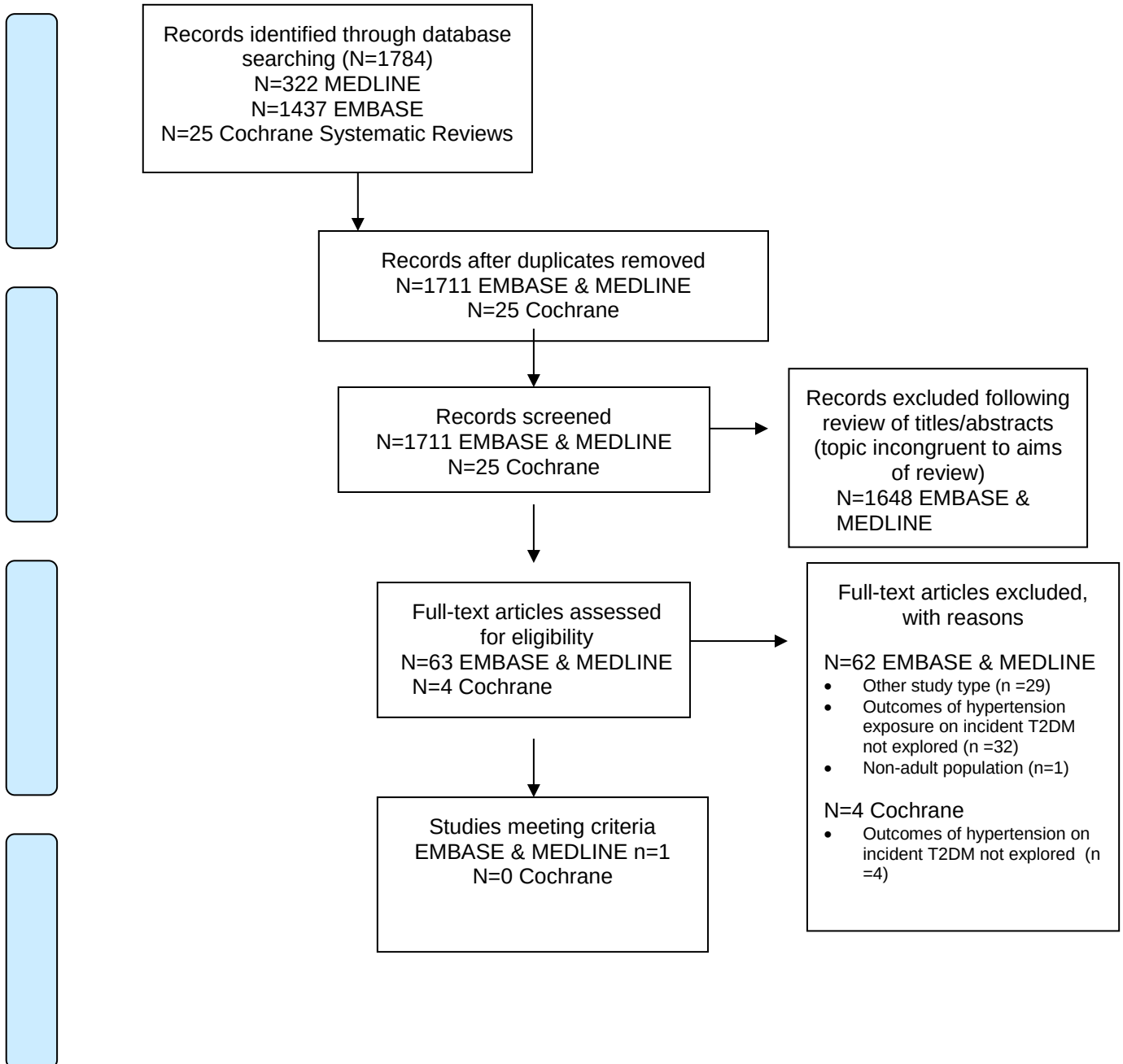
DATABASE	Cochrane Library
Date:	
Strategy	#4 AND #7
	Search
#4 = #1 OR #2 OR #3 (12747)	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees (11939) OR MeSH descriptor: [Glucose Intolerance] explode all trees (618) OR "prediabetes":ti,ab,kw (Word variations have been searched) (605)
#7 = #5 OR #6 (12747)	MeSH descriptor: [cholesterol] explode all trees (9743) OR MeSH descriptor: [hypercholesterolemia] explode all trees (2730)
#4 AND #7*	1234 Of these Cochrane reviews = 6 Other reviews = 25 Trials = 1193 Economic evaluations = 10

