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Prevalence of long-term health conditions in adults with autism - observational study of a whole country population

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Prevalence of long-term health conditions in adults with autism - observational study of a whole country population

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Abstract

Objectives:

To investigate the prevalence of comorbid mental health conditions and physical disabilities in a whole country population of adults aged 25+ with and without reported autism.

Design:

Secondary analysis of Scotland's Census, 2011 data. Cross-sectional study.

Setting:

General population.

Participants:

94% of Scotland's population, including 6,649/3,746,584 adults aged 25+ reported to have autism.

Main outcome measures:

Prevalence of six comorbidities: deafness or partial hearing loss, blindness or partial sight loss, intellectual disabilities, mental health conditions, physical disability, and other condition; odds ratios (OR: 95% confidence intervals) of autism predicting these comorbidities, adjusted for age and gender; and OR for age and gender in predicting comorbidities within the population with reported autism.

Results:

Comorbidities were common: deafness/hearing loss - 17.5%; blindness/sight loss - 12.1%; intellectual disabilities - 29.4%; mental health conditions - 33.0%; physical disability - 30.7%; other condition - 34.1%. Autism statistically predicted all of the conditions: OR=3.3 (3.1 to 3.6) for deafness or partial hearing loss, OR=8.5 (7.9 to 9.2) for blindness or partial sight loss, OR=94.6 (89.4 to 100.0) for intellectual disabilities, OR=8.6 (8.2 to 9.0) for mental health conditions, OR=6.2 (5.8 to 6.6) for physical disability, and OR=2.6 (2.5 to 2.8) for other condition. Contrary to findings within the general population, female gender predicted all conditions within the population with reported autism, including intellectual disabilities (OR=1.4).

Conclusions:

Clinicians need heightened awareness of comorbidities in adults with autism to improve detection and suitable care, especially given the added complexity of assessment in this population and the fact that hearing and visual impairments may cause additional difficulties with reciprocal communication which are also a feature of autism; hence posing further challenges in assessment.

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Keywords: autism, adults, prevalence, comorbidity, mental health, physical disabilities, health inequalities

Strengths and limitations of this study:

- Unique study of comorbidity in adults with reported autism in a whole country population
- High response rate of 94%, and systematic enquiry of everyone regarding autism and comorbidities (deafness, blindness, intellectual disabilities, mental health condition, physical disability, and other condition)
- Results of the study are generalisable to other adult populations in high-income countries
- Findings are limited by the broad survey reporting of comorbidities, rather than detailed examinations

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Introduction

In the last 20 years, there has been a considerable increase in awareness of autism, but research on the comorbid conditions that adults with autism experience is limited.[1] It has been suggested that some comorbidities are more common in children with autism than in the general population,[2] but little research has been conducted with adults. Given the communicative and other problems that are a prominent feature of autism, the detection and management of comorbid conditions in people with autism is more complex than for other people. Therefore, it is important to know whether or not health problems are more common than in the general population. Empirically founded information about autism comorbidity would help to raise clinicians' awareness, and in turn increase identification and appropriate management.

Mental health has been studied more than physical health in adults with autism. However, systematic reviews reveal wide variation in reported prevalence of mental ill-health between studies. This is partly because almost all studies are based on clinical populations. Therefore, findings cannot be generalised with confidence, and additionally most study samples are small in size, and very few have drawn comparisons with the general population. It has been suggested that depression,[3] bipolar disorder,[4] suicidal thoughts/behaviour,[5] non-affective psychosis,[6] and attention-deficit hyperactivity disorder[7,8] may be more common in adults with autism. A further study in North California, USA, used medical records from a single health delivery provider of inpatient and outpatient medical and mental health services to identify 1,507/1,578,658 (0.1%) adults with autism, who were age and gender matched with controls without recorded autism.[9] The study found that 19.2% of the adults with autism also had a record of intellectual disabilities, and 54% also had a record of one or more mental health conditions; with rates of individual mental conditions being 3-22 times higher for the adults with autism than their controls, and higher in the women with autism than in the men with autism.[9] The study does, however, reflect the sampling frame; only those individuals with an existing record of autism in their medical records were identified as having autism.

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Blindness/sight loss, deafness/hearing loss, and physical disabilities may be more common in adults with autism than in other people, but most of the existing literature is drawn from non-representative and/or small populations, and without general population comparisons; hence leaving significant doubts as to the actual degree of overrepresentation. One exception is the North California study of a wide range of conditions recorded in medical records which found 16 (1.1%) adults with autism to have low vision or blindness (OR=7.85), and 71 (4.7%) with hearing impairment (OR=2.35).[9] A further large study across 25 states in USA included 1,002 adults known to have autism, but was drawn from the population receiving intellectual and developmental disabilities services; hence it is clearly not representative of the population of adults with autism.[10] Indeed, only 97 participants (9.7%) did not have intellectual disabilities, so whilst 9.4% had visual impairments, 5.7% had hearing impairments, and 6.0% had physical disability, these rates cannot be generalised to the wider population with autism. In a study of 92/305 adults aged 23-50 who had been identified to have autism in childhood in the 1980s, 11 of whom were deceased, participants answered questions on medical conditions and symptoms.[11] Of the 92, 73% had intellectual disabilities, 12% had hearing impairment, and 25% visual impairment.[11] Neither of these two studies included a general population comparison group. We were unable to identify any other studies on these conditions in adults with autism.

This study aimed to investigate the prevalence and predictors of deafness or partial hearing loss, blindness or partial sight loss, intellectual disabilities, mental health conditions, physical disability, and other condition, in a whole country population of adults with reported autism aged 25+ compared with their peers without autism.

Methods

Data source

Scotland's Census, 2011, provides information on Scotland's population on the census date, 27 March 2011. Approval was gained from the Scottish Government for secondary analysis of the Census data. The Census includes the whole Scottish population, whether living in communal establishments (such as care homes and student halls of residence) or private households. Scotland's Census is one of the

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few country censuses that asks every person in the country whether or not they have autism, indeed it may be unique in this regard. One householder on behalf of all occupants in private households, and manager on behalf of all occupants in communal dwellings, was required to complete the Census information. The Census team also followed up non-responders and provided help to respond when needed. The Census form clearly states that it is a legal requirement to complete the form, and non-completion, or supplying false information attracts a £1,000 fine. The Census is conducted every 10 years. In 2011, it was estimated to have achieved a 94% response rate.[12] During the original data processing, the Census team adjusted for the 6% of the total population of Scotland for whom there was not completed Census data. This used a Census Coverage Survey (including around 40,000 households) to estimate numbers and characteristics. The Coverage Survey and Census records were matched using automated and clerical matching. All Census individuals, including individuals reporting long-term health conditions, were deterministically matched to check if any records were duplicated. Individuals estimated to have been missed from the Census were then imputed, using a subset of characteristics from real individuals, including information on their health, to reach the 100% dataset completeness rate. The process of development of the Scotland's Census 2011 Edit and Imputation Methodology was adapted from the Office for National Statistics rigorous and systematic guidelines, which are available here:

http://webarchive.nationalarchives.gov.uk/20160108193745/http://www.ons.gov.uk/ons/guide-method/method-quality/survey-methodology-bulletin/smb-69/index.html

Further details on how the Census population estimates were arrived at are also available here:

http://www.scotlandscensus.gov.uk/documents/censusresults/release1b/rel1bmethodology.pdf

Full details of the methodology and other background information on Scotland's Census 2011 are available at:

http://www.scotlandscensus.gov.uk/supporting-information.

Census variables

Self/proxy-reporting was used to identify people with autism and other long-term conditions from the Census questionnaire, Question 20: 'Do you have any of the following conditions which have lasted, or are expected to last, at least 12 months?

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Tick all that apply'. Respondents were given a choice of 10 response options: (1) deafness or partial hearing loss, (2) blindness or partial sight loss, (3) learning disability (for example, Down's syndrome), (4) learning difficulty (for example, dyslexia), (5) developmental disorder (for example, autistic spectrum disorder or Asperger's syndrome), (6) physical disability, (7) mental health condition, (8) long-term illness, disease or condition (9) other condition, (10) no condition. Following internal requirements for all Scotland's Census 2011 outputs stipulated by the National Records of Scotland, options 8 (long-term illness, disease or condition) and 9 (other condition) were merged and coded as one category of 'other condition'; thus, this term is used henceforth when referring to both these categories.

Importantly, whilst Question 20: 'Do you have any of the following conditions which have lasted, or are expected to last, at least 12 months?', included the broad term developmental disorder, it only provided reference to 'autistic spectrum disorder' and 'Asperger´s syndrome'. For the purpose of this study we, therefore, interpreted responses to this question as relating to people who know they have these conditions, henceforth referred to as autism. Additionally, the question distinguished autism from learning disability (which in the UK is synonymous to the international term 'intellectual disabilities'), learning difficulty (which in the UK is synonymous to the international term 'specific learning disability' such as dyslexia), and mental health conditions, which are important distinctions.

