Author's response to reviews

Title: Physical and mental health comorbidity in adults with intellectual disabilities: population-based cross-sectional analysis

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Author's response to reviews: see over
The reviewers provide quite detailed but different opinions on our paper, and we are grateful to respond. We have found their comments very helpful, and have used them to improve the paper, and also, where we disagree, to be reflective about this and to ensure that the limitations section of our discussion is comprehensive and accurately identifies the paper’s limitations.

Reviewer 1:

This is a well-written manuscript based on data from a very large general practice population, comparing the scale and character of chronic comorbidity between those with and without intellectual disabilities. Its strength is the large sample, enabling analysis of all age groups over 18 years, and comparisons with persons with a normal intelligence in the same dataset. Main findings are more comorbidity in all age groups with intellectual disabilities, a different distribution of chronic conditions, and no relation with low income neighbourhood. Statistics and conclusions appear adequate. Nevertheless, I have several problems with this study.

Insufficiently innovative
Apart from the lack of a relationship with low income, none of the main findings are new. A comparable study in a large general practice population has been performed by Van Schrojenstein Lantman-de Valk as early as in 2000, whereas several high-quality epidemiologic studies of prevalences and risks of comorbidity, including comparisons with the general population, have been published during recent years, both in 18+ and in 50+ populations with intellectual disabilities (Van Splunder et al, 2006; Meuwese-Jongejeugd et al, 2006; Strydom et al, 2009, 2013; De Winter et al, 2012, 2013, 2014; Zaal-Schuller et al, 2015; Van de Louw et al, 2009; Jansen et al, 2013; Hermans et al, 2012). All groups reported higher prevalences and different distributions. The authors have referred to some of these studies in the introduction, including the two first multimorbidity studies in intellectual disability from the 50+ TILDA (Ireland) and HA-ID (Netherlands) populations. In the second one, comparisons were made with multimorbidity prevalences in different other Dutch 55+ populations, including two general practice-based datasets. The prevalence in the HA-ID group was comparable to that in the Dutch nursing home population. Further, a first attempt of clustering was performed (Hermans et al, 2014).

Response:
We have added a definition of “multimorbidity/comorbidity (two or more conditions in addition to the intellectual disabilities)”, in the abstract and first paragraph of the background section, so this is clearer, as the papers the reviewer quotes are mostly single condition studies. We have also added that “Studies of multi-morbidity in the general population are relatively recent, with increasing awareness of its clinical importance. Multi-morbidity starts to become more common over the age of 50 and increases in the elderly in the general population.”, to strengthen this point in the same paragraph.

Additionally, in the first paragraph of the discussion, we have added “Consequently, any policy initiatives or guidelines on multi-morbidity need to be relevant at a much earlier age in people with intellectual disabilities.”, to highlight the clinical relevance of the findings.

As far as we are aware, multi-morbidity has not previously been reported in younger adults with intellectual disabilities at all; our paper is the first to do so. Of the 14 papers the reviewer quotes, twelve describe prevalence rates of single conditions, not multi-morbidity, and twelve of them have no direct general population comparison group. Eleven of the quoted studies include people with intellectual disabilities who are using specialist intellectual disabilities services, whereas our study is population-based, and ten only include
older adults with intellectual disabilities, so they only provide a partial assessment of the whole adult population with intellectual disabilities.

Of these papers, only two considered multi-morbidity; (1) TILDA (Intellectual Disability Supplement – The Irish Longitudinal Study on Aging), which we quoted in our opening paragraph, reported on multi-morbidity in 695 older adults with intellectual disabilities. (2) Hermans et al, 2014, which we quoted in our opening paragraph, reported on multi-morbidity in 1,047 adult users of specialist intellectual disabilities services aged 50 and over. Hence both included older adults only, neither had a comparison group, and both were smaller in size than our study.