*No limits on search employed

Appendix 10: PRISMA flow diagram: modifiable risk factors for T2DM

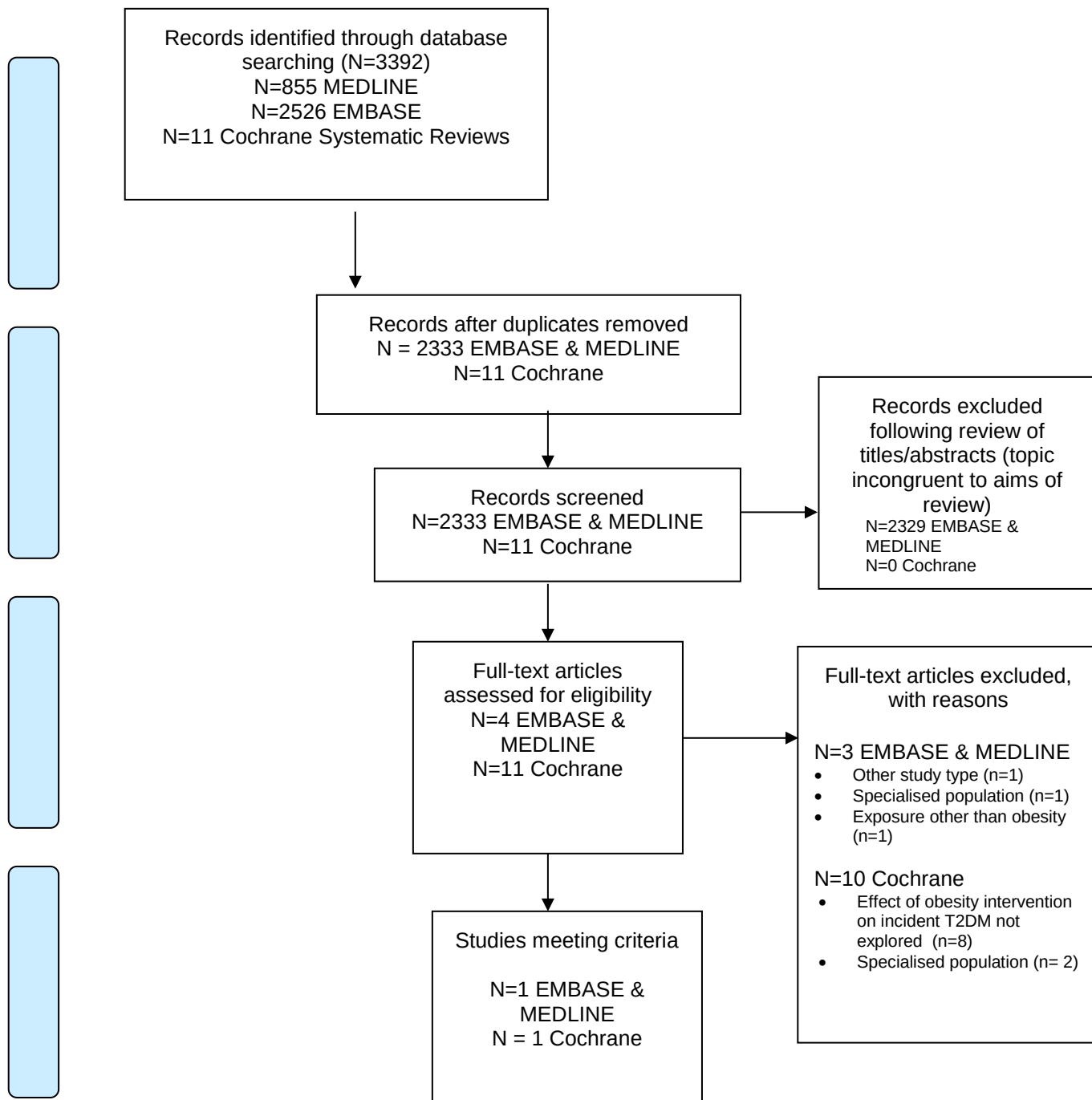


PRISMA 2009 Flow Diagram: Hypertension as a risk factor for T2DM



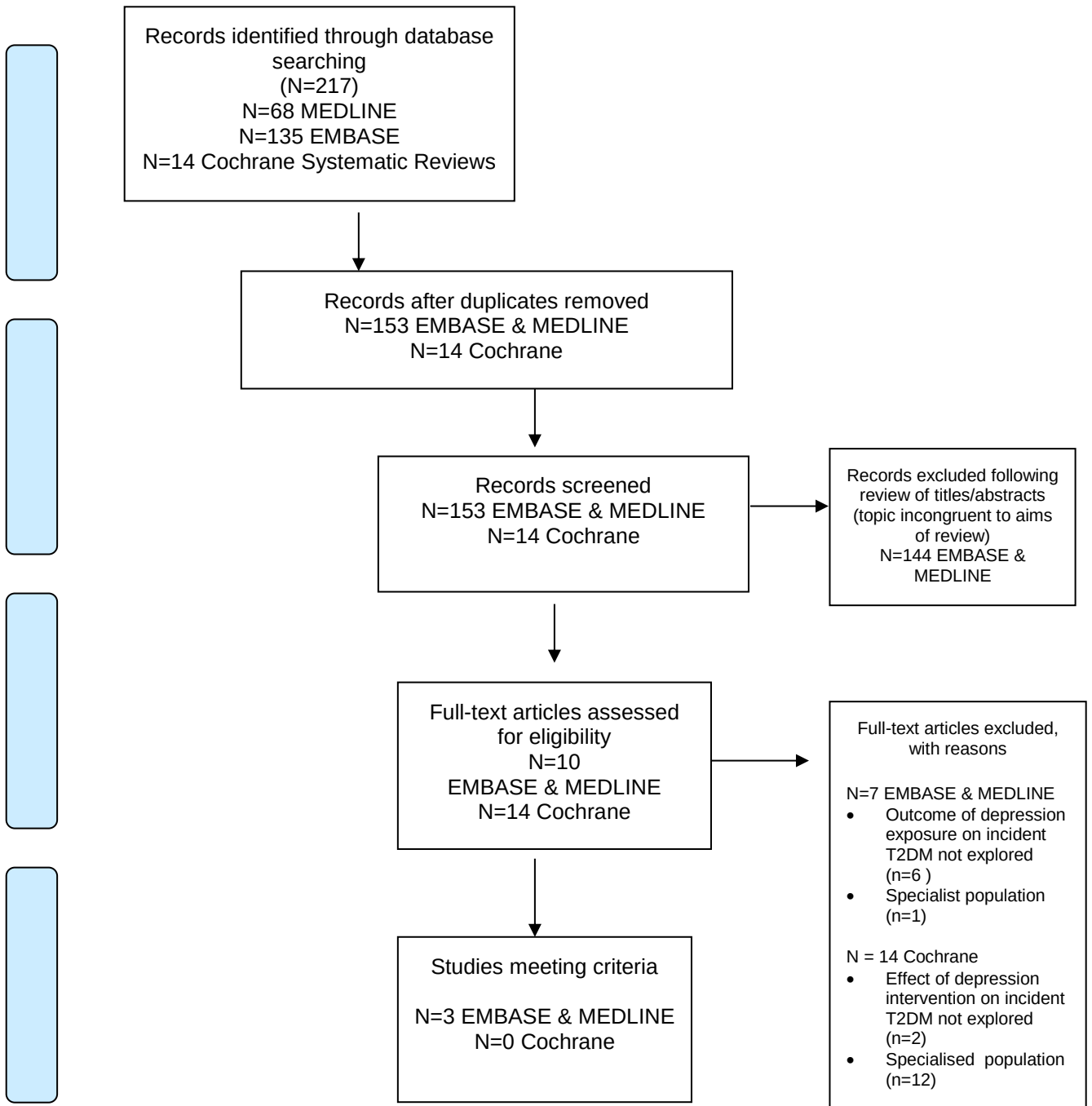


PRISMA 2009 Flow Diagram: Obesity as a risk factor for T2DM



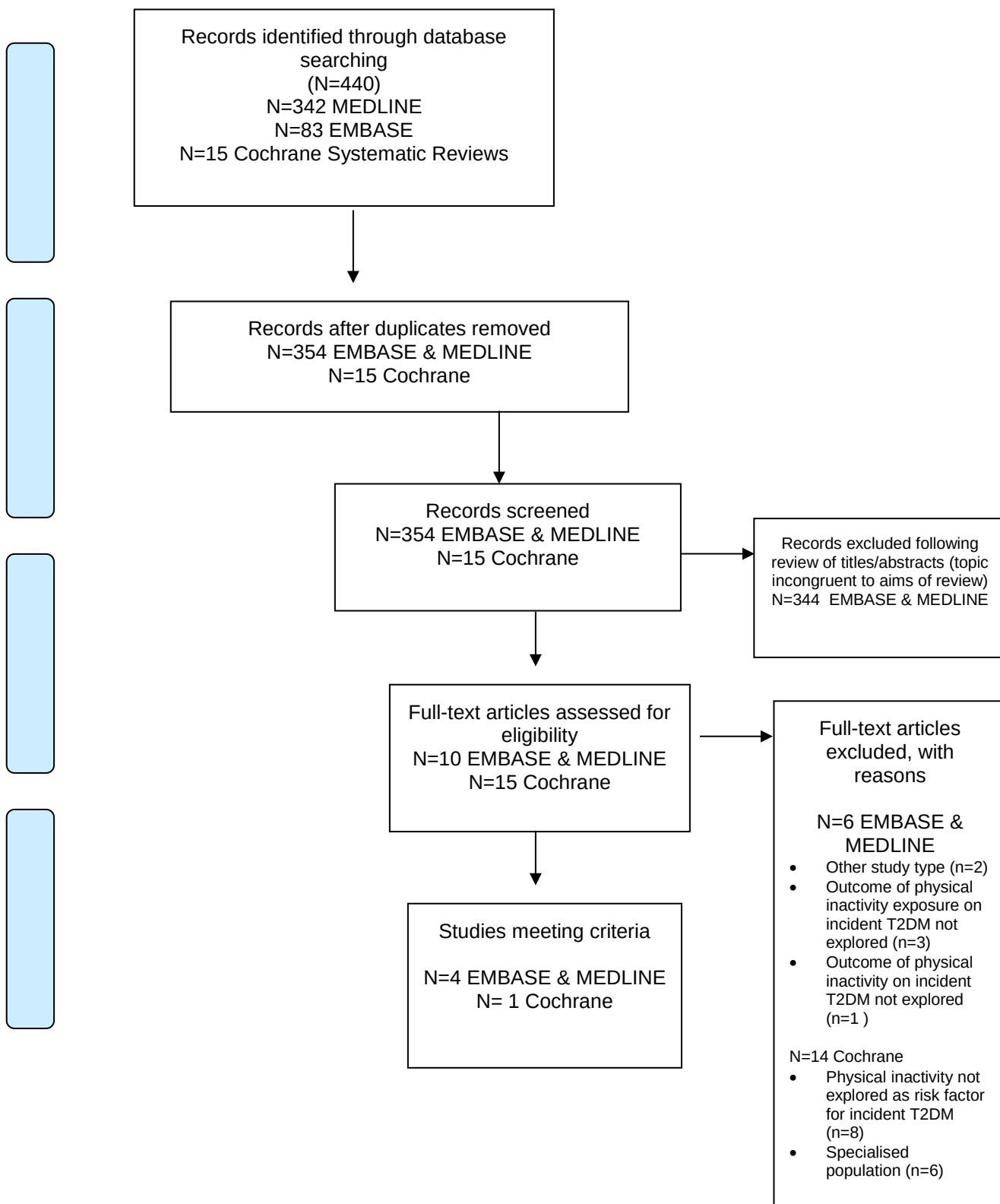


PRISMA 2009 Flow Diagram: Depression as a risk factor for T2DM



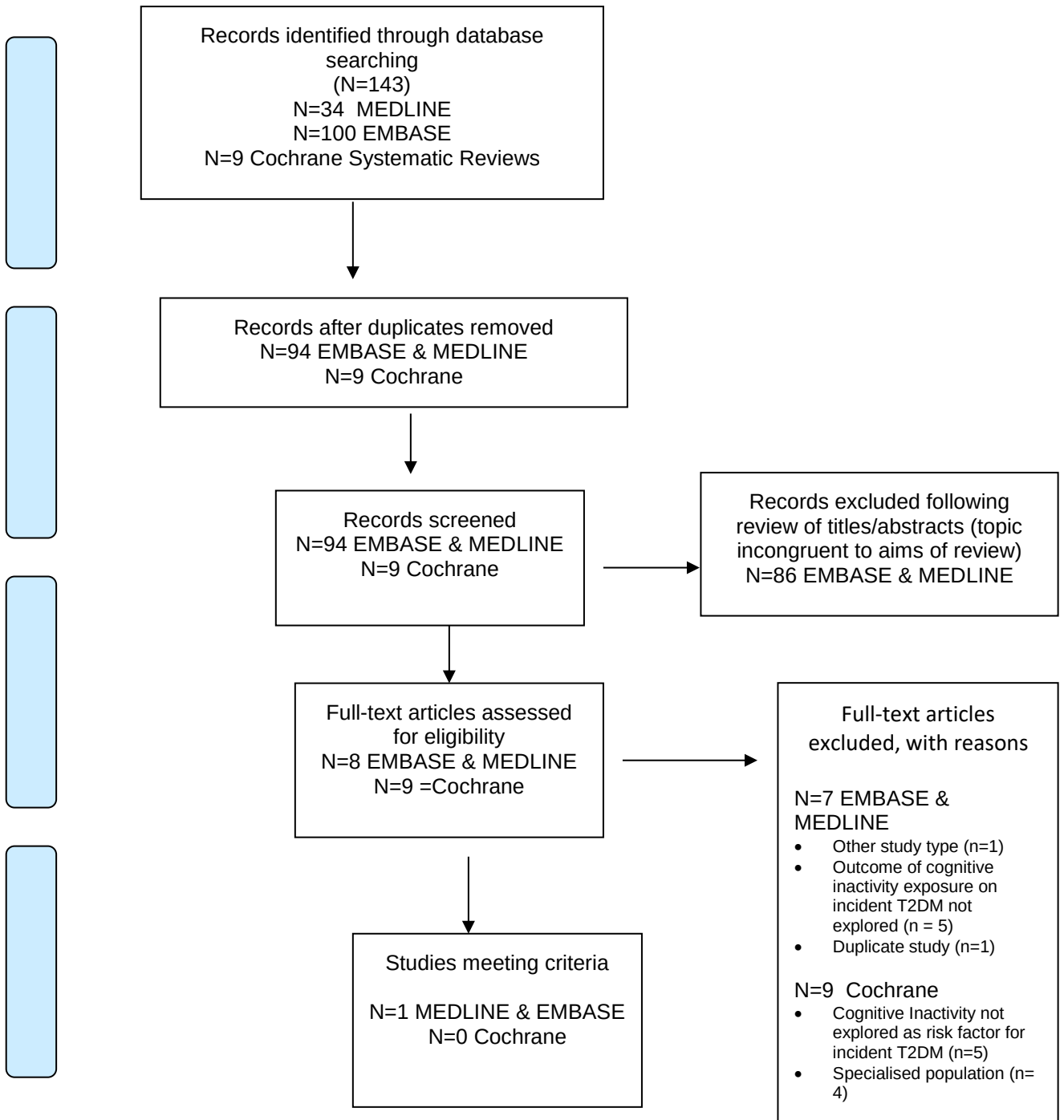


PRISMA 2009 Flow Diagram: Physical Inactivity as a risk factor for T2DM



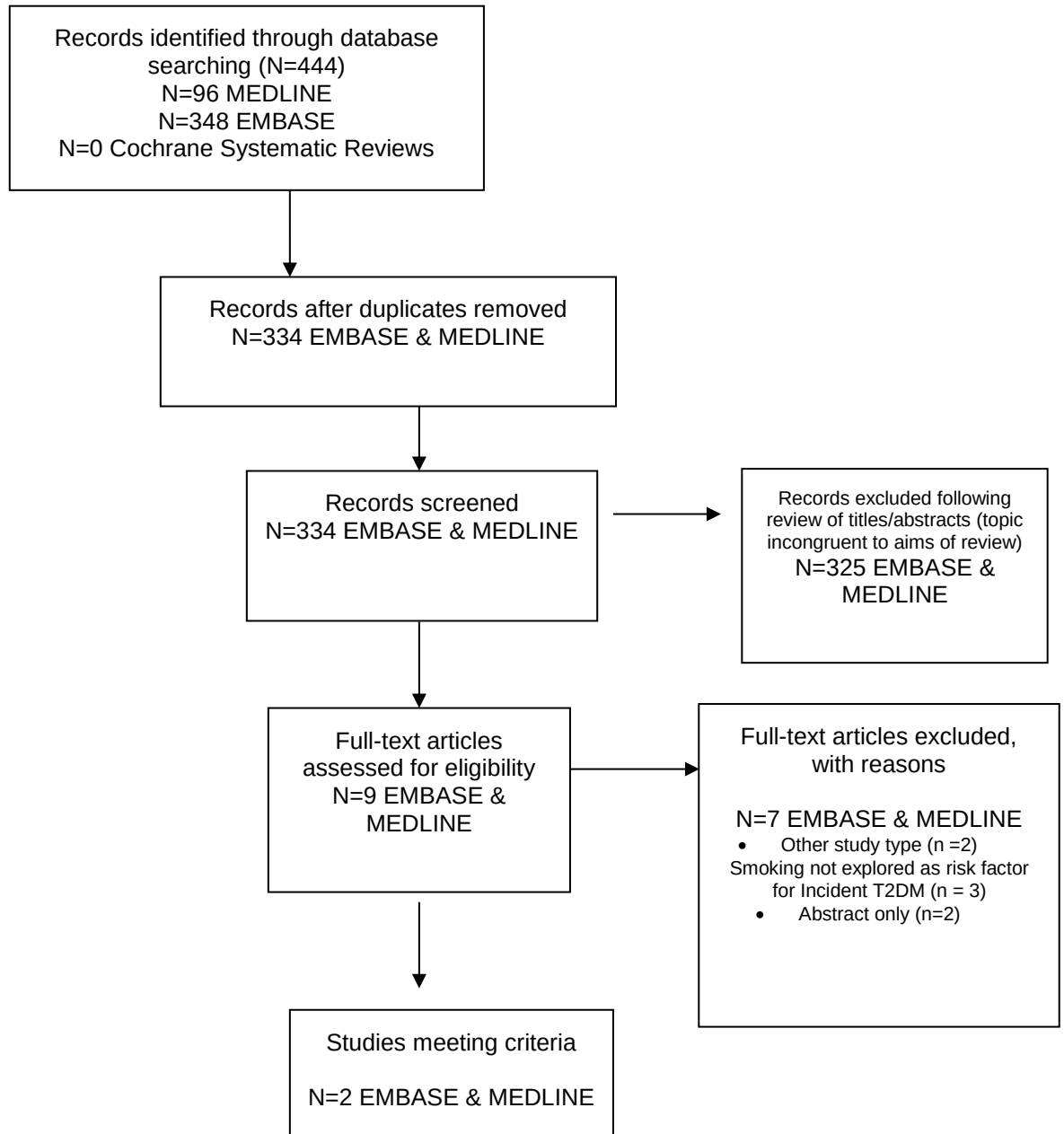


PRISMA 2009 Flow Diagram: Cognitive inactivity as a risk factor for T2DM



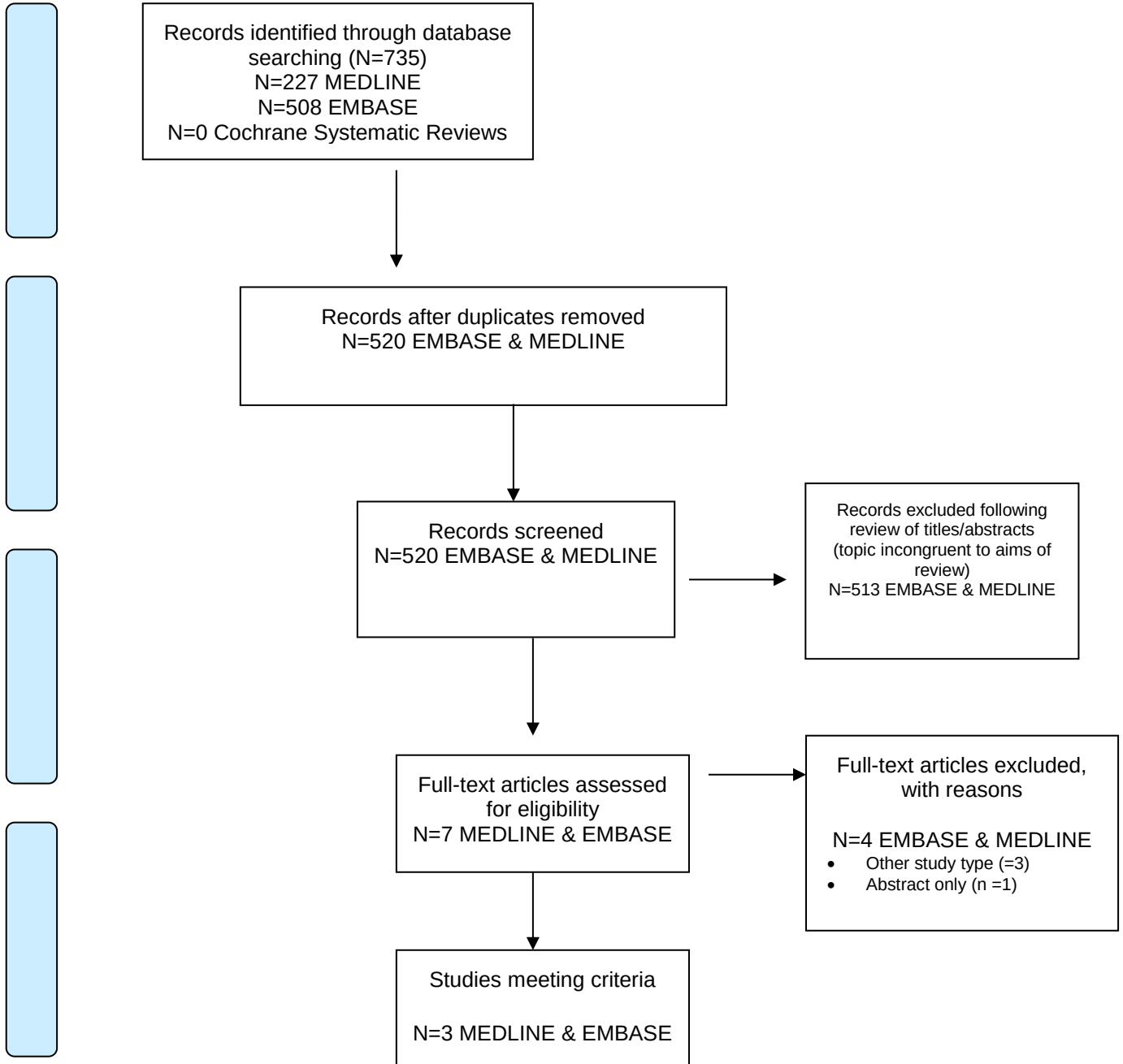


PRISMA 2009 Flow Diagram: Smoking as a risk factor for T2DM



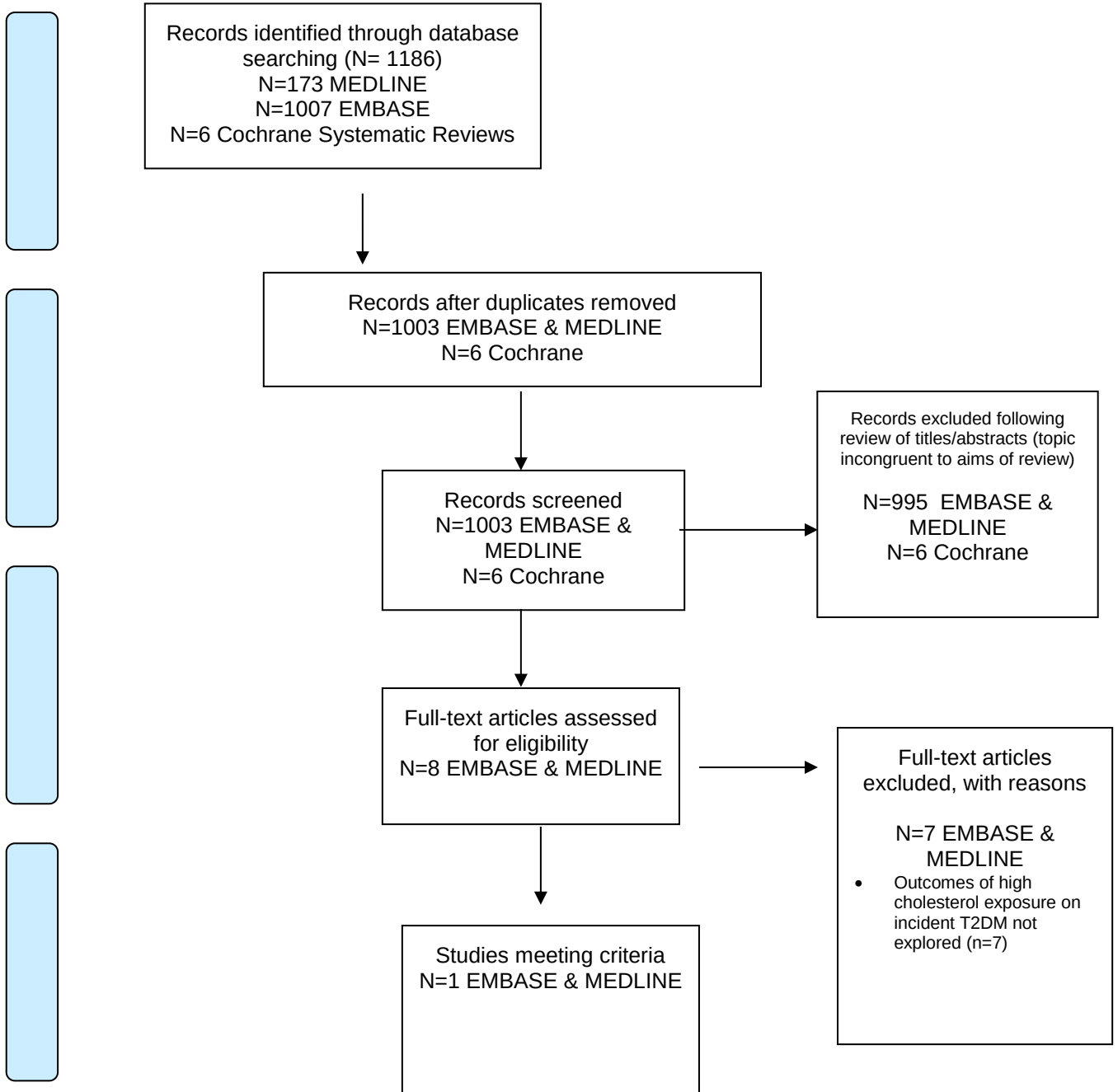


PRISMA 2009 Flow Diagram: Heavy alcohol use as a risk factor for T2DM





PRISMA 2009 Flow Diagram: High cholesterol as a risk factor for T2DM



Appendix 11: Short listed studies with full text review: modifiable risk factors for T2DM

i) Hypertension as a risk factor for T2DM

Meta-analysis of prospective cohort studies

	Study (Author, year)	Study design characteristics	Population characteristics	Systematic review characteristics	Incident diabetes as outcome measured	Exposure characteristics	Statistical findings	Inclusion in qualitative synthesis
1	Emdine¹ (2015) [114]	Meta-analysis of prospective studies and data from a cohort study examining the association between usual blood pressure and new onset diabetes.	Systematic review: general adult population without CVD or diabetes at baseline. Cohort: 4.1 million adults, free of diabetes and cardiovascular disease. Median age 46 years (range 30-90 years) 55.9% female.	30 prospective studies included with 285,664 participants and 17,388 incident diabetes events. At least 1 year follow up.	Yes	20mm Hg higher than usual systolic blood pressure (SBP)	Overall cohort: 20 mmHg higher SBP hazard ratio (HR) = 1.58; 95% confidence interval [CI]: 1.56 to 1.59; Systematic review: pooled relative risk (RR) of diabetes for a 20 mm Hg higher usual SBP across these studies 1.77 (1.53 to 2.05).	Included in qualitative synthesis

ii) Obesity as a risk factor for T2DM

Meta-analysis of prospective cohort studies

	Study (Author, year)	Study design characteristics	Population characteristics	Systematic review/review characteristics	Incident diabetes as outcome measured	Exposure characteristics	Statistical findings	Inclusion in qualitative synthesis
1	Cloostermans (2015) [115]	Meta-analysis of prospective cohort studies exploring independent and combined effects of physical activity (PA) and BMI on incident T2DM	General adult population, 56.2% female, mean age 50 years.	9 prospective cohort studies, 117, 878 participants, 11 237 incident T2DM cases. Mean follow up 9.1 years.	Yes	Measures of PA were based on leisure time physical activities and active commuting and minutes per week spent in low, medium and high physical activity were categorized	Overweight and obese (v normal weight) in adjusted model was associated with increased risk of incident T2DM - HR 2.33 (95% CI 1.95 – 2.78) and HR 6.10 (95% CI 4.63 – 8.04).	Included in qualitative synthesis:

The Cochrane Database of Systematic Reviews

	Study (Author, year)	Population characteristics	Systematic review/review characteristics	Incident diabetes as outcome measured	Intervention characteristics	Statistical findings	Inclusion in qualitative synthesis
1	Norris (2005) [116]	5,168 adult participants with prediabetes in both control and intervention group.	9 RCTs – 1-10 years follow up	Yes – examined in 5 studies (3-6 years follow up)	Long term pharmacological weight loss interventions – weight loss or weight control as primary stated goal via dietary, physical activity or behavioural strategies	Results of 5 studies exploring effect on incident diabetes not pooled but incidence of T2DM was significantly lower in the intervention groups versus the controls.	Included in qualitative synthesis:

iii) Depression as a risk factor for T2DM

Meta-analysis of prospective cohort studies

	Study (Author, year)	Study design characteristics	Population characteristics	Systematic review/review characteristics	Incident diabetes as outcome measured	Exposure characteristics	Statistical Findings	Inclusion in qualitative synthesis
1	Yu¹ (2015)	A systematic review and meta-analysis of a cross-sectional, case-control or cohort studies to assess the association of depression with the risk for developing diabetes.	General adult population	33 studies – (7 cross-sectional, 2 nest case-control and 24 cohort studies) included in the meta-analysis. 2 411 641 participants (3-34 years follow up)	Yes	Depression diagnosis based on screening tool/self-administered questionnaire/medication use/interview/self-report	Pooled RR for diabetes was 1.41 (95% CI, 1.25-1.59) for depression, and the combined RR for T2DM mellitus was 1.32 (95% CI, 1.18-1.47).	No: Cross-sectional studies included
