

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

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| <b>TITLE (PROVISIONAL)</b> | THE PREVALENCE OF PHYSICAL CONDITIONS AND MULTI-MORBIDITY IN A COHORT OF ADULTS WITH INTELLECTUAL DISABILITIES, WITH AND WITHOUT DOWN SYNDROME. CROSS-SECTIONAL STUDY |
| <b>AUTHORS</b>             | Kinnear, Deborah; Morrison, Jill; Allan, Linda; Henderson, Angela; Smiley, Elita; Cooper, Sally-Ann   |

### VERSION 1 – REVIEW

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| <b>REVIEWER</b>        | Iain Carey<br>St George's, University of London<br>No prior competing interests - but I have flagged a potential additional reference on which I am an author on |
| <b>REVIEW RETURNED</b> | 03-Jul-2017  |

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| <b>GENERAL COMMENTS</b> | <p>The paper summarises a cross-sectional study of adults with intellectual disability (ID) in Scotland, and reveals an inordinate high level of multi-morbidity in these patients.</p> <p>The data presented, and its findings, while not entirely surprising are still illuminating. However, the data presentation could be improved, and the discussion of the methods and the findings needs extra detail and expansion (e.g. limitations).</p> <p>My main comment is that I think the 98.7% headline figure of multi-morbidity requires more discussion in relation to a few key points.</p> <p>a) Firstly, there is the issue of how representative of all adults with ID in Scotland or UK they think their study represents. Is the distribution of severity (e.g. 18% with profound ID) comparable to other data? Ditto the 34% with epilepsy, which is higher than some other UK datasets have reported (Cooper et al 2015, reference #8). Can the authors also comment any further on the 35% non-responders and whether their severity might differ? As their adults with ID are those already known to health services, the so-called "hidden majority" of adults with mild ID will presumably not be in their study (see Emerson et al (2016), reference #4). This may be worth a general comment, though I accept this doesn't directly impact on their implications for clinicians.</p> <p>b) The high% invites further scrutiny of their definition of multi-morbidity, of which there is no accepted standard. Most definitions however are based on conditions that are chronic with significant impact on patients in terms of treatment, reduced function, reduced quality of life and risk of future morbidity and mortality Firstly,</p> |
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nowhere in the paper is the complete list of the eligible conditions given, and this need to be included as a supplement. Secondly, the methods fail to make clear what the timing on these are e.g. when infections (fungal, LRTI) are listed are these current or historical? The Barnett et al 2012 paper (reference #5) includes a supplement where it is clear whether the condition is based on a Read code ever recorded (e.g. Stroke) or whether for recent treatment (e.g. Constipation is for  $\geq 4$  laxative prescriptions in last year). This needs to be stated so other researchers can follow and replicate the methods.

c) Lastly the high% does not immediately fit in with other data (also see point Q8 below) and these differences should be discussed and explained further. The most obvious of these would be the Scottish cross-sectional study of primary care data (Cooper et al 2015, reference #8) which is referred to (lines 33-34), but I have to query their interpretation of these findings. They quote 68.2% from this study as having multi-morbidity, but this seems disingenuous as they've counted ID as one. The Cooper paper doesn't do this (e.g. Figure 2) and instead reports "two or more morbidities" as 40.6% (Table 1).

#### Review Checklist

Q2. The Abstract results states "The pattern of multi-morbidity differs to that seen in the general population ..." While this is undoubtedly true, the authors study presents no data on the general population, so this sentence is not justified by their results.

Q4. No full list of the 30 odd conditions is given

Q6. Their top 20 conditions was based on all ID subjects – but does this miss any key differences which may be much higher in Down syndrome subjects such as Hypothyroidism or Dementia?

Q8. The authors state that "Only three studies were identified that investigated multi-morbidity amongst adults with intellectual disabilities" (Lines 29-30). I think two others could be reasonably referred to

- Emerson et al (2016), reference #4, studied adults with mild ID and only found 8% with "multiple morbidity" (their Table 1), although their list focused on more chronic long term conditions.

