Early death and causes of death of people with intellectual disabilities: a systematic review

Title: Life expectancy and cause of death of people with intellectual disabilities: a systematic review

Background: Death of people with intellectual disabilities is considered to be earlier than for the general population.

Methods Databases were searched for key words on intellectual disabilities AND death. Strict inclusion/exclusion criteria were used. Information was extracted from selected papers, tabulated, and synthesised. Prospero registration number: CRD42015020161.

Results: 27/19,111 retrieved articles met criteria. Death was earlier by 20 years. It has improved in recent decades; however the same inequality gap with the general population remains. More severe intellectual disabilities, and/or additional co-morbidities rendered it shortest. Standardised Mortality Rates showed a greater inequality for women than men. Respiratory disease and circulatory diseases (with greater congenital and lesser ischaemic disease compared with the general population) were the main causes of death. Cancer was less common, and cancer profile differed from the general population. Some deaths are potentially avoidable. All research is from high income countries, and cause of death is surprisingly little investigated.

Conclusions: Improved health care, including anticipatory care such as health checks, and initiatives addressing most relevant lifestyle behaviours and health risks are indicated.

Introduction

Life expectancy and mortality rates are important indicators of health status (World Health Organisation, 2015). It has been reported that people with intellectual disabilities die younger and from more avoidable causes amenable to change by good health-care intervention, than the general population (Heslop, 2014, Hosking, 2016). A better understanding of this is important to try to reduce this serious health inequality.

Targeting health inequalities requires identification of the leading causes and rates of mortality for the population with intellectual disabilities, in order to inform appropriate health promotion, health care and environmental interventions (Oullette-Kuntz *et al.* 2015). However it can be challenging to measure premature mortality and causes of death in this population as people with intellectual disabilities are not always identifiable in datasets or national records. Approaches include measuring:

(1) Life expectancy at birth
(2) Probability of dying per 1,000
(3) Additional number of years expected to live at age 75
(4) Standardised Mortality Ratio (SMR) of deaths observed in a specific group compared to those expected in a reference population of identical age structure
(5) Number of years lost due to premature death at age 65 or 70.

(Heslop *et al.* 2015; World Health Organisation, 2015)

Additionally premature or avoidable deaths may be distinguished as amenable and/or preventable. A death is amenable if it is avoidable through health care intervention (depending on age of individual). A death is preventable if it could be avoided through public health interventions focussed on the determinants of health. Avoidable deaths can be preventable, amenable or both (Office for National Statistics, 2012). There have been challenges identified in measuring life expectancy and instances of premature/avoidable deaths in people with intellectual disabilities.

Life expectancy and mortality results may be misleading depending upon the methods of identification of the population with intellectual disabilities and whether, for example, the extent to which people with mild intellectual disabilities are or are not included is clearly reported. Registry based studies using administration services are also dependent on the policies of service providers, which tend not to be consistent across different regions or time periods (Patja *et al.* 2000; Heslop *et al.* 2015). Inconsistent definitions of intellectual disabilities across regions also pose a challenge on the ability to undertake international comparison. Indeed, the size and the characteristics of the population with intellectual disabilities can vary over time and with geography (Cooper *et al.* 2016), and these factors need consideration when interpreting studies on mortality and drawing conclusions on premature mortality. Therefore averaging the age of death across all historic studies may not be appropriate.

There are also challenges related to methods of assessing causes of death in the population with intellectual disabilities. Reliance on death certificate data is open to criticism, as they are completed by many medical practitioners, so often have recording inconsistencies. Identifying the deceased population with intellectual

disabilities via death certification is highly problematic, as intellectual disabilities is often not recorded on death certificates (Glover & Ayub, 2010; Landes & Peek, 2013; Heslop & Glover, 2015; Heslop *et al*. 2015). It is important to know if the leading causes of death are the same as for the general population, as any differences between populations would indicate the need for different approaches to those offered in general, in order to tackle health inequalities.

Given the different reporting methods in mortality studies there is a substantial need to synthesise all the existing evidence on this topic, in order to draw out common themes and trends where they occur. Therefore a systematic review was undertaken, in order to provide more evidence for early deaths and cause of death profile of the population with intellectual disabilities than that contained in single studies. The need for a systematic review has previously been highlighted by Robertson *et al.* (2015).

It is important to undertake a robust appraisal of the evidence on mortality rates and age/causes of death of people with intellectual disabilities. This is needed to determine the extent of early mortality compared with the general population, any trends in terms of the extent of this health inequality, and the pattern of cause of death. This is also needed to inform healthcare decision-making to reduce the inequality. We have not identified an existing synthesis of evidence on mortality in people with intellectual disabilities, and this has been highlighted as a gap in the health and health care evidence for people with intellectual disabilities (Robertson *et al.* 2015). We therefore undertook this systematic review with the aim to identify the life expectancy, age of death, determinants of early mortality, and the main causes of death of people with intellectual disabilities.

Method

The review was registered with the International Prospective Register of Systematic Reviews (Prospero) (registration number: CRD42015020161). A comprehensive search was undertaken of CINAHL, MEDLINE, PsychINFO, Web of Science, and EMBASE databases. The search combined key words related to intellectual disabilities, terminology that is no longer in use, and syndromes associated with intellectual disabilities, with key words related to mortality, causes of death , age of death and life expectancy. The search was completed on 20/10/16. Results were filtered for English language and human. The following inclusion and exclusion criteria were applied in selecting the relevant articles:

Inclusion criteria

- Reports deaths, crude mortality rates, life expectancy from birth or later, standardised mortally ratio and/or age of death
- At least 50% of participants have intellectual disabilities, if not reported separately
- Peer reviewed
- Primary research
- All ages
- All years
- All study designs.

Exclusion criteria

- Full paper not available in English

- Proportion of participants with intellectual disabilities unclear, or <50% of sample if not reported separately
- > 50% of participants live in institutional settings
- Studies focused on hospital resettlement programmes
- Studies focussed on post-operative and post-treatment deaths
- Case studies or case series with <20 participants
- Studies exclusively focussed on individuals with Down Syndrome, or other specific groups.

Studies focussed on deaths following relocation were excluded due to the risk that they may have been influenced by the moving process, and hence not be representative of the wider population with intellectual disabilities. Studies that focussed on reporting Down Syndrome deaths only were excluded, as these individuals have a different mortality and health profile compared to individuals without Down Syndrome. Therefore it is more appropriate to synthesis evidence for Down Syndrome deaths separately where that is possible (Esbensen, 2007).

Study selection and data extraction

Titles retrieved from database searches were entered into the Endnote reference manager software. Duplicates were subsequently removed. Titles and abstracts were then assessed for eligibility against the inclusion criteria. 5% were assessed by a second researcher, with any discrepancies planned to be resolved through discussion. Full papers were then assessed for eligibility. All of these papers were assessed by a second reviewer. Authors were contacted if a full paper could not be retrieved and if the reviewers were not clear if the study met the inclusion criteria. Eleven authors were contacted for these reasons. Reference lists of included studies

and citations to studies were also searched. Information from the included studies was systematically extracted in relation to study characteristics, size, demographics, inclusions/exclusions, context, location, design, data source, comparator groups, method of analysis, outcomes, findings, funding, publication type and risk of bias. Information was tabulated in a database.

Meta-analysis and narrative analysis were two possible analysis options. Meta-analysis entails numerically combining the results of individual studies in order to integrate findings (Glass *et al.*1986). Narrative analysis involves using words and text to synthesise the results from different studies (Popay *et al.* 2006). It is argued that meta-analysis is a more rigorous and objective approach to research (Cooper & Rosenthal, 1980). However, diverse methods were used across the included studies so narrative analysis was undertaken, and study results were tabulated.

Quality appraisal was undertaken using the Critical Appraisal Skills Programme CASP (2013) guidelines. The cohort study appraisal checklist was specifically used to rank the included studies on the basis of their validity, reliability and generalisability. This approach helped to reduce potential bias associated with narrative analysis.