2	Hasan (2014) [117]	A systematic review and meta-analysis of longitudinal studies examining the incidence and risk of diabetes associated with depressive symptoms	General adult population. Range of female participants 0 – 100%.	16 studies included. 208,205 participants, 9,833 incident cases of diabetes. Follow up period range 3 – 16 years.	Yes	Depression diagnosis based on assessment by psychiatrist. (DSM criteria) Depressive symptoms assessed by self-administered questionnaire.	Both RR and HR were significant at 1.67 (95% CI: 1.30–2.15) and 1.45 (95% CI: 1.12–1.87) for incident diabetes associated with depressive symptoms.	Included – most up to date
3	Hasan² (2013)	A systematic review and meta-analysis of longitudinal studies examining the reciprocal relationship between depression and T2DM	General adult population	25 studies - 15 examined depression as a risk factor for T2DM	Yes	Depression diagnosis based on assessment by psychiatrist. (DSM criteria) Depressive symptoms assessed by self-administered questionnaire.	Of 15 studies examining relationship between adults with depression and incident T2DM there was a 1.41 pooled RR and 1.24 pooled HR for T2DM	No

References

1. Yu M, Zhang X, Lu F, Fang L. Depression and Risk for Diabetes: A Meta-Analysis. Can J Diabetes. 2015 Mar 13;
2. Hasan SS, Clavarino AM, Mamun AA, Doi SAR, Kairuz T. Population impact of depression either as a risk factor or consequence of type 2 diabetes in adults: a meta-analysis of longitudinal studies. Asian Journal Of Psychiatry. 2013 Dec;6(6):460–72.

iv) Physical inactivity as a risk factor for T2DM

Meta-analysis of prospective cohort studies

	Study (Author, year)	Study design characteristics	Population characteristics	Systematic review/review characteristics	Incident diabetes as outcome measured	Exposure characteristics	Statistical Findings	Inclusion in qualitative synthesis
1	Cloostermans (2015) [115]	A systematic review and meta-analysis to examine the independent and combined effects of physical activity and BMI on the incidence of T2DM	General adult population - >50 % Caucasian sample. 56.2 % female, mean age 50 years (range 25–65 years).	9 prospective cohort studies included, 117,878 participants, 11,237 incident T2DM cases. Mean follow-up 9.1 years.	Yes	Physical activity included leisure time and active commuting with an indication of frequency, duration and intensity	Increased risk of T2DM if low physical activity compared with high physical activity HR 1.23, (95 % CI: 1.09–1.39,).	Less studies included and less recent than Smith et al 2016
2	Zaccardi¹ (2015)	Cohort study and a meta-analysis of prospective studies examining association between cardiorespiratory fitness (CRF) and risk of T2DM	Cohort: middle-age Finnish men	1.Cohort: population-based sample of 2520 subject with 153 incident T2DM cases 2. Seven studies included in meta-analysis 92,992 participants and 8,564 incident T2DM events	Yes	CRF assessed using respiratory gas exchange analyser	Adjusted HR per 1-MET higher CRF, was 0.93 (95% confidence interval (CI): 0.84, 1.02; p . 0.109); Meta-analysis: pooled risk ratio of T2DM per 1-MET higher CRF level was 0.95 (95% CI: 0.93, 0.98;p . 0.003)	Less studies included and less recent than Smith et al 2016
3	Aune² (2015)	A systematic review and meta-analysis of published studies investigating the association between specific types of physical activity (sum of leisure-time, occupational, and transport activity) and risk of T2DM	General adult population	14 cohort studies including 18,276 cases and 104,908 participants	Yes		Summary RR for high versus low total activity was 0.65 (95 % CI 0.59–0.71) – decreased risk of developing T2DM	Less studies and less recent than Smith et al 2016
4	Smith³ (2016) [118]	A systematic review and dose–response meta-analysis of prospective cohort studies on the association between physical activity and T2DM	General adult population	28 eligible cohort studies included 1,261,991 individuals. 84,134 incident cases of T2DM. Follow-up 3 –23 years.	Yes	Physical activity dose in metabolic equivalent of task (MET) hours/week	RR for T2DM for every 10 MET h/week exposure of physical activity 0.87 (0.84-0.89)	Included in qualitative synthesis

References

1. Zaccardi F, O'Donovan G, Webb DR, Yates T, Kurl S, Khunti K, et al. Cardiorespiratory fitness and risk of type 2 diabetes mellitus: A 23-year cohort study and a meta-analysis of prospective studies. *Atherosclerosis*. 2015 Nov;243(1):13
2. Aune D, Norat T, Leitzmann M, Tonstad S, Vatten LJ. Physical activity and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis. *Eur J Epidemiol*. 2015 Jul;30(7):529–42.

