Epidemiology of Chronic Disease in Adults with Intellectual Disabilities

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I. Abstract

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People with intellectual disabilities [ID] experience a disproportionate burden of health inequalities compared with the general population, including higher rates of obesity. Physical inactivity and sedentary behaviour are both common. As people with ID are now living longer, morbidity due to chronic conditions, including diabetes and CVD, is becoming increasingly important.

I aimed to review existing evidence for the current prevalence of chronic disease and cardiometabolic conditions factors in the ID population and compare them to the general population. In addition, I aimed to review multicomponent lifestyle interventions for primary preventions of chronic disease and cardiometabolic conditions factors in the ID population.

Chapter two shows evidence suggests that prevalence of chronic disease and associated risk factors is similar to that of the general population, and therefore in need of intervention. This is inconsistent with previous research indicating health disparities. However, there may be an influence of under-diagnosis in retrospective datasets. Future research would benefit from further studies with general population comparisons to make more reliable and valid comparisons.

Chapter three shows that generally, significant positive intervention effects can be achieved. The included studies noted similar limitations and made strong recommendations for future research. It also indicated there is a lack of research detailing interventions in this area.

This thesis indicates that levels of cardiometabolic disease in people with ID are generally comparable to that of the general population. However, due to limitations in reported data throughout the literature this conclusion should be treated with some reservations. Chronic disease prevalence is high and reliable methods of improving health in people with ID need researching further because primary prevention is not as easily accomplishable as in the general population.

II. Acknowledgements

The author does not wish to make any acknowledgements for this thesis.

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IV. List of tables shown in this thesis

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VI. List of acronyms used in this thesis

ID – Intellectual disability

IQ – Intelligence quotient

PMID – Profound and multiple intellectual disability

T2DM – Type 2 diabetes mellitus

CVD – Cardiovascular disease

FXS – Fragile-X-Syndrome

DS – Down Syndrome

FASD – Foetal Alcohol Spectrum Disorder

FMR-1 – Fragile-X Mental retardation Gene

BMI – Body mass index

PA – Physical activity

MVPA – Moderate to vigorous physical activity

Kcals – Kilo calories

ICD-10 – International classification of disease codes - volume 10

NHS – National Health Service

GP – General practice

[…] – Square brackets have been used to differentiate from the rounded brackets used for citations.

Chapter 1 Introduction

1.1 Defining intellectual disability

Intellectual disability [ID] is characterised by significant limitations in both intellectual functioning and adaptive behaviour that begin before the age of 18 years old (1). In the government white paper for England 'Valuing People: a new strategy for learning disability for the 21st century' (2), an ID is described as:

- An impairment that started before adulthood, with a lasting effect on development;
- a significantly reduced ability to understand new or complex information or to learn new skills;
- a reduced ability to cope independently.

These criteria are different from criteria used to define learning *difficulty*, in that the term learning difficulty refers to a child or young person, who has a specific learning or educational difficulty such as dyslexia. These difficulties do not have a significant impairment on intelligence and functioning to the extent of ID (3).

Learning disability and ID are often used interchangeably (3). Confusion can occur when ID is used as a term to describe learning difficulties, or vice versa. Throughout this thesis, I will be discussing ID as per the definition above.

Generally, ID means that individuals with certain syndromes and conditions may find it difficult to understand and conduct basic tasks such as communication and learning. This can lead to great difficulty in completing more complex tasks such as organising meals and money. For these tasks, the individual may require a family member and/or carer to assist them in their day to day activities. This may require the individual to be in an assisted living facility. In a report entitled 'Housing for people with a learning disability' by MENCAP (4) it was shown that the majority of the ID population in the UK live in one of three types of accommodation:

- With family and friends [38%]
- In a registered care home [22%]
- In supported accommodation [16%]

Further to this, 12% live as tenants in housing provided by a local authority or housing association and 3% in privately rented housing.

1.2 ID prevalence

A meta-analysis of articles published between 1980 and 2009 confirmed an ID prevalence of 1% [0.05-1.55%] (5). In England, as of 2013 it is estimated that 1,198,000 people have an ID, roughly 2% of the general population (6).

1.3 Categorisation of ID

Often, the choice of housing and level of care for the individual is dictated by the severity of their disability and ability to cope independently. To categorise the range of difficulties experienced by people with ID, the concept of an ID continuum is used and sets out four defined categories for ID [Figure 1] (7).

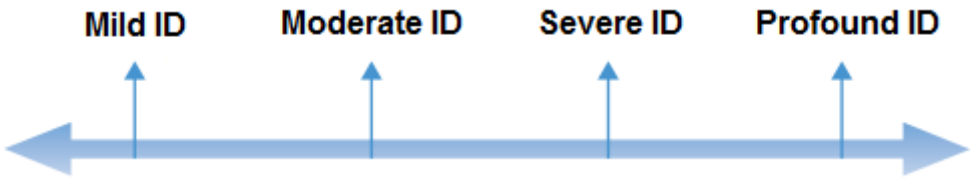


Figure 1. The intellectual disability continuum.

1.3.1 Mild ID

People with mild ID are often the most independent on the continuum. They have an estimated intelligence quotient [IQ] of 50 – 70 (8). In comparison, in

current IQ tests taken by the general population, the majority obtain scores of 85-115 (8). They are often able to care for themselves and complete everyday tasks such as shopping and cleaning the house. They can converse normally and communicate their thoughts verbally. However, they may need further support in understanding more complex ideas. Although, they may have some basic reading and writing skills, they often need help when completing tasks such as budgeting and filling in forms. Due to the mild nature of the person's ID, the condition can often go undiagnosed (8).

1.3.2 Moderate ID

People with moderate ID have an estimated IQ of 35-49 (8). They are likely to be able to communicate effectively, including verbalising their needs. They may need further support in caring for themselves, but the majority will be able to complete everyday tasks without further support (8).

1.3.3 Severe ID

People with severe ID have an estimated IQ of 20-34 (8). They will often need a higher level of support when it comes to everyday activities. They will also find it difficult to verbalise their needs and may only be able to communicate using basic words and gestures. However, they will often be able to look after their own personal care needs but could need support with specific medical care. They may also have mobility issues that require assistance (8).

1.3.4 Profound ID

People with profound ID often have multiple disabilities which require constant care. These people are often termed as having profound and multiple intellectual disabilities [PMID] (9). Other disabilities can include, but are not limited to, impairments in movement, hearing and vision. Profound ID means that the individual's IQ is estimated to be under 20 (8). This means that the individual has very limited understanding and will have great difficulty in communicating their thoughts and needs. It is estimated that there are currently

16,000 individuals with PMID living in England (9). Alongside these issues, PMID can bring further behavioural complications such as self-harm and psychiatric illness which require full time care from a health professional and require the individual to be housed in an assisted living facility or care home (8).

Differences between ID categories are shown in table 1.

Table 1. Characteristics of intellectual disability

Categorisation of ID	IQ (8)	Approximate proportion of ID population (10)	Reading and writing ability (11)	Assistance required (8)	Physical disabilities (8, 9)
Mild	50-70	85%	Generally, can learn to read, write, and do simple mathematics.	Able to live independently, take care of one's self and have a job.	Generally, no physical disabilities.
Moderate	35-49	10%	Can learn some basic reading and writing.	Able to learn functional life-skills but may require further supervision.	May have some physical disabilities, including vision, balance, and hearing problems.
Severe	20-34	5%	Generally, not able to learn to read and write.	Can learn some life-skills but does require supervision during day to day activities.	May have more severe physical disabilities, including vision, balance, and hearing problems.
Profound	<20	1%	Is not able to learn to read and write. Often cannot communicate verbally.	Generally, requires ongoing medical care and therapy.	Profound and multiple disability. Possible severe restrictions in movement, hearing and vision.

ID [intellectual disability]; IQ [intelligence quotient].

1.4 Causes of intellectual disability

ID is a genetically or environmentally determined condition that causes lasting damage in the development of the brain. This can occur either before birth [antenatal], during birth [perinatal], or during childhood [postnatal]. However,

around one-third to half of the causes of ID cannot be determined during childhood (12).

1.4.1 Antenatal problems

Antenatal causes of ID are predominately environmental and genetic in nature and genetic causes account for approximately 45% of ID (13). Alongside genetic causes, other environmental causes such as malnutrition, illnesses such as syphilis and rubella during pregnancy can increase risk of ID (8). One other cause of ID that has been a global health threat recently is microcephaly caused by the Zika virus (14).

Two of the three most common causes of ID are genetic abnormalities: 1. Fragile X syndrome [FXS]; and 2. Down's Syndrome [DS]. The third most common cause is Foetal Alcohol Spectrum Disorder [FASD]. FASD is an environmental influence that is known to be the most preventable cause of ID (15).

1.4.2 Perinatal problems

Babies born prematurely and/or with low birth weights are often found to have health problems in later life, including ID (16, 17). Moreover, other complications during the birth such as birth related injuries and temporary oxygen deprivation can cause ID and a condition known as cerebral palsy (18). Cerebral palsy can, but does not always, present with an ID (19).

1.4.3 Postnatal problems

Illness and injury post-birth can cause ID. This cause is often referred to as 'acquired ID'. Acquired ID can manifest via diseases such as chicken pox, whooping cough, and Hib disease that can lead to meningitis and other conditions that can cause lasting brain damage (20). Other causes such as head injuries and near drowning can also result in irreparable brain damage resulting in ID (21).

1.5 Most common causes

Predominantly, ID is caused by genetic abnormalities (13, 22). Genetic abnormalities often result from inherited gene problems from parents, errors in gene combinations including chromosomal anomalies and genetic metabolic and neurologic disorders, or gene disorders resulting from external factor such as infections (23) or overexposure to x-rays (24). Parents who have an ID are at higher risk of creating offspring with a range of disabilities, but direct passing on of genetically associated ID is unusual (25).

1.5.1 Fragile X syndrome

FXS is the second most common cause of ID (26) with 100-200 people born in the UK each year with FXS, or a prevalence of 2.3/1000 (27). The condition is causes by a mutation of the fragile-X mental retardation gene (FMR-1) which is located on the X chromosome (28). A person with FXS would typically have an IQ <70. Alongside this, they would have physical abnormalities such as a large jaw and long ears, high forehead, large testicles, and noticeable facial asymmetry (29).

1.5.2 Down's Syndrome

DS is the most common genetic cause of ID (30). There are a currently estimated 60,000 people in the UK with DS and it accounts for approximately 15-20% of the entire ID population (30). DS occurs as a result of a trisomy of chromosome 21 (31). This means that the individual is born with 47 chromosomes instead of the normal 46. Currently there is little explanation as to why this happens. However, there is a demonstrated link between the condition and advanced maternal age (32). The average IQ of a person with DS is <50, however, this can vary widely (32).

1.5.3 Foetal Alcohol Spectrum Disorder

FASD presents with neurological and growth impairment and abnormal faces in some infants born to women who consume too much alcohol during pregnancy (33). Smoking, alongside excessive alcohol during pregnancy can make the effects of FASD worse (33). Current estimated prevalence rates in the United States are 0.5 to 2 cases per 1,000 births (34). One study estimated worldwide prevalence is at least 9.1/1,000 (35), however, a reliable contemporary study does has not been published.

1.6 Reasons why people with ID may suffer detriments in health

The need for reductions in health risk factors associated with poorer health in people with ID have gained increased attention within recent decades. Early studies have indicated an imbalance in health problems and health service provision (36). This has led to an increase in research into potential disparities in healthcare leading to increased risk of disease within ID populations (37-39). The increased focus on health disparities has led to improvement in healthcare for people with ID over recent decades. As a result, people with ID are now living longer (40) and becoming more susceptible to chronic diseases common in older age (41, 42).

People with ID experience the same range of diseases as the general population. However, the reality of healthcare and living with poor health is very different for people with ID for a variety of reasons. The history of how people with ID fit within society and the healthcare system has changed over the past four decades. It is important to understand how this influences health for people with ID today. One important influence is the deinstitutionalisation of people with ID.

1.6.1 The deinstitutionalisation of people with ID

The deinstitutionalisation of people with ID (i.e., the process of replacing long-stay hospitals with less isolated community health services) began in the UK during the late 1970s and early 1980s (43). This process is at dissimilar junctures throughout the world. This is predominately due to the attitudes and subsequent treatment of people with ID varying widely from country to country, with higher income countries indicating a more tolerant attitude to people ID (44). Where once large institutions for people with ID were common place, these institutions are being replaced with smaller health services (45). However, progress is slow. Some countries have now closed all large institutions; including the UK, Australia, Italy, and Norway. Whereas other countries still have thousands of individuals residing in institutions (e.g., Israel, Finland). Deinstitutionalisation is seen as beneficial due to the harmful negative effects of being within an institution due to a decrease in quality of life [lack of physical, material, emotional, and social wellbeing] (46).

Yet living a more independent life within a community can bring its own problems for people with ID. People with ID now must rely on the mainstream healthcare system, the same as the general population, but the ability to access the same level of healthcare is made more difficult due to the nature of ID. In this respect, the inequalities in health and healthcare have been made more pronounced by deinstitutionalisation (47). This is due to people with ID facing difficulties when trying to access healthcare. This is not due to healthcare being unavailable, but other barriers, specific to people with ID, that make it difficult to access healthcare. In the following paragraphs, I will outline and describe some of these barriers.

1.6.2 Accommodation type

The type of accommodation in which a person with ID resides has been shown to be an influence on the health of people with intellectual disability (47). Following deinstitutionalisation, it has become a concern that people with ID are not receiving the same quality of healthcare (46). Specifically, people with ID

need more specialised and tailored healthcare, which was more easily accessible within an institution with regular access to healthcare professional (46). Although, some people with ID still live in places where a healthcare professional is at hand, many do not. Research has shown that compared to people with ID who live with friends or family/by themselves, those in a group home are more likely to have a personal doctor and dentist and less likely to be obese (48). However, it should be noted this is not directly related to having a clinician at hand, but rather changing the dynamics of how the person with ID can access healthcare through an increased system of support available through assisted living.

1.6.3 Barriers to exercise

Barriers to exercise can be a major contributor to poor health, such as obesity, diabetes, and heart disease in people with ID or the general population (49). Research has shown that barriers experienced by people with ID are not dissimilar to the general population (e.g., general disinterest, increased age, a preference for other activities, financial restraints) (50). However, there are additional barriers that may be experienced by people with ID (e.g., lack of carer support, travel restraints, segregated facilities). In addition, some people with ID experience physical problems which may prevent them from exercising. For example, those who are at the severe-profound end of the ID continuum tend to experience more motility, vision, and hearing problems (9).

1.6.4 Lack of health literacy

Another potential barrier to exercise, and an additional detriment to health is a lack of health literacy. Health literacy education has become increasingly important with the apparent concern about the possible health inequalities experienced by people with ID. People with ID experience a reduced ability to understand concepts, associations, and actions that are involved with making good health decisions [e.g., healthy food choices and healthy exercise behaviours] (51). Recently, more emphasis has been put on creating health literacy interventions to improve the health education level in people with ID

(52). However, it has been suggested that these interventions teach a somewhat incomplete image of health literacy and do not successfully allow a comprehensive understanding of health and health care (51). The ability to interact with the health education is much more difficult for people with ID compared to the general population due to this limited understanding and inability to make connections (50).

1.6.5 Increased prevalence of mental illness and behavioural problems

Mental illness has been positively associated with chronic diseases such as type 2 diabetes mellitus [T2DM], cardiovascular disease [CVD], and associated risk factors such as obesity (53). These detriments to health are caused by mechanisms such as side effects from medications, depression symptoms causing increased appetite or decreased enthusiasm for exercise, and increased sedentary behaviour (54). People with ID are at higher risk of mental illness and behavioural problems because of difficulties in communication, processing skills, and intelligence (55). Although people with ID experience the same range of mental illnesses as the general population, research has shown the prevalence is higher (56, 57); however, the rates of schizophrenic illness and phobic disorder were significantly higher than the general population [4.4% vs 0.4% and 4.4% vs 1.1% respectively] (58).

Therefore, this increased prevalence of mental illness thereby could increase the possibility of developing an associated cardiometabolic condition.

1.7 National health checks for people with ID

Based on the barriers to health that people with ID face. Strategies and guarding procedures are in place to ensure that people with ID are experiencing the same access to the same quality of healthcare as the general population. Since disparities in health and healthcare for people with ID were made apparent, these strategies have become increasingly important and countries have issued policy surrounding annual health checks for people with ID.

In the UK, the NHS provides an annual health check scheme for adults and young people aged 14 years and above with moderate, severe or profound ID. The policy maintains that in some cases, the health checks can also be given to those with mild ID who have other complex health needs. The general aim of the health checks is to offer a service for those who require more health support and detect health issues that otherwise go undiagnosed. The health check involves the patient attending their local GP clinic and a GP or practice nurse will conduct the following (59):

- a general physical examination, including checking their weight, heart rate, blood pressure and taking blood and urine samples;
- assessing the patient's behaviour, including asking questions about their lifestyle, and mental health;
- a check for epilepsy;
- a check on any prescribed medicines the patient is currently taking;
- a check on whether any chronic illnesses, such as asthma or diabetes, are being well managed;
- a review of any arrangements with other health professionals, such as physiotherapists or speech therapists;

Throughout this process, adjustments to the service are made to account for the difficulties encountered when caring for someone with ID. Examples of these adjustments are (60):

- Using pictures or large print documents to explain to the individual what is happening
- Booking longer appointments
- Carer involvement
- Appointment times changed based on how busy the GP surgery is

Annual health checks for people with ID were brought in after 2009 on the rationale that people with ID have poorer physical and mental health and it is a legal requirement [under the Disability Discrimination Acts 1995, 2005 and the

Equality Act 2010] of primary care services to make sure this ‘at risk’ population are being looked after correctly. The scheme is incentivised with GPs receiving extra money for carrying out health checks. However, in ‘The Uptake of Learning Disability Health Checks 2013-2014’ report by Public Health England’ (61) it is noted that only 49.4% of eligible people have an annual health check performed.

A systematic review of 38 papers presenting results of health checks for people with ID worldwide indicated that the health checks were effective in recognising previously undiagnosed conditions and addressing actions for health improvement (59). Undiagnosed health conditions included psychiatric disorders, hypertension, thyroid disease, and heart (62).

Although annual health checks for persons with ID are somewhat common place in more developed countries, the schemes are still in their infancy and require more attention. Specifically, with under half of all persons with ID taking part in health checks in the UK, there are barriers which needs to be evaluated.

1.8 Chapter summary

The prevalence of CVD and T2DM, along with associated risk factors, is on the rise globally and plays a major part in the financial burden of health services. The ID population has been shown to be more at risk of disparities in health care. Including potential under diagnosis, diagnosis over-shadowing and a lack of suitable interventions to kerb further complications of health problems. However, current research assessing the prevalence and overall risk of CVD, T2DM and associated risk factors in people with ID is relatively scarce and in some cases, contrary.

1.9 Overview of research

The ID population can be described as an ‘at-risk’ population for a variety of reasons indicated above. There is a need to establish current prevalence of chronic disease, co-morbidities, and chronic disease risk factors in the people

with ID and make reliable and valid comparisons to the general population to investigate whether the ID population are more at risk from detrimental lifestyles that can cause chronic disease such as CVD and T2DM. Further to this, it is important to review current literature to assess potentially modifiable causes of conditions in people with ID. The following body of work aims to investigate these areas to influence policy and practice in primary and secondary healthcare.

The remaining chapters of this thesis are described below:

1.9.1 Chapter 2

Chapter 2 provides prevalence data for T2DM, CVD, and associated modifiable risk factors in the ID population via a systematic review and meta-analysis. Secondary to this, it presents data on a comparison of prevalence rates to the general population. This review will seek to inform discussion on current possible health risks and/or health disparities in the ID population.

1.9.2 Chapter 3

Chapter 3 provides data from a systematic descriptive review of the effectiveness and quality of pragmatic lifestyle interventions aimed at primary prevention of T2DM, CVD, and associated modifiable risk factors in the ID population. This review will seek to inform discussion on the management of health conditions in the ID community and specific barriers that may occur during the administration of such interventions.

1.9.3 Chapter 4

Chapter 4 summaries the findings of the two systematic reviews and meta-analyses and discusses the limitations and strengths of this research. From this I will discuss future implications for research in the area.

Supplementary materials used throughout the work are presented in the appendices.

Chapter 2 Chronic disease prevalence in adults with ID

2.1 Introduction

The prevalence T2DM and CVD, alongside the prevalence of the associated risk factors is increasing globally (63). However, people with an ID may be at an increased risk through suggested mechanisms such as increased sedentary behaviour (64), increased anti-psychotic drug use (65), and genetic conditions associated with obesity [e.g., Prada-Willi Syndrome] (66). Many of the barriers to health and healthcare described in chapter one contribute may contribute to an increased prevalence of these types of chronic disease.

The relationship between ID, T2DM, and CVD is currently unclear. While some evidence suggests an increased risk of T2DM and CVD in people with ID owing to increased prevalence of associated risk factors (67), this relationship is not always observed (30).

2.2 Aims

To review and consolidate the evidence for current prevalence of T2DM and CVD, and associated risk factors in adults with ID. A secondary aim was to compare these with prevalence in the general population.

2.3 Methods

Investigators initials and affiliation can be seen in appendix VII.i. This systematic review is registered on PROSPERO – Registration number CRD42015019048 [appendix VII.ii]. The review protocol from the original study can be found in appendix VII. Iii.

2.3.1 Search strategy and study selection

Studies were included if they: 1. involved a cohort consisting of >80% ID persons; 2. were a population based study; 3. involved a cohort consisting of >80% persons on or over the age of 18 years; 4. contained at least one reported outcome of interest [diabetes, CVD, overweight/obesity, hypertension, dyslipidaemia, elevated glucose/impaired glucose tolerance, metabolic syndrome]; 5. reported prevalence rates for outcomes, or data from which these could be calculated. Studies were excluded if they: 1. involved a restrictively selected cohort based on outcome [e.g., all participants were obese at time of data collection]; 2. involved a cohort consisting of >25% persons with a specific ID. This was to reduce the potential bias resulting from associated morbidities from specific genetic syndromes. The percentage was a pragmatic figure based on the current proportion of the most prevalent ID syndrome [DS] (30).

I searched EMBASE, MEDLINE, and PsycINFO from 1st January 2000 to 14th March 2016. This start date was chosen because there was a need to conduct a systematic review of a more contemporary population and establish current prevalence rates due to the increase of T2DM and CVD over recent decades. my search strategy combined MeSH terms and key words including search terms for T2DM, CVD, overweight/obesity, hypertension, dyslipidaemia, elevated glucose/impaired glucose tolerance, metabolic syndrome and intellectual disability [Appendix VII.iv]. I also limited my search to English-language studies and studies with cohorts $\geq$18 years of age. Reference lists of included articles were also searched for relevant studies.

Full text articles were identified after titles and abstracts were read separately by two investigators [T.C and A.D] with discrepancies in selection being discussed. Full texts were then examined by two investigators [T.C and A.D] to check for suitability for inclusion. Only full length articles were included, review articles were removed after reference lists were examined. Lead authors were contacted for further information where inclusion/exclusion could not be determined. The authors of seven studies (68-74) were contacted for further

information. Five authors replied (68, 69, 71, 72, 74) and two provided enough information to be able to include their data within the meta-analysis (68, 74).

2.3.2 Data extraction

A data extraction form was designed and piloted specifically for this review [appendix VII.v]. From each study one investigator [TC] extracted the year of publication, country of the cohort, study type, sampling method, dates of data collection, and inclusion/exclusion criteria. I also extracted total sample size or sub-population size; mean age, proportion of male/female, severity of ID, ethnicity, how the outcomes were measured, and total number measured for outcomes, total number with outcomes, and proportion with outcomes. Alongside ID data, general population comparison data were extracted where available. Due to variation in reporting of outcomes throughout the articles, for analytic purposes descriptions and definitions of each outcome were extracted [Table 2] and then sub-categorised by definition for meta-analyses. All data were checked for accuracy by a second investigator [A.D or R.S].