Results

The steps taken to identify relevant studies are illustrated in Figure 1. A total of 24,702 references were retrieved from searching five databases. An additional two articles were retrieved from references in a relevant paper. N= 19,111 of these articles remained after removing duplicates. These studies dated from 1796-2016.

Following inspection of titles, N=17,010 were excluded for not being relevant to the research question or the population. N=2101 abstracts were examined. N=322 of the abstracts were identified as potentially relevant and were read in full. Both reviewers agreed on the eligibility of the included studies. N=295 of the articles read in full did not meet the inclusion criteria. Some of the excluded articles consisted of specialist populations such as individuals with specific genetic conditions only, mild or severe intellectual disability only, epilepsy only or samples wherein the majority of individuals lived in institutionalised settings. N=27 of the articles that were read in full met the inclusion criteria, so their findings on life expectancy, crude/ standardised mortality rates and age of death (table1) and causes of death (table 2)were synthesised.

Characteristics of studies

All 27 of the studies included in the synthesis were undertaken in high income countries. Ten studies were undertaken within the UK (McGuigan *et al.*1995; Hollins *et al*. 1998;Tyrer *et al*. 2007, Tyrer.& McGrother, 2009; Glover & Ayub, 2010; Emerson e*t a*l. 2014; Glover & Christie, 2014; Heslop *et al*. 2014; Glover *et al.* 2016; Hosking *et al.* 2016), six in Scandinavian regions (Simila *et al*. 1986; Forsgren *et al.* 1996; Patja *et al.* 2000; Patja *et al.* 2001; Gustavson *et al.* 2005, Arvio *et al*. 2016), three in Australia (Bittles *et al*. 2002; Durvasula *et al.* 2002; Florio & Trollor, 2015), two in the USA (Decouflé & Autry, 2002, Lauer & McCallion, 2015), two in Ireland (Lavin *et al .*2006; McCarron *et al*. 2015), one in Germany (Dieckmann *et al*. 2015), and one in Canada (Oullette-Kuntz *et al.* 2015).

Results from studies of early deaths

Different methods were used to assess life expectancy, mortality rates and age of death across the 27 studies. These range from using unstandardized measures to compare age of death/mortality rates with the general population to more recent studies which used more robust measures, through calculating Standardised Mortality Rates (SMR) in order to compare death rates with the age/gender matched general population. Some studies also investigated factors associated with mortality amongst the population with intellectual disabilities. These three types of studies are summarised in Table 1.

All of the studies found that crude mortality rates were higher for the population with intellectual disabilities in comparison to the general population ranging from 4.61/1,000 (Oullette Kuntz *et al.* 2015) to 157.6/1,000 (Simila *et al.* 1986). The former figure is from a population of over 6,000 adults aged 15 years and older and the latter figure is from a study of 65 children up to the age of 1 year. It is therefore important to note that the studies were drawn from a range of differing populations in terms of age groups and countries, and the extent to which people with mild intellectual disabilities were included (see Table 1), which may account for some of the differences found. These differences precluded meta-analysis, and make comparisons difficult. Additionally, temporal trends in mortality rates invalidate - comparison of older studies with more recent studies.

There were some trends identified across the studies. The average age of death was reported to be up to 20 years lower for people with intellectual disabilities in studies that investigated age of death for adults and children (Glover & Ayub, 2010; McCarron *et al*. 2015; Oullette Kuntz *et al.* 2015). In Glover *et al.'s* (2016)

investigation of life expectancy from birth, they also identified that age of deaths was 19.7 times younger than the equivalent general population. Different methods were used across the studies to report age of death including mean (Lavin et al, 2006; Oullette Kuntz *et al.* 2015), median (Heslop *et al.* 2014) and unspecified average (McCarron *et al*. 2015). This challenges comparability across the studies.

Age of death and crude mortality rates were considerably poorer for individuals with profound intellectual disabilities in comparison to the general population, whilst the difference was less for individuals with mild/moderate intellectual disabilities. This trend was noted for all studies comprising samples of children only (Simila *et al.* 1986; Decouflé & Autry, 2002; Gustavson *et al*. 2005). This trend was also noted for some studies that comprised samples of children and adults with intellectual disabilities (Patja *et al.* 2000, Heslop *et al*. 2014; McCarron *et al.* 2015).

Crude mortality rates increased with degree of intellectual disability and support needs (Hosking *et al*. 2016). Co-morbidities such as epilepsy reduced life expectancy (Patja et al. 2000) and mean age of death Oullette-Kuntz et al, 2015).

Mobility, hearing, vison and ambulation problems were associated with poor life expectancy (Patja *et al*. 2000) and higher crude mortality rates (Eyman *at al.* 1989; Oullette-Kuntz *et al* 2015).

The level of support that individuals need to eat and use a toilet was associated with lower mortality rates (Eyman *at al.* 1989) and lower life expectancy (Patja *et al*. 2000). Specific genetic syndromes influenced lower life expectancy (Bittles *et al.* 2002) and higher crude mortality rates (Decoufle & Autry. 2002). Glover & Ayub (2010) found that individuals with microcephaly had a particularly lower age of death

(10 years), compared to individuals with Down Syndrome who had a higher age of death of 56 years.

The majority of studies reported SMRs ranging from 2-5 (table 1). The majority of studies found that SMRs were higher for females with intellectual disabilities in comparison to males with intellectual disabilities. These studies comprised of samples of adults and children (McCarron *et al.* 2015; Florio & Troller, 2015; Arvio *et al.* 2016; Glover *et al.* 2016), individuals aged 15 years (Oullette-Kuntz e*t al*. 2015) and adults only (Tyrer *et al*. 2007). Only one study reported a higher SMR for males (Dieckmann *et al.* 2015). This study comprised of adults with intellectual disabilities, but was drawn from an atypical population due to geographic/historical reasons (Germany). This indicates that the inequality in mortality rates between the population with intellectual disabilities and the general populations is greater for females than males. The reason for this is unclear.

Individuals with more severe intellectual abilities, or comorbidities had higher SMRs (Forsgren *et al.* 1996; Tyrer *et al*. 2007; McCarron *et al*. 2015; Arvio *et al.* 2016). SMRs were highest for young adults (< 29 years), revealing their greater inequality compared with older adults (Forsgren *et al*.1996; Tyrer *et al.* 2007; McCarron *et al.*2015; Oullette-Kuntz *et al*. 2015), and for young children (Simila *et al*.1986).

Emerson et al. (2014) demonstrated that whilst life expectancy had increased for people with intellectual disabilities there was ‘no real closing of the gap’ in differences in life expectancy between the population with intellectual disabilities and the general population from 1980-2012. Helsop *et al*. (2014) provided evidence that this unequal health status and lower age of death amongst people with intellectual disabilities may be influenced by a lack of good quality healthcare for this population.

Studies investigating causes of death

Respiratory disease was one of the leading underlying causes of death in studies that comprised adults and children with intellectual disabilities. For example Patja *et al.* (2001) and Hosking *et al.* (2016) reported that respiratory illness accounted for 36.3% and 18.8% of underlying causes of death in their respective studies. Forsgren *et al.* (1996) and Heslop *et al.* (2014) identified smaller proportions of underlying causes of death from respiratory illness. These accounted for proportions of 10% and 15% of underlying causes of death in their respective studies.

Respiratory disease also accounted for 52% and 29% of immediate causes of death in studies undertaken by Glover and Ayub (2010) and Patja *et al*. (2001). Respiratory disease (specifically pneumonia) accounted for 46.6% of immediate causes of death in Hollins *et al's* (1998) study. Durvasula *et al.* (2002) reported that respiratory illness accounted for 35% of causes of death in their study. However they did not specify whether these were underlying or immediate causes of death.

All studies that compared causes of death with the general population identified higher mortality rates from respiratory illness amongst the population with intellectual disabilities. The majority of these studies included samples of children and adults with intellectual disabilities (Forsgren *et al.* 1996; Patja *et al*. 2001; Durvasula *et al*. 2002; Glover & Ayub, 2010; Heslop *et al.* 2014; Glover *et al*. 2016). Two of these studies included samples of adults only (Tyrer & McGrother, 2009; Hosking *et al*. 2016).

