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# BMJ Open

## Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage

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3 **Rates, causes, place, and predictors of mortality in**  
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6 **adults with intellectual disabilities with and without**  
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9 **Down syndrome: cohort study with record linkage**  
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## Abstract

### **Objectives**

To investigate mortality in adults with intellectual disabilities: rates, causes, place, demographic and clinical predictors.

### **Design**

Cohort study and record linkage to death data.

### **Setting**

General community.

### **Participants**

961/1,023 (94%) adults (16-83 years; mean=44.1 years; 54.6% male) with intellectual disabilities, clinically examined in 2001-2004; subsequently record-linked to their National Health Service number, allowing linkage to death certificate data, 2018.

### **Outcome measures**

Standardised mortality ratios (SMRs), underlying, and all contributing causes of death, avoidable deaths, place, and demographic and clinical predictors of death.

### **Results**

294/961 (30.6%) had died; 64/179 (35.8%) with Down syndrome, 230/783 (29.4%) without Down syndrome. SMR overall=2.24 (1.98, 2.49); Down syndrome adults=5.28 (3.98, 6.57), adults without Down syndrome=1.93 (1.68, 2.18); male=1.69 (1.42, 1.95), female=3.48 (2.90, 4.06). SMRs decreased as age increased. More severe intellectual disabilities increased SMR, but ability was not retained in the multivariate model. SMRs were higher for most ICD-10 chapters. For adults without Down syndrome, aspiration/reflux/choking, and respiratory infection were the commonest underlying causes of mortality; for Down syndrome adults "Down syndrome", and dementia were most common. Amenable deaths (29.8%) were double that in the general population (14%). 60.3% died in hospital. Mortality risk related to: percutaneous endoscopic gastrostomy/tube fed, Down syndrome, diabetes, lower respiratory tract infection at

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3 cohort-entry, smoking, epilepsy, hearing impairment, increasing number of prescribed  
4 drugs, increasing age. Bowel incontinence reduced mortality risk.

### 7 **Conclusions**

9 Adults with intellectual disabilities with and without Down syndrome have different SMRs  
10 and causes of death which should be separately reported. They die younger, from  
11 different causes than other people. Some mortality risks are similar to other people, with  
12 earlier mortality reflecting more multi-morbidity; amenable deaths are also common.  
13 This should inform actions to reduce early mortality, e.g. training to avoid  
14 aspiration/choking, pain identification to address problems before they are advanced,  
15 and reasonable adjustments to improve health-care quality.  
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### 26 **Strengths and limitations of this study**

- 27 • Thorough methods of case ascertainment for intellectual disabilities at baseline.
- 28 • Individual verification of intellectual disabilities and its severity, and detailed health  
29 assessments at baseline.
- 30 • Longitudinal design.
- 31 • Large cohort size and study duration, and successful record linkage for 94% of  
32 participants.
- 33 • Limitations include that the study was conducted in only one part of Scotland, and  
34 the reliance upon recorded cause of death from death certificates.  
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## Introduction

People with intellectual disabilities die at a younger age than other people; on average, 20 years younger,<sup>1</sup> or 28 years younger specifically for people with Down syndrome.<sup>2</sup> It has been demonstrated that people with intellectual disabilities receive poorer management of their long term conditions within primary health care services compared with the general population,<sup>3</sup> and it is conceivable that this is one contributor to earlier mortality. It has been suggested that as many as 40% of deaths of people with intellectual disabilities may have been amenable to good quality health care.<sup>4-6</sup>

Previous studies on death in people with intellectual disabilities had limitations such as small sample sizes, or non-representative populations. More recently, there have been large-scale studies which are more representative, having been drawn from intellectual disabilities registers, or social security or primary care data with record linkage to death certification. These have been undertaken in parts of Sweden, Australia, England, Finland, Canada, Ireland, and USA (supplementary table 1).<sup>5-18</sup> These studies fairly consistently report standardised mortality ratios (SMRs) to be high for people with intellectual disabilities, more so at younger ages, and higher for women than men. Adult studies have tended to report SMRs in the region of 2-4, although in some, SMR is only slightly above 1.<sup>10,18</sup> However, direct comparison between studies is not always possible, due to the different age ranges studied and methods of reporting.

- Supplementary table 1 -

In view of the methods that studies have used for population identification (typically, routine administrative data linked to death certifications), they provide little information on the socio-clinical factors that influence SMR, or the risk factors associated with death, beyond that of age and sex. Three studies reported SMR by level of intellectual disabilities, with, broadly speaking, higher SMR with more severe intellectual

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3 disabilities.<sup>7,10,16</sup> Only three studies (different studies to those that reported on level of  
4 intellectual disabilities) were able to report data separately for adults with intellectual  
5 disabilities with and without Down syndrome; two found higher mortality rates for adults  
6 with Down syndrome (SMR=7.6,<sup>9</sup> and hazard ratio=9.21<sup>5</sup>) than for adults without Down  
7 syndrome, or an odds ratio showing Down syndrome as a risk of death.<sup>12</sup> A further  
8 study reported SMR=5.5 for children and adults (combined) with Down syndrome, but  
9 did not report SMR for those with intellectual disabilities without Down syndrome.<sup>19</sup> Two  
10 studies reported adults with intellectual disabilities to have higher SMRs if they have the  
11 co-morbidities of epilepsy,<sup>5,7</sup> and cerebral palsy,<sup>7</sup> as opposed to not having these  
12 comorbidities. One study reported adults with intellectual disabilities with comorbid  
13 autism to have lower hazard ratios than those without comorbid autism.<sup>5</sup> One study  
14 reported the risk factors for mortality in a population with intellectual disabilities to be:  
15 age, Down syndrome, cerebral palsy, blindness/low vision, technological  
16 dependence/medical fragility, wheelchair dependence, mobility impairment without  
17 wheelchair dependence, and epilepsy.<sup>12</sup> Factors not found to be risks, if any, were not  
18 reported, and a further limitation was that factors were reported by agency staff, rather  
19 than the individuals undergoing health assessments.<sup>12</sup> We have not identified any other  
20 studies that investigated risk factors for time to mortality in adults with intellectual  
21 disabilities.

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44 There is less consistency regarding the most common certified underlying causes of  
45 death in adults with intellectual disabilities, partly as some studies do not report these  
46 separately for children and adults, or by age ranges. Pneumonia, other respiratory  
47 diseases, and diseases of the nervous system were reported to be the most common in  
48 one study,<sup>11</sup> diseases of the circulatory system and respiratory systems in another,<sup>5</sup>  
49 heart disease, neoplasm, and Alzheimer disease in a third,<sup>17</sup> and diseases of the  
50 circulatory system, neoplasm, and the nervous system in a fourth.<sup>18</sup> In adults with  
51 intellectual disabilities, cause specific SMRs have been reported to be high across most  
52 groups of disorders.<sup>5,11</sup> These studies did not report cause of death separately for adults

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3 with and without Down syndrome. Given the different health profile of people with Down  
4 syndrome compared with people with intellectual disabilities of other causes, this is an  
5 important limitation.<sup>20</sup> In people with Down syndrome, most studies on mortality have  
6 been conducted with child populations. The most common causes of death in people with  
7 Down syndrome have been reported to be congenital heart disease, and  
8 pneumonia/diseases of the respiratory system.<sup>2</sup>  
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17 Overall, the existing body of literature on mortality in adults with intellectual disabilities  
18 does not include more detailed information on level of intellectual disabilities, nor  
19 separate out the population with, from those without, Down syndrome (for whom causes  
20 of death may differ), nor investigate health and demographic predictors of death other  
21 than age and sex, and is inconsistent with regards to causes of death. A better  
22 understanding of these factors may provide a pathway to action to reduce the observed  
23 earlier mortality in adults with intellectual disabilities.  
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33 This study aims to investigate the rates, causes, place, and demographic and clinical  
34 associations with mortality in adults with intellectual disabilities, with and without Down  
35 syndrome.  
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## 42 **Methods**

### 43 ***Approval***

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46 Ethical approval was gained from NHS Greater Glasgow Primary Care Trust -  
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48 Community & Mental Health Research Ethics Committee, and NHS Greater Glasgow and  
49  
50 Clyde Safe Haven. Individual consent to participate was taken in line with Scottish law,  
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52 between 2001-2004.  
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## **Participants**

The adult (aged 16+ years) intellectual disabilities population living within the NHS Greater Glasgow area was identified through multiple sources between 2000-2001. General practitioners were financially incentivised to identify their registered patients with intellectual disabilities, and all 631 (100%) did so. Adults were also identified via the intellectual disabilities health and social work services including day services, the Health Board register, and records of financial payments for any service by social work. This process led initially to an over-identification, such as people with IQ scores in the 70–80 range with additional complex health needs. All were systematically reviewed by nurses in the intellectual disabilities health service, and this group were removed. Thus, a register was compiled, and subsequently updated annually via general practices, with central support from the intellectual disabilities health service, until 2017 when services were redesigned. The identified adult prevalence of intellectual disabilities within the area was 3.33 per 1,000.

## **Process and data collection**

With initial piloting in 2001, each participant had a detailed assessment of their general and mental health, and demographic factors, completed 2002-2004. One of six specially trained, registered nurses reviewed each person's primary health care records, then used a semi-structured tool, the C21st Health Check, to assess clinical factors and the level and cause of intellectual disabilities. In addition to a review of existing health problems and all bodily health systems, a physical examination was undertaken, including assessment of vision and hearing, measurement of height and weight, and a phlebotomy protocol followed. All information was then reviewed by the nurse with one of three general practitioners with a special interest in intellectual disabilities, and any further investigations that were indicated were completed. Previously known, and newly identified, conditions were then classified using the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10)*.<sup>21</sup> Anyone identified to have possible, probable, or definite mental ill-health, autism, or problem behaviours was

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3 then fully assessed by the project's intellectual disabilities psychiatrists. Each person's  
4 assessment findings were then case conferenced by the two Consultant psychiatrists,  
5 and diagnoses were derived and agreed according to clinical diagnoses, *ICD-10*  
6 (*Diagnostic Criteria for Research*),<sup>22</sup> *Diagnostic and Statistical Manual of Mental*  
7 (*Disorders-IV-TR*),<sup>23</sup> and *Diagnostic Criteria for Psychiatric Disorders for use with Adults*  
8 (*with Learning Disabilities (DC-LD)*).<sup>24</sup> Information was also collected on demographics,  
9 and community, hospital, and social service use. Further details are provided  
10 elsewhere.<sup>25,26</sup> The data were entered into a database by two dedicated data-entry staff.

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12 Each person in Scotland is given a number unique to them at birth or first registration  
13 with a general practitioner, which is used in almost all subsequent health service  
14 encounters, and on certification of death. The numbers are held on the Community  
15 Health Index (CHI) database at National Services Scotland. These CHI numbers provided  
16 a means to record link each participant with National Records for Scotland death  
17 certification data. This linkage was performed in 2018, and the linked data were held in  
18 the NHS Greater Glasgow & Clyde (NHS GG&C) Safe Haven. Data on immediate,  
19 underlying, and contributory causes of deaths by ICD-10 codes, age at death, and place  
20 of death were extracted.

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22 In order to provide finer granularity of cause of death, and in view of the recognised  
23 issue of variation between health staff in distinguishing and recording immediate, two  
24 clinical academics then grouped individual causes of death into narrower groupings than  
25 those provided by ICD-10 chapter headings (supplementary table 2).

26  
27 - Supplementary table 2 -

## 28 **Analyses**

29 All statistical analyses were conducted using R for Windows v3.3.0 or SAS 9.3 (SAS  
30 Institute, Cary NC) and were performed within the NHS GG&C Safe Haven environment.

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3 Due to disclosure principles of the Safe Haven, results with counts of less than 5 cannot  
4 be released; these have been referred to as <5 throughout. Similarly, if it is deemed  
5 possible that participants may be identified from the results, these may be omitted.  
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7 Details are provided if this occurred.  
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13 Data were summarised for the population of adults aged 16+ years with intellectual  
14 disabilities. Categorical variables were summarised with the number and percentages of  
15 people falling into each category and the number of missing data. Continuous variables  
16 were summarised with the number of observations and those missing, the mean and  
17 standard deviation (SD), and the minimum and maximum values, unless otherwise  
18 stated.  
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27 Participant characteristics were summarised overall and for those alive and those  
28 deceased. For those who are deceased, their data including age at death,  
29 underlying/contributing causes of death, and location of death were summarised for  
30 those with and without Down syndrome. Location codes for place of death are provided  
31 where available. We have assumed that those with the code for non-institutional location  
32 to have died at home. Due to small numbers, location codes have been grouped together  
33 for NHS hospitals, home, and other hospitals/care facilities including hospices.  
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43 Mortality incidence rates have been calculated using the number of deaths in the cohort  
44 divided by the number of person years alive within the study period multiplied by  
45 100,000, overall and for those with and without Down syndrome. Standard mortality  
46 ratios were calculated using population data for those aged 15 and over within NHS  
47 GG&C in 2010.<sup>27,28</sup> Death rates for males and females by 5 year band ages groups  
48 spanning from 15-20 years old to 90 years and over were summed to form the expected  
49 death rates for the general population. The observed death rate for adults with  
50 intellectual disabilities was taken from our study results. The observed/expected death  
51 rates were calculated for the intellectual disabilities cohort overall then separately by age  
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3 group, sex, ability level, and for the adults with, and without, Down syndrome, and ICD-  
4 10 chapter for cause of death, and compared to the general population.  
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9 Deaths were also analysed for those that could be considered as deaths that would have  
10 been avoidable. The Office for National Statistics (ONS) published a definition of  
11 avoidable mortality,<sup>29</sup> which lists the causes of amenable deaths (deaths that should not  
12 occur in the presence of good health care), and causes of preventable deaths, by ICD-10  
13 codes. Causes of death for the adults with intellectual disabilities have been summarised  
14 by ONS definition of avoidable deaths.  
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23 To determine the demographic and clinical factors associated with death in adults with  
24 intellectual disabilities, time to event analyses were explored using univariate Cox  
25 Proportional Hazards models. Variables were selected as potentially relevant on the basis  
26 of what is known on causes of death in people with intellectual disabilities, the 20 most  
27 common physical health conditions reported in the adult population with intellectual  
28 disabilities,<sup>20</sup> and other factors hypothesised as potentially clinically relevant  
29 (supplementary table 3):  
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- 37 • Demographics - 9 variables.
- 38 • Clinical conditions - 33 variables.
- 39 • Service use - 3 variables.
- 40 • Prescriptions - 5 variables.
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45 These models were then extended consider a single multivariable analysis and using a  
46 stepwise regression method, a model of the factors most associated with death was  
47 identified. Results from the univariate Cox Proportional Hazards models (Supplementary  
48 table 3) and the multivariable model from the stepwise results have been presented with  
49 hazard ratios with corresponding 95% confidence intervals (HR, 95% CI) and p-values  
50 were obtained.  
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60 - Supplementary table 3 -

### ***Patient and public involvement***

This study was designed to respond to the growing concern expressed by people with intellectual disabilities, their families, and third sector organisations about the early deaths of people with intellectual disabilities. The Scottish Learning Disabilities Observatory, where this research was undertaken, has a specific remit for people with intellectual disabilities. Its steering group includes partners from third sector organisations, including Down syndrome Scotland, and people with intellectual disabilities, who approved the work plan for this project prior to it commencing. Results from this study will be disseminated for people with intellectual disabilities in an easy-read version via the Scottish Learning Disabilities Observatory.

## **Results**

### ***Population characteristics***

962 of the original 1,023 (94.0%) adults with intellectual disabilities were linked to a CHI number enabling the extraction of relevant death data. Reasons for the unlinked 61 people could be due to moving out of the area, or a recording mistake. 1 further participant was removed from the analysis due to inaccurate recording of dates, leaving 961 adults in the cohort (93.9%). Of these 961 adults, 294 (30.6%) had a record of death. Table 1 shows the baseline characteristics of the full cohort of 961, the adults who died, and those still alive at the time of linkage.

- Insert table 1 about here -

### ***Age at death, and mortality incidence***

The mean age at death was 61.0 years (SD=7.0 years). Of the 961 adults, 64 (35.8%) of the 179 adults with Down syndrome, and 230 (29.4%) of the 782 adults without Down syndrome had a record of death. Their mean age of death was 56.9 years (SD=4.3 years) for the adults with Down syndrome, and 62.2 years (SD=7.5 years) for

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3 the adults without Down syndrome. Mortality incidence for the cohort during the study  
4 period was 3,049.0 per 100,000 person years follow-up, with 3,832.1 per 100,000 for  
5 those with Down Syndrome and 2,885.0 for those without Down syndrome.  
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### 10 **Standardised mortality ratios**

11 Compared with the general population, the SMR was 2.24 (1.98, 2.49) overall; 5.28  
12 (3.98, 6.57) for adults with Down syndrome, 1.93 (1.68, 2.18) for adults without Down  
13 syndrome; 1.69 (1.42, 1.95) for men and 3.48 (2.90, 4.06) for women. SMRs were  
14 higher the more severe the level of intellectual disabilities, with people with profound  
15 intellectual disabilities having an SMR of 4.14 (3.11, 5.17). SMR was high for all age  
16 groups (though for the 15-25 year age group, the wide confidence interval includes one,  
17 perhaps due to the smaller number of deaths in this group); this decreased as age  
18 increased. SMRs were high for most ICD-10 chapter groups of conditions, particularly so  
19 for congenital malformations at 17.26 (10.75, 23.78), diseases of the digestive system  
20 at 16.13 (8.23, 24.04), mental and behavioural disorders at 12.64 (3.27, 22.00), and  
21 external causes at 11.08 (3.40, 18.76). Details are shown in table 2.  
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### 41 **Causes of death**

42 Cause of death data was available from death certificates for 262 (89.1%) of 294  
43 participants who had died, which include 57 (89.1%) participants with Down syndrome,  
44 and 205 (88.7%) participants without Down syndrome. Table 3 shows the underlying  
45 causes of death by ICD-10 chapters separately for the adults with, and without Down  
46 syndrome. For the whole cohort, diseases of the respiratory system were the most  
47 common (21.8%), then diseases of the circulatory system (19.1%), then diseases of the  
48 nervous system (13.0%), and neoplasms, followed by congenital anomalies (10.3%).  
49 For the adults with Down syndrome, congenital anomalies were the most common (in all  
50 cases this was a record of "Down syndrome"), then jointly diseases of the respiratory  
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3 system and diseases of the circulatory system, then diseases of the nervous system,  
4 followed by infections, and mental and behavioural disorders. For the adults without  
5 Down syndrome, diseases of the respiratory system were the most common, then  
6 diseases of the circulatory system, then neoplasms, then diseases of the nervous  
7 system, followed by diseases of the digestive system. Table 4 presents the most  
8 common underlying causes of death by individual causes, or related groups of causes,  
9 with finer granularity than ICD-10 chapter headings (groups are shown in supplementary  
10 table 2). Causes are listed in the order of how common they were in the whole cohort.  
11 Data are presented separately for the adults with, and without Down syndrome. For the  
12 whole cohort, the most common cause was aspiration/reflux/choking, then respiratory  
13 infection, then other malignancy (non gastrointestinal), then other condition (mostly  
14 unrelated conditions that could not be reported individually or as groups, due to  
15 individually occurring at a frequency of <5). For the adults with Down syndrome, Down  
16 syndrome was the most common cause, then dementia, then other infection. For the  
17 adults without Down syndrome, aspiration/reflux/choking was the most common cause,  
18 then respiratory infection, then other malignancy (non gastrointestinal).

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37 - Insert tables 3 and 4 about here -  
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41 Table 5 shows the all contributing causes of death data, again presenting the most  
42 common causes by individual causes, or related groups of causes with finer granularity  
43 than ICD-10 chapter headings. Data is presented separately for the adults with, and  
44 without Down syndrome. For the whole cohort, respiratory infection was the most  
45 common cause (27.1%), followed by aspiration/reflux/choking (19.8%), other conditions  
46 (15.6%), other cardiovascular conditions (non acute myocardial nor other ischaemic  
47 heart disease: 14.5%), then other respiratory conditions. For the adults with Down  
48 syndrome, Down syndrome was the most common, then dementia, then respiratory  
49 infection, then aspiration/reflux/choking. For the adults without Down syndrome,  
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3 respiratory infection was the most common cause, then aspiration/reflux/choking, then  
4 other condition, then other respiratory conditions and intellectual disabilities.  
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### 13 **Avoidable deaths**

14 According to the ONS list of avoidable deaths, 102 (38.9%) of the 262 deaths were  
15 avoidable; 78 (29.8%) were deaths that are amenable to good health care, whilst 51  
16 (19.5%) were preventable deaths. 27 (10.3%) deaths were classed as both amenable  
17 and preventable deaths. This compares to published Scottish death data showing in 2018  
18 that 28% of deaths were avoidable; 14% amenable and 24% preventable, similar to the  
19 figures in the previous four years (data not available prior to 2014).<sup>30</sup> For the 57 deaths  
20 of adults with Down syndrome, 17 (29.8%) deaths were avoidable, 15 (26.3%) deaths  
21 were amenable to good health care, whilst 7 (12.3%) were preventable. 5 (8.8%) were  
22 both amenable and preventable. For the 205 deaths of adults without Down syndrome,  
23 85 (41.5%) were avoidable, 63 (30.7%) deaths were amenable to good health care,  
24 whilst 44 (21.5%) were preventable. 22 (10.7%) were both amenable and preventable.  
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### 40 **Place of death**

41 Of the 262 participants for whom place of death was known, 158 (60.3%) died in an  
42 NHS Hospital, 70 (26.7%) died at home, and 34 (13.0%) died within other  
43 hospitals/care facilities. This was similar for both the adults with Down syndrome: 31  
44 (54.4%) in an NHS hospital, 17 (29.8%) at home, and 9 (15.8%) within other  
45 hospitals/care facilities; and the adults without Down syndrome: 127 (62.0%) in an NHS  
46 hospital, 53 (25.9%) at home, and 25 (12.2%) within other hospitals/care facilities.  
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### **Factors associated with risk of death**

The results from the univariate cox proportional hazards models indicated that of the original 50 potential variables, factors associated with risk of death were (supplementary table 3):

- Demographics – age, more severe learning disabilities, accommodation type (not living with family carer), not having day-time occupation, and being a smoker (but not sex, the extent of neighbourhood deprivation, civil status, nor Down syndrome, in view of the confidence intervals).
- Clinical conditions – having spastic quadriplegia, hearing impairment, visual impairment, diabetes, percutaneous endoscopic gastrostomy/tube fed, constipation, ataxia/gait disorder, osteoporosis, hypertension, dysphagia, dyspnoea, gastro-oesophageal reflux disorder, lower respiratory tract infection, total number of physical health disorders, not having impaired mobility, not having urinary incontinence, not having bowel incontinence, and not having autism (but not epilepsy, body mass index, nail disorder, epidermal thickening, cerebral palsy, fungal infection, musculoskeletal pain, bone deformity, dental/oral problem, eczema/dermatitis, psychosis, affective disorder including bipolar affective disorder, problem behaviour, eating disorder including pica, nor any mental illness).
- Service use – number of general practitioner consultations in the previous 12 months, total number of different types of health professionals providing care at the time of the clinical assessment, (but not number of accident and emergency attendances in the previous 12 months).
- Prescriptions – antiepileptic drugs, total number of different types of drugs, (but not antipsychotic drugs, antidepressant drugs, nor anxiolytic drugs).

Table 6 shows the final model of the variables retained in the multivariable analysis for time to death. The significant factors indicating an increased risk of death were increased age, smoking, Down syndrome, diabetes, being percutaneous endoscopic gastrostomy/tube fed, lower respiratory tract infection at cohort inception, epilepsy,

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3 hearing impairment, and total number of different types of drugs prescribed, whilst  
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5 bowel incontinence showed a reduced risk of death. Of note, level of intellectual  
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7 disabilities whilst significant in the univariate analysis, was not retained in the  
8  
9 multivariable model.

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13 - Insert table 6 about here -  
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## 16 17 **Discussion**

### 18 19 ***Principle findings and interpretation***

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22 As far as we are aware, this is the first population-based study of adults with intellectual  
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24 disabilities to report in detail the factors associated with time to death, and to describe  
25  
26 their causes of death and quantify the SMR separately for adults with Down syndrome  
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28 and adults without Down syndrome. This is important, since adults with Down syndrome  
29  
30 form a notable proportion of all adults with intellectual disabilities (19% in this cohort),  
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32 and because they have a different pattern of clinical conditions compared with other  
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34 adults with intellectual disabilities.<sup>20</sup> We found that aspiration/reflux/choking is the most  
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36 common underlying cause of death in adults with intellectual disabilities, followed by  
37  
38 respiratory infection. They are also the most common all contributing causes of death.  
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40 The profile differed in the adults with Down syndrome for whom "Down syndrome",  
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42 followed by dementia, were recorded as the most common underlying cause of death,  
43  
44 and all contributing causes of death; with the next most common all contributing cause  
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46 of death being respiratory infection, then aspiration/reflux/choking. The proportion of  
47  
48 deaths that would have been amenable to good care for adults with intellectual  
49  
50 disabilities was more than double that seen in the general population. Although  
51  
52 aspiration/reflux/choking is not included in the ONS list of avoidable deaths, and  
53  
54 therefore not included in the figures we report on amenable deaths, we consider that  
55  
56 good care could have prevented many of these deaths. This appears to be very  
57  
58 important for adults with intellectual disabilities irrespective of whether they have Down  
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3 syndrome. Similarly, some other causes of deaths within this cohort, such as  
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5 constipation/mega-colon, and urinary tract infections do not appear on the ONS list of  
6  
7 avoidable deaths.  
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11 Clearly, this pattern of causes of death differs from that seen in the general population,  
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13 in whom the most common underlying causes of death are heart disease, then dementia,  
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15 then lung cancer in men, and dementia, then heart disease, then stroke in women.<sup>31</sup>  
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17 When all cancers are grouped together, in the general population, cancer is the leading  
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19 underlying cause of death in 30% of men and 26% of women, compared with this study  
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21 reporting 0% for adults with Down syndrome, and 15.2% for adults with intellectual  
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23 disabilities without Down syndrome – presumably as the adults with intellectual  
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25 disabilities are dying younger from other causes, and cancers increase with age.  
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29 We found an overall SMR of 2.24; 5.28 in the adults with Down syndrome and 1.93 for  
30  
31 the adults without Down syndrome. SMRs were higher for most ICD-10 chapter  
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33 groupings of conditions. It was higher in the women than the men, as has been  
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35 previously reported in most (supplementary table 1), but not all<sup>10,18</sup> previous reports.  
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37 The reason for this is unknown; in the general population, mortality rates have fallen in  
38  
39 recent decades, and more so in middle and older aged men than women (i.e. the sex  
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41 gap is narrowing at these ages), but we do not know what trends over time there have  
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43 been for people with intellectual disabilities. Having intellectual disabilities removes  
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45 differences in lifespan by sex compared with the general population; but sex was not a  
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47 predictor of mortality in our study, so the SMR difference may only be because of the  
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49 difference found in the general population by sex. SMRs were lowest with older age  
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51 groups, likely to be due to increased illness in the older general population and  
52  
53 conversely a healthier group with intellectual disabilities living to older ages compared  
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55 with those who die younger. Although SMR was higher with increasing severity of  
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57 intellectual disabilities, ability level was not retained within the multivariable model on  
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59 time to death. The factors that were independently associated with increased risk of  
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3 death, in order, were being percutaneous endoscopic gastrostomy/tube fed, Down  
4 syndrome, diabetes, having a lower respiratory tract infection at entry to the cohort,  
5 smoking, epilepsy, hearing impairment, total number of prescribed drugs, and age,  
6 whilst bowel incontinence had a reduced risk of death. Some of these predictors are  
7 similar to those reported in the general population, suggesting earlier mortality of adults  
8 with intellectual disabilities is largely accounted for by the higher rates of multi-  
9 morbidities that they experience compared with other people, and amenable deaths.<sup>32</sup>  
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13 Whilst accommodation type (not living with a family carer), ability level, not having day-  
14 time occupation, having spastic quadriplegia, visual impairment, constipation, ataxia/gait  
15 disorder, osteoporosis, hypertension, dysphagia, dyspnoea, gastro-oesophageal reflux  
16 disorder, total number of physical health disorders, not having impaired mobility, not  
17 having urinary incontinence, and not having autism, number of general practitioner  
18 consultations in the previous 12 months, total number of different types of health  
19 professionals providing care at the time of the health assessment, and antiepileptic  
20 drugs were related to time of death on univariate analyses, they were not retained in the  
21 multivariable model.  
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40 The majority of the adults with intellectual disabilities, with and without Down syndrome,  
41 died in an NHS hospital.  
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### 45 ***Comparison with previous literature***

46  
47 The overall SMR we report, higher SMR in women than men, and higher SMR at younger  
48 age groups is similar to the majority of previous reports. Most mortality studies with  
49 people with Down syndrome have been conducted with children. Previous reports of  
50 children and adults (combined) gave an SMR=5.5,<sup>19</sup> and for adults SMR=7.6,<sup>9</sup> compared  
51 with our finding for adults with Down syndrome of SMR=5.28. Recent systematic reviews  
52 reported people with intellectual disabilities on average died 20 years younger than other  
53 people, and people with Down syndrome died 28 years younger, although the majority  
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3 of the Down syndrome studies were not recent.<sup>1,2</sup> In our study we found the gap  
4 between the age at death of people with intellectual disabilities with and without Down  
5 syndrome to be only 5.3 years, possibly reflecting the increasing lifespan of people with  
6 Down syndrome exceeding increases in lifespan for people with intellectual disabilities  
7 without Down syndrome. Notably, after "Down syndrome", dementia was the most  
8 commonly reported underlying, and all contributing cause of death for the adults with  
9 Down syndrome, whereas studies in the past commented on congenital heart disease  
10 and respiratory causes.  
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21 For the cohort overall, respiratory infection and aspiration/reflux/choking were the most  
22 common all contributing causes of death. These conditions feature in previous studies on  
23 causes of death<sup>5,6,8,10,11</sup>, although there are inconsistencies between studies. By ICD-10  
24 chapter, our study found the most common underlying causes of death were diseases of  
25 the respiratory system, then of the circulatory system, followed by neoplasms. Others  
26 reported the most common to be vascular,<sup>10</sup> circulatory,<sup>5</sup> heart disease,<sup>17</sup> and jointly  
27 circulatory and neoplasm.<sup>18</sup>  
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38 Studies that investigated avoidable deaths in adults with intellectual disabilities found  
39 them to be more common than in the general population, due to deaths that would have  
40 been amenable to good care. Avoidable deaths have been reported in 44.7% of deaths  
41 of people with intellectual disabilities in England (mostly amenable deaths – figure not  
42 reported),<sup>6</sup> and in 31% in Australia,<sup>18</sup> compared with our figure of 38.9%. Avoidable  
43 deaths that would have been amenable to good care have been reported to occur in 37%  
44 of deaths of people with intellectual disabilities in England.<sup>5</sup> Our figure is slightly lower at  
45 29.8% but still more than double that found in the Scottish general population.<sup>30</sup> It  
46 should be noted that the ONS list of avoidable deaths was not designed specifically for  
47 people with intellectual disabilities, and it may emphasise some causes less relevant, and  
48 omit others that might be highly relevant in this population.<sup>5</sup>  
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### ***Strengths and limitations***

The strengths of the study include the thorough methods of case ascertainment for intellectual disabilities at baseline with verification of intellectual disabilities and its severity, suggesting results are generalisable in other high income countries.

Additionally, there were detailed clinical assessments at baseline, and a longitudinal design. The size of the cohort and the duration of follow-up is also a strength, as is the successful record linkage for 94% of participants. Our study does have a couple of limitations, specifically that the study was only conducted in one region of Scotland, and the reliance upon death certificate data to obtain cause of death.

### ***Implications***

It is important to know the factors that are associated with risk of death, and the common causes of death in this population, as these then inform the actions needed to reduce the unacceptably high SMRs experienced by people with intellectual disabilities.

It is not adequate to solely rely on the public health interventions available to everyone, even when they are accessible. Aspiration, reflux, and choking could, and should, be avoided by raising awareness of its consequences (death), and putting in place training on simple measures related to feeding, positioning, food consistency, and when to seek health advice from speech and language therapy, physiotherapy, nursing, and medical advice. Carers need to be aware of how the adults they care for express pain, so that conditions such as gastrointestinal ulcers are attended to, prior to the extreme point of perforation, and so treatable conditions such as constipation and urinary tract infections are managed before they lead to respiratory distress and sepsis. Quality of care is important; adults with intellectual disabilities need just as good care for their diabetes and epilepsy (and other conditions) as the rest of the population, with reasonable adjustments to address accessibility, and accessible smoking cessation programs.

### Future research

Further research on larger samples is needed, particularly with regards to replicating and extending our findings on the factors that are associated with risk of death, and any sex differences in them, so that practitioners can focus on actions to improve the life expectancy of adults with intellectual disabilities, with and without Down syndrome.

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The researchers are independent from the funders.

## Competing interests

The authors declare no competing interests.

## Author's contributions

S-AC is principle investigator, she conceived and managed the project, interpreted data, and wrote the first draft of the manuscript. LA contributed to the conception of the project, and project management. NG designed and supervised the statistical analysis, and contributed to data interpretation and drafting of the manuscript. PMcS implemented and refined the statistical analysis, and contributed to data interpretation, and drafting of the manuscript. AJ implemented and refined the statistical analysis, and contributed to data interpretation. AH contributed to data linkage and interpretation, and drafting of the manuscript. CMcC provided expertise on data linkage and methods, and drafting of the manuscript. DK contributed to data interpretation and drafting of the manuscript. CM contributed to data interpretation, and drafting of the manuscript. All approved the final version of the manuscript. S-AC is the study guarantor.

## Data sharing

Data is available via NHS GG&C safe haven upon application.