Underdiagnosis
As the authors recognise, under-reporting and underdiagnosis are the second problem. In the above epidemiologic studies, data collection had been based on active, standardised diagnostic assessments instead of on clinical practice files. Comparisons with the general population were not based on the same dataset, but on studies, performed in the same period and region, using identical or comparable diagnostic definitions and methods. Because of missing data as a result of non-cooperation or non-understanding, under-reporting was, and will always be, a factor in study populations with intellectual disabilities, but on a different scale than in the current study based on clinical files. One may argue that under-reporting and underdiagnosis will also have been present in the patient group with normal intelligence, but this may be on a different scale. Under-reporting and -diagnosis may not affect the message of more and different comorbidity, even adding to it. However, for individual conditions, this may be different. As an example, findings of this study for the cardiovascular risk are misleading and may hamper timely recognition and treatment, specifically in the large group using antipsychotic drugs. Active diagnostic assessments in the HA-ID and other studies have identified significantly increased risks of diabetes and peripheral vascular disease, which had remained unrecognised in 45% and 97-100%, respectively (De Winter et al, 2012, 2013; Zaal-Schuller, 2015).

Response:
Our data were drawn from a large GP dataset, so there may be under-reporting in both the adults with intellectual disabilities and the general population, and it is possible that this is more of an issue in the intellectually disabled adults. We acknowledged this in our discussion. We have now added data on the extent of measurement of blood pressure in those with and those without intellectual disabilities to provide some reassurance on this point (they are similar), and comment on this in the methods section, the results section, and have added this to the strengths and limitations section of the discussion. “The similarity in extent of blood pressure recording in the population with intellectual disabilities compared with the general population is reassuring in this regard. If there was under-reporting, then the difference between the two groups would be even more marked than that we report, and the key message of our paper still stands i.e. that multi-morbidity is markedly more common in adults with intellectual disabilities than in the general population, and occurs at a much younger age.”

Whilst we recognise and already acknowledged that under-recording is a possibility, the reviewer says our findings on cardiovascular risk are misleading. We disagree. Our figures in the paper cannot be directly compared with the Netherlands HA-ID papers, as our population is aged 18 and over whereas the HA-ID population is aged 50 and over. To address the reviewers comment, we have now examined the prevalence of cardiovascular conditions in people with intellectual disabilities aged 50 and over in our dataset. We find a prevalence of hypertension of 21.1% in our study versus 53% in the HA-ID papers; diabetes was 11.8% compared with 13.7% in the HA-ID papers, and stroke was 4.7% compared with
5.7% in the HA-ID papers. The findings are therefore very similar with the exception of hypertension where the prevalence is less than half compared with HA-ID. The explanation is not due to differences in blood pressure monitoring in our population, since 83.3% of the people with intellectual disabilities aged 50 and over had a blood pressure recorded in the previous three years compared to 84.9% of those without intellectual disabilities, and 79% in the HA-ID papers. We are unable to explain this discrepancy, although it may arise from us examining a population-based sample compared to the HA-ID sample which was drawn from people using specialist intellectual disabilities services, or from differences in blood pressure thresholds used for diagnosis, or because the HA-ID also used prescribed drugs in their definition of hypertension and some of these drugs may have been used for other clinical indications (e.g. ACE-inhibitors for congestive heart failure, diuretics for ankle oedema, beta blockers for anxiety). We have revised our paper by adding the information about extent of blood pressure measuring, but have not added the comparison data with the HA-ID papers, as we feel it would distract from the main thrust of our paper, that of multi-morbidity. However, we would be happy to add it if advised to do so by the editor.

Selection?
The authors conclude that the included study group is representative of the Scottish population with intellectual disabilities, but which population is that? Those using special services and those with mild intellectual disabilities who happen to have been recognised as such? Could the prevalence of mental conditions, such as schizophrenia, have been influenced by selective recognition of mild intellectual disability in psychiatric patients?

As a conclusion, this study is not innovative, underdiagnosis may not have affected the overall pattern of increased comorbidity but has led to misleading outcomes in cardiovascular risk, and selective inclusion of psychiatric patients with mild intellectual disabilities might have influenced prevalences of mental disease.

Response:
Our study is based within primary care, and so is population-based. We have added in the strengths and limitations section of the discussion that “Scottish GP practices have held a register of people with intellectual disabilities since a change in their contract introducing pay-for-performance, which precedes the data extraction this study used. Intellectual disability is a lifetime diagnosis, and once coded at birth or in childhood this remains on the medical record indefinitely.”