Bronchopneumonia was the most common cause of respiratory death. For example Hollins *et al*. (1998) reported that immediate causes of death rates from pneumonia

were 74-135 times more common amongst their sample of children and adults with intellectual disabilities than in the equivalent general population.

A more recent study undertaken by Hosking *et al*. (2016), identified that the underlying cause of death rates for pneumonia and aspiration pneumonia were ten times more common in their sample of adults with intellectual disabilities, compared to the general population.

Circulatory disease was reported as the leading underlying causes of death in studies undertaken by Forsgren *et al*. (1996); Heslop *et al. (*2014); Glover *et al.* (2016) and Hosking *et al,* (2016). These studies included samples of childrena adults with intellectual disabilities. Cerebrovascular disease and ischaemic heart disease combined were marginally more common causes of underlying death than respiratory diseases according to Forsgren *et al. (*1996).

The most common primary, immediate and contributing cause of death reported by Patja *et al.* (2001) was vascular. Cardiac failure was the second most common immediate cause of death according to Hollins *et al*. (1998). Circulatory disease formed a very small proportion of deaths (15%) in the study by Durvasula *et al.* (2002). However they did not specify whether this figure related to immediate or underlying cause of death. Risk of death from circulatory disease was reported to be associated with Down Syndrome by Forsgren *et al.* (1996) and Patja *et al.* (2001), in keeping with the known high rate of congenital cardiac disease in this population. Hence the profile of deaths from circulatory disease shows some differences to the general population in which ischaemic heart disease predominates. Forsgren *et al.* (1996) and Tyrer & McGrother (2009) identified that mortality rates from combined circulatory disease as an underlying cause of death were twice as high in the

population with intellectual disabilities compared to the general population. Hosking *et al.* (2016) identified that these rates were three times higher in their study. However Patja *et al.* (2001), Glover & Ayub (2010) and Heslop *et al.* (2014) identified lower mortality rates from circulatory/vascular disease as an underlying cause of death within their samples of children and adults with intellectual disabilities, in comparison to the general population. Patja *et al.* (2001) proposed that these lower mortality rates may be influenced by protective factors of low blood pressure and non-smoking.

Cancer was another leading underlying cause of death in studies that comprised children and adults with intellectual disabilities (Forsgren *et al.*1996; Heslop *et al.* 2014; Hosking *et al.* 2016; Glover *et al*. 2016), and studies that comprised adults only (Tyrer & McGrother 2009; Hosking *et al.* 2016).

Durvasula *et al.* (2002) identified cancer as the most common cause of death amongst individuals in their study aged >40 years. They did not specify whether this related to underlying or immediate cause of death.

Patja *et al.* (2001) also identified that cancer deaths increased with age. However, the majority of studies that compared causes of death with the general population identified lower mortality rates from cancer amongst the population with intellectual disabilities (Patja *et al*. 2001; Durvasula *et al.* 2002; Glover & Ayub, 2010; Heslop *et al*. 2014). These studies comprised both children and adult samples.

However Tyrer & McGrother (2009) found no difference in cancer mortality rates between their population of adults with intellectual disabilities and the general population. Additionally, of the four studies that specified types of cancer deaths, Tyrer & McGrother (2009), Patja *et al.* (2001) and Glover *et al.* (2016) identified that

the majority of underlying causes of cancer deaths were from diseases of the digestive organs. This differs from the pattern of cancers found in the general population, in whom lung, breast, and prostate cancer predominate. Durvasula *et al.* (2002) found no specific type of cancer accounted for the majority of deaths.

There was mixed evidence in relation to how external causes of death compared with the general population. Five studies identified that external underlying causes of death (accidents, poisoning, violence etc.) were slightly more common in people with intellectual disabilities. These of these studies comprised of children and adults with intellectual disabilities (Forsgren *et al.* 1996; Heslop *et al*. 2014, Glover *et al.* 2016). Two of these studies included adults only (Tyrer & McGrother, 2009; Hosking et al., 2016). Hosking *et al*. (2016) identified that a specific type of external causes of death differed to the general population i.e. accidental poisoning was more common in the population with intellectual disabilities, and suicide/ traffic accidents were more common in the general population. Patja *et al.* (2001); Durvasula *et al*. (2002), and Glover & Ayub (2010) identified that external causes of death were more common in their samples of adults and children with intellectual disabilities than in the equivalent general population.

Other underlying causes of death that were more common amongst the population with intellectual disabilities included congenital malformations, gastrointestinal and neurological disorders. Congenital malformations were 46-86 times more common as an underlying cause of death in the population with intellectual disabilities compared to the general population (Forsgren *et al.*1996; Tyrer & McGrother, 2009; Glover *et al.* 2016). Durvasula *et al.* (2002) and Tyrer & McGrother (2009) identified that digestive disorders were twice as common as a cause of death in people with intellectual disabilities compared to the general population. Neurological disorders

were considerably more common as an underlying or immediate cause of death in the population with intellectual disabilities compared to the equivalent general population (Forsgren *et al*. 1996; Tyrer & McGrother, 2009; Glover & Ayub, 2010; Heslop *et al.* 2014, Glover *et al*. 2016, Hosking *et al.* 2016), with epilepsy alone accounting for 5-11% of immediate or contributory causes of death (Forsgren *et al.* 1996; Hollins *et al.*1998; Patja *et al.* 2001).

Three studies reported incidences of avoidable causes of mortality in the population with intellectual disabilities (Heslop *et al.* 2014; Hosking *et al.* 2016*;* Glover *et al.* 2016). All of these studies reported that people with intellectual disabilities were more likely to die from causes that were amenable to healthcare care intervention such as urinary tract infection, aspiration pneumonitis, ischaemic heart disease, epilepsy, cerebrovascular disease. Hosking *et al.* (2016) also identified that estimates were likely to be an undercount, as definition of amenable deaths excluded some problems that are more common in people with intellectual disabilities. These studies also reported that the population with intellectual disabilities were less likely to die from preventable causes such as suicides or accidents.

Discussion

This is the first systematic review to synthesis what is known about life expectancy, mortality rates, age and causes of death of people with intellectual disabilities. The age of death of people with intellectual disabilities remains up to 20 years less than the general population.

Whilst life expectancy has increased for people with intellectual disabilities overtime, there is evidence of a lack of closure in the gap in the difference in mortality rates

and life expectancy of people with intellectual disabilities (Emerson *et al*. 2014). It is unclear why people with intellectual disabilities continue to be subjected to avoidable deaths that may be amenable to better quality healthcare (Heslop *et al*. 2014).

Age of death is lower for people with more severe intellectual disabilities and for people with additional comorbidities such as epilepsy, genetic syndromes and functional impairments. Hence targeted health care improvements are required for these subgroups of people with intellectual disabilities (Heslop *et al*. 2014). Such preventative measures could include health promotion programs focussed on addressing lifestyle behaviours (Scott & Havercamp, 2016).

There is also a need for investigation of potential social determinants of cause of death and different patterns of long-term disorders and impairments for these specific subgroups. This information may provide an insight into the chain of events leading to the different profile of causes of death for particular sub groups of people with intellectual disabilities (McCallion & McCarron, 2014; Arvio *et al*. 2015; Lauer & McCallion, 2015).

The provision of quality health care is also highly important, with reasonable adjustments to meet their needs and supported by social care. This includes anticipatory care in the form of health checks, which has been shown to improve the management of long term conditions and quality of life and to be dominant with regards to clinical and cost-effectiveness compared with standard care (Cooper *et al.* 2014; Buszewicz *et al.* 2014).

Few studies had investigated cause of death, but consistently, the main causes appeared to be respiratory illness and circulatory disease, but with greater emphasis on congenital heart disease than ischaemia compared with the general population.