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**Table 1. Cohort characteristics at time of the health assessment, summarised overall and by death status during the follow-up period**

| Variable           | Statistics / Groups | All participants (N=961) | Deceased participants (N=294) | Alive participants (N=667) |
|--------------------|---------------------|--------------------------|-------------------------------|----------------------------|
| Age (years)        | Mean (SD)           | 44.1 (14.6)              | 52.4 (13.6)                   | 40.5 (13.6)                |
|                    | Min, max            | 16, 83                   | 18, 83                        | 16, 77                     |
| Age group          | 16-25 years         | 127 (13.2%)              | 10 (3.4%)                     | 117 (17.5%)                |
|                    | 26-35 years         | 153 (15.9%)              | 26 (8.8%)                     | 127 (19.0%)                |
|                    | 36-45 years         | 246 (25.6%)              | 49 (16.7%)                    | 197 (29.5)                 |
|                    | 46-55 years         | 205 (21.3%)              | 85 (28.8%)                    | 120 (18.0%)                |
|                    | >55 years           | 230 (23.9%)              | 124 (42.0%)                   | 106 (15.9%)                |
| Sex                | Male                | 525 (54.6%)              | 154 (52.4%)                   | 371 (55.6%)                |
|                    | Female              | 436 (45.3%)              | 140 (47.5%)                   | 296 (44.4%)                |
| Ability level      | Mild ID             | 382 (39.7%)              | 92 (31.2%)                    | 290 (43.5%)                |
|                    | Moderate ID         | 236 (24.5%)              | 73 (24.7%)                    | 163 (24.4%)                |
|                    | Severe ID           | 180 (18.7%)              | 67 (22.7%)                    | 113 (16.9%)                |
|                    | Profound ID         | 163 (17.0%)              | 62 (21.1%)                    | 101 (15.1%)                |
| Accommodation type | Family carer        | 374 (38.9%)              | 70 (23.8%)                    | 304 (45.6%)                |
|                    | Independent         | 93 (9.7%)                | 36 (12.2%)                    | 57 (8.5%)                  |
|                    | Paid support        | 435 (45.2%)              | 161 (54.6%)                   | 274 (41.1%)                |
|                    | Congregate care     | 59 (6.1%)                | 27 (9.2%)                     | 32 (4.8%)                  |
| Down syndrome      | No                  | 782 (81.4%)              | 230 (78.2%)                   | 552 (82.8%)                |
|                    | Yes                 | 179 (18.6%)              | 64 (21.7%)                    | 115 (17.2%)                |

ID=intellectual disabilities; SD=standard deviation

**Table 2. Standardised mortality ratios**

| Variable   | Groups  | SMR (95% CI)         |
|--|---|----------------------|
| All participants                                       | -   | 2.24 (1.99, 2.50)    |
| Age group*   | 15-25 years   | 18.73 (0.37, 37.09)  |
|  | 26-35 years   | 4.21 (1.29, 7.13)    |
|  | 36-45 years   | 3.86 (2.28, 5.44)    |
|  | 46-55 years   | 3.77 (2.90, 4.74)    |
|  | >55 years   | 1.86 (1.60, 2.12)    |
| Sex  | Male  | 1.69 (1.42, 1.95)    |
|  | Female  | 3.48 (2.90, 4.06)    |
| Ability level  | Mild ID   | 1.60 (1.27, 1.92)    |
|  | Moderate ID   | 2.10 (1.62, 2.58)    |
|  | Severe ID   | 2.78 (2.11, 3.44)    |
|  | Profound ID   | 4.14 (3.11, 5.17)    |
| Down syndrome  | No  | 1.93 (1.68, 2.18)    |
|  | Yes   | 5.28 (3.98, 6.57)    |
| Underlying causes of death grouped by ICD-10 chapter** | Congenital malformations, deformations and chromosomal abnormalities                                | 17.26 (10.75, 23.78) |
|  | Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | 7.50 (-7.20, 22.20)  |
|  | Diseases of the circulatory system  | 5.55 (4.01, 7.09)    |
|  | Diseases of the digestive system  | 16.13 (8.23, 24.04)  |
|  | Diseases of the genitourinary system  | 3.65 (0.73, 6.57)    |
|  | Diseases of the musculoskeletal system and connective tissue  | 5.40 (-0.71, 11.52)  |
|  | Diseases of the nervous system  | 7.73 (5.13, 10.32)   |
|  | Diseases of the respiratory system  | 6.78 (5.02, 8.54)    |

|  |   |                     |
|--|---|---------------------|
|  | Diseases of the skin and subcutaneous tissue  | 2.75 (-2.64, 8.15)  |
|  | Endocrine, nutritional and metabolic diseases   | 3.43 (1.05, 5.81)   |
|  | External causes of morbidity and mobility   | 11.08 (3.40, 18.76) |
|  | Infectious and parasitic diseases   | 8.93 (1.78, 16.07)  |
|  | Mental and behavioural disorders  | 12.64 (3.27, 22.00) |
|  | Neoplasms   | 6.31 (4.19, 8.43)   |
|  | Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified | 19.51 (0.39, 38.63) |

CI=confidence intervals; ID=intellectual disabilities; SMR=standardised mortality ratios

\*Data used for comparison with General Population (GG&C Health Board) provides data in 5 year age bands therefore 15+. Data on adults with ID are 16+

\*\* Negative Lower CI and wide CIs indicate low number of observed deaths in study population

**Table 3. Underlying causes of death grouped by ICD-10 chapter, where cause of death is known**

| ICD-10 chapter  | Participants with Down syndrome (N=57) | Participants without Down syndrome (N=205) |
|---|--|--|
| Certain infectious and parasitic diseases   | 5 (8.8%)                               | <5   |
| Neoplasms   | <5                                     | 33 (16.1%)                                 |
| Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | 0                                      | <5   |
| Endocrine, nutritional and metabolic diseases   | 0                                      | 8 (3.9%)                                   |
| Mental and behavioural disorders  | 5 (8.8%)                               | <5   |
| Diseases of the nervous system  | 7 (12.3%)                              | 27 (13.2%)                                 |
| Diseases of the eye and adnexa  | 0                                      | 0  |
| Diseases of the ear and mastoid process   | 0                                      | 0  |
| Diseases of the circulatory system  | 8 (14.0%)                              | 42 (20.5%)                                 |
| Diseases of the respiratory system  | 8 (14.0%)                              | 49 (23.9%)                                 |
| Diseases of the digestive system  | 0                                      | 16 (7.8%)                                  |
| Diseases of the skin and subcutaneous tissue  | 0                                      | <5   |
| Diseases of the musculoskeletal system and connective tissue  | 0                                      | <5   |
| Diseases of the genitourinary system  | <5                                     | 5 (2.4%)                                   |
| Pregnancy, childbirth and the puerperium  | 0                                      | 0  |
| Certain conditions originating in the perinatal period  | 0                                      | 0  |
| Congenital malformations, deformations and chromosomal abnormalities                                | 21 (36.8%)                             | 6 (2.9%)                                   |
| Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified             | 0                                      | <5   |
| External causes of morbidity and mortality  | <5                                     | 7 (3.4%)                                   |
| All deaths  | 57 (100%)                              | 205 (100%)                                 |

ICD-10=International Statistical Classification of Diseases and Related Health Problems, 10th Revision

**Table 4. Underlying causes of death grouped by specific individual causes or related groups of causes, where cause of death is known**

| <b>Causes</b>                      | <b>Participants with Down syndrome (N=57)</b> | <b>Participants without Down syndrome (N=205)</b> |
|------------------------------------|---|---|
| Aspiration/reflux/choking          | <5  | 22 (10.8%)  |
| Respiratory infection              | <5  | 21 (10.3%)  |
| Down syndrome                      | 21 (36.8%)                                    | 0   |
| Other malignancy                   | 0   | 19 (9.3%)   |
| Other condition                    | <5  | 17 (8.3%)   |
| Epilepsies                         | <5  | 13 (6.4%)   |
| Acute myocardial infarction        | <5  | 13 (6.4%)   |
| Gastro-intestinal malignancy       | <5  | 12 (5.9%)   |
| Stroke                             | <5  | 11 (5.4%)   |
| Other cardiovascular disease       | <5  | 11 (5.4%)   |
| Other respiratory condition        | <5  | 9 (4.4%)  |
| Other infection                    | 5 (8.8%)                                      | 6 (2.9%)  |
| Cerebral palsy                     | 0   | 11 (5.4%)   |
| Dementia                           | 9 (15.8%)                                     | 0   |
| Other gastrointestinal disorders   | 0   | 8 (3.9%)  |
| Ulcer/gastrointestinal perforation | 0   | 7 (3.4%)  |
| Diabetes                           | 0   | 7 (3.4%)  |
| Other congenital condition         | 0   | 6 (2.9%)  |
| Other ischaemic heart condition    | 0   | 6 (2.9)   |
| Mental health                      | 0   | <5  |
| Other neurological conditions      | <5  | <5  |
| Renal failure                      | <5  | <5  |
| All deaths                         | 57 (100%)                                     | 205 (100%)  |

**Table 5. All contributing causes of death grouped by specific individual causes or related groups of causes, where cause of death is known**

| <b>Causes</b>                       | <b>Participants with Down syndrome (N=57)</b> | <b>Participants without Down syndrome (N=205)</b> |
|-------------------------------------|---|---|
| Respiratory infection               | 22 (38.6%)                                    | 49 (23.9%)  |
| Aspiration/reflux/choking           | 11 (19.3%)                                    | 41 (20.0%)  |
| Down syndrome                       | 43 (75.4%)                                    | <5  |
| Other condition                     | 8 (14.0%)                                     | 33 (16.1%)  |
| Other cardiovascular disease        | 8 (14.0%)                                     | 30 (14.6%)  |
| Other respiratory conditions        | <5  | 31 (15.1%)  |
| Other infection                     | 9 (15.8%)                                     | 24 (11.7%)  |
| Intellectual disabilities           | <5  | 31 (15.1%)  |
| Epilepsies                          | 8 (14.0%)                                     | 24 (11.7%)  |
| Dementia                            | 24 (42.1%)                                    | <5  |
| Other neoplasms                     | <5  | 23 (11.2%)  |
| Cerebral palsy                      | <5  | 24 (11.7%)  |
| Acute myocardial infarction         | 5 (8.8%)                                      | 19 (9.3%)   |
| Other gastrointestinal disorders    | <5  | 18 (8.8%)   |
| Diabetes                            | <5  | 19 (9.3%)   |
| Other ischaemic heart disease       | <5  | 19 (9.3%)   |
| Renal failure                       | <5  | 16 (7.8%)   |
| Stroke                              | <5  | 17 (8.3%)   |
| Other congenital condition          | <5  | 15 (7.3%)   |
| Gastrointestinal malignant neoplasm | <5  | 12 (5.9%)   |
| Ulcer/gastrointestinal perforation  | <5  | 10 (4.9%)   |
| Mental health                       | <5  | 10 (4.9%)   |
| Other neurological condition        | <5  | 8 (3.9%)  |
| Heart failure                       | <5  | 7 (3.4%)  |
| Injuries and accidents              | <5  | 8 (3.9%)  |
| Medical/surgical complications      | <5  | <5  |
| Secondary malignancies              | <5  | <5  |
| Thyroid disorders                   | <5  | <5  |
| Metabolic disorder                  | <5  | <5  |
| All deaths                          | 57 (100%)                                     | 205 (100%)  |

**Table 6. Multivariable model results for the outcome time to death**

| Variable                          |     | Hazard ratio | 95% CI        | p-value |
|-----------------------------------|-----|--------------|---------------|---------|
| Age                               |     | 1.056        | 1.046, 1.066  | <0.0001 |
| Smoker                            | No  | 1            | -             |         |
|                                   | Yes | 1.531        | 1.1011, 2.128 | 0.0112  |
| Down syndrome                     | No  | 1            | -             |         |
|                                   | Yes | 2.440        | 1.787, 3.332  | <0.0001 |
| Epilepsy                          | No  | 1            | -             |         |
|                                   | Yes | 1.511        | 1.173, 1.946  | 0.0014  |
| Hearing impairment                | No  | 1            | -             |         |
|                                   | Yes | 1.320        | 1.030, 1.692  | 0.0284  |
| Bowel incontinence                | No  | 1            | -             |         |
|                                   | Yes | 0.490        | 0.376, 0.640  | <0.0001 |
| Diabetes                          | No  | 1            | -             |         |
|                                   | Yes | 2.346        | 1.553, 3.542  | <0.0001 |
| PEG/tube fed                      | No  | 1            | -             |         |
|                                   | Yes | 2.346        | 1.135, 5.989  | 0.00240 |
| Lower respiratory track infection | No  | 1            | -             |         |
|                                   | Yes | 1.782        | 1.315, 2.415  | 0.0002  |
| Total number of prescribed drugs  |     | 1.066        | 1.016, 1.118  | 0.0085  |

CI=confidence interval; PEG=percutaneous endoscopic gastrostomy

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### Supplementary table 1. Previously reported standardised mortality ratios, causes, and risks for death

| Author                                 | Country   | SMR (95% confidence interval)   | Number of deaths                 | Causes of death and risk factors for death   |
|--|-----------|---|----------------------------------|--|
| Forsgren et al (1996) <sup>7</sup>     | Sweden    | 4.2 (3.3, 5.3) at 20-59y; 1.1 (0.9, 1.5) at 60+y<br><i>Without epilepsy:</i><br>3.8 (2.8, 5.0) at 20-59y; 1.1 (0.8, 1.5) at 60+y<br><i>With epilepsy:</i><br>5.0 (2.9, 8.7) at 20-59y; 2.4 (0.9, 6.1) at 60+y<br><i>With epilepsy and cerebral palsy:</i><br>8.0 (4.1, 15.7) at 20-59y; 0.9 (0.1, 6.6) at 60+y<br><i>M:</i> 1.6 (1.2, 2.0) at 0-60+y<br><i>F:</i> 2.6 (2.0, 3.3) at 0-60+y<br><i>Mild ID:</i> 1.8 (1.1, 2.7) at 0-60+y<br><i>Moderate ID:</i> 1.5 (1.1, 2.0) at 0-60+y<br><i>Severe ID:</i> 2.0 (1.5, 2.6) at 0-60+y<br><i>Profound ID:</i> 8.1 (5.6, 11.7) at 0-60+y | 124 at 0-60+y;<br>112 at 20-60+y | <i>Underlying cause at 0-60+y:</i><br>Congenital anomalies: SMR=46.3 (32.9, 65.0)<br>Nervous system: SMR=9.7 (5.5, 17.0)<br>Mental disorder: SMR=4.0 (1.9, 8.4)<br>Respiratory: SMR=3.3 (2.0, 5.5)<br>Circulatory: SMR=2.1 (1.6, 2.7)<br>Violent death: SMR=1.4 (0.6, 2.8)<br>Neoplasm: SMR=0.9 (0.6, 1.6) |
| Durvasula & Beange (2002) <sup>8</sup> | Australia | 4.9 (3.4, 6.4) at 10-59y<br><i>M:</i> 4.1 (2.4, 5.9) at 10-59y<br><i>F:</i> 6.2 (3.3, 9.1) at 10-59y  | 40 at 10-59y;<br>31 at 20-59y    | <i>Underlying cause at 10-59y:</i><br>Respiratory: 30% (pneumonia, aspiration)<br>External cause: 20%<br>Neoplasm: 17%<br>Heart disease: 15% (congenital heart disease 50%)<br>Gastrointestinal: 1.5% (ischaemic bowel, perforated peptic ulcer, post-operative peritonitis)<br>Seizure: 5%                |
| Tyrer et al (2007) <sup>9</sup>        | England   | 3.24 (2.93, 3.56) at 20-70+y<br><i>M:</i> 2.86 (2.50, 3.26) at 20-70+y<br><i>F:</i> 3.63 (3.12, 4.20) at 20-70+y<br>1.51 (1.23, 1.83) to 11.50 (8.14, 15.78) at 20-70+y<br><i>M:</i> 1.39 (1.03, 1.82) to 8.83 (5.60, 13.25) at 20-70+y<br><i>F:</i> 1.60 (1.18, 2.12) to 17.22 (9.64, 28.4) at 20-70+y<br><i>With Down syndrome:</i> 7.60 at 20-70+y<br><i>Without Down syndrome:</i> 2.70 at 20-70+y  | 409 at 20-70+y                   | Not reported   |
| Patja et al (2008) <sup>10</sup>       | Finland   | <i>M:</i> 2.2 at 20-39y, 1.0 at 40-59y, 1.0 at 60+y<br><i>F:</i> 1.4 at 20-39y, 1.1 at 40-49y, 1.0 at 60+y<br><i>Mild ID:</i><br><i>M:</i> 1.6 at 20-39y, 1.0 at 40-59y, 1.0 at 60+y<br><i>F:</i> 1.2 at 20-39y, 1.1 at 40-49y, 1.0 at 60+y   | 1,046 at 20-97y                  | <i>Underlying cause at 2-97y:</i><br>Vascular: 36% (cardiac infarct 33%, cerebral infarct 33%, congenital heart disease 18%, pulmonary infarct 6%)<br>Respiratory: 22% (pneumonia 83%, COPD 11%)   |

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|   |                     |  |                                      |   |
|---|---------------------|--|--------------------------------------|---|
|   |                     | <p><b>Moderate ID:</b><br/>M: 2.3 at 20-39y, 1.1 at 40-59y, 1.0 at 60+y<br/>F: 1.5 at 20-39y, 1.1 at 40-49y, 1.0 at 60+y</p> <p><b>Severe ID:</b><br/>M: 2.6 at 20-39y, 1.2 at 40-59y, 1.0 at 60+y<br/>F: 1.6 at 20-39y, 1.0 at 40-49y, 1.0 at 60+y</p> <p><b>Profound ID:</b><br/>M: 2.1 at 20-39y, 1.1 at 40-59y, 1.0 at 60+y<br/>F: 1.3 at 20-39y, 1.2 at 40-49y, 1.0 at 60+y</p> |                                      | <p>Neoplasm: 11% (Digestive 44%, respiratory 15%, urogenital, 12%)<br/>Digestive: 7% (intestinal obstruction 25%, ulcer perforation 13%)<br/>Accidents and poisonings: 7% (commonest was fatal fracture, then poisoning)<br/>Vascular, neoplasia, and accident causes were less common than sex-age-related general population; Digestive were 2.5 times, Respiratory 2.6-5.8 times more common</p>   |
| Tyrer & McGoher (2009) <sup>11</sup>      | England             | <p>2.77 (2.53, 3.03) at 20+y<br/>M: 2.28 (2.02, 2.56) at 20+y<br/>F: 3.24 (2.83, 3.69) at 20+y</p>   | 503 at 20+y                          | <p><b>Underlying cause of death at 20+y:</b><br/>Pneumonia: 1.3% (OR=6.47 (5.00, 8.23))<br/>Nervous system: 3.1% (OR=16.30 (12.61, 20.74))<br/>Other respiratory: 12.9% (OR=4.64 (3.58, 5.91))<br/>Ischaemic heart disease: 11.5% (OR=1.49 (1.13, 1.92))<br/>Neoplasm: 9.3%<br/>Congenital anomalies: 9.1% (OR=85.60 (62.67, 114.18))<br/>Cerebrovascular disease: 7.8% (OR=2.40 (1.71, 3.28))</p>  |
| Oullette-Kuntz et al (2015) <sup>12</sup> | Canada              | <p>2.5 (2.1, 2.9) at 0-60+y<br/>M: 2.1 (1.7, 2.6) at 0-60+y<br/>F: 3.0 (2.4, 3.8) at 0-60+y<br/>M: 1.7 (1.3, 2.3) to 3.4 (2.3, 4.7) at 20-60+y<br/>F: 2.1 (1.4, 2.9) to 6.1 (4.1, 8.6) at 20-60+y</p>  | 172 at 0-60+y;<br>158 at 20-60+y     | <p><b>Risk factors for death:</b><br/>Age, Down syndrome (OR=1.76 at 20-39y; OR=1.69 at 40-59y; OR=22.3 at 60+y), cerebral palsy (OR=2.39 at 20-39y; OR=0.93 at 40-59y; OR=0.50 at 60+y), blindness/low vision (OR not given), technological dependence/medical fragility (OR=1.95 at 20-39y; OR=7.28 at 40-59y; OR=3.42 at 60+y), wheelchair dependence (OR=5.96 at 20-39y; OR=2.89 at 40-59y; OR=2.56 at 60+y), mobility impairment without wheelchair dependence (OR not given), epilepsy (OR=1.8 at 20-39y; OR=1.80 at 40-59y; OR=1.09 at 60+y)</p> |
| Florio & Troller (2015) <sup>13</sup>     | Australia           | <p>2.48 (2.32, 2.64) at 0-85+y<br/>3.15 (2.94, 3.38) at 5-69y<br/>M: 2.52 (2.29, 2.77) at 5-69y<br/>F: 4.26 (3.83, 4.74) at 5-69y</p>  | 953 at 0-85+y;<br>831 at 15+y        | Not reported  |
| McCarron et al (2015) <sup>14</sup>       | Republic of Ireland | <p>3.85 (3.70, 4.00) at 0-80+y<br/>M: 3.09 (2.93, 3.25) at 0-80+y<br/>F: 4.90 (4.63, 5.17) at 0-80+y<br/>2.71 (2.41, 3.04) to 6.09 (5.29, 6.96) at 20-80y<br/>M: 2.50 (2.18, 2.86) to 4.50 (3.69, 5.44) at 20-80y<br/>F: 2.71 (2.32, 3.14) to 10.07 (8.99, 13.10) at 20-80y</p>  | 2,666 at 0-80+y;<br>2,394 at 20-80+y | Not reported  |

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|                                      |         |  |                                     |  |
|--------------------------------------|---------|--|-------------------------------------|--|
| Heslop & Glover (2015) <sup>15</sup> | England | Median 2.13 (interquartile range 1.09, 2.83) across geographic areas at 18-65+y  | 18-65+y                             | Not reported   |
| Arvio et al (2016) <sup>16</sup>     | Finland | <p><i>Mild ID:</i><br/>                 2.28 (2.18, 2.39) at 0-60+y<br/>                 1.99 (1.85, 2.13) to 2.77 (2.36, 3.23) at 15-60+y<br/> <i>M:</i> 2.01 (1.88, 2.14) at 0-60+y<br/> <i>F:</i> 2.80 (2.60, 3.01) at 0-60+y<br/> <i>Severe ID:</i><br/>                 3.41 (3.30, 3.52) at 0-60+y<br/>                 2.07 (1.96, 2.19) to 8.77 (7.77, 9.87) at 15-60+y<br/> <i>M:</i> 2.59 (2.48, 2.72) at 0-60+y<br/> <i>F:</i> 5.24 (4.99, 5.50) at 0-60+y</p>  | 5,171 at 0-60+y;<br>5,053 at 15-60y | Not reported   |
| Hosking et al (2016) <sup>5</sup>    | England | <p>HR=3.62 (3.33, 3.93) at 18-84y<br/> <i>M:</i> HR=3.30 (2.96, 3.68) at 18-84y<br/> <i>F:</i> HR=4.10 (3.61, 4.66) at 18-84y<br/> <i>With Down syndrome:</i> HR=9.21 (7.22, 11.76)<br/> <i>Without Down syndrome:</i> HR=3.19 (2.92, 3.49)<br/> <i>With epilepsy:</i> HR=6.04 (5.04, 7.24)<br/> <i>Without epilepsy:</i> HR=3.18 (2.90, 3.50)<br/> <i>With high level of support needs:</i> HR=4.77 (4.08, 5.59)<br/> <i>Without high level of support needs:</i> HR=3.28 (2.98, 3.62)<br/> <i>With autism:</i> HR=2.39 (1.45, 3.96)<br/> <i>Without autism:</i> HR=3.66 (3.37, 3.98)<br/> <i>In communal/shared homes:</i> HR=4.99 (4.36, 5.73)<br/> <i>Not in communal/shared homes:</i> HR=3.05 (2.74, 3.30)</p> | 656 at 18-84y                       | <p><i>Underlying cause of death at 18-84y:</i><br/>                 Circulatory: 21.8%, HR=3.05 (2.56, 3.64)<br/>                 Respiratory: 18.8% (pneumonia and aspiration pneumonia), HR=3.68 (5.38, 8.29)<br/>                 Neoplasm: 14.0%, HR=1.44 (1.18, 1.76)<br/>                 Nervous system: 11.6%, HR=13.79 (9.70, 19.62)<br/>                 Digestive: 7.0%, HR=4.02 (2.92, 5.54)<br/>                 Congenital anomalies: 6.9%, HR could not be estimated<br/>                 Mental disorders: 5.3%, HR=7.99 (5.19, 12.31)<br/>                 External causes: 4.1%, HR=1.85 (1.26, 2.71)<br/>                 Genitourinary: 3.1%, HR=10.89 (6.09, 19.47)<br/>                 Endocrine, nutritional, and metabolic: 2.0%, HR=5.38 (2.79, 10.07)<br/> <i>Down syndrome:</i> Respiratory: 20.3% (or 42.4% if "Down syndrome" is excluded as an underlying cause of death)<br/> <i>Avoidable deaths:</i> 37% amenable (27% controls), 19% preventable (40% controls)</p> |
| Lauer (2016) <sup>17</sup>           | USA     | Not reported   | 438 in 2012, 409 in 2013, at 18+y   | <p><i>Major cause of death, 2012, 2013</i><br/>                 Heart disease: 16.0%, 13.7%<br/>                 Neoplasm: 13.7%, 13.4%<br/>                 Alzheimer disease: 13.0%-12.2% (48% in Down syndrome)<br/>                 Aspiration pneumonia: 9.4%, 8.6%<br/>                 Septicaemia: 10.0%, 8.6%<br/>                 Chronic lower respiratory diseases: 4.6%, 6.6%<br/>                 Unintentional injury: 4.8%, 3.2%</p>   |

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|                                    |           |  |                |   |
|------------------------------------|-----------|--|----------------|---|
| Troller et al (2017) <sup>18</sup> | Australia | 1.3 (1.2, 1.5) at 20+y<br>4.0 (3.1, 5.2) at 20-44y<br>2.3 (2.0, 2.7) at 45-64y<br>1.0 (0.8, 1.2) at 65+y<br>M: 1.4 (1.1, 1.6) at 20+y<br>F: 1.3 (1.1, 1.6) at 20+y   | 732 at 20-65+y | <p><i>Underlying cause at 20-65+y:</i><br/>Circulatory: 18%<br/>Neoplasm: 18%<br/>Nervous: 16%<br/>Respiratory: 10%<br/>Congenital anomaly: 11%<br/>Injury and poisoning: 6%<br/>Digestive: 5%<br/>Avoidable deaths: 31%</p>  |
| Glover et al (2017) <sup>6</sup>   | England   | 3.18 (2.94, 3.43) at 0-99y<br>M: 3.03 (2.73, 3.35) at 0-99y<br>F: 3.40 (3.02, 3.81) at 0-99y<br>1.6 (1.2, 2.1) to 7.8 (5.4, 11.1) at 18-99y<br>M: 1.5 (0.9, 2.2) to 6.6 (4.0, 10.1) at 18-99y<br>F: 1.7 (1.1, 2.4) to 11.6 (6.0, 20.2) at 18-99y | 664 at 0-99y   | <p><i>Underlying cause at 0-99y:</i><br/>Circulatory: 22% (ischaemic heart disease 37.5%, cerebrovascular 1.7%, thrombophlebitis 6.6%, cardiomyopathy 9%, PE 3.9%), SMR=2.8 (2.4, 3.3)<br/>Respiratory: 19% (pneumonia 50.0%, pneumonitis 21.0%), SMR=1.9 (4.0, 5.9)<br/>Neoplasm: 3.1% (digestive 36.8%, respiratory 13.8%, female genital tract 10.3%, lymphoid and haematopoietic 10.3%), SMR=1.1 (0.9, 1.4)<br/>Nervous: 12.8%, SMR=9.8 (7.8, 12.1)<br/>Congenital anomalies: 8.4%, SMR=72.9 (55.1, 94.7)<br/>Digestive: 7.8%, SMR=4.0 (3.0, 5.2)<br/>No ICD10 chapter had fewer than expected deaths<br/>Other common single causes: dementia 33/664, epilepsy 26/664, cerebral palsy 23/664<br/><i>Avoidable deaths:</i><br/>44.7% (41.0% to 48.5%), mostly amenable<br/>M: 50.9% (45.0% to 56.0%); F: 36.9% (31.5%, 42.5%)</p> |

COPD=chronic obstructive pulmonary disease; HR=hazard ratio; ID=intellectual disabilities; OR=odds ratio; PE=pulmonary embolism; SMR=standardised mortality ratio; y=years

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## **Supplementary table 2. Groupings of related causes of deaths**

### **Infectious diseases**

#### **Infection**

ENTEROCOLITIS DUE TO CLOSTRIDIUM DIFFICILE  
 SEPSIS DUE TO STAPHYLOCOCCUS AUREUS  
 SEPSIS, UNSPECIFIED  
 BACTERIAL INFECTION, UNSPECIFIED  
 SUBACUTE SCLEROSING PANENCEPHALITIS  
 CHRONIC VIRAL HEPATITIS B WITHOUT DELTA-AGENT  
 PULMONARY CANDIDIASIS  
 NECROTISING FASCIITIS  
 URINARY TRACT INFECTION, SITE NOT SPECIFIED

### **Neoplasms**

#### **Gastrointestinal malignant neoplasms**

MALIGNANT NEOPLASM OF PAROTID GLAND  
 MALIGNANT NEOPLASM, OESOPHAGUS, UNSPECIFIED  
 MALIGNANT NEOPLASM, STOMACH, UNSPECIFIED  
 MALIGNANT NEOPLASM, CAECUM  
 MALIGNANT NEOPLASM, SIGMOID COLON  
 MALIGNANT NEOPLASM, COLON, UNSPECIFIED  
 INTRAHEPATIC BILE DUCT CARCINOMA  
 NEOPLASM OF UNCERTAIN OR UNKNOWN BEHAVIOUR, OTHER DIGESTIVE ORGANS

#### **Other neoplasms**

MALIGNANT NEOPLASM, LOWER LOBE, BRONCHUS OR LUNG  
 MALIGNANT NEOPLASM, BRONCHUS OR LUNG, UNSPECIFIED  
 MALIGNANT NEOPLASM, BREAST, UNSPECIFIED  
 MALIGNANT NEOPLASM, ENDOMETRIUM  
 MALIGNANT NEOPLASM OF OVARY  
 MALIGNANT NEOPLASM, TESTIS, UNSPECIFIED  
 MALIGNANT NEOPLASM, BLADDER, UNSPECIFIED  
 MALIGNANT NEOPLASMS OF THYROID GLAND  
 WALDENSTROM MACROGLOBULINAEMIA  
 NON-HODGKIN'S LYMPHOMA, UNSPECIFIED  
 MALIGNANT NEOPLASM OF UNSPECIFIED SITE  
 NEOPLASM OF UNCERTAIN OR UNKNOWN BEHAVIOUR, TRACHEA, BRONCHUS AND LUNG  
 SECONDARY MALIGNANT NEOPLASM OF LUNG  
 SECONDARY MALIGNANT NEOPLASM OF LIVER AND INTRAHEPATIC BILE DUCT  
 SECONDARY MALIGNANT NEOPLASM OF BRAIN AND CEREBRAL MENINGES  
 SECONDARY MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES

### **Endocrine and metabolic diseases**

#### **Diabetes**

INSULIN-DEPENDENT DIABETES MELLITUS WITHOUT COMPLICATIONS  
 NON-INSULIN-DEPENDENT DIABETES MELLITUS WITH RENAL COMPLICATIONS  
 NON-INSULIN-DEPENDENT DIABETES MELLITUS W. PERIPHERAL CIRC. COMPLICATIONS  
 NON-INSULIN-DEPENDENT DIABETES MELLITUS WITHOUT COMPLICATIONS  
 UNSPECIFIED DIABETES MELLITUS WITH RENAL COMPLICATIONS

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UNSPECIFIED DIABETES MELLITUS WITHOUT COMPLICATIONS

ABNORMAL GLUCOSE TOLERANCE TEST

HYPERGLYCAEMIA, UNSPECIFIED

### **Metabolic disorders**

OTHER HYPERPHENYLALANINAEMIAS

DISORDERS OF PHOSPHORUS METABOLISM & PHOSPHATASES

DISORDERS OF PLASMA-PROTEIN METABOLISM, NOT ELSEWHERE CLASSIFIED

### **Mental disorders**

#### **Dementias**

VASCULAR DEMENTIA, UNSPECIFIED

UNSPECIFIED DEMENTIA

ALZHEIMER'S DISEASE WITH LATE ONSET

ALZHEIMER'S DISEASE, UNSPECIFIED

#### **Mental health**

MENTAL AND BEHAVIOURAL DISORDERS DUE TO ACUTE INTOXICATION WITH ALCOHOL

MENTAL AND BEHAVIOURAL DISORDERS DUE TO ALCOHOL DEPENDENCE SYNDROME

MENTAL AND BEHAVIOURAL DISORDERS DUE TO USE OF TOBACCO, UNSPECIFIED

SCHIZOPHRENIA, UNSPECIFIED

BIPOLAR AFFECTIVE DISORDER, UNSPECIFIED

OTHER & UNSPEC SYMPTOMS & SIGNS INVOLVING COGNITIVE FUNCTIONS & AWARENESS

INTENTIONAL SELF-HARM BY JUMPING FROM A HIGH PLACE

#### **Intellectual disabilities**

UNSPECIFIED MENTAL RETARDATION

DEVELOPMENTAL DISORDER OF SCHOLASTIC SKILLS, UNSPECIFIED

### **Nervous system**

#### **Epilepsies**

GENERALIZED IDIOPATHIC EPILEPSY AND EPILEPTIC SYNDROMES

EPILEPSY, UNSPECIFIED

STATUS EPILEPTICUS, UNSPECIFIED

MYOTONIC DISORDERS

OTHER AND UNSPECIFIED CONVULSIONS

#### **Cerebral palsy**

SPASTIC QUADRAPLEGIC CEREBRAL PALSY

SPASTIC HEMIPLEGIC CEREBRAL PALSY

OTHER CEREBRAL PALSY

CEREBRAL PALSY, UNSPECIFIED

TETRAPLEGIA, UNSPECIFIED

#### **Other neurological conditions**

SEQUELAE OF INFLAMMATORY DISEASES OF CENTRAL NERVOUS SYSTEM

PARKINSON'S DISEASE

MYONEURAL DISORDER, UNSPECIFIED

ENCEPHALITIS, MYELITIS AND ENCEPHALOMYELITIS, UNSPECIFIED

ANOXIC BRAIN DAMAGE, NOT ELSEWHERE CLASSIFIED

BLINDNESS, BINOCULAR

OTHER DISORDERS OF NERVOUS SYSTEM, NOT ELSEWHERE CLASSIFIED

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## **Circulatory system**

### **Acute myocardial infarction**

ACUTE MYOCARDIAL INFARCTION, UNSPECIFIED

CARDIAC ARREST, UNSPECIFIED

### **Other ischaemic heart disease**

HYPERTENSIVE HEART DISEASE WITHOUT (CONGESTIVE) HEART FAILURE

ACUTE ISCHAEMIC HEART DISEASE, UNSPECIFIED

ATHEROSCLEROTIC HEART DISEASE

CHRONIC ISCHAEMIC HEART DISEASE, UNSPECIFIED

ATHEROSCLEROSIS OF AORTA

GENERALIZED AND UNSPECIFIED ATHEROSCLEROSIS

### **Heart failure**

HEART FAILURE, UNSPECIFIED

LEFT VENTRICULAR FAILURE

CONGESTIVE HEART FAILURE

### **Other cardiovascular disease**

PULMONARY EMBOLISM WITHOUT MENTION OF ACUTE COR PULMONALE

OTHER SPECIFIED PULMONARY HEART DISEASES

PULMONARY HEART DISEASE, UNSPECIFIED

AORTIC (VALVE) STENOSIS

ATRIAL FIBRILLATION AND FLUTTER

VENTRICULAR FIBRILLATION AND FLUTTER

OTHER ILL-DEFINED HEART DISEASES

PULMONARY OEDEMA

CARDIOGENIC SHOCK

PERIPHERAL VASCULAR DISEASE, UNSPECIFIED

PHLEBITIS AND THROMBOPHLEBITIS OF OTHER DEEP VESSELS OF LOWER EXTREMITIES

EMBOLISM AND THROMBOSIS OF OTHER SPECIFIED VEINS

ACUTE AND SUBACUTE INFECTIVE ENDOCARDITIS

ACUTE ENDOCARDITIS, UNSPECIFIED

ENDOCARDITIS, VALVE UNSPECIFIED

DILATED CARDIOMYOPATHY

CARDIOMEGALY

ESSENTIAL (PRIMARY) HYPERTENSION

### **Stroke**

INTRACEREBRAL HAEMORRHAGE, UNSPECIFIED

CEREBRAL INFARCTION DUE TO THROMBOSIS OF PRECEREBRAL ARTERIES

CEREBRAL INFARCTION DUE TO UNSPECIFIED OCCLUSION/STENOSIS OF PRECEREBRAL ARTERIES

CEREBRAL INFARCTION, UNSPECIFIED

STROKE, NOT SPECIFIED AS HAEMORRHAGE OR INFARCTION

CEREBROVASCULAR DISEASE, UNSPECIFIED

SEQUELAE OF STROKE, NOT SPECIFIED AS HAEMORRHAGE OR INFARCTION

SEQUELAE OF OTHER AND UNSPECIFIED CEREBROVASCULAR DISEASES

## **Respiratory system**

### **Respiratory infection**

ACUTE UPPER RESPIRATORY INFECTION, UNSPECIFIED

INFLUENZA WITH PNEUMONIA, OTHER INFLUENZA VIRUS IDENTIFIED

INFLUENZA WITH OTHER RESPIRATORY MANIFESTATIONS, OTHER INFLUENZA VIRUS IDENTIFIED

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1  
2 PNEUMONIA DUE TO STREPTOCOCCUS PNEUMONIAE  
3 BRONCHOPNEUMONIA, UNSPECIFIED  
4 LOBAR PNEUMONIA, UNSPECIFIED  
5 HYPOSTATIC PNEUMONIA, UNSPECIFIED  
6 PNEUMONIA, UNSPECIFIED  
7 UNSPECIFIED ACUTE LOWER RESPIRATORY INFECTION  
8 CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH ACUTE LOWER RESP INFECTION  
9  
10

### **Aspiration/reflux/choking**

11 PNEUMONITIS DUE TO FOOD AND VOMIT  
12 GASTRO-OESOPHAGEAL REFLUX DISEASE WITHOUT OESOPHAGITIS  
13 INHALATION AND INGESTION OF FOOD CAUSING OBSTRUCTION OF RESPIRATORY TRACT  
14 FOREIGN BODY IN RESPIRATORY TRACT, PART UNSPECIFIED  
15 INHALATION/INGESTION OF OTHER OBJECTS CAUSING OBSTRUCT OF RESP TRACT  
16  
17  
18

### **Other respiratory disorders**

19 UNSPECIFIED CHRONIC BRONCHITIS  
20 EMPHYSEMA, UNSPECIFIED  
21 CHRONIC OBSTRUCTIVE PULMONARY DISEASE, UNSPECIFIED  
22 ASTHMA, UNSPECIFIED  
23 BRONCHIECTASIS  
24 OTHER INTERSTITIAL PULMONARY DISEASES WITH FIBROSIS  
25 PLEURAL EFFUSION, NOT ELSEWHERE CLASSIFIED  
26 CHRONIC RESPIRATORY FAILURE  
27 RESPIRATORY FAILURE, UNSPECIFIED  
28 OTHER SPECIFIED RESPIRATORY DISORDERS  
29 DYSPNOEA  
30 RESPIRATORY ARREST  
31 ASPHYXIATION  
32 UNSPECIFIED THREAT TO BREATHING  
33  
34  
35  
36  
37

### **Digestive system**

#### **Ulcer/gastrointestinal perforation**

38 OESOPHAGITIS  
39 PERFORATION OF INTESTINE (NONTRAUMATIC  
40 PERITONITIS, UNSPECIFIED  
41 GASTRIC ULCER, CHRONIC OR UNSPECIFIED WITH PERFORATION  
42 OTHER PERITONITIS  
43 ACUTE PERITONITIS  
44 GASTROINTESTINAL HAEMORRHAGE, UNSPECIFIED  
45 ULCER OF INTESTINE  
46  
47  
48  
49  
50

#### **Other gastrointestinal disorders**

51 BARRETT'S OESOPHAGUS  
52 DIAPHRAGMATIC HERNIA WITHOUT OBSTRUCTION OR GANGRENE  
53 OTHER SPECIFIED NONINFECTIVE GASTROENTERITIS AND COLITIS  
54 ACUTE VASCULAR DISORDERS OF INTESTINE  
55 VASCULAR DISORDER OF INTESTINE, UNSPECIFIED  
56 VOLVULUS  
57 OTHER AND UNSPECIFIED INTESTINAL OBSTRUCTION  
58 CONSTIPATION  
59 MEGACOLON, NOT ELSEWHERE CLASSIFIED  
60

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1  
2 ACUTE AND SUBACUTE HEPATIC FAILURE  
3 OTHER AND UNSPECIFIED CIRRHOSIS OF LIVER  
4 AUTOIMMUNE HEPATITIS  
5 INFLAMMATORY LIVER DISEASE, UNSPECIFIED  
6 OTHER SPECIFIED DISEASES OF LIVER  
7 CALCULUS OF GALLBLADDER WITH OTHER CHOLECYSTITIS  
8 CHOLANGITIS  
9 ACUTE PANCREATITIS, UNSPECIFIED  
10 PSEUDOCYST OF PANCREAS  
11 INTESTINAL MALABSORPTION, UNSPECIFIED  
12 DYSPHAGIA  
13  
14  
15  
16

## **Genitourinary system**

### **Renal failure**

17  
18  
19 CHRONIC NEPHRITIC SYNDROME, UNSPECIFIED  
20 OTHER ACUTE RENAL FAILURE  
21 ACUTE RENAL FAILURE, UNSPECIFIED  
22 END-STAGE RENAL DISEASE  
23 CHRONIC KIDNEY DISEASE, STAGE 5  
24 CHRONIC KIDNEY DISEASE, UNSPECIFIED  
25 UNSPECIFIED KIDNEY FAILURE  
26  
27  
28  
29