The Cochrane Database of Systematic Reviews

	Study (Author, year)	Population characteristics	Systematic review/review characteristics	Incident diabetes as outcome measured	Intervention characteristics	Statistical findings	Inclusion in qualitative synthesis
1	Orozco (2008) [119]	5,095 adult participants at risk for T2DM in control and intervention group.	10 RCTs – 1-6 years follow up	Yes	8 trials had exercise plus diet and a standard recommendation arm. Two studies had a diet only and exercise only arm	Overall, exercise plus diet interventions reduced the risk of diabetes compared with standard recommendations (RR 0.63, 95% CI 0.49 to 0.79). No statistical effects were observed when comparing exercise only interventions with standard recommendations or diet only interventions.	Included in qualitative synthesis

v) Cognitive inactivity as a risk factor for T2DM

Meta-analysis of prospective cohort studies

	Study (Author, year)	Study design characteristics	Population characteristics	Systematic review/review characteristics	Incident diabetes as outcome measured	Exposure characteristics	Statistical Findings	Inclusion in qualitative synthesis
1	Agardh (2011) [120]	Systematic review and meta-analysis of case-control and cohort studies on associations between T2DM incidence and socio-economic position (SEP) worldwide	General adult population in high-, middle- and low-income countries	23 studies included – case-control and cohort studies	Yes	Socio-economic position (SEP) measured by educational level, occupation and income	Compared with high educational level, occupation and income, low levels of these determinants were associated with an overall increased risk of T2DM overall.; RR 1.41 95% CI [1.28–1.51], RR.1.31 95% CI [1.09–1.57] and RR.1.40 95% CI [1.04–1.88] respectively.	Included in qualitative synthesis – although case-control studies included

vi) Smoking as a risk factor for T2DM

Meta-analysis of prospective cohort studies

	Study (Author, year)	Study design characteristics	Population characteristics	Systematic review/review characteristics	Incident diabetes as outcome measured	Exposure characteristics	Statistical Findings	Exclusion reason
1	Laaksonen et al.,¹ (2011)	Systematic review and meta-analysis on the relative importance of lifestyle factors on T2DM incidence in those with and without metabolic syndrome (MetS).	2 general adult population Finnish cohorts - aged 40-79 years, free of diabetes and CVD at baseline	2 Finnish cohorts, 8627 individuals. 226 incident T2DM cases, 10- year follow-up	Yes	Participants self-reported smoking status	Pooled RR of incident T2DM in current smoker was 4.34 (95% CI 2.29 – 8.22) for 30 cigarettes or over/day and for less than 30 per day RR 1.29 (95% CI 0.88 - 1.90)	No: Larger number of studies and participants in study by Pan et al
2	Pan et al. (2015) [121]	Systematic review & meta-analysis of prospective studies assessing relation of various smoking behaviours and smoking risk to T2DM incidence.	General adult population. Majority of studies conducted in European countries	88 prospective studies included - 6 million participants, 295,446 incident cases of diabetes. Median follow 9 years	Yes	Never, past and current smoking status, passive smoking, number of cigarettes per day and years since quitting smoking -self reported in all studies but 1	Compared with never smoking pooled RR of T2DM was 1.37 (1.33 – 1.42) for current smoking (84 studies) , 1.14 (1.10-1.18) for former smoking (47 studies) and 1.22 (1.10-1.35) for passive smoking (7 studies). RR 1.21 (1.10 - 1.33) for light smokers and RR 1.57 (1.47 – 1.66) for heavy smokers compared with never smokers	Included in qualitative synthesis

References

1. The relative importance of modifiable risk factors of type 2 diabetes in high- and low-risk populations: Meta-analysis of two cohort studies. Laaksonen M.A. Journal of Diabetes

vii) High Cholesterol as a risk factor for T2DM

Meta-analysis of prospective cohort studies

	Study (Author, year)	Study design characteristics	Population characteristics	Systematic review/review characteristics	Incident diabetes as outcome measured	Exposure characteristics	Statistical Findings	Inclusion/exclusion in qualitative synthesis
1	Tajima et al. (2014) [122]	A meta-analysis of observational longitudinal studies that provided data on the relative risk (RR) for T2D in relation to cholesterol intake	General adult population – studies conducted in the U.S	5 studies total of 203,903 participants and 7589 incident cases of T2DM. Mean follow-up duration 8.8 - 14 years.	Yes – laboratory/self report/medication inventory	Dietary cholesterol intake assessed by valid food frequency questionnaires	Compared with the lowest category, the highest category of cholesterol consumption had a significantly higher association with T2DM risk (RR [95% confidence interval (CI)], 1.25 [1.16-1.36]). The pooled RR for a 100-mg/day increment was also significant (RR [95% CI], 1.11 [1.06-1.15])	Included in qualitative synthesis

viii) Heavy alcohol as a risk factor for T2DM

Meta-analysis of prospective cohort studies

	Study (Author, year)	Study design characteristics	Population characteristics	Systematic review/review characteristics	Incident diabetes as outcome measured	Exposure characteristics	Statistical Findings
1	Knott et al (2015) [123]	Systematic review and meta-analysis of cohort, case-cohort, case-control and nested case-control studies examining an association between alcohol consumption and the risk of T2DM.	Community and occupational data sets considered. Adults aged 16 years or over – 43% female.	38 cohort studies included – 33 non current drinking category and 5 never-drinking category. Participant total was 1,902,605 with 125956 incident cases T2DM	Yes	Self-reported alcohol consumption	Relative to combined abstainers, reductions in the risk of T2DM were present at all levels of alcohol intake <63 g/day, with risks increasing above this threshold. Peak risk reduction was present between 10–14 g/day at an 18% decrease in hazards.
2	Laaksonen ¹	Systematic review and meta-analysis on	Two general adult	2 Finnish cohorts, 8627 individuals.	Yes		Pooled RR of incident T2DM for

	Study (Author, year)	Study design characteristics	Population characteristics	Systematic review/review characteristics	Incident diabetes as outcome measured	Exposure characteristics	Statistical Findings
	(2011)	the relative importance of lifestyle factors on T2DM incidence in those with and without metabolic syndrome (MetS).	population Finnish cohorts- aged 40-79 years, and free of diabetes and CVD	226 incident T2DM cases during a 10- year follow-up			heavy alcohol consumption was 1.03 (95% CI 0.66– 1.63). Alcohol consumption predicted T2DM (PAF = 3%, 95% confidence interval (CI): -2%, 7%)
3	Li ² (2016)	Meta-analysis of prospective observational studies that evaluated the relation between alcohol consumption and the risk of T2DM	General adult population	26 prospective observational studies included. 706,716 individuals with 31,621 T2D cases.	Yes		Compared with the minimal category of alcohol consumption, light (RR: 0.83; 95% CI: 0.73, 0.95; P = 0.005) and moderate (RR: 0.74; 95% CI: 0.67, 0.82; P , 0.001) alcohol consumption was associated with a lower risk of T2D. However, heavy alcohol consumption had little or no effect on subsequent T2D risk.

References

1. The relative importance of modifiable risk factors of type 2 diabetes in high- and low-risk populations: Meta-analysis of two cohort studies. Laaksonen M.A. 2011. Journal of Diabetes
2. Association between alcohol consumption and the risk of incident type 2 diabetes: a systematic review and dose-response meta-analysis. Li. 2016. The American Journal Of Clinical Nutrition

Appendix 12: Delphi Questionnaire: Round 1

Health and Diabetes

STUDY INFORMATION

Thank you for agreeing to participate in this Delphi study, concerned with getting agreement on what experts consider to be the correct answers to questions regarding risk factors for type 2 diabetes mellitus, and complications of diabetes. This Delphi study is concerned with getting agreement from an expert panel on this subject, as definite evidence from the literature is inconsistent. We plan to use results of this Delphi study to develop a valid and reliable Brain Health and Diabetes Knowledge measure designed for use among individuals with diabetes and members of the general public.

This questionnaire is divided into three sections:

Section 1 presents a series of background questions, which will provide a context for analysing your responses.

Section 2 presents statements regarding risk factors for type 2 diabetes mellitus.

Section 3 presents statements regarding potential complications of diabetes mellitus (type 1 and type 2).

You are asked to consider each statement and indicate your level of agreement varying from strongly disagree to strongly agree. For example, if you think there is significant evidence showing high blood pressure is a risk factor for diabetes you could agree or strongly agree with this statement. Alternatively, if you think there is little evidence that high blood pressure is a risk factor for diabetes you could disagree or strongly disagree with this statement.

Please return your completed questionnaire within 3 weeks of receipt of the accompanying email. You will receive the results from this questionnaire at Round 2 of the study when you will be asked to reconsider your answers based on consensus opinion. Responses of individual participants will be confidential and will not be disclosed to other panel members.

Thank you for your time and assistance.

Dr. Catherine Dolan, Specialist Registrar in Old Age Psychiatry, Trinity College Dublin

Dr. Ronan Glynn, Specialist Registrar in Public Health and Epidemiology, Trinity College Dublin

Professor Brian Lawlor, Consultant and Professor in Old Age Psychiatry, Trinity College Dublin

SECTION 1: BACKGROUND INFORMATION

1. What is your name?

2. What is your area of professional expertise?

Other (please specify)

SECTION 2: TYPE 2 DIABETES AND ASSOCIATED RISK FACTORS

Below is the question, worded as we plan to use it in our final questionnaire, which aims to establish participant knowledge of risk factors for developing type 2 diabetes mellitus. We ask that you indicate how strongly you disagree or agree with each statement. We would also be grateful for your opinion and thoughts on the wording of the question and accompanying statements, as well as suggestions for additional risk factors, which we may have omitted. We have left a text box at the end of each section for your comments.

Question

'A risk factor is something that **INCREASES** a persons chance of developing **DIABETES**. Could you tell me whether you believe the following statements to be true or false?'

3. High blood pressure is a risk factor for diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐☐☐☐☐

4. High cholesterol is a risk factor for diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐☐☐☐☐

5. Physical inactivity (low exercise levels) is a risk factor for diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐☐☐☐☐

6. Heavy consumption of alcohol is a risk factor for diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐☐☐☐☐

7. Not keeping your mind active is a risk factor for diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐☐☐☐☐

8. A poor level of engagement in social/leisure activities is a risk factor for diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐☐☐☐☐

9. Getting older is a risk factor for diabetes

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

10. Being obese or overweight is a risk factor for diabetes

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

11. A family history of diabetes is a risk factor for diabetes

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

12. Being a smoker is a risk factor for diabetes

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

13. Frequent exposure to strong sunlight is a risk factor for diabetes

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

14. A past or present diagnosis of depression is a risk factor for diabetes

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

15. Are there any additional risk factor for diabetes which you feel should be included?

Yes	No
☐	☐

16. If yes, please identify those risk factors now, indicating why you feel they should be included.

17. If you have any suggestions for re-phrasing of the above question, or accompanying statements, please give details in the comment box below

SECTION 3: COMPLICATIONS OF DIABETES

Below is the question, worded as we plan to use it in our final questionnaire, which aims to establish participant knowledge of the potential complications of type 1 and type 2 diabetes mellitus. We ask that you indicate how strongly you agree or disagree with each statement. We have left a text box for comments should you wish to add to it. We would be grateful for your opinion and thoughts on the wording of the question and accompanying statements.