Table 2. Outcome definitions from included studies

Author/year	CVD outcomes	Diabetes/blood sugar outcomes	Obesity/Overweight outcomes	Blood pressure outcomes	Lipid outcomes	Metabolic syndrome	Split by M/F	Split by ID severity
Begarie (2013)			**Obese** BMI ≥ 30 **Overweight** BMI ≥ 25 < 30					
Bhaumik (2008)			**Obese *** BMI ≥ 30 **Overweight** BMI 25.1 to 30	**Hypertension** * SBP ≥140 mmHg and/or DBP ≥90mmHg			ALL	
Chang (2012)		**Elevated blood sugar** FPG ≥ 100mg/dl or use of drugs	**Obesity** BMI (definition NR) **Overweight** BMI (definition NR) **Central overweight** FWC ≥ 80cm/MWC ≥ 90cm	**Hypertensive SBP** ≥ 130mmHg or use of drugs **Hypertensive DBP** ≥ 85mmHg or use of drugs	**Elevated triglycerides** ≥ 150mg/dl (or use of drug) **Reduced HDL** HDL Male < 40mg/dl, Female < 50mg/dl (or use of drugs)	3/5 criteria NCEP-ATPIII and MetS criteria for Taiwanese people	ALL	MILD 65% MOD 16% SEV 9% PROF 10%
Chen (2011)	**Heart disease** Such as cardiac arrhythmias and coronary atherosclerosis. Diagnoses based on clinical manifestations or ECG findings.	**Elevated blood glucose** exceeding normal range 3.9-6.1 mmol/L (70~110mg/dl) **Diabetes** FPG ≥ 7mmol/L or 2h plasma glucose≥ 11.1 mmol/L or OGTT 2h >11.1mmol/L		**Hypertension** SBP ≥ 140mmHg or DBP ≥ 90mmHg	**Elevated total cholesterol** ≥6.21 mmol/L [≥240 mg/dl] **Elevated triglycerides** ≥2.26 mmol/L [≥ 200mg/dl]			
De Winter (2009)	**Cerebrovascular disease*** Diagnosed by CT scan **Myocardial infarction*** Diagnosed by ECG changes	**Diabetes** glucose ≥ 7.0 mmol/L or use of anti-diabetic drugs.	**Obese** BMI ≥ 30	**Hypertension** SBP ≥ 140mmHg or use of drugs	**Hypercholesterolemia** Total cholesterol >5.1mmol/L to ≥6.5 mmol/L (depending on laboratory reference values) or use of cholesterol lowering drugs **Elevated LDL** ≥3.5 mmol/L			MILD 12.1% MOD 33.2% SEV 34.3% PROF 20.4%

Author/year	CVD outcomes	Diabetes/blood sugar outcomes	Obesity/Overweight outcomes	Blood pressure outcomes	Lipid outcomes	Metabolic syndrome	Split by M/F	Split by ID severity
De Winter (2013) HA-ID study	**Peripheral arterial disease** Ankle-Brachial-Index ≤ 0.9 (measured only in subjects with >1 CVD risk)							MILD 24.9% MOD 53% SEV 13.4% PROF 4.6%
De Winter (2012)_1 HA-ID study			**Obesity** BMI ≥ 30 **Overweight** BMI ≥ 25 **Central obese** FWC ≥ 88cm/MWC ≥ 102cm **Central overweight** FWC ≥ 80cm/MWC ≥ 94cm				ALL	MILD 24.8% MOD 48% SEV 16% PROF8.9%
De Winter (2012)_2 HA-ID study		**Diabetes** FSG ≥ 6.1 mmol/L or use of drugs		**Hypertension** SBP ≥ 140mmHg Or DBP ≥ 90mmHg and/or medication	**Hypercholesterolemia** Fasting serum total cholesterol >6.5 mmol/L or use of drugs	**Defined separately by:** 3/5 criteria (joint interim statement) and 3/5 criteria NCEP-ATPIII	ALL	MILD 24.5% MOD 48.6% SEV 16% PROF 8.7%
Emerson (2016)	**Cardiovascular disease** ǂ one or more of; congestive heart failure; coronary heart disease; angina; heart attack; myocardial infarction;	**Diabetes** ǂ ever diagnosed by a doctor/relevant healthcare professional	**Obesity** ǂ BMI >30	**High blood pressure** ǂ ever diagnosed by a doctor/relevant healthcare professional				

Author/year	CVD outcomes	Diabetes/blood sugar outcomes	Obesity/Overweight outcomes	Blood pressure outcomes	Lipid outcomes	Metabolic syndrome	Split by M/F	Split by ID severity
	stroke (ever diagnosed by a doctor/relevant healthcare professional).							
Emerson (2004)			**Obese *** BMI >30 **Overweight *** BMI 25.1 - 30					
Frighi (2011)		**Type 2 diabetes** Raised FPG >5.5 mmol/L	**Overweight or above** definition NR – BMI data & WC were collected				ALL	MILD 48% MOD 30.2% SEV/PROF 21.8%
Gale (2009)			**Obese** BMI 30-39.9 **Severely Obese** ≥40 **Overweight** BMI 25-29.9				ALL	
Gazizova (2012)			**Obese** BMI >30 **Overweight** BMI 25.1-30					MILD 61% MOD 24% SEV 15%
Haider (2013)	**Heart disease ₮** ever diagnosed by a doctor/relevant healthcare professional **Stroke ₮** ever diagnosed by a doctor/relevant healthcare professional	**Type 2 diabetes ₮** In the paper, it groups type 1 and 2 together, but in a separate report outcomes are available separately, it also says if been told by doctor	**Obese ₮** BMI >30 **Overweight ₮** 25 - <30					
POMONA II study Haveman (2011) + Martinez-Leal (2011) (Obesity data)	**Heart attack ₮** Definition NR **Cerebrovascular disease ₮** Definition NR	**Diabetes ₮** Definition NR	**Obese** definition NR – BMI data were collected **Overweight** definition NR – BMI data were collected	**Hypertension ₮** Definition NR				Haveman MILD 22.7% MOD 28.2% SEV 20.7% PROF 11.8% Martinez-leal MILD 21.8%

Author/year	CVD outcomes	Diabetes/blood sugar outcomes	Obesity/Overweight outcomes	Blood pressure outcomes	Lipid outcomes	Metabolic syndrome	Split by M/F	Split by ID severity
								MOD 27.7% SEV 19.7% PROF 11.4%
Havercamp (2015)			**Obese*** definition NR **Overweight*** definition NR					MILD 35.7% MOD 26.6% SEV 15.6% PROF 22.1%
Havercamp (2004)	**Cardiovascular disease*** Definition NR	**Diabetes*** Definition NR	**Overweight or above*** Definition NR	**Elevated BP*** Definition NR				MILD 39.4% MOD 26.6% SEV 14.7% PROF 10.6%
Henderson (2008)		**Type 2 diabetes*** Derived from medical problem lists	**Obese*** BMI >30 **Overweight*** BMI ≥ 25 ≤ 30	**Hypertension*** Derived from medical problem lists	**Dyslipidaemia*** Derived from medical problem lists			
Henderson (2009)			**Overweight or above** ǂ** BMI ≥ 25				ALL	MILD/MOD 53% SEV/PROF 47%
Hove (2004)			**Obese** BMI ≥ 30 **Overweight** BMI 25 -29.9				ALL	MILD 39.2% MOD 42.1% SEV 15.5%
Hsieh (2014)			**Obese** ǂ BMI ≥ 30 **Overweight** ǂ BMI ≥ 25 <30				ALL	MILD 44.9% MOD 23.7% SEV/PROF 8.4%
Hsu (2011)			**Overweight or above** * BMI ≥ 24			3/5 criteria NCEP-ATPII	ALL	MILD/MOD 47% SEV/PROF 53%
Ito (2006)			**Obese** BMI >30 **Overweight** BMI 25-30				ALL	
Jansen (2013)	**Cerebrovascular accident*** acute disruption of cerebral circulation with focal neurological						ALL	MILD 6.9% MOD 37.8% SEV 29% PROF 26.3%

Author/year	CVD outcomes	Diabetes/blood sugar outcomes	Obesity/Overweight outcomes	Blood pressure outcomes	Lipid outcomes	Metabolic syndrome	Split by M/F	Split by ID severity
	symptoms ≥24hr **Myocardial infarction*** clinical signs & ECG diagnosis and/or lab results							
Janicki (2002)	**Cardiovascular disease** ₮ NR	**Diabetes** ₮ Adult onset	**Obese** ₮ BMI >27 **Overweight**₮ BMI 22-27	**Hypertension** ₮ NR	**Hyperlipidaemia** ₮ NR		ALL	MILD 1.3% MOD 50.3% SEV/PROF 47%
Lee (2011)	**Cardiac illness*** History of coronary heart disease or congestive cardiac failure	**Diabetes*** implied by prescription of hypoglycaemic drugs	**Obese*** BMI ≥ 31 **Overweight*** BMI 26-30	**Hypertension*** Definition NR				MILD 33% MOD 22% SEV 23% PROF 21%
Lennox (2006)			**Obese** BMI >30 **Overweight** BMI 25-30	**Elevated BP** SBP>140mmHg				
Levy (2006)		**Diabetes*** Definition NR	**Obese *** BMI ≥ 30 **Overweight** BMI 25 – 29.9 **Obese/overweight** ≥25	**Elevated BP*** **Definition NR**	**Hypercholesterolemia*** Definition NR			MILD 47.6% MOD 31.1% SEV 14.6% PROF 6.8%
Levy (2007)		**Diabetes*** Definition NR	**Overweight and above** BMI ≥ 25	**Elevated BP*** Definition NR	**Hypercholesterolemia*** Definition NR			SEV 65.4% PROF 34.6%
Lewis (2002)			**Obese** BMI ≥ 30 **Overweight** BMI 25 – 29.9	**Elevated BP** SBP >140mmHg or DBP >90mmHg	**Hypercholesterolemia** Total cholesterol ≥ 240mg/dl			MILD 37.1% MOD 16.4% SEV 14.7% PROF 15.3%
Lin, J.D. (2013)		**Hyperglycaemia *** FPG ≥ 126mg/dl		**Hypertension *** SBP ≥ 140mmHg or DBP ≥ 90mmHg or use of drugs	**Hyperlipidaemia *** Triglyceride ≥ 200mg/dl or Total cholesterol ≥ 240mg/dl			
Lin, L.P. (2015)			**Obese** BMI ≥ 27 **Overweight**					MILD 6.5% MOD 32.6% SEV 34.8%

Author/year	CVD outcomes	Diabetes/blood sugar outcomes	Obesity/Overweight outcomes	Blood pressure outcomes	Lipid outcomes	Metabolic syndrome	Split by M/F	Split by ID severity
			BMI 24-26.9					PROF 26.1%
Lin, L.P. (2012)				**Hypertension** SBP ≥ 140mmHg or DBP ≥ 90mmHg				
Marshall (2003)			**Obese** BMI ≥ 31 **Overweight** BMI 26-30	**Hypertension** SBP >140mmHg	**Elevated Cholesterol** Definition NR			
Maaskant (2009)			**Obese** BMI ≥ 30 **Overweight** BMI 25 <30					
McCarron (2013)	**Heart disease** ₮ History of Angina, heart attack, coronary heart failure, open heart surgery (ever diagnosed by a doctor/relevant healthcare professional) **Stroke/TIA** ₮ ever diagnosed by a doctor/relevant healthcare professional			**Hypertension** ₮ ever diagnosed by a doctor/relevant healthcare professional				
McDermott (2006)	**Coronary artery disease*** ICD-9-codes **Transient ischemic attack*** ICD-9- codes	**Type 1 & Type 2 Diabetes*** ICD-9- codes	**Obese*** NR	**Hypertension & Elevated BP*** ICD-9- codes				
McDermott (2007)		**Diabetes*** Although a detailed description is given, it is not possible to						

Author/year	CVD outcomes	Diabetes/blood sugar outcomes	Obesity/Overweight outcomes	Blood pressure outcomes	Lipid outcomes	Metabolic syndrome	Split by M/F	Split by ID severity
		define the type of diabetes is used as an outcome.						
McGuire (2007)			**Obese** ǂ BMI >30 **Overweight** ǂ BMI >25					MILD 14.1% MOD 63.5% SEV 12.8% PROF 9%
Melville(2008)			**Obese** BMI ≥30 **Overweight** BMI ≥25<30				ALL	MILD 40.9% MOD 25.1% SEV 18.2% PROF 15.8%
Merrick (2004)	**Heart disease** ǂ Definition NR	**Type 2 diabetes** ǂ Definition NR	**Overweight and above** ǂ BMI >27	**Hypertension** ǂ Definition NR	**Hyperlipidaemia** ǂ Definition NR			
Mikulovic (2014)			**Obese** BMI>30 **Overweight** BMI ≥25				ALL	
Molteno (2000)			**Obese** BMI>30 **Overweight** BMI>25 <30				ALL	MILD 0.3% MOD 18.7% SEV 37.7% PROF 33.5% **MISSING DATA**
Moore (2004)			**Obese** BMI≥30 **Overweight** BMI≥25 <30				ALL	
Morin (2012)	**Heart disease** ǂ ICD-10-codes	**Diabetes** ǂ ICD-10-codes						MILD 32.9% MOD 46.4% SEV 11.2% PROF 5.2%
Moss (2009)		**Elevated glucose** Non-fasting test – definition NR	**Overweight and above** BMI >25	**Hypertension** Definition NR	**Elevated total cholesterol** Non-fasting test – definition NR		WEIGHT ONLY	
Robertson (2000)			**Obese** BMI >30 **Overweight** BMI 25.1-30				ALL	
Rurangirwa (2006)			**Overweight/obese** ǂ ≥ 25					
Shah (2006)		**Diabetes** ǂ Definition NR						
Shireman (2010)		**Diabetes*** ICD-9-codes						

Author/year	CVD outcomes	Diabetes/blood sugar outcomes	Obesity/Overweight outcomes	Blood pressure outcomes	Lipid outcomes	Metabolic syndrome	Split by M/F	Split by ID severity
Sohler (2009)		**Diabetes*** Definition NR	**Obese*** BMI ≥ 30 **Overweight*** BMI 25-29.9	**Hypertension*** Definition NR	**Hypercholesterolemia*** Total cholesterol >240mg/dl			
Stancliffe (2011)			**Obese** BMI≥ 30 **Overweight** BMI≥ 25-29.9 **Overweight and above** BMI ≥25					
Stedman (2010)			**Obese*** BMI ≥ 30 **Overweight*** BMI ≥25-29.9				ALL	
Tyler (2010)	**Coronary heart disease*** ICD-9-codes	**Diabetes*** ICD-9-codes	**Obese*** ICD-9-codes	**Hypertension*** ICD-9-codes	**Hyperlipidaemia*** ICD-9-codes		OBESITY & HYPERTE-NSION ONLY	
Vacek (2013)				**Hypertension*** ICD-9-codes				
Van Den Akker (2006)	**Coronary heart disease*** ICD-10-codes **Cerebrovascular disease*** ICD-10-codes			**Hypertension*** ICD-10-codes				MILD 11% MOD 53% SEV 28% PROF 8%
Van Den Louw (2009)				**Hypertension** SBP >140mmHg				MILD 10% MOD 38% SEV/PROF 52%
Wallace (2008)	**Cardiovascular disease *** History of: Peripheral vascular disease, stroke, or coronary heart disease.	**Elevated glucose *** >6.1mmol/L (fasting and non-fasting tests grouped together in results) **Type 1 & 2 diabetes** *	**Obese *** BMI ≥ 30 **Overweight** BMI 25-29.9	**Hypertension *** SBP >140mmHg	**Elevated cholesterol *** >5.5mmol/L (fasting and non-fasting tests grouped together in results)			
Wang (2007)	**Cardiovascular disease[Ŧ]** ICD-9-codes		**Overweight and above[Ŧ]**					

Author/year	CVD outcomes	Diabetes/blood sugar outcomes	Obesity/Overweight outcomes	Blood pressure outcomes	Lipid outcomes	Metabolic syndrome	Split by M/F	Split by ID severity
Wong (2011)	**Heart disease**[Ŧ] Definition NR **Cerebrovascular disease**[Ŧ] Definition NR	**Diabetes**[Ŧ] Definition NR	**Overweight and above**[Ŧ] BMI >23	**Hypertension**[Ŧ] Definition NR	**Hypercholesterolemia**[Ŧ] Definition NR			MILD 4.9% MOD 41.8% SEV/PROF 51.9%
Yen (2005)			**Obese**[Ŧ] BMI ≥27 **Overweight**[Ŧ] BMI 24-26.9				ALL	MILD 22.2% MOD 34.9% SEV 28.1% PROF 14.8%
Zaal-Schuller (2015)	**Peripheral arterial disease** Ankle-Brachial-Index <0.9						ALL	MILD/MOD 51.1% SEV/PROF 48.9%

***retrospective data extracted from database/medical records, or, Ŧ data self-reported or reported by carer; NR [not reported]; SBP [systolic blood pressure]; DBP [diastolic blood pressure]; HDL [high density lipoprotein]; LDL [low density lipoprotein]; BMI [body mass index]; FPG [fasting plasma glucose]; MWC [male waist circumference]; FWC [female waist circumference].**

2.3.3 Data synthesis

Based on the reported descriptions in the articles, CVD outcomes were sub-categorised as: ischaemic heart disease [including myocardial infarction, congestive heart disease, and coronary arterial disease]; undefined CVD [including outcomes labelled as CVD in articles but without any definition and CVD which was defined as several separate conditions not suited to one specific outcome]; undefined heart disease [including outcomes labelled as heart disease in articles without any definition]; cerebrovascular disease [including stroke and transient ischaemic attack]; and peripheral arterial disease. These outcomes were included in an overall meta-analysis as well as being reported on separately.

Diabetes definitions within the articles varied and included T2DM, combined type 1 and 2 diabetes, and undefined diabetes. Due to varied reporting, a meta-analysis was performed for all diabetes types combined, labelled as 'any diabetes' and a separate meta-analysis was performed for T2DM only. Glucose definitions were varied and a meta-analysis was not possible.

Body Mass Index [BMI] outcomes were labelled as obese [BMI>30 kg/m^2] and overweight [BMI 25-29·9 kg/m^2]. In some articles, a combined overweight and above [BMI $\geq$25 kg/m^2] was used as an outcome. For analytic purposes, where papers reported both obese and overweight data, these were combined to create an overweight and above outcome. Due to varied reporting for lipid outcomes, outcomes were grouped together for one meta-analysis for dyslipidaemia.

Where duplication of data or cohorts was found, the largest sample for each outcome was chosen to include in meta-analyses to avoid duplication of data. Descriptive information for each study is presented in Table 3.

Table 3. Description of included studies

		Severity of ID (%)							Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
CROSS-SECTIONAL STUDIES																						
Begarie (2013) (75)	France	NR				Questionnaire data (CFS)	255	NR	NR	21.9	12.6											
Chang (2012) (76)	Taiwan	65	16	9	10	Annual health check database (NR)	129	56.6	33.0	20.9	28.7		10.1						12.4	20.9		6.2
Chen (2011) (77)	China	NR				Physical exam (2008)	117	NR	NR				11.1	3.4		7.7				13.7		5.1
De Winter (2009) (78)	Netherlands	12.1	33.2	34.3	20.4	GP screened/ medical chart/structured interview (CFS)	470	NR	NR	15			36.7	8.8		1.3	2.3			31.9		

		Severity of ID (%)								Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
De Winter (2015) (79) **HA-ID study**	Netherlands	24.4	47.6	16.7	9	Medical records/Physical examination (CFS)	990	51.3	61.1				52.8 *		12.5				44.7 *	23.1 *	21.1 *	
De Winter (2013) (80) **HA-ID study**	Netherlands	24.9	53	13.4	4.6	Medical records/Physical examination (CFS)	629	53.6	61.5												20.7	
De Winter (2012)_1 (81) **HA-ID study**	Netherlands	24.8	48	16	8.9	Medical records/Physical examination (CFS)	945	51.0	61.5	38.2	25.6											
De Winter (2012)_2 (82) **HA-ID study**	Netherlands	24.5	48.6	16	8.7	Medical records/Physical examination (CFS)	980	51.3	61.5					13.7 *					44.7	23.1		
Emerson (2016) (83)	UK	NR				Questionnaire data (CFS)	299	NR	NR		41.7		5	6				3				

		Severity of ID (%)								Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
Emerson (2005) (84)	UK	NR				Audit review of the quality of supported accommodation (2000-2002)	1304	54.0	49.3	28	27											
Frighi (2011) (85)	UK	48	30.2	21.8		Care home visitation questionnaire data (CFS)	202	52.0	42.1			72.3			4.9							
Gale (2009) (86)	UK	NR				GP survey data collected for study (2007-2009)	1097	58.0	NR	26.9	33.1											
Gazizova (2012) (87)	UK	61	24	15	-	Routine health assessment of people within a	100	67.0	NR	28	25											

		Severity of ID (%)								Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
						service (2009)																
Haveman (2011) (88) **POMONA II study**	14 European countries	22.7	28.2	20.7	11.8	Interview survey data (CFS)	1253	51.0	41.0					4.3		1.8	1.5					
Martinez-Leal (2011) (89) **POMONA II study**	14 European countries	21.8	27.7	19.7	11.4	Interview survey data (CFS)	1257	50.5	41.4	20.5	16.3											
Henderson (2009) (90)	USA	53		47		Health questionnaire data (CFS)	1196	53.0	NR			68.9										
Hove (2004) (91)	Norway	39.2	42.1	15.5	-	Health questionnaire data (CFS)	274	52.0	NR	34.8	19.1											
Hsieh (2014) (92)	USA	44.9	23.7	8.4		Longitudinal study baseline data	1450	55.2	37.1	28.9	38.3											

		Severity of ID (%)								Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
						(2012) questionnaire data (CFS)																
Janicki (2002) (93)	USA	1.3	50.3	47		Health questionnaire data (CFS)	1373	53.0	53.5	55.8	29.9		15	4.4				21.9		4.2		
Lennox (2006) (94)	Australia	NR				Medical history chart/GP examination (CFS)	25	NR	45.0	30.4	34.8		4.3									
Lin, L.P. (2015) (95)	Taiwan	6.5	32.6	34.8	26.1	NR (CFS)	67	NR	NR	15.2	31.5											
Marshall (2003) (96)	UK	NR				Health check questionnaire (CFS)	728	NR	NR	28	36.1		14.6							10.6		
McCarron (2013) (97)	Ireland	NR				Face to face questionnaire – first wave data for a	753	45.0	54.8				15.4			11.8	2.9					

		Severity of ID (%)							Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
						longitudinal study (CFS)																
McGuire (2007) (98)	Ireland	14.1	63.5	12.8	9	Postal questionnaire (CFS)	155	53.5	37.0	37.7	30											
Melville (2008) (99)	UK	40.9	25.1	18.2	15.8	Face to face interview/physical examination by nurse (CFS)	945	55.6	NR	32.9	31.5											
Merrick (2004) (100)	Israel	NR				Health questionnaire data (CFS)	2282	51	49.8				10.9		6.8			14.2		12.7		
Molteno (2000) (101)	South Africa	0.3	18.7	37.7	33.5	Researcher collected data (CFS)	615	51	NR	11.4	21.5											
Moore (2004) (102)	Australia	NR				Researcher collected data (CFS)	93	NR	32.5													

		Severity of ID (%)							Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
Morin (2012) (103)	Canada	32.9	46.4	11.2	5.2	Mail questionnaire data (CFS)	789	NR	NR					8.2				7.2				
Moss (2009) (104)	South Africa	NR				Questionnaire/physical examination by nurse (CFS)	100	47	NR			67	6							23		28
Robertson (2000) (105)	UK	NR				Questionnaire/interview (CFS)	500	60.3	44.4	17.5	26											
Shah (2006) (106)	UK	NR				Mail questionnaire (CFS)	119	NR	NR					5.9								
Stedman (2010) (107)	New Zealand	NR				Service user database data collected by doctor/healthy lifestyles coordinator	98	NR	43	51	30.6											

		Severity of ID (%)							Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
						(6 months prior to study)																
Van Den Louw (2009) (108)	Netherlands	10	38	52		Researcher collected data (CFS)	258	51.6	47				17.4									
Wang (2007) (109)	Taiwan	NR				Health questionnaire data (CFS)	1128	57.6	NR			27.1						6.5				
Wong (2011) (110)	Hong Kong	4.9	41.8	51.9		Survey questionnaire delivered by health professional (CFS)	811	53.3	44			27.3	7.9	5.3			2.2	3.7		1.2		
Zaal-Schuller (2015) (111)	Netherlands	51.1		48.9		Researcher screened (CFS)	407	NR	NR												8.4	
RETROSPECTIVE STUDIES																						

		Severity of ID (%)							Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
Bhaumik (2008) (112)	UK	NR				Questionnaire data register (1998-2001)	1119	59.0	NR	28	20.7		37.5									
Haider (2013) (113)	Australia	NR				Telephone questionnaire (2008-2009)	897	NR	38.4	28	26.6				7		2	8.6				
Havercamp (2004) (114)	USA	39.4	26.6	14.7	10.6	Health survey interview data (2001-2002)	477	56.1	NR			59.6 *	15.9	8				7.1				
Havercamp (2015) (115)	USA	35.7	26.6	15.6	22.1	Health survey interview data (2010)	17679	56.6	NR	29.2	31.1											
Henderson (2008) (116)	USA	NR				Medical chart data (2005)	100	NR	NR	18	39		29		2					39		

		Severity of ID (%)								Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
Hsu (2012) (117)	Taiwan	47		53		Health examination charts (2009)	164	NR	33.0			42.1							11.6			
Ito (2006) (118)	Japan	NR				Care home periodic medical evaluation data (2002)	526	NR	NR	27.2	7											
Jansen (2013) (119)	Netherlands	6.9	37.8	29	26.3	Medical file data (2007)	510	55.7	65.5							1.8	4.1					
Lee (2011) (120)	Australia	33	22	23	21	ID database with medical data (2006-2011)	162	52.0	44.0	19.8	10.5		11.1	10.5		2.5						
Levy (2006) (121)	USA	47.6	31.1	14.6	6.8	Medical record review (NR)	103	52.4	38.2	33	36.9		24.3	10.7						20.4		

		Severity of ID (%)								Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
Levy (2007) (122)	USA	-	-	65.4	34.6	Medical record review/retrospective medical billing data (2006-2007)	52	52.0	NR			69.2	21.2	7.7						19.2		
Lewis (2002) (123)	USA	37.1	16.4	14.7	15.3	Medical records/information from carers/physical exam by nurse (1997)	353	49.9	35.8	25.7	29.1		5.1							9.9		
Lin, J.D. (2013) (124)	Taiwan	NR				Annual health examination chart (2010-2012)	215	NR	NR				24.2	6.5						10.2		
Lin, L.P. (2012) (125)	Taiwan	NR				Annual health examinatio	184	62.5	NR				17.9									

		Severity of ID (%)							Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
						n chart (2010)																
Maaskant (2009) (126)	Netherlands	NR				Database data from a service care provider (2002-2007)	336	55.1	NR	30.5	9.8											
McDermott (2006) (127)	USA	NR				Electronic medical records (1990-2003)	618	NR	NR				29	10.4		2.3	0.3					
McDermott (2007) (128)	USA	NR				Electronic medical records (1990-2003)	585	NR	NR					10.4								
Mikulovic (2014) (129)	France	NR				Face to face interview questionnaire (2007)	570	NR	38.1	45.6	17.2											

		Severity of ID (%)							Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
Rurangirwa (2006) (130)	USA	NR				Study questionnaire data (2004)	173	57.9	23.3			47.4										
Shireman (2010) (74)	USA	NR				Medical care database data (2005-2006)	291	52.6	NR					11.2								
Sohler (2009) (131)	USA	NR				Medical chart data (2001-2005)	5930	NR	NR	27.5	43.3		19.9	4.5						26.5		
Stancliffe (2011) (132)	USA	NR				Consumer survey interview (2008-2009)	8911	NR	43.5	28.6	33.6	62.2										
Tyler (2010) (133)	USA	NR				Electronic medical care database (2005-2008)	1267	53.8	38.8		18.3		24.7	10.3		3.5				35		

		Severity of ID (%)							Prevalence of reported outcomes (%)												
Author/year	**Country**	**Mild ID**	**Moderate ID**	**Severe ID**	**Profound ID**	**Data Source/collection method (year collected if retrospective)**	**Total N**	**Male (%)**	**Mean age**	**Overweight**	**Obesity**	**Overweight and above**	**Hypertension**	**Undefined/other diabetes**	**T2DM**	**Ischaemic heart disease**	**Cerebrovascular disease**	**Undefined CVD or HD**	**Metabolic syndrome**	**Dyslipidaemia**	**Peripheral arterial disease**	**Elevated glucose**
Vacek (2013) (68)	USA	NR				Medical care database data (2006-2007)	3079	NR	NR				9.1									
Van Den Akker (2006) (134)	Netherlands	11	53	28	8	Electronic health service provider database (NR)	436	52	NR				4.1			0.5	0.7					
Wallace (2008) (135)	Australia	NR				Medical chart data from GP n (2002-2005)	155	52	NR	35.3	35.3		18.3	4.6				6.9		26.7		8
Yen (2005) (136)	Taiwan	22.2	34.9	28.1	14.8	Postal questionnaire data (2001)	516	NR	NR	15.7	23.6											

NR (not reported); CFS (collected for study); ID (intellectual disability); CVD (Cardiovascular disease); HD (Heart disease). *Not included in meta-analyses due to duplication of data.