Developmental delay in childhood triggers referral for multidisciplinary assessment of cause, and assessment for additional support at school. This is long before any patients are likely to develop schizophrenia, and it would be exceptionally unusual to diagnose intellectual disabilities in someone without a pre-existing diagnosis, at the time of presenting with schizophrenia as an adult. Rather than stating this in the revision, we have underlined that the data is population based i.e. via general practices. The terms we used to extract this data on intellectual disabilities are included in the appendix to the paper, and were checked by two separate groups, ensuring completeness.

Additionally, the second reviewer’s point 7 suggests that it would be useful to state that the prevalence rate of intellectual disabilities in this sample is similar to that in other Scottish reports – these are based on work in Greater Glasgow and Clyde where there has been extensive work on population identification and checking accuracy of GP records. We have
added this. We also provided a paragraph on the representativeness of the population with intellectual disabilities in the discussion.

**Reviewer 2**

This is a very important and indeed timely paper which address some critical issues in the field of ID. Overall, the analysis the paper has done seems appropriate and correct. They refer to two papers (Smith et al. 2013 and Court et al. 2014) both of which have used very similar methodology. The sample size is very large which is great and this is reflected by the low standard errors and narrow CIs for the odds ratios.

The following comments may help to improve the paper further.

1. Propensity score matching (matching on age, gender and deprivation levels) perhaps could have been used? Rosenbaum and Rubin (1983) showed that treated and untreated subjects with the same propensity scores have identical distributions for all baseline variables. This would result in a lower overall sample size but would address the issue of imbalance in these key identified demographics. Interested in at might be gained or lost from this,? This maybe useful but not necessarily essential.

**Response:**
We deliberately reported data in the same way as the two papers the reviewer mentions (Smith et al, and Court et al). We report data standardised for age group, gender and neighbourhood deprivation, and also show the difference in the effect of deprivation between the population with intellectual disabilities and the general population.

2. Very short paragraphs were used including single sentence paragraphs (page 7 for example). In several places no comma was placed between the ORs and the CIs making it harder for the reader (e.g. OR 1.48 95% CI 1.41-1.55 (page 7)).

**Response:**
Short paragraphs have been reviewed, and commas have been placed between the ORs and the CIs throughout, to improve readability.

3. Personally I wasn’t a fan of how the p-values in tables 2-4 were presented (although this is consistent with Court et al 2014). Either use a format such as * for P # 0.05, ** for P # 0.01 and *** for P # 0.001 or report all p-value for consistency.

**Response:**
We will be happy to change the way the p-values in tables 2-4 are presented, if advised to do so by the editor. We have at present left them as they are, in keeping with the previous general population papers on multimorbidity.

4. Also include a foot note at the end of these tables indicating when the t-test or ANOVA were used etc. Tables should be able to be interpreted as stand alone pieces but these don’t give any indication of what test was used etc.

**Response:**
We have added foot-notes at the end of the tables, as advised by the reviewer.

5. The discussion should address what this study confirms from prior reports (e.g., Heslop, McCarron, Evenhuis) on morbidity differences and contributions to earlier death. It would be helpful to offer some insights into the level of assessment to establish both level of ID and of the different conditions and any data on the validity and reliability of the diagnoses reported in this dataset.
Response:
We have added the comparisons with the studies with older people with intellectual disabilities that the reviewer suggests. We do not have information on the level of intellectual disabilities. The comorbidities were measured in routine clinical care.

6. The measure of deprivation poses a number of concerns. Certainly if people with ID are living independently or with family there postcode deprivation is possible but those living in supervised setting regardless of address likely have a similar and somewhat affluent lifestyle. Perhaps this cannot be ascertained from the dataset and this issues should be discussed more fully as a limitation.

Response:
We are not entirely sure why people living in supervised settings regardless of address would have a similar and somewhat affluent lifestyle. Some supervised settings are individual tenancies with a 24 hour support package; some are congregate care where there might be little individual attention. Unfortunately we do not have this information in the database, and so have added this as a limitation. We hope this addresses the point.

7. It would be helpful to state earlier in the manuscript that the prevalence rate of ID in this sample is similar to other Scottish reports.

Response:
We have stated in the results that the prevalence rate of intellectual disabilities in this sample is similar to other Scottish reports, and provided a reference.

8. The references also need to be checked. For example Court et al 2014 [15] the title of the paper is incorrect.

Response:
The references have been checked, and the error in the title of the Court et al 2014 paper corrected.