### **Chromosomal abnormalities**

#### **Down syndrome**

30  
31  
32 DOWN'S SYNDROME, UNSPECIFIED  
33

#### **Other congenital condition**

34 CONGENITAL HYDROCEPHALUS, UNSPECIFIED  
35 SPINA BIFIDA, UNSPECIFIED  
36 CONGENITAL MALFORMATION OF HEART, UNSPECIFIED  
37 CONGENITAL DEFORMITY OF SPINE  
38 CONGEN MALFORMATION SYNDROMES PREDOMINANTLY ASSOCIATED WITH SHORT  
39 STATURE  
40 MARFAN'S SYNDROME  
41 OTHER SPECIFIED CONGEN MALFORMATION SYNDROMES, NOT ELSEWHERE CLASSIFIED  
42 CONGENITAL MALFORMATION, UNSPECIFIED  
43 KLINEFELTER'S SYNDROME, UNSPECIFIED  
44 FRAGILE X CHROMOSOME  
45 OTHER LACK OF EXPECTED NORMAL PHYSIOLOGICAL DEVELOPMENT  
46  
47  
48  
49

### **Other conditions occurring with small frequency**

#### **Other condition**

50  
51  
52 DECUBITUS ULCER AND PRESSURE AREA  
53 SCOLIOSIS, UNSPECIFIED  
54 URETHRAL STRICTURE, UNSPECIFIED  
55 EPISTAXIS  
56 IMMOBILITY  
57 MALAISE AND FATIGUE  
58 GENERALIZED ENLARGED LYMPH NODES  
59 INSUFFICIENT INTAKE OF FOOD AND WATER DUE TO SELF NEGLECT  
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1  
2 OTHER SPECIFIED GENERAL SYMPTOMS AND SIGNS  
3 OTHER ILL-DEFINED AND UNSPECIFIED CAUSES OF MORTALITY  
4 EXPOSURE TO UNSPECIFIED FACTOR  
5 MULTI-SYSTEM DEGENERATION  
6 BENIGN NEOPLASM, MENINGES, UNSPECIFIED  
7 AGRANULOCYTOSIS  
8 SARCOIDOSIS OF OTHER AND COMBINED SITES  
9 SARCOIDOSIS, UNSPECIFIED  
10 HYPOPITUITARISM  
11 HYPOTHYROIDISM, UNSPECIFIED  
12 OTHER THYROTOXICOSIS  
13 VOLUME DEPLETION  
14  
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16  
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## **Injuries and external causes**

### **Injuries and accidents**

18  
19  
20 INTRACRANIAL INJURY, UNSPECIFIED  
21 UNSPECIFIED INJURY OF HEAD  
22 INJURY OF COLON  
23 FRACTURE OF NECK OF FEMUR  
24 FRACTURE OF SHAFT OF TIBIA  
25 UNSPECIFIED MULTIPLE INJURIES  
26 FAT EMBOLISM (TRAUMATIC)  
27 SEQUELAE OF UNSPECIFIED INJURY OF HEAD  
28 UNSPECIFIED FALL  
29 SEQUELAE OF OTHER ACCIDENTS  
30  
31  
32  
33

### **Medical/surgical complication**

34 POISONING BY OTHER ANTIDYSRHYTHMIC DRUGS, NOT ELSEWHERE CLASSIFIED  
35 ADVERSE EFFECTS OF OTHER ANTIDYSRHYTHMIC DRUGS, NOT ELSEWHERE CLASSIFIED  
36 ABN REACT TO/LATER COMPLIC OF OP WITH IMPLANT OF ARTIFICIAL INTERN DEVICE  
37 ABN REACT TO/LATER COMPLIC OF OP WITH ANASTOMOSIS, BYPASS OR GRAFT  
38 ABN REACT TO/LATER COMPLIC OF OP WITH FORMATION OF EXTERNAL STOMA  
39 ABNORMAL REACTION TO OR LATER COMPLICATION OF OTHER MEDICAL PROCEDURES  
40 SEQ OF PROCED CAUSING ABN REACT/COMPLIC,W/O MENTION OF MISADV AT THE TIME  
41 OTHER POSTPROCEDURAL RESPIRATORY DISORDERS  
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### Supplementary table 3. Predictors of the outcome time to death from univariate analyses

| Variable                  |                     | N with event/<br>N in group | Hazard ratio<br>(95% CI) | Individual p-value | Overall p-value |
|---------------------------|---------------------|-----------------------------|--------------------------|--------------------|-----------------|
| <b>Demographics</b>       |                     |                             |                          |                    |                 |
| Age                       |                     | 294/961                     | 1.05 (1.04, 1.06)        | <0.0001            |                 |
| Sex                       | Male                | 154/525                     | 0.88 (0.70, 1.11)        | 0.2730             |                 |
|                           | Female              | 140/436                     | 1.00 (-)                 |                    |                 |
| Ability level             | Mild ID             | 92/382                      | 1.00 (-)                 |                    | 0.0007          |
|                           | Moderate ID         | 73/236                      | 1.38 (1.01, 1.87)        | 0.0411             |                 |
|                           | Severe ID           | 67/180                      | 1.75 (1.28, 2.40)        | 0.0005             |                 |
|                           | Profound ID         | 62/163                      | 1.77 (1.28, 2.45)        | 0.0005             |                 |
| Type of accommodation     | Family carer        | 70/374                      | 1.00 (-)                 |                    | <0.0001         |
|                           | Independent of care | 36/93                       | 2.35 (1.57, 3.52)        | <0.0001            |                 |
|                           | Paid support        | 161/435                     | 2.18 (1.65, 2.88)        | <0.0001            |                 |
|                           | Congregate          | 27/59                       | 2.87 (1.84, 4.48)        | <0.0001            |                 |
| Neighbourhood deprivation | 1 - most affluent   | 18/73                       | 1.00 (-)                 |                    | 0.1890          |
|                           | 2                   | 56/137                      | 1.92 (1.13, 3.27)        | 0.0158             |                 |
|                           | 3                   | 10/45                       | 0.90 (0.42, 1.95)        | 0.7896             |                 |
|                           | 4                   | 10/40                       | 1.06 (0.49, 2.30)        | 0.8808             |                 |
|                           | 5                   | 12/32                       | 1.71 (0.82, 3.55)        | 0.1527             |                 |
|                           | 6                   | 9/32                        | 1.27 (0.57, 2.82)        | 0.5640             |                 |
|                           | 7                   | 9/34                        | 1.09 (0.49, 2.43)        | 0.8302             |                 |
|                           | 8                   | 15/58                       | 1.21 (0.61, 2.41)        | 0.5818             |                 |
|                           | 9                   | 35/124                      | 1.22 (0.69, 2.16)        | 0.4882             |                 |
|                           | 10 - most deprived  | 120/386                     | 1.41 (0.86, 2.31)        | 0.1782             |                 |
| Civil status              | Single              | 288/938                     | 1.28 (0.57, 2.87)        | 0.5485             |                 |
|                           | Not single          | 6/23                        | 1.00 (-)                 |                    |                 |
| Employment/day activities | Yes                 | 83/231                      | 1.33 (1.03, 1.71)        | 0.0284             |                 |
|                           | No                  | 211/730                     | 1.00 (-)                 |                    |                 |
| Smoker                    | Yes                 | 46/101                      | 1.70 (1.24, 2.33)        | 0.0009             |                 |
|                           | No                  | 248/860                     | 1.00 (-)                 |                    |                 |
| Down syndrome             | Yes                 | 64/179                      | 1.30 (0.98, 1.71)        | 0.0673             |                 |
|                           | No                  | 230/782                     | 1.00 (-)                 |                    |                 |
| Epilepsy                  | Yes                 | 111/325                     | 1.25 (0.99, 1.58)        | 0.0636             |                 |
|                           | No                  | 183/636                     | 1.00 (-)                 |                    |                 |
| Spastic quadriplegia      | Yes                 | 24/325                      | 1.67 (1.10, 2.54)        | 0.0158             |                 |
|                           | No                  | 183/636                     | 1.00 (-)                 |                    |                 |
| Impaired mobility         | Yes                 | 195/735                     | 0.51 (0.40, 0.65)        | <0.0001            |                 |
|                           | No                  | 99/226                      | 1.00 (-)                 |                    |                 |
| Body mass index           | Underweight         | 9/43                        | 0.63 (0.32, 1.25)        | 0.1847             | 0.1865          |
|                           | Acceptable          | 83/265                      | 1.00 (-)                 |                    |                 |
|                           | Overweight          | 75/289                      | 0.78 (0.57, 1.06)        | 0.1132             |                 |
|                           | Obese               | 81/237                      | 1.08 (0.80, 1.47)        | 0.6152             |                 |
|                           | Morbidly obese      | 16/58                       | 0.87 (0.51, 1.48)        | 0.6058             |                 |
| Hearing impairment        | Yes                 | 112/267                     | 1.79 (1.41, 2.26)        | <0.0001            |                 |
|                           | No                  | 182/694                     | 1.00 (-)                 |                    |                 |
| Visual impairment         | Yes                 | 154/449                     | 1.29 (1.02, 1.62)        | 0.0317             |                 |
|                           | No                  | 140/512                     | 1.00 (-)                 |                    |                 |

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|  |     |          |                    |         |  |
|--|-----|----------|--------------------|---------|--|
| Urinary incontinence                             | Yes | 158/632  | 0.52 (0.41, 0.65)  | <0.0001 |  |
|  | No  | 136/329  | 1.00 (-)           |         |  |
| Bowel incontinence                               | Yes | 197/733  | 0.55 (0.43, 0.70)  | <0.0001 |  |
|  | No  | 97/228   | 1.00 (-)           |         |  |
| Diabetes   | Yes | 29/47    | 2.72 (1.86, 4.00)  | <0.0001 |  |
|  | No  | 265/914  | 1.00 (-)           |         |  |
| PEG/tube fed                                     | Yes | N/7      | 4.99 (2.22, 11.20) | 0.0001  |  |
|  | No  | 288/954  |                    |         |  |
| Constipation                                     | Yes | 112/316  | 1.34 (1.06, 1.70)  | 0.0145  |  |
|  | No  | 182/645  | 1.00 (-)           |         |  |
| Ataxia/gait disorder                             | Yes | 104/276  | 1.50 (1.18, 1.90)  | 0.0009  |  |
|  | No  | 190/685  | 1.00 (-)           |         |  |
| Nail disorder                                    | Yes | 74/223   | 1.18 (0.91, 1.54)  | 0.2120  |  |
|  | No  | 220/738  | 1.00 (-)           |         |  |
| Epidermal thickening                             | Yes | 66/207   | 1.10 (0.84, 1.45)  | 0.4947  |  |
|  | No  | 228/754  | 1.00 (-)           |         |  |
| Cerebral palsy                                   | Yes | 54/175   | 1.02 (0.76, 1.37)  | 0.8792  |  |
|  | No  | 240/786  | 1.00 (-)           |         |  |
| Osteoporosis                                     | Yes | 76/174   | 1.71 (1.32, 2.22)  | <0.0001 |  |
|  | No  | 218/786  | 1.00 (-)           |         |  |
| Fungal infection                                 | Yes | 42/158   | 0.83 (0.61, 1.18)  | 0.3366  |  |
|  | No  | 252/803  | 1.00 (-)           |         |  |
| Hypertension                                     | Yes | 56/146   | 1.36 (1.01, 1.82)  | 0.0399  |  |
|  | No  | 238/815  | 1.00 (-)           |         |  |
| Dysphagia  | Yes | 51/132   | 1.51 (1.11, 2.04)  | 0.0080  |  |
|  | No  | 243/829  | 1.00 (-)           |         |  |
| Dyspnoea   | Yes | 49/130   | 1.41 (1.04, 1.92)  | 0.0285  |  |
|  | No  | 245/831  | 1.00 (-)           |         |  |
| Musculoskeletal pain                             | Yes | 48/148   | 1.14 (0.83, 1.55)  | 0.4153  |  |
|  | No  | 246/813  | 1.00 (-)           |         |  |
| Bone deformity                                   | Yes | 50/139   | 1.32 (0.97, 1.79)  | 0.0769  |  |
|  | No  | 244/822  | 1.00 (-)           |         |  |
| Dental/oral problem                              | Yes | 38/120   | 1.07 (0.76, 1.50)  | 0.7128  |  |
|  | No  | 256/841  | 1.00 (-)           |         |  |
| Eczema/dermatitis                                | Yes | 38/138   | 0.86 (0.61, 1.21)  | 0.3790  |  |
|  | No  | 256/823  | 1.00 (-)           |         |  |
| GORD   | Yes | 51/133   | 1.43 (1.06, 1.94)  | 0.0198  |  |
|  | No  | 243/828  | 1.00 (-)           |         |  |
| Lower respiratory tract infection                | Yes | 55/126   | 1.75 (1.30, 2.34)  | 0.0002  |  |
|  | No  | 239/835  | 1.00 (-)           |         |  |
| Total number of physical conditions              |     | 294/961  | 1.06 (1.04, 1.08)  | <0.0001 |  |
| Psychosis  | Yes | 11 /42   | 0.81 (0.44, 1.48)  | 0.4990  |  |
|  | No  | 283 /919 | 1.00 (-)           |         |  |
| Affective disorder including bipolar             | Yes | 24/68    | 1.19 (0.78, 1.80)  | 0.4216  |  |
|  | No  | 270/893  | 1.00 (-)           |         |  |
| Autism   | Yes | 13/69    | 0.54 (0.31, 0.94)  | 0.0306  |  |
|  | No  | 281/892  | 1.00 (-)           |         |  |
| Problem behaviour                                | Yes | 71/218   | 1.09 (0.83, 1.42)  | 0.5251  |  |
|  | No  | 223/743  | 1.00 (-)           |         |  |
| Eating disorder, including pica                  | Yes | 5/17     | 0.99 (0.41, 2.40)  | 0.9857  |  |
|  | No  | 289/944  | 1.00 (-)           |         |  |
| Any mental illness, excluding problem behaviours | Yes | 73/217   | 1.16 (0.89, 1.51)  | 0.2849  |  |
|  | No  | 221/744  | 1.00 (-)           |         |  |
| <b>Service use</b>                               |     |          |                    |         |  |
| Number of GP consultations in last 12 months     |     | 287/951  | 1.05 (1.03, 1.06)  | <0.0001 |  |

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|   |     |         |                   |         |  |
|---|-----|---------|-------------------|---------|--|
| Number of A&E attendances in last 12 months |     | 280/938 | 1.09 (0.99, 1.20) | 0.0847  |  |
| Number of health professions providing care |     | 294/961 | 1.10 (1.03, 1.16) | 0.0023  |  |
| <b>Prescriptions</b>                        |     |         |                   |         |  |
| Antipsychotics                              | Yes | 79/226  | 1.12 (0.94, 1.57) | 0.1421  |  |
|   | No  | 215/735 | 1.00 (-)          |         |  |
| Antidepressants                             | Yes | 39/118  | 1.16 (0.83, 1.63) | 0.3778  |  |
|   | No  | 255/843 | 1.00 (-)          |         |  |
| Anxiolytic/hypnotics                        | Yes | 20/68   | 0.95 (0.60, 1.49) | 0.8159  |  |
|   | No  | 274/893 | 1.00 (-)          |         |  |
| Antiepileptics                              | Yes | 90/253  | 1.31 (1.02, 1.68) | 0.0315  |  |
|   | No  | 204/708 | 1.00 (-)          |         |  |
| Number of drug classes taken                |     | 294/961 | 1.16 (1.12, 1.21) | <0.0001 |  |

A&E=accident and emergency; CI=confidence interval; GORD=gastro-oesophageal reflux disorder; PEG=percutaneous endoscopic gastrostomy

## STROBE Statement—checklist of items that should be included in reports of observational studies

|                              | Item No. | Recommendation   | Page No. | Relevant text from manuscript    |
|------------------------------|----------|--|----------|----------------------------------|
| <b>Title and abstract</b>    | 1        | (a) Indicate the study's design with a commonly used term in the title or the abstract   |          | p1                               |
|                              |          | (b) Provide in the abstract an informative and balanced summary of what was done and what was found  |          | p2                               |
| <b>Introduction</b>          |          |  |          |                                  |
| Background/rationale         | 2        | Explain the scientific background and rationale for the investigation being reported   |          | p4-6, supplementary table 1      |
| Objectives                   | 3        | State specific objectives, including any prespecified hypotheses   |          | 6, paragraph 3                   |
| <b>Methods</b>               |          |  |          |                                  |
| Study design                 | 4        | Present key elements of study design early in the paper  |          | p6-10, supplementary tables 2/3  |
| Setting                      | 5        | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection  |          | p7, paragraph 1, 7-8             |
| Participants                 | 6        | (a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br><i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br><i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants |          | p7, paragraph 1                  |
|                              |          | (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed<br><i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case   |          | p7, paragraph 2, p9, paragraph 4 |
| Variables                    | 7        | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable   |          | p7-8, supplementary table 2      |
| Data sources/<br>measurement | 8*       | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group   |          | p7-8, p9, paragraph 4            |
| Bias                         | 9        | Describe any efforts to address potential sources of bias  |          | p9, paragraph 4                  |
| Study size                   | 10       | Explain how the study size was arrived at  |          | P7, paragraph2, p9, paragraph 4  |

Continued on next page

|                        |     |  |  |
|------------------------|-----|--|--|
| Quantitative variables | 11  | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why   | p8-10                                  |
| Statistical methods    | 12  | (a) Describe all statistical methods, including those used to control for confounding  | p8-10                                  |
|                        |     | (b) Describe any methods used to examine subgroups and interactions  | p8-10                                  |
|                        |     | (c) Explain how missing data were addressed  | p11, paragraph 2                       |
|                        |     | (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed  | p11, paragraph 2                       |
|                        |     | <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed   |  |
|                        |     | <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy   |  |
|                        |     | (e) Describe any sensitivity analyses  | N/A                                    |
| <b>Results</b>         |     |  |  |
| Participants           | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed            | p11, paragraph 2                       |
|                        |     | (b) Give reasons for non-participation at each stage   | p11, paragraph 2                       |
|                        |     | (c) Consider use of a flow diagram   | -                                      |
| Descriptive data       | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders   | p11-12, Table 1, supplementary table 3 |
|                        |     | (b) Indicate number of participants with missing data for each variable of interest  | table 1, supplementary table 3         |
|                        |     | (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)   | p12, paragraph 1                       |
| Outcome data           | 15* | <i>Cohort study</i> —Report numbers of outcome events or summary measures over time  | p11, paragraph 2                       |
|                        |     | <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure   |  |
|                        |     | <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures   |  |
| Main results           | 16  | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | P15, table 6                           |
|                        |     | (b) Report category boundaries when continuous variables were categorized  | N/A                                    |
|                        |     | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period   | -                                      |

Continued on next page

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|                          |    |  |                  |
|--------------------------|----|--|------------------|
| Other analyses           | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses   | p11-16           |
| <b>Discussion</b>        |    |  |                  |
| Key results              | 18 | Summarise key results with reference to study objectives   | p16, paragraph 2 |
| Limitations              | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias                 | p20, paragraph 1 |
| Interpretation           | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | p20, paragraph 2 |
| Generalisability         | 21 | Discuss the generalisability (external validity) of the study results  | p20, paragraph 1 |
| <b>Other information</b> |    |  |                  |
| Funding                  | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based              | P24              |

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage

|                                 |   |
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3 **Rates, causes, place, and predictors of mortality in**  
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6 **adults with intellectual disabilities with and without**  
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9 **Down syndrome: cohort study with record linkage**  
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## Abstract

### **Objectives**

To investigate mortality in adults with intellectual disabilities: rates, causes, place, demographic and clinical predictors.

### **Design**

Cohort study with record linkage to death data.

### **Setting**

General community.

### **Participants**

961/1,023 (94%) adults (16-83 years; mean=44.1 years; 54.6% male) with intellectual disabilities, clinically examined in 2001-2004; subsequently record-linked to their National Health Service number, allowing linkage to death certificate data, 2018.

### **Outcome measures**

Standardised mortality ratios (SMRs), underlying, and all contributing causes of death, avoidable deaths, place, and demographic and clinical predictors of death.

### **Results**

294/961 (30.6%) had died; 64/179 (35.8%) with Down syndrome, 230/783 (29.4%) without Down syndrome. SMR overall=2.24 (1.98, 2.49); Down syndrome adults=5.28 (3.98, 6.57), adults without Down syndrome=1.93 (1.68, 2.18); male=1.69 (1.42, 1.95), female=3.48 (2.90, 4.06). SMRs decreased as age increased. More severe intellectual disabilities increased SMR, but ability was not retained in the multivariable model. SMRs were higher for most ICD-10 chapters. For adults without Down syndrome, aspiration/reflux/choking, and respiratory infection were the commonest underlying causes of mortality; for Down syndrome adults "Down syndrome", and dementia were most common. Amenable deaths (29.8%) were double that in the general population (14%). 60.3% died in hospital. Mortality risk related to: percutaneous endoscopic gastrostomy/tube fed, Down syndrome, diabetes, lower respiratory tract infection at

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3 cohort-entry, smoking, epilepsy, hearing impairment, increasing number of prescribed  
4 drugs, increasing age. Bowel incontinence reduced mortality risk.

### 7 **Conclusions**

9 Adults with intellectual disabilities with and without Down syndrome have different SMRs  
10 and causes of death which should be separately reported. Both die younger, from  
11 different causes than other people. Some mortality risks are similar to other people, with  
12 earlier mortality reflecting more multi-morbidity; amenable deaths are also common.

13 This should inform actions to reduce early mortality, e.g. training to avoid  
14 aspiration/choking, pain identification to address problems before they are advanced,  
15 and reasonable adjustments to improve health-care quality.

### 24 **Strengths and limitations of this study**

- 25 • Thorough methods of case ascertainment for intellectual disabilities at baseline.
- 26 • Individual verification of intellectual disabilities and its severity, and detailed health  
27 assessments at baseline.
- 28 • Longitudinal design.
- 29 • Large cohort size and study duration, and successful record linkage for 94% of  
30 participants.
- 31 • Limitations include that the study was conducted in only one part of Scotland, and  
32 the reliance upon recorded cause of death from death certificates.

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49 Word count: 5,605

## Introduction

People with intellectual disabilities die at a younger age than other people; on average, 20 years younger,<sup>1</sup> or 28 years younger specifically for people with Down syndrome.<sup>2</sup> It has been demonstrated that people with intellectual disabilities receive poorer management of their long term conditions within primary health care services compared with the general population,<sup>3</sup> and it is conceivable that this is one contributor to earlier mortality. It has been suggested that as many as 40% of deaths of people with intellectual disabilities may have been amenable to good quality health care.<sup>4-6</sup> There has been a recent increase in research on mortality in people with intellectual disabilities, but very little research has distinguished people with intellectual disabilities with and without Down syndrome, or investigated the factors associated with risk of mortality, and causes of mortality.

Previous studies on death in people with intellectual disabilities had limitations such as small sample sizes, or non-representative populations. More recently, there have been large-scale studies which are more representative, having been drawn from intellectual disabilities registers, or social security or primary care data with record linkage to death certification. These have been undertaken in parts of Sweden, Australia, England, Finland, Canada, Ireland, and USA (supplementary table 1).<sup>5-19</sup> These studies fairly consistently report standardised mortality ratios (SMRs) to be high for people with intellectual disabilities, more so at younger ages, and higher for women than men. Adult studies have tended to report SMRs in the region of 2-4, although in some, SMR is only slightly above 1.<sup>10,16,19</sup> However, direct comparison between studies is not always possible, due to the different age ranges studied and methods of reporting.

- Supplementary table 1 -

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3 In view of the methods that studies have used for population identification (typically,  
4 routine administrative data linked to death certifications), they provide little information  
5 on the socio-clinical factors that influence SMR, or the risk factors associated with death,  
6 beyond that of age and sex. Three studies reported SMR by level of intellectual  
7 disabilities, with, broadly speaking, higher SMR with more severe intellectual  
8 disabilities.<sup>7,10,17</sup> Only three studies (different studies to those that reported on level of  
9 intellectual disabilities) were able to report data separately for adults with intellectual  
10 disabilities with and without Down syndrome; two found higher mortality rates for adults  
11 with Down syndrome (SMR=7.6,<sup>9</sup> and hazard ratio=9.21<sup>5</sup>) than for adults without Down  
12 syndrome, or an odds ratio showing Down syndrome as a risk of death.<sup>12</sup> A further  
13 study reported SMR=5.5 for children and adults (combined) with Down syndrome, but  
14 did not report SMR for those with intellectual disabilities without Down syndrome.<sup>20</sup> Two  
15 studies reported adults with intellectual disabilities to have higher SMRs if they have the  
16 co-morbidities of epilepsy,<sup>5,7</sup> and cerebral palsy,<sup>7</sup> as opposed to not having these  
17 comorbidities. One study reported adults with intellectual disabilities with comorbid  
18 autism to have lower risk of mortality than those without comorbid autism.<sup>5</sup> One study  
19 reported the risk factors for mortality in a population with intellectual disabilities to be:  
20 age, Down syndrome, cerebral palsy, blindness/low vision, technological  
21 dependence/medical fragility, wheelchair dependence, mobility impairment without  
22 wheelchair dependence, and epilepsy.<sup>12</sup> Factors not found to be risks, if any, were not  
23 reported, and a further limitation was that factors were reported by agency staff, rather  
24 than the individuals undergoing health assessments.<sup>12</sup> We have not identified any other  
25 studies that investigated risk factors for time to mortality in adults with intellectual  
26 disabilities.

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54 There is less consistency regarding the most common certified underlying causes of  
55 death in adults with intellectual disabilities, partly as some studies do not report these  
56 separately for children and adults, or by age ranges. Additionally, studies group causes  
57 of death in different ways (e.g. pneumonia versus respiratory system), which can affect  
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3 prevalence rankings between studies. Pneumonia, other respiratory diseases, and  
4 diseases of the nervous system were reported to be the most common in one study,<sup>11</sup>  
5 diseases of the circulatory system and respiratory systems in another,<sup>5</sup> heart disease,  
6 neoplasm, and Alzheimer disease in a third,<sup>18</sup> and diseases of the circulatory system,  
7 neoplasm, and the nervous system in a fourth.<sup>19</sup> In adults with intellectual disabilities,  
8 cause specific SMRs have been reported to be high across most groups of disorders.<sup>5,11</sup>  
9 These studies did not report cause of death separately for adults with and without Down  
10 syndrome. Given the different health profile of people with Down syndrome compared  
11 with people with intellectual disabilities of other causes, this is an important limitation.<sup>21</sup>  
12 In people with Down syndrome, most studies on mortality have been conducted with  
13 child populations, and report the most common causes of death to be congenital heart  
14 disease, and pneumonia/diseases of the respiratory system.<sup>2</sup>

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30 Overall, the existing body of literature on mortality in adults with intellectual disabilities  
31 does not include more detailed information on level of intellectual disabilities, nor  
32 separate out the population with, from those without, Down syndrome (for whom causes  
33 of death may differ), nor investigate health and demographic predictors of death other  
34 than age and sex, and is inconsistent with regards to causes of death. A better  
35 understanding of these factors may provide a pathway to action to reduce the observed  
36 earlier mortality in adults with intellectual disabilities.

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46 This study aims to investigate the rates, causes, place, and demographic and clinical  
47 associations with mortality in adults with intellectual disabilities, with and without Down  
48 syndrome.

## 49 50 51 52 53 **Methods**

### 54 55 56 57 58 **Approval**

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3 Ethical approval was gained from NHS Greater Glasgow Primary Care Trust -  
4  
5 Community & Mental Health Research Ethics Committee, and NHS Greater Glasgow and  
6  
7 Clyde Safe Haven. Individual consent to participate was taken in line with Scottish law,  
8  
9 between 2001-2004.  
10

### 11 12 13 **Participants**

14  
15 The adult (aged 16+ years) intellectual disabilities population living within the NHS  
16  
17 Greater Glasgow area was identified through multiple sources between 2000-2001.  
18  
19 General practitioners were financially incentivised to identify their registered patients  
20  
21 with intellectual disabilities, and all 631 (100%) did so. Adults were also identified via  
22  
23 the intellectual disabilities health and social work services including day services, the  
24  
25 Health Board register, and records of financial payments for any service by social work.  
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27 This process led initially to an over-identification, such as people with IQ scores in the  
28  
29 70–80 range with additional complex health needs. All were systematically reviewed by  
30  
31 nurses in the intellectual disabilities health service, and this group were removed. Thus,  
32  
33 a register was compiled, and subsequently updated annually via general practices, with  
34  
35 central support from the intellectual disabilities health service, until 2017 when services  
36  
37 were redesigned. The identified adult prevalence of intellectual disabilities within the  
38  
39 area was 3.33 per 1,000 in 2000-2001.  
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### 44 **Process and data collection**

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46 With initial piloting in 2001, each participant had a detailed assessment of their general  
47  
48 and mental health, and demographic factors, completed 2002-2004. One of six specially  
49  
50 trained, registered nurses reviewed each person's primary health care records, then  
51  
52 used a semi-structured tool, the C21st Health Check, to assess clinical factors and the  
53  
54 level and cause of intellectual disabilities. In addition to a review of existing health  
55  
56 problems and all bodily health systems, a physical examination was undertaken,  
57  
58 including assessment of vision and hearing, measurement of height and weight, and a  
59  
60 phlebotomy protocol followed. All information was then reviewed by the nurse with one

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3 of three general practitioners with a special interest in intellectual disabilities, and any  
4 further investigations that were indicated were completed. Previously known, and newly  
5 identified, conditions were then classified using the *International Statistical Classification*  
6 *of Diseases and Related Health Problems, 10th Revision (ICD-10)*.<sup>22</sup> Anyone identified to  
7 have possible, probable, or definite mental ill-health, autism, or problem behaviours was  
8 then fully assessed by the project's intellectual disabilities psychiatrists. Each person's  
9 assessment findings were then case conferenced by the two Consultant psychiatrists,  
10 and diagnoses were derived and agreed according to clinical diagnoses, *ICD-10*  
11 *(Diagnostic Criteria for Research)*,<sup>23</sup> *Diagnostic and Statistical Manual of Mental*  
12 *Disorders-IV-TR*,<sup>24</sup> and *Diagnostic Criteria for Psychiatric Disorders for use with Adults*  
13 *with Learning Disabilities (DC-LD)*.<sup>25</sup> Information was also collected on demographics,  
14 and community, hospital, and social service use. Further details are provided  
15 elsewhere.<sup>26,27</sup> The data were entered into a database by two dedicated data-entry staff.

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31 Each person in Scotland is given a number unique to them at birth or first registration  
32 with a general practitioner, which is used in almost all subsequent health service  
33 encounters, and on certification of death. The numbers are held on the Community  
34 Health Index (CHI) database at National Services Scotland. These CHI numbers provided  
35 a means to record link each participant with National Records for Scotland death  
36 certification data. This linkage was performed in 2018, and the linked data were held in  
37 the NHS Greater Glasgow & Clyde (NHS GG&C) Safe Haven. Data on immediate,  
38 underlying, and contributory causes of deaths by ICD-10 codes, age at death, and place  
39 of death were extracted.

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51 In order to provide finer granularity of cause of death, two clinical academics then  
52 grouped specific causes of death into narrower groupings than those provided by ICD-10  
53 chapter headings (supplementary table 2). This approach was also in view of the  
54 recognised issue of variation between health staff in distinguishing and recording  
55 immediate causes of death, and because some causes occurred in low numbers so could

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3 not be individually reported due to the risk of statistical disclosure. Additionally, some  
4 conditions likely to be the same are spilt between different ICD-10 chapters, e.g.  
5 dementia in Alzheimer disease (F00) and unspecified dementia (F03) in the ICD-10  
6 mental and behavioural disorders chapter, and Alzheimer's disease (G30) and  
7 Alzheimer's disease, unspecified (G30.9) in the ICD-10 diseases of the nervous system  
8 chapter. A list of related conditions was generated by one of the clinical academics and  
9 then checked by the second.  
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19 - Supplementary table 2 -  
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### 23 **Analyses**

24 All statistical analyses were conducted using R for Windows v3.3.0 or SAS 9.3 (SAS  
25 Institute, Cary NC) and were performed within the NHS GG&C Safe Haven environment.  
26 Due to disclosure principles of the Safe Haven, results with counts of less than 5 cannot  
27 be released; these have been referred to as <5 throughout. Similarly, if it is deemed  
28 possible that participants may be identified from the results, these may be omitted.  
29 Details are provided if this occurred.  
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40 Data were summarised for the population of adults aged 16+ years with intellectual  
41 disabilities. Categorical variables were summarised with the number and percentages of  
42 people falling into each category and the number of missing data. Continuous variables  
43 were summarised with the number of observations and those missing, the mean and  
44 standard deviation (SD), and the minimum and maximum values, unless otherwise  
45 stated.  
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54 Participant characteristics were summarised overall and for those alive and those  
55 deceased. For those who are deceased, their data including age at death,  
56 underlying/contributing causes of death, and location of death were summarised for  
57 those with and without Down syndrome. Location codes for place of death are provided  
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3 where available. We assumed those with the code for non-institutional location to have  
4 died at home. Due to small numbers, location codes have been grouped together for  
5 NHS hospitals, home, and other hospitals/care facilities including hospices.  
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11 Mortality incidence rates have been calculated using the number of deaths in the cohort  
12 divided by the number of person years alive within the study period multiplied by  
13 100,000, overall and for those with and without Down syndrome. SMRs were calculated  
14 using population data for those aged 15 and over within NHS GG&C in 2010.<sup>28,29</sup> Death  
15 rates for males and females by 5 year band ages groups spanning from 15-20 years old  
16 to 90 years and over were summed to form the expected death rates for the general  
17 population. The observed death rate for adults with intellectual disabilities was taken  
18 from our study results. The observed/expected death rates were calculated for the  
19 intellectual disabilities cohort overall then separately by age group, sex, ability level, and  
20 for the adults with, and without, Down syndrome, and ICD-10 chapter for cause of  
21 death, and compared to the general population.  
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36 Deaths were also analysed for those that could be considered as deaths that would have  
37 been avoidable. The Office for National Statistics (ONS) published a definition of  
38 avoidable mortality,<sup>30</sup> which lists the causes of amenable deaths (deaths that should not  
39 occur in the presence of good health care, e.g. respiratory disease), and causes of  
40 preventable deaths (e.g. from diseases that could have been avoided by prior  
41 immunisation), by ICD-10 codes. Causes of death for the adults with intellectual  
42 disabilities have been summarised by ONS definition of avoidable deaths.  
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51 To determine the demographic and clinical factors associated with death in adults with  
52 intellectual disabilities, time to event analyses were explored using univariate Cox  
53 Proportional Hazards models. Variables were selected as potentially relevant on the basis  
54 of what is known on causes of death in people with intellectual disabilities, the 20 most  
55 common physical health conditions reported in the adult population with intellectual  
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3 disabilities,<sup>21</sup> and other factors hypothesised as potentially clinically relevant  
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5 (supplementary table 3):

- 6 • Demographics - 9 variables.
- 7 • Clinical conditions - 33 variables.
- 8 • Service use - 3 variables.
- 9 • Prescriptions - 5 variables.

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11 All 50 variables were then permitted entry in to a single multivariable analysis using  
12 stepwise regression methods, in order to identify a model containing the statistically  
13 significant factors associated with death. Age at date of the health assessment was  
14 entered in to the model as a continuous measure. Results from the univariate Cox  
15 Proportional Hazards models (Supplementary table 3) and the statistically significant  
16 multivariable model from the stepwise results have been presented with hazard ratios  
17 with corresponding 95% confidence intervals (HR, 95% CI) and p-values were obtained.  
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31 - Supplementary table 3 -  
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### 33 ***Patient and public involvement***

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35 This study was designed to respond to the growing concern expressed by people with  
36 intellectual disabilities, their families, and third sector organisations about the early  
37 deaths of people with intellectual disabilities. The Scottish Learning Disabilities  
38 Observatory, where this research was undertaken, has a specific remit for people with  
39 intellectual disabilities. Its steering group includes partners from third sector  
40 organisations, including Down syndrome Scotland, and people with intellectual  
41 disabilities, who approved the work plan for this project prior to it commencing. Results  
42 from this study will be disseminated for people with intellectual disabilities in an easy-  
43 read version via the Scottish Learning Disabilities Observatory.  
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### 58 **Results**

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### ***Population characteristics***

962 of the original 1,023 (94.0%) adults with intellectual disabilities who were assessed were linked to a CHI number enabling the extraction of relevant death data. Reasons for the unlinked 61 people could be due to moving out of the area, or a recording mistake. 1 further participant was removed from the analysis due to inaccurate recording of dates, leaving 961 adults in the cohort (93.9%). Of these 961 adults, 294 (30.6%) had a record of death. Table 1 shows the baseline characteristics of the full cohort of 961, the adults who died, and those still alive at the time of linkage.

- Insert table 1 about here -

### ***Age at death, and mortality incidence***

The mean age at death was 61.0 years (SD=7.0 years). Of the 961 adults, 64 (35.8%) of the 179 adults with Down syndrome, and 230 (29.4%) of the 782 adults without Down syndrome had a record of death. Their mean age of death was 56.9 years (SD=4.3 years) for the adults with Down syndrome, and 62.2 years (SD=7.5 years) for the adults without Down syndrome. Mortality incidence for the cohort during the study period was 3,049.0 per 100,000 person years follow-up, with 3,832.1 per 100,000 for those with Down Syndrome and 2,885.0 for those without Down syndrome.