For the primary objectives, random effects models were used to pool point prevalence for each outcome. Random effects models were used due to the high amount of variability between studies of this nature. A secondary meta-analysis was conducted using general population comparison data for each outcome where data were presented from the same population and time period as the population with ID. Heterogeneity was assessed using the I^2 statistic. Meta-regression and sub-group analysis was used to determine if study level characteristics explained heterogeneity. These study characteristics were severity of ID, mean age, continent, and method of data collection [self/carer reported, researcher collected, retrospective records/database]. All analyses were conducted using STATA statistical software, version 14·0 [Stata Corp]. Significance level was set at $p<0·05$.

2.3.4 Risk of bias

Risk of bias was assessed using the Joanna Brigg's Institute critical appraisal tool for studies reporting prevalence data (137); the assessment consists of a checklist of ten items focused on sampling, data analysis, and reporting. Each item was assessed independently by two investigators [T.C and L.C] and categorised as yes/no/unclear/not applicable. Disagreements were discussed between the two investigators. Funnel plots and the Egger test were used to examine potential publication bias for outcomes with more than 10 studies.

2.4 Results

2.4.1 Identification of studies

I identified 4782 articles via the literature searches. After duplicates were removed, 3845 articles were screened [figure 2]. The full-texts of 162 articles were reviewed after seven articles were added from other sources. The articles from other sources were picked up in a scoping search from Google Scholar but were not included on returned searches of our chosen databases. Sixty-four articles (32, 38, 39-100) from 60 studies were included for quantitative analysis after review. Four of these articles reported findings from one study (43-46) and a further two articles reported findings from another study (52, 53)

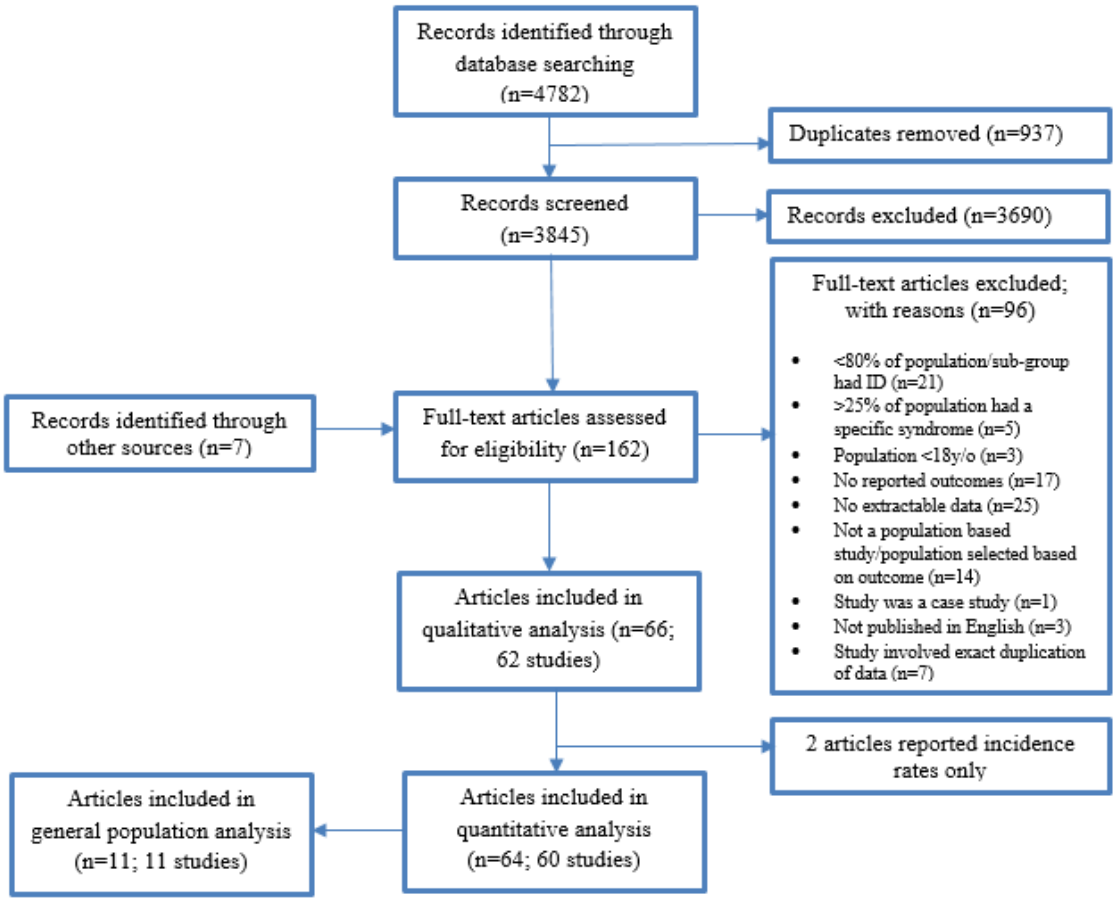


Figure 2. Flow diagram of study selection

2.4.2 Study characteristics

Included studies involved participants from 23 countries over five continents. Two articles from one study covered 14 European countries (52, 53). Most studies were conducted in the USA/Canada [n=18]. The remaining studies were conducted in Europe [Netherlands [n=7]; UK [n=9]; France [n=2]; Norway [n=1]; Ireland [n=2] and Israel [n=1]], Asia (China [n=1]; Taiwan [n=8]; Hong Kong [n=1]; Japan [n=1]], Australia/NZ [n=6], and South Africa [n=2].

Most of the studies presented researcher collected screening data [n=25]. The remaining studies used retrospective database/medical records data [n=19];

self/carer reported questionnaire data [n=12]. Four studies used a combination of the above methods.

Studies were published between 2000 and 2016. The average mean age was 44·1 years with a range of 23·3 to 65·5 years. The average percentage male was 53·9%. The number of people included in the studies ranged from 25 to 17,679 with a mean of 1088 and a median of 505.

Eleven of the studies presented general population comparison data for inclusion in the secondary meta-analysis. (78, 82, 87, 114-116, 118, 119, 127, 128, 133). The studies presented data for over 342,000 people from the general population and over 69,600 for the ID population. Number of people included in the studies ranged from 195 to 312,144 for the general population and 100 to 20,395 for the ID population.

2.4.3 Risk of bias

Most articles received a high-quality grading for sample bias [50/66, 75·8%]; data collection methods (57/66, 86·4%); and confounding and explanatory factors [57/66, 86·4%] [table 4].

Table 4. Quality assessment grading for included studies.

	Sample bias						Data collection				Confounding factors		
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?	**OVERALL**	Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?	**OVERALL**	Confounding factors, subgroups, and differences	Identified subpopulations?	**OVERALL**
Begarie (2013)	+	+	+	++	+	+	+	++	++	++	++	++	++
Bhaumik (2008)	++	++	++	++	++	++	++	++	+	++	++	NA	++
Chang (2012)	++	+	+	++	++	++	++	+	++	++	++	NA	++

	Sample bias						Data collection				Confounding factors		
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?	**OVERALL**	Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?	**OVERALL**	Confounding factors, subgroups, and differences	Identified subpopulations?	**OVERALL**
Chen (2011)	++	++	++	-	++	++	++	+	++	++	++	++	++
De Winter (2009)	+	+	++	++	++	++	++	+	++	++	++	NA	++
De Winter (2015) **HA-ID study**	++	++	++	++	++	++	++	++	++	++	++	NA	++

	Sample bias						Data collection				Confounding factors		
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?	**OVERALL**	Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?	**OVERALL**	Confounding factors, subgroups, and differences	Identified subpopulations?	**OVERALL**
De Winter (2013) **HA-ID study**	++	++	++	++	++	++	++	++	++	++	++	NA	++
De Winter (2012)_1 **HA-ID study**	++	++	++	++	++	++	++	++	++	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
De Winter (2012)_2 **HA-ID study**	++	++	++	++	++	++	++	++	++	++	++	NA	++
Emerson (2016)	++	++	+	+	++	++	+	+	++	++	++	++	++
Emerson (2004)	++	+	+	++	+	++	++	+	+	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Frighi (2011)	++	++	+	++	++	++	++	+	++	++	++	NA	++
Gale (2009)	++	++	+	-	++	++	+	++	++	++	++	NA	++
Gazizova (2012)	++	+	+	++	++	++	+	++	++	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Haider (2013)	++	++	++	++	++	++	++	+	++	++	+	NA	+
Haveman (2011) **POMONA II study**	+	+	+	++	+	+	+	+	++	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Martinez-Leal (2011) **POMONA II study**	+	++	+	++	+	++	+	+	++	++	++	NA	++
Haverkamp (2015)	+	++	++	++	+	++	+	+	++	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Haverca mp (2004)	+	++	++	++	+	++	+	+	+	+	++	NA	++
Henderso n (2008)	-	+	-	-	+	-	+	+	++	++	+	NA	+
Henderso n (2009)	+	+	+	++	+	+	+	+	++	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Hove (2004)	+	-	+	++	+	+	+	++	++	++	++	NA	++
Hsieh (2014)	++	++	+	++	++	++	++	+	++	++	++	NA	++
Hsu (2011)	+	+	+	++	+	+	++	+	++	++	++	NA	++
Ito (2006)	+	+	+	-	++	+	++	+	++	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Jansen (2013)	+	+	+	++	++	++	+	++	++	++	++	NA	++
Janicki (2002)	+	++	+	++	++	++	+	+	+	+	++	NA	++
Lee (2011)	+	++	+	++	++	++	+	+	+	+	+	NA	+

	Sample bias						Data collection				Confounding factors		
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?	**OVERALL**	Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?	**OVERALL**	Confounding factors, subgroups, and differences	Identified subpopulations?	**OVERALL**
Lennox (2006)	-	+	+	-	++	+	++	+	+	++	+	NA	+
Levy (2006)	+	+	+	++	+	+	+	+	++	++	++	NA	++
Levy (2007)	-	+	-	++	++	+	+	+	++	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Lewis (2002)	++	++	+	++	++	++	++	+	++	++	-	NA	-
Lin, J.D. (2013)	++	++	+	++	++	++	++	+	++	++	++	NA	++
Lin, L.P. (2015)	+	+	+	++	++	++	++	++	++	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Lin, L.P. (2012)	++	++	++	++	++	++	++	+	++	++	++	NA	++
Marshall (2003)	++	++	++	++	++	++	++	++	+	++	++	NA	++
Maaskant (2009)	+	+	+	++	++	++	++	+	++	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
McCarron (2013)	++	++	+	++	+	++	+	-	-	-	++	NA	++
McDermott (2006)	+	++	++	++	+	++	+	+	++	++	-	NA	-
McDermott (2007)	+	++	+	-	+	+	++	+	++	++	-	NA	-

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
McGuire (2007)	+	++	+	++	+	++	+	+	+	+	++	NA	++
Melville(2008)	++	++	+	++	++	++	++	++	++	++	++	NA	++
Merrick (2004)	+	+	+	++	++	++	+	+	+	+	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Mikulovic (2014)	+	+	+	++	++	++	++	+	++	++	++	NA	++
Molteno (2000)	+	+	-	-	-	-	++	+	+	++	++	NA	++
Moore (2004)	+	+	+	++	+	+	++	++	+	++	++	NA	++

	Sample bias						Data collection				Confounding factors		
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?	**OVERALL**	Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?	**OVERALL**	Confounding factors, subgroups, and differences	Identified subpopulations?	**OVERALL**
Morin (2012)	++	+	+	++	+	++	+	+	++	++	++	NA	++
Moss (2009)	+	+	+	++	++	++	++	++	++	++	++	NA	++
Robertson (2000)	+	+	+	++	+	+	+	+	+	+	+	NA	+

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Rurangirwa (2006)	+	++	+	++	++	++	+	++	++	++	++	NA	++
Shah (2006)	+	+	+	-	++	+	+	+	+	+	NA	NA	NA
Shireman (2010)	++	++	+	+	++	++	++	++	++	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Sohler (2009)	++	++	+	++	++	++	++	++	++	++	++	NA	++
Stancliffe (2011)	++	++	++	++	++	++	+	+	+	+	+	NA	+
Stedman (2010)	+	+	+	-	++	+	++	++	++	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Tyler (2010)	++	++	++	++	++	++	+	+	+	+	++	NA	++
Vacek (2013)	+	++	+	+	++	++	+	+	++	++	++	NA	++
Van Den Akker (2006)	++	++	+	++	++	++	++	++	++	++	++	NA	++

	Sample bias						Data collection				Confounding factors		
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?	**OVERALL**	Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?	**OVERALL**	Confounding factors, subgroups, and differences	Identified subpopulations?	**OVERALL**
Van Den Louw (2009)	++	+	++	++	++	++	++	++	++	++	++	NA	`++
Wallace (2008)	+	+	+	-	++	+	++	++	++	++	++	NA	++
Wang (2007)	+	+	+	+	++	+	+	+	++	++	++	NA	++

	Sample bias					OVERALL	Data collection			OVERALL	Confounding factors		OVERALL
Author/year	Representative of population?	Recruited appropriately?	Adequate sample size?	Subjects and setting described in detail?	Data analysis conducted with sufficient coverage?		Objective & standard criteria used for measurement of	Conditions measured reliably?	Appropriate statistical analysis?		Confounding factors, subgroups, and differences	Identified subpopulations?	
Wong (2011)	+	++	+	++	++	++	+	+	++	++	++	NA	++
Yen (2005)	+	+	+	++	++	++	++	+	+	++	++	NA	++
Zaal-Schuller (2015)	+	+	+	-	+	+	++	+	++	++	++	NA	++

++ [Yes]; - [No]; + [Unsure]; NA [Not applicable].

The results of the Egger's test and funnel plots indicated no publication bias for the outcomes with more than 10 studies [any CVD/heart disease, hypertension, obesity, overweight, overweight and above, any diabetes, and dyslipidaemia] [appendix VII.vi].

2.4.4 Meta-analyses

2.4.4.1 Prevalence of diabetes

Results of the diabetes meta-analyses are shown in figure 3 and table 5. Prevalence estimates for T2DM ranged from 2% to 13%. The pooled prevalence for T2DM was 7·6% [95% CI 4·7%-10·6%; I^2= 0%]. The pooled prevalence for other diabetes was 8.9% [7.3-10.4; I^2= 0%]. The overall prevalence of any diabetes ranged from 2% to 11%. The pooled prevalence for any diabetes was 8·6% [7·2-9·9; I^2=0%].

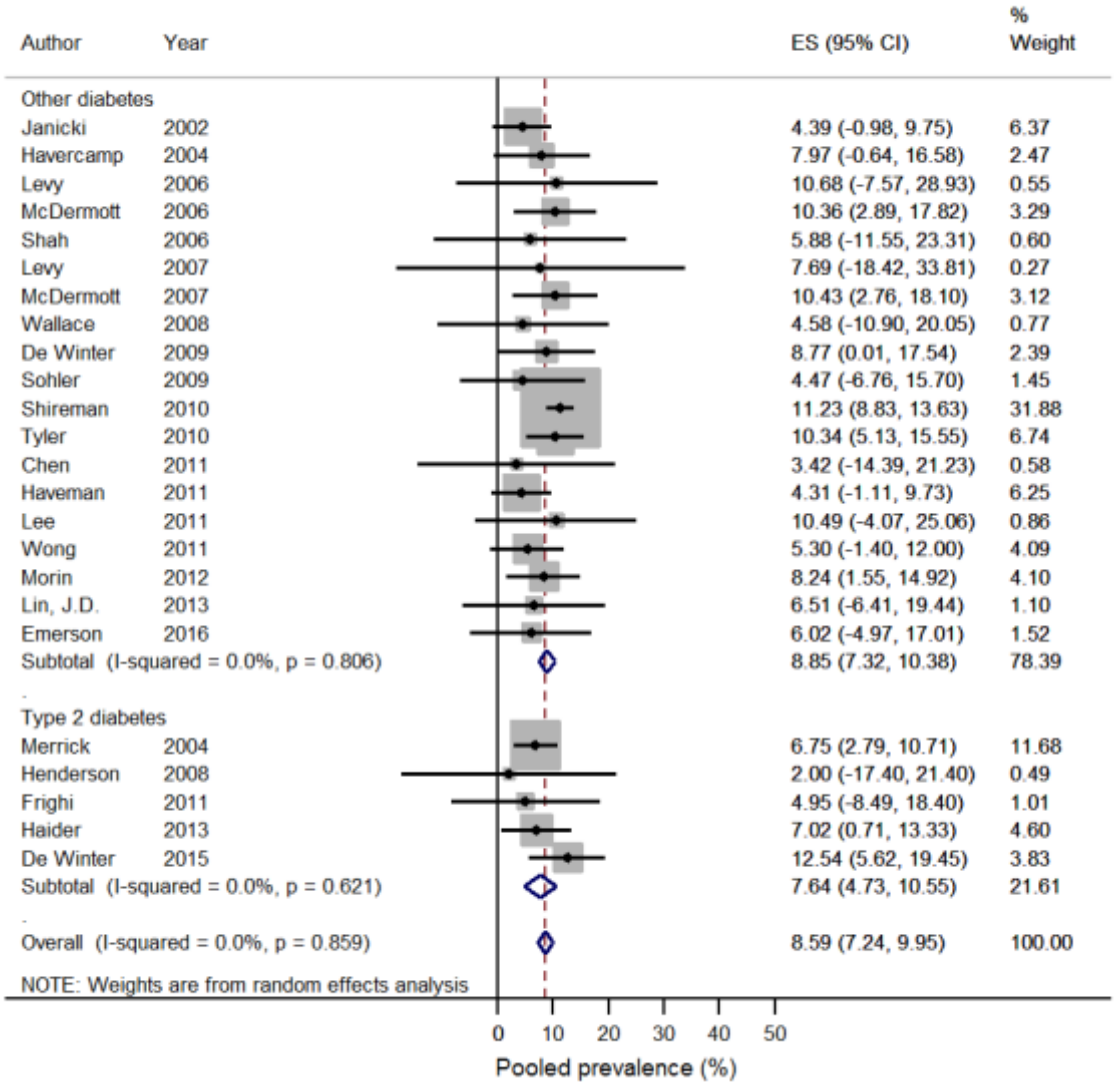


Figure 3. Pooled prevalence for diabetes outcomes

2.4.4.2 Prevalence of cardiovascular disease

Prevalence estimates for ischaemic heart disease ranged from 0·5% to 12% and pooled prevalence was 3·7% [1·1-6·3; I^2=0%]. For peripheral arterial disease, pooled prevalence was 14·9% [2.9-27; I^2=76.8%]; undefined CVD 9·8% [1·1-18·5; I^2=82.8%]; and for undefined heart disease 8·9% [4-13·8; I^2=65.6%]. The overall pooled prevalence for all CVD/heart disease was 7·5% [4·3-10·8; I^2=74%]; however, this ranged by individual study from 4% to 22% [figure 4]. Prevalence estimates for cerebrovascular disease ranged from 0·5%

to 4%. The pooled prevalence for cerebrovascular disease was 2% [0-4·6; I^2=0%] [figure 5].

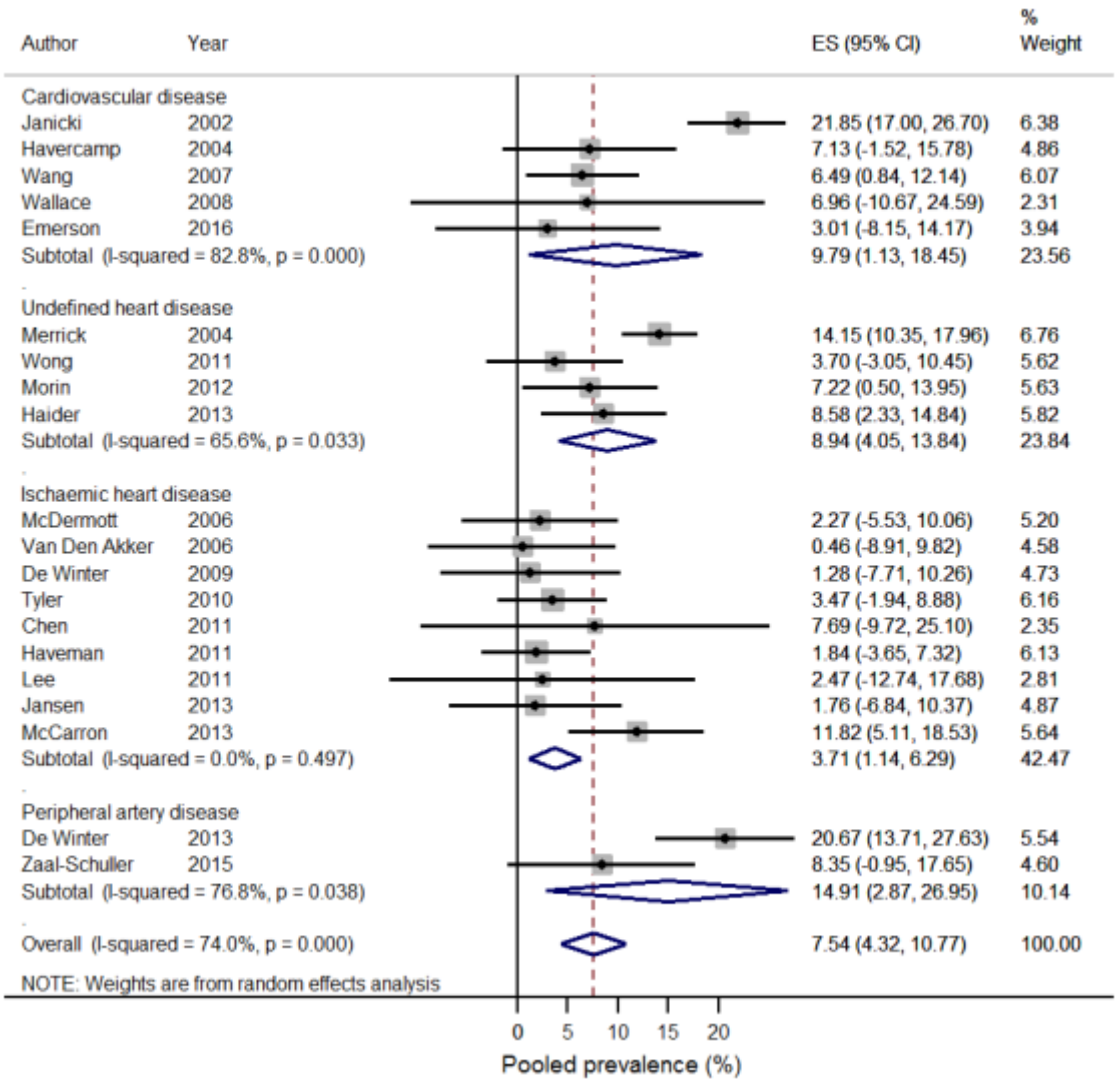


Figure 4. Pooled prevalence for CVD outcomes.