As part of the methodological preparations for Scotland's Census, 2011, the General Register Office for Scotland commissioned Ipsos MORI Scotland to undertake cognitive question testing of the question 20 long term health conditions and disabilities. The aim was primarily to test whether the questions were answered accurately and willingly by respondents, and what changes might be required to improve data quality and/or the acceptability of the response options. Cognitive interviewing is a widely used approach to critically evaluate survey questionnaires.[13] It enables researchers to modify survey material to enhance clarity. Retrospective probing was deemed to be the most appropriate of the different techniques for the Census. The questions were tested with 102 participants with a mix of gender and age, both with and without the health conditions and disabilities (including people with more than one of the conditions), to ensure accurate and willing completion, and

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included people with autism, intellectual disabilities, dyslexia, dyspraxia, speech impairment, mental health conditions (both milder and more serious), and other long-term conditions. This resulted in a redesign of the question on autism, to 'Developmental disorder, for example autism spectrum disorder or Asperger's syndrome' in order to accurately capture specifically the data on autism. The questions on the other conditions tested (some of which, from a medical perspective, can be considered as developmental disorders) did not require any modification. Further information can be found at:

http://www.scotlandscensus.gov.uk/documents/research/2011-census-health-disability-questions.pdf

http://www.scotlandscensus.gov.uk/documents/legislation/changes-to-gov-statement-report.pdf

Data Analysis

We calculated the numbers and percentages of people with and without reported autism reporting deafness or partial hearing loss, blindness or partial sight loss, intellectual disabilities, mental health conditions, physical disability, and other condition. We compared differences between the populations with and without reported autism using chi-square tests. Within the whole population, we then used six binary logistic regressions to calculate odds ratios (OR: 95% confidence intervals) of autism predicting having each of the six types of additional health conditions, adjusted for age group and gender. We then calculated the ORs for age group and gender in predicting each of the six comorbidities within the population with reported autism. All analyses were conducted with SPSS software version 22.

Patient and Public Involvement

The question on autism was included in Scotland's Census, 2011 at the behest of third sector organisations for people with autism. This study was undertaken by the Scottish Learning Disabilities Observatory, which has a specific remit for people with autism; its steering group includes partners from the third sector organisations. Results from this study will be disseminated for people with autism in easy-read version via the Scottish Learning Disabilities Observatory website and newsletters.

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Results

Participant characteristics

Scotland's Census 2011 included records on 5,295,403 people. There were 6,649/3,746,584 (0.2%) adults aged 25+ recorded to have autism as defined here, 4,610 (69.3%) of whom were men and 2,039 (30.7%) women compared with 1,776,845 (47.5%) men and 1,963,090 (52.5%) women in the adult population without autism (Table 1).

- Insert Table 1 here -

Prevalence of reported comorbidities

The adult population with reported autism was significantly more likely to have each of the additional health conditions when compared to the population without reported autism, with each at the p<0.001 level (Table 2).

- Insert Table 2 here -

Table 3 shows the OR (95% Confidence intervals) of autism predicting each of the six conditions: OR=3.3 (3.1-3.6) for deafness or partial hearing loss, OR=8.5 (7.9-9.2) for blindness or partial sight loss, OR=94.6 (89.4-100.0) for intellectual disabilities, OR=8.6 (8.2-9.0) for mental health conditions, OR=6.2 (5.8-6.6) for physical disability, and OR=2.6 (2.5-2.8) for other condition. Table 4 shows the OR (95% Confidence interval) of age and gender in predicting comorbidities within the population with autism aged 25+. As one would expect, in the whole population, older age group statistically predicted blindness, deafness, physical disability and other condition, whilst age over 55 reduced the likelihood of intellectual disabilities (presumably due to early death), as did the 65+ age group for mental health conditions. Female gender predicted blindness, mental health conditions, physical disability and other condition, whilst male gender predicted deafness and intellectual disabilities. Within the population with reported autism, older age group also statistically predicted blindness, deafness, physical disability and other condition, but

not intellectual disabilities and mental health conditions. Contrary to findings in the general population, female gender predicted all conditions within the population with reported autism.

- Insert Tables 3 and 4 here –

Discussion

Principal findings and comparison with existing literature

Comorbidity is substantially greater in adults with reported autism than in other people; with odds ratios of 95 for intellectual disabilities, 9 for mental health conditions, 9 for deafness or partial hearing loss, 6 for physical disability, 3 for blindness or partial sight loss, and 3 for other condition. All these conditions were common in adults with reported autism. These findings are important given the gap in evidence, as clinicians need to have heightened awareness of potential comorbidities in order to provide suitable investigation and management to maximise functioning and therefore improve quality of life. Findings on hearing and visual impairments for people with reported autism are perhaps particularly important, given the impact of these impairments on reciprocal communication, which is also an integral underlying impairment in autism. Clinical assessments of people with autism are more complex and take longer than for the average person. Nevertheless, our findings have demonstrated that investment in such assessments is necessary and important given the much higher prevalence of comorbidities.

We found mental health conditions in 33% of all adults with reported autism (range 23-37% depending on age group; 27%-37% for men and 30%-40% for women). This high rate is lower than a previous report of 54%[9], but their sample may have been biased to a more severely affected/complex population given their sampling, as shown by their lower identification rate for autism. We found 14% with hearing impairment (range 7%-46% depending on age group; 5%-44% for men and 11%-47% for women), and 12% with visual impairments (range 7%-30% depending on age group; 7%-27% for men and 10%-35% for women), notably higher than the rates recorded in medical records reported in the North California study (4.7% and 1.1%

respectively, though ORs were not dissimilar)[9] likely reflecting the different study methodologies. In the study of 92 adults with autism, 12% had hearing impairment, and 25% visual impairment,[11] respectively, though the study was much smaller and of limited age range than in our study. A high rate of intellectual disabilities in children with autism has been described previously; we have now quantified the extent of this - 29% (25%-32% depending on age group; 22%-35% for men and 31%-42% for women) - in a much larger study of adults. There are few other studies with which we can draw comparisons, and we identified none on physical disability in adults with autism with which we could compare the high rate of 24% for all adults aged 25+ (range 15%-45% depending on age group; 14%-42% for men and 24%-45% for women).

A view has been expressed that autism is currently underdiagnosed in more intellectually-able females compared with males.[14] We found that 34% of women compared with only 27% of men with autism reported accompanying intellectual disabilities, so the female population with autism was intellectually less able than the male population with autism. Our findings may therefore provide some evidence to support the view of under-diagnosis of autism in the more intellectually-able women. Alternatively, women and men with autism may actually be intellectually different.

We have previously reported Census findings on comorbidities for people with intellectual disabilites.[15] Many conditions are related to intellectual level, with there being a gradient across the whole spread of intelligence (not just intellectual disabilities).[16] Given the lower average intelligence we found in the autistic women than the autistic men, one might expect more comorbidities to be found in the women than the men. Indeed, the women with autism had higher rates of all six comorbidities than did the men with autism; odds ratio of female gender predicting each of the six comorbidities was greater for all conditions (except mental health) in the population with autism compared with the whole population, and indeed reversed for deafness and intellectual disabilities which were more common in men in the whole population. Alternatively, these findings could support the view that in some cases it is the concept of 'Autism Plus' (i.e. autism co-occurring with any other major neurodevelopmental disorder),[17] which ultimately results in people receiving a diagnosis of autism. Whilst this Plus element of co-occurring conditions is currently

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often neglected in assessment, diagnosis and intervention, in some populations, possibly including women, it may be the initial or primary reason for considering a diagnosis of autism.

Strengths and limitations

We believe this study to be unique in including the whole population of a country, with a high response rate, and systematic enquiry of everyone regarding autism and selected long-term conditions. The results of this study are generalisable to other adult populations in high-income countries. The concept of autistic spectrum disorder has broadened in recent years; hence our findings relate to the narrower definition that was used to diagnose autism in the past, as the study is one of adults who most likely were originally diagnosed in childhood. This accounts for the 0.2% identified prevalence; more recent studies conducting autism assessments have reported higher prevalence.[18] Limitations may include the use of the term developmental disorders in the Census, although the clarification of this term provided on the Census form included only autistic spectrum disorder and Asperger's syndrome, and the phrasing of the question was carefully selected specifically to capture autism, from results of the cognitive question testing procedure. Furthermore, this category was distinguished from intellectual disabilities, specific learning disability, and mental health conditions, and tested with people with all these conditions. Hence, we consider that respondents will have replied accordingly, i.e. responded regarding autism. However, we have no further means to check this on the whole population. Respondents reported whether or not each person was known to have autism rather than each person having an assessment for autism, so some reporting error is possible. The Census form was also broad-brush in its questioning rather than including detailed sub-questions on each of the six categories of health conditions. Finally, whilst we describe the imputation process, we cannot state with certainty whether or not the imputed 6% of records contained the same, more or fewer proportion of adults with autism, but note that this missing 6% is a small proportion overall. Despite this, we believe the results of this study are generalisable to other high-income countries, as well as filling a significant gap in existing research on the prevalence of long-term health conditions in adults with autism.