- Carey et al (BJGP 2016 <http://bjgp.org/content/66/645/e264>), used primary care data on a large group of ID patients and found "22.9% having  $\geq 2$  recorded conditions". Again the list of conditions was shorter, but could be discussed.

Q10. In terms of data presentation in the Tables and figures, I have the following comments

- Table 1. Since Down syndrome is in the title of the paper, and obviously of interest in the study, I think Table 1 needs expanding with extra columns to show the N and % for each of the demographics by Down syndrome. Currently I cannot ascertain whether Down subjects are older or more deprived for example. The authors may also want to consider presenting mean age by each of the demographic categories too, as there are likely to be differences.

- Table 1. In the results the authors quote the mean number of conditions by gender & severity. It would be a useful addition to have a table that showed these means by the demographics in Table 1. This could replace Figure 3, which is barely referred to, and whose similar means would be included in such a table. This could allow some of accompanying text (see point 8) to be shortened or simplified.

- Figure 1 mentions "ICD-10 physical health conditions" but I am not clear how ICD-10 is being used or referred to here. This could easily be an e-figure.

- Table 3 is too busy and not an effective presentation of the data. I presume from the methods that all the odds ratios are unadjusted. The question is then, should they be? What are the authors trying to achieve in Table 3? The authors suggest in the discussion there may be age differences by severity, so are some differences in the prevalence of conditions by severity explained by age for example? Presenting unadjusted ORs is OK, but the authors should make clear that any adjustment does not explain or change their findings.

- Additionally in Table 3 there are insufficient frequencies for them to present age in this way (e.g. there are only N=16 in the 75+ groups). If age is to be presented, fewer larger groups ( would be more effective. Similarly, combing severity (Severe or Profound vs Mild or Moderate) might be more effective to summarise their results.

- Figure 2. In the text the authors say "For women, mean number of physical health conditions was higher for individuals with severe (M = 12.02, SD = 3.91) and profound intellectual disabilities (M = 12.55, SD = 4.35) than for individuals with mild (M = 11.64, SD = 5.27) and moderate intellectual disabilities (M = 11.46, SD = 4.97)." But in Figure 2 all the lines intersect across different ages, so this seems a rather strong interpretation (and is not based on any statistical test). The accompanying text for men is confusing as it compared mild and profound versus moderate and severe. The lack of visual associations in Figure 2 also don't at first glance match up with some of the odds ratios in Table 3. For example, the ORs for Severe or Profound vs. Mild are all much greater than 1 for Vision/Epilepsy/Constipation/Gait Disorder which are the top 4 conditions. The authors need to expand and explain whether there is an association with severity (either before or after adjustment for age).

- Figure 4 could again be an e-figure as I don't think it adds much. The presentation would be better if it was using percentages rather than percentages.

Q12. The limitations section should be extended light of some other comments above. Was there a reason the authors focussed on physical conditions, and excluded mental health from their study and/or definition of multi-morbidity? Both the Cooper at al (2015) and Carey et al (2016) studies referred to above, I believe counted these in their definitions of multi-morbidity, and showed high recorded prevalence in patients with ID compared to the general population.

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| <b>REVIEWER</b>        | Dr Eilish Burke<br>Ussher Assistant Professor in Ageing and Intellectual Disability<br>Trinity College Dublin<br>Ireland |
| <b>REVIEW RETURNED</b> | 15-Jul-2017  |