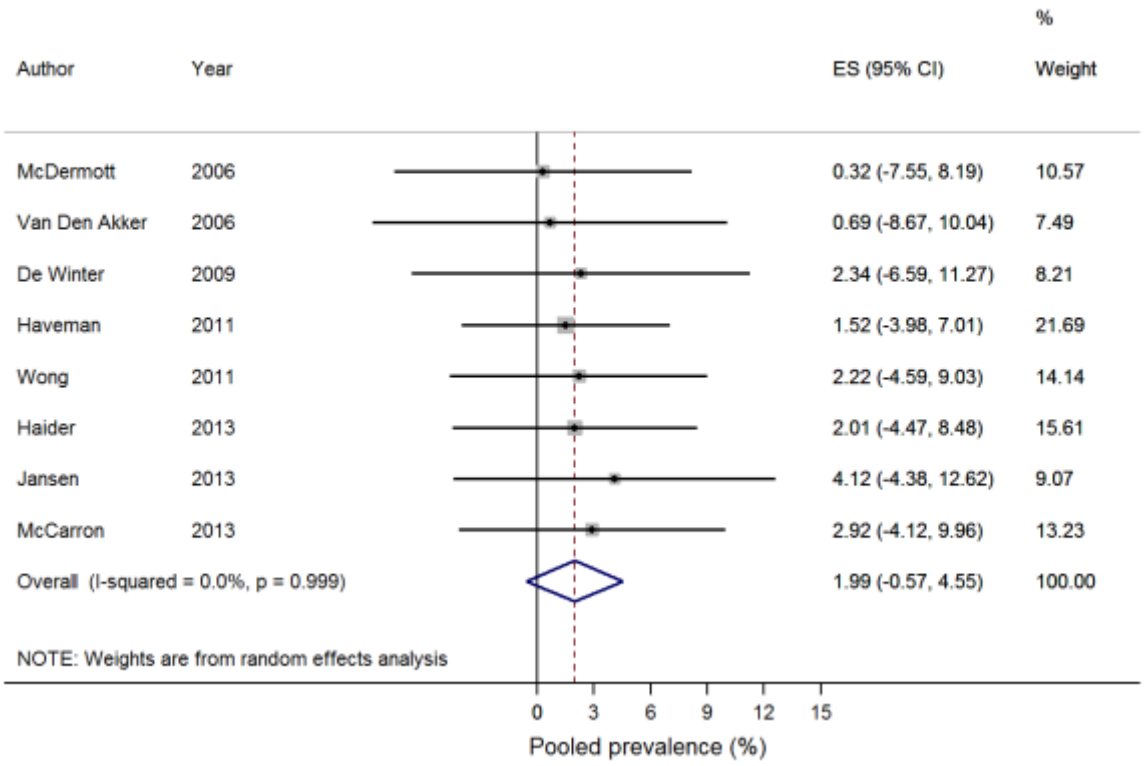


Figure 5. Pooled prevalence for cerebrovascular disease.

2.4.4.3 Prevalence of associated risk factors

The overall estimated prevalence of hypertension was 18·1% [12·6-23·5]. The estimated prevalence of overweight was 29·3% [26·3-32.3] [figure 6], obesity was 27·7% [24·1-31·2] [figure 7], and the prevalence of combined overweight and obesity was 53·4% [49·8-56.9]. The prevalence of dyslipidaemia was 18·4% [16·5-20·3] [figure 8] and metabolic syndrome was 23·7% [0-49]. However, all risk factors were associated with high heterogeneity [table 6].

Table 5. Point prevalence for outcomes in the intellectual disability population.

Outcome	Study n	Total n	Total n with outcome	Pooled prevalence (95% CI)	I^2
T2DM	5	4183	372	7.6% (4.7%-10.6%)	0%
Any diabetes	24	19157	1630	8.6% (7.2%-9.9%)	0%
Ischaemic heart disease	9	5586	200	3.7% (1.1%-6.3%)	0%
Peripheral arterial disease	2	1036	164	14.9% (2.9%-27%)	76.8%
Undefined CVD	5	3293	403	9.8% (1.1%-18.5%)	82.8%
Undefined heart disease	4	4779	487	8.9% (4%-13.8%)	65.6%
Any CVD/heart disease	20	14694	1254	7.5% (4.3%-10.8%)	74%
Cerebrovascular disease	8	5748	114	2% (0%-4.6%)	0%
Hypertension	29	17460	3023	18.1% (12.6%-23.5%)	93%
Overweight	33	45318	13389	29.3% (26.3%-32.3%)	89.4%
Obese	37	47729	14109	27.7% (24.1%-31.2%)	93.2%
Overweight and above	41	51090	28539	53.4% (49.8%-56.9%)	96.5%
Dyslipidaemia	17	8578	1434	18.4 % (16.5%-20.3%)	88.9%
Metabolic syndrome	3	877	296	23.7% (0%-49%)	92.6%

Where confidence intervals [CI] were negative they have been rounded up to 0%; CVD [Cardiovascular disease].

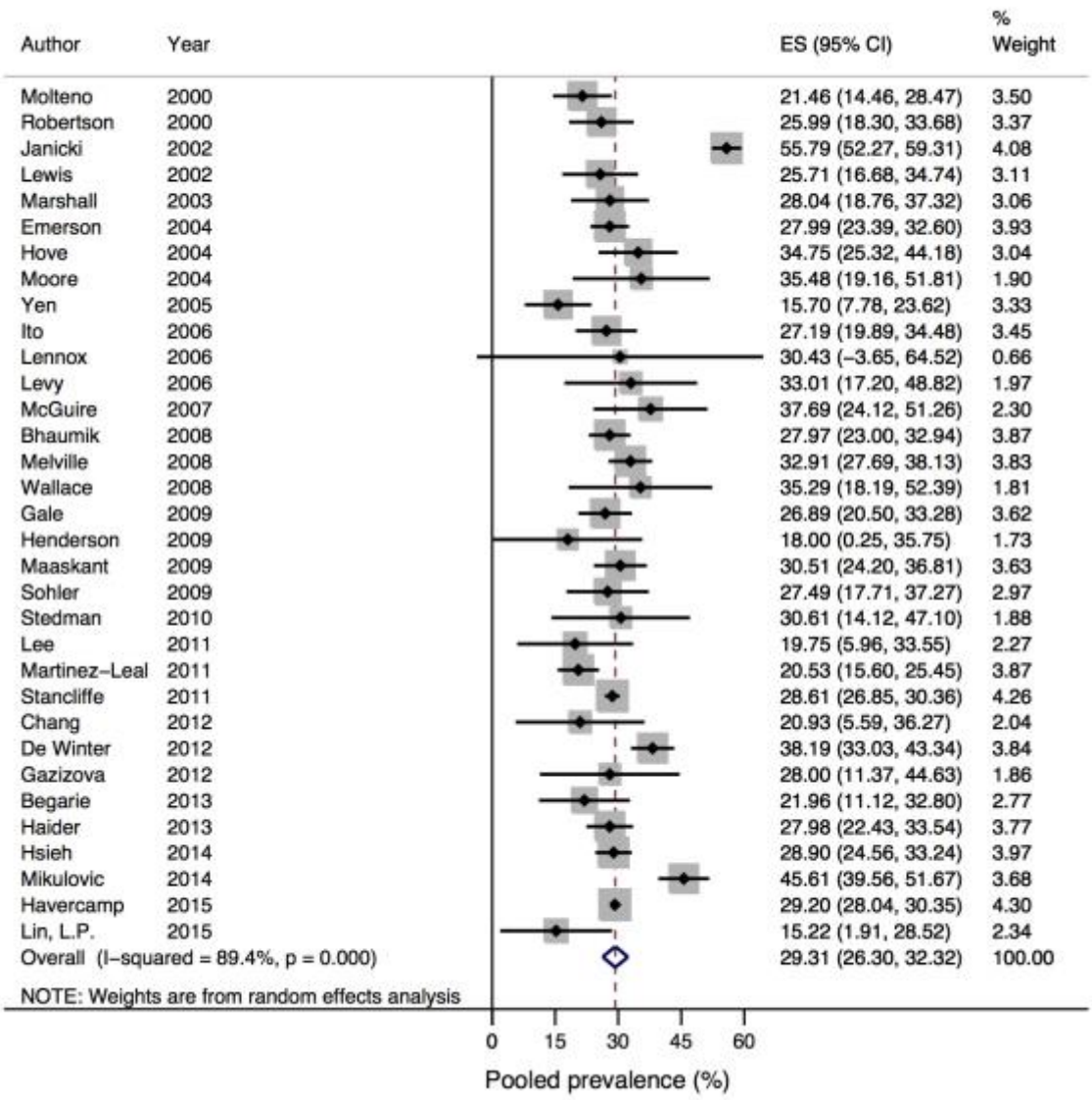


Figure 6. Pooled prevalence of overweight

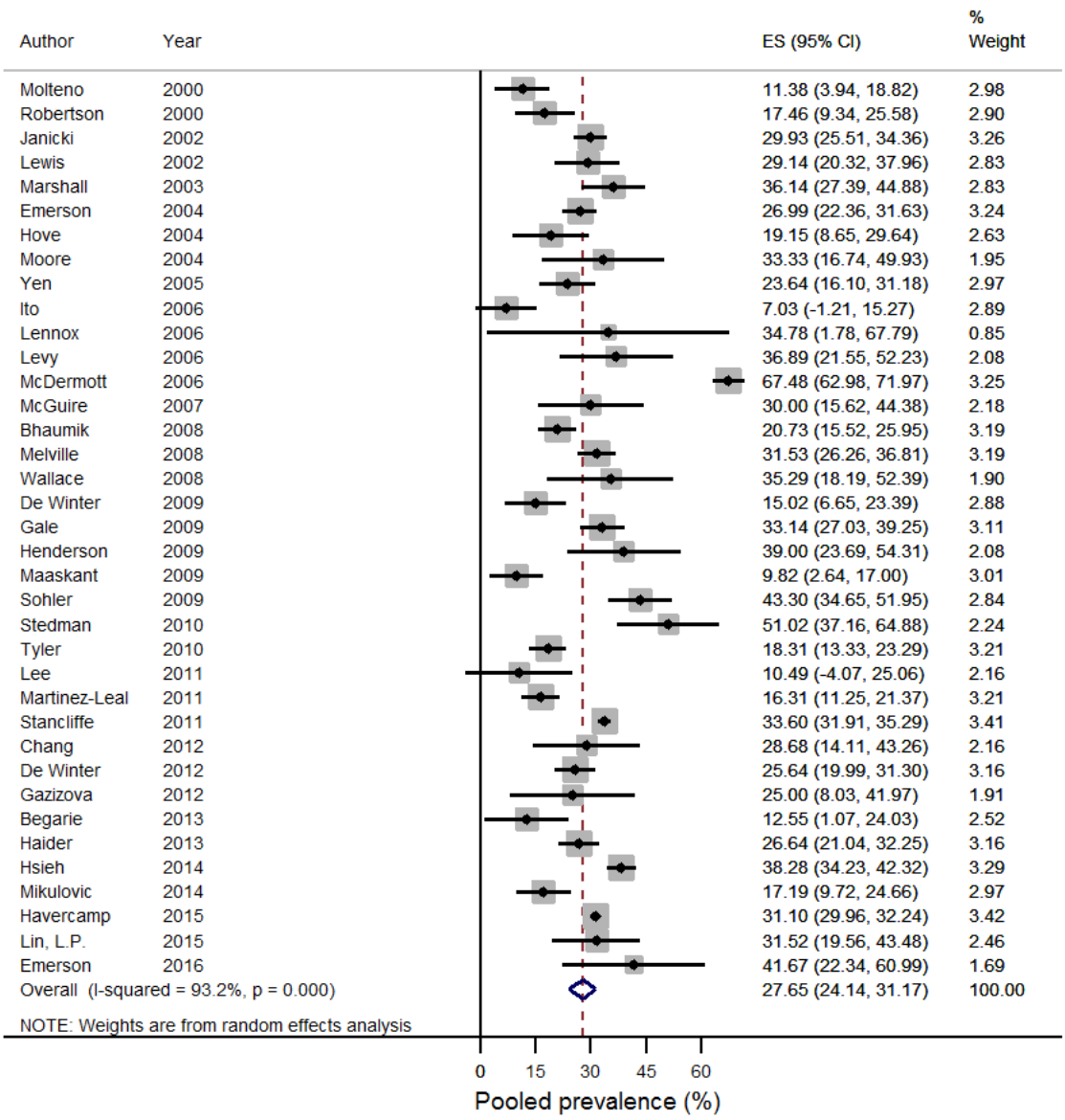


Figure 7. Pooled prevalence of obesity.

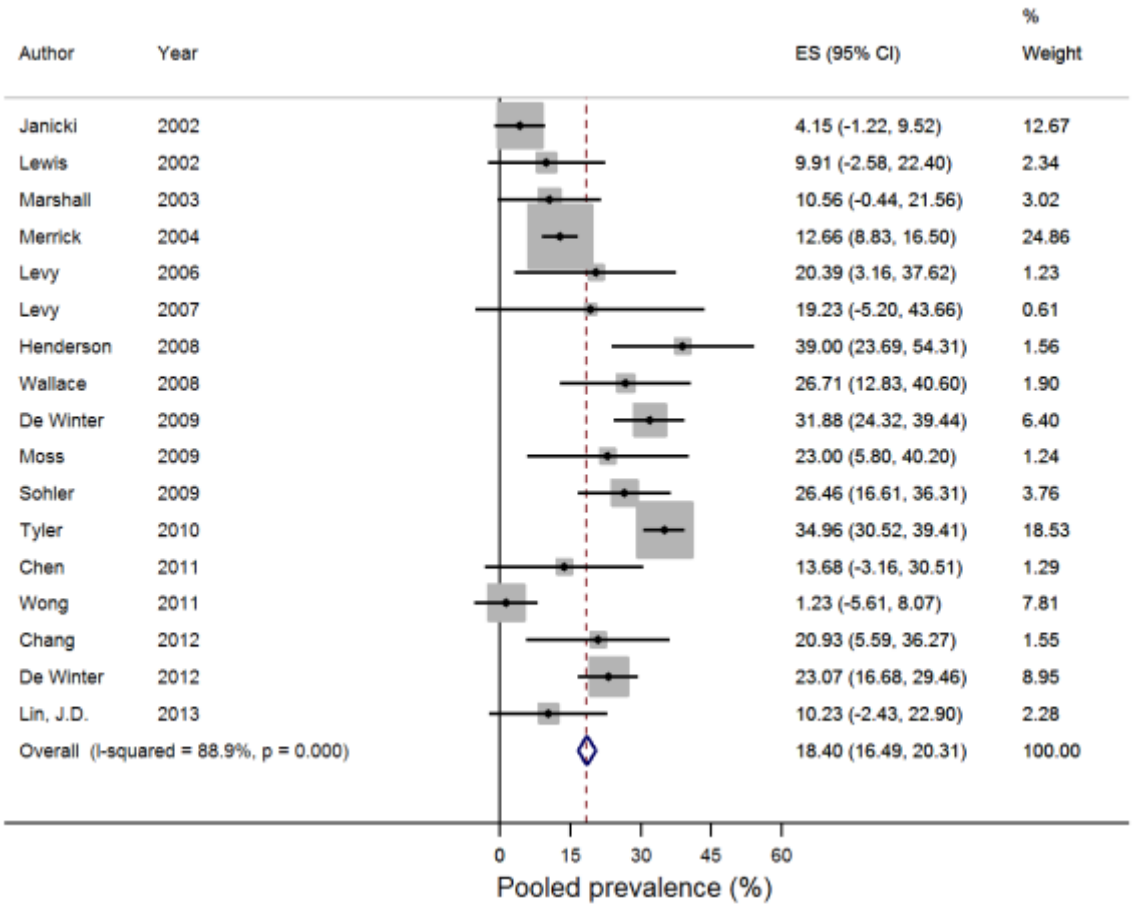


Figure 8. Pooled prevalence for dyslipidaemia.

2.4.4.4 Comparisons with the general population

People with ID were at decreased odds of having ischaemic heart disease [OR 0·44 [0·34-0·58] P<0·01] compared to the general population [Table 6]. There was no significant difference in prevalence for other conditions or risk factors. High heterogeneity was associated with all outcomes except for ischaemic heart disease.

Table 6. Results of the general population comparison meta-analyses

Outcomes	Study n	ID total n	ID total n with outcome	GP total n	GP total n with outcome	Odds ratio (95% CI)	I^2
Ischaemic heart disease	3	2395	67	5441	335	0.44 (0.34, 0.58)*	0%
Pooled diabetes	6	4014	411	13404	1371	0.96 (0.61, 1.5)	92.2%
Hypertension	6	3588	1097	14262	4598	0.76 (0.58, 0.99)	86.9%
Overweight	5	21882	6432	329963	121791	0.83 (0.45, 1.5)	97.2%
Obese	8	24233	7347	335374	81114	0.94 (0.63, 1.39)	97%

ID [Intellectual Disability]; GP [General Population]; *P<0.01.

2.4.4.5 Variation in estimates

Meta-regression was used to investigate the effects of mean age, severity of ID, continent, and data collection method [researcher collected data, self/carer reported data, or retrospective records data] on prevalence of outcomes [table 8]. An association approaching significance was observed between mean age and hypertension with each year increase in mean age causing a 0·1% increase in prevalence of hypertension [p=0·05]. Severity of ID had no significant effect on prevalence for any condition or associated risk factor.

Data collection method was found to have an effect on all combined diabetes with higher prevalence observed in database reported data [10·5% [8·6-12·4]] when compared to self/carer reported data [6·1% [4-8·2]; p<0·01]. Higher obesity prevalence was observed when database collected data (35% (21·4-48·6) when compared to researcher collected data [22·8% [18·1-27·6]; p=0·02].

Obesity and overweight rates were 8·9% [1-29] and 11·5% [1-24] higher, respectively, in North America when compared to Asia. No other significant continental differences were observed [table 7]

Table 7. Meta-regression analyses

Variable	No. obs	Effect (95% CI)	P-value
Ischaemic heart disease			
Method of data collection			
Database vs self/carer reported data	9	0.06 (-0.02, 0.14)	0.14
Database vs researcher collected data	9	0.001 (-0.08, 0.08)	0.98
Mean age	5	0.0001 (-0.01, 0.01)	0.66
% mild/moderate ID	5	0.001 (-0.01, 0.01)	0.88
Continent			
Asia vs Australasia	9	-0.05 (-0.37, 0.27)	0.69
Asia vs Europe	9	-0.04 (-0.28, 0.21)	0.7
Asia vs North America	9	-0.05 (-0.3, 0.2)	0.65
Asia vs South Africa	-	Insufficient observations	-
Type 2 diabetes			
Method of data collection			
Database vs self/carer reported data	5	0.05 (0.21, 0.12)	0.35
Database vs researcher collected data	5	0.06 (0.39, 0.26)	0.49
Mean age	3	-0.00005 (-0.04, 0.04)	0.99
% mild/moderate ID	-	Insufficient observations	-
Continent			
Australasia vs Europe	5	0.01 (-0.18, 0.2)	0.8
Australasia vs North America	5	-0.05 (-0.51, 0.41)	0.69
Australasia vs Asia	-	Insufficient observations	-
Australasia vs South Africa	-	Insufficient observations	-
All diabetes			
Method of data collection			
Database vs self/carer reported data	24	-0.05 (-0.08, -0.02)	0.01*
Database vs researcher collected data	24	-0.04 (-0.11, 0.04)	0.33
Mean age	10	0.001 (0.00, 0.00)	0.7
% mild/moderate ID	11	0.001 (0.00, 0.00)	0.23
Continent			
Asia vs Australasia	24	0.02 (-0.07, 0.11)	0.66
Asia vs Europe	24	0.03 (-0.04, 0.1)	0.45
Asia vs North America	24	0.04 (-0.03, 0.11)	0.23
Asia vs South Africa	-	Insufficient observations	-
Obesity			

Method of data collection			
Database vs self/carer reported data **Database vs researcher collected data**	37 37	-0.05 (-0.19, 0.08) -0.12 (-0.21, -0.02)	0.44 0.02*
Mean age	18	-0.001 (-0.01, 0.01)	0.77
% mild/moderate ID	18	0.002 (0.00, 0.01)	0.07
Continent			
Asia vs Australasia **Asia vs Europe** **Asia vs North America** **Asia vs South Africa**	37 37 37 37	0.09 (-0.07, 0.25) 0.004 (-0.13, 0.14) 0.15 (0.01, 0.29) -0.11 (-0.36, 0.15)	0.25 0.95 0.04* 0.4
Overweight			
Method of data collection			
Database vs self/carer reported data **Database vs researcher collected data**	32 32	0.06 (-0.05, 0.17) 0.01 (-0.07, 0.1)	0.26 0.8
Mean age	17	0.01 (0.00, 0.01)	0.16
% mild/moderate ID	16	0.002 (-0.00, 0.01)	0.27
Continent			
Asia vs Australasia **Asia vs Europe** **Asia vs North America** **Asia vs South Africa**	32 32 32 32	0.09 (-0.04, 0.22) 0.1 (-0.002, 0.21) 0.13 (0.01, 0.24) 0.01 (-0.18, 0.21)	0.17 0.06 0.04* 0.89
Hypertension			
Method of data collection			
Database vs self/carer reported data **Database vs researcher collected data**	29 29	-0.08 (-0.21, 0.04) -0.01 (-0.12, 0.11)	0.17 0.89
Mean age	13	0.01 (0.00, 0.02)	0.05*
% mild/moderate ID	13	0.001 (-0.01, 0.01)	0.74
Continent			
Asia vs Australasia **Asia vs Europe** **Asia vs North America** **Asia vs South Africa**	29 29 29 29	-0.01 (-0.2, 0.22) 0.09 (-0.06, 0.24) 0.05 (-0.1, 0.19) -0.08 (-0.41, 0.25)	0.94 0.33 0.5 0.63

ID [intellectual disability]; * [significant result].

2.5 Discussion

2.5.1 Key findings

From this comprehensive systematic review, I was able to obtain current prevalence rates for T2DM and CVD, and associated risk factors. my findings indicate that there is no evidence to suggest that the prevalence of T2DM or associated risk factors are different from the general population. However, ischaemic heart disease was demonstrated to be significantly lower in the ID population when compared with the general population. Meta-regression showed that the method of data collection had minor effects on pooled prevalence for diabetes and obesity, mean age had minor effects on prevalence of hypertension, and that obesity and overweight prevalence were higher in North America compared with Asia.

2.5.2 Comparison to other knowledge

To my knowledge, this is the first systematic review and meta-analysis of prevalence of diabetes alongside CVD and associated risk factors in a population with ID. In addition, it is the first review of its kind to make comparisons with the general population.

Two other systematic reviews have been carried out which considered diabetes prevalence in people with ID. Specifically, McVilly *et al*. (138) reviewed 13 papers with an aim of establishing prevalence and incidence rates for non-specific diabetes in the ID population. The reported prevalence of 8.7% was similar to my result of 8.6%.

MacRae *et al.* (139) reviewed 22 papers reporting any type of diabetes in the ID population and reported a similar range to that found in the current study of 0·4% – 25%. However, it was noted that due to 16 out of the 22 papers not reporting type of diabetes, specific diabetes outcomes could not be reported. This lack of consistent detailed reporting throughout the literature is consistent with what was found during my investigation. However, in contrast to these two studies, of the 24 papers found reporting diabetes in my review, I was able to isolate five for a separate meta-analysis for T2DM.