### ***Standardised mortality ratios***

Compared with the general population, the SMR was 2.24 (1.98, 2.49) overall; 5.28 (3.98, 6.57) for adults with Down syndrome, 1.93 (1.68, 2.18) for adults without Down syndrome; 1.69 (1.42, 1.95) for men and 3.48 (2.90, 4.06) for women. SMRs were higher the more severe the level of intellectual disabilities, with people with profound intellectual disabilities having an SMR of 4.14 (3.11, 5.17). SMR was high for all age groups (though for the 15-25 year age group, the wide confidence interval includes one, perhaps due to the smaller number of deaths in this group); this decreased as age increased. SMRs were high for most ICD-10 chapter groups of conditions, particularly so

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3 for congenital malformations at 17.26 (10.75, 23.78), diseases of the digestive system  
4 at 16.13 (8.23, 24.04), mental and behavioural disorders at 12.64 (3.27, 22.00), and  
5 external causes at 11.08 (3.40, 18.76). Details are shown in table 2.  
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11 - Insert table 2 about here -  
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### 14 15 **Causes of death**

16 Cause of death data was available from death certificates for 262 (89.1%) of 294  
17 participants who had died, which include 57 (89.1%) participants with Down syndrome,  
18 and 205 (88.7%) participants without Down syndrome. Table 3 shows the underlying  
19 causes of death by ICD-10 chapters separately for the adults with, and without Down  
20 syndrome. For the whole cohort, diseases of the respiratory system were the most  
21 common (21.8%), then diseases of the circulatory system (19.1%), then diseases of the  
22 nervous system (13.0%), and neoplasms, followed by congenital anomalies (10.3%).  
23 For the adults with Down syndrome, congenital anomalies were the most common (in all  
24 cases this was a record of "Down syndrome"), then jointly diseases of the respiratory  
25 system and diseases of the circulatory system, then diseases of the nervous system,  
26 followed by infections, and mental and behavioural disorders. For the adults without  
27 Down syndrome, diseases of the respiratory system were the most common, then  
28 diseases of the circulatory system, then neoplasms, then diseases of the nervous  
29 system, followed by diseases of the digestive system. Table 4 presents the most  
30 common underlying causes of death by individual causes, or related groups of causes,  
31 with finer granularity than ICD-10 chapter headings (groups are shown in supplementary  
32 table 2). Causes are listed in the order of how common they were in the whole cohort.  
33 Data are presented separately for the adults with, and without Down syndrome. For the  
34 whole cohort, the most common cause was aspiration/reflux/choking, then respiratory  
35 infection, then other malignancy (non gastrointestinal), then other condition (mostly  
36 unrelated conditions that could not be reported individually or as groups, due to  
37 individually occurring at a frequency of <5). For the adults with Down syndrome, Down  
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3 syndrome was the most common cause, then dementia, then other infection. For the  
4 adults without Down syndrome, aspiration/reflux/choking was the most common cause,  
5 then respiratory infection, then other malignancy (non gastrointestinal). For the 21  
6 people whose death certificate listed Down syndrome as their underlying cause of death,  
7 the death certificates were reviewed and underlying cause of death reclassified, as a  
8 sensitivity check. Following this, the most common underlying causes of death for the  
9 adults with Down syndrome were dementia (n=20; 35.1%), then other infection (n=7;  
10 12.3%).

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21 - Insert tables 3 and 4 about here -  
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25 Table 5 shows the all contributing causes of death data, again presenting the most  
26 common causes by individual causes, or related groups of causes with finer granularity  
27 than ICD-10 chapter headings. Data is presented separately for the adults with, and  
28 without Down syndrome. For the whole cohort, respiratory infection was the most  
29 common cause (27.1%), followed by aspiration/reflux/choking (19.8%), other conditions  
30 (15.6%), other cardiovascular conditions (non acute myocardial nor other ischaemic  
31 heart disease: 14.5%), then other respiratory conditions. For the adults with Down  
32 syndrome, Down syndrome was the most common, then dementia, then respiratory  
33 infection, then aspiration/reflux/choking. For the adults without Down syndrome,  
34 respiratory infection was the most common cause, then aspiration/reflux/choking, then  
35 other condition, then other respiratory conditions, and intellectual disabilities.  
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### 52 53 **Avoidable deaths**

54 According to the ONS list of avoidable deaths, 102 (38.9%) of the 262 deaths were  
55 avoidable; most notably, respiratory infection and epilepsies (table 4). 78 (29.8%) were  
56 deaths that are amenable to good health care, whilst 51 (19.5%) were preventable  
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3 deaths. 27 (10.3%) deaths were classed as both amenable and preventable deaths. This  
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5 compares to published Scottish death data showing in 2018 that 28% of deaths were  
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7 avoidable; 14% amenable and 24% preventable, similar to the figures in the previous  
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9 four years (data not available prior to 2014).<sup>31</sup> For the 57 deaths of adults with Down  
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11 syndrome, 17 (29.8%) deaths were avoidable, 15 (26.3%) deaths were amenable to  
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13 good health care, whilst 7 (12.3%) were preventable. 5 (8.8%) were both amenable and  
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15 preventable. For the 205 deaths of adults without Down syndrome, 85 (41.5%) were  
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17 avoidable, 63 (30.7%) deaths were amenable to good health care, whilst 44 (21.5%)  
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19 were preventable. 22 (10.7%) were both amenable and preventable.  
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### 23 **Place of death**

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25 Of the 262 participants for whom place of death was known, 158 (60.3%) died in an  
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27 NHS Hospital, 70 (26.7%) died at home, and 34 (13.0%) died within other  
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29 hospitals/care facilities. This was similar for both the adults with Down syndrome: 31  
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31 (54.4%) in an NHS hospital, 17 (29.8%) at home, and 9 (15.8%) within other  
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33 hospitals/care facilities; and the adults without Down syndrome: 127 (62.0%) in an NHS  
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35 hospital, 53 (25.9%) at home, and 25 (12.2%) within other hospitals/care facilities.  
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### 39 **Factors associated with risk of death**

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41 The results from the univariate cox proportional hazards models indicated that of the  
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43 original 50 potential variables, factors associated with risk of death were (supplementary  
44  
45 table 3):  
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- 47 • Demographics – age at the time of the health assessment, more severe learning  
48 disabilities, accommodation type (not living with family carer), not having day-time  
49 occupation, and being a smoker (but not sex, the extent of neighbourhood  
50 deprivation, civil status, nor Down syndrome, in view of the confidence intervals).
- 51 • Clinical conditions – having spastic quadriplegia, hearing impairment, visual  
52 impairment, diabetes, percutaneous endoscopic gastrostomy/tube fed, constipation,  
53 ataxia/gait disorder, osteoporosis, hypertension, dysphagia, dyspnoea, gastro-  
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oesophageal reflux disorder, lower respiratory tract infection, total number of physical health disorders, not having impaired mobility, not having urinary incontinence, not having bowel incontinence, and not having autism (but not epilepsy, body mass index, nail disorder, epidermal thickening, cerebral palsy, fungal infection, musculoskeletal pain, bone deformity, dental/oral problem, eczema/dermatitis, psychosis, affective disorder including bipolar affective disorder, problem behaviour, eating disorder including pica, nor any mental illness).

- Service use – number of general practitioner consultations in the previous 12 months, total number of different types of health professionals providing care at the time of the clinical assessment, (but not number of accident and emergency attendances in the previous 12 months).
- Prescriptions – antiepileptic drugs, total number of different types of drugs, (but not antipsychotic drugs, antidepressant drugs, nor anxiolytic drugs).

Table 6 shows the final model of the variables retained in the multivariable analysis for time to death. The significant factors indicating an increased risk of death were increased age at the time of the health assessment, smoking, Down syndrome, diabetes, being percutaneous endoscopic gastrostomy/tube fed, lower respiratory tract infection at cohort inception, epilepsy, hearing impairment, and total number of different types of drugs prescribed, whilst bowel incontinence showed a reduced risk of death. Of note, level of intellectual disabilities whilst significant in the univariate analysis, was not retained in the multivariable model.

- Insert table 6 about here -

## Discussion

### *Principle findings and interpretation*

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3 As far as we are aware, this is the first population-based study of adults with intellectual  
4 disabilities to report in detail the factors associated with time to death, and to describe  
5 their causes of death and quantify the SMR separately for adults with Down syndrome  
6 and adults without Down syndrome. This is important, since adults with Down syndrome  
7 form a notable proportion of all adults with intellectual disabilities (19% in this cohort),  
8 and because they have a different pattern of clinical conditions compared with other  
9 adults with intellectual disabilities.<sup>21</sup> We found that aspiration/reflux/choking is the most  
10 common underlying cause of death in adults with intellectual disabilities, followed by  
11 respiratory infection. They are also the most common all contributing causes of death.  
12 The profile differed in the adults with Down syndrome for whom "Down syndrome",  
13 followed by dementia, were recorded as the most common underlying cause of death,  
14 and all contributing causes of death (or alternatively, dementia, then other infection  
15 were the most common underlying causes when "Down syndrome" deaths were  
16 reclassified); with the next most common all contributing cause of death being  
17 respiratory infection, then aspiration/reflux/choking. The proportion of deaths that would  
18 have been amenable to good care for adults with intellectual disabilities was more than  
19 double that seen in the general population. Although aspiration/reflux/choking is not  
20 included in the ONS list of avoidable deaths, and therefore not included in the figures we  
21 report on amenable deaths, we consider that good care could have prevented many of  
22 these deaths. This appears to be very important for adults with intellectual disabilities  
23 irrespective of whether they have Down syndrome. Similarly, some other causes of  
24 deaths within this cohort (supplementary table 2), such as constipation/mega-colon, and  
25 urinary tract infections do not appear on the ONS list of avoidable deaths.

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52 Clearly, this pattern of causes of death differs from that seen in the general population,  
53 in whom the most common underlying causes of death are heart disease, then dementia,  
54 then lung cancer in men, and dementia, then heart disease, then stroke in women.<sup>32</sup>  
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When all cancers are grouped together, in the general population, cancer is the leading  
underlying cause of death in 30% of men and 26% of women, compared with this study

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3 reporting 0% for adults with Down syndrome, and 15.2% for adults with intellectual  
4 disabilities without Down syndrome – presumably as the adults with intellectual  
5 disabilities are dying younger from other causes, and cancers increase with age.  
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11 We found an overall SMR of 2.24; 5.28 in the adults with Down syndrome and 1.93 for  
12 the adults without Down syndrome. SMRs were higher for most ICD-10 chapter  
13 groupings of conditions. It was higher in the women than the men, as has been  
14 previously reported in most (supplementary table 1), but not all<sup>10,19</sup> previous reports.  
15 The reason for this is unknown; in the general population, mortality rates have fallen in  
16 recent decades, and more so in middle and older aged men than women (i.e. the sex  
17 gap is narrowing at these ages), but we do not know what trends over time there have  
18 been for people with intellectual disabilities. Having intellectual disabilities removes  
19 differences in lifespan by sex compared with the general population; but sex was not a  
20 predictor of mortality in our study, so the SMR difference may only be because of the  
21 difference found in the general population by sex. SMRs were lowest with older age  
22 groups, likely to be due to increased illness in the older general population and  
23 conversely a healthier group with intellectual disabilities living to older ages compared  
24 with those who die younger. Although SMR was higher with increasing severity of  
25 intellectual disabilities, ability level was not retained within the multivariable model on  
26 time to death. The factors that were independently associated with increased risk of  
27 death, in order, were being percutaneous endoscopic gastrostomy/tube fed, Down  
28 syndrome, diabetes, having a lower respiratory tract infection at entry to the cohort,  
29 smoking, epilepsy, hearing impairment, total number of prescribed drugs, and age,  
30 whilst bowel incontinence had a reduced risk of death. Some of these predictors are  
31 similar to those reported in the general population, suggesting earlier mortality of adults  
32 with intellectual disabilities is largely accounted for by the higher rates of multi-  
33 morbidities that they experience compared with other people, and amenable deaths.<sup>33</sup>  
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3 Whilst accommodation type (not living with a family carer), ability level, not having day-  
4 time occupation, having spastic quadriplegia, visual impairment, constipation, ataxia/gait  
5 disorder, osteoporosis, hypertension, dysphagia, dyspnoea, gastro-oesophageal reflux  
6 disorder, total number of physical health disorders, not having impaired mobility, not  
7 having urinary incontinence, and not having autism, number of general practitioner  
8 consultations in the previous 12 months, total number of different types of health  
9 professionals providing care at the time of the health assessment, and antiepileptic  
10 drugs were related to time of death on univariate analyses, they were not retained in the  
11 multivariable model.  
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23 The majority of the adults with intellectual disabilities, with and without Down syndrome,  
24 died in an NHS hospital.  
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### 29 ***Comparison with previous literature***

30 The overall SMR we report, higher SMR in women than men, and higher SMR at younger  
31 age groups is similar to the majority of previous reports. Most mortality studies with  
32 people with Down syndrome have been conducted with children. Previous reports of  
33 children and adults (combined) gave an SMR=5.5,<sup>20</sup> and for adults SMR=7.6,<sup>9</sup> compared  
34 with our finding for adults with Down syndrome of SMR=5.28. Recent systematic reviews  
35 reported people with intellectual disabilities on average died 20 years younger than other  
36 people, and people with Down syndrome died 28 years younger, although the majority  
37 of the Down syndrome studies were not recent.<sup>1,2</sup> In our study we found the gap  
38 between the age at death of people with intellectual disabilities with and without Down  
39 syndrome to be only 5.3 years, possibly reflecting the increasing lifespan of people with  
40 Down syndrome exceeding increases in lifespan for people with intellectual disabilities  
41 without Down syndrome. Notably, after "Down syndrome", dementia was the most  
42 commonly reported underlying, and all contributing cause of death for the adults with  
43 Down syndrome, whereas studies in the past commented on congenital heart disease  
44 and respiratory causes.  
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5 For the cohort overall, respiratory infection and aspiration/reflux/choking were the most  
6 common all contributing causes of death. These conditions feature in previous studies on  
7 causes of death,<sup>5,6,8,10,11</sup> although there are inconsistencies between studies. By ICD-10  
8 chapter, our study found the most common underlying causes of death were diseases of  
9 the respiratory system, then of the circulatory system, followed by neoplasms. Others  
10 reported the most common to be vascular,<sup>10</sup> circulatory,<sup>5</sup> heart disease,<sup>17</sup> and jointly  
11 circulatory and neoplasm.<sup>19</sup>  
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22 Previous research from other countries has highlighted that listing Down syndrome or  
23 intellectual disabilities as the underlying cause of death obscures actual causes of death for  
24 this population.<sup>34</sup> We therefore presented data on revised cause of death for the 21 people  
25 for whom it was listed as Down syndrome (as a sensitivity check), and highlight with interest  
26 that in this Scottish cohort no-one had intellectual disabilities listed as underlying cause of  
27 death. This may reflect different medical death certificate recording practices in Scotland  
28 compared to e.g. USA.  
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41 Studies that investigated avoidable deaths in adults with intellectual disabilities found  
42 them to be more common than in the general population, due to deaths that would have  
43 been amenable to good care. Avoidable deaths have been reported in 44.7% of deaths  
44 of people with intellectual disabilities in England (mostly amenable deaths – figure not  
45 reported),<sup>6</sup> and in 31% in Australia,<sup>19</sup> compared with our figure of 38.9%. Avoidable  
46 deaths that would have been amenable to good care have been reported to occur in 37%  
47 of deaths of people with intellectual disabilities in England.<sup>5</sup> Our figure is slightly lower at  
48 29.8% but still more than double that found in the Scottish general population.<sup>31</sup> It  
49 should be noted that the ONS list of avoidable deaths was not designed specifically for  
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3 people with intellectual disabilities, and it may emphasise some causes less relevant, and  
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5 omit others that might be highly relevant in this population.<sup>5</sup>  
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### 8 9 **Strengths and limitations**

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11 The strengths of the study include the thorough methods of case ascertainment for  
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13 intellectual disabilities at baseline with verification of intellectual disabilities and its  
14  
15 severity, suggesting results are generalisable in other high income countries. Whilst our  
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17 Identification of the population will not have identified everyone with intellectual  
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19 impairment (an IQ<70), in view of the multiple sources used, we believe it will have  
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21 identified the adults with intellectual disabilities (IQ<70, plus need for support in daily  
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23 activities, and onset in the developmental period). Additionally, there were detailed  
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25 clinical assessments at baseline, and a longitudinal design. The size of the cohort and the  
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27 duration of follow-up is also a strength, as is the successful record linkage for 94% of  
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29 participants. Our study does have limitations, specifically that the study was only  
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31 conducted in one region of Scotland, and the reliance upon death certificate data to  
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33 obtain cause of death. Additionally, the characteristics and health of the participants was  
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35 collected in 2002-2004. The health conditions we investigated tend to be long-standing  
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37 or remitting/relapsing conditions, and psychotropic prescribing also once initiated tends  
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39 to be long-standing in people with intellectual disabilities. However, it is possible that  
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41 extent of neighbourhood deprivation, type of accommodation, employment, and civil  
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43 status (though few marry) might have changed for some people between 2002-2004 and  
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45 2018; we have no further information to check this. There were no concerns regarding  
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47 the proportional hazards assumption in the multivariable model. The linkage was also  
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49 reliant on the accuracy of the CHI number as a sole source of linkage.  
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### 53 **Implications**

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55 It is important to know the factors that are associated with risk of death, and the  
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57 common causes of death in this population, as these then inform the actions needed to  
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59 reduce the unacceptably high SMRs experienced by people with intellectual disabilities.  
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3 Awareness of these factors may provide a pathway to action to reduce the observed  
4 earlier mortality in adults with intellectual disabilities. It is not adequate to solely rely on  
5 the public health interventions available to everyone, even when they are accessible.  
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7 Aspiration, reflux, and choking could, and should, be avoided by raising awareness of its  
8 consequences (death), and putting in place training on simple measures related to  
9 feeding, positioning, food consistency, and when to seek health advice from speech and  
10 language therapy, physiotherapy, nursing, and medical advice. Carers need to be aware  
11 of how the adults they care for express pain, so that conditions such as gastrointestinal  
12 ulcers are attended to, prior to the extreme point of perforation, and so treatable  
13 conditions such as constipation and urinary tract infections are managed before they  
14 lead to respiratory distress and sepsis. Quality of care is important; adults with  
15 intellectual disabilities need just as good care for their diabetes and epilepsy (and other  
16 conditions) as the rest of the population, with reasonable adjustments to address  
17 accessibility, and accessible smoking cessation programs.  
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### 35 **Future research**

36 Further research on larger samples is needed, particularly with regards to replicating and  
37 extending our findings on the factors that are associated with risk of death, and any sex  
38 differences in them, so that practitioners can focus on actions to improve the life  
39 expectancy of adults with intellectual disabilities, with and without Down syndrome.  
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## 56 **Author's contributions**

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5 S-AC is principle investigator, she conceived and managed the project, interpreted data,  
6 and wrote the first draft of the manuscript. LA contributed to the conception of the  
7 project, and project management. NG designed and supervised the statistical analysis,  
8 and contributed to data interpretation and drafting of the manuscript. PMcS implemented  
9 and refined the statistical analysis, and contributed to data interpretation, and drafting of  
10 the manuscript. AJ implemented and refined the statistical analysis, and contributed to  
11 data interpretation. AH contributed to data linkage and interpretation, and drafting of the  
12 manuscript. CMcC provided expertise on data linkage and methods, and drafting of the  
13 manuscript. DK contributed to data interpretation and drafting of the manuscript. CM  
14 contributed to data interpretation, and drafting of the manuscript. All approved the final  
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## 30 **Data sharing**

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**Table 1. Cohort characteristics at time of the health assessment, summarised overall and by death status during the follow-up period**

| Variable           | Statistics / Groups | All participants (N=961) | Deceased participants (N=294) | Alive participants (N=667) |
|--------------------|---------------------|--------------------------|-------------------------------|----------------------------|
| Age (years)        | Mean (SD)           | 44.1 (14.6)              | 52.4 (13.6)                   | 40.5 (13.6)                |
|                    | Min, max            | 16, 83                   | 18, 83                        | 16, 77                     |
| Age group          | 16-25 years         | 127 (13.2%)              | 10 (3.4%)                     | 117 (17.5%)                |
|                    | 26-35 years         | 153 (15.9%)              | 26 (8.8%)                     | 127 (19.0%)                |
|                    | 36-45 years         | 246 (25.6%)              | 49 (16.7%)                    | 197 (29.5)                 |
|                    | 46-55 years         | 205 (21.3%)              | 85 (28.8%)                    | 120 (18.0%)                |
|                    | >55 years           | 230 (23.9%)              | 124 (42.0%)                   | 106 (15.9%)                |
| Sex                | Male                | 525 (54.6%)              | 154 (52.4%)                   | 371 (55.6%)                |
|                    | Female              | 436 (45.3%)              | 140 (47.5%)                   | 296 (44.4%)                |
| Ability level      | Mild ID             | 382 (39.7%)              | 92 (31.2%)                    | 290 (43.5%)                |
|                    | Moderate ID         | 236 (24.5%)              | 73 (24.7%)                    | 163 (24.4%)                |
|                    | Severe ID           | 180 (18.7%)              | 67 (22.7%)                    | 113 (16.9%)                |
|                    | Profound ID         | 163 (17.0%)              | 62 (21.1%)                    | 101 (15.1%)                |
| Accommodation type | Family carer        | 374 (38.9%)              | 70 (23.8%)                    | 304 (45.6%)                |
|                    | Independent         | 93 (9.7%)                | 36 (12.2%)                    | 57 (8.5%)                  |
|                    | Paid support        | 435 (45.2%)              | 161 (54.6%)                   | 274 (41.1%)                |
|                    | Congregate care     | 59 (6.1%)                | 27 (9.2%)                     | 32 (4.8%)                  |
| Down syndrome      | No                  | 782 (81.4%)              | 230 (78.2%)                   | 552 (82.8%)                |
|                    | Yes                 | 179 (18.6%)              | 64 (21.7%)                    | 115 (17.2%)                |

ID=intellectual disabilities; SD=standard deviation

**Table 2. Standardised mortality ratios**

| Variable   | Groups  | SMR (95% CI)         |
|--|---|----------------------|
| All participants                                       | -   | 2.24 (1.99, 2.50)    |
| Age group*   | 15-25 years   | 18.73 (0.37, 37.09)  |
|  | 26-35 years   | 4.21 (1.29, 7.13)    |
|  | 36-45 years   | 3.86 (2.28, 5.44)    |
|  | 46-55 years   | 3.77 (2.90, 4.74)    |
|  | >55 years   | 1.86 (1.60, 2.12)    |
| Sex  | Male  | 1.69 (1.42, 1.95)    |
|  | Female  | 3.48 (2.90, 4.06)    |
| Ability level  | Mild ID   | 1.60 (1.27, 1.92)    |
|  | Moderate ID   | 2.10 (1.62, 2.58)    |
|  | Severe ID   | 2.78 (2.11, 3.44)    |
|  | Profound ID   | 4.14 (3.11, 5.17)    |
| Down syndrome  | No  | 1.93 (1.68, 2.18)    |
|  | Yes   | 5.28 (3.98, 6.57)    |
| Underlying causes of death grouped by ICD-10 chapter** | Congenital malformations, deformations and chromosomal abnormalities                                | 17.26 (10.75, 23.78) |
|  | Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | 7.50 (-7.20, 22.20)  |
|  | Diseases of the circulatory system  | 5.55 (4.01, 7.09)    |
|  | Diseases of the digestive system  | 16.13 (8.23, 24.04)  |
|  | Diseases of the genitourinary system  | 3.65 (0.73, 6.57)    |
|  | Diseases of the musculoskeletal system and connective tissue  | 5.40 (-0.71, 11.52)  |
|  | Diseases of the nervous system  | 7.73 (5.13, 10.32)   |
|  | Diseases of the respiratory system  | 6.78 (5.02, 8.54)    |

|  |   |                     |
|--|---|---------------------|
|  | Diseases of the skin and subcutaneous tissue  | 2.75 (-2.64, 8.15)  |
|  | Endocrine, nutritional and metabolic diseases   | 3.43 (1.05, 5.81)   |
|  | External causes of morbidity and mobility   | 11.08 (3.40, 18.76) |
|  | Infectious and parasitic diseases   | 8.93 (1.78, 16.07)  |
|  | Mental and behavioural disorders  | 12.64 (3.27, 22.00) |
|  | Neoplasms   | 6.31 (4.19, 8.43)   |
|  | Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified | 19.51 (0.39, 38.63) |

CI=confidence intervals; ID=intellectual disabilities; SMR=standardised mortality ratios

\*Data used for comparison with General Population (GG&C Health Board) provides data in 5 year age bands therefore 15+. Data on adults with ID are 16+

\*\* Negative Lower CI and wide CIs indicate low number of observed deaths in study population

**Table 3. Underlying causes of death grouped by ICD-10 chapter, where cause of death is known**

| ICD-10 chapter  | Participants with Down syndrome (N=57) | Participants without Down syndrome (N=205) |
|---|--|--|
| Certain infectious and parasitic diseases   | 5 (8.8%)                               | <5   |
| Neoplasms   | <5                                     | 33 (16.1%)                                 |
| Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | <5                                     | <5   |
| Endocrine, nutritional and metabolic diseases   | <5                                     | 8 (3.9%)                                   |
| Mental and behavioural disorders  | 5 (8.8%)                               | <5   |
| Diseases of the nervous system  | 7 (12.3%)                              | 27 (13.2%)                                 |
| Diseases of the eye and adnexa  | <5                                     | <5   |
| Diseases of the ear and mastoid process   | <5                                     | <5   |
| Diseases of the circulatory system  | 8 (14.0%)                              | 42 (20.5%)                                 |
| Diseases of the respiratory system  | 8 (14.0%)                              | 49 (23.9%)                                 |
| Diseases of the digestive system  | <5                                     | 16 (7.8%)                                  |
| Diseases of the skin and subcutaneous tissue  | <5                                     | <5   |
| Diseases of the musculoskeletal system and connective tissue  | <5                                     | <5   |
| Diseases of the genitourinary system  | <5                                     | 5 (2.4%)                                   |
| Pregnancy, childbirth and the puerperium  | <5                                     | <5   |
| Certain conditions originating in the perinatal period  | <5                                     | <5   |
| Congenital malformations, deformations and chromosomal abnormalities                                | 21 (36.8%)                             | 6 (2.9%)                                   |
| Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified             | <5                                     | <5   |
| External causes of morbidity and mortality  | <5                                     | 7 (3.4%)                                   |
| All deaths  | 57 (100%)                              | 205 (100%)                                 |

ICD-10=International Statistical Classification of Diseases and Related Health Problems, 10th Revision

**Table 4. Underlying causes of death grouped by specific individual causes or related groups of causes, where cause of death is known**

| <b>Causes</b>                      | <b>Participants with Down syndrome (N=57)</b> | <b>Participants without Down syndrome (N=205)</b> |
|------------------------------------|---|---|
| Aspiration/reflux/choking          | <5  | 22 (10.8%)  |
| Respiratory infection              | <5  | 21 (10.3%)  |
| Down syndrome                      | 21 (36.8%)                                    | <5  |
| Other malignancy                   | <5  | 19 (9.3%)   |
| Other condition                    | <5  | 17 (8.3%)   |
| Epilepsies                         | <5  | 13 (6.4%)   |
| Acute myocardial infarction        | <5  | 13 (6.4%)   |
| Gastro-intestinal malignancy       | <5  | 12 (5.9%)   |
| Stroke                             | <5  | 11 (5.4%)   |
| Other cardiovascular disease       | <5  | 11 (5.4%)   |
| Other respiratory condition        | <5  | 9 (4.4%)  |
| Other infection                    | 5 (8.8%)                                      | 6 (2.9%)  |
| Cerebral palsy                     | <5  | 11 (5.4%)   |
| Dementia                           | 9 (15.8%)                                     | <5  |
| Other gastrointestinal disorders   | <5  | 8 (3.9%)  |
| Ulcer/gastrointestinal perforation | <5  | 7 (3.4%)  |
| Diabetes                           | <5  | 7 (3.4%)  |
| Other congenital condition         | <5  | 6 (2.9%)  |
| Other ischaemic heart condition    | <5  | 6 (2.9)   |
| Mental health                      | <5  | <5  |
| Other neurological conditions      | <5  | <5  |
| Renal failure                      | <5  | <5  |
| All deaths                         | 57 (100%)                                     | 205 (100%)  |

**Table 5. All contributing causes of death grouped by specific individual causes or related groups of causes, where cause of death is known**

| <b>Causes</b>                       | <b>Participants with Down syndrome (N=57)</b> | <b>Participants without Down syndrome (N=205)</b> |
|-------------------------------------|---|---|
| Respiratory infection               | 22 (38.6%)                                    | 49 (23.9%)  |
| Aspiration/reflux/choking           | 11 (19.3%)                                    | 41 (20.0%)  |
| Down syndrome                       | 43 (75.4%)                                    | <5  |
| Other condition                     | 8 (14.0%)                                     | 33 (16.1%)  |
| Other cardiovascular disease        | 8 (14.0%)                                     | 30 (14.6%)  |
| Other respiratory conditions        | <5  | 31 (15.1%)  |
| Other infection                     | 9 (15.8%)                                     | 24 (11.7%)  |
| Intellectual disabilities           | <5  | 31 (15.1%)  |
| Epilepsies                          | 8 (14.0%)                                     | 24 (11.7%)  |
| Dementia                            | 24 (42.1%)                                    | <5  |
| Other neoplasms                     | <5  | 23 (11.2%)  |
| Cerebral palsy                      | <5  | 24 (11.7%)  |
| Acute myocardial infarction         | 5 (8.8%)                                      | 19 (9.3%)   |
| Other gastrointestinal disorders    | <5  | 18 (8.8%)   |
| Diabetes                            | <5  | 19 (9.3%)   |
| Other ischaemic heart disease       | <5  | 19 (9.3%)   |
| Renal failure                       | <5  | 16 (7.8%)   |
| Stroke                              | <5  | 17 (8.3%)   |
| Other congenital condition          | <5  | 15 (7.3%)   |
| Gastrointestinal malignant neoplasm | <5  | 12 (5.9%)   |
| Ulcer/gastrointestinal perforation  | <5  | 10 (4.9%)   |
| Mental health                       | <5  | 10 (4.9%)   |
| Other neurological condition        | <5  | 8 (3.9%)  |
| Heart failure                       | <5  | 7 (3.4%)  |
| Injuries and accidents              | <5  | 8 (3.9%)  |
| Medical/surgical complications      | <5  | <5  |
| Secondary malignancies              | <5  | <5  |
| Thyroid disorders                   | <5  | <5  |
| Metabolic disorder                  | <5  | <5  |
| All deaths                          | 57 (100%)                                     | 205 (100%)  |

**Table 6. Multivariable model results for the outcome time to death**

| Variable                          |     | Hazard ratio | 95% CI        | p-value |
|-----------------------------------|-----|--------------|---------------|---------|
| Age at time of health assessment  |     | 1.056        | 1.046, 1.066  | <0.0001 |
| Smoker                            | No  | 1            | -             |         |
|                                   | Yes | 1.531        | 1.1011, 2.128 | 0.0112  |
| Down syndrome                     | No  | 1            | -             |         |
|                                   | Yes | 2.440        | 1.787, 3.332  | <0.0001 |
| Epilepsy                          | No  | 1            | -             |         |
|                                   | Yes | 1.511        | 1.173, 1.946  | 0.0014  |
| Hearing impairment                | No  | 1            | -             |         |
|                                   | Yes | 1.320        | 1.030, 1.692  | 0.0284  |
| Bowel incontinence                | No  | 1            | -             |         |
|                                   | Yes | 0.490        | 0.376, 0.640  | <0.0001 |
| Diabetes                          | No  | 1            | -             |         |
|                                   | Yes | 2.346        | 1.553, 3.542  | <0.0001 |
| PEG/tube fed                      | No  | 1            | -             |         |
|                                   | Yes | 2.346        | 1.135, 5.989  | 0.00240 |
| Lower respiratory track infection | No  | 1            | -             |         |
|                                   | Yes | 1.782        | 1.315, 2.415  | 0.0002  |
| Total number of prescribed drugs  |     | 1.066        | 1.016, 1.118  | 0.0085  |

CI=confidence interval; PEG=percutaneous endoscopic gastrostomy

Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage

### Supplementary table 1. Previously reported standardised mortality ratios, causes, and risks for death

| Author                                 | Country   | SMR (95% confidence interval)   | Number of deaths                 | Causes of death and risk factors for death   |
|--|-----------|---|----------------------------------|--|
| Forsgren et al (1996) <sup>7</sup>     | Sweden    | 4.2 (3.3, 5.3) at 20-59y; 1.1 (0.9, 1.5) at 60+y<br><i>Without epilepsy:</i><br>3.8 (2.8, 5.0) at 20-59y; 1.1 (0.8, 1.5) at 60+y<br><i>With epilepsy:</i><br>5.0 (2.9, 8.7) at 20-59y; 2.4 (0.9, 6.1) at 60+y<br><i>With epilepsy and cerebral palsy:</i><br>8.0 (4.1, 15.7) at 20-59y; 0.9 (0.1, 6.6) at 60+y<br><i>M:</i> 1.6 (1.2, 2.0) at 0-60+y<br><i>F:</i> 2.6 (2.0, 3.3) at 0-60+y<br><i>Mild ID:</i> 1.8 (1.1, 2.7) at 0-60+y<br><i>Moderate ID:</i> 1.5 (1.1, 2.0) at 0-60+y<br><i>Severe ID:</i> 2.0 (1.5, 2.6) at 0-60+y<br><i>Profound ID:</i> 8.1 (5.6, 11.7) at 0-60+y | 124 at 0-60+y;<br>112 at 20-60+y | <i>Underlying cause at 0-60+y:</i><br>Congenital anomalies: SMR=46.3 (32.9, 65.0)<br>Nervous system: SMR=9.7 (5.5, 17.0)<br>Mental disorder: SMR=4.0 (1.9, 8.4)<br>Respiratory: SMR=3.3 (2.0, 5.5)<br>Circulatory: SMR=2.1 (1.6, 2.7)<br>Violent death: SMR=1.4 (0.6, 2.8)<br>Neoplasm: SMR=0.9 (0.6, 1.6) |
| Durvasula & Beange (2002) <sup>8</sup> | Australia | 4.9 (3.4, 6.4) at 10-59y<br><i>M:</i> 4.1 (2.4, 5.9) at 10-59y<br><i>F:</i> 6.2 (3.3, 9.1) at 10-59y  | 40 at 10-59y;<br>31 at 20-59y    | <i>Underlying cause at 10-59y:</i><br>Respiratory: 30% (pneumonia, aspiration)<br>External cause: 20%<br>Neoplasm: 17%<br>Heart disease: 15% (congenital heart disease 50%)<br>Gastrointestinal: 1.5% (ischaemic bowel, perforated peptic ulcer, post-operative peritonitis)<br>Seizure: 5%                |
| Tyrer et al (2007) <sup>9</sup>        | England   | 3.24 (2.93, 3.56) at 20-70+y<br><i>M:</i> 2.86 (2.50, 3.26) at 20-70+y<br><i>F:</i> 3.63 (3.12, 4.20) at 20-70+y<br>1.51 (1.23, 1.83) to 11.50 (8.14, 15.78) at 20-70+y<br><i>M:</i> 1.39 (1.03, 1.82) to 8.83 (5.60, 13.25) at 20-70+y<br><i>F:</i> 1.60 (1.18, 2.12) to 17.22 (9.64, 28.4) at 20-70+y<br><i>With Down syndrome:</i> 7.60 at 20-70+y<br><i>Without Down syndrome:</i> 2.70 at 20-70+y  | 409 at 20-70+y                   | Not reported   |
| Patja et al (2008) <sup>10</sup>       | Finland   | <i>M:</i> 2.2 at 20-39y, 1.0 at 40-59y, 1.0 at 60+y<br><i>F:</i> 1.4 at 20-39y, 1.1 at 40-49y, 1.0 at 60+y<br><i>Mild ID:</i><br><i>M:</i> 1.6 at 20-39y, 1.0 at 40-59y, 1.0 at 60+y<br><i>F:</i> 1.2 at 20-39y, 1.1 at 40-49y, 1.0 at 60+y   | 1,046 at 20-97y                  | <i>Underlying cause at 2-97y:</i><br>Vascular: 36% (cardiac infarct 33%, cerebral infarct 33%, congenital heart disease 18%, pulmonary infarct 6%)<br>Respiratory: 22% (pneumonia 83%, COPD 11%)   |

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|   |                     |  |                                      |   |
|---|---------------------|--|--------------------------------------|---|
|   |                     | <p><b>Moderate ID:</b><br/>M: 2.3 at 20-39y, 1.1 at 40-59y, 1.0 at 60+y<br/>F: 1.5 at 20-39y, 1.1 at 40-49y, 1.0 at 60+y</p> <p><b>Severe ID:</b><br/>M: 2.6 at 20-39y, 1.2 at 40-59y, 1.0 at 60+y<br/>F: 1.6 at 20-39y, 1.0 at 40-49y, 1.0 at 60+y</p> <p><b>Profound ID:</b><br/>M: 2.1 at 20-39y, 1.1 at 40-59y, 1.0 at 60+y<br/>F: 1.3 at 20-39y, 1.2 at 40-49y, 1.0 at 60+y</p> |                                      | <p>Neoplasm: 11% (Digestive 44%, respiratory 15%, urogenital, 12%)<br/>Digestive: 7% (intestinal obstruction 25%, ulcer perforation 13%)<br/>Accidents and poisonings: 7% (commonest was fatal fracture, then poisoning)<br/>Vascular, neoplasia, and accident causes were less common than sex-age-related general population; Digestive were 2.5 times, Respiratory 2.6-5.8 times more common</p>   |
| Tyrer & McGoher (2009) <sup>11</sup>      | England             | <p>2.77 (2.53, 3.03) at 20+y<br/>M: 2.28 (2.02, 2.56) at 20+y<br/>F: 3.24 (2.83, 3.69) at 20+y</p>   | 503 at 20+y                          | <p><b>Underlying cause of death at 20+y:</b><br/>Pneumonia: 1.3% (OR=6.47 (5.00, 8.23))<br/>Nervous system: 3.1% (OR=16.30 (12.61, 20.74))<br/>Other respiratory: 12.9% (OR=4.64 (3.58, 5.91))<br/>Ischaemic heart disease: 11.5% (OR=1.49 (1.13, 1.92))<br/>Neoplasm: 9.3%<br/>Congenital anomalies: 9.1% (OR=85.60 (62.67, 114.18))<br/>Cerebrovascular disease: 7.8% (OR=2.40 (1.71, 3.28))</p>  |
| Oullette-Kuntz et al (2015) <sup>12</sup> | Canada              | <p>2.5 (2.1, 2.9) at 0-60+y<br/>M: 2.1 (1.7, 2.6) at 0-60+y<br/>F: 3.0 (2.4, 3.8) at 0-60+y<br/>M: 1.7 (1.3, 2.3) to 3.4 (2.3, 4.7) at 20-60+y<br/>F: 2.1 (1.4, 2.9) to 6.1 (4.1, 8.6) at 20-60+y</p>  | 172 at 0-60+y;<br>158 at 20-60+y     | <p><b>Risk factors for death:</b><br/>Age, Down syndrome (OR=1.76 at 20-39y; OR=1.69 at 40-59y; OR=22.3 at 60+y), cerebral palsy (OR=2.39 at 20-39y; OR=0.93 at 40-59y; OR=0.50 at 60+y), blindness/low vision (OR not given), technological dependence/medical fragility (OR=1.95 at 20-39y; OR=7.28 at 40-59y; OR=3.42 at 60+y), wheelchair dependence (OR=5.96 at 20-39y; OR=2.89 at 40-59y; OR=2.56 at 60+y), mobility impairment without wheelchair dependence (OR not given), epilepsy (OR=1.8 at 20-39y; OR=1.80 at 40-59y; OR=1.09 at 60+y)</p> |
| Florio & Troller (2015) <sup>13</sup>     | Australia           | <p>2.48 (2.32, 2.64) at 0-85+y<br/>3.15 (2.94, 3.38) at 5-69y<br/>M: 2.52 (2.29, 2.77) at 5-69y<br/>F: 4.26 (3.83, 4.74) at 5-69y</p>  | 953 at 0-85+y;<br>831 at 15+y        | Not reported  |
| McCarron et al (2015) <sup>14</sup>       | Republic of Ireland | <p>3.85 (3.70, 4.00) at 0-80+y<br/>M: 3.09 (2.93, 3.25) at 0-80+y<br/>F: 4.90 (4.63, 5.17) at 0-80+y<br/>2.71 (2.41, 3.04) to 6.09 (5.29, 6.96) at 20-80y<br/>M: 2.50 (2.18, 2.86) to 4.50 (3.69, 5.44) at 20-80y<br/>F: 2.71 (2.32, 3.14) to 10.07 (8.99, 13.10) at 20-80y</p>  | 2,666 at 0-80+y;<br>2,394 at 20-80+y | Not reported  |