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| <b>GENERAL COMMENTS</b> | <p>The authors use a comprehensive health assessment tool which identifies a broad range of conditions however one major drawback of this approach is that it is true the more conditions you look for the more conditions you will identify. The authors should consider highlighting this as not only a strength but also a weakness which contributed to such a high prevalence of multimorbidity. However in doing so the authors highlight the level of morbidity and perhaps conditions like 'ingrown toe nail' whilst considered minor and perhaps frequently overlooked are painful and debilitating however conditions that are easily remedied. This highlights the need for a standardised approach to health assessment among people with intellectual disability across all health settings.</p> <p>With regards the discussion greater exploration of the main finding, the high prevalence of multimorbidity is needed, drawing out the impact and contribution this can make on the lives of people with intellectual disability. The authors fail to strongly highlight how their findings can challenge the single disease approach to medical training, education and care, the findings have the potential to support policy and practice change to ensure comprehensive continuity of care in the lives of people with intellectual disability especially as more and more begin to live to old age. Improving healthcare provision can only contribute to making the lives of people with intellectual disability better.</p> <p>The authors present the conditions identified in rank order however discuss them randomly with no systematic or orderly approach. The reader would have expected consistency in the approach to the discussion which would improve the overall flow.</p> <p>The focus is very much on constipation, which is a life threatening condition and requires increased awareness among health providers and health care workers, however there is no mention of epilepsy which is the second more common condition reported and whilst epilepsy is common within the intellectual disability field it is not within the general field. This is critical to highlight as many primary health professionals are not familiar or knowledgeable of the field of intellectual disability a point which contributes greatly to conditions being missed or misdiagnosed.</p> <p>Table 1: The authors present the accommodation type, a deprivation category index and ethnicity for the participants however do not refer to this data within the body of the paper or do not appear to utilise the data within the analysis. Why collect and present data if it is not used or investigated? The deprivation scale scoring used is not explained therefore utility it redundant. However deprivation has been highlighted within the general population as having an impact on health and wellbeing with reports of associations between higher morbidity consistent with lower socio-economic status. Considering that people with intellectual disability are more likely to be socially and economically improvised it would be interesting to identify if the same social gradient applies. Which would have indications for health budget distribution.</p> |
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Table 3: This is a very crowded table and does not lend itself to easy interpretation, with no measurement guide. There is no clear indication of the reference group for Down syndrome whilst it can be assumed it's those without Down syndrome however with convention the authors ought to indicate this. The authors should consider splitting this table or reducing the number of items included. It is also questionable using the youngest age group as reference for all other age groups, it is well known that there is an associated age gradient with the presence of chronic health conditions. Therefore comparing 75 year olds with teenagers is problematic.

Other specific areas to address

Page 2 line 21 - Make it clear and explicit what definition you are using for your study - you mention 2 or more health conditions in the introduction but do not state that this is the definition adopted for your study.

Page 3 Methods – Clarify what measures were in place to support the individual to say no, make it clear how the rights of the individual were upheld especially as objective measures were conducted and the likelihood of acquiescence among people with intellectual disability is high.

Page 6 line 15 – rephrase ‘not picked up’

Page 7 line 3 – rephrase ‘but they can make visual ....-worse’

Some interesting areas the authors may consider highlighting

On examination of figure 2 Women – it is interesting that those females with moderate level of intellectual disability in the younger age group had an equal number of physical health conditions to those with profound intellectual disability, however within the next category the number falls – did the authors consider why this is, is there something particular here? Similarly for those with mild level of intellectual disability in the middle age group (45-54) there is a peak which teeters out as the age groups range increases. Again have the authors considered why this is?

Overall this is an interesting paper highlighting the complex issue of multimorbidity among people with intellectual disability. As people with intellectual disability now live well into old age addressing the emerging challenges and improving healthcare delivery where multimorbidity is becoming the norm can only improve the lives of adults as they grow older.

## VERSION 1 – AUTHOR RESPONSE

### Reviewer: 1

Reviewer Name: Iain Carey

Institution and Country: St George's, University of London, UK Competing Interests: No prior competing interests - but I have flagged a potential additional reference on which I am an author on

### General Comment

The paper summarises a cross-sectional study of adults with intellectual disability (ID) in Scotland, and reveals an inordinate high level of multi-morbidity in these patients.

The data presented, and its findings, while not entirely surprising are still illuminating. However, the data presentation could be improved, and the discussion of the methods and the findings needs extra detail and expansion (e.g. limitations).

My main comment is that I think the 98.7% headline figure of multi-morbidity requires more discussion in relation to a few key points.