2.5.3 Strengths and limitations

The aim of this review was to report a current ID population prevalence and therefore stringent criteria concerning heterogeneous ID cohorts were enforced. This removed the possibility of potential bias introduced by cohorts with certain syndromes which may be at increased risk of specific outcomes. Although heterogeneity was non-existent for disease outcomes, high heterogeneity was seen in associated risk factors for pooled prevalence. I was unable to explain this with meta-regression. However, high heterogeneity is commonly seen in evidence syntheses investigating prevalence across large numbers of studies from a global population (140, 141).

A limitation to my review was the lack of demographic data extracted from articles which reported general population comparison data. Because of this I was unable to adjust for confounding factors or perform a meta-regression. The lack of demographic data could result from poorly recorded data from retrospective databases. Studies using prospective screening data could provide more meaningful and reliable data. Future research of this nature would provide valid comparisons to the general population.

There were large differences in observed in the upper and lower prevalence range for some outcomes, this could be due to confounding variables [e.g., age or BMI]. Additional data such as this was often not reported leaving no explanation for these large ranges. Moreover, outcome definitions were often poorly reported in the studies and separate health conditions were often grouped together [e.g., type 1 and T2DM]. Improved reporting would help to derive more accurate prevalence estimates. However, when using population based approaches with ID cohorts, it is likely that people who get involved in the studies are the same people who are likely to engage with health care, leaving out people who may be truly vulnerable, meaning the sample may not be representative. Currently, the only factor which indicates the true health inequality in the ID population is premature mortality, which has been consistently replicated in studies (40, 142, 143).

The lower prevalence of ischaemic heart disease observed in the ID population could be explained by mortality in the ID population occurring at a younger age, mainly due to non-cardiovascular causes (144). Therefore, the results observed may be explained by survival bias. Under-diagnosis or mismanagement of conditions is a suggested contributor to the health disadvantages for people with ID (145), this may also go some way to explaining the observed lower prevalence. Further analysis needs to take place taking account of confounding factors (i.e., age). Due to lack of data, I could not adjust for the effects of age.

The time that has elapsed since the last search was performed is a limitation of this chapter. Due to time constraints, I was unable to conduct an updated search prior to writing this thesis. However, I am aware that an updated search may reveal new eligible studies that would make for a more robust analysis.

2.5.4 Conclusions

This systematic review shows that there is no evidence to suggest that prevalence of T2DM, CVD, and associated risk factors are dissimilar to the general population. The prevalence of ischaemic heart disease was significantly lower in people with ID but may be explained by survival bias. Studies comparing health conditions in people with ID to the general population are currently sparse, and often important confounding variables are missing or poorly reported; more research with a focus on making comparisons to the general population is needed to investigate possible health disparities.

Chapter 3 Systematic review of interventions to lower chronic disease prevalence in adults with ID

3.1 Introduction

Conditions such as CVD and T2DM share similar risk factors, including dyslipidaemia, hypertension, obesity, and impaired glucose regulation [IGR]. In the general population, these risk factors can be effectively lowered through interventions focusing on changes in nutrition and physical activity [PA] (64). However, an international review of PA levels in people with ID revealed that they were less likely to meet the government recommended guidelines for PA, with only 9% of individuals meeting recommended levels of PA (146).

Interventions of this nature predominantly incorporate increasing PA and making better diet choices. Combining the two can result in a more pronounced effects [i.e., diet and PA will increase weight loss vs diet alone] (147). In addition, research has indicated that sustained health improvement can be difficult over the long-term, with longer term interventions providing the best chance of long-term success (148). Based on this the aim of this review was to consolidate and describe the evidence assessing the effectiveness of multi-component and long-term lifestyle interventions for people with ID aimed at primary prevention of T2DM, CVD, or associated risk factors.

As indicated above, these types of interventions have been shown to work in the general population (147, 148). In the introduction, I discussed barriers to health experienced by people with ID. When considering barriers of this nature, it is important to tailor interventions to people with ID in order to achieve maximum effectiveness. However, past studies of this nature have often had limitations (149). It was the aim of this chapter to consolidate evidence for primary prevention of chronic disease through multi-component lifestyle interventions and look for strengths and limitations of each in order to make future recommendations.

3.2 Methods

Investigator initials and details can be found in appendix VII. vii. This systematic review is registered on PROSPERO – Registration number 42015020758 [appendix VII. Viii]. The review protocol from the original study can be found in appendix VII.ix.

3.2.1 Search strategy and study selection

Studies were included if they: 1. involved a cohort consisting of ≥ 80% ID persons; 2. assessed a multi-component lifestyle behaviour change intervention aimed at primary prevention of T2DM or CVD or reduction of risk factors; 3. reported data for changes in anthropometric and/or biomedical measures associated with primary reduction of T2DM or CVD [BMI, weight, body fat measures, waist circumference, blood pressure, lipid levels, glucose levels, PA level, sedentary behaviour, or dietary habits]; 4. were published in English; 5. had a follow up period of six months or 24 weeks [based on recommended clinical guidelines for interventions of this type]. Studies were excluded if they: 1. involved a restrictively selected cohort based on outcome [e.g., all participants already had diabetes before the intervention]; 2. involved surgical interventions, pharmacological interventions, meal replacement interventions, or interventions aimed at increasing specific aspects of physical fitness for athletic gain as opposed to changes in levels of physical activity; 3. involved a cohort consisting of ≥25% persons with a specific ID. This was to reduce the potential bias resulting from associated morbidities from specific genetic syndromes. The percentage was a pragmatic figure based on the current proportion of the most prevalent ID syndrome [DS] (30).

I searched EMBASE, MEDLINE, CINAHL, CENTRAL and PsycINFO from January 01, 2000 through May 24, 2015. This start date was chosen because of three reasons; 1. there was a need to conduct a systematic review of a more contemporary population; 2. related systematic reviews of the topic area revealed no research published before 2000 (149-151); and 3. there was a need to include interventions with modern outcome testing techniques. Over the

previous two decades, modern testing techniques [i.e., accelerometers] for PA have improved and are now becoming a gold standard for this type of intervention (152). There was a need for new types of measurement for day-to-day PA, as self-reported data can often be unreliable by comparison (153).

My search strategy included search terms for health improvement programmes, health behavioural change programmes, exercise programmes, nutrition programmes, intervention study design, and intellectual disability [appendix VII.x]. I also limited my search by English-language studies and studies with cohorts >18 years of age, depending on database. Reference lists of relevant articles were also searched for possible included studies.

Full text articles were identified after titles and abstracts were read separately by two investigators [TC and AD] with discrepancies in selection being discussed. Full texts were then examined by two investigators [TC and AD] to check for suitability for inclusion. Only full length articles were included, review articles were removed after reference lists were examined. Lead authors were contacted for further information where inclusion/exclusion could not be determined. Two authors of articles were contacted for information regarding their studies. One did not reply (154) and the other supplied enough information to exclude them from the review (155).

3.2.2 Data extraction

A data extraction form was designed and piloted specifically for this review [appendix VII.xi]. From each study, I extracted the first author's name, title of the paper, country of the author's affiliation, year of publication, country of the cohort, study type, sampling method, dates of data collection, and inclusion/exclusion criteria. For each group within the study design, I also extracted total sample size or sub-population size; mean ages, proportion of male/female, severity of ID, ethnicity, and withdrawals. For each reported outcome, I extracted information on the definition of the outcomes, how the outcomes were measured, total number measured for outcomes, length of follow up, baseline mean, post intervention mean, and mean differences

between groups and/or from pre-to-post intervention. Data were extracted separately by male and female where reported. Data were extracted by one investigator [TC] and verified for accuracy by another [RS].

3.2.3 Risk of bias

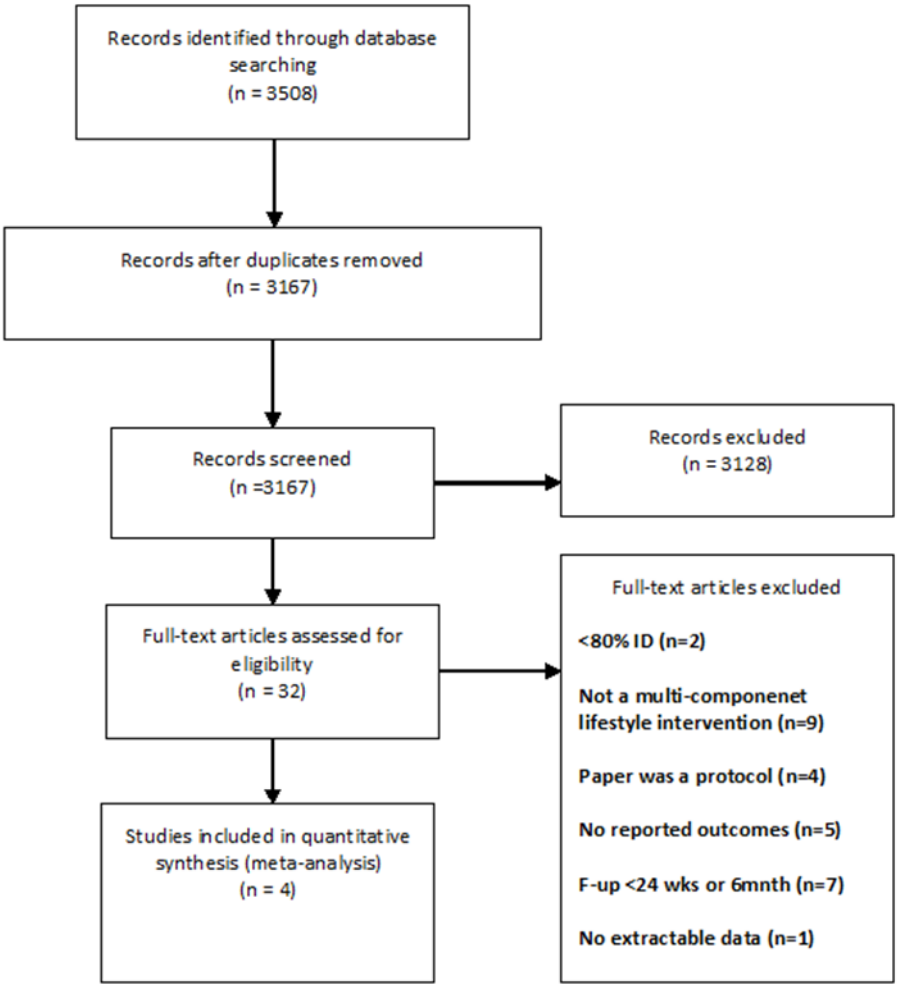
The risk of bias for included studies was assessed using the UK's National Institute for Health and Clinical Excellence [NICE] quality appraisal checklist for quantitative intervention studies 3rd edition (156). The checklist included criteria for assessing the internal and external validity of experimental and observational quantitative studies [randomised controlled trials [RCTs], non-randomised controlled trials, before and after studies] and grades studies according to overall quality [categories ++, + or -].

3.3 Results

3.3.1 Identification of studies

I identified 3,508 articles via the literature searches [Figure 9]. After duplicates were removed, 3,167 articles remained to be screened. The full-text of 32 articles were reviewed. Overall, four studies were included for descriptive analysis (157-160)

Figure 9. Flow diagram of included studies



3.3.2 Quality of included articles

A breakdown of study quality is presented in table 9. Overall, 50% of studies received a high grading for external validity, and 50% received a good grade. 100% of studies received a good grade for internal validity [Table 8].

Table 8. Quality assessment table

	Bazzano et al.	Bergstrom et al.	McDermott at al.	Melville at al.
SECTION 1 - Population				
Was the source population or source area well described?	+	++	++	++
Was the eligible population or area representative of the source population or area?	++	++	++	+
Do the selected participants or areas represent the eligible population?	+	+	++	++
SECTION 2 – Method of allocation to intervention (or comparison) ++				
Allocation to intervention (or comparison). How was selection bias minimised?	NA	++	++	NA
Were interventions (and comparisons) well described and appropriate?	++	++	++	++
Was the allocation concealed?	NA	++	NR	NA
Were participants or investigators blind to exposure and comparison?	NA	NA	NA	NA
Was the exposure to the intervention and comparison adequate?	++	++	++	++
Was contamination acceptably low?	NA	++	++	NA
Were other interventions similar in both groups?	NA	++	++	NA
Were all participants accounted for at study conclusion?	-	++	-	++
Did the setting reflect usual UK practice?	++	++	++	++
Did the intervention or control comparison reflect usual UK practice?	++	++	+	+
SECTION 3 – Outcomes				
Were outcome measures reliable	+	+	++	+
Were all outcome measurements complete?	++	-	+	++
Were all important outcomes assessed?	++	++	++	++
Were outcomes relevant?	++	+	++	++
Were there similar follow-up times in exposure and comparison groups?	NA	+	++	NA
Was follow-up time meaningful?	+	++	++	++
SECTION 4 – Analyses				
Were exposure and comparison groups similar at baseline? If not, where these adjusted?	NA	++	NR	NA

Was intention to treat (ITT) analysis conducted?	-	++	++	-
Was the study sufficiently powered to detect an intervention effect (if one exists)?	NR	++	NR	NR
Were the estimates of effect size given or calculable?	NR	+	++	++
Were the analytical methods appropriate?	+	+	++	-
Was the precision of intervention effects given or calculable? Were they meaningful?	+	++	++	++
SECTION 5 – Summary				
Are the study results internally valid (i.e., unbiased)	+	+	++	+
Are the findings generalisable to the source population (i.e., externally valid)?	++	+	++	+

++ (All the checklist criteria have been fulfilled). + (Some of the checklist criteria have been fulfilled). – (Few or no criteria have been fulfilled). NR (not reported). NA (not applicable).

3.3.3 Descriptive overview of interventions

In the following section I will give a brief overview of the included studies and compare the strengths and limitations of each. Descriptive information from the included studies can be seen in table 9; results are summarised in table 10.

3.3.3.1 Bazzano et al., (157)

The authors conducted a one arm before and after intervention in already overweight or obese adults with an ID (BMI >25) who also had either, another risk factor for diabetes or metabolic syndrome, or already had diabetes. The starting sample size of the study was 85. The community based health intervention, named ‘The Healthy Lifestyle Change Programme’ [HLCP] involved peer-mentoring, one-to-one health education, supervised PA, and clinical support aimed at reducing weight, diet & increasing PA. The intervention ran for seven months and participants were seen twice per week for education and exercise classes. The overall aim was to increase self-efficacy regarding health, nutrition, and fitness. A one arm approach was taken due to financial constraints and the perception that if an intervention was being offered within a community then all eligible should be able to participate.

Outcomes were changes in: Body mass; BMI; waist circumference; access to care; self-reported nutrition; self-reported PA; and life satisfaction. Just under half of the study participants [39/85 or 45.9%] dropped-out before the post-intervention measurements could be taken, this was mentioned as a limitation of the study in the discussion. However, the author notes that small scale of the intervention then allowed the project to be flexible in nature.

The results showed an overall improvement in all outcomes [table 11] indicating that the intervention works well as a lifestyle change intervention. However, the author notes the limitation of selection bias. Meaning that those who volunteered to take part were also most likely to be motivated to lose weight. The outcomes were self-reported. Self-reported outcomes have been found to be unreliable (150).

The attrition rate was attributed to several reasons including: Lack of motivation to exercise; transportation problems; childcare issues; conflict with work schedules; and language translation needs. However, the author notes that the attrition rate is consistent with other interventions of this nature.

Overall, the author promoted the peer-led community based approach to lifestyle interventions for people with ID. It meant the intervention could be flexible and adapted as necessary. However, for future research of this nature the author recommends that an RCT approach is used with longer term outcomes.

3.3.3.2 Bergstrom et al., (158)

The authors conducted a two-arm intervention which took place at residences caring for people with ID. The intervention offered a ‘study circle’ for caregivers, and an appointed health ambassador at each residence. An educational health course for the residents was provided with the primary outcome of increasing PA and the secondary outcome of decreasing weight and BMI. The study involved people with mild and moderate ID only. This is common in

interventions of this nature due to the increased physical limitations of people with severe to profound ID.

The primary outcome of this study was PA [measured in steps per day]. This was measured via pedometer; based on the literature indicating that self-report methods both under- and overestimate PA levels (161), a pedometer would be a more accurate method.

Secondary outcomes included BMI, waist circumference, dietary quality [measured by digital photography], satisfaction with life, and work routines. A positive intervention effect was seen for PA, with a significant increase in steps per day demonstrated. However, this increase in PA was not translated into any improvements in BMI, diet improvement, or waist circumference [the applicable outcomes for my review]. This study was a cluster study involving separate residences housing people with ID. The author noted that the type of residence was found to be an effect moderator, and that this should be accounted for in future research. The type of home [i.e., group home vs assisted living] may increase the positive outcomes of an intervention due to the support systems in place for the participants. This indicates that the level of support that is in place for people with an ID during a lifestyle intervention is an important aspect for success.

Again, not everyone who enrolled took part in final measurements with some measures for work routine outcomes having only 14/64 measured on follow-up. Fortunately, the PA, anthropometric, and diet outcomes were all above 70% complete for follow-up, offering a more reliable result. Consistent with Bazzano *et al.,* the author notes that they encountered several challenged when collecting data in the target group including: Both the participant and/or the care-giver motivation to take part in the intervention and/or measurement; seasonal differences affecting motivation; and the nature of self-reported data being unreliable. Which is consistent with my previous suggestions.

Overall, the author remains positive that the results are encouraging. However, admits that there are areas for improvement. One key area that is necessary for

improvement is a consistent implementation strategy to increase fidelity. This is something that is specific to this study to the clustered nature of the intervention across different residences. It could be suggested that the decreased fidelity arising from the differing implementation technique and management for the intervention within individual residences led to the difference in results between Bergstrom et al., and Bazzano *et al.* Where anthropometric measures were seen to improve in Bazzano *et al*., possibly due to the smaller group size allowing for more control over participants and the flexible nature of the intervention this caused.

Table 9. Descriptive information for included studies.

Study [year]	Arms	Country	Study n	Mean age		% male	Severity of ID [%]		% white
Bazzano et al., [2013]	1	USA	85	44		38.6	NR		20.5
Bergstrom et al., [2009]	2	Sweden	129	Interven.	Control	43.4	Mild / Moderate	100	NR
				36.2 [10.1]	39.4 [11.3]		Severe	0	
							Profound	0	
McDermott et al., [2012]	2	USA	432	38.8		49.2	Mild / Moderate	100	41.7
							Severe	0	
							Profound	0	
Melville et al., [2011]	1	UK	54	NR		40.7	Mild	31.5	96.3
							Moderate	31.5	
							Severe	35.2	
							Profound	1.9	

3.3.3.3 McDermott et al., (159)

The authors conducted an active randomised control trial for 432 people with mild to moderate ID. Intervention participants were assigned to eight weekly lessons involving nutrition, exercise, and changing ways of thinking. The lessons focused on stress management, complications of obesity, and behaviour management. The classes emphasised moderate to vigorous physical activity, healthy eating and BMI reduction. The active control group were assigned to eight weekly lessons on safety and hygiene.

The outcomes included: Increase in moderate-to-vigorous PA [MVPA]; BMI reduction; food availability; and life stress. However, results were published for MVPA and BMI only. No significant intervention effects were seen in any of the outcomes.

This study started with the largest sample size [n=432]. However, the attrition rate was also the highest with 54.6% of participants not taking part in the follow-up measurements. The author notes this is a major challenge to their study and as an area that is important for future research. This is a consistent area in which these types of interventions experience limitations. Alongside drop-outs, the author notes that refusal to take part in aspects of the intervention throughout the time-period was an issue that affected results. Reasons for drop-out of inability to take part included: Job-related conflicts; preference to go on other outings with family or carers; not wanting repeat home visits to measure their food availability or complete questionnaires. In addition to these issues, many participants refused to wear the accelerometers. When trying to move away from self-reporting data, this issue makes it difficult to find an effective and reliable method for PA data collection. Although the author does not allude to it in the article, other behavioural issues (162) and issues in understanding (163) that are common in people with ID may contribute to participants not wanting to wear the accelerometer.

3.3.3.4 Melville et al., (160)

The authors conducted a single arm intervention in 57 already obese adults with ID (BMI > 30) that had been referred to a dietician by their general practitioner in the UK. The intervention consisted of nine lessons, every 2-3 weeks were provided for participants and their carers. Lessons were aimed at increasing PA and better diet, via personalised diet prescriptions, as well weight loss. Interventions also consisted of personalised diet plans with a daily energy deficit [600kcals per day].

The outcomes were: Body weight; BMI; waist circumference; and levels of PA and sedentary behaviour. PA and sedentary behaviour was measured using an

accelerometer. The study saw only seven drop-outs before follow-up measurement could be taken [12.3%]. This was the smallest number of drop-outs of all included studies.

The study demonstrated positive intervention effects. With significant reductions in body weight, BMI, waist circumference, and sedentary behaviour. No significant increase was seen in PA.

The author notes the one-to-one nature of intervention delivery as a strength, this is consistent with Bazzano *et al.* However, the author writes that financial implications need to be considered for future research because one-to-one lessons are an expensive option. The study incorporated carers where possible, this was perceived as a positive motivator on participants. This is also consistent throughout the studies. It shows that with a higher level of support, the person with ID is more likely to do well. Regarding the accelerometer use, the author collected data for over 70% of the participants. This is higher than McDermott *et al.,* where most participants refused to wear the accelerometer. Limitations of the study were a lack of control group and a short follow-up period.

I will discuss and compare the included studies in further detail in chapter four of this thesis.

Table 10. Summarised results of the included studies

Descriptive information			Intervention effects [% difference]					
Author [year] Study name	Study n after drop-outs	Baseline to final data collection	Anthropometrics			PA outcome [measurement]		Vegetable servings [per day]
			Body weight	BMI	Waist circum.			
Bazzano (2009) **"Healthy Lifestyle Change Program (HLCP)"**	44	7 months	-1.34% *	-1.502% *	-2.179% **	**Minutes PA per week** +54.887% ** **Sessions per week** +21.875 **		+10%
Bergstrom (2013)Ψ	14-63 depending on outcome measured	12-16 months	-1%	-1.799%	NR	**Steps per day [pedometer]** +19.995% *		+14.286%
McDermott (2012) **"Steps to Your Health (STYH)"**	196	12 months	**Interven.** -0.779%	**Control** -0.664%	NR	NR	**MVPA ratio [Accelerometer]** **Intervention** -4.167%	**Control** -4.762%	NR
Melville (2011) **"TAKE-5 STUDY"**	47	24 weeks	-4.445% **		-4.55% **	-5.152% **	**Sedentary [mins per day]** -6.642% * **Light intensity [mins per day]** +10.763% **MVPA [mins per day]** +25.423%		NR

ᵠResults were shown for intervention group only; * P < 0.05; ** P < 0.01; PA – Physical Activity; MVPA – Moderate to Vigorous Physical Activity.

3.4 Discussion

3.4.1 Summary of results

Out of the four included studies, two single arm studies with a follow up of seven months (157) and 24 weeks (164) respectively indicated significantly improved outcomes. Reductions in weight, BMI, and waist circumference were demonstrated after implementation of a lifestyle intervention programme aimed at increasing physical activity and improving diet. Additionally, both studies demonstrate a significant improvement in PA outcomes. Specifically, 'minutes per week' and 'frequency of sessions' (157) and a 'reduction in sedentary behaviour' (164). These positive intervention effects may be explained by both cohorts being overweight-obese upon commencement of the study. This was not the case in the further two studies (158, 159) where the cohort was not recruited based on health status. Significant positive improvements in waist circumference, BMI, and steps per day were seen in the intervention group of one of the two studies with a control group (158); between group data was not reported for the other study (159). However, there were no significant differences between control and intervention reported for either of the two-armed studies.

3.4.2 Comparison to other knowledge

To my knowledge, this is the first systematic review and meta-analysis focusing on pragmatic long-term lifestyle interventions for adults with ID in order to reduce CVD and/or T2DM risk. I will briefly discuss similar reviews that have been conducted:

Jinks *et al.,* (165) conducted a systematic review around qualitative studies focused on behavioural change approaches within the ID community to aid weight loss and health. The review found 12 papers, of which only one was qualitative in nature. The author notes that not enough research focuses on behavioural approaches and more research with a qualitative basis needs to be performed.

Spanos et al., (166) reviewed 22 papers assessing interventions for weight loss in people with ID. The review concluded that not enough interventions met the recommended duration in clinical guidelines. Also, the interventions were too specific and differed in the nature, concluding that more multi-component interventions need to take place.

Brooker et al., (167) reviewed interventions with a primary focus on PA. The review noted small sample sizes and invalid measurement tools were an issue, concluding that PA does have the ability to improve health in the ID population but longer term multi-component interventions need to take place.