Question

'A complication is a health problem that can occur because of having DIABETES. Could you tell me whether you believe the following statements to be true or false?'

18. Kidney damage is a potential complication of diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐	☐	☐	☐	☐
-----------------------	-----------------------	-----------------------	-----------------------	-----------------------

19. Memory problems are a potential complication of diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐	☐	☐	☐	☐
-----------------------	-----------------------	-----------------------	-----------------------	-----------------------

20. Leg ulcers are a potential complication of diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐	☐	☐	☐	☐
-----------------------	-----------------------	-----------------------	-----------------------	-----------------------

21. Multiple sclerosis is a potential complication of diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐	☐	☐	☐	☐
-----------------------	-----------------------	-----------------------	-----------------------	-----------------------

22. Breathing problems are a potential complication of diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐	☐	☐	☐	☐
-----------------------	-----------------------	-----------------------	-----------------------	-----------------------

23. Depression is a potential complication of diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐	☐	☐	☐	☐
-----------------------	-----------------------	-----------------------	-----------------------	-----------------------

24. Damage to the back of the eye is a potential complication of diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐ ☐ ☐ ☐ ☐

25. A lack of feeling or tingling in legs or feet due to nerve damage is a potential complication of diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐ ☐ ☐ ☐ ☐

26. Lung cancer is a potential complication of diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐ ☐ ☐ ☐ ☐

27. Dementia is a potential complication of diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐ ☐ ☐ ☐ ☐

28. Stroke is a potential complication of diabetes

Strongly disagree

Disagree

Don't know

Agree

Strongly agree

☐ ☐ ☐ ☐ ☐

29. Are there any additional complications of diabetes which you feel should be included?

Yes

No

☐ ☐

30. If yes, please identify those complications now, indicating why you feel they should be included.

31. If you have any suggestions for re-phrasing of the above question, or accompanying statements, please give details in the comment box below.

EXPERT PANEL MEMBERSHIP IDENTIFICATION

32. Would you be willing to be identified as a member of the expert panel in future publications?

(NB individual panel members responses will remain confidential and known only to the lead researcher)

☐ Yes

☐ No

Thank you for participating in the Delphi study, which was set up to assist with the development of a questionnaire to assess knowledge levels of modifiable risk factors for type 2 diabetes mellitus, and complications of diabetes among individuals with diabetes and the general public.

Appendix 13: Delphi Questionnaire: Round 2

Round Two: Brain Health and Diabetes Delphi Study

ROUND TWO STUDY INFORMATION

Thank you for participating in Round Two of this Delphi study. You will recall the purpose of this study is to establish consensus on risk factors for type 2 diabetes (T2DM), and potential complications of diabetes mellitus with the help of an expert panel. Consensus was reached on a number of risk factors and complications following Round One of this Delphi study, as outlined in the Round Two invitation email.

However, there were a number of items in the Round One questionnaire which did not achieve panel agreement of 70% or more. Results from Round One questionnaire have been included in this updated questionnaire for these items.

In this questionnaire you will be asked to:

- 1) Reflect on the group response in Round One to a number of diabetes risk factor and complication items, on which expert panel members did not achieve a consensus. You have also been provided with a summary of your own responses in Round One in the invitation email. Following consideration please indicate your level of agreement, varying from strongly disagree to strongly agree, with each of these items.**
- 2) Indicate whether you agree with updated wording of a number of questionnaire items driven by expert panelists suggestions in Round One.**
- 3) Indicate your agreement with new risk factor and complication items proposed by expert panel members during Round One of the Delphi study.**

Please return your completed questionnaire within 3 weeks of receipt of the accompanying email.

Once again, responses of individual participants will be confidential and will not be disclosed to other panel members.

Thank you for your time and assistance.

**Dr. Catherine Dolan, Specialist Registrar in Old Age Psychiatry, Trinity College Dublin
Dr. Ronan Glynn, Specialist Registrar in Public Health and Epidemiology, Trinity College Dublin
Professor Brian Lawlor, Consultant and Professor in Old Age Psychiatry, Trinity College Dublin**

SECTION 1: BACKGROUND INFORMATION

1. What is your name?

Round Two: Brain Health and Diabetes Delphi Study

SECTION 2: RISK FACTOR STATEMENTS WITH LESS THAN 70% EXPERT AGREEMENT IN ROUND ONE

In this section five T2DM risk factor items which did not reach consensus in Round One are presented to the expert panel once again. The Round One expert group response is outlined, which we ask you consider before indicating your level of agreement with the Round Two item. The wording of Round Two items (question and statement) are updated based on expert panel suggestions in the first round.

2.

Round One

'A risk factor is something that INCREASES a persons chance of developing DIABETES. Could you tell me whether you believe the following statements to be true or false?'

'High blood pressure is a risk factor for diabetes'

Strongly disagree	Disagree	Don't know	Agree	Strongly Agree
0% (n=0)	50% (n=7)	7.1% (n=1)	35.7% (n=5)	7.1% (n=1)

Round Two

'Several risk factors have been associated with TYPE 2 DIABETES. Could you tell me whether you believe the following to be true or false?'

'T2DM is more common in individuals with high blood pressure (hypertension)'

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

3. Round One

'A risk factor is something that INCREASES a persons chance of developing DIABETES. Could you tell me whether you believe the following statements to be true or false?'

'A past or present diagnosis of depression is a risk factor for diabetes'

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
7.1% (n=1)	42.9% (n=6)	14.3% (n=2)	21.4% (n=3)	14.4% (n=2)

Round Two

'Several risk factors have been associated with TYPE 2 DIABETES. Could you tell me whether you believe the following to be true or false?'

'T2DM is more common in individuals with a history of depression'

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

4.

Round One

'A risk factor is something that INCREASES a persons chance of developing DIABETES. Could you tell me whether you believe the following statements to be true or false?'

'High cholesterol is a risk factor for diabetes'

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
0% (n=0)	57.1% (n=8)	14.3% (n=2)	28.6% (n=4)	0% (n=0)

Round Two

'Several risk factors have been associated with TYPE 2 DIABETES. Could you tell me whether you believe the following to be true or false?'

'T2DM is more common in individuals with individuals with high cholesterol'

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

5.

Round One

'A risk factor is something that INCREASES a persons chance of developing DIABETES. Could you tell me whether you believe the following statements to be true or false?'

'Being a smoker is a risk factor for diabetes'

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
14.3% (n=2)	35.7% (n=5)	14.3% (n=2)	28.6% (n=4)	7.1% (n=1)

Round Two

'Several risk factors have been associated with TYPE 2 DIABETES. Could you tell me whether you believe the following to be true or false?'

'T2DM is more common in individuals who smoke'

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

6.

Round One

'A risk factor is something that INCREASES a persons chance of developing DIABETES. Could you tell me whether you believe the following statements to be true or false?'

'A poor level of engagement in social/leisure activities is a risk factor for diabetes'

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
21.4% (n=3)	21.4% (n=3)	28.6% (n=4)	28.6% (n=4)	0% (n=0)

Round Two

'Several risk factors have been associated with TYPE 2 DIABETES. Could you tell me whether you believe the following to be true or false?'

'T2DM is more common in individuals with a poor level of engagement in social activities'

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

7. If you have any suggestions (e.g. re-phrasing of the question, or accompanying statements) please give details in the comment box below

Round Two: Brain Health and Diabete

SECTION 3: RISK FACTORS STATEMENTS WITH EXPERT PANEL CONSENSUS IN ROUND ONE

The section outlines T2DM risk factor items from Round One on which the panel reached a consensus. These items are therefore accepted as risk factors, or not risk factors for T2DM as the case may be, for the purpose of development of a brain health and diabetes questionnaire. Of note we plan to include items in the brain health and diabetes questionnaire which are NOT risk factors for T2DM in addition to items which are risk factors for T2DM.

However, in response to suggestions made by expert panel members in Round One we have amended the wording of a number of items. We ask that you please indicate if you are satisfied with the updated wording of the items by responding 'yes'. If you are not satisfied with the updated wording please answer 'no' and kindly qualify your response in the comment box.

8. Round One statement: 100% expert panel agreement

'Physical inactivity (low exercise levels) is a risk factor for diabetes'.

Round Two updated wording:

'The risk of developing type 2 diabetes increases with lack of physical activity'

Are you satisfied with the updated statement?

☐ Yes

☐ No

Comments on wording of this question?

9. Round One statement: 71.3% expert panel disagreement

'Not keeping your mind active is a risk factor for diabetes'

Round Two updated wording:

'T2DM is more common in individuals with low levels of mental stimulation'

Are you satisfied with the updated statement?

☐

Yes

☐

No

Comments on wording of this question?

10. Round One statement: 92.9% expert panel agreement

'Getting older is a risk factor for diabetes'

Round Two updated wording:

'The risk of developing type 2 diabetes increases with age'

Are you satisfied with the updated statement?

☐

Yes

☐

No

Comments on wording of this question?

11. Round One statement: 85.8% expert panel disagreement

'T2DM is more common in individuals with frequent exposure to strong sunlight'

Round Two updated wording:

'The risk of developing type 2 diabetes increases with frequent exposure to strong sunlight'

Are you satisfied with the updated statement?

☐ Yes

☐ No

Comments on wording of this question?

12. Round One statement: 84.6% expert panel agreement

'Heavy consumption of alcohol is a risk factor for diabetes'

Round Two updated statement:

'The risk of developing type 2 diabetes increases with heavy consumption of alcohol'

Are you satisfied with the updated statement?

☐ Yes

☐ No

Comments on wording of this question?

13. Round One statement: 100% expert panel agreement

'Being obese or overweight is a risk factor for diabetes'

Round Two updated statement:

'The risk of developing type 2 diabetes increases when an individual is overweight or obese'

Are you satisfied with the updated statement?

☐ Yes

☐ No

Comments on wording of this question?

14. Round One statement: 100% expert panel agreement

'T2DM is more common in individuals with a family history of diabetes'

Round Two updated statement:

'The risk of developing type 2 diabetes increases when an individual has a family history of diabetes' Are you satisfied with the updated statement?

☐ Yes

☐ No

Comments on wording of this question?

Round Two: Brain Health and Diabetes Delphi Study

SECTION 4: ADDITIONAL RISK FACTORS SUGGESTED BY EXPERT PANEL IN
ROUND ONE OF DELPHI STUDY

This section outlines a number of risk factors for T2DM suggested by expert panel members in Round One as additional items for inclusion in a Diabetes and Brain Health questionnaire.

We ask that you indicate your level of agreement with these items in response to the question:

'Several risk factors have been associated with TYPE 2 DIABETES. Could you tell me whether you believe the following to be true or false?'

15. *'T2DM is more common in individuals with abnormal fasting blood sugar levels'*

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

16. *'T2DM is more common in individuals with a history of cardiovascular disease'*

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

17. *'T2DM is more common in individuals of a certain race or ethnicity e.g. individuals from South-East Asia'*

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

18. *'T2DM is more common in women who have had diabetes when pregnant (i.e. gestational diabetes)'*

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

19. *'T2DM is more common in individuals who were a lower than normal weight at birth'*

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

20. *'T2DM is more common in individuals who have an unhealthy diet'*

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

SECTION 5: COMPLICATION OF DIABETES NOT REACHING CONSENSUS BY
EXPERT PANEL IN ROUND ONE

Below is one complication of diabetes items from Round One, which had less than 70% expert panel agreement.

In Round Two we ask that you once again indicate how strongly you disagree or agree with the statement below following consideration of the expert group response. Group response in Round One is outlined.

In addition we have updated the wording of this complication statements in response to expert panel comments in Round One of the Delphi survey.

'A complication is a health problem that can occur because of having DIABETES. Could you tell me whether you believe the following statements to be true or false?'

21.

Round One

'Breathing problems are a potential complication of diabetes'

Strongly disagree	Disagree	Don't know	Agree	Strongly Agree
7.1%	35.7%	0%	57.14%	0%
(n=1)	(n=5)	(n=0)	(n=8)	(n=0)

Round Two with updated wording

'Pneumonia is a potential complication of diabetes'

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

22. If you have any comments on the above items please give details in the comment box below.

SECTION 6: UPDATED WORDING TO COMPLICATION STATEMENT REACHING
EXPERT PANEL CONSENSUS IN ROUND ONE

In response to suggestions made by expert panel members in Round One we have amended the wording of the item below. We ask that you please indicate if you are satisfied with the updated wording of this item by responding 'yes'. If you are not satisfied with the updated wording please answer 'no' and kindly qualify your response in the comment box.

23. Round One statement: 71.4% expert panel agreement

'Depression is a complication of diabetes'

Round Two updated statement:

'People with diabetes have a greater risk of depression than people without diabetes'

Are you satisfied with the updated statement?

☐ Yes

☐ No

Comments on wording of this question?

SECTION 7: ADDITIONAL DIABETES COMPLICATIONS SUGGESTED BY EXPERT
PANEL IN ROUND ONE

This section outlines a number of complications of diabetes suggested by expert panel members in Round One as additional items for inclusion in a Diabetes and Brain Health questionnaire.