Lower smoking rates in people with intellectual disabilities may contribute to these differences, and obesity and sedentary lifestyles which are more common in people with intellectual disabilities may contribute to cardio-vascular disease and respiratory disease (Melville *et al.* 2008; Haveman *et al.* 2011; Hsieh *et al.* 2014; Robertson *et al.* 2014; Scott & Havercamp, 2016).

Also Down syndrome may contribute to respiratory disease, as people with Down Syndrome are susceptible to respiratory infection due to physiological differences in pulmonary cilia (Watts & Vyas, 2013). Robertson *et al.* (2015) revealed that no heath care focussed systematic reviews have addressed respiratory or vascular diseases among people with intellectual disabilities, highlighting a significant and important gap in the evidence evidence-base.

Cancer deaths were less common in the population with intellectual disabilities, compared to the general population. This difference may be due to lower smoking rates, and the lower life expectancy of people with intellectual disabilities, and therefore reduced risk of reaching an age where they are at risk of certain cancers (Glover & Ayub, 2011). Digestive system cancers were the most common type of cancer death. Cooke (1997) hypothesised that digestive system cancers may be influenced by gastrointestinal tract dysfunction, gastro-oesophageal reflux disease, chronic constipation and poor diet. These health risks are common in people with intellectual disabilities, so greater awareness of this amongst support staff and health professionals is important so that active management can be accessed/ provided to ease suffering as well as to reduce longer term sequelae.

It is important to understand these differences compared with the general population, as it highlights that programmes to address lifestyle behaviours need to be

accessible for people with intellectual disabilities including more severe disabilities, and also importantly need to address the issues that are most relevant to them, such as sedentary and dietary habits, poor mobility, and education on common long-term conditions such as gut disorders and epilepsy (Gustavson *et al.* 2005).

Training for support staff is also important, to reduce accidents, and for example to reduce the risk of choking and respiratory infection through safe feeding methods following swallowing assessments (Finlayson *et al.* 2010; Perez *et al.* 2015).

The possible contribution of restraint and medication use on mortality risk was not captured in the included studies, although poisoning was reported as a cause of death by Patja *et al.* (2001) and Glover & Ayub (2010). Hosking *et al.* (2016) specifically identified how people with intellectual disabilities were more likely to die from accidental poisoning than the general population (see table 2). Therefore healthcare and support staff should be trained and educated to implement strategies to reduce this risk of accidental poisoning.

Limitations of studies

The studies had several limitations, and this limited the conclusions we could draw. Some studies used crude methods to measure life expectancy, including age of death and survival curves. Not all studies made comparisons with the general population using matched or standardised samples.

The majority of intellectual disability cohorts were administrative samples of service users, who may have greater health problems and under-represent people with mild intellectual disabilities (Oullette-Kuntz *et al*., 2015). A further consideration is that all studies were from high income countries, so are unlikely to be representative of life

expectancy and causes of death in low and middle income countries. There were also challenges surrounding the completeness and accuracies in relation to linkage of administration data sets (Heslop *et al.* 2013; Heslop & Glover, 2015).

The majority of studies on cause of death relied on death certificates. Death certificates often have coding errors (Glover & Ayub, 2010; Landes & Peek, 2013). Examples of missing information/coding errors in death certificates related to coding for people with intellectual disabilities were reported in the studies by Forsgren *et al.* (1996); Hollins *et al.* (1998) and Durvasula *et al.* (2002). Comparability and generalisability may also be compromised by the fact that primary, underlying, and immediate causes of death are often recorded inconsistently across different local practices and regions (Patja *et al*. 2001; Forsgren *et al.*1996; Hollins *et al.*1998).

According to the World Health Organisation Guidelines, Part 1 of the death certificate should record the immediate cause of death, and then work back in time to the disease or condition that started the process. Part 2 of the certificate should be used to record other significant diseases, conditions or accidents which contributed to the occurrence of the death, but were not part of the main sequence leading to the death (Office for National certificates, 2010). However, as many medical practitioners complete death certificates, there is variability in coding practices across local practices. For example, a person with Down syndrome, congenital heart valvular disease and heart failure may have any of or all three conditions listed in Part 1, depending on the practice of the medical practitioner completing the certificate.

Some studies provided limited baseline data on level of intellectual disabilities, gender, age, and not all reported age-specific death rates. These are fundamental limitations, as all of these characteristics influence mortality rates.

Strengths and weaknesses of the review

The quality of the review was assessed using the Methodological Quality of Systematic Reviews checklist (AMSTAR, 2015).Strengths of the review include the provision of an a priori design, as the protocol and research objectives were registered with the International Prospective Register of Systematic Reviews.

The review was also robust, as a proportion of the study titles, abstracts and full papers were checked by two independent researchers. Quality appraisal was ensured through checking the eligibility of the included titles, abstracts, full paper and checking the data extraction process, and the quality assessment with a second reviewer. A comprehensive searching strategy was undertaken comprising key words, papers were selected against pre-defined inclusion and exclusion criteria, and their quality systematically reviewed. However quality appraisal of the review was undertaken by the authors, which limits objectivity.

All of these studies were undertaken in high income countries and were restricted to English publications. This limits generalisability in terms of investigating causes of death and life expectancy on a global scale. It was not possible to statistically integrate results of studies using meta-analysis because of variability between studies. Therefore the findings from the studies had to be pooled using narrative analysis, which has the risk of being a more biased than a meta-analysis (Cooper & Rosenthal, 1980). The CASP checklist was used to minimise this bias, as each

specific study was given a formal quality assessment score. This assessment process was verified with one other reviewer.

There are many causes of intellectual disabilities and some are associated with a shorter lifespan, most notably Down Syndrome. Other examples include rarer syndromes such as Rett syndrome and San Fillippo syndrome. Individuals with Down Syndrome are likely to be included in all the papers in Table 1 and 2, but in many cases were not reported separately. Therefore these papers are incomparable in this respect, and it was not possible to identify and report on individuals with these syndromes separately in this review.

Conclusions

It is difficult to draw definitive conclusions about the evidence for early deaths and specific causes of death of people with intellectual disabilities and how this compares to the general population, in light of the lack of standardised procedures for reporting mortality across different countries and service providers. However, some patterns have been identified in this review.

People with intellectual disabilities die 20 years younger than the general population in high income countries, with women with intellectual disabilities experiencing a greater inequality compared to the general population, than do men compared to the general population. These trends have emerged across studies comprising adults and children with intellectual disabilities. The pattern of cause of death also differs from the general population, with respiratory disease and circulatory disease being the most common underlying causes of death, and likely to be preventable in some cases.

Improved health care, including anticipatory care such as health checks, and initiatives that address the lifestyle behaviours and health risks that are most relevant for people with intellectual disabilities are indicated.

However lack of detailed information regarding immediate and contributory causes of death has reduced the potential to acquire a clear and concrete picture of the leading factors that influence specific causes of death in people with intellectual disabilities. There is a need for improved recording of this information.

There is need for more robust, standardised data in relation to identification and characteristics of people with intellectual disabilities, and standard age bandings and definition of intellectual disabilities across countries. This would help advance knowledge in this area. However, this will be challenging in view of the differences in death certification, and definitions of intellectual disabilities, and procedures in different regions.