3.4.3 Strengths and limitations of my review

The aim of this review was to evaluate multi-component lifestyle interventions with a follow-up period of more than six months or 24 weeks. An initial plan was to conduct meta-analyses on the extracted data. Unfortunately, any subsequent meta-analyses would not have been useful or reliable due to the lack of data overall, and the mixed data collection methods and reporting methods throughout the studies.

A strength of this review is the stringent criteria used to form an unbiased selection of studies. This is demonstrated in our inclusion criteria for percent of specific ID and age. Also, we only selected studies that involved longer-term follow-up periods to be consistent with clinical guidelines for lifestyle interventions. However, this could also be considered a weakness.

Only four studies were included in this review. This shows that multi-component lifestyle intervention research in people with ID is scarce. However, there were seven studies which could have been included if we had set our inclusion criteria to include studies that were of a shorter follow-up period (96, 104, 168-172). We considered studies with a longer-term follow-up only. This was based on the recommended clinical guideline's advice on length of lifestyle intervention playing a part in sustained weight-loss. With longer term interventions providing the best chance of long-term success (148). However, in

a future review it may be prudent to include all lengths of review and then split the results by length of study. There is clearly some added complexity in running interventions with people with ID compared to the general population. In this respect, it would be helpful to compile and analyse all available literature to help collate themes, regardless of study length.

The searches for this study need to be updated. It was my aim to update these searches prior to the writing of this thesis. Unfortunately, due to my focus being on other streams of work that were to form part of a wider PhD, I was unable to find time to update the searches in time.

3.4.4 Conclusion

Multi-component lifestyle interventions with a follow-up time of 12 months are the current recommendation for weight-loss intervention studies (173). Literature adhering to these guidelines with general population samples are common (174). However, it is the finding of this review that the literature focusing on lifestyle interventions in people with ID is currently scarce by comparison. People with ID have distinctive health needs and due to specific challenges [e.g., level of disability, level of communication ability]. The nature of an ID means that interventions must be carefully planned and structured to achieve maximum positive intervention effects. This is especially important when trying to adhere to the recommended length of intervention set by NICE because the studies within this review have consistently noted high drop-outs as a weakness of their respective intervention results.

Chapter 4 Discussion

It was the purpose of this thesis to address gaps in the published literature. Two systematic reviews were conducted to form the basis of this thesis. This discussion will summarise the findings from both reviews and then present the implications of the thesis before making recommendations for future research.

4.1 Implications

4.1.1 Disparities in health compared to the general population

Chapter two showed that there are comparable rates of cardiometabolic conditions seen in people with ID and the general population. This was not as expected based on previous literature. However, the systematic review that was conducted has limitations due to the varied reporting and lack of comparison data. In this respect, the question of whether people with ID suffer from health disparities by comparison to the general population has not been answered.

Possible health disparities have been the focus of much research over the previous decade and this increased research has resulted in changes to policy and practice in the health care of people with ID. It may be the case that previous research and subsequent changes in policy and practice have led to a stabilisation of health disparities between people with ID and the general population. Issues also surround the reliability of the results shown and the limitations discussed within the chapter.

Briefly, there was a lack of consistent reporting which led to me being unable to reliably account for confounding variables within the data. Therefore, the key implication from this review is the recommendations it makes to future research in standardisation of reporting sample descriptive information; definition of outcomes; and most importantly, providing general population comparison data. It is also important to consider the implication of grouping many syndromes and conditions, diagnosable in their own right, under one label – ‘ID’. This is

especially important to consider in cardiometabolic condition research, due to the nature of the effects of severity on cardiometabolic outcomes.

4.1.2 A move to the separation of severity of ID as individual conditions

Although it is the finding of chapter two that the level of overweight and obesity is high in people with ID, a problem also exists in people with ID being underweight (84), with evidence that underweight prevalence is nearly as high as obesity [18.6% and 20.7% respectively] (112). One important thing to consider when analysing ID research is the implications of grouping people with an ID under on blanket term. As discussed in the introduction, the term 'ID' is used to encompass all people who can be placed on the ID continuum from mild to profound. I would recommend that researcher be cautions with this way of grouping people with ID. It has been suggested that people who have severe of profound ID are more likely to be underweight than those who are at the mild/moderate end of the continuum (160), and on study has shown that increased severity of ID is associated with being underweight [bivariate association: $p<0.001$; OR = 2.7] (84).

Therefore, it should be the case that research moves towards a separation of the continuum of ID into two categories [mild/moderate and severe/profound], and research should take place as if these were two distinct conditions. If researchers are to group these severities together in one study, it is important that they report the percentage of each severity so results can be separated accordingly.

4.1.3 Improved health screening for people with ID

T2DM, CVD, and obesity have become highly prevalent across the world in recent decades and there is increasing emphasis on reducing mortality and financial burden that these conditions cause (175). There is a current focus on obesity management and non-communicable disease prevention. A significant proportion of people with ID have difficulty accessing health services and therefore the physical health conditions in this population remain under

diagnosed (176). The ID health checks are in place to provide opportunity for specialised health screening to take account of complexities associated with ID. However, a recent evaluation of these health checks in the UK reports that only 49.4% of eligible persons have taken part in the checks (61). Although health checks in the UK are incentivised for general practices, there is currently no provision for the ID community to attend. Higher participation rates in annual health checks would facilitate diagnoses and prevention of conditions through educational interventions by healthcare professionals.

One potential issue faced by year-on-year health check data is that we do not know whether the people who attended the previous year are the people who continue to attend. Moreover, those who interact with their healthcare are also more likely to be healthy. This is an issue than can also arise in selection bias during studies, and was alluded to in the included studies from chapter three, in that those who are willing to participate in weight-loss research are more likely to go forward and lose weight. One way to research this to check this problem with ID health check attendance prevalence is to analyse patient level history of attendance data. This way, we can gauge the consistency of attendances. There needs to be more focus on these possible confounders to the attendance statistics so we can gain more insight.

An important aspect of the ID health check is the increased appointment length. This is an important issue to consider when NHS GPs are constantly under pressure to meet appointment waiting time targets in an overloaded system. This surely means that offering extended appointment times to people with ID is a difficult undertaking. An additional important piece of research would be to look at the length of these appointments for ID health checks and see if they are adhering to the recommended appointment times. One suggestion is to schedule these appointments in less busy times to account for appointments taking longer than planned. This is a good idea in principle, but surely impossible bearing in mind the burden that GPs face with an overloaded system. Although the health checks are incentivised and provide additional benefit to the health of people with ID, 24.1% of GP surgeries still do not perform ID health checks (58).

One way to counteract the lack of GP availability to suitably screen people with ID is to provide screening elsewhere – a shared responsibility to relieve the burden and improve health for those with ID. One organisation that is already doing this is the Special Olympics. The Special Olympics are a registered charity and the largest provider of sports opportunities to people with ID. They hold annual events, nationally and internationally, in which 1000s of individuals with ID attend. At these events, health screening provided by volunteer nurses, doctors, and other medical professionals screen the 'athletes' for potential medical issues. If a problem is found, an official referral to the athletes GP is made. Not only does this offer an opportunity for health screening in people with ID, but it offers a rich data set for analysis. In fact, many articles were found during the search for chapter two which provided prevalence results for people with ID for the outcomes we were looking for. Special Olympics samples were excluded from this review due to the perception that they may take part in regular PA and therefore bias the sample. However, in future it may be prudent to include such prevalence rates for a better overall analysis and then split the results accordingly to account for any bias. These added data would provide for a more comprehensive analysis.

4.2 Weaknesses in study methodology

Study methodology was heterogeneous within included studies for both my systematic reviews, therefore I included rigorous inclusion criteria. This was due to our specific outcomes (population based sample of adults with ID). This was considered a strength of my systematic review and meta-analysis. However, this strict inclusion criteria mean that I could potentially have missed papers that would have influenced my results. Based on this, I will critically discuss the knock-on effects of each inclusion criteria and how this may have changed the meta-analysis results.

For the first review in chapter 2 we selected inclusion criteria that helped us form a non-biased study sample. Inclusion criteria 1 was selecting papers that involved cohorts consisting of >80% ID persons. This was a pragmatic figure chosen such that any non-ID person in the sample would not influence the

results. It is important to note that this '>80%' figure was not based on any statistical result and should be treated with caution. However, it is also important to note that no papers were excluded based on this criterion. All studies that were included had ID specific samples. Based on this it may have been pertinent to perform a more thorough scoping search, and based on knowledge gained from said search, not have used this inclusion criteria. This inclusion criteria did not affect the results of the systematic review and meta-analysis.

Inclusion criteria 2 was to include 'population based studies' only. This was a strong inclusion criteria in principle. It meant that we were only included studies that were representative of an entire population (e.g., the UK population that includes proportions of ID people). However, this inclusion criteria was ill-defined in itself and upon further analysis it could be said the exclusion criteria had covered the issue of population based studies. For example, excluding cohorts with >25% of people with a specific ID syndrome, or excluding studies that included a cohort selected based on outcome (e.g., all obese). These exclusion criteria were selected to remove the risk of biasing a sample and to make the cohort a good representation of a population. Based on this, this specific inclusion criteria was not necessary.

Inclusion criteria 3 was to include samples where >80% of people were over the age of 18. This was included because we wanted to include a sample of adults. However, again, the 80% figure was a pragmatic decision based on no statistical input. In future, it would be better to base these figures on statistically valid output to validate our decision.

Inclusion criteria 4 and 5 (included health outcome of interest and reported data that prevalence rates could be extracted from, respectively) were included so we could focus research on cardiometabolic outcomes and the prevalence thereof. These criteria were a good choice based on the outcomes of the systematic review.

We used inclusion and exclusion criteria to help us collect an unbiased sample representative of the population. However, some of the studies we have included could be deemed as potentially biased and could have affected the results of the meta-analysis. We accounted for this by using meta-regression but I will briefly discuss some of the types of papers that were included that could have had an effect.

The need to have a sample representative of the population may have led to us excluding potentially useful papers. An example of this was the exclusion of papers that used sampled from Special Olympics. The Special Olympics is the world's largest provider of sporting activities an opportunity for people with ID. They also collect scientifically rigorous data from large sporting events to track people's health and offer referral for those with health issues. The majority of published papers using Special Olympic samples are based on cardiometabolic outcomes such as obesity and blood pressure which are easy to measure during events. I did not include papers from Special Olympic samples because of potential bias caused by the Special Olympic 'athletes' having regularly partaken in exercise and could therefore be deemed as healthy people based on performing more exercise than a population average. This was a naïve assumption. Special Olympics 'athletes' are a wide-ranging population including people who attend clubs for social activities as well as sporting activities. They also include athletes with PMLD who have limited movement such that they cannot perform exercise to the extent that fitness betterment can be achieved. Based on this it would have been a better decision to include these studies published using Special Olympic samples and include the criteria as a confounding variable during the meta-regression. Not including these studies has led to me excluding valid and useful data.

Papers from the HA-ID study (n=5) used a sample of older people (age = 45+). Although these were not excluded due to our inclusion criteria including of population >80% 18+ years, the sample of people may have biased results. The sample in this study were older and therefore more susceptible to later life disease and illnesses such as cardiometabolic conditions that were the basis of my systematic review. This weakness can be further compounded by other

research indicating that people with ID can experience cardiometabolic ta younger ages and that life expectancy is younger for the ID population.

There are studies within my systematic review which may be biased in other ways not considered by our inclusion criteria. These include smaller studies and studies where the sample is all female or all male. Males and females have different rates of cardiometabolic disease and this was not addressed in my inclusion criteria. I did not account for male and female split during my meta-regression, this is something that should be considered for future research. Moreover, it should be considered by anyone collecting data on ID populations, often male female split, amongst other important influential criteria, was not reported and therefore I was unable to account or it during meta-regression. This means that the true influence of confounding variables could not be demonstrated.

4.3 Recommendations for future research

Within this thesis, I have conducted two systematic reviews. Chapter two was a large-scale and comprehensive review of the literature and included 64 individual articles. This is a high number of papers compared to chapter three, where only four were included. The most obvious reason for this is the nature of the research, whereby retrospective data analysis is a cheaper and quicker method of providing insight compared to running long-term intervention studies. However, a consistent issue I have faced throughout the assessment of studies in people with ID is the varying standards of reporting and inconsistent definitions leading to a poorer evaluation of literature.

The studies within chapter two had inconsistent definitions of diseases, this lead to difficulty in grouping diseases for meta-analyses. I tried to group the diseases the best I could, based on the descriptions in the text. However, due to the poor definitions in some papers I had to create separate meta-analyses for undefined diseases. This varied reporting nature may result from language

differences, or a general misunderstanding of the definition of a disease the author is trying to report. One example of this is the reporting of ‘heart disease’. This can take on different definitions depending on your medical background. To be able to make the most of the results published in these papers, it would be beneficial to standardise reporting of diseases according to specific disease level ICD-10 (177). This would avoid confusion. Additionally, a common reporting method defining the disease would be beneficial when it comes to pooling results together for meta-analyses.

Chapter two set out to make a comparison of pooled prevalence of disease between people with ID and the general population. Chapter two showed that there is no evidence to suggest that prevalence of T2DM, CVD, and associated risk factors are dissimilar to the general population. The prevalence of ischaemic heart disease was significantly lower in people with ID but may be explained by survival bias. Studies comparing health conditions in people with ID to the general population are currently sparse, and often important confounding variables are missing or poorly reported; more research with a focus on making comparisons to the general population is needed to investigate possible health disparities.

Only 11 articles reported general population data alongside ID data. This was a limitation. To make true reliable comparisons, more like-for-like data needs to be published comparing the two populations. One major problem for this is the availability and quality of datasets alongside the complexities researchers face in matching datasets together.

In comparison to the general population, data indicating health measures in the ID population are relatively sparse. Although there have been recent additions to health care provisions for this at risk community, additional, better maintained databases would help fill this gap in data and provide better estimates of health in people with ID (178). As well as investigation of health conditions, future research is required to investigate methods of reducing the severity and risk of these conditions through modifiable behaviours.

In chapter two I tried to analyse the effects of severity of ID using meta-regression. However, only half of the included studies reported severity of ID. During my implications section of this discussion I have discussed the importance of separating mild/moderate ID from severe/profound. The lack of reporting of severity of ID may make the reliability of the meta-regression output unreliable. Future research should be considerate of the severity of ID when reporting prevalence results. In addition to this, in those studies where severity was reported it is clear to see that most samples were predominately mild/moderate. It could be suggested that this would bias the result if people with mild/moderate ID are more likely to be obese. It is difficult to account for this using the meta-regression when only half of includes studies reported severity of ID.

Research limitations were also shown in chapter three. Only half of included studies were given a high-quality grading and the respective authors discussed several limitations that were consistent across studies and that are important consideration for future research in multi-component lifestyle interventions for primary preventions of chronic disease.

Within my introduction, I described barriers to health faced by people with ID and this is consistent with the behavioural barriers the researchers describe during their intervention studies. A person with ID may have a decreased understanding of new concepts (50, 51) and it can then be difficult to try and explain why something is necessary. This was shown in interventions where the researchers used accelerometers. The researchers found it difficult to collect results because of the participant's refusal to wear the device. Although the accelerometer is fast becoming the most accepted method of measuring day-to-day PA (179). However, an issue clearly exists in using this type of measurement in people with ID.

One other issue that arises from behavioural and intelligence barriers is attrition rates during studies. Again, this may arise from a general lack of understanding of concepts are complications due to increased behavioural issues exhibited by people with ID. It also touches on another point brought up during my

introduction, a lack of health literacy. This concept evolves from a lack of understanding about what is involved in being healthy. This isn't an issue unique to people with ID and many people in the general population face the same lack of understanding. If in a research intervention, the participant with ID may struggle to understand the need to complete the intervention and need to maintain a healthy lifestyle. This is one issue that is addressed with the multi-component nature of the interventions. It is important to have an educational aspect alongside exercise and diet intervention to help participants understand why they are taking part. One way of increasing understanding is by increasing the interaction and guidance from the researchers throughout the study.

A way to counteract this would be to utilise a strength of two of the studies (157, 160). It was noted that studies in which the participants had an increased level of guidance and care throughout the intervention provided a better intervention environment with more reliable and complete results. This can be seen in Melville *et al.,* where one-to-one guidance for participants was used, and the data collected for the accelerometers was over 70% complete. A recommendation for future research would be to use accelerometers alongside increased interaction from researchers and carers to support the participant during the intervention. This would help provide more complete and reliable data.

One way to ensure a more personalised guided intervention would be to keep intervention group sizes small. This is counterintuitive for research because researchers require large sample sizes to increase power. However, in Bergstrom *et al.,* the author notes that a smaller group size allowed for a more flexible intervention which was a strength. Therefore, it is the finding of this review that interventions should be smaller and more personalised with more assistance provided to the participant to achieve maximum positive intervention effects.

One important issue to be raised when considering increased research and carer presence during interventions is the financial implications. A consistent theme throughout the included studies was a lack of funding to make the

intervention the best it could be. An increased researcher presence within an intervention would only increase cost and this would be tough to deal with unless more research funding can be sought.

Overall, multi-component lifestyle interventions have been shown to be somewhat beneficial in health improvement in people with ID. Currently, studies with long-term follow up periods are scarce and more research needs to take place in the best way to conduct these interventions to maintain a long-term benefit. It is the findings of this research that longer term studies may be difficult due to high study attrition. This can be counteracted by taking note of the future research recommendations from the studies. The main recommendation being that increased assistance and smaller groups will provide a better environment for the participant to make the most of the intervention.

4.4 Conclusions

This body of research indicates that levels of cardiometabolic disease in people with ID are generally comparable to that of the general population. However, due to limitations in reported data throughout the literature this conclusion should be treated with some reservations. However, rates of cardiometabolic disease are high and reliable methods of improving health in people with ID are not as easily accomplishable as in the general population for a variety of reasons.

Although, health and the reduction in health disparity has improved in people with ID in the UK, and most countries in the western world, there are issues that still need urgently addressing to investigate existing health related issues arising from cardiometabolic conditions. More reliable results from robust analyses can be achieved via changes in the way ID research is conducted and reported.

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VIII. Appendix

i. Chapter two – investigators

Initial	Investigator	Position	Affiliation
TC	Thomas Chalk	Author; MPhil student	Health Sciences – University of Leicester
AD	Alison Dunkley	Research Associate	Diabetes Research Centre
RS	Rebecca Spong	Research Assistant	Diabetes Research Centre
LC	Lynsey Chudleigh	Research Assistant	Health Sciences - University of Leicester

ii. Chapter two - PROSPERO protocol

UNIVERSITY of York
Centre for Reviews and Dissemination

NHS
National Institute for Health Research

PROSPERO International prospective register of systematic reviews

Review title and timescale

1 Review title
Give the working title of the review. This must be in English. Ideally it should state succinctly the interventions or exposures being reviewed and the associated health or social problem being addressed in the review.
Evidence for primary prevention of diabetes and cardiovascular disease in people with intellectual disabilities: a systematic review of the effectiveness of lifestyle interventions aimed at reducing modifiable risk factors

2 Original language title
For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3 Anticipated or actual start date
Give the date when the systematic review commenced, or is expected to commence.
20/04/2015

4 Anticipated completion date
Give the date by which the review is expected to be completed.
31/12/2015

5 Stage of review at time of this submission
Indicate the stage of progress of the review by ticking the relevant boxes. Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. This field should be updated when any amendments are made to a published record.

The review has not yet started x

Review stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	No	No

Provide any other relevant information about the stage of the review here.

Review team details

6 Named contact
The named contact acts as the guarantor for the accuracy of the information presented in the register record.
Mr Chalk

7 Named contact email
Enter the electronic mail address of the named contact.
tc207@le.ac.uk

8 Named contact address
Enter the full postal address for the named contact.
Leicester Diabetes Centre Leicester General Hospital Gwendolen Road Leicester LE5 4PW

9 Named contact phone number
Enter the telephone number for the named contact, including international dialing code.

10 Organisational affiliation of the review
Full title of the organisational affiliations for this review, and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.
Diabetes Research Centre, University of Leicester, Leicester Diabetes Centre, Leicester General Hospital, Leicester,

UK

Website address:

11 Review team members and their organisational affiliations

Give the title, first name and last name of all members of the team working directly on the review. Give the organisational affiliations of each member of the review team.

Title	First name	Last name	Affiliation
Mr	Thomas. E. W.	Chalk	(PhD student) Department of Health Sciences, University of Leicester, Leicester, UK
Dr	Alison. J.	Dunkley	(Research associate in nursing) Department of Health Sciences, University of Leicester, Leicester, UK
Dr	Laura	Gray	(Senior Lecturer of Population and Public Health Sciences) Department of Health Sciences, University of Leicester, Leicester, UK
Professor	Kamlesh	Khunti	(Professor of Primary Care Diabetes and Vascular Medicine) Diabetes Research Centre, University of Leicester, Leicester, UK
Miss	Rebecca	Spong	(Research Assistant) Department of Health Sciences, University of Leicester, Leicester, UK

12 Funding sources/sponsors

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Any unique identification numbers assigned to the review by the individuals or bodies listed should be included.

This project is supported by The National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care – East Midlands (NIHR CLAHRC – EM), the University of Leicester Clinical Trials Unit, and the NIHR Leicester-Loughborough Diet, Lifestyle and Physical Activity Biomedical Research Unit. Sources of support for researcher time include a University of Leicester PhD studentship, and an NIHR Programme Grant for Applied Research (RP-PG-1209-10057). This is independent research and the views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. No funding bodies will have any role in study design, data collection and analysis.

13 Conflicts of interest

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

Are there any actual or potential conflicts of interest?

None known

14 Collaborators

Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

Title	First name	Last name	Organisation details
Dr	Satheesh Kumar	Gangadharan	(Medical Director and Consultant Psychiatrist in Learning Disability), Learning Disability Service, Leicestershire Partnership NHS Trust, Leicester, UK.

Review methods

15 Review question(s)

State the question(s) to be addressed / review objectives. Please complete a separate box for each question.

The overall aim is to review and consolidate the evidence for reduction of risk of CVD and/or T2DM through lifestyle

interventions in the ID population. The focus of the review will be on lifestyle interventions aimed at increasing physical activity, reducing sedentary behaviour, reducing weight, and/or increasing healthy dietary behaviours in order to reduce CVD or T2DM, or their associated risk factors (obesity, impaired glucose metabolism, elevated blood pressure, dyslipidaemia).

16 Searches

Give details of the sources to be searched, and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.

Separate searches of the following databases will be used to identify relevant studies: MEDLINE PsycINFO EMBASE Cochrane Central Register of Controlled Trials (CENTRAL) CINAHL Reference lists of other applicable articles will also be inspected to obtain any other relevant studies.

17 URL to search strategy

If you have one, give the link to your search strategy here. Alternatively you can e-mail this to PROSPERO and we will store and link to it.

I give permission for this file to be made publicly available

Yes

18 Condition or domain being studied

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

Intellectual disability (ID), commonly referred to as learning disability, can be characterised as arrested development from childhood in intellectual functioning and adaptive skills, leading to a reduction in ability to cope independently. ID has an estimated current prevalence of 10.37/1000 worldwide. The need for reductions in health risk factors in this population have gained increased attention within the previous two decades, with international publications indicating an imbalance in health problems, and health services. Specifically, issues and solutions were addressed in the World Health Organisation's 2001 report 'Healthy Ageing – Adults with Intellectual Disabilities: Physical Health Issues'. Such publications have caused an increase in research into important issues surrounding the disparities in healthcare, and possible increased risk of disease within ID populations. Non-communicable diseases (NCDs) are on the rise globally, and the need for lifestyle interventions to reduce morbidity and mortality, as well as rising health costs, are being called for on a large scale. The suggested mechanisms for this rise in NCD are an increased availability of energy rich foods and a decrease in physical activity. Cardiovascular diseases (CVD) and type 2 diabetes mellitus (T2DM), and shared associated risk factors are major contributors to NCD deaths. Within ID populations, the literature has indicated possible disparities in prevalence between ID populations and the general population, indicating that persons with ID could be at increased risk of NCD. Those with ID could be at higher risk of T2DM due to an increased prevalence of risk factors, including obesity. Specifically, a study in an older ID population from the Netherlands demonstrated a 16% higher prevalence of obesity compared to the general population. Alongside this, a comprehensive review of the prevalence of CVD in ID populations noted that although prevalence of CVD has fallen over the last two decades, the reduction in ID populations has been smaller when compared to the general population, calling for suitable lifestyle measures to be enforced. Conditions such as CVD and T2DM share similar risk factors, including dyslipidaemia, hypertension, obesity, and impaired glucose regulation (IGR). In the general population, these risk factors can be effectively lowered through interventions focusing on changes in nutrition and physical activity. With an indicated increased risk of NCD being present within ID populations, special attention needs to be paid to the efficacy and effectiveness of pragmatic lifestyle interventions to reverse the disparity. However, the literature focusing on lifestyle behaviour change interventions in people with ID is currently scarce in comparison to the general population.

19 Participants/population

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

Included: People with an intellectual disability (whole study population or a defined sub-sample); Adults (>18 years).
Excluded: Study population includes any of the following (50%) sub-group analysis will be used to test for study level covariates, e.g., intervention type.