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|  |         |   |  |   |
|--|---------|---|--|---|
| Heslop & Glover (2015) <sup>15</sup>   | England | Median 2.13 (interquartile range 1.09, 2.83) across geographic areas at 18-65+y   | 18-65+y  | Not reported  |
| Lauer & McCallion (2015) <sup>16</sup> | USA     | <i>Intellectual and developmental disabilities*:</i><br>1.19 at all ages, 2011<br>1.49 at 18+y, 2009  | 120,913 in 2009 at 18+y, 140,104 in 2011 at all ages | Not reported  |
| Arvio et al (2016) <sup>17</sup>       | Finland | <i>Mild ID:</i><br>2.28 (2.18, 2.39) at 0-60+y<br>1.99 (1.85, 2.13) to 2.77 (2.36, 3.23) at 15-60+y<br><i>M:</i> 2.01 (1.88, 2.14) at 0-60+y<br><i>F:</i> 2.80 (2.60, 3.01) at 0-60+y<br><i>Severe ID:</i><br>3.41 (3.30, 3.52) at 0-60+y<br>2.07 (1.96, 2.19) to 8.77 (7.77, 9.87) at 15-60+y<br><i>M:</i> 2.59 (2.48, 2.72) at 0-60+y<br><i>F:</i> 5.24 (4.99, 5.50) at 0-60+y  | 5,171 at 0-60+y; 5,053 at 15-60y                     | Not reported  |
| Hosking et al (2016) <sup>5</sup>      | England | HR=3.62 (3.33, 3.93) at 18-84y<br><i>M:</i> HR=3.30 (2.96, 3.68) at 18-84y<br><i>F:</i> HR=4.10 (3.61, 4.66) at 18-84y<br><i>With Down syndrome:</i> HR=9.21 (7.22, 11.76)<br><i>Without Down syndrome:</i> HR=3.19 (2.92, 3.49)<br><i>With epilepsy:</i> HR=6.04 (5.04, 7.24)<br><i>Without epilepsy:</i> HR=3.18 (2.90, 3.50)<br><i>With high level of support needs:</i> HR=4.77 (4.08, 5.59)<br><i>Without high level of support needs:</i> HR=3.28 (2.98, 3.62)<br><i>With autism:</i> HR=2.39 (1.45, 3.96)<br><i>Without autism:</i> HR=3.66 (3.37, 3.98)<br><i>In communal/shared homes:</i> HR=4.99 (4.36, 5.73)<br><i>Not in communal/shared homes:</i> HR=3.05 (2.74, 3.30) | 656 at 18-84y  | <i>Underlying cause at 18-84y:</i><br>Circulatory: 2.6%, HR=3.05 (2.56, 3.64)<br>Respiratory: 1.8% (pneumonia and aspiration pneumonia), HR=1.68 (5.38, 8.29)<br>Neoplasm: 14%, HR=1.44 (1.18, 1.76)<br>Nervous system: 1.6%, HR=13.79 (9.70, 19.62)<br>Digestive: 7.0%, HR=4.02 (2.92, 5.54)<br>Congenital anomalies: 6.9%, HR could not be estimated<br>Mental disorders: 2.3%, HR=7.99 (5.19, 12.31)<br>External causes: 4.1%, HR=1.85 (1.26, 2.71)<br>Genitourinary: 3.5%, HR=10.89 (6.09, 19.47)<br>Endocrine, nutritional, and metabolic: 2.0%, HR=5.38 (2.79, 10.07)<br><i>Down syndrome:</i> Respiratory: 20.3% (or 42.4% if "Down syndrome" is excluded as an underlying cause of death)<br><i>Avoidable deaths:</i> 37% amenable (20% controls), 19% preventable (40% controls) |

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|                                    |           |   |                                   |  |
|------------------------------------|-----------|---|-----------------------------------|--|
| Lauer (2016) <sup>18</sup>         | USA       | Not reported  | 438 in 2012, 409 in 2013, at 18+y | <p><i>Major cause of death, 2012, 2013</i></p> <p>Heart disease: 16.9%, 13.7%</p> <p>Neoplasm: 13.0%, 13.4%</p> <p>Alzheimer disease: 13.0%-12.2% (48% in Down syndrome)</p> <p>Aspiration pneumonia: 9.4%, 8.6%</p> <p>Septicaemia: 10.0%, 8.6%</p> <p>Chronic lower respiratory diseases: 4.6%, 6.6%</p> <p>Unintentional injury: 4.8%, 3.2%</p>   |
| Troller et al (2017) <sup>19</sup> | Australia | <p>1.3 (1.2, 1.5) at 20+y</p> <p>4.0 (3.1, 5.2) at 20-44y</p> <p>2.3 (2.0, 2.7) at 45-64y</p> <p>1.0 (0.8, 1.2) at 65+y</p> <p>M: 1.4 (1.1, 1.6) at 20+y</p> <p>F: 1.3 (1.1, 1.6) at 20+y</p>   | 732 at 20-65+y                    | <p><i>Underlying cause at 20-65+y:</i></p> <p>Circulatory: 18%</p> <p>Neoplasm: 18%</p> <p>Nervous: 16%</p> <p>Respiratory: 11%</p> <p>Congenital anomalies: 11%</p> <p>Injury and poisoning: 6%</p> <p>Digestive: 5%</p> <p><i>Avoidable deaths: 31%</i></p>  |
| Glover et al (2017) <sup>6</sup>   | England   | <p>3.18 (2.94, 3.43) at 0-99y</p> <p>M: 3.03 (2.73, 3.35) at 0-99y</p> <p>F: 3.40 (3.02, 3.81) at 0-99y</p> <p>1.6 (1.2, 2.1) to 7.8 (5.4, 11.1) at 18-99y</p> <p>M: 1.5 (0.9, 2.2) to 6.6 (4.0, 10.1) at 18-99y</p> <p>F: 1.7 (1.1, 2.4) to 11.6 (6.0, 20.2) at 18-99y</p> | 664 at 0-99y                      | <p><i>Underlying cause at 0-99y:</i></p> <p>Circulatory: 22.9% (ischaemic heart disease 37.5%, cerebrovascular 2.7%, thrombophlebitis 6.6%, cardiomyopathy 9.9%, PE 3.9%), SMR=2.8 (2.4, 3.3)</p> <p>Respiratory: 14.2% (pneumonia 50.0%, pneumonitis 21.0%), SMR=4.9 (4.0, 5.9)</p> <p>Neoplasm: 3.1% (digestive 36.8%, respiratory 13.8%, female genital tract 10.3%, lymphoid and haematopoietic 10.3%), SMR=1.1 (0.9, 1.4)</p> <p>Nervous: 12.8%, SMR=9.8 (7.8, 12.1)</p> <p>Congenital anomalies: 8.4%, SMR=72.9 (55.1, 94.7)</p> <p>Digestive: 7.8%, SMR=4.0 (3.0, 5.2)</p> <p>No ICD10 chapter had fewer than expected deaths</p> <p>Other common single causes: dementia 33/664, epilepsy 26/664, cerebral palsy 23/664</p> <p><i>Avoidable deaths:</i></p> <p>44.7% (41.0%, 48.5%), mostly amenable</p> <p>M: 50.9% (45.9%, 56.0%); F: 36.9% (31.5%, 42.5%)</p> |

COPD=chronic obstructive pulmonary disease; HR=hazard ratio; ID=intellectual disabilities; OR=odds ratio; PE=pulmonary embolism; SMR=standardised mortality ratio; y=years

\*Includes some individuals with IQ>70

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## Supplementary table 2. Groupings of related causes of deaths

|   | <b>ICD10</b> |
|---|--------------|
| <b>Infectious diseases</b>  |              |
| <b>Infection</b>  |              |
| ENTEROCOLITIS DUE TO CLOSTRIDIUM DIFFICILE                                | A047         |
| SEPSIS DUE TO STAPHYLOCOCCUS AUREUS                                       | A410         |
| SEPSIS, UNSPECIFIED   | A419         |
| BACTERIAL INFECTION, UNSPECIFIED  | A499         |
| SUBACUTE SCLEROSING PANENCEPHALITIS                                       | A811         |
| CHRONIC VIRAL HEPATITIS B WITHOUT DELTA-AGENT                             | B181         |
| PULMONARY CANDIDIASIS   | B371         |
| NECROTISING FASCIITIS   | M726         |
| URINARY TRACT INFECTION, SITE NOT SPECIFIED                               | N390         |
| <b>Neoplasms</b>  |              |
| <b>Gastrointestinal malignant neoplasms</b>                               |              |
| MALIGNANT NEOPLASM OF PAROTID GLAND                                       | C07          |
| MALIGNANT NEOPLASM, OESOPHAGUS, UNSPECIFIED                               | C159         |
| MALIGNANT NEOPLASM, STOMACH, UNSPECIFIED                                  | C169         |
| MALIGNANT NEOPLASM, CAECUM  | C180         |
| MALIGNANT NEOPLASM, SIGMOID COLON   | C187         |
| MALIGNANT NEOPLASM, COLON, UNSPECIFIED                                    | C189         |
| INTRAHEPATIC BILE DUCT CARCINOMA  | C221         |
| NEOPLASM OF UNCERTAIN OR UNKNOWN BEHAVIOUR, OTHER DIGESTIVE ORGANS        | D377         |
| <b>Other neoplasms</b>  |              |
| MALIGNANT NEOPLASM, LOWER LOBE, BRONCHUS OR LUNG                          | C343         |
| MALIGNANT NEOPLASM, BRONCHUS OR LUNG, UNSPECIFIED                         | C349         |
| MALIGNANT NEOPLASM, BREAST, UNSPECIFIED                                   | C509         |
| MALIGNANT NEOPLASM, ENDOMETRIUM   | C541         |
| MALIGNANT NEOPLASM OF OVARY   | C56          |
| MALIGNANT NEOPLASM, TESTIS, UNSPECIFIED                                   | C629         |
| MALIGNANT NEOPLASM, BLADDER, UNSPECIFIED                                  | C679         |
| MALIGNANT NEOPLASMS OF THYROID GLAND                                      | C73          |
| WALDENSTROM MACROGLOBULINAEMIA  | C880         |
| NON-HODGKIN'S LYMPHOMA, UNSPECIFIED                                       | C859         |
| MALIGNANT NEOPLASM OF UNSPECIFIED SITE                                    | C80          |
| NEOPLASM OF UNCERTAIN OR UNKNOWN BEHAVIOUR, TRACHEA, BRONCHUS AND LUNG    | D381         |
| SECONDARY MALIGNANT NEOPLASM OF LUNG                                      | C780         |
| SECONDARY MALIGNANT NEOPLASM OF LIVER AND INTRAHEPATIC BILE DUCT          | C787         |
| SECONDARY MALIGNANT NEOPLASM OF BRAIN AND CEREBRAL MENINGES               | C793         |
| SECONDARY MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES                     | C798         |
| <b>Endocrine and metabolic diseases</b>                                   |              |
| <b>Diabetes</b>   |              |
| INSULIN-DEPENDENT DIABETES MELLITUS WITHOUT COMPLICATIONS                 | E109         |
| NON-INSULIN-DEPENDENT DIABETES MELLITUS WITH RENAL COMPLICATIONS          | E112         |
| NON-INSULIN-DEPENDENT DIABETES MELLITUS W. PERIPHERAL CIRC. COMPLICATIONS | E115         |
| NON-INSULIN-DEPENDENT DIABETES MELLITUS WITHOUT COMPLICATIONS             | E119         |
| UNSPECIFIED DIABETES MELLITUS WITH RENAL COMPLICATIONS                    | E142         |

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|    |   |      |
|----|---|------|
| 1  |   |      |
| 2  | UNSPECIFIED DIABETES MELLITUS WITHOUT COMPLICATIONS                     | E149 |
| 3  | ABNORMAL GLUCOSE TOLERANCE TEST   | R730 |
| 4  | HYPERGLYCAEMIA, UNSPECIFIED   | R739 |
| 5  |   |      |
| 6  | <b>Metabolic disorders</b>  |      |
| 7  | OTHER HYPERPHENYLALANINAEMIAS   | E701 |
| 8  | DISORDERS OF PHOSPHORUS METABOLISM & PHOSPHATASES                       | E833 |
| 9  | DISORDERS OF PLASMA-PROTEIN METABOLISM, NOT ELSEWHERE CLASSIFIED        | E880 |
| 10 |   |      |
| 11 |   |      |
| 12 | <b>Mental disorders</b>   |      |
| 13 | <b>Dementias</b>  |      |
| 14 | VASCULAR DEMENTIA, UNSPECIFIED  | F019 |
| 15 | UNSPECIFIED DEMENTIA  | F03  |
| 16 | ALZHEIMER'S DISEASE WITH LATE ONSET                                     | G301 |
| 17 | ALZHEIMER'S DISEASE, UNSPECIFIED  | G309 |
| 18 |   |      |
| 19 | <b>Mental health</b>  |      |
| 20 |   |      |
| 21 | MENTAL AND BEHAVIOURAL DISORDERS DUE TO ACUTE INTOXICATION WITH ALCOHOL | F100 |
| 22 | MENTAL AND BEHAVIOURAL DISORDERS DUE TO ALCOHOL DEPENDENCE SYNDROME     | F102 |
| 23 | MENTAL AND BEHAVIOURAL DISORDERS DUE TO USE OF TOBACCO, UNSPECIFIED     | F179 |
| 24 | SCHIZOPHRENIA, UNSPECIFIED  | F209 |
| 25 | BIPOLAR AFFECTIVE DISORDER, UNSPECIFIED                                 | F319 |
| 26 | OTHER & UNSPEC SYMPTOMS & SIGNS INVOLVING COGNITIVE FUNCTIONS &         | R418 |
| 27 | AWARENESS   |      |
| 28 | INTENTIONAL SELF-HARM BY JUMPING FROM A HIGH PLACE                      | X80  |
| 29 |   |      |
| 30 | <b>Intellectual disabilities</b>  |      |
| 31 | UNSPECIFIED MENTAL RETARDATION  | F79  |
| 32 | DEVELOPMENTAL DISORDER OF SCHOLASTIC SKILLS, UNSPECIFIED                | F819 |
| 33 |   |      |
| 34 |   |      |
| 35 | <b>Nervous system</b>   |      |
| 36 | <b>Epilepsies</b>   |      |
| 37 | GENERALIZED IDIOPATHIC EPILEPSY AND EPILEPTIC SYNDROMES                 | G403 |
| 38 | EPILEPSY, UNSPECIFIED   | G409 |
| 39 | STATUS EPILEPTICUS, UNSPECIFIED   | G419 |
| 40 | MYOTONIC DISORDERS  | G711 |
| 41 | OTHER AND UNSPECIFIED CONVULSIONS                                       | R568 |
| 42 |   |      |
| 43 | <b>Cerebral palsy</b>   |      |
| 44 | SPASTIC QUADRAPLEGIC CEREBRAL PALSY                                     | G800 |
| 45 | SPASTIC HEMIPLEGIC CEREBRAL PALSY                                       | G802 |
| 46 | OTHER CEREBRAL PALSY  | G808 |
| 47 | CEREBRAL PALSY, UNSPECIFIED   | G809 |
| 48 | TETRAPLEGIA, UNSPECIFIED  | G825 |
| 49 |   |      |
| 50 | <b>Other neurological conditions</b>                                    |      |
| 51 | SEQUELAE OF INFLAMMATORY DISEASES OF CENTRAL NERVOUS SYSTEM             | G09  |
| 52 | PARKINSON'S DISEASE   | G20  |
| 53 | MYONEURAL DISORDER, UNSPECIFIED   | G709 |
| 54 | ENCEPHALITIS, MYELITIS AND ENCEPHALOMYELITIS, UNSPECIFIED               | G049 |
| 55 | ANOXIC BRAIN DAMAGE, NOT ELSEWHERE CLASSIFIED                           | G931 |
| 56 | BLINDNESS, BINOCULAR  | H540 |
| 57 | OTHER DISORDERS OF NERVOUS SYSTEM, NOT ELSEWHERE CLASSIFIED             | G98  |
| 58 |   |      |
| 59 |   |      |
| 60 |   |      |

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## **Circulatory system**

### **Acute myocardial infarction**

ACUTE MYOCARDIAL INFARCTION, UNSPECIFIED I219

CARDIAC ARREST, UNSPECIFIED I469

### **Other ischaemic heart disease**

HYPERTENSIVE HEART DISEASE WITHOUT (CONGESTIVE) HEART FAILURE I119

ACUTE ISCHAEMIC HEART DISEASE, UNSPECIFIED I249

ATHEROSCLEROTIC HEART DISEASE I251

CHRONIC ISCHAEMIC HEART DISEASE, UNSPECIFIED I259

ATHEROSCLEROSIS OF AORTA I700

GENERALIZED AND UNSPECIFIED ATHEROSCLEROSIS I709

### **Heart failure**

HEART FAILURE, UNSPECIFIED I509

LEFT VENTRICULAR FAILURE I501

CONGESTIVE HEART FAILURE I500

### **Other cardiovascular disease**

PULMONARY EMBOLISM WITHOUT MENTION OF ACUTE COR PULMONALE I269

OTHER SPECIFIED PULMONARY HEART DISEASES I278

PULMONARY HEART DISEASE, UNSPECIFIED I279

AORTIC (VALVE) STENOSIS I350

ATRIAL FIBRILLATION AND FLUTTER I48

VENTRICULAR FIBRILLATION AND FLUTTER I490

OTHER ILL-DEFINED HEART DISEASES I518

PULMONARY OEDEMA J81

CARDIOGENIC SHOCK R570

PERIPHERAL VASCULAR DISEASE, UNSPECIFIED I739

PHLEBITIS AND THROMBOPHLEBITIS OF OTHER DEEP VESSELS OF LOWER EXTREMITIES I802

EMBOLISM AND THROMBOSIS OF OTHER SPECIFIED VEINS I828

ACUTE AND SUBACUTE INFECTIVE ENDOCARDITIS I330

ACUTE ENDOCARDITIS, UNSPECIFIED I339

ENDOCARDITIS, VALVE UNSPECIFIED I38

DILATED CARDIOMYOPATHY I420

CARDIOMEGALY I517

ESSENTIAL (PRIMARY) HYPERTENSION I10

### **Stroke**

INTRACEREBRAL HAEMORRHAGE, UNSPECIFIED I619

CEREBRAL INFARCTION DUE TO THROMBOSIS OF PRECEREBRAL ARTERIES I630

CEREBRAL INFARCTION DUE TO UNSPECIFIED OCCLUSION/STENOSIS OF PRECEREBRAL ARTERIES I632

CEREBRAL INFARCTION, UNSPECIFIED I639

STROKE, NOT SPECIFIED AS HAEMORRHAGE OR INFARCTION I64

CEREBROVASCULAR DISEASE, UNSPECIFIED I679

SEQUELAE OF STROKE, NOT SPECIFIED AS HAEMORRHAGE OR INFARCTION I694

SEQUELAE OF OTHER AND UNSPECIFIED CEREBROVASCULAR DISEASES I698

## **Respiratory system**

### **Respiratory infection**

ACUTE UPPER RESPIRATORY INFECTION, UNSPECIFIED J069

INFLUENZA WITH PNEUMONIA, OTHER INFLUENZA VIRUS IDENTIFIED J100

INFLUENZA WITH OTHER RESPIRATORY MANIFESTATIONS, OTHER INFLUENZA VIRUS IDENTIFIED J101

*Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage*

|    |   |      |
|----|---|------|
| 1  |   |      |
| 2  | PNEUMONIA DUE TO STREPTOCOCCUS PNEUMONIAE                             | J13  |
| 3  | BRONCHOPNEUMONIA, UNSPECIFIED   | J180 |
| 4  | LOBAR PNEUMONIA, UNSPECIFIED  | J181 |
| 5  | HYPOSTATIC PNEUMONIA, UNSPECIFIED                                     | J182 |
| 6  | PNEUMONIA, UNSPECIFIED  | J189 |
| 7  | UNSPECIFIED ACUTE LOWER RESPIRATORY INFECTION                         | J22  |
| 8  | CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH ACUTE LOWER RESP INFECTION | J440 |
| 9  |   |      |
| 10 |   |      |
| 11 | <b>Aspiration/reflux/choking</b>                                      |      |
| 12 | PNEUMONITIS DUE TO FOOD AND VOMIT                                     | J690 |
| 13 | GASTRO-OESOPHAGEAL REFLUX DISEASE WITHOUT OESOPHAGITIS                | K219 |
| 14 | INHALATION AND INGESTION OF FOOD CAUSING OBSTRUCTION OF RESPIRATORY   | W79  |
| 15 | TRACT   |      |
| 16 |   |      |
| 17 | FOREIGN BODY IN RESPIRATORY TRACT, PART UNSPECIFIED                   | T179 |
| 18 | INHALATION/INGESTION OF OTHER OBJECTS CAUSING OBSTRUCT OF RESP TRACT  | W80  |
| 19 |   |      |
| 20 | <b>Other respiratory disorders</b>                                    |      |
| 21 | UNSPECIFIED CHRONIC BRONCHITIS  | J42  |
| 22 | EMPHYSEMA, UNSPECIFIED  | J439 |
| 23 | CHRONIC OBSTRUCTIVE PULMONARY DISEASE, UNSPECIFIED                    | J440 |
| 24 | ASTHMA, UNSPECIFIED   | J459 |
| 25 | BRONCHIECTASIS  | J47  |
| 26 | OTHER INTERSTITIAL PULMONARY DISEASES WITH FIBROSIS                   | J841 |
| 27 | PLEURAL EFFUSION, NOT ELSEWHERE CLASSIFIED                            | J90  |
| 28 | CHRONIC RESPIRATORY FAILURE   | J961 |
| 29 | RESPIRATORY FAILURE, UNSPECIFIED                                      | J969 |
| 30 | OTHER SPECIFIED RESPIRATORY DISORDERS                                 | J988 |
| 31 | DYSPNOEA  | R060 |
| 32 | RESPIRATORY ARREST  | R092 |
| 33 | ASPHYXIATION  | T71  |
| 34 | UNSPECIFIED THREAT TO BREATHING                                       | W84  |
| 35 |   |      |
| 36 |   |      |
| 37 |   |      |
| 38 |   |      |
| 39 | <b>Digestive system</b>   |      |
| 40 | <b>Ulcer/gastrointestinal perforation</b>                             |      |
| 41 | OESOPHAGITIS  | K20  |
| 42 | PERFORATION OF INTESTINE (NONTRAUMATIC)                               | K631 |
| 43 | PERITONITIS, UNSPECIFIED  | K659 |
| 44 | GASTRIC ULCER, CHRONIC OR UNSPECIFIED WITH PERFORATION                | K255 |
| 45 | OTHER PERITONITIS   | K658 |
| 46 | ACUTE PERITONITIS   | K650 |
| 47 | GASTROINTESTINAL HAEMORRHAGE, UNSPECIFIED                             | K922 |
| 48 | ULCER OF INTESTINE  | K633 |
| 49 |   |      |
| 50 | <b>Other gastrointestinal disorders</b>                               |      |
| 51 | BARRETTS OESOPHAGUS   | K227 |
| 52 | DIAPHRAGMATIC HERNIA WITHOUT OBSTRUCTION OR GANGRENE                  | K449 |
| 53 | OTHER SPECIFIED NONINFECTIVE GASTROENTERITIS AND COLITIS              | K528 |
| 54 | ACUTE VASCULAR DISORDERS OF INTESTINE                                 | K550 |
| 55 | VASCULAR DISORDER OF INTESTINE, UNSPECIFIED                           | K559 |
| 56 | VOLVULUS  | K562 |
| 57 | OTHER AND UNSPECIFIED INTESTINAL OBSTRUCTION                          | K566 |
| 58 | CONSTIPATION  | K590 |
| 59 |   |      |
| 60 |   |      |

*Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage*

|    |  |      |
|----|--|------|
| 1  |  |      |
| 2  | MEGACOLON, NOT ELSEWHERE CLASSIFIED              | K593 |
| 3  | ACUTE AND SUBACUTE HEPATIC FAILURE               | K720 |
| 4  | OTHER AND UNSPECIFIED CIRRHOSIS OF LIVER         | K746 |
| 5  | AUTOIMMUNE HEPATITIS                             | K754 |
| 6  | INFLAMMATORY LIVER DISEASE, UNSPECIFIED          | K759 |
| 7  | OTHER SPECIFIED DISEASES OF LIVER                | K768 |
| 8  | CALCULUS OF GALLBLADDER WITH OTHER CHOLECYSTITIS | K801 |
| 9  | CHOLANGITIS                                      | K830 |
| 10 | ACUTE PANCREATITIS, UNSPECIFIED                  | K859 |
| 11 | PSEUDOCYST OF PANCREAS                           | K863 |
| 12 | INTESTINAL MALABSORPTION, UNSPECIFIED            | K909 |
| 13 | DYSPHAGIA  | R13  |

## **Genitourinary system**

### **Renal failure**

|    |   |      |
|----|---|------|
| 14 | CHRONIC NEPHRITIC SYNDROME, UNSPECIFIED | N039 |
| 15 | OTHER ACUTE RENAL FAILURE               | N178 |
| 16 | ACUTE RENAL FAILURE, UNSPECIFIED        | N179 |
| 17 | END-STAGE RENAL DISEASE                 | N180 |
| 18 | CHRONIC KIDNEY DISEASE, STAGE 5         | N185 |
| 19 | CHRONIC KIDNEY DISEASE, UNSPECIFIED     | N189 |
| 20 | UNSPECIFIED KIDNEY FAILURE              | N19  |

### **Chromosomal abnormalities**

#### **Down syndrome**

|    |                              |      |
|----|------------------------------|------|
| 21 | DOWN'S SYNDROME, UNSPECIFIED | Q909 |
|----|------------------------------|------|

#### **Other congenital condition**

|    |   |      |
|----|---|------|
| 22 | CONGENITAL HYDROCEPHALUS, UNSPECIFIED                                     | Q039 |
| 23 | SPINA BIFIDA, UNSPECIFIED   | Q059 |
| 24 | CONGENITAL MALFORMATION OF HEART, UNSPECIFIED                             | Q249 |
| 25 | CONGENITAL DEFORMITY OF SPINE   | Q675 |
| 26 | CONGEN MALFORMATION SYNDROMES PREDOMINANTLY ASSOCIATED WITH SHORT STATURE | Q871 |
| 27 | MARFAN'S SYNDROME   | Q874 |
| 28 | OTHER SPECIFIED CONGEN MALFORMATION SYNDROMES, NOT ELSEWHERE CLASSIFIED   | Q878 |
| 29 | CONGENITAL MALFORMATION, UNSPECIFIED                                      | Q899 |
| 30 | KLINEFELTER'S SYNDROME, UNSPECIFIED                                       | Q984 |
| 31 | FRAGILE X CHROMOSOME  | Q992 |
| 32 | OTHER LACK OF EXPECTED NORMAL PHYSIOLOGICAL DEVELOPMENT                   | R628 |

### **Other conditions occurring with small frequency**

#### **Other condition**

|    |                                   |      |
|----|-----------------------------------|------|
| 33 | DECUBITUS ULCER AND PRESSURE AREA | L89  |
| 34 | SCOLIOSIS, UNSPECIFIED            | M419 |
| 35 | URETHRAL STRICTURE, UNSPECIFIED   | N359 |
| 36 | EPISTAXIS                         | R040 |
| 37 | IMMOBILITY                        | R263 |
| 38 | MALAISE AND FATIGUE               | R53  |
| 39 | GENERALIZED ENLARGED LYMPH NODES  | R591 |

*Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage*

|    |   |      |
|----|---|------|
| 1  |   |      |
| 2  | INSUFFICIENT INTAKE OF FOOD AND WATER DUE TO SELF NEGLECT                 | R636 |
| 3  | OTHER SPECIFIED GENERAL SYMPTOMS AND SIGNS                                | R688 |
| 4  | OTHER ILL-DEFINED AND UNSPECIFIED CAUSES OF MORTALITY                     | R99  |
| 5  | EXPOSURE TO UNSPECIFIED FACTOR  | X59  |
| 6  | MULTI-SYSTEM DEGENERATION   | G903 |
| 7  | BENIGN NEOPLASM, MENINGES, UNSPECIFIED                                    | D329 |
| 8  | AGRANULOCYTOSIS   | D70  |
| 9  | SARCOIDOSIS OF OTHER AND COMBINED SITES                                   | D868 |
| 10 | SARCOIDOSIS, UNSPECIFIED  | D869 |
| 11 | HYPOPITUITARISM   | E230 |
| 12 | HYPOTHYROIDISM, UNSPECIFIED   | E039 |
| 13 | OTHER THYROTOXICOSIS  | E058 |
| 14 | VOLUME DEPLETION  | E86  |
| 15 |   |      |
| 16 |   |      |
| 17 |   |      |
| 18 |   |      |
| 19 |   |      |
| 20 | <b>Injuries and external causes</b>                                       |      |
| 21 | <b>Injuries and accidents</b>   |      |
| 22 | INTRACRANIAL INJURY, UNSPECIFIED  | S069 |
| 23 | UNSPECIFIED INJURY OF HEAD  | S099 |
| 24 | INJURY OF COLON   | S365 |
| 25 | FRACTURE OF NECK OF FEMUR   | S720 |
| 26 | FRACTURE OF SHAFT OF TIBIA  | S822 |
| 27 | UNSPECIFIED MULTIPLE INJURIES   | T07  |
| 28 | FAT EMBOLISM (TRAUMATIC)  | T791 |
| 29 | SEQUELAE OF UNSPECIFIED INJURY OF HEAD                                    | T909 |
| 30 | UNSPECIFIED FALL  | W19  |
| 31 | SEQUELAE OF OTHER ACCIDENTS   | Y86  |
| 32 |   |      |
| 33 | <b>Medical/surgical complication</b>                                      |      |
| 34 | POISONING BY OTHER ANTIDYSRHYTHMIC DRUGS, NOT ELSEWHERE CLASSIFIED        | T462 |
| 35 | ADVERSE EFFECTS OF OTHER ANTIDYSRHYTHMIC DRUGS, NOT ELSEWHERE CLASSIFIED  | Y522 |
| 36 | ABN REACT TO/LATER COMPLIC OF OP WITH IMPLANT OF ARTIFICIAL INTERN DEVICE | Y831 |
| 37 | ABN REACT TO/LATER COMPLIC OF OP WITH ANASTOMOSIS, BYPASS OR GRAFT        | Y832 |
| 38 | ABN REACT TO/LATER COMPLIC OF OP WITH FORMATION OF EXTERNAL STOMA         | Y833 |
| 39 | ABNORMAL REACTION TO OR LATER COMPLICATION OF OTHER MEDICAL PROCEDURES    | Y848 |
| 40 | SEQ OF PROCED CAUSING ABN REACT/COMPLIC,W/O MENTION OF MISADV AT THE TIME | Y883 |
| 41 | OTHER POSTPROCEDURAL RESPIRATORY DISORDERS                                | J958 |
| 42 |   |      |
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*Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage*

### Supplementary table 3. Predictors of the outcome time to death from univariate analyses

| Variable                         |                     | N with event/<br>N in group | Hazard ratio<br>(95% CI) | Individual p-value | Overall p-value |
|----------------------------------|---------------------|-----------------------------|--------------------------|--------------------|-----------------|
| <b>Demographics</b>              |                     |                             |                          |                    |                 |
| Age at time of health assessment |                     | 294/961                     | 1.05 (1.04, 1.06)        | <0.0001            |                 |
| Sex                              | Male                | 154/525                     | 0.88 (0.70, 1.11)        | 0.2730             |                 |
|                                  | Female              | 140/436                     | 1.00 (-)                 |                    |                 |
| Ability level                    | Mild ID             | 92/382                      | 1.00 (-)                 |                    | 0.0007          |
|                                  | Moderate ID         | 73/236                      | 1.38 (1.01, 1.87)        | 0.0411             |                 |
|                                  | Severe ID           | 67/180                      | 1.75 (1.28, 2.40)        | 0.0005             |                 |
|                                  | Profound ID         | 62/163                      | 1.77 (1.28, 2.45)        | 0.0005             |                 |
| Type of accommodation            | Family carer        | 70/374                      | 1.00 (-)                 |                    | <0.0001         |
|                                  | Independent of care | 36/93                       | 2.35 (1.57, 3.52)        | <0.0001            |                 |
|                                  | Paid support        | 161/435                     | 2.18 (1.65, 2.88)        | <0.0001            |                 |
|                                  | Congregate          | 27/59                       | 2.87 (1.84, 4.48)        | <0.0001            |                 |
| Neighbourhood deprivation        | 1 - most affluent   | 18/73                       | 1.00 (-)                 |                    | 0.1890          |
|                                  | 2                   | 56/137                      | 1.92 (1.13, 3.27)        | 0.0158             |                 |
|                                  | 3                   | 10/45                       | 0.90 (0.42, 1.95)        | 0.7896             |                 |
|                                  | 4                   | 10/40                       | 1.06 (0.49, 2.30)        | 0.8808             |                 |
|                                  | 5                   | 12/32                       | 1.71 (0.82, 3.55)        | 0.1527             |                 |
|                                  | 6                   | 9/32                        | 1.27 (0.57, 2.82)        | 0.5640             |                 |
|                                  | 7                   | 9/34                        | 1.09 (0.49, 2.43)        | 0.8302             |                 |
|                                  | 8                   | 15/58                       | 1.21 (0.61, 2.41)        | 0.5818             |                 |
|                                  | 9                   | 35/124                      | 1.22 (0.69, 2.16)        | 0.4882             |                 |
|                                  | 10 - most deprived  | 120/386                     | 1.41 (0.86, 2.31)        | 0.1782             |                 |
| Civil status                     | Single              | 288/938                     | 1.28 (0.57, 2.87)        | 0.5485             |                 |
|                                  | Not single          | 6/23                        | 1.00 (-)                 |                    |                 |
| Employment/day activities        | Yes                 | 83/231                      | 1.33 (1.03, 1.71)        | 0.0284             |                 |
|                                  | No                  | 211/730                     | 1.00 (-)                 |                    |                 |
| Smoker                           | Yes                 | 46/101                      | 1.70 (1.24, 2.33)        | 0.0009             |                 |
|                                  | No                  | 248/860                     | 1.00 (-)                 |                    |                 |
| <b>Health</b>                    |                     |                             |                          |                    |                 |
| Down syndrome                    | Yes                 | 64/179                      | 1.30 (0.98, 1.71)        | 0.0673             |                 |
|                                  | No                  | 230/782                     | 1.00 (-)                 |                    |                 |
| Epilepsy                         | Yes                 | 111/325                     | 1.25 (0.99, 1.58)        | 0.0636             |                 |
|                                  | No                  | 183/636                     | 1.00 (-)                 |                    |                 |
| Spastic quadriplegia             | Yes                 | 24/325                      | 1.67 (1.10, 2.54)        | 0.0158             |                 |
|                                  | No                  | 183/636                     | 1.00 (-)                 |                    |                 |
| Impaired mobility                | Yes                 | 195/735                     | 0.51 (0.40, 0.65)        | <0.0001            |                 |
|                                  | No                  | 99 /226                     | 1.00 (-)                 |                    |                 |
| Body mass index                  | Underweight         | 9/43                        | 0.63 (0.32, 1.25)        | 0.1847             | 0.1865          |
|                                  | Acceptable          | 83/265                      | 1.00 (-)                 |                    |                 |
|                                  | Overweight          | 75/289                      | 0.78 (0.57, 1.06)        | 0.1132             |                 |
|                                  | Obese               | 81/237                      | 1.08 (0.80, 1.47)        | 0.6152             |                 |
|                                  | Morbidly obese      | 16/58                       | 0.87 (0.51, 1.48)        | 0.6058             |                 |
| Hearing impairment               | Yes                 | 112/267                     | 1.79 (1.41, 2.26)        | <0.0001            |                 |
|                                  | No                  | 182/694                     | 1.00 (-)                 |                    |                 |
| Visual impairment                | Yes                 | 154/449                     | 1.29 (1.02, 1.62)        | 0.0317             |                 |
|                                  | No                  | 140/512                     | 1.00 (-)                 |                    |                 |