We ask that you indicate your level of agreement with these proposed new items. Of note developing an exhaustive list of complications is not the intent of the researchers in development of a Diabetes and Brain Health questionnaire and therefore there will be a number of complication items not included.

24. *'Cardiovascular disease is a potential complication of diabetes'*

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

25. *'Erectile dysfunction is a potential complication of diabetes'*

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

26. *'Problems with attention and concentration are a potential complication of diabetes'*

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

27. *'Cataracts are a potential complication of diabetes'*

Strongly disagree	Disagree	Don't know	Agree	Strongly agree
☐	☐	☐	☐	☐

Round Two: Brain Health and Diabetes Delphi Study

Thank you once again for participating.

You will be provided with results of this Round Two of the Delphi study in the coming weeks.

Appendix 14: Diabetes and Brain Health (DBH) study participant information sheet



Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

ST. JAMES'S
HOSPITAL
DUBLIN, IRELAND



Study title: General Health Knowledge Survey

You are invited to take part in a study, by undertaking a brief questionnaire, which will take approximately 5-10 minutes to complete.

You may decide not to take part in this study, which will have no impact on your treatment as usual by your doctor.

What is the purpose of the study?

The aim of this simple study is to establish what knowledge the general public and patients have about general health. Any gaps in knowledge identified during this study will be used to improve education of patients and the public to help in prevention of common illnesses.

What will I be asked to do?

Complete a brief questionnaire with a trained interviewer, which includes questions about your background, health knowledge and lifestyle.

Your identity, and all responses received in the study will remain strictly confidential.

Why have I been invited to take part?

We plan to recruit 500 participants in total among patients attending a GP practice or hospital diabetes clinic.

Individuals will be eligible to take part in the study if you are English speaking and aged over 18.

What are the potential benefits and risks of participating in this study?

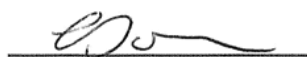
By participating in this research you are helping us identify gaps in what the general public and patients know about common health conditions. We hope results will inform educational programmes in Ireland to address prevention of common health conditions.

What do I do now?

Thank you if you have volunteered to participate in this study. This document includes information on consent to take part, which you can keep for your records. Please be aware you can withdraw from the study prior to completing the questionnaire. However, as research involves a questionnaire, withdrawal from the study once questionnaire is completed cannot be guaranteed. It is hoped the results of this study will be disseminated at appropriate research conferences, published in an academic journal and the principal researcher's thesis.

The study has St. James's Hospital Research Ethics Committee approval.

If you want any information about the study please contact lead researcher, Dr. Catherine Dolan on email at dolanc8@tcd.ie



Dr. Catherine Dolan

Lead Researcher,

Specialty Registrar in Old Age Psychiatry

St. James's Hospital and Trinity College Dublin

Consent information: General Health Knowledge Survey

Research assistant **SARAH GRIFFIN** has explained the nature, purpose, procedures, benefits and, alternatives to, this research study. I have been provided with written study information and this consent form has been explained to me. Research assistant has offered to answer any questions regarding the study.

I now understand:

- What will happen if I agree to be part of this study.
- That my participation is voluntary and that I am free to withdraw from the study at any time, without having to give a reason and without any consequence.
- That any information recorded in the study will remain confidential and no information that identifies me will be made publically available.

I have freely and voluntarily agreed to be part of this research study, though without prejudice to my legal and ethical rights.

Appendix 15: Diabetes and Brain Health (DBH) questionnaire

Diabetes and Brain Complication Questionnaire

STUDY INFORMATION: This questionnaire aims to gather information on what people with diabetes know about general health matters. Please answer all questions honestly. You may skip any questions you do not wish to answer. You have a right to stop the questionnaire at any point. All your responses will be confidential. Should you need any further information about health topics mentioned in this questionnaire please ask the interviewer.

CONSENT: I confirm that I have received information on this study and understand: Ø What will happen if I agree to be part of this study. Ø That my participation is voluntary Ø I am free to withdraw from the study at any time. Ø All information recorded in the study will remain confidential and no information that identifies me will be made publically available. I confirm that I am aged over 18 years and have a diagnosis of diabetes. I have read and agree to the above statements and am willing to participate in the project.

☐ I agree (1)

Q1 Are you?

☐ Male (1)

☐ Female (

Q2 What age are you currently?

☐ 18 (1)

☐ 19 (2)

☐ 20 (3)

☐ 21 (4)

☐ 22 (5)

☐ 23 (6)

☐ 24 (7)

☐ 25 (8)

☐ 26 (9)

☐ 27 (67)

☐ 28 (10)

☐ 29 (11)

☐ 30 (12)

☐ 31 (13)

☐ 32 (14)

☐ 33 (15)

☐ 34 (16)

☐ 35 (17)

☐ 36 (18)

☐ 37 (19)

☐ 38 (20)

☐ 39 (21)

☐ 40 (22)

☐ 41 (23)

☐ 42 (24)

☐ 43 (25)

☐ 44 (26)

- 45 (27)
- 46 (28)
- 47 (29)
- 48 (30)
- 49 (31)
- 50 (32)
- 51 (33)
- 52 (34)
- 53 (35)
- 54 (36)
- 55 (37)
- 56 (38)
- 57 (39)
- 58 (40)
- 59 (41)
- 60 (42)
- 61 (43)
- 62 (44)
- 63 (45)
- 64 (46)
- 65 (47)
- 66 (48)
- 67 (49)
- 68 (50)
- 69 (51)
- 70 (52)
- 71 (53)
- 72 (54)
- 73 (55)
- 74 (56)
- 75 (57)
- 76 (58)
- 77 (59)
- 78 (60)
- 79 (61)
- 80 (62)
- 81 (63)
- 82 (64)
- 83 (65)
- 84 (66)
- 85 (68)
- 86 (69)
- 87 (70)
- 88 (71)
- 89 (72)
- 90 + (73)

Q3 Age Bracket

- ☐ 18 - 44 years (1)
- ☐ 45 - 64 years (2)
- ☐ 65 years plus (3)
- ☐ Unsure/don't know (4)
- ☐ Refusal (5)

Q4 Where were you born?

- ☐ Republic of Ireland (1)
- ☐ A country other than Republic of Ireland (2)
- ☐ Unsure/don't know (3)
- ☐ Refusal (4)

Q5 Please tell me whether you believe the following statement to be true or false. There are things you can do to reduce your risk of getting type 2 diabetes

- ☐ Yes (1)
- ☐ No (2)
- ☐ Unsure/Don't Know (3)

Q6 A risk factor is something that INCREASES your chance of getting a disorder/disease. Please tell me whether you believe the following statements to be true or false. The following factors increase your chance of getting type 2 diabetes:

	True (1)	False (2)	Unsure/Don't Know (3)
Physical inactivity (1)	☐	☐	☐
Heavy consumption of alcohol (2)	☐	☐	☐
Increasing age (3)	☐	☐	☐
Obesity (4)	☐	☐	☐
Having a family history of diabetes (5)	☐	☐	☐
Frequent exposure to strong sunlight (6)	☐	☐	☐
High blood pressure (hypertension) (7)	☐	☐	☐
A history of heart disease (8)	☐	☐	☐
An unhealthy diet (9)	☐	☐	☐

Q7 A complication is a health problem that can occur because of having a disorder/disease. Please tell me whether you believe the following statements to be true or false. A potential complication of diabetes (type 1 and type 2 diabetes) is:

	True (1)	False (2)	Unsure/Don't Know (3)
Kidney damage (1)	☐	☐	☐
Heart disease (2)	☐	☐	☐
Dementia (3)	☐	☐	☐
Multiple sclerosis (MS) (4)	☐	☐	☐
Memory problems (5)	☐	☐	☐
Damage to the back of the eyes (6)	☐	☐	☐
Depression (7)	☐	☐	☐
Nerve damage (e.g tingling in feet, legs or hands) (8)	☐	☐	☐
Lung cancer (9)	☐	☐	☐
Leg ulcers (10)	☐	☐	☐
Stroke (11)	☐	☐	☐

Q8 Please tell me whether you believe the following statement to be true or false. There are things you can do to reduce your risk of getting dementia

- ☐ True (1)
- ☐ False (2)
- ☐ Unsure/Don't Know (3)

Q9 A risk factor is something that INCREASES your chance of getting a disorder/disease. Please tell me whether you believe the following statements to be true or false. The following factors increase your chance of getting dementia

	True (1)	False (2)	Unsure/Don't Know (3)
High blood pressure (1)	☐	☐	☐
A family history of dementia (2)	☐	☐	☐
Being a smoker (3)	☐	☐	☐
Living in a city (4)	☐	☐	☐
Low level of education (5)	☐	☐	☐
Depression (6)	☐	☐	☐
Obesity (7)	☐	☐	☐
Increasing age (8)	☐	☐	☐
Physical inactivity (9)	☐	☐	☐
Diabetes (10)	☐	☐	☐

Q10 Have you been diagnosed with, or treated for, any of the following conditions in the past 12 months?

	Yes (1)	No (2)	Unsure/Don't Know (3)
High Blood Pressure (1)	☐	☐	☐
Depression (2)	☐	☐	☐
Memory problems (3)	☐	☐	☐
Diabetes (4)	☐	☐	☐
High Cholesterol (5)	☐	☐	☐
Stroke/mini-stroke (6)	☐	☐	☐
Heart problems (7)	☐	☐	☐
Dementia (or Alzheimer's disease) (8)	☐	☐	☐

Display This Question:

If Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Dementia (or Alzheimer's disease) - No Is Selected

And Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Dementia (or Alzheimer's disease) - Unsure/Don't Know Is Selected

Q 10.1 Do you currently know, or have you known, someone who has dementia?

- ☐ Yes (31)
- ☐ No (32)
- ☐ Unsure/Don't Know (33)

Display This Question:

If Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Dementia (or Alzheimer's disease) - No Is Selected

And Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Dementia (or Alzheimer's disease) - Unsure/Don't Know Is Selected

And Do you currently know someone who has dementia? Yes Is Selected

Q 10.2 Is the person with dementia that you know

- ☐ A partner or a member of my family (1)
- ☐ Other acquaintance (2)

Display This Question:

If Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Diabetes - No Is Selected

And Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Diabetes - Unsure/Don't Know Is Selected

Q10.3 Do you currently know, or have you known, someone who has diabetes?

- ☐ Yes (1)
- ☐ No (3)
- ☐ Unsure/Don't Know (4)

Display This Question:

If Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Diabetes - No Is Selected

And Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Diabetes - Unsure/Don't Know Is Selected

And DIABETES: Doyou currently meone who has diabetes? Yes Is Selected

Q10.4 If yes, is the person with diabetes that you know

- ☐ A partner or a member of my family (1)
- ☐ Other acquaintance (2)

Q11 How much do you feel you know about each of the following conditions?

	A great deal (20)	A lot (21)	A moderate amount (22)	A little (23)	None at all (24)
High blood pressure (8)	☐	☐	☐	☐	☐
Depression (9)	☐	☐	☐	☐	☐
Memory problems (10)	☐	☐	☐	☐	☐
Diabetes (11)	☐	☐	☐	☐	☐
High cholesterol (12)	☐	☐	☐	☐	☐
Stroke/mini-stroke (13)	☐	☐	☐	☐	☐
Heart problems (14)	☐	☐	☐	☐	☐

Display This Question:

If HEALTH INFORMATION Have you been diagnosed with or treated for any of the following conditions in... Diabetes - Yes Is Selected

Q12 Which type of diabetes have you been diagnosed with (please tick the relevant box)

- ☐ Type 1 diabetes (1)
- ☐ Type 2 diabetes (2)
- ☐ Pre-diabetes (3)
- ☐ Unsure/Don't Know (4)
- ☐ Refusal (5)

Display This Question:

If Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Diabetes - Yes Is Selected

Q12.1 Approximately how old were you when you were first told by a doctor that you had diabetes or pre-diabetes

- ☐ Unsure/don't know (1)
- ☐ 5 (2)
- ☐ 6 (4)
- ☐ 7 (5)
- ☐ 8 (6)
- ☐ 9 (7)
- ☐ 10 (8)
- ☐ 11 (9)
- ☐ 12 (10)
- ☐ 13 (11)
- ☐ 14 (12)
- ☐ 15 (13)
- ☐ 16 (14)
- ☐ 17 (15)
- ☐ 18 (16)
- ☐ 19 (17)
- ☐ 20 (18)
- ☐ 21 (19)
- ☐ 22 (20)
- ☐ 23 (21)
- ☐ 24 (22)
- ☐ 25 (23)
- ☐ 26 (24)
- ☐ 27 (25)
- ☐ 28 (26)
- ☐ 29 (27)
- ☐ 30 (28)
- ☐ 31 (29)
- ☐ 32 (30)
- ☐ 33 (31)
- ☐ 34 (32)
- ☐ 35 (33)
- ☐ 36 (34)
- ☐ 37 (35)
- ☐ 38 (36)
- ☐ 39 (37)
- ☐ 40 (38)
- ☐ 41 (39)
- ☐ 42 (40)
- ☐ 43 (41)
- ☐ 44 (42)
- ☐ 45 (43)
- ☐ 46 (44)

- ☐ 47 (45)
- ☐ 48 (46)
- ☐ 49 (47)
- ☐ 50 (48)
- ☐ 51 (49)
- ☐ 52 (50)
- ☐ 53 (51)
- ☐ 54 (52)
- ☐ 55 (53)
- ☐ 56 (54)
- ☐ 57 (55)
- ☐ 58 (56)
- ☐ 59 (57)
- ☐ 60 (58)
- ☐ 61 (59)
- ☐ 62 (60)
- ☐ 63 (61)
- ☐ 64 (62)
- ☐ 65 (63)
- ☐ 66 (64)
- ☐ 67 (65)
- ☐ 68 (66)
- ☐ 69 (67)
- ☐ 70 (68)
- ☐ 71 (69)
- ☐ 72 (70)
- ☐ 73 (71)
- ☐ 74 (72)
- ☐ 75 (73)
- ☐ 76 (74)
- ☐ 77 (75)
- ☐ 78 (76)
- ☐ 79 (77)
- ☐ 80 (78)
- ☐ 81 (79)
- ☐ 82 (80)
- ☐ 83 (81)
- ☐ 84 (82)
- ☐ 85 (83)
- ☐ 86 (84)
- ☐ 87 (85)
- ☐ 88 (86)
- ☐ 89 (87)
- ☐ 90 + (88)
- ☐ Refusal (89)

Display This Question:

If Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Diabetes - Yes Is Selected

Q12.2 Are you currently taking medication (tablets or injections) for diabetes ?