Review general information

30 Type and method of review

Select the type of review and the review method from the drop down list.

Intervention, Prevention, Systematic review

31 Language
Select the language(s) in which the review is being written and will be made available, from the drop down list. Use the control key to select more than one language.
English

Will a summary/abstract be made available in English?
Yes

32 Country
Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved. Use the control key to select more than one country.
England

33 Other registration details
Give the name of any organisation where the systematic review title or protocol is registered together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here.

34 Reference and/or URL for published protocol
Give the citation for the published protocol, if there is one.
Give the link to the published protocol, if there is one. This may be to an external site or to a protocol deposited with CRD in pdf format.

I give permission for this file to be made publicly available
Yes

35 Dissemination plans
Give brief details of plans for communicating essential messages from the review to the appropriate audiences.
This systematic review will be submitted for publiction in a peer reviewed journal.

Do you intend to publish the review on completion?
Yes

36 Keywords
Give words or phrases that best describe the review. (One word per box, create a new box for each term)
Intellectual disabilities

Type 2 diabetes

Cardiovascular disease

Lifestyle and behaviour interventions

37 Details of any existing review of the same topic by the same authors
Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38 Current review status
Review status should be updated when the review is completed and when it is published.
Ongoing

39 Any additional information
Provide any further information the review team consider relevant to the registration of the review.

40 Details of final report/publication(s)

iii. Chapter two – review protocol

Background

Intellectual disability

Intellectual disability (ID), commonly referred to as learning disability, can be characterised as arrested development from childhood in intellectual functioning and adaptive skills, leading to a reduction in ability to cope independently [1] and has an estimated current prevalence of 10.37/1000 worldwide [2]. Increased risk factors for cardiovascular disease (CVD) and Type 2 diabetes mellitus (T2DM) have been demonstrated in specific ID sub-groups defined throughout the literature including those with sedentary lifestyles [3], those with a less severe ID [4] and with more independence [5]. Importantly, the high rate of anti-psychotic medication use amongst those with ID [6] adversely causes metabolic changes associated with CVD and T2DM, including excessive weight gain [7]. A retrospective study conducted in the Netherlands [8] demonstrated a prevalence of multi-morbidity (two chronic conditions or more) of 79.8% in an ID population.

Type 2 diabetes

The prevalence of T2DM is increasing globally [9] through suggested mechanisms such as decreased physical activity levels [10] an increase in availability of cheaper, energy rich foods providing an increase in energy intake [11]. It is estimated that 360 million people worldwide will be diagnosed with T2DM by 2030 [12]. The increased prevalence of T2DM is causing worldwide increases in medical costs [13]. The predicted rise in cost globally is estimated to rise to $627 billion by 2035 [14]. Moreover, the predicted rise in cost to the NHS is estimated to rise to £16.9 billion per annum by 2035 [15]. Those with ID are likely to be more at risk of T2DM due to an increased prevalence of risk factors, including obesity. Specifically, a study in an older population from the Netherlands [16] indicated an increased risk of T2DM via high prevalence of risk factors in an ID population. However, other studies have been contrary, with no differences seen at all between ID and non-ID populations [17].

Cardiovascular conditions

Cardiovascular disease is the UK's largest cause of death, with responsibility for over a third of all deaths in the UK and is also the largest cause of death in ID populations [18]. These figures are predicted to rise and lead to an overall annual cost to the NHS of £50 billion per year by 2030 in the general population [19]. Multiple modifiable risk factors such as dyslipidaemia, hypertension, and hyperglycaemia can all be noted as responsible mechanisms in increasing CVD risk. These mechanisms are all increasing in prevalence due to the nature of the increase in obesity caused by poor diet and sedentary behaviour - physical inactivity is currently estimated to be responsible for 10.5% of all coronary heart disease cases in the UK [20]. A comprehensive review focused on the literature indicating prevalence of CVD in ID populations noted an increased prevalence overall and a smaller reduction in prevalence over the last two decades when compared to the general population, calling for suitable lifestyle measures to be enforced [21]. Conversely, A large American survey study [22] demonstrated a lower overall reported frequency of CVD in ID samples, however, it is noted that these results were not consistent with mortality data indicating either a discrepancy in the self-

reported nature of the study or an under-diagnosis of conditions in this sample. Discrepancies within the literature are common and need to be further investigated in ID populations.

Risk factors for T2DM and CVD

Established risk factors heavily contribute to the development T2DM and CVD as well as the long-term vascular risks associated with these conditions [23]. Risk factors for T2DM and/or CVD that are frequently measured as part of risk assessment in routine care include obesity, impaired glucose regulation (IGR), hypertension, and hyperlipidemia. These risk factors have all been noted as contributory factors to T2DM and CVD. Alongside the conditions themselves, risk factor prevalence is also increasing. The DECODE study, a large European epidemiological study demonstrates that half of all Europeans will experience IGR or T2DM within their lifetimes [24]. Hypertension is also on the rise, with a 26.4% global prevalence recorded in 2000 predicted to rise to 29.2% by 2025 [25]. And hyperlipidaemia, including raised cholesterol, increases the risks of CVD with raised cholesterol levels accounting for over 30% of ischemic disease worldwide and is accountable for 2.6 million deaths annually [26]

The suggested associated mechanisms for T2DM prevalence (i.e., increased energy intake) is also a direct cause of increased obesity. The current estimated worldwide prevalence of adults with a body-mass index (BMI) of 25 kg/m^2 or greater (classed as overweight) increased between 1980 and 2013 by 8.1% in men and 8.2% in women [27] and at the time of diagnosis of T2DM, 80% of individuals are categorised as obese [28]. Some investigation into this area indicates the at risk nature of ID populations. A UK based study with a population of mild-moderate people with ID living in supported accommodation demonstrated an increased obesity prevalence in older people and, overall, only 4% of participants reaching minimum standards of physical activity – a major contributor to obesity.

Rationale

Research indicates that ID populations may be at increased risk of developing T2DM and subsequent CVD through increased risk factors such as obesity. The global increase of obesity, CVD and T2DM and current discrepancies between studies focusing on incidence and prevalence of such conditions in those with ID indicates a need for a systematic review of literature in this area.

Two reviews have been conducted in this area focusing on combined type 1 and type 2 diabetes prevalence [29] and CVD and risk factors [21] respectively. However, to our knowledge a systematic review focusing on CVD, T2DM, and associated risk factors inclusive of meta-analytic techniques does not currently exist.

Aims

The overall aim is to review and consolidate the evidence for current rates of T2DM, CVD, and associated risk factors, in people with ID. If sufficient data are available, a meta-analysis will also be conducted.

The original plan was to only examine rates of T2DM and CVD in people with ID. However, an initial scoping search suggested a lack of studies reporting relevant outcome data. The focus of the

review will therefore be widened to include risk factors for T2DM and/or CVD that are currently considered as part of risk assessment in routine clinical practice (obesity, impaired glucose metabolism, elevated blood pressure, dyslipidaemia).

Physical activity levels/sedentary behaviour and dietary factors will not be considered when framing the research question and designing the search strategy. However, where studies report data related to the above, these data will be extracted.

Objectives

- To establish the prevalence and incidence of T2DM in the ID population.
- To establish the prevalence of previous CVD and incidence of CVD in the ID population.
- To establish the prevalence of risk factors for T2DM and/or CVD (adverse lipid profiles, IGR, obesity, and hypertension) in the ID population.

Methods

Search strategy

Separate searches of the following electronic databases will be conducted to identify relevant studies from the year 2000 to current.

- MEDLINE
- PsycINFO
- EMBASE

The search strategy will combine MeSH terms and keywords relating to intellectual disabilities, T2DM, CVD, and risk factors for T2DM and/or CVD (Table 1). An initial scoping search suggests that this is the most appropriate approach.

Study Selection

The planned inclusion and exclusion criteria are summarised in Table 1. Only studies published as full length articles in English language will be included in the review. Titles and abstracts will be reviewed independently by two reviewers (TC and AD). Following retrieval of potentially relevant articles,full-text review will be carried out by two reviewers (TC and AD). Any differences will be resolved by a third party.

Reference lists of papers identified for inclusion and other applicable articles will be examined for other relevant studies. Experts in the field and first authors of included papers will also be contacted.

	Inclusion	Exclusion
P - population	• People with an intellectual disability (whole study population or a defined sub-sample)	• Study population includes any of the following (≤ 20% permitted): - People with an identified developmental disability in

	• Adults (>18 years)	the absence of intellectual impairment. - People identified as having a learning difficulty as opposed to a learning (intellectual) disability. - People with specific syndromes linked to a genetic pre-disposition to diabetes, obesity or CVD e.g. Prader Willi. - People selected on the basis of having a specific syndrome e.g. all have Down's - People with acquired ID (e.g., from head injury)
I – item of interest	• Type 2 diabetes • Cardiovascular disease (atherosclerotic) • Risk factors for T2DM and/or CVD: - Overweight/obesity - Hypertension - Metabolic syndrome - Hyperlipidaemia - Impaired glucose regulation	• Type 1 diabetes or if type of diabetes not specified. • Heart disease not classified as CVD e.g. congenital heart disease; or if type not specified.
C - context	• Population based studies	
O - outcome	• Prevalence and/or incidence rates (or data to enable calculation)	
S – study design	• Cross-sectional studies • Retrospective or prospective cohort studies	• Randomised controlled trials • Intervention studies • Case studies

Table 1: Inclusion and exclusion criteria for the systematic review

Data extraction

Data will be extracted by one reviewer (TC) and checked by another (AD) using a standardised data extraction form. All included studies will have the following data recorded on the data extraction form:

- Study characteristics (author, year, country, study type)

- Participant characteristics (number, percentage male, mean age, percentage of participants within categories of severity of ID [if noted])
- Definition of diabetes, CVD, and associated risk factors.
- Prevalence and/or incidence data of T2DM, CVD, and associated risk factors or data extractable for use when calculating prevalence and/or incidence.
- Length of follow up if a prospective study
- Inclusion/exclusion criteria

Obesity data will be extracted from BMI data wherever possible, when studies report obesity prevalence, classification methods will be scrutinised and standardised where possible.

Incidence and prevalence data will be extracted and calculated in order to be on the same scale, specifically, prevalence data is the percentage of people with a specific condition at one point in time and will be calculated as a percentage. Incidence data is the number of new cases of a specific condition over a specific period of time and incidence data will be extracted and converted into cases per 100 person-years. 95% confidence intervals will be calculated from data where none are reported.

Quality assessment

Quality will be assessed using the Joanna Brigg's Institute critical appraisal tool for studies reporting prevalence data. Quality assessment will consist of a checklist of 10 items focused on sampling, data analysis, and reporting. Each item will be assessed using YES/NO/UNCLEAR [30].

Data synthesis and analysis

Data analysis

Data will be pooled using a random effects model using Stata (version 13.0). Separate analysis will be carried out for each outcome. Statistical significance relates to $p < 0.05$, and 95% confidence intervals (95% CIs) will be presented throughout.

Assessment of heterogeneity

Between-study heterogeneity will be assessed using the I^2 statistic in conjunction with Cochrane's Q (significance for chi-squared set at $p < 0.01$). When heterogeneity is deemed high (>50%) [31] meta-regression will be used to adjust for study level covariates the following covariates will be used: mean age, percentage male, severity of condition, and study quality.

Assessment of risk of biases

Publication bias will be assessed for syntheses with five or more studies included with a funnel plot and the Egger test. This will be carried out separately for CVD and diabetes and separately for prevalence and incidence.

References

1. World-Health-Organisation, *The ICD-10 Classification of Mental and Behavioural Disorders*. 1993, World Health Organisation: Geneva.
2. Maulik, P.K., et al., *Prevalence of intellectual disability: A meta-analysis of population-based studies*. Research in Developmental Disabilities, 2011. 32(2): p. 419-436.
3. Draheim, C.C., J.A. McCubbin, and D.P. Williams, *Differences in cardiovascular disease risk between nondiabetic adults with mental retardation with and without Down syndrome*. Am J Ment Retard, 2002. 107(3): p. 201-11.
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6. Kiernan, C., D. Reeves, and A. Alborz, *The use of anti-psychotic drugs with adults with learning disabilities and challenging behaviour*. J Intellect Disabil Res, 1995. 39 (Pt 4): p. 263-74.
7. Tek, C., et al., *Investigating the safety and efficacy of naltrexone for anti-psychotic induced weight gain in severe mental illness: study protocol of a double-blind, randomized, placebo-controlled trial*. BMC Psychiatry, 2013. 13: p. 176.
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9. Shaw, J.E., R.A. Sicree, and P.Z. Zimmet, *Global estimates of the prevalence of diabetes for 2010 and 2030*. Diabetes Research and Clinical Practice, 2010. 87(1): p. 4-14.
10. Hallal, P.C., et al., *Global physical activity levels: surveillance progress, pitfalls, and prospects*. Lancet, 2012. 380(9838): p. 247-57.
11. Salmeron, J., et al., *Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women*. Jama, 1997. 277(6): p. 472-7.
12. Wild, S., et al., *Global prevalence of diabetes: estimates for the year 2000 and projections for 2030*. Diabetes Care, 2004. 27(5): p. 1047-53.
13. Caro, J.J., A.J. Ward, and J.A. O'Brien, *Lifetime costs of complications resulting from type 2 diabetes in the U.S.* Diabetes Care, 2002. 25(3): p. 476-81.
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19. Quality-Care-Comission, *National study – Closing the gap: tackling cardiovascular disease and health inequalities by prescribing statins and stop smoking services*. 2009.
20. Lee, I.M., et al., *Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy*. Lancet, 2012. 380(9838): p. 219-29.
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22. Janicki, M.P., et al., *Health characteristics and health services utilization in older adults with intellectual disability living in community residences*. J Intellect Disabil Res, 2002. 46(Pt 4): p. 287-98.

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27. Ng, M., et al., *Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013.* The Lancet. 384(9945): p. 766-781.
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30. Munn, Z., et al., *The Development of a Critical Appraisal Tool for Use in Systematic Reviews: Addressing Questions of Prevalence.* International Journal of Health Policy and Management, 2014. 3(3): p. 123-128.
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iv. Chapter two search strategy

1. Exp Diabetes Mellitus, Type 2/
2. (diabet* adj3 type adj "2").ti,ab.
3. T2DM.ti,ab.
4. (diabet* adj3 type adj ii).ti,ab.
5. niddm.ti,ab.
6. (non-insulin-dependent adj2 diabet*).ti,ab.
7. (adult-onset adj2 diabet*).ti,ab.
8. Or/1-7
9. Exp Hypertension/
10. hypertens*.ti,ab.
11. (blood adj pressure adj3 (high or elevated or increased or raised)).ti,ab.
12. Or/9-11
13. Exp Metabolic syndrome x/
14. (metabolic adj syndrome).ti,ab.
15. (cardiometabolic adj syndrome).ti,ab.
16. (Insulin adj resistance adj syndrome).ti,ab.
17. MetSyn.ti,ab.
18. MetS.ti,ab.
19. Or/13-18
20. Exp. Hyperlipidemias/
21. Hyperlipid*.ti,ab.
22. dyslipid*.ti,ab.
23. hypercholes*.ti,ab.
24. hypertriglycer*.ti,ab.
25. (cholesterol* adj2(high or elevated or raised or increased)).ti,ab.
26. (triglcerid* adj2(high or elevated or raised or increased)).ti,ab.
27. (lipid adj profile adj2(adverse or abnormal)).ti,ab.
28. Or/20-27
29. Exp. Glucose intolerance/
30. (impaired adj glucose adj(tolerance or regulation)).ti,ab.

31. (impaired adj fasting adj glucose).ti,ab.
32. IGT.ti,ab.
33. IFG.ti,ab.
34. IGR.ti,ab.
35. Exp Prediabetic state/
36. prediabet*.ti,ab.
37. pre-diabet*.ti,ab.
38. Or/29-37
39. (cardiovascular adj diseas*).ti,ab.
40. CVD.ti,ab.
41. CHD.ti,ab.
42. Exp. Myocardial infarction/
43. (infarct* adj2 myocardial).ti,ab.
44. Exp Coronary disease/
45. (coronary adj2 diseas*).ti,ab.
46. (acute adj coronary adj syndrom*).ti,ab.
47. Exp angina pectoris/
48. angina.ti,ab.
49. Exp myocardial ischemia/
50. (isch* adj2 heart adj2 diseas*).ti,ab.
51. (Myocardial adj2 isch*).ti,ab.
52. Exp. Stroke/
53. strok*.ti,ab.
54. (cerebrovascular adj2 diseas*).ti,ab.
55. (cerebrovascular adj2 accident*).ti,ab.
56. (cerebral adj2 diseas*).ti,ab.
57. (cerebral adj2 accident*).ti,ab.
58. CVA.ti,ab.
59. TIA.ti,ab.
60. (brain adj1 infarc*).ti,ab.

61. (brainstem adj1 infarc*).ti,ab.
62. Exp ischemic attack, transient/
63. (isch* adj2 attac* adj2 transient).ti,ab.
64. Exp Atherosclerosis/
65. atheroscle*.ti,ab.
66. (arteriosclerotic adj vascular adj diseas*).ti,ab.
67. exp Peripheral Arterial Disease/ or exp Peripheral Vascular Diseases/
68. (peripheral adj2 arter* adj2 diseas*).ti,ab.
69. (peripheral adj2 vascular adj2 diseas*).ti,ab.
70. (peripheral adj1 angiopath*).ti,ab.
71. or/39-70
72. exp obesity/
73. obes*.ti,ab.
74. overweight.ti,ab.
75. (body adj weight adj2 (high or elevated or increase*)).ti,ab.
76. (bodyweight adj2 (high or elevated or increase*)).ti,ab.
77. (body adj mass adj3 (high or elevated or increase*)).ti,ab.
78. (waist adj2 (large or elevated or increas*)).ti,ab.
79. Exp body mass index
80. (BMI adj2 (high or elevated or increase*)).ti,ab.
81. or/72-80
82. exp Intellectual disability/
83. (learning adj1 disabilit*).ti,ab.
84. (developmental adj1 disabilit*).ti,ab.
85. (intellectual adj1 disabilit*).ti,ab.
86. (impair* adj2 intellectual adj2 function*).ti,ab.
87. (mental* adj1 impair*).ti,ab.
88. (mental* adj1 handicap*).ti,ab.

89. Exp mentally disabled persons/
90. (mental* adj1 disabl*).ti,ab.
91. (mental* adj2 retard*).ti,ab.

92. Or/82-91
93. 9 or 12 or 19 or 28 or 38 or 71 or 81
94. 92 and 93
95. Limit 94 to yr=2000-current
96. Limit 95 to English language
97. (animals not humans).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier
98. 96 not 97

v. Chapter two data extraction form

ELIGIBILITY CHECKLIST	YES	NO	NOTES
Population or sub-group has ID (>80%)			If no, exclude
Population has a specific syndrome, acquired ID, or a learning difficulty/developmental disability.			If yes, exclude if >25%
Population >= 18 years			If no, exclude
Reported outcomes CVD, T2DM &/or risk factors (obesity, hypertension, MetS, dyslipidemia, IGR)			If no, exclude
Extractable data (prevalence, incidence or data to calculate)			If no, exclude
Population based study			If no, exclude
Study involves an intervention (RCT/non-randomised) or is a case study			If yes, exclude
Published year 2000 or after			If no, exclude

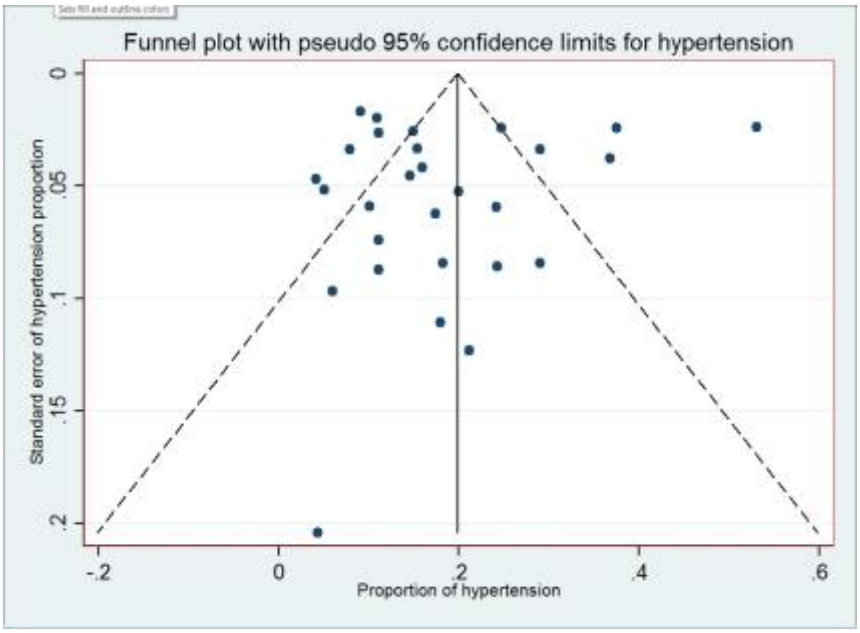
STUDY DETAILS			
First author		Publication date	
Title of paper			
Journal			
Language and country of first author			
Important notes (include any significant issues here: eg validity, areas of uncertainty etc)			
Country/countries			
Study type			

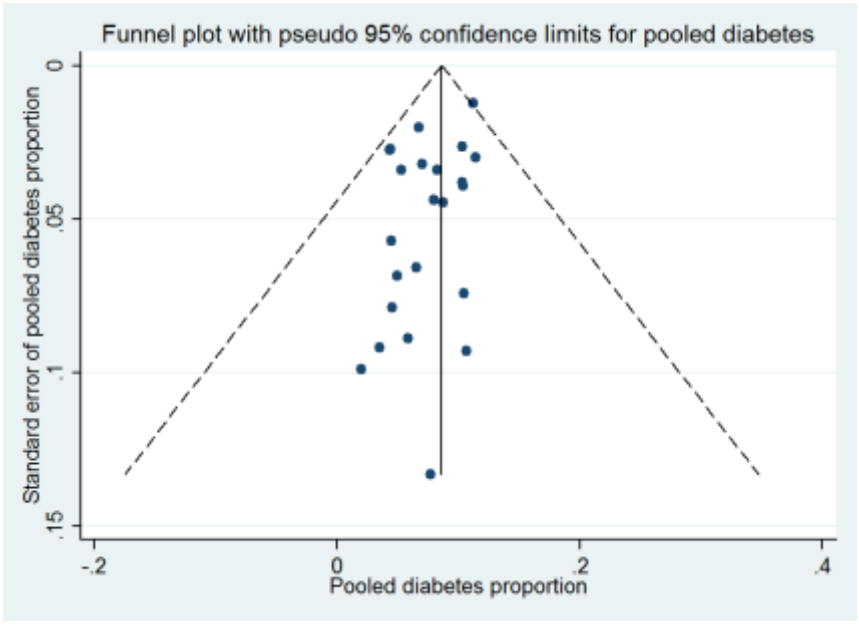
POPULATION				
Sampling method				
Dates of data collection				
Exclusion criteria				
Population	**Overall**	**Subgroup:**		
Number				
Subjects	**Total**	**Proportion (%)**		
Men				
Women				
Age	**Overall**	**Male**	**Female**	
Mean age (+/- SD)				
Age range				
Ethnicity	**Group 1:**	**Group 2:**	**Group 3:**	
Total				
Proportion (%)				
ID severity	**Mild**	**Moderate**	**Severe**	**Profound**
Total				
Proportion				

OUTCOME MEASURE			
Type (if CVD)			
Definition/Method of measuring			
	MALE	**FEMALE**	**OVERALL**
Total number measured			
Number with outcome			
Proportion			
95% CI			
Standardised proportion			
95% CI			
Standardised by:			
OUTCOME MEASURE			
Type			
Definition/Method of measuring			
	MALE	**FEMALE**	**OVERALL**
Total number measured			
Number with outcome			
Proportion			
95% CI			
Standardised proportion			
95% CI			
Standardised by:			

OUTCOME MEASURE			
Type (if CVD)			
Definition/Method of measuring			
	MALE	**FEMALE**	**OVERALL**
Total number measured			
Number with outcome			
Proportion			
95% CI			
Standardised proportion			
95% CI			
Standardised by:			
OUTCOME MEASURE			
Type			
Definition/Method of measuring			
	MALE	**FEMALE**	**OVERALL**
Total number measured			
Number with outcome			
Proportion			
95% CI			
Standardised proportion			
95% CI			
Standardised by:			

vi. Chapter two funnel plots





vii. Chapter three – investigators

Initial	Investigator	Position	Affiliation
TC	Thomas Chalk	Author; MPhil student	Leicester Diabetes Centre & Health Sciences – University of Leicester
AD	Alison Dunkley	Research Associate	Leicester Diabetes Centre
RS	Rebecca Spong	Research Assistant	Leicester Diabetes Centre

viii. Chapter three PROSPERO protocol

UNIVERSITY of York
Centre for Reviews and Dissemination

NHS
National Institute for Health Research

PROSPERO International prospective register of systematic reviews

Review title and timescale

1 Review title
Give the working title of the review. This must be in English. Ideally it should state succinctly the interventions or exposures being reviewed and the associated health or social problem being addressed in the review.
Evidence for primary prevention of diabetes and cardiovascular disease in people with intellectual disabilities: a systematic review of the effectiveness of lifestyle interventions aimed at reducing modifiable risk factors

2 Original language title
For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3 Anticipated or actual start date
Give the date when the systematic review commenced, or is expected to commence.
20/04/2015

4 Anticipated completion date
Give the date by which the review is expected to be completed.
31/12/2015

5 Stage of review at time of this submission
Indicate the stage of progress of the review by ticking the relevant boxes. Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. This field should be updated when any amendments are made to a published record.

