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Deposited on: 26 July 2016
Epidemiology of autism in adults across age groups and ability levels

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Word count: 2988 words

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Abstract.

Background. The epidemiology of autism in adults has relied on untested projections using childhood research. Aims. To derive representative estimates of the prevalence of autism and key associations in adults of all ages and ability levels. Method. Comparable clinical diagnostic assessments of 7274 Adult Psychiatric Morbidity Survey participants combined with a population case register survey of 290 adults with intellectual disability. Results. The combined prevalence of autism in adults of all ages in England was 11/1000 (95% CI 3-19/1000). It was higher in those with moderate to profound intellectual disability (odds ratio 63.5; 95% CI 27.4-147.2). Male sex was a strong predictor of autism only in those with no or mild intellectual disability (adjusted OR=8.5; 95% CI 2.0-34.9; interaction with sex, p=0.03).

Conclusions. Few adults with autism have intellectual disability; however, autism is more prevalent in this population. Autism measures may miss cases more in women. Declaration of interest. None.

(All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author). The authors declare that that they have no conflicts of interest.)
Introduction

Globally, in 2010, there were an estimated 52 million people with autism that accounted for more than 111 DALYs per 100,000 population (1). Until recently, information on the epidemiology of autism was based on childhood studies (2;3). A complete understanding of the nature, causes and public health impact of autism should consider the interplay of genetic, epigenetic and environmental associations throughout the life course (4). There is a widespread but largely uninformed assumption (5;6) that as many as a half of all adults with autism have intellectual disability, which, if untrue, could distort planning a balanced range of services for the whole population with autism. As childhood diagnoses of autism (or of Asperger syndrome) have increased (7;8), parental fears remain undiminished concerning the future care of their offspring with little prospect of funded services when they can no longer provide support.

Two UK studies limited to adults with intellectual disability (9;10) suggest autism rates between 70/1000 and 210/1000 but lacked a validated systematic diagnostic assessment. Recently the prevalence of autism was reported as 9.8/1000 in the Adult Psychiatric Morbidity Survey, a nationally representative sample of adults capable of giving informed consent and of taking part in a survey interview, living in private households (11). That study (11) found autism was associated with reduced verbal IQ, low educational achievement, male gender and epilepsy (12). However, by excluding people without the decision-making capacity to consent or to take part in a standard survey interview, or who were living in care settings such as institutions or care homes for the intellectually disabled, adults with moderate to profound intellectual disability were unrepresented.
Given the strong association between intellectual disability and a childhood (13) and adulthood (9) diagnosis of autism, knowledge of the overall prevalence and age (11) and gender (2) (3) profile of autism in adults requires adults of all ability levels to be examined using comparable methods. This paper reports on the epidemiology of autism drawing on samples combined to reflect the full range of ability levels in the adult general population. The sample from the first general population study (11) was extended with the inclusion of representative samples of adults with intellectual disability omitted from the earlier survey. The aims were to provide an estimate of the overall prevalence of autism and to examine key associations in adults at all intellectual ability levels.

**Method**

Data from a multi-phase survey of adults in private households throughout England (*Adult Psychiatric Morbidity Survey*: APMS (11); field work 2007), and a single-phase survey of a representative group of adults with intellectual disability drawn from intellectual disability case registers in three areas of England (*The Intellectual Disability Case Register study*: IDCR (14); field work 2010) were combined.

The APMS employed a stratified two phase design based on a random probability sample of one adult per private household (15), throughout England (as already described (11)) followed by diagnostic assessments of respondents at an increased risk of autism (16).

For the IDCR, adults not considered in the APMS, by design, and living in communal care establishments and private households, were randomly sampled from three adult intellectual disability registers in England, in Leicestershire, Lambeth and Sheffield, stratified by age,
sex and type of residence (detailed in eSupplement 1). For the adults living in private households, those judged sufficiently able to have taken part in the APMS were then excluded. All adults living in communal care establishments were included, as these establishments were excluded from the APMS, yet a lot of people with intellectual disabilities live in such establishments. The sample size in APMS phase 2 was chosen to reflect the sample sizes and precision of psychosis prevalence estimates required to monitor trends in each APMS survey since the first APMS in 1993 (17). The IDCR sample was designed to achieve similar precision.