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|  |     |          |                    |         |  |
|--|-----|----------|--------------------|---------|--|
| Urinary incontinence                             | Yes | 158/632  | 0.52 (0.41, 0.65)  | <0.0001 |  |
|  | No  | 136/329  | 1.00 (-)           |         |  |
| Bowel incontinence                               | Yes | 197/733  | 0.55 (0.43, 0.70)  | <0.0001 |  |
|  | No  | 97/228   | 1.00 (-)           |         |  |
| Diabetes   | Yes | 29/47    | 2.72 (1.86, 4.00)  | <0.0001 |  |
|  | No  | 265/914  | 1.00 (-)           |         |  |
| PEG/tube fed                                     | Yes | N/7      | 4.99 (2.22, 11.20) | 0.0001  |  |
|  | No  | 288/954  |                    |         |  |
| Constipation                                     | Yes | 112/316  | 1.34 (1.06, 1.70)  | 0.0145  |  |
|  | No  | 182/645  | 1.00 (-)           |         |  |
| Ataxia/gait disorder                             | Yes | 104/276  | 1.50 (1.18, 1.90)  | 0.0009  |  |
|  | No  | 190/685  | 1.00 (-)           |         |  |
| Nail disorder                                    | Yes | 74/223   | 1.18 (0.91, 1.54)  | 0.2120  |  |
|  | No  | 220/738  | 1.00 (-)           |         |  |
| Epidermal thickening                             | Yes | 66/207   | 1.10 (0.84, 1.45)  | 0.4947  |  |
|  | No  | 228/754  | 1.00 (-)           |         |  |
| Cerebral palsy                                   | Yes | 54/175   | 1.02 (0.76, 1.37)  | 0.8792  |  |
|  | No  | 240/786  | 1.00 (-)           |         |  |
| Osteoporosis                                     | Yes | 76/174   | 1.71 (1.32, 2.22)  | <0.0001 |  |
|  | No  | 218/786  | 1.00 (-)           |         |  |
| Fungal infection                                 | Yes | 42/158   | 0.83 (0.61, 1.18)  | 0.3366  |  |
|  | No  | 252/803  | 1.00 (-)           |         |  |
| Hypertension                                     | Yes | 56/146   | 1.36 (1.01, 1.82)  | 0.0399  |  |
|  | No  | 238/815  | 1.00 (-)           |         |  |
| Dysphagia  | Yes | 51/132   | 1.51 (1.11, 2.04)  | 0.0080  |  |
|  | No  | 243/829  | 1.00 (-)           |         |  |
| Dyspnoea   | Yes | 49/130   | 1.41 (1.04, 1.92)  | 0.0285  |  |
|  | No  | 245/831  | 1.00 (-)           |         |  |
| Musculoskeletal pain                             | Yes | 48/148   | 1.14 (0.83, 1.55)  | 0.4153  |  |
|  | No  | 246/813  | 1.00 (-)           |         |  |
| Bone deformity                                   | Yes | 50/139   | 1.32 (0.97, 1.79)  | 0.0769  |  |
|  | No  | 244/822  | 1.00 (-)           |         |  |
| Dental/oral problem                              | Yes | 38/120   | 1.07 (0.76, 1.50)  | 0.7128  |  |
|  | No  | 256/841  | 1.00 (-)           |         |  |
| Eczema/dermatitis                                | Yes | 38/138   | 0.86 (0.61, 1.21)  | 0.3790  |  |
|  | No  | 256/823  | 1.00 (-)           |         |  |
| GORD   | Yes | 51/133   | 1.43 (1.06, 1.94)  | 0.0198  |  |
|  | No  | 243/828  | 1.00 (-)           |         |  |
| Lower respiratory tract infection                | Yes | 55/126   | 1.75 (1.30, 2.34)  | 0.0002  |  |
|  | No  | 239/835  | 1.00 (-)           |         |  |
| Total number of physical conditions              |     | 294/961  | 1.06 (1.04, 1.08)  | <0.0001 |  |
| Psychosis  | Yes | 11 /42   | 0.81 (0.44, 1.48)  | 0.4990  |  |
|  | No  | 283 /919 | 1.00 (-)           |         |  |
| Affective disorder including bipolar             | Yes | 24/68    | 1.19 (0.78, 1.80)  | 0.4216  |  |
|  | No  | 270/893  | 1.00 (-)           |         |  |
| Autism   | Yes | 13/69    | 0.54 (0.31, 0.94)  | 0.0306  |  |
|  | No  | 281/892  | 1.00 (-)           |         |  |
| Problem behaviour                                | Yes | 71/218   | 1.09 (0.83, 1.42)  | 0.5251  |  |
|  | No  | 223/743  | 1.00 (-)           |         |  |
| Eating disorder, including pica                  | Yes | 5/17     | 0.99 (0.41, 2.40)  | 0.9857  |  |
|  | No  | 289/944  | 1.00 (-)           |         |  |
| Any mental illness, excluding problem behaviours | Yes | 73/217   | 1.16 (0.89, 1.51)  | 0.2849  |  |
|  | No  | 221/744  | 1.00 (-)           |         |  |
| <b>Service use</b>                               |     |          |                    |         |  |
| Number of GP consultations in last 12 months     |     | 287/951  | 1.05 (1.03, 1.06)  | <0.0001 |  |

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|   |     |         |                   |         |  |
|---|-----|---------|-------------------|---------|--|
| Number of A&E attendances in last 12 months |     | 280/938 | 1.09 (0.99, 1.20) | 0.0847  |  |
| Number of health professions providing care |     | 294/961 | 1.10 (1.03, 1.16) | 0.0023  |  |
| <b>Prescriptions</b>                        |     |         |                   |         |  |
| Antipsychotics                              | Yes | 79/226  | 1.12 (0.94, 1.57) | 0.1421  |  |
|   | No  | 215/735 | 1.00 (-)          |         |  |
| Antidepressants                             | Yes | 39/118  | 1.16 (0.83, 1.63) | 0.3778  |  |
|   | No  | 255/843 | 1.00 (-)          |         |  |
| Anxiolytic/hypnotics                        | Yes | 20/68   | 0.95 (0.60, 1.49) | 0.8159  |  |
|   | No  | 274/893 | 1.00 (-)          |         |  |
| Antiepileptics                              | Yes | 90/253  | 1.31 (1.02, 1.68) | 0.0315  |  |
|   | No  | 204/708 | 1.00 (-)          |         |  |
| Number of drug classes taken                |     | 294/961 | 1.16 (1.12, 1.21) | <0.0001 |  |

A&E=accident and emergency; CI=confidence interval; GORD=gastro-oesophageal reflux disorder; PEG=percutaneous endoscopic gastrostomy

## STROBE Statement—checklist of items that should be included in reports of observational studies

|                              | Item No. | Recommendation   | Page No. | Relevant text from manuscript    |
|------------------------------|----------|--|----------|----------------------------------|
| <b>Title and abstract</b>    | 1        | (a) Indicate the study's design with a commonly used term in the title or the abstract   |          | p1                               |
|                              |          | (b) Provide in the abstract an informative and balanced summary of what was done and what was found  |          | p2                               |
| <b>Introduction</b>          |          |  |          |                                  |
| Background/rationale         | 2        | Explain the scientific background and rationale for the investigation being reported   |          | p4-6, supplementary table 1      |
| Objectives                   | 3        | State specific objectives, including any prespecified hypotheses   |          | 6, paragraph 3                   |
| <b>Methods</b>               |          |  |          |                                  |
| Study design                 | 4        | Present key elements of study design early in the paper  |          | p6-10, supplementary tables 2/3  |
| Setting                      | 5        | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection  |          | p7, paragraph 1, 7-8             |
| Participants                 | 6        | (a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br><i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br><i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants |          | p7, paragraph 1                  |
|                              |          | (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed<br><i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case   |          | p7, paragraph 2, p9, paragraph 4 |
| Variables                    | 7        | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable   |          | p7-8, supplementary table 2      |
| Data sources/<br>measurement | 8*       | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group   |          | p7-8, p9, paragraph 4            |
| Bias                         | 9        | Describe any efforts to address potential sources of bias  |          | p9, paragraph 4                  |
| Study size                   | 10       | Explain how the study size was arrived at  |          | P7, paragraph2, p9, paragraph 4  |

Continued on next page

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|------------------------|-----|--|--|
| Quantitative variables | 11  | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why   | p8-10                                  |
| Statistical methods    | 12  | (a) Describe all statistical methods, including those used to control for confounding  | p8-10                                  |
|                        |     | (b) Describe any methods used to examine subgroups and interactions  | p8-10                                  |
|                        |     | (c) Explain how missing data were addressed  | p11, paragraph 2                       |
|                        |     | (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed  | p11, paragraph 2                       |
|                        |     | <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed   |  |
|                        |     | <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy   |  |
|                        |     | (e) Describe any sensitivity analyses  | N/A                                    |
| <b>Results</b>         |     |  |  |
| Participants           | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed            | p11, paragraph 2                       |
|                        |     | (b) Give reasons for non-participation at each stage   | p11, paragraph 2                       |
|                        |     | (c) Consider use of a flow diagram   | -                                      |
| Descriptive data       | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders   | p11-12, Table 1, supplementary table 3 |
|                        |     | (b) Indicate number of participants with missing data for each variable of interest  | table 1, supplementary table 3         |
|                        |     | (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)   | p12, paragraph 1                       |
| Outcome data           | 15* | <i>Cohort study</i> —Report numbers of outcome events or summary measures over time  | p11, paragraph 2                       |
|                        |     | <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure   |  |
|                        |     | <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures   |  |
| Main results           | 16  | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | P15, table 6                           |
|                        |     | (b) Report category boundaries when continuous variables were categorized  | N/A                                    |
|                        |     | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period   | -                                      |

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|--------------------------|----|--|------------------|
| Other analyses           | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses   | p11-16           |
| <b>Discussion</b>        |    |  |                  |
| Key results              | 18 | Summarise key results with reference to study objectives   | p16, paragraph 2 |
| Limitations              | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias                 | p20, paragraph 1 |
| Interpretation           | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | p20, paragraph 2 |
| Generalisability         | 21 | Discuss the generalisability (external validity) of the study results  | p20, paragraph 1 |
| <b>Other information</b> |    |  |                  |
| Funding                  | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based              | P24              |

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage

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3 **Rates, causes, place, and predictors of mortality in**  
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6 **adults with intellectual disabilities with and without**  
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9 **Down syndrome: cohort study with record linkage**  
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## Abstract

### **Objectives**

To investigate mortality in adults with intellectual disabilities: rates, causes, place, demographic and clinical predictors.

### **Design**

Cohort study with record linkage to death data.

### **Setting**

General community.

### **Participants**

961/1,023 (94%) adults (16-83 years; mean=44.1 years; 54.6% male) with intellectual disabilities, clinically examined in 2001-2004; subsequently record-linked to their National Health Service number, allowing linkage to death certificate data, 2018.

### **Outcome measures**

Standardised mortality ratios (SMRs), underlying, and all contributing causes of death, avoidable deaths, place, and demographic and clinical predictors of death.

### **Results**

294/961 (30.6%) had died; 64/179 (35.8%) with Down syndrome, 230/783 (29.4%) without Down syndrome. SMR overall=2.24 (1.98, 2.49); Down syndrome adults=5.28 (3.98, 6.57), adults without Down syndrome=1.93 (1.68, 2.18); male=1.69 (1.42, 1.95), female=3.48 (2.90, 4.06). SMRs decreased as age increased. More severe intellectual disabilities increased SMR, but ability was not retained in the multivariable model. SMRs were higher for most ICD-10 chapters. For adults without Down syndrome, aspiration/reflux/choking, and respiratory infection were the commonest underlying causes of mortality; for Down syndrome adults "Down syndrome", and dementia were most common. Amenable deaths (29.8%) were double that in the general population (14%). 60.3% died in hospital. Mortality risk related to: percutaneous endoscopic gastrostomy/tube fed, Down syndrome, diabetes, lower respiratory tract infection at

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3 cohort-entry, smoking, epilepsy, hearing impairment, increasing number of prescribed  
4 drugs, increasing age. Bowel incontinence reduced mortality risk.

### 7 **Conclusions**

9 Adults with intellectual disabilities with and without Down syndrome have different SMRs  
10 and causes of death which should be separately reported. Both die younger, from  
11 different causes than other people. Some mortality risks are similar to other people, with  
12 earlier mortality reflecting more multi-morbidity; amenable deaths are also common.  
13 This should inform actions to reduce early mortality, e.g. training to avoid  
14 aspiration/choking, pain identification to address problems before they are advanced,  
15 and reasonable adjustments to improve health-care quality.  
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### 26 **Strengths and limitations of this study**

- 27 • Thorough methods of case ascertainment for intellectual disabilities at baseline.
- 28 • Individual verification of intellectual disabilities and its severity, and detailed health  
29 assessments at baseline.
- 30 • Longitudinal design.
- 31 • Large cohort size and study duration, and successful record linkage for 94% of  
32 participants.
- 33 • Limitations include that the study was conducted in only one part of Scotland, and  
34 the reliance upon recorded cause of death from death certificates.  
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49 Word count: 5,610  
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## Introduction

People with intellectual disabilities die at a younger age than other people; on average, 20 years younger,<sup>1</sup> or 28 years younger specifically for people with Down syndrome.<sup>2</sup> It has been demonstrated that people with intellectual disabilities receive poorer management of their long term conditions within primary health care services compared with the general population,<sup>3</sup> and it is conceivable that this is one contributor to earlier mortality. It has been suggested that as many as 40% of deaths of people with intellectual disabilities may have been amenable to good quality health care.<sup>4-6</sup> There has been a recent increase in research on mortality in people with intellectual disabilities, but very little research has distinguished people with intellectual disabilities with and without Down syndrome, or investigated the factors associated with risk of mortality, and causes of mortality.

Previous studies on death in people with intellectual disabilities had limitations such as small sample sizes, or non-representative populations. More recently, there have been large-scale studies which are more representative, having been drawn from intellectual disabilities registers, or social security or primary care data with record linkage to death certification. These have been undertaken in parts of Sweden, Australia, England, Finland, Canada, Ireland, and USA (supplementary table 1).<sup>5-19</sup> These studies fairly consistently report standardised mortality ratios (SMRs) to be high for people with intellectual disabilities, more so at younger ages, and higher for women than men. Adult studies have tended to report SMRs in the region of 2-4, although in some, SMR is only slightly above 1.<sup>10,16,19</sup> However, direct comparison between studies is not always possible, due to the different age ranges studied and methods of reporting.

- Supplementary table 1 -

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3 In view of the methods that studies have used for population identification (typically,  
4 routine administrative data linked to death certifications), they provide little information  
5 on the socio-clinical factors that influence SMR, or the risk factors associated with death,  
6 beyond that of age and sex. Three studies reported SMR by level of intellectual  
7 disabilities, with, broadly speaking, higher SMR with more severe intellectual  
8 disabilities.<sup>7,10,17</sup> Only three studies (different studies to those that reported on level of  
9 intellectual disabilities) were able to report data separately for adults with intellectual  
10 disabilities with and without Down syndrome; two found higher mortality rates for adults  
11 with Down syndrome (SMR=7.6,<sup>9</sup> and hazard ratio=9.21<sup>5</sup>) than for adults without Down  
12 syndrome, or an odds ratio showing Down syndrome as a risk of death.<sup>12</sup> A further  
13 study reported SMR=5.5 for children and adults (combined) with Down syndrome, but  
14 did not report SMR for those with intellectual disabilities without Down syndrome.<sup>20</sup> Two  
15 studies reported adults with intellectual disabilities to have higher SMRs if they have the  
16 co-morbidities of epilepsy,<sup>5,7</sup> and cerebral palsy,<sup>7</sup> as opposed to not having these  
17 comorbidities. One study reported adults with intellectual disabilities with comorbid  
18 autism to have lower risk of mortality than those without comorbid autism.<sup>5</sup> One study  
19 reported the risk factors for mortality in a population with intellectual disabilities to be:  
20 age, Down syndrome, cerebral palsy, blindness/low vision, technological  
21 dependence/medical fragility, wheelchair dependence, mobility impairment without  
22 wheelchair dependence, and epilepsy.<sup>12</sup> Factors not found to be risks, if any, were not  
23 reported, and a further limitation was that factors were reported by agency staff, rather  
24 than the individuals undergoing health assessments.<sup>12</sup> We have not identified any other  
25 studies that investigated risk factors for time to mortality in adults with intellectual  
26 disabilities.

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54 There is less consistency regarding the most common certified underlying causes of  
55 death in adults with intellectual disabilities, partly as some studies do not report these  
56 separately for children and adults, or by age ranges. Additionally, studies group causes  
57 of death in different ways (e.g. pneumonia versus respiratory system), which can affect  
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3 prevalence rankings between studies. Pneumonia, other respiratory diseases, and  
4 diseases of the nervous system were reported to be the most common in one study,<sup>11</sup>  
5 diseases of the circulatory system and respiratory systems in another,<sup>5</sup> heart disease,  
6 neoplasm, and Alzheimer disease in a third,<sup>18</sup> and diseases of the circulatory system,  
7 neoplasm, and the nervous system in a fourth.<sup>19</sup> In adults with intellectual disabilities,  
8 cause specific SMRs have been reported to be high across most groups of disorders.<sup>5,11</sup>  
9 These studies did not report cause of death separately for adults with and without Down  
10 syndrome. Given the different health profile of people with Down syndrome compared  
11 with people with intellectual disabilities of other causes, this is an important limitation.<sup>21</sup>  
12 In people with Down syndrome, most studies on mortality have been conducted with  
13 child populations, and report the most common causes of death to be congenital heart  
14 disease, and pneumonia/diseases of the respiratory system.<sup>2</sup>

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30 Overall, the existing body of literature on mortality in adults with intellectual disabilities  
31 does not include more detailed information on level of intellectual disabilities, nor  
32 separate out the population with, from those without, Down syndrome (for whom causes  
33 of death may differ), nor investigate health and demographic predictors of death other  
34 than age and sex, and is inconsistent with regards to causes of death. A better  
35 understanding of these factors may provide a pathway to action to reduce the observed  
36 earlier mortality in adults with intellectual disabilities.

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46 This study aims to investigate the rates, causes, place, and demographic and clinical  
47 associations with mortality in adults with intellectual disabilities, with and without Down  
48 syndrome.

## 49 50 51 52 53 **Methods**

### 54 55 56 57 58 **Approval**

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3 Ethical approval was gained from NHS Greater Glasgow Primary Care Trust -  
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5 Community & Mental Health Research Ethics Committee, and NHS Greater Glasgow and  
6  
7 Clyde Safe Haven. Individual consent to participate was taken in line with Scottish law,  
8  
9 between 2001-2004.  
10

### 11 12 13 **Participants**

14  
15 The adult (aged 16+ years) intellectual disabilities population living within the NHS  
16  
17 Greater Glasgow area was identified through multiple sources between 2000-2001.  
18  
19 General practitioners were financially incentivised to identify their registered patients  
20  
21 with intellectual disabilities, and all 631 (100%) did so. Adults were also identified via  
22  
23 the intellectual disabilities health and social work services including day services, the  
24  
25 Health Board register, and records of financial payments for any service by social work.  
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27 This process led initially to an over-identification, such as people with IQ scores in the  
28  
29 70–80 range with additional complex health needs. All were systematically reviewed by  
30  
31 nurses in the intellectual disabilities health service, and this group were removed. Thus,  
32  
33 a register was compiled, and subsequently updated annually via general practices, with  
34  
35 central support from the intellectual disabilities health service, until 2017 when services  
36  
37 were redesigned. The identified adult prevalence of intellectual disabilities within the  
38  
39 area was 3.33 per 1,000 in 2000-2001.  
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### 44 **Process and data collection**

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46 With initial piloting in 2001, each participant had a detailed assessment of their general  
47  
48 and mental health, and demographic factors, completed 2002-2004. One of six specially  
49  
50 trained, registered nurses reviewed each person's primary health care records, then  
51  
52 used a semi-structured tool, the C21st Health Check, to assess clinical factors and the  
53  
54 level and cause of intellectual disabilities. In addition to a review of existing health  
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56 problems and all bodily health systems, a physical examination was undertaken,  
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58 including assessment of vision and hearing, measurement of height and weight, and a  
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60 phlebotomy protocol followed. All information was then reviewed by the nurse with one

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3 of three general practitioners with a special interest in intellectual disabilities, and any  
4 further investigations that were indicated were completed. Previously known, and newly  
5 identified, conditions were then classified using the *International Statistical Classification*  
6 *of Diseases and Related Health Problems, 10th Revision (ICD-10)*.<sup>22</sup> Anyone identified to  
7 have possible, probable, or definite mental ill-health, autism, or problem behaviours was  
8 then fully assessed by the project's intellectual disabilities psychiatrists. Each person's  
9 assessment findings were then case conferenced by the two Consultant psychiatrists,  
10 and diagnoses were derived and agreed according to clinical diagnoses, *ICD-10*  
11 *(Diagnostic Criteria for Research)*,<sup>23</sup> *Diagnostic and Statistical Manual of Mental*  
12 *Disorders-IV-TR*,<sup>24</sup> and *Diagnostic Criteria for Psychiatric Disorders for use with Adults*  
13 *with Learning Disabilities (DC-LD)*.<sup>25</sup> Information was also collected on demographics,  
14 and community, hospital, and social service use. Further details are provided  
15 elsewhere.<sup>26,27</sup> The data were entered into a database by two dedicated data-entry staff.

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31 Each person in Scotland is given a number unique to them at birth or first registration  
32 with a general practitioner, which is used in almost all subsequent health service  
33 encounters, and on certification of death. The numbers are held on the Community  
34 Health Index (CHI) database at National Services Scotland. These CHI numbers provided  
35 a means to record link each participant with National Records for Scotland death  
36 certification data. This linkage was performed in 2018, and the linked data were held in  
37 the NHS Greater Glasgow & Clyde (NHS GG&C) Safe Haven. Data on immediate,  
38 underlying, and contributory causes of deaths by ICD-10 codes, age at death, and place  
39 of death were extracted.

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51 In order to provide finer granularity of cause of death, two clinical academics then  
52 grouped specific causes of death into narrower groupings than those provided by ICD-10  
53 chapter headings (supplementary table 2). This approach was also in view of the  
54 recognised issue of variation between health staff in distinguishing and recording  
55 immediate causes of death, and because some causes occurred in low numbers so could

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3 not be individually reported due to the risk of statistical disclosure. Additionally, some  
4 conditions likely to be the same are spilt between different ICD-10 chapters, e.g.  
5 dementia in Alzheimer disease (F00) and unspecified dementia (F03) in the ICD-10  
6 mental and behavioural disorders chapter, and Alzheimer's disease (G30) and  
7 Alzheimer's disease, unspecified (G30.9) in the ICD-10 diseases of the nervous system  
8 chapter. A list of related conditions was generated by one of the clinical academics and  
9 then checked by the second.  
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19 - Supplementary table 2 -  
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### 23 **Analyses**

24 All statistical analyses were conducted using R for Windows v3.3.0 or SAS 9.3 (SAS  
25 Institute, Cary NC) and were performed within the NHS GG&C Safe Haven environment.  
26 Due to disclosure principles of the Safe Haven, results with counts of less than 5 cannot  
27 be released; these have been referred to as <5 throughout. Similarly, if it is deemed  
28 possible that participants may be identified from the results, these may be omitted.  
29 Details are provided if this occurred.  
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40 Data were summarised for the population of adults aged 16+ years with intellectual  
41 disabilities. Categorical variables were summarised with the number and percentages of  
42 people falling into each category and the number of missing data. Continuous variables  
43 were summarised with the number of observations and those missing, the mean and  
44 standard deviation (SD), and the minimum and maximum values, unless otherwise  
45 stated.  
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54 Participant characteristics were summarised overall and for those alive and those  
55 deceased. For those who are deceased, their data including age at death,  
56 underlying/contributing causes of death, and location of death were summarised for  
57 those with and without Down syndrome. Location codes for place of death are provided  
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3 where available. We assumed those with the code for non-institutional location to have  
4 died at home. Due to small numbers, location codes have been grouped together for  
5 NHS hospitals, home, and other hospitals/care facilities including hospices.  
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11 Mortality incidence rates have been calculated using the number of deaths in the cohort  
12 divided by the number of person years alive within the study period multiplied by  
13 100,000, overall and for those with and without Down syndrome. SMRs were calculated  
14 using population data for those aged 15 and over within NHS GG&C in 2010.<sup>28,29</sup> Death  
15 rates for males and females by 5 year band ages groups spanning from 15-20 years old  
16 to 90 years and over were summed to form the expected death rates for the general  
17 population. The observed death rate for adults with intellectual disabilities was taken  
18 from our study results. The observed/expected death rates were calculated for the  
19 intellectual disabilities cohort overall then separately by age group, sex, ability level, and  
20 for the adults with, and without, Down syndrome, and ICD-10 chapter for cause of  
21 death, and compared to the general population.  
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36 Deaths were also analysed for those that could be considered as deaths that would have  
37 been avoidable. The Office for National Statistics (ONS) published a definition of  
38 avoidable mortality,<sup>30</sup> which lists the causes of amenable deaths (deaths that should not  
39 occur in the presence of good health care, e.g. respiratory disease), and causes of  
40 preventable deaths (e.g. from diseases that could have been avoided by prior  
41 immunisation), by ICD-10 codes. Causes of death for the adults with intellectual  
42 disabilities have been summarised by ONS definition of avoidable deaths.  
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51 To determine the demographic and clinical factors associated with death in adults with  
52 intellectual disabilities, time to event analyses were explored using univariate Cox  
53 Proportional Hazards models. Variables were selected as potentially relevant on the basis  
54 of what is known on causes of death in people with intellectual disabilities, the 20 most  
55 common physical health conditions reported in the adult population with intellectual  
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3 disabilities,<sup>21</sup> and other factors hypothesised as potentially clinically relevant

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5 (supplementary table 3):

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7
- 8 • Demographics - 9 variables.
  - 9 • Clinical conditions - 33 variables.
  - 10 • Service use - 3 variables.
  - 11 • Prescriptions - 5 variables.
- 12  
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15 All 50 variables were then permitted entry in to a single multivariable analysis using  
16 stepwise regression methods, in order to identify a model containing the statistically  
17 significant factors associated with death. Age at date of the health assessment was  
18 entered in to the model as a continuous measure. Results from the univariate Cox  
19 Proportional Hazards models (Supplementary table 3) and the statistically significant  
20 multivariable model from the stepwise results have been presented with hazard ratios  
21 with corresponding 95% confidence intervals (HR, 95% CI) and p-values were obtained.  
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31 - Supplementary table 3 -  
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### 33 34 35 ***Patient and public involvement***

36 This study was designed to respond to the growing concern expressed by people with  
37 intellectual disabilities, their families, and third sector organisations about the early  
38 deaths of people with intellectual disabilities. The Scottish Learning Disabilities  
39 Observatory, where this research was undertaken, has a specific remit for people with  
40 intellectual disabilities. Its steering group includes partners from third sector  
41 organisations, including Down syndrome Scotland, and people with intellectual  
42 disabilities, who approved the work plan for this project prior to it commencing. Results  
43 from this study will be disseminated for people with intellectual disabilities in an easy-  
44 read version via the Scottish Learning Disabilities Observatory.  
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### 58 **Results**

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### ***Population characteristics***

962 of the original 1,023 (94.0%) adults with intellectual disabilities who were assessed were linked to a CHI number enabling the extraction of relevant death data. Reasons for the unlinked 61 people could be due to moving out of the area, or a recording mistake. 1 further participant was removed from the analysis due to inaccurate recording of dates, leaving 961 adults in the cohort (93.9%). Of these 961 adults, 294 (30.6%) had a record of death. Table 1 shows the baseline characteristics of the full cohort of 961, the adults who died, and those still alive at the time of linkage.

- Insert table 1 about here -

### ***Age at death, and mortality incidence***

The mean age at death was 61.0 years (SD=7.0 years). Of the 961 adults, 64 (35.8%) of the 179 adults with Down syndrome, and 230 (29.4%) of the 782 adults without Down syndrome had a record of death. Their mean age of death was 56.9 years (SD=4.3 years) for the adults with Down syndrome, and 62.2 years (SD=7.5 years) for the adults without Down syndrome. Mortality incidence for the cohort during the study period was 3,049.0 per 100,000 person years follow-up, with 3,832.1 per 100,000 for those with Down Syndrome and 2,885.0 for those without Down syndrome.

### ***Standardised mortality ratios***

Compared with the general population, the SMR was 2.24 (1.98, 2.49) overall; 5.28 (3.98, 6.57) for adults with Down syndrome, 1.93 (1.68, 2.18) for adults without Down syndrome; 1.69 (1.42, 1.95) for men and 3.48 (2.90, 4.06) for women. SMRs were higher the more severe the level of intellectual disabilities, with people with profound intellectual disabilities having an SMR of 4.14 (3.11, 5.17). SMR was high for all age groups (though for the 15-25 year age group, the wide confidence interval includes one, perhaps due to the smaller number of deaths in this group); this decreased as age increased. SMRs were high for most ICD-10 chapter groups of conditions, particularly so

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3 for congenital malformations at 17.26 (10.75, 23.78), diseases of the digestive system  
4 at 16.13 (8.23, 24.04), mental and behavioural disorders at 12.64 (3.27, 22.00), and  
5 external causes at 11.08 (3.40, 18.76). Details are shown in table 2.  
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11 - Insert table 2 about here -  
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### 14 15 **Causes of death**

16 Cause of death data was available from death certificates for 262 (89.1%) of 294  
17 participants who had died, which include 57 (89.1%) participants with Down syndrome,  
18 and 205 (88.7%) participants without Down syndrome. Table 3 shows the underlying  
19 causes of death by ICD-10 chapters separately for the adults with, and without Down  
20 syndrome. For the whole cohort, diseases of the respiratory system were the most  
21 common (21.8%), then diseases of the circulatory system (19.1%), then diseases of the  
22 nervous system (13.0%), and neoplasms, followed by congenital anomalies (10.3%).  
23 For the adults with Down syndrome, congenital anomalies were the most common (in all  
24 cases this was a record of "Down syndrome"), then jointly diseases of the respiratory  
25 system and diseases of the circulatory system, then diseases of the nervous system,  
26 followed by infections, and mental and behavioural disorders. For the adults without  
27 Down syndrome, diseases of the respiratory system were the most common, then  
28 diseases of the circulatory system, then neoplasms, then diseases of the nervous  
29 system, followed by diseases of the digestive system. Table 4 presents the most  
30 common underlying causes of death by individual causes, or related groups of causes,  
31 with finer granularity than ICD-10 chapter headings (groups are shown in supplementary  
32 table 2). Causes are listed in the order of how common they were in the whole cohort.  
33 Data are presented separately for the adults with, and without Down syndrome. For the  
34 whole cohort, the most common cause was aspiration/reflux/choking, then respiratory  
35 infection, then other malignancy (non gastrointestinal), then other condition (mostly  
36 unrelated conditions that could not be reported individually or as groups, due to  
37 individually occurring at a frequency of <5). For the adults with Down syndrome, Down  
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3 syndrome was the most common cause, then dementia, then other infection. For the  
4 adults without Down syndrome, aspiration/reflux/choking was the most common cause,  
5 then respiratory infection, then other malignancy (non gastrointestinal). For the 21  
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7 people whose death certificate listed Down syndrome as their underlying cause of death,  
8  
9 the death certificates were reviewed and underlying cause of death reclassified, as a  
10  
11 sensitivity check. Following this, the most common underlying causes of death for the  
12  
13 adults with Down syndrome were dementia (n=20; 35.1%), then other infection (n=7;  
14  
15 12.3%).  
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21 - Insert tables 3 and 4 about here -  
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25 Table 5 shows the all contributing causes of death data, again presenting the most  
26  
27 common causes by individual causes, or related groups of causes with finer granularity  
28  
29 than ICD-10 chapter headings. Data is presented separately for the adults with, and  
30  
31 without Down syndrome. For the whole cohort, respiratory infection was the most  
32  
33 common cause (27.1%), followed by aspiration/reflux/choking (19.8%), other conditions  
34  
35 (15.6%), other cardiovascular conditions (non acute myocardial nor other ischaemic  
36  
37 heart disease: 14.5%), then other respiratory conditions. For the adults with Down  
38  
39 syndrome, Down syndrome was the most common, then dementia, then respiratory  
40  
41 infection, then aspiration/reflux/choking. For the adults without Down syndrome,  
42  
43 respiratory infection was the most common cause, then aspiration/reflux/choking, then  
44  
45 other condition, then other respiratory conditions, and intellectual disabilities.  
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49 - Insert table 5 about here -  
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### 51 52 53 **Avoidable deaths**

54  
55 According to the ONS list of avoidable deaths, 102 (38.9%) of the 262 deaths were  
56  
57 avoidable; most notably, respiratory infection and epilepsies (table 4). 78 (29.8%) were  
58  
59 deaths that are amenable to good health care, whilst 51 (19.5%) were preventable  
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3 deaths. 27 (10.3%) deaths were classed as both amenable and preventable deaths. This  
4  
5 compares to published Scottish death data showing in 2018 that 28% of deaths were  
6  
7 avoidable; 14% amenable and 24% preventable, similar to the figures in the previous  
8  
9 four years (data not available prior to 2014).<sup>31</sup> For the 57 deaths of adults with Down  
10  
11 syndrome, 17 (29.8%) deaths were avoidable, 15 (26.3%) deaths were amenable to  
12  
13 good health care, whilst 7 (12.3%) were preventable. 5 (8.8%) were both amenable and  
14  
15 preventable. For the 205 deaths of adults without Down syndrome, 85 (41.5%) were  
16  
17 avoidable, 63 (30.7%) deaths were amenable to good health care, whilst 44 (21.5%)  
18  
19 were preventable. 22 (10.7%) were both amenable and preventable.  
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### 23 **Place of death**

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25 Of the 262 participants for whom place of death was known, 158 (60.3%) died in an  
26  
27 NHS Hospital, 70 (26.7%) died at home, and 34 (13.0%) died within other  
28  
29 hospitals/care facilities. This was similar for both the adults with Down syndrome: 31  
30  
31 (54.4%) in an NHS hospital, 17 (29.8%) at home, and 9 (15.8%) within other  
32  
33 hospitals/care facilities; and the adults without Down syndrome: 127 (62.0%) in an NHS  
34  
35 hospital, 53 (25.9%) at home, and 25 (12.2%) within other hospitals/care facilities.  
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### 40 **Factors associated with risk of death**

41  
42 The results from the univariate cox proportional hazards models indicated that of the  
43  
44 original 50 potential variables, factors associated with risk of death were (supplementary  
45  
46 table 3):

- 47 • Demographics – age at the time of the health assessment, more severe learning  
48 disabilities, accommodation type (not living with family carer), not having day-time  
49 occupation, and being a smoker (but not sex, the extent of neighbourhood  
50 deprivation, civil status, nor Down syndrome, in view of the confidence intervals).
- 51 • Clinical conditions – having spastic quadriplegia, hearing impairment, visual  
52 impairment, diabetes, percutaneous endoscopic gastrostomy/tube fed, constipation,  
53 ataxia/gait disorder, osteoporosis, hypertension, dysphagia, dyspnoea, gastro-  
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oesophageal reflux disorder, lower respiratory tract infection, total number of physical health disorders, not having impaired mobility, not having urinary incontinence, not having bowel incontinence, and not having autism (but not epilepsy, body mass index, nail disorder, epidermal thickening, cerebral palsy, fungal infection, musculoskeletal pain, bone deformity, dental/oral problem, eczema/dermatitis, psychosis, affective disorder including bipolar affective disorder, problem behaviour, eating disorder including pica, nor any mental illness).

- Service use – number of general practitioner consultations in the previous 12 months, total number of different types of health professionals providing care at the time of the clinical assessment, (but not number of accident and emergency attendances in the previous 12 months).
- Prescriptions – antiepileptic drugs, total number of different types of drugs, (but not antipsychotic drugs, antidepressant drugs, nor anxiolytic drugs).

Table 6 shows the final model of the variables retained in the multivariable analysis for time to death. The significant factors indicating an increased risk of death were increased age at the time of the health assessment, smoking, Down syndrome, diabetes, being percutaneous endoscopic gastrostomy/tube fed, lower respiratory tract infection at cohort inception, epilepsy, hearing impairment, and total number of different types of drugs prescribed, whilst bowel incontinence showed a reduced risk of death. Of note, level of intellectual disabilities whilst significant in the univariate analysis, was not retained in the multivariable model.

- Insert table 6 about here -

## Discussion

### *Principle findings and interpretation*

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3 As far as we are aware, this is the first population-based study of adults with intellectual  
4 disabilities to report in detail the factors associated with time to death, and to describe  
5 their causes of death and quantify the SMR separately for adults with Down syndrome  
6 and adults without Down syndrome. This is important, since adults with Down syndrome  
7 form a notable proportion of all adults with intellectual disabilities (19% in this cohort),  
8 and because they have a different pattern of clinical conditions compared with other  
9 adults with intellectual disabilities.<sup>21</sup> We found that aspiration/reflux/choking is the most  
10 common underlying cause of death in adults with intellectual disabilities, followed by  
11 respiratory infection. They are also the most common all contributing causes of death.  
12 The profile differed in the adults with Down syndrome for whom "Down syndrome",  
13 followed by dementia, were recorded as the most common underlying cause of death,  
14 and all contributing causes of death (or alternatively, dementia, then other infection  
15 were the most common underlying causes when "Down syndrome" deaths were  
16 reclassified); with the next most common all contributing cause of death being  
17 respiratory infection, then aspiration/reflux/choking. The proportion of deaths that would  
18 have been amenable to good care for adults with intellectual disabilities was more than  
19 double that seen in the general population. Although aspiration/reflux/choking is not  
20 included in the ONS list of avoidable deaths, and therefore not included in the figures we  
21 report on amenable deaths, we consider that good care could have prevented many of  
22 these deaths. This appears to be very important for adults with intellectual disabilities  
23 irrespective of whether they have Down syndrome. Similarly, some other causes of  
24 deaths within this cohort (supplementary table 2), such as constipation/mega-colon, and  
25 urinary tract infections do not appear on the ONS list of avoidable deaths.