Implications for clinicians

This study advances our knowledge of comorbidities in adults with autism, which is otherwise somewhat invisible in previous studies. Adults with reported autism have very high rates of comorbid physical disabilities as well as mental health conditions. Hearing and visual impairments are also very common, and their impact on reciprocal communication, especially if undiagnosed/unattended, may compound core features of autism. Clinicians require a heightened awareness of this, especially given the greater complexity of health assessments in adults with autism compared with other people. It is essential to have accurate information on the prevalence of comorbid conditions in adults with autism in order to accurately plan for service provision and to tackle health inequalities. Our study is large scale and robust in design, but requires replication given the relative lack of previous study on this topic.

Word count: 3,153

Competing interests:

All authors have completed the Unified Competing Interest form (available on request from the corresponding author) at www.icmje.org/coi_disclosure.pdf and declare: all authors had financial support from the Scottish Government for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Patient consent:

Not applicable

Ethical approval:

Permission to access data was granted by the Scottish Government.

Provenance and peer review:

Not commissioned; externally peer reviewed.

Data sharing statement:

Data available at:

http://www.scotlandscensus.gov.uk/ods-web/data-warehouse.html#additionaltab

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Table 1. Number and proportion of adults with autism by age and gender

Age	Gender	Autism	Without autism
All adults aged 25+	Male N=1,781,455 (100%)	4,610 (0.3%)	1,776,845 (99.7%)
	Female N=1,965,129 (100%)	2,039 (0.1%)	1,963,090 (99.9%)
	All N=3,746,584 (100%)	6,649 (0.2%)	3,739,935 (99.8%)
25-34 y	Male N= 328,607 (100%)	1,753 (0.5%)	326,854 (99.5%)
	Female N= 338,720 (100%)	636 (0.2%)	338,084 (99.8%)
	All N= 632,488 (100%)	2,389 (0.4%)	664,938 (99.6%)
35-44 y	Male N= 357,670 (100%)	1,117 (0.3%)	356,553 (99.7%)
	Female N= 377,084 (100%)	471 (0.1%)	376,613 (99.9%)
	All N= 734,754 (100%)	1,588 (0.2%)	733,166 (99.8%)
45-54 y	Male N= 384,517 (100%)	890 (0.2%)	383,627 (99.8%)
	Female N= 402,239 (100%)	377 (0.1%)	401,862 (99.9%)
	All N=786,756 (100%)	1,267 (0.2%)	785,489 (99.8%)
55-64 y	Male N= 326,922 (100%)	474 (0.1%)	326,448 (99.9%)
	Female N= 340,491 (100%)	233 (0.1%)	340,258 (99.9%)
	All N=667,413 (100%)	707 (0.1%)	666,706 (99.9%)
65+ y	Male N= 383,739 (100%)	376 (0.1%)	383,363 (99.9%)
	Female N= 506,595 (100%)	322 (0.1%)	506,273 (99.9%)
	All N=890,334 (100%)	698 (0.1%)	889,636 (99.9%)

Table 2. Prevalence of comorbidities in adults with and without autism by age and gender

Age group	Condition	Autism			Without autism		
All adults aged 25+		**Men N=4,610 (100%)**	**Women N=2,039 (100%)**	**Total N=6,649 (100%)**	**Men N=1,776,845 (100%)**	**Women N=1,963,090 (100%)**	**Total N=3,739,935 (100%)**
	Deafness/partial hearing loss	583 (12.6%)	356 (17.5%)	939 (14.1%)	178,994 (10.1%)	160,495 (8.2%)	339,489 (9.1%)
	Blindness/partial sight loss	503 (10.9%)	304 (14.9%)	807 (12.1%)	52,351 (2.9%)	65,198 (3.3%)	117,549 (3.1%)
	Intellectual disabilities	1,254 (27.2%)	699 (34.3%)	1,953 (29.4%)	8,141 (0.5%)	6,859 (0.3%)	15,000 (0.4%)
	Mental health condition	1,468 (31.8%)	728 (35.7%)	2,196 (33.0%)	90,292 (5.1%)	121,584 (6.2%)	211,876 (5.7%)
	Physical disability	973 (21.1%)	626 (30.7%)	1,599 (24.0%)	150,896 (8.5%)	188,347 (9.6%)	339,243 (9.1%)
	Other condition	1,402 (30.4%)	864 (42.4%)	2,266 (34.1%)	407,090 (22.9%)	489,875 (25.0%)	896,965 (24.0%)
25-34 y		**Men N=1,753 (100%)**	**Women N=636 (100%)**	**Total N=2,389 (100%)**	**Men N=326,854 (100%)**	**Women N=338,084 (100%)**	**Total N=664,938 (100%)**
	Deafness/partial hearing loss	94 (5.4%)	68 (10.7%)	162 (6.8%)	4,341 (1.3%)	3,651 (1.1%)	7,992 (1.2%)
	Blindness/partial sight loss	118 (6.7%)	62 (9.7%)	180 (7.5%)	2,382 (0.7%)	1,698 (0.5%)	4,080 (0.6%)
	Intellectual disabilities	391 (22.3%)	211 (33.2%)	602 (25.2%)	1,634 (0.5%)	1,239 (0.4%)	2,873 (0.4%)

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		Men N=1,117 (100%)	Women N=471 (100%)	Total N=1,588 (100%)	Men N=356,553 (100%)	Women N=376,613 (100%)	Total N=733,166 (100%)
	Mental health condition	466 (26.6%)	188 (29.6%)	654 (27.4%)	13,522 (4.1%)	19,428 (5.7%)	32,950 (5.0%)
	Physical disability	253 (14.4%)	163 (25.6%)	416 (17.4%)	5,616 (1.7%)	5,200 (1.5%)	10,816 (1.6%)
	Other condition	420 (24.0%)	218 (34.3%)	638 (26.7%)	23,726 (7.3%)	31,470 (9.3%)	55,196 (8.3%)
35-44 y		Men N=1,117 (100%)	Women N=471 (100%)	Total N=1,588 (100%)	Men N=356,553 (100%)	Women N=376,613 (100%)	Total N=733,166 (100%)
	Deafness/partial hearing loss	83 (7.4%)	44 (9.3%)	127 (8.0%)	8,442 (2.4%)	7,067 (1.9%)	15,509 (2.1%)
	Blindness/partial sight loss	94 (8.4%)	46 (9.8%)	140 (8.8%)	3,664 (1.0%)	2,498 (0.7%)	6,162 (0.8%)
	Intellectual disabilities	304 (27.2%)	146 (31.0%)	450 (28.3%)	1,905 (0.5%)	1,504 (0.4%)	3,409 (0.5%)
	Mental health condition	377 (33.8%)	187 (39.7%)	564 (35.5%)	22,156 (6.2%)	27,844 (7.4%)	50,000 (6.8%)
	Physical disability	216 (19.3%)	112 (23.8%)	328 (20.7%)	12,711 (3.6%)	12,727 (3.4%)	25,438 (3.5%)
	Other condition	318 (28.5%)	190 (40.3%)	508 (32.0%)	43,670 (12.2%)	54,825 (14.6%)	98,495 (13.4%)
45-54 y		Men N=890 (100%)	Women N=377 (100%)	Total N=1,267 (100%)	Men N=383,627 (100%)	Women N=401,862 (100%)	Total N=785,489 (100%)
	Deafness/partial hearing loss	116 (13.0%)	58 (15.4%)	174 (13.7%)	19,115 (5.0%)	13,565 (3.4%)	32,680 (4.2%)
	Blindness/partial sight loss	113 (12.7%)	46 (12.2%)	159 (12.5%)	6,753 (1.8%)	4,554 (1.1%)	11,307 (1.4%)