APMS participants gave informed consent directly to APMS phase one interviewers. In the IDCR, following the English Mental Capacity Act, 2005, consent was taken wherever possible with input from consultees as appropriate. In keeping with the requirements of the ethics committees, participants in Leicestershire were telephoned by the research team (‘opt-out consent procedure’); those in Lambeth and Sheffield contacted the research team only if they wished to take part in the study (‘opt-in consent procedure’).

The 20-item self completion Autism-spectrum Quotient (AQ) (15:18) was used in phase one of the APMS to select participants for a second phase evaluation using detailed clinical assessments based on Module-4 of the Autism Diagnostic Observation Schedule (ADOS-Mod4) (16). In the IDCR study, most participants were assessed at first interview with the ADOS Module-1 (19), which is designed for individuals who do not consistently use phrase speech. The ADOS-Mod4 was used for verbally fluent adults living in communal care establishments.
Threshold scores of 12+ in the ADOS-1 and 10+ in the ADOS-4 were used to define an autism case. Both the ADOS-1 and ADOS-4 were subject to validation and calibration work (eSupplement 3) within the study general population samples (11, 14) based on developmental assessments using the ADI-R (20) and the DISCO (21) and, in the APMS, a consensus clinical diagnosis evaluation (N=200 (22)). In the IDCR a random sample of 30 carers of individuals who scored high in the ADOS-1 (≥7) and a random sample of 30 carers of individuals who scored low in the ADOS-1 (<7) were invited to take part in an interview by a senior research psychologist (JS) using the DISCO and ADI-R, to test the accuracy of the ADOS-1 in identifying autism cases. Both studies confirmed the diagnostic thresholds for autism originally recommended by the developers of the ADOS (19).

Diagnostic interviewers were experienced in psychological research, and received an induction and training programme, run by a senior research psychologist (JS), a psychiatrist (TSB) and a qualified ADOS trainer (FS). Training experience was gained through assessing adults living in settings in which fieldwork subsequently took place. Field interviews did not commence until the interviewers achieved at least 90% agreement on ratings of jointly observed ADOS examinations. During fieldwork, interviewers received supervision sessions and prepared case vignette reports. They took part in post fieldwork debriefing to add further contextual information.

Intellectual disability was defined as a significant intellectual impairment with onset before adulthood and deficits in skills needed for daily functioning (23-25) assessed in the IDCR by the carer report version of the Vineland II Adaptive Behaviour Scales (26). In the APMS, predicted Verbal IQ (V-IQ; range estimate 70-130) was derived using the National Adult Reading Test (NART) (27). The NART requires a high reading age, leaving gaps in its
completion for adults with literacy problems of a wide range of causes, including mild intellectual disability, dementia, dyslexia, lack of education. Given this limitation (eSupplement 3), we were unable to identify those in the APMS with mild intellectual disability, so all were included in a category of none to mild intellectual disability. This assumption is reasonable, as ability to participate in the APMS would be extremely unlikely at an ability level of moderate intellectual disabilities or lower.

In both surveys questionnaires were completed covering participant’s physical and mental health, socio-economic factors and use of services, using comparable measures (15).

**Statistical Analysis**

eSupplement 1 describes how the APMS and IDCR samples were combined for analysis, which is illustrated in an explanatory Figure. The svytabulate procedure (STATA 12.0 for Windows) was used to estimate prevalence of autism by intellectual disability, age, and sex; svylogistic was used to fit logistic regression models for autism by age and sex, taking the complex survey design into account and adjusting for the presence of epilepsy; confidence intervals were calculated using Taylor linearization (28). To examine whether predictors of autism are the same in those with and without moderate intellectual disability, models were fitted for univariable predictors with an interaction term, allowing odds ratios to vary by disability level. The significance of interaction terms was tested using an adjusted Wald test (29) and where significant (p<0.05) was included in the final multivariable model.