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52 Clearly, this pattern of causes of death differs from that seen in the general population,  
53 in whom the most common underlying causes of death are heart disease, then dementia,  
54 then lung cancer in men, and dementia, then heart disease, then stroke in women.<sup>32</sup>  
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3 reporting 0% for adults with Down syndrome, and 15.2% for adults with intellectual  
4 disabilities without Down syndrome – presumably as the adults with intellectual  
5 disabilities are dying younger from other causes, and cancers increase with age.  
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11 We found an overall SMR of 2.24; 5.28 in the adults with Down syndrome and 1.93 for  
12 the adults without Down syndrome. SMRs were higher for most ICD-10 chapter  
13 groupings of conditions. It was higher in the women than the men, as has been  
14 previously reported in most (supplementary table 1), but not all<sup>10,19</sup> previous reports.  
15 The reason for this is unknown; in the general population, mortality rates have fallen in  
16 recent decades, and more so in middle and older aged men than women (i.e. the sex  
17 gap is narrowing at these ages), but we do not know what trends over time there have  
18 been for people with intellectual disabilities. Having intellectual disabilities removes  
19 differences in lifespan by sex compared with the general population; but sex was not a  
20 predictor of mortality in our study, so the SMR difference may only be because of the  
21 difference found in the general population by sex. SMRs were lowest with older age  
22 groups, likely to be due to increased illness in the older general population and  
23 conversely a healthier group with intellectual disabilities living to older ages compared  
24 with those who die younger (as has previously been reported<sup>33</sup>). Although SMR was  
25 higher with increasing severity of intellectual disabilities, ability level was not retained  
26 within the multivariable model on time to death. The factors that were independently  
27 associated with increased risk of death, in order, were being percutaneous endoscopic  
28 gastrostomy/tube fed, Down syndrome, diabetes, having a lower respiratory tract  
29 infection at entry to the cohort, smoking, epilepsy, hearing impairment, total number of  
30 prescribed drugs, and age, whilst bowel incontinence had a reduced risk of death. Some  
31 of these predictors are similar to those reported in the general population, suggesting  
32 earlier mortality of adults with intellectual disabilities is largely accounted for by the  
33 higher rates of multi-morbidities that they experience compared with other people, and  
34 amenable deaths.<sup>34</sup>  
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3 Whilst accommodation type (not living with a family carer), ability level, not having day-  
4 time occupation, having spastic quadriplegia, visual impairment, constipation, ataxia/gait  
5 disorder, osteoporosis, hypertension, dysphagia, dyspnoea, gastro-oesophageal reflux  
6 disorder, total number of physical health disorders, not having impaired mobility, not  
7 having urinary incontinence, and not having autism, number of general practitioner  
8 consultations in the previous 12 months, total number of different types of health  
9 professionals providing care at the time of the health assessment, and antiepileptic  
10 drugs were related to time of death on univariate analyses, they were not retained in the  
11 multivariable model.  
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23 The majority of the adults with intellectual disabilities, with and without Down syndrome,  
24 died in an NHS hospital.  
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### 29 ***Comparison with previous literature***

30 The overall SMR we report, higher SMR in women than men, and higher SMR at younger  
31 age groups is similar to the majority of previous reports. Most mortality studies with  
32 people with Down syndrome have been conducted with children. Previous reports of  
33 children and adults (combined) gave an SMR=5.5,<sup>20</sup> and for adults SMR=7.6,<sup>9</sup> compared  
34 with our finding for adults with Down syndrome of SMR=5.28. Recent systematic reviews  
35 reported people with intellectual disabilities on average died 20 years younger than other  
36 people, and people with Down syndrome died 28 years younger, although the majority  
37 of the Down syndrome studies were not recent.<sup>1,2</sup> In our study we found the gap  
38 between the age at death of people with intellectual disabilities with and without Down  
39 syndrome to be only 5.3 years, possibly reflecting the increasing lifespan of people with  
40 Down syndrome exceeding increases in lifespan for people with intellectual disabilities  
41 without Down syndrome. Notably, after "Down syndrome", dementia was the most  
42 commonly reported underlying, and all contributing cause of death for the adults with  
43 Down syndrome, whereas studies in the past commented on congenital heart disease  
44 and respiratory causes.  
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5 For the cohort overall, respiratory infection and aspiration/reflux/choking were the most  
6 common all contributing causes of death. These conditions feature in previous studies on  
7 causes of death,<sup>5,6,8,10,11</sup> although there are inconsistencies between studies. By ICD-10  
8 chapter, our study found the most common underlying causes of death were diseases of  
9 the respiratory system, then of the circulatory system, followed by neoplasms. Others  
10 reported the most common to be vascular,<sup>10</sup> circulatory,<sup>5</sup> heart disease,<sup>17</sup> and jointly  
11 circulatory and neoplasm.<sup>19</sup>

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21 Previous research from other countries has highlighted that listing Down syndrome or  
22 intellectual disabilities as the underlying cause of death obscures actual causes of death  
23 for this population.<sup>35</sup> We therefore presented data on revised cause of death for the 21  
24 people for whom it was listed as Down syndrome (as a sensitivity check), and highlight  
25 with interest that in this Scottish cohort no-one had intellectual disabilities listed as  
26 underlying cause of death. This may reflect different medical death certificate recording  
27 practices in Scotland compared to e.g. USA.

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38 Studies that investigated avoidable deaths in adults with intellectual disabilities found  
39 them to be more common than in the general population, due to deaths that would have  
40 been amenable to good care. Avoidable deaths have been reported in 44.7% of deaths  
41 of people with intellectual disabilities in England (mostly amenable deaths – figure not  
42 reported),<sup>6</sup> and in 31% in Australia,<sup>19</sup> compared with our figure of 38.9%. Avoidable  
43 deaths that would have been amenable to good care have been reported to occur in 37%  
44 of deaths of people with intellectual disabilities in England.<sup>5</sup> Our figure is slightly lower at  
45 29.8% but still more than double that found in the Scottish general population.<sup>31</sup> It  
46 should be noted that the ONS list of avoidable deaths was not designed specifically for  
47 people with intellectual disabilities, and it may emphasise some causes less relevant, and  
48 omit others that might be highly relevant in this population.<sup>5</sup>

### ***Strengths and limitations***

The strengths of the study include the thorough methods of case ascertainment for intellectual disabilities at baseline with verification of intellectual disabilities and its severity, suggesting results are generalisable in other high income countries. Whilst our Identification of the population will not have identified everyone with intellectual impairment (an IQ<70), in view of the multiple sources used, we believe it will have identified the adults with intellectual disabilities (IQ<70, plus need for support in daily activities, and onset in the developmental period). Additionally, there were detailed clinical assessments at baseline, and a longitudinal design. The size of the cohort and the duration of follow-up is also a strength, as is the successful record linkage for 94% of participants. Our study does have limitations, specifically that the study was only conducted in one region of Scotland, and the reliance upon death certificate data to obtain cause of death. Additionally, the characteristics and health of the participants was collected in 2002-2004. The health conditions we investigated tend to be long-standing or remitting/relapsing conditions, and psychotropic prescribing also once initiated tends to be long-standing in people with intellectual disabilities. However, it is possible that extent of neighbourhood deprivation, type of accommodation, employment, and civil status (though few marry) might have changed for some people between 2002-2004 and 2018; we have no further information to check this. There were no concerns regarding the proportional hazards assumption in the multivariable model. The linkage was also reliant on the accuracy of the CHI number as a sole source of linkage.

### ***Implications***

It is important to know the factors that are associated with risk of death, and the common causes of death in this population, as these then inform the actions needed to reduce the unacceptably high SMRs experienced by people with intellectual disabilities. Awareness of these factors may provide a pathway to action to reduce the observed earlier mortality in adults with intellectual disabilities. It is not adequate to solely rely on the public health interventions available to everyone, even when they are accessible.

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3 Aspiration, reflux, and choking could, and should, be avoided by raising awareness of its  
4 consequences (death), and putting in place training on simple measures related to  
5 feeding, positioning, food consistency, and when to seek health advice from speech and  
6 language therapy, physiotherapy, nursing, and medical advice. Carers need to be aware  
7 of how the adults they care for express pain, so that conditions such as gastrointestinal  
8 ulcers are attended to, prior to the extreme point of perforation, and so treatable  
9 conditions such as constipation and urinary tract infections are managed before they  
10 lead to respiratory distress and sepsis. Quality of care is important; adults with  
11 intellectual disabilities need just as good care for their diabetes and epilepsy (and other  
12 conditions) as the rest of the population, with reasonable adjustments to address  
13 accessibility, and accessible smoking cessation programs.  
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### 28 **Future research**

29 Further research on larger samples is needed, particularly with regards to replicating and  
30 extending our findings on the factors that are associated with risk of death, and any sex  
31 differences in them, so that practitioners can focus on actions to improve the life  
32 expectancy of adults with intellectual disabilities, with and without Down syndrome.  
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44 The researchers are independent from the funders.  
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## 48 **Competing interests**

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52 The authors declare no competing interests.  
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## 56 **Author's contributions**

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3 S-AC is principle investigator, she conceived and managed the project, interpreted data,  
4 and wrote the first draft of the manuscript. LA contributed to the conception of the  
5 project, and project management. NG designed and supervised the statistical analysis,  
6 and contributed to data interpretation and drafting of the manuscript. PMcS implemented  
7 and refined the statistical analysis, and contributed to data interpretation, and drafting of  
8 the manuscript. AJ implemented and refined the statistical analysis, and contributed to  
9 data interpretation. AH contributed to data linkage and interpretation, and drafting of the  
10 manuscript. CMcC provided expertise on data linkage and methods, and drafting of the  
11 manuscript. DK contributed to data interpretation and drafting of the manuscript. CM  
12 contributed to data interpretation, and drafting of the manuscript. All approved the final  
13 version of the manuscript. S-AC is the study guarantor.

## 24 25 26 27 **Data sharing**

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32 Data is available via NHS GG&C Safe Haven upon application.

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**Table 1. Cohort characteristics at time of the health assessment, summarised overall and by death status during the follow-up period**

| Variable           | Statistics / Groups | All participants (N=961) | Deceased participants (N=294) | Alive participants (N=667) |
|--------------------|---------------------|--------------------------|-------------------------------|----------------------------|
| Age (years)        | Mean (SD)           | 44.1 (14.6)              | 52.4 (13.6)                   | 40.5 (13.6)                |
|                    | Min, max            | 16, 83                   | 18, 83                        | 16, 77                     |
| Age group          | 16-25 years         | 127 (13.2%)              | 10 (3.4%)                     | 117 (17.5%)                |
|                    | 26-35 years         | 153 (15.9%)              | 26 (8.8%)                     | 127 (19.0%)                |
|                    | 36-45 years         | 246 (25.6%)              | 49 (16.7%)                    | 197 (29.5)                 |
|                    | 46-55 years         | 205 (21.3%)              | 85 (28.8%)                    | 120 (18.0%)                |
|                    | >55 years           | 230 (23.9%)              | 124 (42.0%)                   | 106 (15.9%)                |
| Sex                | Male                | 525 (54.6%)              | 154 (52.4%)                   | 371 (55.6%)                |
|                    | Female              | 436 (45.3%)              | 140 (47.5%)                   | 296 (44.4%)                |
| Ability level      | Mild ID             | 382 (39.7%)              | 92 (31.2%)                    | 290 (43.5%)                |
|                    | Moderate ID         | 236 (24.5%)              | 73 (24.7%)                    | 163 (24.4%)                |
|                    | Severe ID           | 180 (18.7%)              | 67 (22.7%)                    | 113 (16.9%)                |
|                    | Profound ID         | 163 (17.0%)              | 62 (21.1%)                    | 101 (15.1%)                |
| Accommodation type | Family carer        | 374 (38.9%)              | 70 (23.8%)                    | 304 (45.6%)                |
|                    | Independent         | 93 (9.7%)                | 36 (12.2%)                    | 57 (8.5%)                  |
|                    | Paid support        | 435 (45.2%)              | 161 (54.6%)                   | 274 (41.1%)                |
|                    | Congregate care     | 59 (6.1%)                | 27 (9.2%)                     | 32 (4.8%)                  |
| Down syndrome      | No                  | 782 (81.4%)              | 230 (78.2%)                   | 552 (82.8%)                |
|                    | Yes                 | 179 (18.6%)              | 64 (21.7%)                    | 115 (17.2%)                |

ID=intellectual disabilities; SD=standard deviation

**Table 2. Standardised mortality ratios**

| Variable   | Groups  | SMR (95% CI)         |
|--|---|----------------------|
| All participants                                       | -   | 2.24 (1.99, 2.50)    |
| Age group*   | 15-25 years   | 18.73 (0.37, 37.09)  |
|  | 26-35 years   | 4.21 (1.29, 7.13)    |
|  | 36-45 years   | 3.86 (2.28, 5.44)    |
|  | 46-55 years   | 3.77 (2.90, 4.74)    |
|  | >55 years   | 1.86 (1.60, 2.12)    |
| Sex  | Male  | 1.69 (1.42, 1.95)    |
|  | Female  | 3.48 (2.90, 4.06)    |
| Ability level  | Mild ID   | 1.60 (1.27, 1.92)    |
|  | Moderate ID   | 2.10 (1.62, 2.58)    |
|  | Severe ID   | 2.78 (2.11, 3.44)    |
|  | Profound ID   | 4.14 (3.11, 5.17)    |
| Down syndrome  | No  | 1.93 (1.68, 2.18)    |
|  | Yes   | 5.28 (3.98, 6.57)    |
| Underlying causes of death grouped by ICD-10 chapter** | Congenital malformations, deformations and chromosomal abnormalities                                | 17.26 (10.75, 23.78) |
|  | Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | 7.50 (-7.20, 22.20)  |
|  | Diseases of the circulatory system  | 5.55 (4.01, 7.09)    |
|  | Diseases of the digestive system  | 16.13 (8.23, 24.04)  |
|  | Diseases of the genitourinary system  | 3.65 (0.73, 6.57)    |
|  | Diseases of the musculoskeletal system and connective tissue  | 5.40 (-0.71, 11.52)  |
|  | Diseases of the nervous system  | 7.73 (5.13, 10.32)   |
|  | Diseases of the respiratory system  | 6.78 (5.02, 8.54)    |

|  |   |                     |
|--|---|---------------------|
|  | Diseases of the skin and subcutaneous tissue  | 2.75 (-2.64, 8.15)  |
|  | Endocrine, nutritional and metabolic diseases   | 3.43 (1.05, 5.81)   |
|  | External causes of morbidity and mobility   | 11.08 (3.40, 18.76) |
|  | Infectious and parasitic diseases   | 8.93 (1.78, 16.07)  |
|  | Mental and behavioural disorders  | 12.64 (3.27, 22.00) |
|  | Neoplasms   | 6.31 (4.19, 8.43)   |
|  | Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified | 19.51 (0.39, 38.63) |

CI=confidence intervals; ID=intellectual disabilities; SMR=standardised mortality ratios

\*Data used for comparison with General Population (GG&C Health Board) provides data in 5 year age bands therefore 15+. Data on adults with ID are 16+

\*\* Negative Lower CI and wide CIs indicate low number of observed deaths in study population

**Table 3. Underlying causes of death grouped by ICD-10 chapter, where cause of death is known**

| ICD-10 chapter  | Participants with Down syndrome (N=57) | Participants without Down syndrome (N=205) |
|---|--|--|
| Certain infectious and parasitic diseases   | 5 (8.8%)                               | <5   |
| Neoplasms   | <5                                     | 33 (16.1%)                                 |
| Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | <5                                     | <5   |
| Endocrine, nutritional and metabolic diseases   | <5                                     | 8 (3.9%)                                   |
| Mental and behavioural disorders  | 5 (8.8%)                               | <5   |
| Diseases of the nervous system  | 7 (12.3%)                              | 27 (13.2%)                                 |
| Diseases of the eye and adnexa  | <5                                     | <5   |
| Diseases of the ear and mastoid process   | <5                                     | <5   |
| Diseases of the circulatory system  | 8 (14.0%)                              | 42 (20.5%)                                 |
| Diseases of the respiratory system  | 8 (14.0%)                              | 49 (23.9%)                                 |
| Diseases of the digestive system  | <5                                     | 16 (7.8%)                                  |
| Diseases of the skin and subcutaneous tissue  | <5                                     | <5   |
| Diseases of the musculoskeletal system and connective tissue  | <5                                     | <5   |
| Diseases of the genitourinary system  | <5                                     | 5 (2.4%)                                   |
| Pregnancy, childbirth and the puerperium  | <5                                     | <5   |
| Certain conditions originating in the perinatal period  | <5                                     | <5   |
| Congenital malformations, deformations and chromosomal abnormalities                                | 21 (36.8%)                             | 6 (2.9%)                                   |
| Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified             | <5                                     | <5   |
| External causes of morbidity and mortality  | <5                                     | 7 (3.4%)                                   |
| All deaths  | 57 (100%)                              | 205 (100%)                                 |

ICD-10=International Statistical Classification of Diseases and Related Health Problems, 10th Revision

**Table 4. Underlying causes of death grouped by specific individual causes or related groups of causes, where cause of death is known**

| <b>Causes</b>                      | <b>Participants with Down syndrome (N=57)</b> | <b>Participants without Down syndrome (N=205)</b> |
|------------------------------------|---|---|
| Aspiration/reflux/choking          | <5  | 22 (10.8%)  |
| Respiratory infection              | <5  | 21 (10.3%)  |
| Down syndrome                      | 21 (36.8%)                                    | <5  |
| Other malignancy                   | <5  | 19 (9.3%)   |
| Other condition                    | <5  | 17 (8.3%)   |
| Epilepsies                         | <5  | 13 (6.4%)   |
| Acute myocardial infarction        | <5  | 13 (6.4%)   |
| Gastro-intestinal malignancy       | <5  | 12 (5.9%)   |
| Stroke                             | <5  | 11 (5.4%)   |
| Other cardiovascular disease       | <5  | 11 (5.4%)   |
| Other respiratory condition        | <5  | 9 (4.4%)  |
| Other infection                    | 5 (8.8%)                                      | 6 (2.9%)  |
| Cerebral palsy                     | <5  | 11 (5.4%)   |
| Dementia                           | 9 (15.8%)                                     | <5  |
| Other gastrointestinal disorders   | <5  | 8 (3.9%)  |
| Ulcer/gastrointestinal perforation | <5  | 7 (3.4%)  |
| Diabetes                           | <5  | 7 (3.4%)  |
| Other congenital condition         | <5  | 6 (2.9%)  |
| Other ischaemic heart condition    | <5  | 6 (2.9)   |
| Mental health                      | <5  | <5  |
| Other neurological conditions      | <5  | <5  |
| Renal failure                      | <5  | <5  |
| All deaths                         | 57 (100%)                                     | 205 (100%)  |

**Table 5. All contributing causes of death grouped by specific individual causes or related groups of causes, where cause of death is known**

| <b>Causes</b>                       | <b>Participants with Down syndrome (N=57)</b> | <b>Participants without Down syndrome (N=205)</b> |
|-------------------------------------|---|---|
| Respiratory infection               | 22 (38.6%)                                    | 49 (23.9%)  |
| Aspiration/reflux/choking           | 11 (19.3%)                                    | 41 (20.0%)  |
| Down syndrome                       | 43 (75.4%)                                    | <5  |
| Other condition                     | 8 (14.0%)                                     | 33 (16.1%)  |
| Other cardiovascular disease        | 8 (14.0%)                                     | 30 (14.6%)  |
| Other respiratory conditions        | <5  | 31 (15.1%)  |
| Other infection                     | 9 (15.8%)                                     | 24 (11.7%)  |
| Intellectual disabilities           | <5  | 31 (15.1%)  |
| Epilepsies                          | 8 (14.0%)                                     | 24 (11.7%)  |
| Dementia                            | 24 (42.1%)                                    | <5  |
| Other neoplasms                     | <5  | 23 (11.2%)  |
| Cerebral palsy                      | <5  | 24 (11.7%)  |
| Acute myocardial infarction         | 5 (8.8%)                                      | 19 (9.3%)   |
| Other gastrointestinal disorders    | <5  | 18 (8.8%)   |
| Diabetes                            | <5  | 19 (9.3%)   |
| Other ischaemic heart disease       | <5  | 19 (9.3%)   |
| Renal failure                       | <5  | 16 (7.8%)   |
| Stroke                              | <5  | 17 (8.3%)   |
| Other congenital condition          | <5  | 15 (7.3%)   |
| Gastrointestinal malignant neoplasm | <5  | 12 (5.9%)   |
| Ulcer/gastrointestinal perforation  | <5  | 10 (4.9%)   |
| Mental health                       | <5  | 10 (4.9%)   |
| Other neurological condition        | <5  | 8 (3.9%)  |
| Heart failure                       | <5  | 7 (3.4%)  |
| Injuries and accidents              | <5  | 8 (3.9%)  |
| Medical/surgical complications      | <5  | <5  |
| Secondary malignancies              | <5  | <5  |
| Thyroid disorders                   | <5  | <5  |
| Metabolic disorder                  | <5  | <5  |
| All deaths                          | 57 (100%)                                     | 205 (100%)  |

**Table 6. Multivariable model results for the outcome time to death**

| Variable                          |     | Hazard ratio | 95% CI        | p-value |
|-----------------------------------|-----|--------------|---------------|---------|
| Age at time of health assessment  |     | 1.056        | 1.046, 1.066  | <0.0001 |
| Smoker                            | No  | 1            | -             |         |
|                                   | Yes | 1.531        | 1.1011, 2.128 | 0.0112  |
| Down syndrome                     | No  | 1            | -             |         |
|                                   | Yes | 2.440        | 1.787, 3.332  | <0.0001 |
| Epilepsy                          | No  | 1            | -             |         |
|                                   | Yes | 1.511        | 1.173, 1.946  | 0.0014  |
| Hearing impairment                | No  | 1            | -             |         |
|                                   | Yes | 1.320        | 1.030, 1.692  | 0.0284  |
| Bowel incontinence                | No  | 1            | -             |         |
|                                   | Yes | 0.490        | 0.376, 0.640  | <0.0001 |
| Diabetes                          | No  | 1            | -             |         |
|                                   | Yes | 2.346        | 1.553, 3.542  | <0.0001 |
| PEG/tube fed                      | No  | 1            | -             |         |
|                                   | Yes | 2.346        | 1.135, 5.989  | 0.00240 |
| Lower respiratory track infection | No  | 1            | -             |         |
|                                   | Yes | 1.782        | 1.315, 2.415  | 0.0002  |
| Total number of prescribed drugs  |     | 1.066        | 1.016, 1.118  | 0.0085  |

CI=confidence interval; PEG=percutaneous endoscopic gastrostomy

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### Supplementary table 1. Previously reported standardised mortality ratios, causes, and risks for death

| Author                                 | Country   | SMR (95% confidence interval)   | Number of deaths                 | Causes of death and risk factors for death   |
|--|-----------|---|----------------------------------|--|
| Forsgren et al (1996) <sup>7</sup>     | Sweden    | 4.2 (3.3, 5.3) at 20-59y; 1.1 (0.9, 1.5) at 60+y<br><i>Without epilepsy:</i><br>3.8 (2.8, 5.0) at 20-59y; 1.1 (0.8, 1.5) at 60+y<br><i>With epilepsy:</i><br>5.0 (2.9, 8.7) at 20-59y; 2.4 (0.9, 6.1) at 60+y<br><i>With epilepsy and cerebral palsy:</i><br>8.0 (4.1, 15.7) at 20-59y; 0.9 (0.1, 6.6) at 60+y<br><i>M:</i> 1.6 (1.2, 2.0) at 0-60+y<br><i>F:</i> 2.6 (2.0, 3.3) at 0-60+y<br><i>Mild ID:</i> 1.8 (1.1, 2.7) at 0-60+y<br><i>Moderate ID:</i> 1.5 (1.1, 2.0) at 0-60+y<br><i>Severe ID:</i> 2.0 (1.5, 2.6) at 0-60+y<br><i>Profound ID:</i> 8.1 (5.6, 11.7) at 0-60+y | 124 at 0-60+y;<br>112 at 20-60+y | <i>Underlying cause at 0-60+y:</i><br>Congenital anomalies: SMR=46.3 (32.9, 65.0)<br>Nervous system: SMR=9.7 (5.5, 17.0)<br>Mental disorder: SMR=4.0 (1.9, 8.4)<br>Respiratory: SMR=3.3 (2.0, 5.5)<br>Circulatory: SMR=2.1 (1.6, 2.7)<br>Violent death: SMR=1.4 (0.6, 2.8)<br>Neoplasm: SMR=0.9 (0.6, 1.6) |
| Durvasula & Beange (2002) <sup>8</sup> | Australia | 4.9 (3.4, 6.4) at 10-59y<br><i>M:</i> 4.1 (2.4, 5.9) at 10-59y<br><i>F:</i> 6.2 (3.3, 9.1) at 10-59y  | 40 at 10-59y;<br>31 at 20-59y    | <i>Underlying cause at 10-59y:</i><br>Respiratory: 30% (pneumonia, aspiration)<br>External cause: 20%<br>Neoplasm: 17%<br>Heart disease: 15% (congenital heart disease 50%)<br>Gastrointestinal: 1.5% (ischaemic bowel, perforated peptic ulcer, post-operative peritonitis)<br>Seizure: 5%                |
| Tyrer et al (2007) <sup>9</sup>        | England   | 3.24 (2.93, 3.56) at 20-70+y<br><i>M:</i> 2.86 (2.50, 3.26) at 20-70+y<br><i>F:</i> 3.63 (3.12, 4.20) at 20-70+y<br>1.51 (1.23, 1.83) to 11.50 (8.14, 15.78) at 20-70+y<br><i>M:</i> 1.39 (1.03, 1.82) to 8.83 (5.60, 13.25) at 20-70+y<br><i>F:</i> 1.60 (1.18, 2.12) to 17.22 (9.64, 28.4) at 20-70+y<br><i>With Down syndrome:</i> 7.60 at 20-70+y<br><i>Without Down syndrome:</i> 2.70 at 20-70+y  | 409 at 20-70+y                   | Not reported   |
| Patja et al (2008) <sup>10</sup>       | Finland   | <i>M:</i> 2.2 at 20-39y, 1.0 at 40-59y, 1.0 at 60+y<br><i>F:</i> 1.4 at 20-39y, 1.1 at 40-49y, 1.0 at 60+y<br><i>Mild ID:</i><br><i>M:</i> 1.6 at 20-39y, 1.0 at 40-59y, 1.0 at 60+y<br><i>F:</i> 1.2 at 20-39y, 1.1 at 40-49y, 1.0 at 60+y   | 1,046 at 20-97y                  | <i>Underlying cause at 2-97y:</i><br>Vascular: 36% (cardiac infarct 33%, cerebral infarct 33%, congenital heart disease 18%, pulmonary infarct 6%)<br>Respiratory: 22% (pneumonia 83%, COPD 11%)   |

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|   |                     |  |                                      |   |
|---|---------------------|--|--------------------------------------|---|
|   |                     | <p><b>Moderate ID:</b><br/>M: 2.3 at 20-39y, 1.1 at 40-59y, 1.0 at 60+y<br/>F: 1.5 at 20-39y, 1.1 at 40-49y, 1.0 at 60+y</p> <p><b>Severe ID:</b><br/>M: 2.6 at 20-39y, 1.2 at 40-59y, 1.0 at 60+y<br/>F: 1.6 at 20-39y, 1.0 at 40-49y, 1.0 at 60+y</p> <p><b>Profound ID:</b><br/>M: 2.1 at 20-39y, 1.1 at 40-59y, 1.0 at 60+y<br/>F: 1.3 at 20-39y, 1.2 at 40-49y, 1.0 at 60+y</p> |                                      | <p>Neoplasm: 11% (Digestive 44%, respiratory 15%, urogenital, 12%)<br/>Digestive: 7% (intestinal obstruction 25%, ulcer perforation 13%)<br/>Accidents and poisonings: 7% (commonest was fatal fracture, then drowning)<br/>Vascular, neoplasia, and accident causes were less common than sex-age-related in the general population; Digestive were 2.5 times, Respiratory 2.6-5.8 times more common</p>   |
| Tyrer & McGoher (2009) <sup>11</sup>      | England             | <p>2.77 (2.53, 3.03) at 20+y<br/>M: 2.28 (2.02, 2.56) at 20+y<br/>F: 3.24 (2.83, 3.69) at 20+y</p>   | 503 at 20+y                          | <p><b>Underlying cause of death at 20+y:</b><br/>Pneumonia: 1.9%, SMR=6.47 (5.00, 8.23)<br/>Nervous system: 3.1%, SMR=16.30 (12.61, 20.74)<br/>Other respiratory: 12.9%, SMR=4.64 (3.58, 5.91)<br/>Ischaemic heart disease: 11.5%, SMR=1.49 (1.13, 1.92)<br/>Neoplasm: 9.3%<br/>Congenital anomalies: 9.1%, SMR=85.60 (62.67, 114.18)<br/>Cerebrovascular disease: 7.8%, SMR=2.40 (1.71, 3.28)</p>  |
| Oullette-Kuntz et al (2015) <sup>12</sup> | Canada              | <p>2.5 (2.1, 2.9) at 0-60+y<br/>M: 2.1 (1.7, 2.6) at 0-60+y<br/>F: 3.0 (2.4, 3.8) at 0-60+y<br/>M: 1.7 (1.3, 2.3) to 3.4 (2.3, 4.7) at 20-60+y<br/>F: 2.1 (1.4, 2.9) to 6.1 (4.1, 8.6) at 20-60+y</p>  | 172 at 0-60+y;<br>158 at 20-60+y     | <p><b>Risk factors for death:</b><br/>Age, Down syndrome (OR=1.76 at 20-39y; OR=1.69 at 40-59y; OR=22.3 at 60+y), cerebral palsy (OR=2.39 at 20-39y; OR=0.93 at 40-59y; OR=0.50 at 60+y), blindness/low vision (OR not given), technological dependence/medical fragility (OR=1.95 at 20-39y; OR=7.28 at 40-59y; OR=3.42 at 60+y), wheelchair dependence (OR=5.96 at 20-39y; OR=2.89 at 40-59y; OR=2.56 at 60+y), mobility impairment without wheelchair dependence (OR not given), epilepsy (OR=1.8 at 20-39y; OR=1.80 at 40-59y; OR=1.09 at 60+y)</p> |
| Florio & Troller (2015) <sup>13</sup>     | Australia           | <p>2.48 (2.32, 2.64) at 0-85+y<br/>3.15 (2.94, 3.38) at 5-69y<br/>M: 2.52 (2.29, 2.77) at 5-69y<br/>F: 4.26 (3.83, 4.74) at 5-69y</p>  | 953 at 0-85+y;<br>831 at 15+y        | Not reported  |
| McCarron et al (2015) <sup>14</sup>       | Republic of Ireland | <p>3.85 (3.70, 4.00) at 0-80+y<br/>M: 3.09 (2.93, 3.25) at 0-80+y<br/>F: 4.90 (4.63, 5.17) at 0-80+y<br/>2.71 (2.41, 3.04) to 6.09 (5.29, 6.96) at 20-80y<br/>M: 2.50 (2.18, 2.86) to 4.50 (3.69, 5.44) at 20-80y<br/>F: 2.71 (2.32, 3.14) to 10.07 (8.99, 13.10) at 20-80y</p>  | 2,666 at 0-80+y;<br>2,394 at 20-80+y | Not reported  |

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|  |         |   |  |   |
|--|---------|---|--|---|
| Heslop & Glover (2015) <sup>15</sup>   | England | Median 2.13 (interquartile range 1.09, 2.83) across geographic areas at 18-65+y   | 18-65+y  | Not reported  |
| Lauer & McCallion (2015) <sup>16</sup> | USA     | <i>Intellectual and developmental disabilities*:</i><br>1.19 at all ages, 2011<br>1.49 at 18+y, 2009  | 120,913 in 2009 at 18+y, 140,104 in 2011 at all ages | Not reported  |
| Arvio et al (2016) <sup>17</sup>       | Finland | <i>Mild ID:</i><br>2.28 (2.18, 2.39) at 0-60+y<br>1.99 (1.85, 2.13) to 2.77 (2.36, 3.23) at 15-60+y<br><i>M:</i> 2.01 (1.88, 2.14) at 0-60+y<br><i>F:</i> 2.80 (2.60, 3.01) at 0-60+y<br><i>Severe ID:</i><br>3.41 (3.30, 3.52) at 0-60+y<br>2.07 (1.96, 2.19) to 8.77 (7.77, 9.87) at 15-60+y<br><i>M:</i> 2.59 (2.48, 2.72) at 0-60+y<br><i>F:</i> 5.24 (4.99, 5.50) at 0-60+y  | 5,171 at 0-60+y; 5,053 at 15-60y                     | Not reported  |
| Hosking et al (2016) <sup>5</sup>      | England | HR=3.62 (3.33, 3.93) at 18-84y<br><i>M:</i> HR=3.30 (2.96, 3.68) at 18-84y<br><i>F:</i> HR=4.10 (3.61, 4.66) at 18-84y<br><i>With Down syndrome:</i> HR=9.21 (7.22, 11.76)<br><i>Without Down syndrome:</i> HR=3.19 (2.92, 3.49)<br><i>With epilepsy:</i> HR=6.04 (5.04, 7.24)<br><i>Without epilepsy:</i> HR=3.18 (2.90, 3.50)<br><i>With high level of support needs:</i> HR=4.77 (4.08, 5.59)<br><i>Without high level of support needs:</i> HR=3.28 (2.98, 3.62)<br><i>With autism:</i> HR=2.39 (1.45, 3.96)<br><i>Without autism:</i> HR=3.66 (3.37, 3.98)<br><i>In communal/shared homes:</i> HR=4.99 (4.36, 5.73)<br><i>Not in communal/shared homes:</i> HR=3.05 (2.74, 3.30) | 656 at 18-84y  | <i>Underlying cause at 18-84y:</i><br>Circulatory: 21.6%, HR=3.05 (2.56, 3.64)<br>Respiratory: 18.8% (pneumonia and aspiration pneumonia), HR=1.68 (5.38, 8.29)<br>Neoplasm: 14.1%, HR=1.44 (1.18, 1.76)<br>Nervous system: 1.6%, HR=13.79 (9.70, 19.62)<br>Digestive: 7.0%, HR=4.02 (2.92, 5.54)<br>Congenital anomalies: 6.9%, HR could not be estimated<br>Mental disorders: 2.3%, HR=7.99 (5.19, 12.31)<br>External causes: 4.1%, HR=1.85 (1.26, 2.71)<br>Genitourinary: 3.5%, HR=10.89 (6.09, 19.47)<br>Endocrine, nutritional, and metabolic: 2.0%, HR=5.38 (2.79, 10.07)<br><i>Down syndrome:</i> Respiratory: 20.3% (or 42.4% if "Down syndrome" is excluded as an underlying cause of death)<br><i>Avoidable deaths:</i> 37% amenable (20% controls), 19% preventable (40% controls) |

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|                                    |           |  |                                   |   |
|------------------------------------|-----------|--|-----------------------------------|---|
| Lauer (2016) <sup>18</sup>         | USA       | Not reported   | 438 in 2012, 409 in 2013, at 18+y | <p><i>Major cause of death, 2012, 2013</i><br/> Heart disease: 16.9%, 13.7%<br/> Neoplasm: 13.3%, 13.4%<br/> Alzheimer disease: 13.0%-12.2% (48% in Down syndrome)<br/> Aspiration pneumonia: 9.4%, 8.6%<br/> Septicaemia: 10.0%, 8.6%<br/> Chronic lower respiratory diseases: 4.6%, 6.6%<br/> Unintentional injury: 4.8%, 3.2%</p>  |
| Troller et al (2017) <sup>19</sup> | Australia | 1.3 (1.2, 1.5) at 20+y<br>4.0 (3.1, 5.2) at 20-44y<br>2.3 (2.0, 2.7) at 45-64y<br>1.0 (0.8, 1.2) at 65+y<br>M: 1.4 (1.1, 1.6) at 20+y<br>F: 1.3 (1.1, 1.6) at 20+y   | 732 at 20-65+y                    | <p><i>Underlying cause at 20-65+y:</i><br/> Circulatory: 18%<br/> Neoplasm: 18%<br/> Nervous: 16%<br/> Respiratory: 11%<br/> Congenital anomalies: 11%<br/> Injury and poisoning: 6%<br/> Digestive: 5%<br/> Avoidable deaths: 31%</p>  |
| Glover et al (2017) <sup>6</sup>   | England   | 3.18 (2.94, 3.43) at 0-99y<br>M: 3.03 (2.73, 3.35) at 0-99y<br>F: 3.40 (3.02, 3.81) at 0-99y<br>1.6 (1.2, 2.1) to 7.8 (5.4, 11.1) at 18-99y<br>M: 1.5 (0.9, 2.2) to 6.6 (4.0, 10.1) at 18-99y<br>F: 1.7 (1.1, 2.4) to 11.6 (6.0, 20.2) at 18-99y | 664 at 0-99y                      | <p><i>Underlying cause at 0-99y:</i><br/> Circulatory: 22.9% (ischaemic heart disease 37.5%, cerebrovascular 2.7%, thrombophlebitis 6.6%, cardiomyopathy 9%, PE 3.9%), SMR=2.8 (2.4, 3.3)<br/> Respiratory: 14.2% (pneumonia 50.0%, pneumonitis 21.0%), SMR=4.9 (4.0, 5.9)<br/> Neoplasm: 3.1% digestive 36.8%, respiratory 13.8%, female genital tract 10.3%, lymphoid and haematopoietic 10.3%), SMR=1.1 (0.9, 1.4)<br/> Nervous: 12.8%, SMR=9.8 (7.8, 12.1)<br/> Congenital anomalies: 8.4%, SMR=72.9 (55.1, 94.7)<br/> Digestive: 7.8%, SMR=4.0 (3.0, 5.2)<br/> No ICD10 chapter had fewer than expected deaths<br/> Other common single causes: dementia 33/664, epilepsy 26/664, cerebral palsy 23/664<br/> Avoidable deaths: 44.7% (41.0%, 48.5%), mostly amenable<br/> M: 50.9% (45.9%, 56.0%); F: 36.9% (31.5%, 42.5%)</p> |

COPD=chronic obstructive pulmonary disease; HR=hazard ratio; ID=intellectual disabilities; OR=odds ratio; PE=pulmonary embolism; SMR=standardised mortality ratio; y=years