- ☐ Yes (1)
- ☐ No (2)
- ☐ Unsure/Don't Know (3)
- ☐ Refusal (4)

Display This Question:

If Are you currently taking medication (tablets or injections) for diabetes ? Yes Is Selected

And Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Diabetes - Yes Is Selected

Q12.3 If yes, do you take insulin (injections or pump)?

- ☐ Yes (1)
- ☐ No (2)
- ☐ Unsure/Don't Know (3)
- ☐ Refusal (4)

Display This Question:

If Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Diabetes - Yes Is Selected

Q12.4 Do you have any complications of diabetes?

- ☐ Yes (1)
- ☐ No (3)
- ☐ Unsure/Don't Know (4)
- ☐ Refusal (5)

Display This Question:

If Do you have any complications of diabetes? Yes Is Selected

And Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Diabetes - Yes Is Selected

Q12.5 What complications of diabetes do you have?

- ☐ None (1)
- ☐ Leg/foot ulcers or amputations (2)
- ☐ Eye problems/Damage to the back of the eye (3)
- ☐ Nerve damage (tingling in hands or feet) (4)
- ☐ Kidney damage (5)
- ☐ Other (6)
- ☐ Refusal (7)

Display This Question:

If Have you been diagnosed with, or treated for, any of the following conditions in the past 12 mont... Diabetes - Yes Is Selected

Q12.6 Have you undertaken a formal diabetes education programme/session with a healthcare professional?

- ☐ Yes (20)
- ☐ No (21)
- ☐ Unsure/Don't Know (22)

Q13 Are you?

- ☐ Single (never married) (1)
- ☐ Married/living with a partner as if married/in a civil partnership (2)
- ☐ Separated/divorced (3)
- ☐ Widowed (4)
- ☐ Refusal (5)

Q14 What is the highest level of education you have completed?

- ☐ No education or primary education only (1)
- ☐ Lower secondary education (completed Junior/Intermediate Certificate) (2)
- ☐ Upper secondary education (completed Leaving Cert or equivalent) (4)
- ☐ Third level qualification non- degree (7)
- ☐ Third level qualification degree or higher (8)
- ☐ Refusal (9)

Q15 Which one of these would you say best describes your current situation?

- ☐ Retired from employment (1)
- ☐ Employed (2)
- ☐ Self-employed (3)
- ☐ Unemployed (4)
- ☐ Permanently sick or disabled (5)
- ☐ Looking after home or family (6)
- ☐ In education or training (7)
- ☐ Other (8)
- ☐ Refusal (9)

Q16 What is the name or title of your current/most recent occupation?

Q17 Are/were you a health care worker ?

- ☐ Yes (1)
- ☐ No (2)

Display This Question:

If Are you a healthcare worker

Yes Is Selected

Q17.1 What is/was your job title in health care?

- ☐ Care assistant/health assistant (1)
- ☐ Nurse (any level) (2)
- ☐ Doctor (3)
- ☐ Physiotherapist (4)
- ☐ Social worker (5)
- ☐ Occupational therapist (6)
- ☐ Psychologist (including counsellor, psychotherapist) (7)
- ☐ Health researcher (8)
- ☐ Radiation therapist (9)
- ☐ Health administrator/clerical officer in health care (10)
- ☐ Dietician/nutritionist (11)
- ☐ Health education/promotion officer (13)
- ☐ Pharmacist (14)
- ☐ Paramedic (15)
- ☐ Dentist (16)
- ☐ Podiatrist/Chiropodist (17)
- ☐ Optician/Optometrlist (18)
- ☐ Complimentary therapist (non-professional background) (19)
- ☐ Other non-professional job in health care setting (20)
- ☐ Other professional job in health care setting (21)

Q18 Do you smoke tobacco products (defined as having smoked at least once every month in the previous year) at present?

- ☐ Yes (1)
- ☐ No (2)
- ☐ Refusal (3)

Display This Question:

If LIFESTYLE: SMOKING Do you smoke tobacco products (defined as having smoked at least once every month in the previous year) at present? No Is Selected

Q18.1 If no, are you an ex-smoker (defined as not having smoked at least once every month in the previous year)?

- ☐ Yes (1)
- ☐ No (2)
- ☐ Refusal (3)

Q 19 Do you consume alcohol?

- ☐ Yes (1)
- ☐ No (2)
- ☐ Refusal (3)

Display This Question:

If Do you consume alcohol? Yes Is Selected

Q 19.1 If yes, what alcoholic drink?

- ☐ Glass (half pint) of beer/cider/stout (1)
- ☐ Pint of beer/cider/stout (2)
- ☐ Can of beer/cider/stout (3)
- ☐ Bottle of beer/cider/stout (4)
- ☐ Measures of spirits (5)
- ☐ Bottle of alcopops (6)
- ☐ Glass of wine (7)
- ☐ Bottle of wine (8)

Display This Question:

If If yes, what alcoholic drink? glass (half pint) of beer/cider/stout Is Selected

Q 19.2 If yes, how many glasses (half pints) of beer/cider/stout do you consume on average per week?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)
- ☐ 13 (13)
- ☐ 14 (14)
- ☐ 15 (15)
- ☐ 16 (16)
- ☐ 17 (17)
- ☐ 18 (18)
- ☐ 19 (19)
- ☐ 20 + (20)
- ☐ Refusal (21)

Display This Question:

If If yes, what alcoholic drink? pint of beer/cider/stout Is Selected

Q 19.3 If yes, how many pints of beer/cider/stout do you consume on average per week?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)
- ☐ 13 (13)
- ☐ 14 (14)
- ☐ 15 + (15)
- ☐ Refusal (16)

Display This Question:

If If yes, what alcoholic drink? can of beer/cider/stout Is Selected

Q 19.4 If yes, how many cans of beer/cider/stout do you consume on average per week?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)
- ☐ 13 (13)
- ☐ 14 (14)
- ☐ 15 (15)
- ☐ 16 (16)
- ☐ 17 (17)
- ☐ 18 (18)
- ☐ 19 (19)
- ☐ 20+ (20)
- ☐ Refusal (21)

Display This Question:

If If yes, what alcoholic drink? bottles of beer/cider/stout Is Selected

Q 19.5 If yes, how many bottles of beer/cider/stout do you consume on average per week?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)
- ☐ 13 (13)
- ☐ 14 (14)
- ☐ 15 (15)
- ☐ 16 (16)
- ☐ 17 (17)
- ☐ 18 (18)
- ☐ 19 (19)
- ☐ 20 (20)
- ☐ 21 (21)
- ☐ 22 (22)
- ☐ 23 (23)
- ☐ 24 (24)
- ☐ 25 + (25)
- ☐ Refusal (26)

Display This Question:

If If yes, what alcoholic drink? Measures of spirits Is Selected

Q 19.6 If yes, how many measures of spirits do you consume on average per week?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)
- ☐ 13 (13)
- ☐ 14 (14)
- ☐ 15 (15)
- ☐ 16 (16)
- ☐ 17 (17)
- ☐ 18 (18)
- ☐ 19 (19)
- ☐ 20 + (20)
- ☐ Refusal (21)

Display This Question:

If If yes, what alcoholic drink? bottles of alcopops Is Selected

Q 19.7 If yes, how many bottles of alcopops do you consume on average per week?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)
- ☐ 13 (13)
- ☐ 14 (14)
- ☐ 15 (15)
- ☐ 16 (16)
- ☐ 17 (17)
- ☐ 18 (18)
- ☐ 19 (19)
- ☐ 20+ (20)
- ☐ Refusal (21)

Display This Question:

If If yes, what alcoholic drink? glass of wine Is Selected

Q 19.8 If yes, how many glasses of wine do you consume on average per week?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)
- ☐ 13 (13)
- ☐ 14 (14)
- ☐ 15+ (15)
- ☐ Refusal (16)

Display This Question:

If If yes, what alcoholic drink? bottle of wine Is Selected

Q 19.9 If yes, how many bottles of wine do you consume on average per week?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (16)
- ☐ 10+ (17)
- ☐ Refusal (18)

Display This Question:

If Do you consume alcohol? Yes Is Selected

Q20 How many units of alcohol do you consume on average per week?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)
- ☐ 13 (13)
- ☐ 14 (14)
- ☐ 15 (15)
- ☐ 16 (16)
- ☐ 17 (17)
- ☐ 18 (18)
- ☐ 19 (19)
- ☐ 20 (20)
- ☐ 21 (21)
- ☐ 22 (22)
- ☐ 23 (23)
- ☐ 24 (24)
- ☐ 25 (25)
- ☐ 26 (26)
- ☐ 27 (27)
- ☐ 28 (28)
- ☐ 29 (29)
- ☐ 30 (30)
- ☐ 31 (31)
- ☐ 32 (32)
- ☐ 33 (33)
- ☐ 34 (34)
- ☐ 35 (35)
- ☐ 36 (36)
- ☐ 37 (37)
- ☐ 38 (38)
- ☐ 39 (39)
- ☐ 40 (40)
- ☐ 41 (41)
- ☐ 42 (42)
- ☐ 43 (43)
- ☐ 44 (44)
- ☐ 45 (45)

- ☐ 46 (46)
- ☐ 47 (47)
- ☐ 48 (48)
- ☐ 49 (49)
- ☐ 50 + (50)
- ☐ Refusal (51)

Q 21 Do you know how much you weigh?

- ☐ Yes (1)
- ☐ No (2)

Display This Question:

If Do you know how much you weight? Yes Is Selected

Q 21.1 If yes, do you know how much you weigh in kilograms, stones or pounds?

- ☐ Kilograms (kg) (1)
- ☐ Stones (st) and pounds (lb) (4)

Display This Question:

If If yes, do you know how much you weigh in kilograms, stones or pounds?

Kilograms (kg) Is Selected

Q 21.2 How much do you weigh in kilograms?