**Results**

*Achieved sample and response rate*
Of 13,171 households identified as potentially eligible in the APMS, 7,461 (57%) provided a complete phase-one interview of whom 849 were selected for phase-two interviews. Of these 630 (74%) completed phase-two assessments: 618 full ADOS-4 assessments were carried out in the APMS. Analyses reported previously (11) found no evidence of non-response bias.

In the IDCR study, response rates were much higher in Leicestershire under the opt-out ethical approval procedure than for Lambeth or Sheffield. There were only 5 individuals assessed from Sheffield. Response rates were also higher in communal care establishments. Overall, 75/118 (64%) establishments took part and, in these 207/300 (69%) eligible individuals approached took part. In the IDCR private households, however, only 83/410 (20%) individuals took part, of whom 78 were from Leicestershire. Very few family carers of adults living in private households in Lambeth or Sheffield responded to the written invitation so, under ‘opt in’ procedures, almost all could not be contacted further. Nevertheless, the achieved communal care establishments sample in Leicestershire compared well with the case register population (see eSupplement 2), although the participants in the private household sample were more likely to be male and have more severe intellectual disability.

Of 290 individuals interviewed, 276 were assessed for autism. Assessments with the remaining 14 were attempted but could not be completed because participants had profound and multiple disabilities and assessors were unable to give a confident assessment.

Missing values in the APMS were minimal (<1% on all variables): there were 12 (4.3%) individuals in the IDCR study who had no Vineland assessment but were assessed for autism. Sensitivity analyses with these sequentially counted as having and not having
intellectual disability had no effect on the findings. Other missing values in the IDCR study were infrequent and are shown in the tables where they amount to more than 5% of N.

**Sample characteristics by intellectual ability**

Participants with moderate to profound intellectual disability were more likely to be male, younger, and were more ethnically diverse than those with no or mild intellectual disability (Table 1). The increased prevalence of South Asian ethnicity reflects the location of most of the IDCR sample in Leicestershire. Those in the sample with moderate to profound intellectual disability were more likely to be disabled and less likely to have ever worked.

Table 1 near here

**Autism prevalence by age, sex and intellectual ability**

There were 14 male and 4 female autism cases in the APMS subsample, and 49 male and 40 female cases in the IDCR subsample. The prevalence of autism in England, estimated from the combined reweighted sample, was 1.1% (95% CI 0.3-1.9%). Because people with moderate to profound intellectual disability make up just 0.3% of the total population, overall associations of autism with age and sex for the population as a whole are unchanged by the inclusion of rates for people with intellectual disability. There was a gradient of autism prevalence by intellectual ability (Figure 1), with prevalence considerably higher in those with moderate to profound intellectual disability (39.3%; 95% CI 31.0-48.4, compared with 1.0%; 95% CI 0.4-2.2 in those with no or mild intellectual disability (OR 63.5; 95% CI 27.4-147.2)).
In the population with moderate to profound intellectual disability, prevalence of autism was not specifically associated with sex, being (42.3% (31.1-54.3) in men and 35.2% (23.5-49.0) in women, p=0.43 (Table 2). However, in the population with no or mild intellectual disability, prevalence was considerably higher in men at 1.9% (0.8-4.2) than in women 0.2% (0.0-0.7). The interaction between intellectual disability and sex on the prevalence of autism was statistically significant (p=0.02; Wald test) and remained statistically significant when adjusted for age and presence of epilepsy (Table 3).

There was evidence of a small decline in the prevalence of autism with age statistically significant only in those with moderate to profound intellectual disability (table 2).

**Discussion**

This standardised whole population sample case finding study has yielded new understanding of the prevalence of autism and its associations in adults with intellectual disability, gender and age. The usual male gender excess for autism in childhood (2) (3) was not evident among adults with intellectual disability, showing a significant sex by intellectual disability interaction on autism prevalence, with men and women with at least moderate intellectual disability having similar prevalence. Previous studies of adults with intellectual disability have found a higher rate of autism in men than women (9) (30) (31), although not as high as for the rest of the population (32). Childhood population estimates (33) have reported a male/female ratio of 2.1 for children with IQ<70 and 3.7 for those without; an administrative study (34) also found that the sex-ratio diminished with increasing disability.
level in children; the Global Burden of Disease (GBD) project estimate (1), based on childhood, incidence and mortality data, was three times commoner in males than females with autistic disorders (autism with delay in language or cognitive development) and over four times commoner for other forms of autism.