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		Men	Women	Total	Men	Women	Total
	Intellectual disabilities	268 (30.1%)	133 (35.3%)	401 (31.6%)	2,188 (0.6%)	1,712 (0.4%)	3,900 (0.5%)
	Mental health condition	316 (35.5%)	140 (37.1%)	456 (36.0%)	23,060 (6.0%)	29,734 (7.4%)	52,794 (6.7%)
	Physical disability	195 (21.9%)	110 (29.2%)	305 (24.1%)	22,783 (5.9%)	24,340 (6.1%)	47,123 (6.0%)
	Other condition	283 (31.8%)	152 (40.3%)	435 (34.3%)	74,773 (19.5%)	86,373 (21.5%)	161,146 (20.5%)
55-64 y		**Men N=474 (100%)**	**Women N=233 (100%)**	**Total N=707 (100%)**	**Men N=326,448 (100%)**	**Women N=340,258 (100%)**	**Total N=666,706 (100%)**
	Deafness/partial hearing loss	123 (25.9%)	35 (15.0%)	158 (6.7%)	35,743 (10.9%)	21,889 (6.4%)	57,632 (3.4%)
	Blindness/partial sight loss	77 (16.2%)	39 (16.7%)	116 (6.5%)	9,193 (2.8%)	6,640 (2.0%)	15,833 (1.2%)
	Intellectual disabilities	158 (33.3%)	98 (42.1%)	256 (22.7%)	1,381 (0.4%)	1,226 (0.4%)	2,607 (0.4%)
	Mental health condition	175 (36.9%)	87 (37.3%)	262 (22.9%)	16,848 (5.2%)	18,483 (5.4%)	35,331 (5.3%)
	Physical disability	150 (31.6%)	85 (36.5%)	235 (15.1%)	36,100 (11.1%)	37,034 (10.9%)	73,134 (4.7%)
	Other condition	199 (42.0%)	114 (48.9%)	313 (24.6%)	106,897 (32.7%)	109,001 (32.0%)	215,898 (16.4%)
65+ y		**Men N=376 (100%)**	**Women N=322 (100%)**	**Total N=698 (100%)**	**Men N=383,363 (100%)**	**Women N=506,273 (100%)**	**Total N=889,636 (100%)**
	Deafness/partial hearing loss	167 (44.4%)	151 (46.9%)	318 (45.6%)	111,353 (29.0%)	114,323 (22.6%)	225,676 (25.4%)

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	Blindness/partial sight loss	101 (26.9%)	111 (34.5%)	212 (30.4%)	30,359 (7.9%)	49,808 (9.8%)	80,167 (9.0%)
	Intellectual disabilities	133 (35.4%)	111 (34.5%)	244 (35.0%)	1,033 (0.3%)	1,178 (0.2%)	2,211 (0.2%)
	Mental health condition	134 (35.6%)	126 (39.1%)	260 (37.2%)	14,706 (3.8%)	26,095 (5.2%)	40,801 (4.6%)
	Physical disability	159 (42.3%)	156 (48.4%)	315 (45.1%)	73,686 (19.2%)	109,046 (21.5%)	182,732 (20.5%)
	Other condition	182 (48.4%)	190 (59.0%)	372 (53.3%)	158,024 (41.2%)	208,206 (41.1%)	366,230 (41.2%)

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Table 3. Results of six regressions showing independent predictors of comorbid conditions in the whole adult population

Condition	Variable		Odds ratio	95% confidence interval
Deafness or partial hearing loss	Autism	No autism (reference)	-	
		Autism	3.320	3.075-3.585
	Age	25-34 (reference)	-	
		35-44	1.768	1.721-1.817
		45-54	3.550	3.464-3.638
		55-64	7.742	7.563-7.926
		65+	28.621	27.987-29.269
	Gender	Male (reference)	-	
		Female	.683	.678-.688
	Constant		.015	
Blindness or partial sight loss	Autism	No autism (reference)	-	
		Autism	8.514	7.861-9.220
	Age	25-34 (reference)	-	
		35-44	1.360	1.308-1.414
		45-54	2.335	2.254-2.419
		55-64	3.882	3.752-4.016
		65+	15.769	15.287-16.267
	Gender	Male (reference)	-	
		Female	1.018	1.006-1.030
	Constant		.006	
Intellectual disabilities	Autism	No autism (reference)	-	
		Autism	94.571	89.409-100.032
	Age	25-34 (reference)	-	
		35-44	1.101	1.050-1.154
		45-54	1.187	1.134-1.243
		55-64*	.958	.910-1.008
		65+	.631	.598-.665
	Gender	Male (reference)	-	
		Female	.812	.788-.838
	Constant		.005	
Mental health condition	Autism	No autism (reference)	-	
		Autism	8.595	8.163-9.050
	Age	25-34 (reference)	-	
		35-44	1.404	1.384-1.424
		45-54	1.383	1.364-1.403
		55-64	1.076	1.060-1.093
		65+	.913	.899-.926

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	Gender	Male (reference)	-	
		Female	1.247	1.236-1.258
	Constant		.046	
Physical disability	Autism	No autism (reference)	-	
		Autism	6.210	5.841-6.603
	Age	25-34 (reference)	-	
		35-44	2.138	2.091-2.186
		45-54	3.786	3.708-3.866
		55-64	7.311	7.164-7.460
		65+	15.288	14.994-15.587
	Gender	Male (reference)	-	
		Female	1.064	1.056-1.072
	Constant		.016	
Other condition	Autism	No autism (reference)	-	
		Autism	2.640	2.502-2.786
	Age	25-34 (reference)	-	
		35-44	1.709	1.690-1.728
		45-54	2.839	2.810-2.868
		55-64	5.269	5.217-5.323
		65+	7.671	7.597-7.745
	Gender	Male (reference)	-	
		Female	1.068	1.063-1.074
	Constant		.088	

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Table 4. Results of six regressions showing independent predictors of comorbid conditions in the adult population with autism

Condition	Variable		Odds ratio	95% confidence interval
Deafness or partial hearing loss	Age	25-34 (reference)	-	
		35-44	1.189	.934-1.514
		45-54	2.178	1.738-2.731
		55-64	3.920	3.088-4.975
		65+	11.179	8.972-13.929
	Gender	Male (reference)	-	
		Female	1.169	1.001-1.365
	Constant		.070	
Blindness or partial sight loss	Age	25-34 (reference)	-	
		35-44	1.179	.936-1.485
		45-54	1.750	1.397-2.192
		55-64	2.378	1.851-3.056
		65+	5.148	4.117-6.438
	Gender	Male (reference)	-	
		Female	1.232	1.051-1.443
	Constant		.077	
Intellectual disabilities	Age	25-34 (reference)	-	
		35-44	1.163	1.008-1.343
		45-54	1.363	1.172-1.584
		55-64	1.656	1.384-1.981
		65+	1.505	1.254-1.807
	Gender	Male (reference)	-	
		Female	1.354	1.209-1.516
	Constant		.309	
Mental health condition	Age	25-34 (reference)	-	
		35-44	1.455	1.269-1.668
		45-54	1.485	1.284-1.719
		55-64	1.548	1.297-1.849
		65+	1.531	1.280-1.832
	Gender	Male (reference)	-	
		Female	1.155	1.034-1.291
	Constant		.362	
Physical disability	Age	25-34 (reference)	-	
		35-44	1.220	1.038-1.434
		45-54	1.487	1.258-1.758
		55-64	2.312	1.913-2.795

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		65+	3.634	3.022-4.370
	Gender	Male (reference)	-	
		Female	1.504	1.333-1.697
	Constant		.187	
Other condition	Age	25-34 (reference)	-	
		35-44	1.276	1.109-1.467
		45-54	1.419	1.224-1.645
		55-64	2.134	1.792-2.542
		65+	2.901	2.433-3.459
	Gender	Male (reference)	-	
		Female	1.563	1.400-1.745
	Constant		.321	

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4-5 Section: Introduction
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 5 Section: Introduction
Methods			
Study design	4	Present key elements of study design early in the paper	Page 5-6 Section: Methods/Data source
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5-6 Section: Methods/Data source
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Page 6-8 Section: Methods/Census variables
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 6-8 Section: Methods/Census variables
Data sources/ 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	Page 6-8 Section: Methods/Census variables
Bias	9	Describe any efforts to address potential sources of bias	Page 5-8 Section: Methods
Study size	10	Explain how the study size was arrived at	Page 5-6 Section: Methods/Data

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			source
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 8 Section: Methods/Data analysis
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 8 Section: Methods/Data analysis
		(*b*) Describe any methods used to examine subgroups and interactions	Page 8 Section: Methods/Data analysis
		(*c*) Explain how missing data were addressed	Page 5-6 Section: Methods/Data source
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
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	Page 9 Section: Results/Participant characteristics
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 9 Section: Results/Participant characteristics Page 16 Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Page 5-6 Section: Methods/Data source
Outcome data	15*	Report numbers of outcome events or summary measures	N/A

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Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Pages 9-10 Section: results/Prevalence of reported comorbidities Pages 17-24 Tables 2-4
		(*b*) Report category boundaries when continuous variables were categorized	Page 8 Section: Methods/data analysis Pages 16-24 Tables 1-4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 10-11 Section: Discussion/ Principal findings and comparison with existing literature
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	Page 12 Section: Strengths and limitations
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 10-11 Section: Discussion/ Principal findings and comparison with existing literature
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 12-13 Section: Implications for clinicians
Other information			
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	Page 13 Section: Funding

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*Give information separately for exposed and unexposed groups.

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.

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BMJ Open

Prevalence of long-term health conditions in adults with autism - observational study of a whole country population

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Prevalence of long-term health conditions in adults with autism - observational study of a whole country population

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1

Abstract

Objectives:

To investigate the prevalence of comorbid mental health conditions and physical disabilities in a whole country population of adults aged 25+ with and without reported autism.

Design:

Secondary analysis of Scotland's Census, 2011 data. Cross-sectional study.