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Table 1: Studies on life expectancy, standardised mortality rates, and associated factors

Study	ID cohort	ID level	Data sources	Comparison group	Analyses	Findings	Critique/Quality
	Studies of life expectancy, mortality rates, age at death						
Simila et al, 1986	N=165 total with ID (N=26 deaths) Age: up to 17 (born in 1966) Gender proportions not given	Mild (N=68), Moderate (N=51), Severe (N=28), Pofound (N=18)	Oulu and Lapland, Finland. Prospective cohort ID: identified via numerous sources including hospital and school registers Deaths: identified via death certificates from population registers, hospital notes and autopsies	General population in same birth cohort N=11,731 total (N=267 deaths)	Mortality rate up to age 17	Mortality rate=157.6/1,000 (7 times that of general population) *Higher at lower ability *Highest at <1y * Mild ID level similar to general population	CASP score :12/14 Limitations: *Small ID sample *Administrative sample
Patja et al, 2000	N=2,366 total with ID (N=1108 deaths) Age: 2-64y in 1962 Gender: M 50%, F:50%	Mild (N=1101), Moderate (N=606), Profound (N=368), Severe, (N=280)	Finland. Prospective cohort ID: identified via individual medical examination organised by the National Board of Health Deaths: identified via population registers of death	General population survival curves	Life expectancy by 5year age bands, sex, ability level, and ID aetiology Expected life lost over the timeframe: 1.1.63-31.12.97 Mean expected life span over the time frame: 1.1.63-31.12.97	Mortality rate=18/1000 *Close to general population for mild ID; worse for profound ID * lower life expectancy for epilepsy, DS, visual/hearing impairment, over 30 years age group *Mean expected life span for the ID population ranged from 19-69.3 years across different age ranges * Mean expected life span for general population ranged from 23.6—67.8 years *Expected life lost for ID population compared to general population ranged from -7.7-42.9 years	CASP score: 14/14 Strengths: *Population-based sample *High retention *Long follow-up
Decouflé & Autry, 2002	N=1,062 total with ID (N=23 deaths)	Mild (N= 746), Severe (N=316)	ID: identified via multiple administrative	Georgia population, 1989-1991	Mortality ratios, matched by	Mortality ratio=3.3 *Higher at lower ability *Higher at younger age	CASP score: 12 /14 Limitations: *Small sample

	Age:10y in 1985-1987 Gender proportions not given		sources, Atlanta, USA Deaths: identified via linkage to national death index, and death certificates (1985-1995		age, gender, race, per PY over the timeframe: (01.1. 85-31.12.95)	*Higher for genetic syndromes *Higher if other co-morbidities for all types of developmental disability	* Administration sample
Gustavson et al, 2005	N=213 total with ID (N=57 deaths) Age: up to 15y in 1974 Gender: M:62%, F:38%	Mild (N=91) Severe (N=122)	ID: identified Uppsala county, Sweden, population registers Deaths: identified via the National Death Records, medical examinations	Age matched general population, Sweden	Mortality rates on 13.12.2002	Mortality rate= 27% *A lot higher than 2% general population *Twice as high for profound ID	CASP score :12/14 Limitations: *Small sample *Administrative sample
Lavin et al, 2006	Unidentified total with ID (N=1,120 deaths) All ages Gender: M: 53%)F: 47%	Proportions not given	ID: identified from National ID database, Ireland, Deaths:: identified from National ID database, Ireland	Irish general population, 1996	Mean age of death over the timeframe: 1996-2001	Mean age of death: 46y, versus 76y for general population * Lowest for profound ID (29y) *Highest for moderate ID (51y) *No effect for gender	CASP score : 11/14 Limitations: *Only one data source was used to identify age of death so open to bias *Small sample *Administrative sample
Glover and Ayub (2010)	N=undefined total with ID (N=984 deaths) All ages Gender proportions not given	Proportions not given	ID: identified from death certificates, England Deaths: identified from computerised records, England, and death certificates	General population, England	Age of death by specific condition over the timeframe (2004-20080	ID (no condition): >50% die before 65y, versus 50% die at or before 80y in general population *Lowest for microcephaly (10y) *Highest for DS (56y)	CASP score: 13/14 Limitations: *Administration sample

Heslop et al, 2014	N=undefined total with ID (N=247 deaths) Age4+y Gender: M:57.9% , F: 42.1`%	Mild (N=98), Moderate (N= 77), Severe (N=53), Profound and multiple,([N=1 9)	ID: identified from GP records England Deaths: identified from multiple agencies including office for National Statistics	England and Wales general population	Median age of death over the timeframe, (01.6.10-31.5.12)	Median age of death: M: 65y (IQR 54-76), 13 years younger than comparison group *Fs 63y (IQR 54-75), 20 years younger than comparison group *22% <50y at death, versus 9% in comparison group <50y at death *Younger age of death for more severe ID population	CASP score: 13/14 Limitations: *General population comparison group drawn from a wider area than ID population (England and Wales)
McCarron et al, 2015	N=31,943 total with ID (N=2,666 deaths) All ages Gender: M: 58,19% F: 41.81%	Mild (N=9 601), Moderate (N=11,993), Severe (4,782), Profound (N=1,281) Other or undefined (N=4,286)	ID: identified from National ID database, Ireland, Deaths: identified from National ID database (2003-2012), Ireland	Not applicable	Age of death over the time-frame 2003-2012 (Irish Central Statistics Office)	Mortality rate=8.35% *Increased with age *Higher than 5.9% in general population *Average age of death:(mean, median or mode unspecified) F:56y; M:53y *Lowest for profound ID (44y), rising to moderate ID (62y)	CASP score : 12/14 Limitations: * Administrative sample *Only one data source used to identify age of death
Oullette-Kuntz et al, 2015	N=6,048 total with ID (N=134 deaths) Age15+y Gender proportions not given	Proportions not given	ID: identified from multiple administrative databases, Manitoba, Canada Deaths: identified from vital statistics mortality database, Manitoba, Canada	Age, gender, post-code matched Manitoba general population (N=12,069)	Age-specific mortality rates, per PY over the timeframe: (01.4.00-31.3.05)	Mortality rate: 4.61/ 1,000 PY *5.69 times that of general population *Mean age of death 10 years less for ID population *Premature mortality 6.13 times higher than general population	CASP score: 12/14 Limitations: *administration sample *only used one death data source

Glover et al, 2016	N=59,165 PY with ID: (N=664 deaths) All ages Gender: M: 0.62% of general population , F: 0.45% of general population	Proportions not given	ID: identified from Clinical Practice Research Database, England (registered: 01.04.10-31.03.14) Deaths: identified from individuals who had complete data for linkage mortality records, England	11.16 million PY (N=98,035 deaths in general population) Clinical Practice Research Database, England	Age/gender specific mortality rates, per PY over the timeframe: (01.04.10-31.03.14)	Mortality rate:11.2 /1,000 PY *1.27 times that of general population *Difference more marked for females and younger age groups *Age of death 19.7 years less for ID population	CASP: 14/14
Hosking et al, 2016	N=16,666 total with ID (N=656 deaths) Age 18-84 yrs Gender M=48%, F=42%,	Proportions not given	ID: identified from Clinical Practice Research Database, England (registered 01.01.09-31.03.13) Deaths: identified from Office of National Statistics (ONS) death registration data.	Gender and practice matched general population N=113,562 total (N=1358 deaths)	Age/gender specific mortality rates, per PY over the timeframe: (01.04.10-31.03.14)	Mortality rate: I3.2/ 1,000 *3-4 times that of general population *Higher in DS, individuals with support needs , *Higher in males (not significant)	CASP: 14/14:
	Studies of standardised mortality rates						
McGuigan et al, 1995	N=1,756 total with ID (N=270 deaths) All ages Gender proportions not given	Proportions not given	ID: identified from ID registers London, England (two boroughs) Deaths: identified from registers (1992-1990) London, England, and death certificates	England & Wales general population	SMR by 5y age groups and gender over the timeframe (1982-1990)	SMRs>1; 22 groups significant, 13 not significant due to wide confidence intervals	CASP score :12/14 Limitations: *Wide confidence intervals *Administration sample