The strength of this study lies in the comprehensive epidemiological sampling of adults of all ability levels in defined geographic areas and the use of direct diagnostic assessments of autism carefully validated in the study samples with the aim of achieving comparable measurement across intellectual ability levels. However, there is potential for selection bias on the estimate of autism prevalence in the IDCR study due to low response in the IDCR private household sample. Detailed investigation of the pattern of non response by age, sex, residence and presence of autistic traits in Leicestershire (eSupplement 2), makes type II error unlikely (i.e. failure to find a relationship between gender and prevalence of intellectual disability where it really exists).

We used moderate intellectual disability assessed by the Vineland II caregiver rating form in the IDCR as a threshold for intellectual disability in the logistic regression, with none or mild intellectual disability imputed for the APMS sample. This measure is consistent with other recent prevalence studies of adults (35;36), giving a standardised but more exclusive measure of intellectual disability. Our results were substantially unchanged when we reanalysed with intellectual disability defined pragmatically as lack of decision-making capacity to consent and to participate in a household survey. This is closer to a threshold of mild intellectual disability, but with unavoidable undercounting of those with mild disability in the APMS.
Analysis was limited by the small number of autism cases, particularly in the APMS sample. The presented analyses are weighted to represent the national population by age, sex, intellectual disability and type of residence. Calculation of the IDCR weights was subject to error as it relied upon incomplete official statistics, and on the assumption that the three case register areas represent the English population as a whole. Detailed sensitivity analyses found that the effects of estimating unknown population quantities on the overall prevalence estimates was minimal, giving prevalence of between 1.1% and 1.2%, regardless of assumptions made (37).

There are two main hypotheses that could account for this pattern: females with autism could be more severely impaired (38) or there could be more ‘missed’ cases of autism in women without intellectual disability. Missed cases could result from male bias in autism diagnostic markers (39); female presentation of autism may differ from male presentation and measures may be less able to detect the female presentation (39;40). Autism in women of average or above average intelligence may be ‘masked’ by other conditions, such as eating disorders (41), anxiety disorders (42) and borderline personality disorders (43). They may be better than women with intellectual disability at hiding their difficulties by imitating social interactions (44), having better language skills, different special interests, less hyperactivity and aggression (45). If more able women with autism are not diagnosed or are incorrectly diagnosed, then the prevalence of autism could be under estimated and their needs unmet. Biological theories for the male excess of autism (46) may benefit from reconsideration.

Although almost 2 in 5 adults with moderate to profound intellectual disability had autism, higher than expected based on previous research (9) (32) (47), only 1% of adults with no or
mild intellectual disability had autism. But because moderate to profound intellectual
disability only affects 0.3% of all adults (9) the point estimate for the prevalence of autism in
the population as a whole only changed from 1.0% to 1.1% when adults with intellectual
disability were included in the overall prevalence estimate. This finding runs counter to a
widespread assumption that as many as half of autistic adults have intellectual disability (6).

Only a small decline in the prevalence of autism with increasing age in adults with moderate
to profound intellectual disability emerged, the same in magnitude to that reported previously
in the household population (11), but the finding was only statistically significant in the
intellectually disabled population and not in the combined or household population samples.
The GBD (1) showed no clear evidence of a change in prevalence of autism between 1990
and 2010 but as there was no information on prevalence in adulthood, age pattern findings
were informed entirely by remission and mortality data. Although our finding does not
support the suggestion that rates of autism are increasing rapidly (although diagnosis may
be (8;48)), further independent work on this association using case finding population
research methods is needed.