Setting:

General population.

Participants:

94% of Scotland's population, including 6,649/3,746,584 adults aged 25+ reported to have autism.

Main outcome measures:

Prevalence of six comorbidities: deafness or partial hearing loss, blindness or partial sight loss, intellectual disabilities, mental health conditions, physical disability, and other condition; odds ratios (OR: 95% confidence intervals) of autism predicting these comorbidities, adjusted for age and gender; and OR for age and gender in predicting comorbidities within the population with reported autism.

Results:

Comorbidities were common: deafness/hearing loss - 17.5%; blindness/sight loss - 12.1%; intellectual disabilities - 29.4%; mental health conditions - 33.0%; physical disability - 30.7%; other condition - 34.1%. Autism statistically predicted all of the conditions: OR=3.3 (3.1 to 3.6) for deafness or partial hearing loss, OR=8.5 (7.9 to 9.2) for blindness or partial sight loss, OR=94.6 (89.4 to 100.0) for intellectual disabilities, OR=8.6 (8.2 to 9.0) for mental health conditions, OR=6.2 (5.8 to 6.6) for physical disability, and OR=2.6 (2.5 to 2.8) for other condition. Contrary to findings within the general population, female gender predicted all conditions within the population with reported autism, including intellectual disabilities (OR=1.4).

Conclusions:

Clinicians need heightened awareness of comorbidities in adults with autism to improve detection and suitable care, especially given the added complexity of assessment in this population and the fact that hearing and visual impairments may cause additional difficulties with reciprocal communication which are also a feature of autism; hence posing further challenges in assessment.

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Strengths and limitations of this study:

- Unique study of comorbidity in adults with reported autism in a whole country population
- High response rate of 94%, and systematic enquiry of everyone regarding autism and comorbidities (deafness, blindness, intellectual disabilities, mental health condition, physical disability, and other condition)
- Results of the study are generalisable to other adult populations in high-income countries
- Findings are limited by the broad survey reporting of comorbidities, rather than detailed examinations

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Introduction

In the last 20 years, there has been a considerable increase in awareness of autism, but research on the comorbid conditions that adults with autism experience is limited.[1] It has been suggested that some comorbidities are more common in children with autism than in the general population,[2] but little research has been conducted with adults. Given the communicative and other problems that are a prominent feature of autism, the detection and management of comorbid conditions in people with autism is more complex than for other people. Therefore, it is important to know whether or not health problems are more common than in the general population. Empirically founded information about autism comorbidity would help to raise clinicians' awareness, and in turn increase identification and appropriate management.

Mental health has been studied more than physical health in adults with autism. However, systematic reviews reveal wide variation in reported prevalence of mental ill-health between studies. This is partly because almost all studies are based on clinical populations. Therefore, findings cannot be generalised with confidence, and additionally most study samples are small in size, and very few have drawn comparisons with the general population. It has been suggested that depression,[3] bipolar disorder,[4] suicidal thoughts/behaviour,[5] non-affective psychosis,[6] and attention-deficit hyperactivity disorder[7,8] may be more common in adults with autism. A further study in North California, USA, used medical records from a single health delivery provider of inpatient and outpatient medical and mental health services to identify 1,507/1,578,658 (0.1%) adults with autism, who were age and gender matched with controls without recorded autism.[9] The study found that 19.2% of the adults with autism also had a record of intellectual disabilities, and 54% also had a record of one or more mental health conditions; with rates of individual mental conditions being 3-22 times higher for the adults with autism than their controls, and higher in the women with autism than in the men with autism.[9] The study does, however, reflect the sampling frame; only those individuals with an existing record of autism in their medical records were identified as having autism.

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Blindness/sight loss, deafness/hearing loss, and physical disabilities may be more common in adults with autism than in other people, but most of the existing literature is drawn from non-representative and/or small populations, and without general population comparisons; hence leaving significant doubts as to the actual degree of overrepresentation. One exception is the North California study of a wide range of conditions recorded in medical records which found 16 (1.1%) adults with autism to have low vision or blindness (OR=7.85), and 71 (4.7%) with hearing impairment (OR=2.35).[9] A further large study across 25 states in USA included 1,002 adults known to have autism, but was drawn from the population receiving intellectual and developmental disabilities services; hence it is clearly not representative of the population of adults with autism.[10] Indeed, only 97 participants (9.7%) did not have intellectual disabilities, so whilst 9.4% had visual impairments, 5.7% had hearing impairments, and 6.0% had physical disability, these rates cannot be generalised to the wider population with autism. In a study of 92/305 adults aged 23-50 who had been identified to have autism in childhood in the 1980s, 11 of whom were deceased, participants answered questions on medical conditions and symptoms.[11] Of the 92, 73% had intellectual disabilities, 12% had hearing impairment, and 25% visual impairment.[11] Neither of these two studies included a general population comparison group. We were unable to identify any other studies on these conditions in adults with autism.

This study aimed to investigate the prevalence and predictors of deafness or partial hearing loss, blindness or partial sight loss, intellectual disabilities, mental health conditions, physical disability, and other condition, in a whole country population of adults with reported autism aged 25+ compared with their peers without autism.

Methods

Data source

Scotland's Census, 2011, provides information on Scotland's population on the census date, 27 March 2011. Approval was gained from the Scottish Government for secondary analysis of the Census data. The Census includes the whole Scottish population, whether living in communal establishments (such as care homes and student halls of residence) or private households. Scotland's Census is one of the

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few country censuses that asks every person in the country whether or not they have autism, indeed it may be unique in this regard. One householder on behalf of all occupants in private households (the household reference person), and manager on behalf of all occupants in communal dwellings, was required to complete the Census information. The Census team also followed up non-responders and provided help to respond when needed. The Census form clearly states that it is a legal requirement to complete the form, and non-completion, or supplying false information attracts a £1,000 fine. The Census is conducted every 10 years. In 2011, it was estimated to have achieved a 94% response rate.[12] During the original data processing, the Census team adjusted for the 6% of the total population of Scotland for whom there was not completed Census data. This used a Census Coverage Survey (including around 40,000 households) to estimate numbers and characteristics. The Coverage Survey and Census records were matched using automated and clerical matching. All Census individuals, including individuals reporting long-term health conditions, were deterministically matched to check if any records were duplicated. Individuals estimated to have been missed from the Census were then imputed, using a subset of characteristics from real individuals, including information on their health, to reach the 100% dataset completeness rate. The process of development of the Scotland's Census 2011 Edit and Imputation Methodology was adapted from the Office for National Statistics rigorous and systematic guidelines, which are available here: http://webarchive.nationalarchives.gov.uk/20160108193745/http://www.ons.gov.uk/ons/guide-method/method-quality/survey-methodology-bulletin/smb-69/index.html

Further details on how the Census population estimates were arrived at are also available here:

http://www.scotlandscensus.gov.uk/documents/censusresults/release1b/rel1bmethodology.pdf

Full details of the methodology and other background information on Scotland's Census 2011 are available at:

http://www.scotlandscensus.gov.uk/supporting-information.

Census variables

Self/proxy-reporting was used to identify people with autism and other long-term conditions from the Census questionnaire, Question 20: 'Do you have any of the following conditions which have lasted, or are expected to last, at least 12 months?

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Tick all that apply'. Respondents were given a choice of 10 response options: (1) deafness or partial hearing loss, (2) blindness or partial sight loss, (3) learning disability (for example, Down's syndrome), (4) learning difficulty (for example, dyslexia), (5) developmental disorder (for example, autistic spectrum disorder or Asperger's syndrome), (6) physical disability, (7) mental health condition, (8) long-term illness, disease or condition (9) other condition, (10) no condition. Following internal requirements for all Scotland's Census 2011 outputs stipulated by the National Records of Scotland, options 8 (long-term illness, disease or condition) and 9 (other condition) were merged and coded as one category of 'other condition'; thus, this term is used henceforth when referring to both these categories.

Importantly, whilst Question 20: 'Do you have any of the following conditions which have lasted, or are expected to last, at least 12 months?', included the broad term developmental disorder, it only provided reference to 'autistic spectrum disorder' and 'Asperger´s syndrome'. For the purpose of this study we, therefore, interpreted responses to this question as relating to people who know they have these conditions, henceforth referred to as autism. Additionally, the question distinguished autism from learning disability (which in the UK is synonymous to the international term 'intellectual disabilities'), learning difficulty (which in the UK is synonymous to the international term 'specific learning disability' such as dyslexia), and mental health conditions, which are important distinctions.