Forsgren et al, 1996	N=1,478 total with ID (N=124 deaths) All ages on 31.12.85 Gender M: 0.67%, F: 0.54% *percentage out of total population	Mild (2,460 PY), Moderate (3,454 PY), Severe (3,158 PY), Profound (849 PY)	ID: identified Swedish province. Register for ID services Deaths: identified from cause of death registries linked to the Swedish National central bureau of statistics	Same Swedish province general population	SMR by 10y age groups and gender over the timeframe: (1986-1992)	SMR=2.0 *Higher if epilepsy and ID *Higher if cerebral palsy and ID *Higher in F *Higher at lower ability	CASP score :13/14 Limitations: *Administration sample
Durvasula et al, 2002	N=693 total with ID (N=40 deaths) Age 4-60y in 1989 Gender: M=55%, F=45%	Proportions not given	ID: identified from a previous prevalence study undertaken in (1989-1990) , Lower North Shore Sydney, Australia. Deaths: identified via NSW Register of births, deaths and marriages (1989-1999)	Lower North Shore Sydney general population (1989-1999)	SMR by 5y age group and gender Years of potential life lost ratio (YPLL) over the timeframe: (1989-1999)	SMR=4.9 *Higher for F YPLL ratio=6.7	CASP score :10/14 Limitations: * Unclear if child cohort age 4-20y were followed up * Results of child cohort age 4-20y not reported *Small sample *Only used one death data source
Tyrer et al, 2007	N=2,436 total with ID (N=409 deaths) Age 20+y Gender: M: 56.8% F: 43.2%	Moderate (N=751), Profound (N=791), Severe (N= 894)	ID: identified from ID case register, Leicestershire, England. Deaths: identified Office of National Statistics	Leicestershire and Rutland general population (1993-2004)	SMRs by age and gender, per PY over the time frame: (01.1.93-31.12.05)	SMR=3.2 *Largest difference at younger age groups especially 20-29 Y *Older individuals similar to general population (70+) *Higher in F (even after external causes excluded) *Higher in DS *Higher in city than county for F	CASP score12 /14 Limitations: *Administration sample *Only used one death data source
Ouellette Kuntz et al (2015)	N=3,388 with ID (N=172 deaths) All ages Gender M:57.97% F: 42.03%	Proportions not given	ID: known to community partner agencies Ontario, Canada Research alliance - Deaths: identified from Geographic Registry in ID (GRID)	South East Ontario general population, 2007	SMR by age groups (<20, 20-40, 40-60, 60+y) and gender, per PY (2004-2011)	SMR=2.5 *Higher at older age groups, except highest in <20y *Higher in F	CASP score: 12/14 Limitations: *Administration sample * Only one data source used to identify age of death

Glover and Christie, 2014	N= 154 total with ID (N=68 deaths) , from 01/04/12-31/03/13 Age and gender proportions unspecified	Proportions not given	ID: identified from 68 health boards, England Deaths: identified via numerous sources	General population in 68 health boards, England	Local age/death specific SMRs	Median SMR across regions=2.1 *Highest in East England=3.3 *Lowest in West Midlands=0.4	CASP score: 11/14 Limitations: *Small sample *Short follow up *Age not reported
Heslop & Glover, 2015	Unspecified total population, and number of deaths not stated Age: 18+ Gender proportions not given	Proportions not given	ID: identified from GP records England Deaths: identified via Local Authority self-assessment exercise reports	General practice registered general population in same area	SMR over the timeframe: (01.4.12-31.3.13)	SMR=1.92	CASP score 12/14 Limitations: *Unclear sample size *Best estimate based on available data sources
Lauer & McCallion, 2015	N=120,913 total with ID (N=2,369 deaths) Age 18+y Gender proportions not given	Proportions not given	ID: identified Massachusetts, Connecticut, Ohio, Louisiana, USA State ID service systems Deaths: identified from staff reports, some external review of deaths via national death index	General population in same USA states; US standard population	Age of death and crude mortality rate over the time frames: (01.1.09-31.12.11) and (01.7.08-30.6.11)	Age adjusted SMR=1.8	CASP score 12/14 Limitations: *Lack of standardised measurement of death/age groups reporting across states *Administration sample
McCarron et al, 2015	N=31,943 total with ID (N=2666 deaths) All ages Gender: M: 58,19% F: 41.81%	Mild (N=9601), Moderate (11,993), Severe (4,782), Profound (1,281), Other or undefined (4,286)	ID: identified from National ID database, Ireland, Deaths: identified from National ID database (2003-2012) , Ireland	Irish central statistics for births and deaths	SMR by 10y age groups and gender, per person years over the timeframe: (2003-2012)	SMR=3.7 *Highest SMR aged 0-19y *Higher in F *Higher at lower ability	CASP score : 12/14 Limitations: * Administrative sample *Only one data source was used to identify age of death

Florio & Troller, 2015	N=40,705 total with ID (N=953 deaths) Gender proportions not given Age :5-69y	Proportions not given	ID: identified NSW services register, Australia Death: identified from NSW births deaths and marriages linked to death records of people with ID	NSW general population, N=45818,946 PY (312, 649 deaths)	SMR by age, per PY over the timeframe: (01.6.05-31.12.11) Comparison of age standardised death rates with general population	SMR=3.15 (age 5-69Y) *Higher in F Comparative mortality ratio= 2.55	CASP score : 13/14 Limitations: *Administration sample
Dieckmann et al, 2015	N=11,000 total with ID (N=468 deaths) Gender proportions not given Age 18+	Proportions not given	ID: identified from 12 disabilities service providers, Baden-Wuerttemberb, Germany. Deaths: identified Baden-Wuerttemberb, Germany. 12 disabilities service providers	WHO global standard population	SMR by age and gender over the timeframe: (2007-2010)	SMRs were calculated for males and females separately *SMR=13.2 (M) *SMR=8.9 (F) *Mortality rates of older age groups almost the same as general population	CASP score: 12/14 Limitations: *Atypical older population - healthy survivors of Nazi atrocities *Administration sample
Arvio et al, 2016	N= 378,987 PY with ID (N=5171 deaths) Gender proportions not given All ages	Mild (N=151,835 PY), Severe (N=227,152 PY)	ID: identified from Finland social insurance institution Deaths: identified from record of terminated benefits due to death for mild or severe ID (identified 1996-2011)	Finnish general population (1996-2011)	SMR by 5y age groups and gender, per PY; over the time frame (1996-2011)	SMR=2.0-4.2 (mild ID) SMR=2.1-13.3 (severe ID) *Higher in older age groups *Higher in F	CASP score:12 /14 Limitations: *Administration sample *Only one data source used to identify age of death
Glover et al, 2016	N=59,165 PY with ID: (N=664 deaths) All ages	Proportions not given	ID: identified from Clinical Practice Research Database , England	11.16 million PY (N=98,035 deaths in general	SMR by age groups (<9, 9-17, 18-24, 25-34, 35-44,	SMR=3.18 *Higher in F	CASP 13/14 Limitations: *Risk of not representing all

	Gender: M: 0.62% of general population F: 0.45% of general population		(registered: 01.04.10-31.03.14) Deaths: identified from records of individuals who had complete data for linkage mortality records, England	population), Clinical Practice Research Database, England	45-54, 55-64,65-74, 75-84, 85-99) and gender, per PY over the timeframe: (2010-2014)		individuals with mild ID in sample
Studies of factors associated with mortality and life expectancy (other than lower level of ability, and age {childhood, and older age})							
Eyman et al, 1989	N=undefined total with ID (N=87,352 deaths) All ages	Mild (N=13,175 deaths), Moderate (9,360 deaths), Severe (4,980 deaths), Suspected or unknown (6,575)	Oulu and Lapland, Finland. Prospective cohort ID: identified via numerous sources including hospital and school registers Deaths: identified via death certificates from population registers, hospital notes and autopsies	None	Associations with deaths. Age groups (0-20, 21-54, >55y) over the time frame (March 1984-October 1987)	Mortality rate lower in middle age group (21-54); higher with lower ability, reduced mobility, poorer ambulation, eating problems, toileting problems, DS	CASP score: 13/14 Limitations: *Administration sample
Patja et al, 2000	N=2,366 total with ID (N=1,108 deaths) Age 2-64y in 1962 Gender: M 50%, F:50% [0.7% of general population]	Mild (=1101), Moderate, (N=606), Profound, (N=368), Severe, (N=280)	Finland. Prospective cohort; ID: identified via individual medical examination organised by the National Board of Health Deaths: identified via population registers of death	Not applicable	Life expectancy by 5y age groups, sex, ability level, and ID aetiology, per PYover the timeframe : (01.1.63-31.12.97)	Reduced life expectancy with age, lower ability, more severe ID, epilepsy, hearing impairment, visual impairment, especially after 49y, lower in males	CASP score: 14/14 Additional strengths: *Population-based sample *High retention *Long follow-up
Bittles et al, 2002	N=8,724 total with ID (N=1,162 deaths) Age unclear Gender:	Mild (N=4773), Moderate (N=2422),	ID: identified from record of referrals to ID services in Western Australia since 1953	None	Survival probabilities	Highest mortality in men, indigenous ethnicity, genetic syndromes, lower ability	CASP score: 12/14 Limitations: *Follow up of cohort not consistent i.e. changes in age at