The review has not yet started x

Review stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	No	No

Provide any other relevant information about the stage of the review here.

Review team details

6 Named contact
The named contact acts as the guarantor for the accuracy of the information presented in the register record.
Mr Chalk

7 Named contact email
Enter the electronic mail address of the named contact.
tc207@le.ac.uk

8 Named contact address
Enter the full postal address for the named contact.
Leicester Diabetes Centre Leicester General Hospital Gwendolen Road Leicester LE5 4PW

9 Named contact phone number
Enter the telephone number for the named contact, including international dialing code.

10 Organisational affiliation of the review
Full title of the organisational affiliations for this review, and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.
Diabetes Research Centre, University of Leicester, Leicester Diabetes Centre, Leicester General Hospital, Leicester,

UK

Website address:

11 Review team members and their organisational affiliations

Give the title, first name and last name of all members of the team working directly on the review. Give the organisational affiliations of each member of the review team.

Title	First name	Last name	Affiliation
Mr	Thomas. E. W.	Chalk	(PhD student) Department of Health Sciences, University of Leicester, Leicester, UK
Dr	Alison. J.	Dunkley	(Research associate in nursing) Department of Health Sciences, University of Leicester, Leicester, UK
Dr	Laura	Gray	(Senior Lecturer of Population and Public Health Sciences) Department of Health Sciences, University of Leicester, Leicester, UK
Professor	Kamlesh	Khunti	(Professor of Primary Care Diabetes and Vascular Medicine) Diabetes Research Centre, University of Leicester, Leicester, UK
Miss	Rebecca	Spong	(Research Assistant) Department of Health Sciences, University of Leicester, Leicester, UK

12 Funding sources/sponsors

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Any unique identification numbers assigned to the review by the individuals or bodies listed should be included.

This project is supported by The National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care – East Midlands (NIHR CLAHRC – EM), the University of Leicester Clinical Trials Unit, and the NIHR Leicester-Loughborough Diet, Lifestyle and Physical Activity Biomedical Research Unit. Sources of support for researcher time include a University of Leicester PhD studentship, and an NIHR Programme Grant for Applied Research (RP-PG-1209-10057). This is independent research and the views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. No funding bodies will have any role in study design, data collection and analysis.

13 Conflicts of interest

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

Are there any actual or potential conflicts of interest?

None known

14 Collaborators

Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

Title	First name	Last name	Organisation details
Dr	Satheesh Kumar	Gangadharan	(Medical Director and Consultant Psychiatrist in Learning Disability), Learning Disability Service, Leicestershire Partnership NHS Trust, Leicester, UK.

Review methods

15 Review question(s)

State the question(s) to be addressed / review objectives. Please complete a separate box for each question.

The overall aim is to review and consolidate the evidence for reduction of risk of CVD and/or T2DM through lifestyle

interventions in the ID population. The focus of the review will be on lifestyle interventions aimed at increasing physical activity, reducing sedentary behaviour, reducing weight, and/or increasing healthy dietary behaviours in order to reduce CVD or T2DM, or their associated risk factors (obesity, impaired glucose metabolism, elevated blood pressure, dyslipidaemia).

16 Searches

Give details of the sources to be searched, and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.

Separate searches of the following databases will be used to identify relevant studies: MEDLINE PsycINFO EMBASE Cochrane Central Register of Controlled Trials (CENTRAL) CINAHL Reference lists of other applicable articles will also be inspected to obtain any other relevant studies.

17 URL to search strategy

If you have one, give the link to your search strategy here. Alternatively you can e-mail this to PROSPERO and we will store and link to it.

I give permission for this file to be made publicly available

Yes

18 Condition or domain being studied

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

Intellectual disability (ID), commonly referred to as learning disability, can be characterised as arrested development from childhood in intellectual functioning and adaptive skills, leading to a reduction in ability to cope independently. ID has an estimated current prevalence of 10.37/1000 worldwide. The need for reductions in health risk factors in this population have gained increased attention within the previous two decades, with international publications indicating an imbalance in health problems, and health services. Specifically, issues and solutions were addressed in the World Health Organisation's 2001 report 'Healthy Ageing – Adults with Intellectual Disabilities: Physical Health Issues'. Such publications have caused an increase in research into important issues surrounding the disparities in healthcare, and possible increased risk of disease within ID populations. Non-communicable diseases (NCDs) are on the rise globally, and the need for lifestyle interventions to reduce morbidity and mortality, as well as rising health costs, are being called for on a large scale. The suggested mechanisms for this rise in NCD are an increased availability of energy rich foods and a decrease in physical activity. Cardiovascular diseases (CVD) and type 2 diabetes mellitus (T2DM), and shared associated risk factors are major contributors to NCD deaths. Within ID populations, the literature has indicated possible disparities in prevalence between ID populations and the general population, indicating that persons with ID could be at increased risk of NCD. Those with ID could be at higher risk of T2DM due to an increased prevalence of risk factors, including obesity. Specifically, a study in an older ID population from the Netherlands demonstrated a 16% higher prevalence of obesity compared to the general population. Alongside this, a comprehensive review of the prevalence of CVD in ID populations noted that although prevalence of CVD has fallen over the last two decades, the reduction in ID populations has been smaller when compared to the general population, calling for suitable lifestyle measures to be enforced. Conditions such as CVD and T2DM share similar risk factors, including dyslipidaemia, hypertension, obesity, and impaired glucose regulation (IGR). In the general population, these risk factors can be effectively lowered through interventions focusing on changes in nutrition and physical activity. With an indicated increased risk of NCD being present within ID populations, special attention needs to be paid to the efficacy and effectiveness of pragmatic lifestyle interventions to reverse the disparity. However, the literature focusing on lifestyle behaviour change interventions in people with ID is currently scarce in comparison to the general population.

19 Participants/population

Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

Included: People with an intellectual disability (whole study population or a defined sub-sample); Adults (>18 years).
Excluded: Study population includes any of the following (50%) sub-group analysis will be used to test for study level covariates, e.g., intervention type.

Review general information

30 Type and method of review

Select the type of review and the review method from the drop down list.

Intervention, Prevention, Systematic review

31 Language
Select the language(s) in which the review is being written and will be made available, from the drop down list. Use the control key to select more than one language.
English

Will a summary/abstract be made available in English?
Yes

32 Country
Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved. Use the control key to select more than one country.
England

33 Other registration details
Give the name of any organisation where the systematic review title or protocol is registered together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here.

34 Reference and/or URL for published protocol
Give the citation for the published protocol, if there is one.
Give the link to the published protocol, if there is one. This may be to an external site or to a protocol deposited with CRD in pdf format.

I give permission for this file to be made publicly available
Yes

35 Dissemination plans
Give brief details of plans for communicating essential messages from the review to the appropriate audiences.
This systematic review will be submitted for publiction in a peer reviewed journal.

Do you intend to publish the review on completion?
Yes

36 Keywords
Give words or phrases that best describe the review. (One word per box, create a new box for each term)
Intellectual disabilities

Type 2 diabetes

Cardiovascular disease

Lifestyle and behaviour interventions

37 Details of any existing review of the same topic by the same authors
Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38 Current review status
Review status should be updated when the review is completed and when it is published.
Ongoing

39 Any additional information
Provide any further information the review team consider relevant to the registration of the review.

40 Details of final report/publication(s)

ix. Chapter three – review protocol

Background

Intellectual disability

Intellectual disability (ID), commonly referred to as learning disability, can be characterised as arrested development from childhood in intellectual functioning and adaptive skills, leading to a reduction in ability to cope independently [1]. ID has an estimated current prevalence of 10.37/1000 worldwide [2]. The need for reductions in health risk factors in this population have gained increased attention within the previous two decades, with international publications indicating an imbalance in health problems and health service provision. Specifically, issues and solutions were addressed in the World Health Organisation's 2001 report 'Healthy Ageing – Adults with Intellectual Disabilities: Physical Health Issues' [3]. Such publications have caused an increase in research into important issues surrounding the disparities in healthcare [4-6], and possible increased risk of disease within ID populations [7-10].

The rise of non-communicable disease

Non-communicable diseases (NCDs) are on the rise globally and the need for lifestyle interventions to reduce morbidity and mortality, as well as rising health costs, are being called for on a large scale [11]. The suggested mechanisms for this rise in NCD are an increased availability of energy rich foods and a decrease in physical activity [12]. Cardiovascular diseases (CVD) and type 2 diabetes mellitus (T2DM), and shared associated risk factors, are major contributors to NCD deaths [13]. Within ID populations, the literature has indicated possible disparities in prevalence of non-communicable disease and their associated risk factors between ID populations and the general population, indicating that persons with ID could be at increased risk of NCD [4-10]. Those with ID could be at higher risk of T2DM due to an increased prevalence of risk factors, including obesity. Specifically, a study in an older ID population from the Netherlands [9] demonstrated a 16% higher prevalence of obesity when compared to the general population. Alongside this, a comprehensive review focusing on the prevalence of CVD in ID populations noted that although prevalence of CVD has fallen over the last two decades. However, the reduction in ID populations has been much smaller when compared to the general population. calling for suitable lifestyle measures to be enforced [14].

Implementation of lifestyle interventions

Conditions such as CVD and T2DM share similar risk factors, including dyslipidaemia, hypertension, obesity, and impaired glucose regulation (IGR). In the general population, these risk factors can be effectively lowered through interventions focusing on changes in nutrition and physical activity [15-18]. With an indicated increased risk of NCD being present within ID populations, special attention needs to be paid to the efficacy and effectiveness of lifestyle behaviour change interventions to reverse this disparity. However, the literature focusing on lifestyle interventions in people with ID is currently scarce in comparison to the general population.

Aim

The overall aim is to review and consolidate the evidence for reduction of risk of CVD and/or T2DM through lifestyle interventions in the ID population. The focus of the review will be on lifestyle interventions aimed at increasing physical activity, reducing sedentary behaviour, reducing weight, and/or increasing healthy dietary behaviours in order to reduce CVD or T2DM, or their associated risk factors (obesity, impaired glucose metabolism, elevated blood pressure, dyslipidaemia, metabolic syndrome).

Primary objectives

- To establish the effectiveness of lifestyle interventions in promoting weight loss in the ID population

Secondary objectives

- To establish the effectiveness of lifestyle interventions in improving other modifiable risk factors for T2DM and/or CVD in the ID population.
- To establish the effectiveness of lifestyle interventions in reducing risk of T2DM and/or CVD in the ID population.

Methods

Search Methods

Separate searches of the following electronic databases will be conducted to identify relevant studies from the year 2000 to current.

- MEDLINE
- PsycINFO
- EMBASE
- CINAHL
- Cochrane Central Register of Controlled Trials (CENTRAL)

The search strategy will combine MeSH terms and keywords relating to intellectual disabilities, physical activity, behavioural change and diet. An initial scoping search suggests that this is the most appropriate approach.

Studies

Participants

Studies including participants deemed as having an ID will be included in this review.

Study Selection

The planned inclusion and exclusion criteria are summarised in Table 1. Only studies published as full length articles in English language will be included in the review. Titles and

abstracts will be reviewed independently by two reviewers. Following retrieval of potentially relevant articles, full-text review will be carried out by two reviewers. Any differences will be resolved by a third party.

Reference lists of papers identified for inclusion and other applicable articles will be examined for other relevant studies. Experts in the field and first authors of included papers will also be contacted.

	Inclusion	**Exclusion**
P - population	• People with an intellectual disability (whole study population or a defined sub-sample) • Adults (>18 years)	• Study population includes any of the following (≤ 25% permitted): - People with an identified developmental disability in the absence of intellectual impairment. - People identified as having a learning difficulty as opposed to a learning (intellectual) disability. - People having a specific syndrome e.g. all participants have Prada Willi - People with acquired ID (e.g., from head injury • Studies where the whole population already have CVD and/or T2DM
I – Intervention	• Multi-component lifestyle behaviour change interventions aimed at primary prevention of T2DM or CVD or reduction of risk factors: o Weight management o Increasing physical activity/reducing sedentary behaviour o Dietary improvement • Intervention aimed at ID population and/or their carer	• Surgical interventions • Pharmacological interventions • Meal replacement interventions • Interventions aimed at increasing physical fitness as opposed to changes in levels of physical activity.

C - Comparator	• Studies with and without comparators will be included.	
O - outcome	Changes in: • anthropometric measures (e.g., BMI, weight, body fat measures, waist circumference) • Blood pressure • Lipid levels • Glucose levels • Physical activity level • Sedentary behaviour • Dietary habits	
S – study design	• Experimental studies: o Before and after studies o Randomised control trials o Non-randomised control trials • All studies must have a follow up period of at least 24 weeks or 6 months from baseline	• Studies that do not involve an intervention • Observational studies

Data extraction

Data will be extracted by one reviewer (TC) and checked by another using a standardised data extraction form. All included studies will have the following data recorded on the data extraction form:

- Study characteristics (author, year, country, study type)
- Intervention details
- Participant characteristics (number, percentage male, mean age, percentage of participants within categories of severity of ID [if noted])
- Changes in mean physical activity data
- Changes in mean BMI, weight, body fat measures, waist measurement, blood pressure, lipid levels, glucose levels.
- Dietary habits
- Length of follow up from baseline, and program completion.

- Inclusion/exclusion criteria

Risk of bias assessment

The quality of selected studies will be assessed according to the UK's National Institute for Health and Clinical Excellence (NICE) quality appraisal checklist for quantitative intervention studies [19]. The checklist includes criteria for assessing the internal and external validity of experimental and observational quantitative studies (randomized controlled trials (RCTs), non-randomised controlled trials, before and after studies) and allows assignment of an overall quality grade (categories ++, + or -).

Data synthesis and analysis

Data analysis

Data will be pooled using a random effects model using Stata (version 13.0). Separate analysis will be carried out for each outcome. Statistical significance relates to $p < 0.05$, and 95% confidence intervals (95% CIs) will be presented throughout.

Separate analyses will be carried out based on the structure of the study, i.e., whether the study is within group (single arm), or between intervention and control groups (multiple arms).

Assessment of heterogeneity

Between-study heterogeneity will be assessed using the I^2 statistic in conjunction with Cochrane's Q (significance for chi-squared set at $p < 0.01$). When heterogeneity is deemed high (>50%) [20] sub-group analysis will be used to test for study level covariates, e.g., intervention type.

Assessment of risk of biases

Publication bias will be assessed for syntheses with five or more studies included with a funnel plot and the Egger test. This will be carried out separately for each variable identified from the literature found.

References

1. World-Health-Organisation, *The ICD-10 Classification of Mental and Behavioural Disorders*. 1993, World Health Organisation: Geneva.
2. Maulik, P.K., et al., *Prevalence of intellectual disability: A meta-analysis of population-based studies*. Research in Developmental Disabilities, 2011. **32**(2): p. 419-436.

3. Evenhuis, H., et al., *Healthy Ageing – Adults with Intellectual Disabilities: Physical Health Issues*. Journal of Applied Research in Intellectual Disabilities, 2001. **14**(3): p. 175-194.
4. Buszewicz, M., et al., *Assessment of an incentivised scheme to provide annual health checks in primary care for adults with intellectual disability: a longitudinal cohort study*. The Lancet Psychiatry. **1**(7): p. 522-530.
5. Robertson, J., et al., *The impact of health checks for people with intellectual disabilities: a systematic review of evidence*. Journal of Intellectual Disability Research, 2011. **55**(11): p. 1009-1019.
6. Krahn, G.L. and M.H. Fox, *Health Disparities of Adults with Intellectual Disabilities: What Do We Know? What Do We Do?* Journal of Applied Research in Intellectual Disabilities, 2014. **27**(5): p. 431-446.
7. Haveman, M., et al., *Ageing and health status in adults with intellectual disabilities: results of the European POMONA II study*. Journal of Intellectual & Developmental Disability, 2011. **36**(1): p. 49-60.
8. de Winter, C.F., et al., *Cardiovascular risk factors (diabetes, hypertension, hypercholesterolemia and metabolic syndrome) in older people with intellectual disability: results of the HA-ID study*. Research in Developmental Disabilities, 2012. **33**(6): p. 1722-31.
9. de Winter, C.F., et al., *Overweight and obesity in older people with intellectual disability*. Research in Developmental Disabilities, 2012. **33**(2): p. 398-405.
10. de Winter, C.F., et al., *Peripheral arterial disease in older people with intellectual disability in The Netherlands using the ankle-brachial index: results of the HA-ID study*. Research in Developmental Disabilities, 2013. **34**(5): p. 1663-8.
11. Beaglehole, R., et al., *Priority actions for the non-communicable disease crisis*. The Lancet. **377**(9775): p. 1438-1447.
12. Swinburn, B.A., et al., *The global obesity pandemic: shaped by global drivers and local environments*. The Lancet. **378**(9793): p. 804-814.
13. WHO, *Mortality and burden of disease estimates for WHO Member States in 2004*. 2004: Geneva, Switzerland.
14. Draheim, C.C., *Cardiovascular disease prevalence and risk factors of persons with mental retardation*. Ment Retard Dev Disabil Res Rev, 2006. **12**(1): p. 3-12.
15. Dunkley, A.J., et al., *Diabetes prevention in the real world: effectiveness of pragmatic lifestyle interventions for the prevention of type 2 diabetes and of the impact of adherence to guideline recommendations: a systematic review and meta-analysis*. Diabetes Care, 2014. **37**(4): p. 922-33.
16. Dunkley, A.J., et al., *Effectiveness of interventions for reducing diabetes and cardiovascular disease risk in people with metabolic syndrome: systematic review and mixed treatment comparison meta-analysis*. Diabetes Obes Metab, 2012. **14**(7): p. 616-25.
17. Katzmarzyk, P.T. and S.A. Lear, *Physical activity for obese individuals: a systematic review of effects on chronic disease risk factors*. Obesity Reviews, 2012. **13**(2): p. 95-105.

18. Gillies, C.L., et al., *Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis.* Bmj, 2007. **334**(7588): p. 299.
19. Excellence, N.I.f.H.a.C., *Methods for the development of NICE public health guidance (third edition)*. 2006 (updated 2012), NICE: Lonon.
20. Higgins JPT, 5.1.0 [updat Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version ed March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

x. Chapter three - search strategy

1. Exp exercise/
2. Exp diet/
3. Aerobic train*.tw.
4. Behav* Modif*.tw.
5. Behav* therap*.tw.
6. Cognitive* therap*.tw.
7. counsel*.ti.
8. Health* Educ*.tw.
9. Health* Promot*.tw.
10. Health* behav*.tw.
11. Educat* program*.tw.
12. Patient Educ*.tw.
13. (Diet* adj2 Intervention*).tw.
14. (Diet* adj2 Modif*).tw.
15. Food habit*.tw.
16. (Health* adj2 Eating).tw.
17. (Nutrition* adj2 Counselling).tw.
18. (Nutrition* adj2 Therap*).tw.
19. (Exercis* adj2 intervention*).tw.
20. Physical Exercise.tw.
21. (Exercis* adj2 therap*).tw.
22. Physical endurance.tw.
23. Physical education.tw.
24. Physical Fitness.tw.
25. Physical Activit*.tw.
26. Physical Train*.tw.
27. Resistance Train*.tw.
28. Strength Train*.tw.
29. (Lifestyle adj2 advice).tw.
30. (Lifestyle adj2 Guid*).tw.
31. (Lifestyle adj2 Modif*).tw.
32. Lifestyle Program*.tw.
33. Weight control*.tw.
34. Weight Train*.tw.
35. Weight reduc*.tw.
36. Weight loss program*.tw.
37. weight loss.tw.

38. (Weight adj loss adj program*).tw.
39. (lifestyle adj2 intervention).tw.
40. Sport*.tw.
41. walk*.tw.
42. jog*.tw.
43. swim*.tw.
44. cycle*.tw.
45. Bicycle*.tw.
46. exp Health Promotion/
47. exp Program Evaluation/
48. exp Patient Education as Topic/
49. exp Diet Therapy/
50. exp Nutrition Therapy/
51. exp Exercise Therapy/
52. exp Diet, Reducing/
53. exp Exercise/
54. exp Diet/
55. or/1-52
56. OBSERVATIONAL.ti,ab.
57. RCT.ti,ab.
58. (RANDOMI*4 adj CONTROL adj TRIAL*).ti,ab.
59. Experimental studies.ti,ab.
60. (QUASI adj EXPERIMENTAL).ti,ab.
61. TRIAL*.ti,ab.
62. Time-series.ti,ab.
63. Cross-sectional.ti,ab.
64. Cross-sectional studies.ti,ab.
65. longitudinal study.ti,ab.
66. Clinical trial.ti,ab.
67. randomized.ab.
68. placebo.ab.
69. dt.fs.
70. randomly.ab.
71. trial.ab.
72. groups.ab.
73. (Before adj2 after).ab.
74. Cohort analy*.ab.
75. exp cohort studies/

76. (cohort adj (study or studies)).ab.
77. (follow up adj (study or studies)).ab.
78. Retrospective.ab.
79. 0r/56-78
80. exp Intellectual disability/
81. (learning adj1 disabilit*).ti,ab.
82. (developmental adj1 disabilit*).ti,ab.
83. (intellectual adj1 disabilit*).ti,ab.
84. (impair* adj2 intellectual adj2 function*).ti,ab.
85. (mental* adj1 impair*).ti,ab.
86. (mental* adj1 handicap*).ti,ab.
87. Exp mentally disabled persons/
88. (mental* adj1 disabl*).ti,ab.
89. (mental* adj2 retard*).ti,ab.
90. Or/80-89
91. animal/ not (animal/ and human/)
92. 90 not 91
93. limit 92 to english language
94. limit 93 to yr=2000-current

xi. Chapter three - data extraction form

ELIGIBILITY CHECKLIST	YES	NO	NOTES
Population or sub-group has ID (>80%)			If no, exclude
Population has a specific syndrome, acquired ID, or a learning difficulty/developmental disability			If yes, exclude if >25%
Population >= 18 years			If no, exclude
Reported outcomes incidence of CVD, T2DM &/or changes in risk factors (anthropometrics, hypertension, hyperglycemia, hyperlipidemia, MetS, PA, SB, or diet)			If no, exclude
Extractable data (differences to/from baseline or calculable data)			If no, exclude
Study is a multi-component lifestyle behavior change intervention aimed at ID person &/or carer			If no, exclude
Study aimed at prevention of CVD or T2DM, weight management, PA, SB, or diet			
Study has a f-up period ≥ 24 wk or 6 mths			If no, exclude
Published year 2000 or after			If no, exclude

STUDY DETAILS			
First author		Publication date	
Title of paper			
Journal			
Language and country of first author			
Name of study			
Other associated papers			
Country/countries			
Study type			

POPULATION								
Recruitment method								
Dates of data collection								
Exclusion criteria								
Subjects	**Overall**		**Arm 1:**		**Arm 2:**			
Total number								
Male (%)								
Age	**Overall**		**Arm 1:**		**Arm 2:**			
Mean age (+/- SD)								
Age range								
Ethnicity	**Group 1:**		**Group 2:**		**Group 3:**			
Total								
Proportion (%)								
ID severity	**Mild (n / %)**		**Moderate (n / %)**		**Severe (n / %)**		**Profound (n /%)**	
Total								

INTERVENTION	Overall	Arm 1:	Arm 2:
Withdrawal			
Aimed at care provider or participant			
Type of targeted behavior change (e.g., PA/diet)			
Method of intervention (e.g., group/individual)			
Follow up	**Time-point 1**	**Time-point 2**	**Time-point 3**
Length			
Exclusion criteria			
Notes on mobility at baseline			
Outcomes measured			
Important notes (include any significant issues here: eg validity, areas of uncertainty etc)			

Time-point:	Arm 1						Arm 2						Difference					
	N	Mean	SD	SE	% L CL	% U CL	N	Mean	SD	SE	% L CL	% U CL	N	Mean	SD	SE	% L CL	% U CL
Weight (kg) Baseline																		
Change																		
Percentage loss																		
BMI (kg/m^2) Baseline																		
Change																		
Percentage loss																		
O/C: Baseline																		
Change																		
Percentage loss																		
O/C: Baseline																		
Change																		
Percentage loss																		