It was noted that research identified cases of autism reported previously in the able
household population (11) had not been recognised or diagnosed by health services. New
findings reported here suggest that the research case finding measures used may also fail to
identify women with autism who do not have intellectual disabilities, possibly adding further
to the invisibility of autism in society. The picture that emerges is of a large population of
significantly disabled adults whose needs remain unmet because they are not recognised,
particularly when they do not have intellectual disabilities. The clinical, health and economic
implications are potentially enormous and urgently merit the attention of further research.
Acknowledgements
Our recently deceased colleague Professor Howard Meltzer played a key role in the design and development of this study; we would like to express our appreciation for his insight, knowledge and contribution. We acknowledge all the carers and adults with intellectual disability who participated in this study. We are grateful to Susan Purdon for advice and comments on study design and analysis and to Abdolreza Ashtarikiani, Sabyashi Bhaumik, Gyles Glover, Richard Mills and Patricia Howlin for advice.

Funding
The study was funded by the Department of Health, London, through the Health and Social Care information Centre, Leeds, United Kingdom. The funder played a substantial role in determining the content of the surveys, but played no part in the design, analysis or interpretation of this study, in drafting this article or in the decision to submit it for publication.

Ethical approval for the APMS was obtained from the Royal Free Medical School Research Ethics Committee, London, England. Ethical approval for the IDCR was obtained in Leicestershire from the Derbyshire Ethics Committee and for Sheffield and Lambeth from the “Essex 2” Research Ethics Committee, UK.

Authorship contributions:
All authors contributed to interpretation of data for the work, drafting or revising the work for critically important intellectual content, approved the final version of the paper to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. TSB, NS, JB, SAC, SM, FJS, FT contributed substantially to the
design or conception of the work; TSB, SM, FJS, JS, FT contributed substantially to data acquisition.

TSB had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Previous presentations of the information reported in the manuscript**


TSB (the manuscript's guarantor) affirms that 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 that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

**Data Sharing**

Anonymised data arising from this survey have been archived following standard procedures by the UK Data Service
As the survey involved a case register, particular care was taken to ensure that the data were anonymised, including using a new numeric identifier, removing place of recruitment and presenting broad age groups. Cross-tabulations of all variables archived were conducted to ensure that no fewer than 6 individuals fell into each 'cell'.

(http://discover.ukdataservice.ac.uk/Catalogue/?sn=7082&type=Data%20catalogue)
Reference List


Table 1: Sample Characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Moderate to Profound Intellectual Disability</th>
<th>No or mild/borderline Intellectual Disability</th>
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* Classified using the Vineland II caregiver rating form (26) for the IDCR sample, and the National Adult Reading Test for APMS sample. 12 adults from the IDCR study are excluded because they could not be classified.
† Self- or carer-reported epilepsy or fits since age 16.
‡ Difficulty with seven Activities of Daily Living including personal care, getting out and about and using transport, medical care, household activities, practical activities, paperwork, and managing money.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Moderate to Profound Intellectual Disability†</th>
<th>No or mild/borderline Intellectual Disability</th>
<th>P-value for variable by intellectual disability interaction</th>
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* Weighted to represent the English population by age, sex, intellectual disability and type of residence

† Classified using the Vineland II caregiver rating form in the IDCR; those in the APMS sample are assumed to have no or mild intellectual disability

‡ Self- or carer-reported epilepsy or fits since age 16
Table 3  Multivariate Predictors of Autism by Intellectual Disability, with Sex by Intellectual Disability Interaction *.

<table>
<thead>
<tr>
<th>Characteristic</th>
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<th>No or mild/borderline intellectual disability OR(95%CI)</th>
<th>P-value for variable by intellectual disability interaction</th>
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<td>-</td>
<td>1.31(0.58-2.99)</td>
<td>8.46(2.05-34.80)</td>
<td>.03</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year</td>
<td>0.98(0.92-1.05)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* Reweighted to represent the English population by age, sex, intellectual disability and type of residence and adjusted for carer or self-reported epilepsy or fits since age 16.
† Classified using the Vineland II caregiver rating form in the IDCR; those in the APMS sample are assumed to have no or mild intellectual disability ‡ P<0.01
Figure 1. Gradient of autism prevalence by intellectual ability; combined sample.

Intellectual ability is classified using the Vineland II caregiver rating form (24) for the IDCR sample; those in the APMS sample are assumed to have no or mild intellectual disability.