	M :58.4%. F: 41.6%	Severe (N=1529)	Deaths: identified from state mortality registers (1969-2000) and Disability services commission database				registration over time (11y in 1953; 32y in 2000) *Administration sample
Ouellette et al (2015)	N=3,388 with ID (N=172 deaths) All ages	Proportions not given	ID: known to community partner agencies Ontario, Canada. Research alliance Deaths: identified from Geographic Registry in Intellectual Disabilities (GRID)	Not applicable	Logistic regression for survival versus death (<20, 20-40,40-60, 60+) over the timeframe: (2004-2011)	Mortality higher and life expectancy lower for DS, cerebral palsy, blind, technology dependent/medical fragility, wheelchair user/mobility impairment, epilepsy	CASP score: 12/14 Limitations: *Administration sample * Only one data source used to identify age of death
Emerson et al, 2014	N=84,262 total with ID (N=1,313 deaths) All ages Gender proportions not given	Proportions not given	ID: identified from ID case register, Sheffield England Deaths: identified from ID case register Sheffield, England. (1980-2012)	England & Wales general population (1980-2012)	N of deaths in 10y age groups by number registered, per person years; Mortality rates by age over the timeframe: (1980-2012)	Life expectancy risen for ID population (2.78 per decade versus 2.24 for general population from (1980-2012) *No closing of the gap between ID and general population over time	CASP score: 11/14 Limitations: *Administrative sample *Changes in the register over time not known *Only one data source used to identify age of death
Heslop et al, 2014	N=undefined total with ID (N=247 deaths) Age: 4+y M: 57.9% F: 42.1% [0.5% of adult general population}	Mild (N=98), Moderate (N= 77), Severe (N=53), Profound and multiple (N=19)	ID: identified from GP records, part of England (1.7 million general population). Deaths: identified from multiple agencies including office for National Statistics	Age, gender, ICD-10 cause of death category, GP records, matched general population	ID deaths compared with general population over the timeframe: (01.6.10-31.5.12)	Age of death: M, 65y (IQR 54-76), 13 years younger than comparison group, F,63y (IQR 54-75), 20 years younger than comparison *22% < age 50Y at death versus 9% in comparison group age<50Y at death *Younger age of death for severe/profound ID	CASP score:13/14 Limitations: *General population comparison group drawn from a wider area

Glover et al, 2016	N=59165.14 PY with ID, (N=664 deaths) All ages Gender: M: 0.62% of general population F: 0.45% of general population	Proportions not given	ID: identified from Clinical Practice Research Database (01.04.10-31.03.14) Deaths: identified from death certificates of individuals who had complete data for linkage mortality records, England	11.16 million PY(N=98,035 deaths in general population), Clinical Practice Research Database, England	Avoidable causes of death (amenable versus preventable)	Avoidable deaths:44.7% (lower than general population ages 10-74Ys) *34.9% amenable to good health care (higher than general population) * preventable deaths lower than general population	CASP score:14/14
Hosking et al, 2016	N=16,666 total with ID (N=656 deaths) Age: 18-84 Y Gender F=42%, M=48%	Proportions not given	ID: identified from Clinical Practice Research Database (01.01.09-31.03.13) Deaths: identified from Office of National Statistics (ONS) death registration data	Gender and practice matched general population N=113,562 total (N=1358 deaths)	Avoidable causes of death (amenable versus preventable)	Avoidable deaths: 46. 3% (lower than 47.5% in general population) *37% amenable to good health care (higher than 22.5% in general population) *19% preventable lower than 40% in general population)	CASP score :14/14:

CASP: Critical Appraisal Skills Programme
F: female
ID: intellectual disabilities
ICD-10: 10th revision of the International Statistical Classification of Diseases and Related Health Problems
IQR: Interquartile range (IQR)
M: male
N: number
PY: Person Years
YPLL: Years of potential life lost ratio
SMR: standardised mortality ratio

Table 2: Studies on causes of death

Study	ID cohort	Id level	Data sources	Comparison group	Analyses	Primary/underlying/ leading cause of death	Immediate cause of death	Other contributory factors	Critique/ Quality
Simila et al, 1986	N=165 total with ID (N=26 deaths) Age: up to 17 (born in 1966) Gender proportions not given	Mild (N=68), Moderate (N=51), Severe (N=28), Profound (N=18)	Oulu and Lapland, Finland. Prospective cohort ID: identified via numerous sources including hospital and school registers Deaths: identified via death certificates, population registers, hospital notes and autopsies	General population in same birth cohort N=11,731 total (N=267 deaths)	Immediate cause of death on death certificates,	Not applicable	Congenital anomalies (N=14, 53.8%), infectious disease (N=7, 26.9%), injuries (N=2, 7.7%), neoplasms (N=1, .8%,) *Congenital anomalies and infectious disease significantly higher mortality rates versus comparison group	Not applicable	CASP score: 11/14 Limitations: *Small ID sample *Administrative sample *Reliance on death certificates
Forsgren et al, 1996	N=1,478 total with ID (124 deaths) All ages on 31.12.85 Gender [M: 0.67%, F: 0.54%]	Mild (N=2430 PY) Moderate (N=3454 PY), Severe (N=3158 PY), Profound(N=849)	ID: identified from Register for ID services, Swedish province Deaths: identified from cause of death registries linked to the Swedish National central bureau of statistics	Västerbotten, Sweden general population	Most common underlying causes of death from death certificates SMR for cause of death (1986-1992)	Circulatory (N=58, 46.8%) specifically IHD/CVD); *heart failure common cause of death in people with DS, neoplasm (N=14, 11.3%); respiratory (N=13, 10.5%); congenital malformation (N=11 8.9%); violent death (N=7, 5.6%) Highest SMRs: congenital (46.3); neurological (9.7); mental disorder (4.0); respiratory (3.3);	Not applicable	N=6 (4.8%) listed epilepsy as contributory cause	CASP score: 12/14 Limitations: *Administrative sample *Reliance on death certificates

						circulatory (2.1); violent death (1.4) Less common SMRs cancer (0.9)			
Hollins et al, 1998	N= 2,026 total with ID (268 deaths) Gender proportions not given All ages	Proportions not given	ID: identified from ID registers London, England (two boroughs) Deaths identified from death certificates from registers (1992-1990) London, England	Same two boroughs of London general population	Most common immediate causes of death reported in death certificates SMR for pneumonia for each borough (1982-1990)	Not applicable	Pneumonia (N=125, 46.6%); other cardiovascular disease/cerebrovascular disease (N=21, 8%); cancer (N=21, 7.8%); cardiac failure (N=17, 6.3%), myocardial infarction (17, 6.3%); status epilepticus (N=11, 4.1.5%); GI (N=10, 3.7%) SMR pneumonia: 74.1 (Wandsworth borough 35.4 (KCW borough)	N=30 (11.2%) listed epilepsy as contributory cause	CASP score: 11/14 Limitations: *SMR age groups unclear *Only one database to identify deaths (ID registers) *Reliance on death certificates
Patja et al, 2001	N=2,366 total with ID (1,095 deaths) Age 2-64y in 1962 Gender: M 50%, F:50% [0.7% of general population]	Mild (N=11,01), Moderate (N=606), Profound, (N=368), Severe, (N=280)	Prospective cohort, Finland. ID: identified via individual medical examination organised by the National Board of Health Deaths: identified via population registers of death	Finnish general population	Most common underlying immediate and contributory cause of deaths on death certificates; age and gender Relative risk for cause of death, (01.1.63-31.12.97)	Vascular (N=398, 36.3%); respiratory (N=241, 22%); tumours (N=124, 11.3%); accidents and poisonings (N=80, 7.3%); digestive system (N=77, 7%) Age standardized: excess mortality in respiratory (RR: 2.7-6.2), digestive (RR 0.8-4.3), and infectious diseases (RR 1.5-4.1) *Cancer and external causes were less common than comparison group, vascular was similar or less common (at younger ages they related to DS and congenital anomalies)	Vascular (N=402, 36.7%); respiratory (322, 29.4%); tumours (102, 9.3%); digestive (76, 3.2%); accidents and poisonings (69, 6.3%)	Mental illness (262, 36.7%); vascular (170, 15.5%); nervous system (164, 15%); congenital malformations (59, 5.4%); epilepsy (54, 5.1%), respiratory (46, 4.2%)	CASP score:13 /14 Limitations: *Reliance on death certificates Additional strengths: *Population-based sample *High retention *Long follow-up