As part of the methodological preparations for Scotland's Census, 2011, the General Register Office for Scotland commissioned Ipsos MORI Scotland to undertake cognitive question testing of the question 20 long term health conditions and disabilities. The aim was primarily to test whether the questions were answered accurately and willingly by respondents, and what changes might be required to improve data quality and/or the acceptability of the response options. Cognitive interviewing is a widely used approach to critically evaluate survey questionnaires.[13] It enables researchers to modify survey material to enhance clarity. Retrospective probing was deemed to be the most appropriate of the different techniques for the Census. The questions were tested with 102 participants with a mix of gender and age, both with and without the health conditions and disabilities (including people with more than one of the conditions), to ensure accurate and willing completion, and

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included people with autism, intellectual disabilities, dyslexia, dyspraxia, speech impairment, mental health conditions (both milder and more serious), and other long-term conditions. This resulted in a redesign of the question on autism, to 'Developmental disorder, for example autism spectrum disorder or Asperger's syndrome' in order to accurately capture specifically the data on autism. The questions on the other conditions tested (some of which, from a medical perspective, can be considered as developmental disorders) did not require any modification. Further information can be found at:

http://www.scotlandscensus.gov.uk/documents/research/2011-census-health-disability-questions.pdf

http://www.scotlandscensus.gov.uk/documents/legislation/changes-to-gov-statement-report.pdf

Data Analysis

We calculated the numbers and percentages of people with and without reported autism reporting deafness or partial hearing loss, blindness or partial sight loss, intellectual disabilities, mental health conditions, physical disability, and other condition. We compared differences between the populations with and without reported autism using chi-square tests. Within the whole population, we then used six binary logistic regressions to calculate odds ratios (OR: 95% confidence intervals) of autism predicting having each of the six types of additional health conditions, adjusted for age group and gender. We then calculated the ORs for age group and gender in predicting each of the six comorbidities within the population with reported autism. All analyses were conducted with SPSS software version 22.

Patient and Public Involvement

The question on autism was included in Scotland's Census, 2011 at the behest of third sector organisations for people with autism. This study was undertaken by the Scottish Learning Disabilities Observatory, which has a specific remit for people with autism; its steering group includes partners from the third sector organisations. Results from this study will be disseminated for people with autism in easy-read version via the Scottish Learning Disabilities Observatory website and newsletters.

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Results

Participant characteristics

Scotland's Census 2011 included records on 5,295,403 people. There were 6,649/3,746,584 (0.2%) adults aged 25+ recorded to have autism as defined here, 4,610 (69.3%) of whom were men and 2,039 (30.7%) women compared with 1,776,845 (47.5%) men and 1,963,090 (52.5%) women in the adult population without autism (Table 1). The rate of autism was lowest in the oldest age groups (autism may be associated with reduced life expectancy).

- Insert Table 1 here -

Prevalence of reported comorbidities

The adult population with reported autism was significantly more likely to have each of the additional health conditions when compared to the population without reported autism, with each at the p<0.001 level (Table 2).

- Insert Table 2 here -

Table 3 shows the OR (95% Confidence intervals) of autism predicting each of the six conditions: OR=3.3 (3.1-3.6) for deafness or partial hearing loss, OR=8.5 (7.9-9.2) for blindness or partial sight loss, OR=94.6 (89.4-100.0) for intellectual disabilities, OR=8.6 (8.2-9.0) for mental health conditions, OR=6.2 (5.8-6.6) for physical disability, and OR=2.6 (2.5-2.8) for other condition. Table 4 shows the OR (95% Confidence interval) of age and gender in predicting comorbidities within the population with autism aged 25+. As one would expect, in the whole population, older age group statistically predicted blindness, deafness, physical disability and other condition, whilst age over 55 reduced the likelihood of intellectual disabilities (presumably due to early death), as did the 65+ age group for mental health conditions. Female gender predicted blindness, mental health conditions, physical disability and other condition, whilst male gender predicted deafness and intellectual

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disabilities. Within the population with reported autism, older age group also statistically predicted blindness, deafness, physical disability and other condition, but not intellectual disabilities and mental health conditions. Contrary to findings in the general population, female gender predicted all conditions within the population with reported autism.

-   Insert Tables 3 and 4 here –

Discussion

Principal findings and comparison with existing literature

Comorbidity is substantially greater in adults with reported autism than in other people; with odds ratios of 95 for intellectual disabilities, 9 for mental health conditions, 9 for deafness or partial hearing loss, 6 for physical disability, 3 for blindness or partial sight loss, and 3 for other condition. All these conditions were common in adults with reported autism. These findings are important given the gap in evidence, as clinicians need to have heightened awareness of potential comorbidities in order to provide suitable investigation and management to maximise functioning and therefore improve quality of life. Findings on hearing and visual impairments for people with reported autism are perhaps particularly important, given the impact of these impairments on reciprocal communication, which is also an integral underlying impairment in autism. Clinical assessments of people with autism are more complex and take longer than for the average person. Nevertheless, our findings have demonstrated that investment in such assessments is necessary and important given the much higher prevalence of comorbidities.

We found mental health conditions in 33% of all adults with reported autism (range 23-37% depending on age group; 27%-37% for men and 30%-40% for women). This high rate is lower than a previous report of 54%[9], but their sample may have been biased to a more severely affected/complex population given their sampling, as shown by their lower identification rate for autism. We found 14% with hearing impairment (range 7%-46% depending on age group; 5%-44% for men and 11%-47% for women), and 12% with visual impairments (range 7%-30% depending on

age group; 7%-27% for men and 10%-35% for women), notably higher than the rates recorded in medical records reported in the North California study (4.7% and 1.1% respectively, though ORs were not dissimilar)[9] likely reflecting the different study methodologies. In the study of 92 adults with autism, 12% had hearing impairment, and 25% visual impairment,[11] respectively, though the study was much smaller and of limited age range than in our study. A high rate of intellectual disabilities in children with autism has been described previously; we have now quantified the extent of this - 29% (25%-32% depending on age group; 22%-35% for men and 31%-42% for women) - in a much larger study of adults. There are few other studies with which we can draw comparisons, and we identified none on physical disability in adults with autism with which we could compare the high rate of 24% for all adults aged 25+ (range 15%-45% depending on age group; 14%-42% for men and 24%-45% for women).

A view has been expressed that autism is currently underdiagnosed in more intellectually-able females compared with males.[14] We found that 34% of women compared with only 27% of men with autism reported accompanying intellectual disabilities, so the female population with autism was intellectually less able than the male population with autism. Our findings may therefore provide some evidence to support the view of under-diagnosis of autism in the more intellectually-able women. Alternatively, women and men with autism may actually be intellectually different.

We have previously reported Census findings on comorbidities for people with intellectual disabilites.[15] Many conditions are related to intellectual level, with there being a gradient across the whole spread of intelligence (not just intellectual disabilities).[16] Given the lower average intelligence we found in the autistic women than the autistic men, one might expect more comorbidities to be found in the women than the men. Indeed, the women with autism had higher rates of all six comorbidities than did the men with autism; odds ratio of female gender predicting each of the six comorbidities was greater for all conditions (except mental health) in the population with autism compared with the whole population, and indeed reversed for deafness and intellectual disabilities which were more common in men in the whole population. Alternatively, these findings could support the view that in some cases it is the concept of 'Autism Plus' (i.e. autism co-occurring with any other major

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neurodevelopmental disorder),[17] which ultimately results in people receiving a diagnosis of autism. Whilst this Plus element of co-occurring conditions is currently often neglected in assessment, diagnosis and intervention, in some populations, possibly including women, it may be the initial or primary reason for considering a diagnosis of autism.

Strengths and limitations

We believe this study to be unique in including the whole population of a country, with a high response rate, and systematic enquiry of everyone regarding autism and selected long-term conditions. The results of this study are generalisable to other adult populations in high-income countries. The concept of autistic spectrum disorder has broadened in recent years; hence our findings relate to the narrower definition that was used to diagnose autism in the past, as the study is one of adults who most likely were originally diagnosed in childhood. This accounts for the 0.2% identified prevalence; more recent studies conducting autism assessments have reported higher prevalence.[18] It is important to note that undiagnosed adults with milder forms of autism may have lower levels of comorbidity than those with more severe autism. Limitations may include the use of the term developmental disorders in the Census, although the clarification of this term provided on the Census form included only autistic spectrum disorder and Asperger's syndrome, and the phrasing of the question was carefully selected specifically to capture autism, from results of the cognitive question testing procedure. Furthermore, this category was distinguished from intellectual disabilities, specific learning disability, and mental health conditions, and tested with people with all these conditions. Hence, we consider that respondents will have replied accordingly, i.e. responded regarding autism. However, we have no further means to check this on the whole population. Furthermore, respondents reported whether or not each person was known to have autism rather than each person having an assessment for autism, so some reporting error is possible. Given the large number of households, we are unable to state how each household reference person approached completing the Census form, although cognitive question testing was completed with a broad range of 70 respondents on the whole questionnaire in advance of the Census (in addition to the 102 respondents who completed cognitive question testing interviews specifically on the health questions). The Census form was also broad-brush in its questioning rather than including detailed sub-questions on each of the six categories of health

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conditions. Finally, whilst we describe the imputation process, we cannot state with certainty whether or not the imputed 6% of records contained the same, more or fewer proportion of adults with autism, but note that this missing 6% is a small proportion overall. Despite this, we believe the results of this study are generalisable to other high-income countries, as well as filling a significant gap in existing research on the prevalence of long-term health conditions in adults with autism.