- ☐ Refusal (1)
- ☐ 39 or less (2)
- ☐ 40 (4)
- ☐ 41 (5)
- ☐ 42 (6)
- ☐ 43 (7)
- ☐ 44 (8)
- ☐ 45 (9)
- ☐ 46 (10)
- ☐ 47 (11)
- ☐ 48 (12)
- ☐ 49 (13)
- ☐ 50 (14)
- ☐ 51 (15)
- ☐ 52 (16)
- ☐ 53 (17)
- ☐ 54 (18)
- ☐ 55 (19)
- ☐ 56 (20)
- ☐ 57 (21)
- ☐ 58 (22)
- ☐ 59 (23)
- ☐ 60 (24)
- ☐ 61 (25)
- ☐ 62 (26)
- ☐ 63 (27)
- ☐ 64 (28)
- ☐ 65 (29)
- ☐ 66 (30)
- ☐ 67 (31)
- ☐ 68 (32)
- ☐ 69 (33)
- ☐ 70 (34)
- ☐ 71 (35)
- ☐ 72 (36)
- ☐ 73 (37)
- ☐ 74 (38)
- ☐ 75 (39)
- ☐ 76 (40)
- ☐ 77 (41)
- ☐ 78 (42)
- ☐ 79 (43)
- ☐ 80 (44)
- ☐ 81 (45)

- 82 (46)
- 83 (47)
- 84 (48)
- 85 (49)
- 86 (50)
- 87 (51)
- 88 (52)
- 89 (53)
- 90 (54)
- 91 (55)
- 92 (56)
- 93 (57)
- 94 (58)
- 95 (59)
- 96 (60)
- 97 (61)
- 98 (62)
- 99 (63)
- 100 (64)
- 101 (65)
- 102 (66)
- 103 (67)
- 104 (68)
- 105 (69)
- 106 (70)
- 107 (71)
- 108 (72)
- 109 (73)
- 110 (74)
- 111 (75)
- 112 (76)
- 113 (77)
- 114 (78)
- 115 (79)
- 116 (80)
- 117 (81)
- 118 (82)
- 119 (83)
- 120 (84)
- 121 (85)
- 122 (86)
- 123 (87)
- 124 (88)
- 125 (89)
- 126 (90)
- 127 (91)
- 128 (92)
- 129 (93)

- 130 (94)
- 131 (95)
- 132 (96)
- 133 (97)
- 134 (98)
- 135 (99)
- 136 (100)
- 137 (101)
- 138 (102)
- 139 (103)
- 140 (104)
- 141 (105)
- 142 (106)
- 143 (107)
- 144 (108)
- 145 (109)
- 146 (110)
- 147 (111)
- 148 (112)
- 149 (113)
- 150 (114)
- 151 (115)
- 152 (116)
- 153 (117)
- 154 (118)
- 155 (119)
- 156 (120)
- 157 (121)
- 158 (122)
- 159 (123)
- 160 (124)
- 161 (125)
- 162 (126)
- 163 (127)
- 164 (128)
- 165 (129)
- 166 (130)
- 167 (131)
- 168 (132)
- 169 (133)
- 170 (134)
- 171 (135)
- 172 (136)
- 173 (137)
- 174 (138)
- 175 (139)
- 176 (140)
- 177 (141)

- 178 (142)
- 179 (143)
- 180 (144)
- 181 (145)
- 182 (146)
- 183 (147)
- 184 (148)
- 185 (149)
- 186 (150)
- 187 (151)
- 188 (152)
- 189 (153)
- 190 (154)
- 191 (155)
- 192 (156)
- 193 (157)
- 194 (158)
- 195 (159)
- 196 (160)
- 197 (161)
- 198 (191)
- 199 (192)
- 200 (193)

Display This Question:

If If yes, do you know how much you weigh in kilograms, stones or pounds?

Stones (st) and pounds (lb) Is Selected

Q 21.3 How much do you weigh in stones?

- ☐ 6 or less (1)
- ☐ 7 (2)
- ☐ 8 (3)
- ☐ 9 (4)
- ☐ 10 (5)
- ☐ 11 (6)
- ☐ 12 (7)
- ☐ 13 (8)
- ☐ 14 (9)
- ☐ 15 (10)
- ☐ 16 (11)
- ☐ 17 (12)
- ☐ 18 (13)
- ☐ 19 (14)
- ☐ 20 (15)
- ☐ 21 (16)
- ☐ 22 (17)
- ☐ 23 (18)
- ☐ 24 (19)
- ☐ 25 (20)
- ☐ 26 + (21)
- ☐ Refusal (22)

Display This Question:

If If yes, do you know how much you weigh in kilograms, stones or pounds?

Stones (st) and pounds (lb) Is Selected

Q 21.4 How much do you weigh in pounds?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)
- ☐ 13 (13)
- ☐ 14 (14)
- ☐ Refusal (15)

Q22 Do you know what height you are?

- ☐ Yes (1)
- ☐ No (2)

Display This Question:

If Do you know what height you are? Yes Is Selected

Q 22.1 If yes, do you know what height you are in feet/inches or metres/centimetres?

- ☐ feet/inches (1)
- ☐ metres/centimetres (2)

Display This Question:

If If yes, do you know what height you are in feet/inches or metres/centimetres? feet/inches Is Selected

Q22.2 What height you are in feet?

- ☐ 4 (1)
- ☐ 5 (2)
- ☐ 6 (3)
- ☐ 7 (4)
- ☐ Refusal (5)

Display This Question:

If If yes, do you know what height you are in feet/inches or metres/centimetres? feet/inches Is Selected

Q22.3 What height you are in inches?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)

Display This Question:

If If yes, do you know what height you are in feet/inches or metres/centimetres? metres/centimetres Is Selected

Q22.4 What height you are in metres?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ Refusal (3)

Display This Question:

If If yes, do you know what height you are in feet/inches or metres/centimetres?

metres/centimetres Is Selected

Q22.5 What height you are in centimetres?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)
- ☐ 13 (13)
- ☐ 14 (14)
- ☐ 15 (15)
- ☐ 16 (16)
- ☐ 17 (17)
- ☐ 18 (18)
- ☐ 19 (19)
- ☐ 20 (20)
- ☐ 21 (21)
- ☐ 22 (22)
- ☐ 23 (23)
- ☐ 24 (24)
- ☐ 25 (25)
- ☐ 26 (26)
- ☐ 27 (27)
- ☐ 28 (28)
- ☐ 29 (29)
- ☐ 30 (30)
- ☐ 31 (31)
- ☐ 32 (32)
- ☐ 33 (33)
- ☐ 34 (34)
- ☐ 35 (35)
- ☐ 36 (36)
- ☐ 37 (37)
- ☐ 38 (38)
- ☐ 39 (39)
- ☐ 40 (40)
- ☐ 41 (41)
- ☐ 42 (42)
- ☐ 43 (43)
- ☐ 44 (44)

- ☐ 45 (45)
- ☐ 46 (46)
- ☐ 47 (47)
- ☐ 48 (48)
- ☐ 49 (49)
- ☐ 50 (50)
- ☐ 51 (51)
- ☐ 52 (52)
- ☐ 53 (53)
- ☐ 54 (54)
- ☐ 55 (55)
- ☐ 56 (56)
- ☐ 57 (57)
- ☐ 58 (58)
- ☐ 59 (59)
- ☐ 60 (60)
- ☐ 61 (61)
- ☐ 62 (62)
- ☐ 63 (63)
- ☐ 64 (64)
- ☐ 65 (65)
- ☐ 66 (66)
- ☐ 67 (67)
- ☐ 68 (68)
- ☐ 69 (69)
- ☐ 70 (70)
- ☐ 71 (71)
- ☐ 72 (72)
- ☐ 73 (73)
- ☐ 74 (74)
- ☐ 75 (75)
- ☐ 76 (76)
- ☐ 77 (77)
- ☐ 78 (78)
- ☐ 79 (79)
- ☐ 80 (80)
- ☐ 81 (81)
- ☐ 82 (82)
- ☐ 83 (83)
- ☐ 84 (84)
- ☐ 85 (85)
- ☐ 86 (86)
- ☐ 87 (87)
- ☐ 88 (88)
- ☐ 89 (89)
- ☐ 90 (90)
- ☐ 91 (91)
- ☐ 92 (92)

- ☐ 93 (93)
- ☐ 94 (94)
- ☐ 95 (95)
- ☐ 96 (96)
- ☐ 97 (97)
- ☐ 98 (98)
- ☐ 99 (99)
- ☐ Refusal (100)

PHYSICAL ACTIVITYThe following questions will ask you about the time you spent being physically active in the last 7 days. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Q23 Think about all the vigorous activities that you did in the last 7 days. Vigorous physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time. During the last 7 days, did you do vigorous physical activities like heavy lifting, digging, aerobics, or fast bicycling?

- ☐ Yes (1)
- ☐ No (2)

Display This Question:

If During the last 7 days, did you do vigorous physical activities like heavy lifting, digging, aerobics, or fast bicycling? <o:p></o:p> Yes Is Selected

Q23.1 During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, digging, aerobics, or fast bicycling?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)

Display This Question:

If During the last 7 days, did you do vigorous physical activities like heavy lifting, digging, aerobics, or fast bicycling? <o:p></o:p> Yes Is Selected

Q23.2 How many hours did you usually spend doing vigorous physical activities on one of those days?

- ☐ 1 (2)
- ☐ 2 (3)
- ☐ 3 (4)
- ☐ 4 (5)
- ☐ 5 (6)
- ☐ 6 (7)
- ☐ 7 (8)
- ☐ 8 (9)
- ☐ 9 (10)
- ☐ 10 (11)
- ☐ 11 (12)
- ☐ 12 (13)

Display This Question:

If Think about all the vigorous activities that you did in the last 7 days. Vigorous physical acti... Yes Is Selected

Q23.3 How many minutes did you usually spend doing vigorous physical activities on one of those days?

- ☐ 5 (1)
- ☐ 10 (2)
- ☐ 15 (3)
- ☐ 20 (4)
- ☐ 25 (5)
- ☐ 30 (6)
- ☐ 35 (7)
- ☐ 40 (8)
- ☐ 45 (9)
- ☐ 50 (10)
- ☐ 55 (11)

Q24 Think about all the moderate activities that you did in the last 7 days. Moderate activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time. During the last 7 days, did you do moderate physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

- ☐ Yes (1)
- ☐ No (2)

Display This Question:

If During the last 7 days, did you do moderate physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking. Yes
Is Selected

Q24.1 During the last 7 days, on how many days did you do moderate physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)

Display This Question:

If During the last 7 days, did you do moderate physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking. Yes
Is Selected

Q24.2 How many hours did you usually spend doing moderate physical activities on one of those days?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)

Display This Question:

If Think about all the moderate activities that you did in the last 7 days. Moderate activities refe... Yes Is Selected

Q24.3 How many minutes did you usually spend doing moderate physical activities on one of those days?

- ☐ 5 (1)
- ☐ 10 (2)
- ☐ 15 (3)
- ☐ 20 (4)
- ☐ 25 (5)
- ☐ 30 (6)
- ☐ 35 (7)
- ☐ 40 (8)
- ☐ 45 (9)
- ☐ 50 (10)
- ☐ 55 (11)

Q25 Think about the time you spent walking in the last 7 days. This includes at work and at home, walking to travel from place to place, and any other walking that you have done solely for recreation, sport, exercise, or leisure. During the last 7 days, on any day did you walk for at least 10 minutes at a time?

- ☐ Yes (1)
- ☐ No (2)

Display This Question:

If During the last 7 days, on any day did you walk for at least 10 minutes at a time? <o:p></o:p> Yes Is Selected

Q25.1 During the last 7 days, on how many days did you walk for at least 10 minutes at a time?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)

Display This Question:

If During the last 7 days, on any day did you walk for at least 10 minutes at a time? <o:p></o:p> Yes Is Selected

Q25.2 How many hours did you usually spend walking on one of those days?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)

Display This Question:

If Think about the time you spent walking in the last 7 days. This includes at work and at home, w... Yes Is Selected

Q25.3 How many minutes did you usually spend walking on one of those days?

- ☐ 5 (1)
- ☐ 10 (2)
- ☐ 15 (3)
- ☐ 20 (4)
- ☐ 25 (5)
- ☐ 30 (6)
- ☐ 35 (7)
- ☐ 40 (8)
- ☐ 45 (9)
- ☐ 50 (10)
- ☐ 55 (11)

The last question is about the time you spent sitting on weekdays during the last 7 days. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

Q26 During the last 7 days,how many hours did you spend sitting on a weekday?

- ☐ 1 (1)
- ☐ 2 (2)
- ☐ 3 (3)
- ☐ 4 (4)
- ☐ 5 (5)
- ☐ 6 (6)
- ☐ 7 (7)
- ☐ 8 (8)
- ☐ 9 (9)
- ☐ 10 (10)
- ☐ 11 (11)
- ☐ 12 (12)
- ☐ 13 (13)
- ☐ 14 (14)
- ☐ 15 (15)
- ☐ 16 (16)

Q26.1 During the last 7 days,how many minutes did you spend sitting on a weekday?

- ☐ 5 (1)
- ☐ 10 (2)
- ☐ 15 (3)
- ☐ 20 (4)
- ☐ 25 (5)
- ☐ 30 (6)
- ☐ 35 (7)
- ☐ 40 (8)
- ☐ 45 (9)
- ☐ 50 (10)
- ☐ 55 (11)

Q27 Do you participate in any groups such as a sports or social group or club, a religious connected group, a self-help or charitable body or other community group or a day care centre?

- ☐ Yes (1)
- ☐ No (2)
- ☐ Unsure/Don't Know (3)
- ☐ Refusal (4)

Q28 Into which socio-economic grouping does the respondent belong as per CSO?

- ☐ Employers and managers (A) (1)
- ☐ Higher professional (B) (2)
- ☐ Lower professional (C) (3)
- ☐ Non-manual (D) (4)
- ☐ Manual skilled (E) (5)
- ☐ Semi-skilled (F) (6)
- ☐ Unskilled (G) (7)
- ☐ Own account workers (H) (8)
- ☐ Farmers (I) (9)
- ☐ Agricultural workers (J) (10)
- ☐ All others gainfully occupied and unknown (Z) (11)