						*Cause specific mortality gender differences were smaller than for comparison group			
Durvasula et al, 2002	N=693 total with ID (N=40 deaths) Age :4-60y in 1989 Gender: M=55%, F=45%	Proportions not given	ID: identified (1989-1990) Lower North Shore Sydney, Australia in a previous prevalence study Deaths: identified in NSW Register of births, deaths and marriages (1989-1999)	Lower North Shore, Sydney general population	Causes of deaths (% of all causes) across the timeframe (1989-1999) from death certificates	Respiratory (N=14, 35%); external causes (N=8, 20%); cancer (N=7, 17.5%), heart disease (N=6, 15%), digestive (N=3, 7.5%), seizure (N=2, 5%) Comparison group (exact N not reported): cancer (38.7%), external (21.4%), heart disease (10.3%), endocrine (7.2%), other (8.8%), digestive (3.1%), respiratory (2.8%)	Not applicable	Not applicable	CASP score 10/14 Limitations: * Unclear if child cohort aged 4-20 y were followed up (-1) * Results of child cohort age 4-20 y not reported *Small sample *Reliance on death certificates
Tyrer & McGrother, 2009	N=2,995 with ID (503 deaths) Age: 20+ Gender: M=56.8% F=43.2%	Moderate (N=751), Profound (N=791), Severe (N=894)	ID: identified from Leicestershire, England. ID case register Deaths: identified Office of National Statistics	Leicestershire general population	Underlying causes of death in death certificates SMR of underlying cause of death by ICD chapters and conditions (01.1.93-31.12.06)	SMR congenital malformations (85.6), nervous system (16.3). mental disorders (11.4), pneumonia (6.5), other respiratory (4.6), genitourinary (6), cerebrovascular (2.4), digestive (2.4)	Not applicable	ID (3%), DS (18%), congenital (7%), chromosome anomalies, (6%),cerebral palsy (4%)	CASP score :12/14: Limitations * Administration sample (though included population based data from primary care) *Reliance on death certificates
Glover and Ayub (2010)	Undefined total with ID (N= 984 deaths) from 2004-2008	Not given	ID: identified from death certificates, England Deaths: identified from computerised	General population, England	Underlying and immediate cause of death reported in death	More common in ID: congenital, respiratory (specifically pneumonia, genito-urinary, infectious, nervous, accidents (specifically foreign body n respiratory tract), epilepsy	Respiratory (N=3,866, 52%), circulatory (N=898, 12.1%), *most common age> 65 infectious (N=459, 6.2%), nervous	Not applicable	CASP score:12 /14 Limitations * Administration sample *Reliance on death certificates

	All ages Gender proportions not given		records. England, and death certificates (2004-2008)		certificates cross reference with list of conditions	Less common in ID: cancer, circulatory, injury and poisoning, * Preventable causes: Lung inflammation (14% versus 2% in general population Epilepsy and convulsions (13% versus 0.4% in general population)	(N=393, 5.3%), congenital (N=301, 4%), cancer (N=284, 3.8%) *most common age 35-64, genito-urinary (N=202, 2.7%), Injury and poisoning (N=197, 2.6%), *most common age 5-34 digestive (N=191, 2.6%)		
Heslop et al, 2014	N=undefined total with ID (N=247 deaths) Age: 4+y Gender: M:58% F: 42%	Mild (N=98), Moderate (N= 77), Severe, (N=53), Profound and multiple, (N=19)	ID cases identified from GP records England Deaths: identified by multiple agencies including office for National Statistics	England and Wales general population	Underlying causes of deaths by ICD-10 chapter reported in death certificates (% of all causes) (01.6.10-31.5.12)	Heart and circulatory (N=53, 21.5%); cancer (N=50, 20.2%); nervous system (N=39, 16%); respiratory (N=37, 15%); congenital (N=18,7.3%); digestive (N=12. 4.9%); external (N=10, 4.1%); endocrine (N=7,2.8%); mental (N=6, 2.4%); other (N=15, 6.1%) Comparison group: heart and circulatory (28.8%); cancer (29.6%); nervous system (3.8%); respiratory (14.0%); congenital (0.2%); digestive (5.1%); external (3.6%); endocrine (1.3%); mental (6.4%); *More common in ID: nervous system, congenital *Less common in ID: heart, cancer, mental disorders	Not applicable	Not applicable	CASP score 12/14 Limitations *reliance on death certificates as data source *comparison group drawn from a wider area
Glover et al, 2016	N=59165	Not given	ID cases: identified from	11.16 million PY	Underlying causes of	Circulatory (N=152, 22.9%), respiratory			CASP: 13/14

	PY with ID (N=664 deaths) All ages		Clinical Practice Research Database , England (registered: 01.04.10-31.03.14), Deaths: identified from individuals who had complete data for linkage mortality records, England	(N=98035 deaths), Clinical Practice Research Database, England	deaths by ICD10 chapter Avoidable cause of death categories as amenable to health care or preventable	(N=114, 17.17%), neoplasms (digestive most common) (N=87, 13.1%) , nervous system (N=85, 12.8%), congenital (N=56, 8.4%), mental and behavioural (N=43, 6.5%), external (N=25, 3.8%) Highest SMRs congenital (72.9), nervous system (9.8), mental and behavioural disorders (5.4), genitourinary system (5.4), endocrine, nutritional and metabolic (5.1), respiratory system (4.9), digestive system (4) , infectious and parasite disease (3.2) *more likely to die from causes amenable to good healthcare			Limitations *Reliance on death certificates
Hosking *et al.* 2016	N=16,666 with ID (N=656 deaths) Age :18-84 Y Gender F=42%, M=48%	Not given	ID: identified from Clinical Practice Research Database , England (registered 01.01.09-31.03.13) Deaths: identified from Office of National Statistics (ONS) death registration data	N=113,562 (N=1358 deaths), gender and practice matched	Underlying cause of death reported in death certificates	Circulatory (21.6%), respiratory disease (18.8%), neoplasm (14.9%), nervous system diseases (11.6%), External: *accidental poisoning most common (0.6%) Most common general population: neoplasms (37.4%), circulatory (26.5%, respiratory diseases (9.9%), external causes (7.4%) Highest HR:			CASP:13/14 Limitations *Reliance on death certificates (-1)

						nervous (13.79), genitourinary (10.89), respiratory (6.68) * pneumonia and aspiration pneumonia (>10) endocrine (5.38), mental and behavioural disorders (7.99), musculoskeletal (5.5) , digestive (4.02), circulatory (3.05)			

CASP: Critical Appraisal Skills Programme
CVD: Cardio Vascular Disease
DS: Down syndrome
F: female
GI: Gastrointestinal disorder
HR: Hazard Ratio
ICD-10: International statistical Classification of Diseases, 10th Revision
ID: intellectual disabilities
IHD: Ischemic heart disease
KCW: Kensington, Chelsea and Westminster boroughs
N: number
M: male
NSW: New South Wales
PY: Person Years
RR: relative risk
SMR: standardised mortality ratio
Y: years
YPPL: Years of life lost ratio