Implications for clinicians

This study advances our knowledge of comorbidities in adults with autism, which is otherwise somewhat invisible in previous studies. Adults with reported autism have very high rates of comorbid physical disabilities as well as mental health conditions. Hearing and visual impairments are also very common, and their impact on reciprocal communication, especially if undiagnosed/unattended, may compound core features of autism. Clinicians require a heightened awareness of this, especially given the greater complexity of health assessments in adults with autism compared with other people. It is essential to have accurate information on the prevalence of comorbid conditions in adults with autism in order to accurately plan for service provision and to tackle health inequalities. Our study is large scale and robust in design, but requires replication given the relative lack of previous study on this topic.

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Contributors:

ER analysed the data, jointly interpreted it, and wrote the first draft of the manuscript, LAH-M, CG, and AH jointly interpreted the data, and contributed to the manuscript, CM and JR worked on the Census, jointly interpreted the data, and contributed to the manuscript, S-AC conceived the project, interpreted the data, and contributed to the manuscript. All authors approved the final version of the manuscript. S-AC is the study guarantor.

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S-AC confirms the manuscript is an honest, accurate and transparent account of the study being reported, that no important aspects of the study have been omitted, and there has been no discrepancies from the study as planned.

Competing interests:

All authors have completed the Unified Competing Interest form (available on request from the corresponding author) at www.icmje.org/coi_disclosure.pdf and declare: all authors had financial support from the Scottish Government for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Data available at:

http://www.scotlandscensus.gov.uk/ods-web/data-warehouse.html#additionaltab

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Table 1. Number and proportion of adults with autism by age and gender

Age	Gender	Autism	Without autism
All adults aged 25+	Male N=1,781,455 (100%)	4,610 (0.3%)	1,776,845 (99.7%)
	Female N=1,965,129 (100%)	2,039 (0.1%)	1,963,090 (99.9%)
	All N=3,746,584 (100%)	6,649 (0.2%)	3,739,935 (99.8%)
25-34 y	Male N= 328,607 (100%)	1,753 (0.5%)	326,854 (99.5%)
	Female N= 338,720 (100%)	636 (0.2%)	338,084 (99.8%)
	All N= 632,488 (100%)	2,389 (0.4%)	664,938 (99.6%)
35-44 y	Male N= 357,670 (100%)	1,117 (0.3%)	356,553 (99.7%)
	Female N= 377,084 (100%)	471 (0.1%)	376,613 (99.9%)
	All N= 734,754 (100%)	1,588 (0.2%)	733,166 (99.8%)
45-54 y	Male N= 384,517 (100%)	890 (0.2%)	383,627 (99.8%)
	Female N= 402,239 (100%)	377 (0.1%)	401,862 (99.9%)
	All N=786,756 (100%)	1,267 (0.2%)	785,489 (99.8%)
55-64 y	Male N= 326,922 (100%)	474 (0.1%)	326,448 (99.9%)
	Female N= 340,491 (100%)	233 (0.1%)	340,258 (99.9%)
	All N=667,413 (100%)	707 (0.1%)	666,706 (99.9%)
65+ y	Male N= 383,739 (100%)	376 (0.1%)	383,363 (99.9%)
	Female N= 506,595 (100%)	322 (0.1%)	506,273 (99.9%)
	All N=890,334 (100%)	698 (0.1%)	889,636 (99.9%)

Table 2. Prevalence of comorbidities in adults with and without autism by age and gender

Age group	Condition	Autism			Without autism		
All adults aged 25+		**Men N=4,610 (100%)**	**Women N=2,039 (100%)**	**Total N=6,649 (100%)**	**Men N=1,776,845 (100%)**	**Women N=1,963,090 (100%)**	**Total N=3,739,935 (100%)**
	Deafness/partial hearing loss	583 (12.6%)	356 (17.5%)	939 (14.1%)	178,994 (10.1%)	160,495 (8.2%)	339,489 (9.1%)
	Blindness/partial sight loss	503 (10.9%)	304 (14.9%)	807 (12.1%)	52,351 (2.9%)	65,198 (3.3%)	117,549 (3.1%)
	Intellectual disabilities	1,254 (27.2%)	699 (34.3%)	1,953 (29.4%)	8,141 (0.5%)	6,859 (0.3%)	15,000 (0.4%)
	Mental health condition	1,468 (31.8%)	728 (35.7%)	2,196 (33.0%)	90,292 (5.1%)	121,584 (6.2%)	211,876 (5.7%)
	Physical disability	973 (21.1%)	626 (30.7%)	1,599 (24.0%)	150,896 (8.5%)	188,347 (9.6%)	339,243 (9.1%)
	Other condition	1,402 (30.4%)	864 (42.4%)	2,266 (34.1%)	407,090 (22.9%)	489,875 (25.0%)	896,965 (24.0%)
25-34 y		**Men N=1,753 (100%)**	**Women N=636 (100%)**	**Total N=2,389 (100%)**	**Men N=326,854 (100%)**	**Women N=338,084 (100%)**	**Total N=664,938 (100%)**
	Deafness/partial hearing loss	94 (5.4%)	68 (10.7%)	162 (6.8%)	4,341 (1.3%)	3,651 (1.1%)	7,992 (1.2%)
	Blindness/partial sight loss	118 (6.7%)	62 (9.7%)	180 (7.5%)	2,382 (0.7%)	1,698 (0.5%)	4,080 (0.6%)
	Intellectual disabilities	391 (22.3%)	211 (33.2%)	602 (25.2%)	1,634 (0.5%)	1,239 (0.4%)	2,873 (0.4%)

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		Men	Women	Total	Men	Women	Total
	Mental health condition	466 (26.6%)	188 (29.6%)	654 (27.4%)	13,522 (4.1%)	19,428 (5.7%)	32,950 (5.0%)
	Physical disability	253 (14.4%)	163 (25.6%)	416 (17.4%)	5,616 (1.7%)	5,200 (1.5%)	10,816 (1.6%)
	Other condition	420 (24.0%)	218 (34.3%)	638 (26.7%)	23,726 (7.3%)	31,470 (9.3%)	55,196 (8.3%)
35-44 y		**Men N=1,117 (100%)**	**Women N=471 (100%)**	**Total N=1,588 (100%)**	**Men N=356,553 (100%)**	**Women N=376,613 (100%)**	**Total N=733,166 (100%)**
	Deafness/partial hearing loss	83 (7.4%)	44 (9.3%)	127 (8.0%)	8,442 (2.4%)	7,067 (1.9%)	15,509 (2.1%)
	Blindness/partial sight loss	94 (8.4%)	46 (9.8%)	140 (8.8%)	3,664 (1.0%)	2,498 (0.7%)	6,162 (0.8%)
	Intellectual disabilities	304 (27.2%)	146 (31.0%)	450 (28.3%)	1,905 (0.5%)	1,504 (0.4%)	3,409 (0.5%)
	Mental health condition	377 (33.8%)	187 (39.7%)	564 (35.5%)	22,156 (6.2%)	27,844 (7.4%)	50,000 (6.8%)
	Physical disability	216 (19.3%)	112 (23.8%)	328 (20.7%)	12,711 (3.6%)	12,727 (3.4%)	25,438 (3.5%)
	Other condition	318 (28.5%)	190 (40.3%)	508 (32.0%)	43,670 (12.2%)	54,825 (14.6%)	98,495 (13.4%)
45-54 y		**Men N=890 (100%)**	**Women N=377 (100%)**	**Total N=1,267 (100%)**	**Men N=383,627 (100%)**	**Women N=401,862 (100%)**	**Total N=785,489 (100%)**
	Deafness/partial hearing loss	116 (13.0%)	58 (15.4%)	174 (13.7%)	19,115 (5.0%)	13,565 (3.4%)	32,680 (4.2%)
	Blindness/partial sight loss	113 (12.7%)	46 (12.2%)	159 (12.5%)	6,753 (1.8%)	4,554 (1.1%)	11,307 (1.4%)