\*Includes some individuals with IQ>70

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## Supplementary table 2. Groupings of related causes of deaths

|   | <b>ICD10</b> |
|---|--------------|
| <b>Infectious diseases</b>  |              |
| <b>Infection</b>  |              |
| ENTEROCOLITIS DUE TO CLOSTRIDIUM DIFFICILE                                | A047         |
| SEPSIS DUE TO STAPHYLOCOCCUS AUREUS                                       | A410         |
| SEPSIS, UNSPECIFIED   | A419         |
| BACTERIAL INFECTION, UNSPECIFIED  | A499         |
| SUBACUTE SCLEROSING PANENCEPHALITIS                                       | A811         |
| CHRONIC VIRAL HEPATITIS B WITHOUT DELTA-AGENT                             | B181         |
| PULMONARY CANDIDIASIS   | B371         |
| NECROTISING FASCIITIS   | M726         |
| URINARY TRACT INFECTION, SITE NOT SPECIFIED                               | N390         |
| <b>Neoplasms</b>  |              |
| <b>Gastrointestinal malignant neoplasms</b>                               |              |
| MALIGNANT NEOPLASM OF PAROTID GLAND                                       | C07          |
| MALIGNANT NEOPLASM, OESOPHAGUS, UNSPECIFIED                               | C159         |
| MALIGNANT NEOPLASM, STOMACH, UNSPECIFIED                                  | C169         |
| MALIGNANT NEOPLASM, CAECUM  | C180         |
| MALIGNANT NEOPLASM, SIGMOID COLON   | C187         |
| MALIGNANT NEOPLASM, COLON, UNSPECIFIED                                    | C189         |
| INTRAHEPATIC BILE DUCT CARCINOMA  | C221         |
| NEOPLASM OF UNCERTAIN OR UNKNOWN BEHAVIOUR, OTHER DIGESTIVE ORGANS        | D377         |
| <b>Other neoplasms</b>  |              |
| MALIGNANT NEOPLASM, LOWER LOBE, BRONCHUS OR LUNG                          | C343         |
| MALIGNANT NEOPLASM, BRONCHUS OR LUNG, UNSPECIFIED                         | C349         |
| MALIGNANT NEOPLASM, BREAST, UNSPECIFIED                                   | C509         |
| MALIGNANT NEOPLASM, ENDOMETRIUM   | C541         |
| MALIGNANT NEOPLASM OF OVARY   | C56          |
| MALIGNANT NEOPLASM, TESTIS, UNSPECIFIED                                   | C629         |
| MALIGNANT NEOPLASM, BLADDER, UNSPECIFIED                                  | C679         |
| MALIGNANT NEOPLASMS OF THYROID GLAND                                      | C73          |
| WALDENSTROM MACROGLOBULINAEMIA  | C880         |
| NON-HODGKIN'S LYMPHOMA, UNSPECIFIED                                       | C859         |
| MALIGNANT NEOPLASM OF UNSPECIFIED SITE                                    | C80          |
| NEOPLASM OF UNCERTAIN OR UNKNOWN BEHAVIOUR, TRACHEA, BRONCHUS AND LUNG    | D381         |
| SECONDARY MALIGNANT NEOPLASM OF LUNG                                      | C780         |
| SECONDARY MALIGNANT NEOPLASM OF LIVER AND INTRAHEPATIC BILE DUCT          | C787         |
| SECONDARY MALIGNANT NEOPLASM OF BRAIN AND CEREBRAL MENINGES               | C793         |
| SECONDARY MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES                     | C798         |
| <b>Endocrine and metabolic diseases</b>                                   |              |
| <b>Diabetes</b>   |              |
| INSULIN-DEPENDENT DIABETES MELLITUS WITHOUT COMPLICATIONS                 | E109         |
| NON-INSULIN-DEPENDENT DIABETES MELLITUS WITH RENAL COMPLICATIONS          | E112         |
| NON-INSULIN-DEPENDENT DIABETES MELLITUS W. PERIPHERAL CIRC. COMPLICATIONS | E115         |
| NON-INSULIN-DEPENDENT DIABETES MELLITUS WITHOUT COMPLICATIONS             | E119         |
| UNSPECIFIED DIABETES MELLITUS WITH RENAL COMPLICATIONS                    | E142         |

*Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage*

|    |   |      |
|----|---|------|
| 1  |   |      |
| 2  | UNSPECIFIED DIABETES MELLITUS WITHOUT COMPLICATIONS                     | E149 |
| 3  | ABNORMAL GLUCOSE TOLERANCE TEST   | R730 |
| 4  | HYPERGLYCAEMIA, UNSPECIFIED   | R739 |
| 5  |   |      |
| 6  | <b>Metabolic disorders</b>  |      |
| 7  | OTHER HYPERPHENYLALANINAEMIAS   | E701 |
| 8  | DISORDERS OF PHOSPHORUS METABOLISM & PHOSPHATASES                       | E833 |
| 9  | DISORDERS OF PLASMA-PROTEIN METABOLISM, NOT ELSEWHERE CLASSIFIED        | E880 |
| 10 |   |      |
| 11 |   |      |
| 12 | <b>Mental disorders</b>   |      |
| 13 | <b>Dementias</b>  |      |
| 14 | VASCULAR DEMENTIA, UNSPECIFIED  | F019 |
| 15 | UNSPECIFIED DEMENTIA  | F03  |
| 16 | ALZHEIMER'S DISEASE WITH LATE ONSET                                     | G301 |
| 17 | ALZHEIMER'S DISEASE, UNSPECIFIED  | G309 |
| 18 |   |      |
| 19 | <b>Mental health</b>  |      |
| 20 |   |      |
| 21 | MENTAL AND BEHAVIOURAL DISORDERS DUE TO ACUTE INTOXICATION WITH ALCOHOL | F100 |
| 22 | MENTAL AND BEHAVIOURAL DISORDERS DUE TO ALCOHOL DEPENDENCE SYNDROME     | F102 |
| 23 | MENTAL AND BEHAVIOURAL DISORDERS DUE TO USE OF TOBACCO, UNSPECIFIED     | F179 |
| 24 | SCHIZOPHRENIA, UNSPECIFIED  | F209 |
| 25 | BIPOLAR AFFECTIVE DISORDER, UNSPECIFIED                                 | F319 |
| 26 | OTHER & UNSPEC SYMPTOMS & SIGNS INVOLVING COGNITIVE FUNCTIONS &         | R418 |
| 27 | AWARENESS   |      |
| 28 | INTENTIONAL SELF-HARM BY JUMPING FROM A HIGH PLACE                      | X80  |
| 29 |   |      |
| 30 | <b>Intellectual disabilities</b>  |      |
| 31 | UNSPECIFIED MENTAL RETARDATION  | F79  |
| 32 | DEVELOPMENTAL DISORDER OF SCHOLASTIC SKILLS, UNSPECIFIED                | F819 |
| 33 |   |      |
| 34 |   |      |
| 35 | <b>Nervous system</b>   |      |
| 36 | <b>Epilepsies</b>   |      |
| 37 | GENERALIZED IDIOPATHIC EPILEPSY AND EPILEPTIC SYNDROMES                 | G403 |
| 38 | EPILEPSY, UNSPECIFIED   | G409 |
| 39 | STATUS EPILEPTICUS, UNSPECIFIED   | G419 |
| 40 | MYOTONIC DISORDERS  | G711 |
| 41 | OTHER AND UNSPECIFIED CONVULSIONS                                       | R568 |
| 42 |   |      |
| 43 | <b>Cerebral palsy</b>   |      |
| 44 | SPASTIC QUADRAPLEGIC CEREBRAL PALSY                                     | G800 |
| 45 | SPASTIC HEMIPLEGIC CEREBRAL PALSY                                       | G802 |
| 46 | OTHER CEREBRAL PALSY  | G808 |
| 47 | CEREBRAL PALSY, UNSPECIFIED   | G809 |
| 48 | TETRAPLEGIA, UNSPECIFIED  | G825 |
| 49 |   |      |
| 50 | <b>Other neurological conditions</b>                                    |      |
| 51 | SEQUELAE OF INFLAMMATORY DISEASES OF CENTRAL NERVOUS SYSTEM             | G09  |
| 52 | PARKINSON'S DISEASE   | G20  |
| 53 | MYONEURAL DISORDER, UNSPECIFIED   | G709 |
| 54 | ENCEPHALITIS, MYELITIS AND ENCEPHALOMYELITIS, UNSPECIFIED               | G049 |
| 55 | ANOXIC BRAIN DAMAGE, NOT ELSEWHERE CLASSIFIED                           | G931 |
| 56 | BLINDNESS, BINOCULAR  | H540 |
| 57 | OTHER DISORDERS OF NERVOUS SYSTEM, NOT ELSEWHERE CLASSIFIED             | G98  |
| 58 |   |      |
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| 60 |   |      |

*Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage*

## **Circulatory system**

### **Acute myocardial infarction**

ACUTE MYOCARDIAL INFARCTION, UNSPECIFIED I219

CARDIAC ARRECT, UNSPECIFIED I469

### **Other ischaemic heart disease**

HYPERTENSIVE HEART DISEASE WITHOUT (CONGESTIVE) HEART FAILURE I119

ACUTE ISCHAEMIC HEART DISEASE, UNSPECIFIED I249

ATHEROSCLEROTIC HEART DISEASE I251

CHRONIC ISCHAEMIC HEART DISEASE, UNSPECIFIED I259

ATHEROSCLEROSIS OF AORTA I700

GENERALIZED AND UNSPECIFIED ATHEROSCLEROSIS I709

### **Heart failure**

HEART FAILURE, UNSPECIFIED I509

LEFT VENTRICULAR FAILURE I501

CONGESTIVE HEART FAILURE I500

### **Other cardiovascular disease**

PULMONARY EMBOLISM WITHOUT MENTION OF ACUTE COR PULMONALE I269

OTHER SPECIFIED PULMONARY HEART DISEASES I278

PULMONARY HEART DISEASE, UNSPECIFIED I279

AORTIC (VALVE) STENOSIS I350

ATRIAL FIBRILLATION AND FLUTTER I48

VENTRICULAR FIBRILLATION AND FLUTTER I490

OTHER ILL-DEFINED HEART DISEASES I518

PULMONARY OEDEMA J81

CARDIOGENIC SHOCK R570

PERIPHERAL VASCULAR DISEASE, UNSPECIFIED I739

PHLEBITIS AND THROMBOPHLEBITIS OF OTHER DEEP VESSELS OF LOWER EXTREMITIES I802

EMBOLISM AND THROMBOSIS OF OTHER SPECIFIED VEINS I828

ACUTE AND SUBACUTE INFECTIVE ENDOCARDITIS I330

ACUTE ENDOCARDITIS, UNSPECIFIED I339

ENDOCARDITIS, VALVE UNSPECIFIED I38

DILATED CARDIOMYOPATHY I420

CARDIOMEGALY I517

ESSENTIAL (PRIMARY) HYPERTENSION I10

### **Stroke**

INTRACEREBRAL HAEMORRHAGE, UNSPECIFIED I619

CEREBRAL INFARCTION DUE TO THROMBOSIS OF PRECEREBRAL ARTERIES I630

CEREB INFARCT DUE TO UNSPEC OCCL/STENOSIS OF PRECEREB ARTERIES I632

CEREBRAL INFARCTION, UNSPECIFIED I639

STROKE, NOT SPECIFIED AS HAEMORRHAGE OR INFARCTION I64

CEREBROVASCULAR DISEASE, UNSPECIFIED I679

SEQUELAE OF STROKE, NOT SPECIFIED AS HAEMORRHAGE OR INFARCTION I694

SEQUELAE OF OTHER AND UNSPECIFIED CEREBROVASCULAR DISEASES I698

## **Respiratory system**

### **Respiratory infection**

ACUTE UPPER RESPIRATORY INFECTION, UNSPECIFIED J069

INFLUENZA WITH PNEUMONIA, OTHER INFLUENZA VIRUS IDENTIFIED J100

INFLUENZA WITH OTHER RESP MANIFESTATIONS, OTHER INFLUENZA VIRUS IDENTIFIED J101

*Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage*

|    |   |      |
|----|---|------|
| 1  |   |      |
| 2  | PNEUMONIA DUE TO STREPTOCOCCUS PNEUMONIAE                             | J13  |
| 3  | BRONCHOPNEUMONIA, UNSPECIFIED   | J180 |
| 4  | LOBAR PNEUMONIA, UNSPECIFIED  | J181 |
| 5  | HYPOSTATIC PNEUMONIA, UNSPECIFIED                                     | J182 |
| 6  | PNEUMONIA, UNSPECIFIED  | J189 |
| 7  | UNSPECIFIED ACUTE LOWER RESPIRATORY INFECTION                         | J22  |
| 8  | CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH ACUTE LOWER RESP INFECTION | J440 |
| 9  |   |      |
| 10 |   |      |
| 11 | <b>Aspiration/reflux/choking</b>                                      |      |
| 12 | PNEUMONITIS DUE TO FOOD AND VOMIT                                     | J690 |
| 13 | GASTRO-OESOPHAGEAL REFLUX DISEASE WITHOUT OESOPHAGITIS                | K219 |
| 14 | INHALATION AND INGESTION OF FOOD CAUSING OBSTRUCTION OF RESPIRATORY   | W79  |
| 15 | TRACT   |      |
| 16 |   |      |
| 17 | FOREIGN BODY IN RESPIRATORY TRACT, PART UNSPECIFIED                   | T179 |
| 18 | INHALATION/INGESTION OF OTHER OBJECTS CAUSING OBSTRUCT OF RESP TRACT  | W80  |
| 19 |   |      |
| 20 | <b>Other respiratory disorders</b>                                    |      |
| 21 | UNSPECIFIED CHRONIC BRONCHITIS  | J42  |
| 22 | EMPHYSEMA, UNSPECIFIED  | J439 |
| 23 | CHRONIC OBSTRUCTIVE PULMONARY DISEASE, UNSPECIFIED                    | J440 |
| 24 | ASTHMA, UNSPECIFIED   | J459 |
| 25 | BRONCHIECTASIS  | J47  |
| 26 | OTHER INTERSTITIAL PULMONARY DISEASES WITH FIBROSIS                   | J841 |
| 27 | PLEURAL EFFUSION, NOT ELSEWHERE CLASSIFIED                            | J90  |
| 28 | CHRONIC RESPIRATORY FAILURE   | J961 |
| 29 | RESPIRATORY FAILURE, UNSPECIFIED                                      | J969 |
| 30 | OTHER SPECIFIED RESPIRATORY DISORDERS                                 | J988 |
| 31 | DYSPNOEA  | R060 |
| 32 | RESPIRATORY ARREST  | R092 |
| 33 | ASPHYXIATION  | T71  |
| 34 | UNSPECIFIED THREAT TO BREATHING                                       | W84  |
| 35 |   |      |
| 36 |   |      |
| 37 |   |      |
| 38 |   |      |
| 39 | <b>Digestive system</b>   |      |
| 40 | <b>Ulcer/gastrointestinal perforation</b>                             |      |
| 41 | OESOPHAGITIS  | K20  |
| 42 | PERFORATION OF INTESTINE (NONTRAUMATIC)                               | K631 |
| 43 | PERITONITIS, UNSPECIFIED  | K659 |
| 44 | GASTRIC ULCER, CHRONIC OR UNSPECIFIED WITH PERFORATION                | K255 |
| 45 | OTHER PERITONITIS   | K658 |
| 46 | ACUTE PERITONITIS   | K650 |
| 47 | GASTROINTESTINAL HAEMORRHAGE, UNSPECIFIED                             | K922 |
| 48 | ULCER OF INTESTINE  | K633 |
| 49 |   |      |
| 50 | <b>Other gastrointestinal disorders</b>                               |      |
| 51 | BARRETTS OESOPHAGUS   | K227 |
| 52 | DIAPHRAGMATIC HERNIA WITHOUT OBSTRUCTION OR GANGRENE                  | K449 |
| 53 | OTHER SPECIFIED NONINFECTIVE GASTROENTERITIS AND COLITIS              | K528 |
| 54 | ACUTE VASCULAR DISORDERS OF INTESTINE                                 | K550 |
| 55 | VASCULAR DISORDER OF INTESTINE, UNSPECIFIED                           | K559 |
| 56 | VOLVULUS  | K562 |
| 57 | OTHER AND UNSPECIFIED INTESTINAL OBSTRUCTION                          | K566 |
| 58 | CONSTIPATION  | K590 |
| 59 |   |      |
| 60 |   |      |

*Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage*

|    |  |      |
|----|--|------|
| 1  |  |      |
| 2  | MEGACOLON, NOT ELSEWHERE CLASSIFIED              | K593 |
| 3  | ACUTE AND SUBACUTE HEPATIC FAILURE               | K720 |
| 4  | OTHER AND UNSPECIFIED CIRRHOSIS OF LIVER         | K746 |
| 5  | AUTOIMMUNE HEPATITIS                             | K754 |
| 6  | INFLAMMATORY LIVER DISEASE, UNSPECIFIED          | K759 |
| 7  | OTHER SPECIFIED DISEASES OF LIVER                | K768 |
| 8  |  |      |
| 9  | CALCULUS OF GALLBLADDER WITH OTHER CHOLECYSTITIS | K801 |
| 10 | CHOLANGITIS                                      | K830 |
| 11 | ACUTE PANCREATITIS, UNSPECIFIED                  | K859 |
| 12 | PSEUDOCYST OF PANCREAS                           | K863 |
| 13 | INTESTINAL MALABSORPTION, UNSPECIFIED            | K909 |
| 14 | DYSPHAGIA  | R13  |
| 15 |  |      |
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## **Genitourinary system**

### **Renal failure**

|    |   |      |
|----|---|------|
| 20 |   |      |
| 21 | CHRONIC NEPHRITIC SYNDROME, UNSPECIFIED | N039 |
| 22 | OTHER ACUTE RENAL FAILURE               | N178 |
| 23 | ACUTE RENAL FAILURE, UNSPECIFIED        | N179 |
| 24 | END-STAGE RENAL DISEASE                 | N180 |
| 25 | CHRONIC KIDNEY DISEASE, STAGE 5         | N185 |
| 26 | CHRONIC KIDNEY DISEASE, UNSPECIFIED     | N189 |
| 27 | UNSPECIFIED KIDNEY FAILURE              | N19  |
| 28 |   |      |
| 29 |   |      |
| 30 |   |      |

### **Chromosomal abnormalities**

#### **Down syndrome**

|    |                              |      |
|----|------------------------------|------|
| 31 |                              |      |
| 32 |                              |      |
| 33 | DOWN'S SYNDROME, UNSPECIFIED | Q909 |
| 34 |                              |      |

#### **Other congenital condition**

|    |   |      |
|----|---|------|
| 35 |   |      |
| 36 | CONGENITAL HYDROCEPHALUS, UNSPECIFIED                                     | Q039 |
| 37 | SPINA BIFIDA, UNSPECIFIED   | Q059 |
| 38 | CONGENITAL MALFORMATION OF HEART, UNSPECIFIED                             | Q249 |
| 39 | CONGENITAL DEFORMITY OF SPINE   | Q675 |
| 40 | CONGEN MALFORMATION SYNDROMES PREDOMINANTLY ASSOCIATED WITH SHORT STATURE | Q871 |
| 41 | MARFAN'S SYNDROME   | Q874 |
| 42 | OTHER SPECIFIED CONGEN MALFORMATION SYNDROMES, NOT ELSEWHERE CLASSIFIED   | Q878 |
| 43 | CONGENITAL MALFORMATION, UNSPECIFIED                                      | Q899 |
| 44 | KLINEFELTER'S SYNDROME, UNSPECIFIED                                       | Q984 |
| 45 | FRAGILE X CHROMOSOME  | Q992 |
| 46 | OTHER LACK OF EXPECTED NORMAL PHYSIOLOGICAL DEVELOPMENT                   | R628 |
| 47 |   |      |
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### **Other conditions occurring with small frequency**

#### **Other condition**

|    |                                   |      |
|----|-----------------------------------|------|
| 51 |                                   |      |
| 52 |                                   |      |
| 53 | DECUBITUS ULCER AND PRESSURE AREA | L89  |
| 54 | SCOLIOSIS, UNSPECIFIED            | M419 |
| 55 | URETHRAL STRICTURE, UNSPECIFIED   | N359 |
| 56 | EPISTAXIS                         | R040 |
| 57 | IMMOBILITY                        | R263 |
| 58 | MALAISE AND FATIGUE               | R53  |
| 59 | GENERALIZED ENLARGED LYMPH NODES  | R591 |
| 60 |                                   |      |

*Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage*

|    |   |      |
|----|---|------|
| 1  |   |      |
| 2  | INSUFFICIENT INTAKE OF FOOD AND WATER DUE TO SELF NEGLECT | R636 |
| 3  | OTHER SPECIFIED GENERAL SYMPTOMS AND SIGNS                | R688 |
| 4  | OTHER ILL-DEFINED AND UNSPECIFIED CAUSES OF MORTALITY     | R99  |
| 5  | EXPOSURE TO UNSPECIFIED FACTOR                            | X59  |
| 6  | MULTI-SYSTEM DEGENERATION                                 | G903 |
| 7  | BENIGN NEOPLASM, MENINGES, UNSPECIFIED                    | D329 |
| 8  | AGRANULOCYTOSIS   | D70  |
| 9  | SARCOIDOSIS OF OTHER AND COMBINED SITES                   | D868 |
| 10 | SARCOIDOSIS, UNSPECIFIED                                  | D869 |
| 11 | HYPOPITUITARISM   | E230 |
| 12 | HYPOTHYROIDISM, UNSPECIFIED                               | E039 |
| 13 | OTHER THYROTOXICOSIS                                      | E058 |
| 14 | VOLUME DEPLETION  | E86  |
| 15 |   |      |
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## **Injuries and external causes**

### **Injuries and accidents**

|    |  |      |
|----|--|------|
| 21 | INTRACRANIAL INJURY, UNSPECIFIED       | S069 |
| 22 | UNSPECIFIED INJURY OF HEAD             | S099 |
| 23 | INJURY OF COLON                        | S365 |
| 24 | FRACTURE OF NECK OF FEMUR              | S720 |
| 25 | FRACTURE OF SHAFT OF TIBIA             | S822 |
| 26 | UNSPECIFIED MULTIPLE INJURIES          | T07  |
| 27 | FAT EMBOLISM (TRAUMATIC)               | T791 |
| 28 | SEQUELAE OF UNSPECIFIED INJURY OF HEAD | T909 |
| 29 | UNSPECIFIED FALL                       | W19  |
| 30 | SEQUELAE OF OTHER ACCIDENTS            | Y86  |
| 31 |  |      |
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### **Medical/surgical complication**

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|----|---|------|
| 35 | POISONING BY OTHER ANTIDYSRHYTHMIC DRUGS, NOT ELSEWHERE CLASSIFIED        | T462 |
| 36 | ADVERSE EFFECTS OF OTHER ANTIDYSRHYTHMIC DRUGS, NOT ELSEWHERE CLASSIFIED  | Y522 |
| 37 | ABN REACT TO/LATER COMPLIC OF OP WITH IMPLANT OF ARTIFICIAL INTERN DEVICE | Y831 |
| 38 | ABN REACT TO/LATER COMPLIC OF OP WITH ANASTOMOSIS, BYPASS OR GRAFT        | Y832 |
| 39 | ABN REACT TO/LATER COMPLIC OF OP WITH FORMATION OF EXTERNAL STOMA         | Y833 |
| 40 | ABNORMAL REACTION TO OR LATER COMPLICATION OF OTHER MEDICAL PROCEDURES    | Y848 |
| 41 | SEQ OF PROCED CAUSING ABN REACT/COMPLIC,W/O MENTION OF MISADV AT THE TIME | Y883 |
| 42 | OTHER POSTPROCEDURAL RESPIRATORY DISORDERS                                | J958 |
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*Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage*

### Supplementary table 3. Predictors of the outcome time to death from univariate analyses

| Variable                         |                     | N with event/<br>N in group | Hazard ratio<br>(95% CI) | Individual p-value | Overall p-value |
|----------------------------------|---------------------|-----------------------------|--------------------------|--------------------|-----------------|
| <b>Demographics</b>              |                     |                             |                          |                    |                 |
| Age at time of health assessment |                     | 294/961                     | 1.05 (1.04, 1.06)        | <0.0001            |                 |
| Sex                              | Male                | 154/525                     | 0.88 (0.70, 1.11)        | 0.2730             |                 |
|                                  | Female              | 140/436                     | 1.00 (-)                 |                    |                 |
| Ability level                    | Mild ID             | 92/382                      | 1.00 (-)                 |                    | 0.0007          |
|                                  | Moderate ID         | 73/236                      | 1.38 (1.01, 1.87)        | 0.0411             |                 |
|                                  | Severe ID           | 67/180                      | 1.75 (1.28, 2.40)        | 0.0005             |                 |
|                                  | Profound ID         | 62/163                      | 1.77 (1.28, 2.45)        | 0.0005             |                 |
| Type of accommodation            | Family carer        | 70/374                      | 1.00 (-)                 |                    | <0.0001         |
|                                  | Independent of care | 36/93                       | 2.35 (1.57, 3.52)        | <0.0001            |                 |
|                                  | Paid support        | 161/435                     | 2.18 (1.65, 2.88)        | <0.0001            |                 |
|                                  | Congregate          | 27/59                       | 2.87 (1.84, 4.48)        | <0.0001            |                 |
| Neighbourhood deprivation        | 1 - most affluent   | 18/73                       | 1.00 (-)                 |                    | 0.1890          |
|                                  | 2                   | 56/137                      | 1.92 (1.13, 3.27)        | 0.0158             |                 |
|                                  | 3                   | 10/45                       | 0.90 (0.42, 1.95)        | 0.7896             |                 |
|                                  | 4                   | 10/40                       | 1.06 (0.49, 2.30)        | 0.8808             |                 |
|                                  | 5                   | 12/32                       | 1.71 (0.82, 3.55)        | 0.1527             |                 |
|                                  | 6                   | 9/32                        | 1.27 (0.57, 2.82)        | 0.5640             |                 |
|                                  | 7                   | 9/34                        | 1.09 (0.49, 2.43)        | 0.8302             |                 |
|                                  | 8                   | 15/58                       | 1.21 (0.61, 2.41)        | 0.5818             |                 |
|                                  | 9                   | 35/124                      | 1.22 (0.69, 2.16)        | 0.4882             |                 |
|                                  | 10 - most deprived  | 120/386                     | 1.41 (0.86, 2.31)        | 0.1782             |                 |
| Civil status                     | Single              | 288/938                     | 1.28 (0.57, 2.87)        | 0.5485             |                 |
|                                  | Not single          | 6/23                        | 1.00 (-)                 |                    |                 |
| Employment/day activities        | Yes                 | 83/231                      | 1.33 (1.03, 1.71)        | 0.0284             |                 |
|                                  | No                  | 211/730                     | 1.00 (-)                 |                    |                 |
| Smoker                           | Yes                 | 46/101                      | 1.70 (1.24, 2.33)        | 0.0009             |                 |
|                                  | No                  | 248/860                     | 1.00 (-)                 |                    |                 |
| <b>Health</b>                    |                     |                             |                          |                    |                 |
| Down syndrome                    | Yes                 | 64/179                      | 1.30 (0.98, 1.71)        | 0.0673             |                 |
|                                  | No                  | 230/782                     | 1.00 (-)                 |                    |                 |
| Epilepsy                         | Yes                 | 111/325                     | 1.25 (0.99, 1.58)        | 0.0636             |                 |
|                                  | No                  | 183/636                     | 1.00 (-)                 |                    |                 |
| Spastic quadriplegia             | Yes                 | 24/325                      | 1.67 (1.10, 2.54)        | 0.0158             |                 |
|                                  | No                  | 183/636                     | 1.00 (-)                 |                    |                 |
| Impaired mobility                | Yes                 | 195/735                     | 0.51 (0.40, 0.65)        | <0.0001            |                 |
|                                  | No                  | 99/226                      | 1.00 (-)                 |                    |                 |
| Body mass index                  | Underweight         | 9/43                        | 0.63 (0.32, 1.25)        | 0.1847             | 0.1865          |
|                                  | Acceptable          | 83/265                      | 1.00 (-)                 |                    |                 |
|                                  | Overweight          | 75/289                      | 0.78 (0.57, 1.06)        | 0.1132             |                 |
|                                  | Obese               | 81/237                      | 1.08 (0.80, 1.47)        | 0.6152             |                 |
|                                  | Morbidly obese      | 16/58                       | 0.87 (0.51, 1.48)        | 0.6058             |                 |
| Hearing impairment               | Yes                 | 112/267                     | 1.79 (1.41, 2.26)        | <0.0001            |                 |
|                                  | No                  | 182/694                     | 1.00 (-)                 |                    |                 |
| Visual impairment                | Yes                 | 154/449                     | 1.29 (1.02, 1.62)        | 0.0317             |                 |
|                                  | No                  | 140/512                     | 1.00 (-)                 |                    |                 |

*Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage*

|  |     |          |                    |         |  |
|--|-----|----------|--------------------|---------|--|
| Urinary incontinence                             | Yes | 158/632  | 0.52 (0.41, 0.65)  | <0.0001 |  |
|  | No  | 136/329  | 1.00 (-)           |         |  |
| Bowel incontinence                               | Yes | 197/733  | 0.55 (0.43, 0.70)  | <0.0001 |  |
|  | No  | 97/228   | 1.00 (-)           |         |  |
| Diabetes   | Yes | 29/47    | 2.72 (1.86, 4.00)  | <0.0001 |  |
|  | No  | 265/914  | 1.00 (-)           |         |  |
| PEG/tube fed                                     | Yes | N/7      | 4.99 (2.22, 11.20) | 0.0001  |  |
|  | No  | 288/954  |                    |         |  |
| Constipation                                     | Yes | 112/316  | 1.34 (1.06, 1.70)  | 0.0145  |  |
|  | No  | 182/645  | 1.00 (-)           |         |  |
| Ataxia/gait disorder                             | Yes | 104/276  | 1.50 (1.18, 1.90)  | 0.0009  |  |
|  | No  | 190/685  | 1.00 (-)           |         |  |
| Nail disorder                                    | Yes | 74/223   | 1.18 (0.91, 1.54)  | 0.2120  |  |
|  | No  | 220/738  | 1.00 (-)           |         |  |
| Epidermal thickening                             | Yes | 66/207   | 1.10 (0.84, 1.45)  | 0.4947  |  |
|  | No  | 228/754  | 1.00 (-)           |         |  |
| Cerebral palsy                                   | Yes | 54/175   | 1.02 (0.76, 1.37)  | 0.8792  |  |
|  | No  | 240/786  | 1.00 (-)           |         |  |
| Osteoporosis                                     | Yes | 76/174   | 1.71 (1.32, 2.22)  | <0.0001 |  |
|  | No  | 218/786  | 1.00 (-)           |         |  |
| Fungal infection                                 | Yes | 42/158   | 0.83 (0.61, 1.18)  | 0.3366  |  |
|  | No  | 252/803  | 1.00 (-)           |         |  |
| Hypertension                                     | Yes | 56/146   | 1.36 (1.01, 1.82)  | 0.0399  |  |
|  | No  | 238/815  | 1.00 (-)           |         |  |
| Dysphagia  | Yes | 51/132   | 1.51 (1.11, 2.04)  | 0.0080  |  |
|  | No  | 243/829  | 1.00 (-)           |         |  |
| Dyspnoea   | Yes | 49/130   | 1.41 (1.04, 1.92)  | 0.0285  |  |
|  | No  | 245/831  | 1.00 (-)           |         |  |
| Musculoskeletal pain                             | Yes | 48/148   | 1.14 (0.83, 1.55)  | 0.4153  |  |
|  | No  | 246/813  | 1.00 (-)           |         |  |
| Bone deformity                                   | Yes | 50/139   | 1.32 (0.97, 1.79)  | 0.0769  |  |
|  | No  | 244/822  | 1.00 (-)           |         |  |
| Dental/oral problem                              | Yes | 38/120   | 1.07 (0.76, 1.50)  | 0.7128  |  |
|  | No  | 256/841  | 1.00 (-)           |         |  |
| Eczema/dermatitis                                | Yes | 38/138   | 0.86 (0.61, 1.21)  | 0.3790  |  |
|  | No  | 256/823  | 1.00 (-)           |         |  |
| GORD   | Yes | 51/133   | 1.43 (1.06, 1.94)  | 0.0198  |  |
|  | No  | 243/828  | 1.00 (-)           |         |  |
| Lower respiratory tract infection                | Yes | 55/126   | 1.75 (1.30, 2.34)  | 0.0002  |  |
|  | No  | 239/835  | 1.00 (-)           |         |  |
| Total number of physical conditions              |     | 294/961  | 1.06 (1.04, 1.08)  | <0.0001 |  |
| Psychosis  | Yes | 11 /42   | 0.81 (0.44, 1.48)  | 0.4990  |  |
|  | No  | 283 /919 | 1.00 (-)           |         |  |
| Affective disorder including bipolar             | Yes | 24/68    | 1.19 (0.78, 1.80)  | 0.4216  |  |
|  | No  | 270/893  | 1.00 (-)           |         |  |
| Autism   | Yes | 13/69    | 0.54 (0.31, 0.94)  | 0.0306  |  |
|  | No  | 281/892  | 1.00 (-)           |         |  |
| Problem behaviour                                | Yes | 71/218   | 1.09 (0.83, 1.42)  | 0.5251  |  |
|  | No  | 223/743  | 1.00 (-)           |         |  |
| Eating disorder, including pica                  | Yes | 5/17     | 0.99 (0.41, 2.40)  | 0.9857  |  |
|  | No  | 289/944  | 1.00 (-)           |         |  |
| Any mental illness, excluding problem behaviours | Yes | 73/217   | 1.16 (0.89, 1.51)  | 0.2849  |  |
|  | No  | 221/744  | 1.00 (-)           |         |  |
| <b>Service use</b>                               |     |          |                    |         |  |
| Number of GP consultations in last 12 months     |     | 287/951  | 1.05 (1.03, 1.06)  | <0.0001 |  |

*Rates, causes, place, and predictors of mortality in adults with intellectual disabilities with and without Down syndrome: cohort study with record linkage*

|   |     |         |                   |         |  |
|---|-----|---------|-------------------|---------|--|
| Number of A&E attendances in last 12 months |     | 280/938 | 1.09 (0.99, 1.20) | 0.0847  |  |
| Number of health professions providing care |     | 294/961 | 1.10 (1.03, 1.16) | 0.0023  |  |
| <b>Prescriptions</b>                        |     |         |                   |         |  |
| Antipsychotics                              | Yes | 79/226  | 1.12 (0.94, 1.57) | 0.1421  |  |
|   | No  | 215/735 | 1.00 (-)          |         |  |
| Antidepressants                             | Yes | 39/118  | 1.16 (0.83, 1.63) | 0.3778  |  |
|   | No  | 255/843 | 1.00 (-)          |         |  |
| Anxiolytic/hypnotics                        | Yes | 20/68   | 0.95 (0.60, 1.49) | 0.8159  |  |
|   | No  | 274/893 | 1.00 (-)          |         |  |
| Antiepileptics                              | Yes | 90/253  | 1.31 (1.02, 1.68) | 0.0315  |  |
|   | No  | 204/708 | 1.00 (-)          |         |  |
| Number of drug classes taken                |     | 294/961 | 1.16 (1.12, 1.21) | <0.0001 |  |

A&E=accident and emergency; CI=confidence interval; GORD=gastro-oesophageal reflux disorder; PEG=percutaneous endoscopic gastrostomy

## STROBE Statement—checklist of items that should be included in reports of observational studies

|                              | Item No. | Recommendation   | Page No. | Relevant text from manuscript    |
|------------------------------|----------|--|----------|----------------------------------|
| <b>Title and abstract</b>    | 1        | (a) Indicate the study's design with a commonly used term in the title or the abstract   |          | p1                               |
|                              |          | (b) Provide in the abstract an informative and balanced summary of what was done and what was found  |          | p2                               |
| <b>Introduction</b>          |          |  |          |                                  |
| Background/rationale         | 2        | Explain the scientific background and rationale for the investigation being reported   |          | p4-6, supplementary table 1      |
| Objectives                   | 3        | State specific objectives, including any prespecified hypotheses   |          | 6, paragraph 3                   |
| <b>Methods</b>               |          |  |          |                                  |
| Study design                 | 4        | Present key elements of study design early in the paper  |          | p6-10, supplementary tables 2/3  |
| Setting                      | 5        | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection  |          | p7, paragraph 1, 7-8             |
| Participants                 | 6        | (a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br><i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br><i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants |          | p7, paragraph 1                  |
|                              |          | (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed<br><i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case   |          | p7, paragraph 2, p9, paragraph 4 |
| Variables                    | 7        | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable   |          | p7-8, supplementary table 2      |
| Data sources/<br>measurement | 8*       | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group   |          | p7-8, p9, paragraph 4            |
| Bias                         | 9        | Describe any efforts to address potential sources of bias  |          | p9, paragraph 4                  |
| Study size                   | 10       | Explain how the study size was arrived at  |          | P7, paragraph2, p9, paragraph 4  |

Continued on next page

|                        |     |  |  |
|------------------------|-----|--|--|
| Quantitative variables | 11  | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why   | p8-10                                  |
| Statistical methods    | 12  | (a) Describe all statistical methods, including those used to control for confounding  | p8-10                                  |
|                        |     | (b) Describe any methods used to examine subgroups and interactions  | p8-10                                  |
|                        |     | (c) Explain how missing data were addressed  | p11, paragraph 2                       |
|                        |     | (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed  | p11, paragraph 2                       |
|                        |     | <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed   |  |
|                        |     | <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy   |  |
|                        |     | (e) Describe any sensitivity analyses  | N/A                                    |
| <b>Results</b>         |     |  |  |
| Participants           | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed            | p11, paragraph 2                       |
|                        |     | (b) Give reasons for non-participation at each stage   | p11, paragraph 2                       |
|                        |     | (c) Consider use of a flow diagram   | -                                      |
| Descriptive data       | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders   | p11-12, Table 1, supplementary table 3 |
|                        |     | (b) Indicate number of participants with missing data for each variable of interest  | table 1, supplementary table 3         |
|                        |     | (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)   | p12, paragraph 1                       |
| Outcome data           | 15* | <i>Cohort study</i> —Report numbers of outcome events or summary measures over time  | p11, paragraph 2                       |
|                        |     | <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure   |  |
|                        |     | <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures   |  |
| Main results           | 16  | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | P15, table 6                           |
|                        |     | (b) Report category boundaries when continuous variables were categorized  | N/A                                    |
|                        |     | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period   | -                                      |

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|                          |    |  |                  |
|--------------------------|----|--|------------------|
| Other analyses           | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses   | p11-16           |
| <b>Discussion</b>        |    |  |                  |
| Key results              | 18 | Summarise key results with reference to study objectives   | p16, paragraph 2 |
| Limitations              | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias                 | p20, paragraph 1 |
| Interpretation           | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | p20, paragraph 2 |
| Generalisability         | 21 | Discuss the generalisability (external validity) of the study results  | p20, paragraph 1 |
| <b>Other information</b> |    |  |                  |
| Funding                  | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based              | P24              |

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).