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		Men N=474 (100%)	Women N=233 (100%)	Total N=707 (100%)	Men N=326,448 (100%)	Women N=340,258 (100%)	Total N=666,706 (100%)
	Intellectual disabilities	268 (30.1%)	133 (35.3%)	401 (31.6%)	2,188 (0.6%)	1,712 (0.4%)	3,900 (0.5%)
	Mental health condition	316 (35.5%)	140 (37.1%)	456 (36.0%)	23,060 (6.0%)	29,734 (7.4%)	52,794 (6.7%)
	Physical disability	195 (21.9%)	110 (29.2%)	305 (24.1%)	22,783 (5.9%)	24,340 (6.1%)	47,123 (6.0%)
	Other condition	283 (31.8%)	152 (40.3%)	435 (34.3%)	74,773 (19.5%)	86,373 (21.5%)	161,146 (20.5%)
55-64 y		**Men N=474 (100%)**	**Women N=233 (100%)**	**Total N=707 (100%)**	**Men N=326,448 (100%)**	**Women N=340,258 (100%)**	**Total N=666,706 (100%)**
	Deafness/partial hearing loss	123 (25.9%)	35 (15.0%)	158 (6.7%)	35,743 (10.9%)	21,889 (6.4%)	57,632 (3.4%)
	Blindness/partial sight loss	77 (16.2%)	39 (16.7%)	116 (6.5%)	9,193 (2.8%)	6,640 (2.0%)	15,833 (1.2%)
	Intellectual disabilities	158 (33.3%)	98 (42.1%)	256 (22.7%)	1,381 (0.4%)	1,226 (0.4%)	2,607 (0.4%)
	Mental health condition	175 (36.9%)	87 (37.3%)	262 (22.9%)	16,848 (5.2%)	18,483 (5.4%)	35,331 (5.3%)
	Physical disability	150 (31.6%)	85 (36.5%)	235 (15.1%)	36,100 (11.1%)	37,034 (10.9%)	73,134 (4.7%)
	Other condition	199 (42.0%)	114 (48.9%)	313 (24.6%)	106,897 (32.7%)	109,001 (32.0%)	215,898 (16.4%)
65+ y		**Men N=376 (100%)**	**Women N=322 (100%)**	**Total N=698 (100%)**	**Men N=383,363 (100%)**	**Women N=506,273 (100%)**	**Total N=889,636 (100%)**
	Deafness/partial hearing loss	167 (44.4%)	151 (46.9%)	318 (45.6%)	111,353 (29.0%)	114,323 (22.6%)	225,676 (25.4%)

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	Blindness/partial sight loss	101 (26.9%)	111 (34.5%)	212 (30.4%)	30,359 (7.9%)	49,808 (9.8%)	80,167 (9.0%)
	Intellectual disabilities	133 (35.4%)	111 (34.5%)	244 (35.0%)	1,033 (0.3%)	1,178 (0.2%)	2,211 (0.2%)
	Mental health condition	134 (35.6%)	126 (39.1%)	260 (37.2%)	14,706 (3.8%)	26,095 (5.2%)	40,801 (4.6%)
	Physical disability	159 (42.3%)	156 (48.4%)	315 (45.1%)	73,686 (19.2%)	109,046 (21.5%)	182,732 (20.5%)
	Other condition	182 (48.4%)	190 (59.0%)	372 (53.3%)	158,024 (41.2%)	208,206 (41.1%)	366,230 (41.2%)

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Table 3. Results of six regressions showing independent predictors of comorbid conditions in the whole adult population

Condition	Variable		Odds ratio	95% confidence interval
Deafness or partial hearing loss	Autism	No autism (reference)	-	
		Autism	3.320	3.075-3.585
	Age	25-34 (reference)	-	
		35-44	1.768	1.721-1.817
		45-54	3.550	3.464-3.638
		55-64	7.742	7.563-7.926
		65+	28.621	27.987-29.269
	Gender	Male (reference)	-	
		Female	.683	.678-.688
	Constant		.015	
Blindness or partial sight loss	Autism	No autism (reference)	-	
		Autism	8.514	7.861-9.220
	Age	25-34 (reference)	-	
		35-44	1.360	1.308-1.414
		45-54	2.335	2.254-2.419
		55-64	3.882	3.752-4.016
		65+	15.769	15.287-16.267
	Gender	Male (reference)	-	
		Female	1.018	1.006-1.030
	Constant		.006	
Intellectual disabilities	Autism	No autism (reference)	-	
		Autism	94.571	89.409-100.032
	Age	25-34 (reference)	-	
		35-44	1.101	1.050-1.154
		45-54	1.187	1.134-1.243
		55-64*	.958	.910-1.008
		65+	.631	.598-.665
	Gender	Male (reference)	-	
		Female	.812	.788-.838
	Constant		.005	
Mental health condition	Autism	No autism (reference)	-	
		Autism	8.595	8.163-9.050
	Age	25-34 (reference)	-	
		35-44	1.404	1.384-1.424
		45-54	1.383	1.364-1.403
		55-64	1.076	1.060-1.093
		65+	.913	.899-.926

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	Gender	Male (reference)	-	
		Female	1.247	1.236-1.258
	Constant		.046	
Physical disability	Autism	No autism (reference)	-	
		Autism	6.210	5.841-6.603
	Age	25-34 (reference)	-	
		35-44	2.138	2.091-2.186
		45-54	3.786	3.708-3.866
		55-64	7.311	7.164-7.460
		65+	15.288	14.994-15.587
	Gender	Male (reference)	-	
		Female	1.064	1.056-1.072
	Constant		.016	
Other condition	Autism	No autism (reference)	-	
		Autism	2.640	2.502-2.786
	Age	25-34 (reference)	-	
		35-44	1.709	1.690-1.728
		45-54	2.839	2.810-2.868
		55-64	5.269	5.217-5.323
		65+	7.671	7.597-7.745
	Gender	Male (reference)	-	
		Female	1.068	1.063-1.074
	Constant		.088	

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Table 4. Results of six regressions showing independent predictors of comorbid conditions in the adult population with autism

Condition	Variable		Odds ratio	95% confidence interval
Deafness or partial hearing loss	Age	25-34 (reference)	-	
		35-44	1.189	.934-1.514
		45-54	2.178	1.738-2.731
		55-64	3.920	3.088-4.975
		65+	11.179	8.972-13.929
	Gender	Male (reference)	-	
		Female	1.169	1.001-1.365
	Constant		.070	
Blindness or partial sight loss	Age	25-34 (reference)	-	
		35-44	1.179	.936-1.485
		45-54	1.750	1.397-2.192
		55-64	2.378	1.851-3.056
		65+	5.148	4.117-6.438
	Gender	Male (reference)	-	
		Female	1.232	1.051-1.443
	Constant		.077	
Intellectual disabilities	Age	25-34 (reference)	-	
		35-44	1.163	1.008-1.343
		45-54	1.363	1.172-1.584
		55-64	1.656	1.384-1.981
		65+	1.505	1.254-1.807
	Gender	Male (reference)	-	
		Female	1.354	1.209-1.516
	Constant		.309	
Mental health condition	Age	25-34 (reference)	-	
		35-44	1.455	1.269-1.668
		45-54	1.485	1.284-1.719
		55-64	1.548	1.297-1.849
		65+	1.531	1.280-1.832
	Gender	Male (reference)	-	
		Female	1.155	1.034-1.291
	Constant		.362	
Physical disability	Age	25-34 (reference)	-	
		35-44	1.220	1.038-1.434
		45-54	1.487	1.258-1.758
		55-64	2.312	1.913-2.795

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		65+	3.634	3.022-4.370
	Gender	Male (reference)	-	
		Female	1.504	1.333-1.697
	Constant		.187	
Other condition	Age	25-34 (reference)	-	
		35-44	1.276	1.109-1.467
		45-54	1.419	1.224-1.645
		55-64	2.134	1.792-2.542
		65+	2.901	2.433-3.459
	Gender	Male (reference)	-	
		Female	1.563	1.400-1.745
	Constant		.321	

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4-5 Section: Introduction
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 5 Section: Introduction
Methods			
Study design	4	Present key elements of study design early in the paper	Page 5-6 Section: Methods/Data source
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5-6 Section: Methods/Data source
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Page 6-8 Section: Methods/Census variables
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 6-8 Section: Methods/Census variables
Data sources/ 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	Page 6-8 Section: Methods/Census variables
Bias	9	Describe any efforts to address potential sources of bias	Page 5-8 Section: Methods
Study size	10	Explain how the study size was arrived at	Page 5-6 Section: Methods/Data

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			source
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 8 Section: Methods/Data analysis
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 8 Section: Methods/Data analysis
		(*b*) Describe any methods used to examine subgroups and interactions	Page 8 Section: Methods/Data analysis
		(*c*) Explain how missing data were addressed	Page 5-6 Section: Methods/Data source
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
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	Page 9 Section: Results/Participant characteristics
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 9 Section: Results/Participant characteristics Page 16 Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Page 5-6 Section: Methods/Data source
Outcome data	15*	Report numbers of outcome events or summary measures	N/A

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Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Pages 9-10 Section: results/Prevalence of reported comorbidities Pages 17-24 Tables 2-4
		(*b*) Report category boundaries when continuous variables were categorized	Page 8 Section: Methods/data analysis Pages 16-24 Tables 1-4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 10-11 Section: Discussion/ Principal findings and comparison with existing literature
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	Page 12-13 Section: Strengths and limitations
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 10-11 Section: Discussion/ Principal findings and comparison with existing literature
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 13 Section: Implications for clinicians
Other information			
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	Page 13-14 Section: Funding

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*Give information separately for exposed and unexposed groups.

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.

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