Reviewer comment: Please see response to the key points raised below.

a) Firstly, there is the issue of how representative of all adults with ID in Scotland or UK they think their study represents. Is the distribution of severity (e.g. 18% with profound ID) comparable to other data? Ditto the 34% with epilepsy, which is higher than some other UK datasets have reported (Cooper et al 2015, reference #8). Can the authors also comment any further on the 35% non-responders and whether their severity might differ? As their adults with ID are those already known to health services, the so-called "hidden majority" of adults with mild ID will presumably not be in their study (see Emerson et al (2016), reference #4). This may be worth a general comment, though I accept this doesn't directly impact on their implications for clinicians.

Response: The distribution of severity of intellectual disabilities is highly dependant upon the age of the population, and as the majority of studies in this regard have been conducted with children they are not comparable. In a recent meta-analysis of studies on the prevalence of intellectual disabilities, only 5 of 52 included studies were of adults (Maulik et al (2011) Res. Dev. Disabil. 32, 419). None of the adult studies separately reported the prevalence of profound intellectual disabilities; moderate to profound intellectual disabilities was reported to account for 65-66% of the adults with intellectual disabilities in these studies, compared with 61% in ours, i.e. our rates are similar. Additionally, of the few studies on adults with intellectual disabilities focussed on other principal outcomes that have been conducted in primary care, extrapolation as to distribution of severity of intellectual disabilities is very limited due to incomplete recording of severity of intellectual disabilities in primary care. The epilepsy rate reported in Cooper et al (2015) is not directly comparable, due to the different methodologies – Cooper et al (2015) only included information already Read coded in primary care records, so as expected provides a lower rate than that in this current study submitted to BMJ Open. Hence, whilst the amount of existing literature is small, it suggests our cohort is representative on distribution of level of intellectual disabilities; and we can think of no reason to suggest it is not. We have added a comment on representativeness in the discussion on page 8.

We cannot comment on whether there is a difference in severity of intellectual disabilities in the 34% non-participants, as their level of intellectual disabilities is unknown (indeed, some might not have intellectual disabilities, as some who agreed to participate in our cohort study where subsequently excluded as not having intellectual disabilities following our assessment of this). We note however, that the 66% participation rate was high, and that there is a body of literature, chiefly from the UK and Australia that highlights that non-recruitment to intellectual disabilities studies relates to the characteristics of carers, practitioners, and other intermediaries rather than to characteristics of the persons with intellectual disabilities (e.g. Lennox et al (2005) JIDR, 46, 296; Oliver-Africano et al (2010) JIDR, 54, 17).

This proposed BMJ Open study is not just of people known to health services; it is rare, in that it used an extensive process to ascertain the population with intellectual disabilities from multiple sources, and directly assessed level of intellectual disabilities in all participants. This has been highlighted in the manuscript text, and a reference is now added to further detail the ascertainment process (page 3). Emerson has a long record of important and influential research which we greatly admire. His (unproven) theory of the hidden majority is a statistical concept based on an assumption of a normal distribution of IQ, with just an estimated loss with age due to death. We consider that other factors also account for the prevalence of intellectual disabilities in adults: 1. the normal distribution of IQ is less reliable at its extreme ends; 2. the ICD-10 definition of intellectual disabilities requires social as well as statistical criteria to be met; an impairment in adaptive functioning/requirement for support in daily activities. Many individuals who may require additional support at school to learn to read and write may not require support in adulthood having gradually acquired skills, so do not identify with nor meet classification requirements for intellectual disabilities; 3. an over-recording of intellectual disabilities in pupil/school data, to the advantage of the child in terms of securing additional support for learning (and very apparent through quite marked shifts in the proportions so recorded when criteria change) - but hence a much lower rate in adults when these factors are no longer a personal advantage; 4. the actual rate of early death in the population. The statistical "cut-off" for intellectual disabilities is of course also completely arbitrary, and given the approximation of population IQ to the normal distribution, the proportion of the population just above the IQ cut-off exceeds that below it whatever cut-off is used. These issues are complex and vary geographically and over time, see e.g. <https://www.sldo.ac.uk/media/1610/what-are-learning-disabilities-how-common-are-learning-disabilities.pdf>

In support of our ascertainment rate being representative, we note that it is similar to that reported in Scotland's Census 2011 (4.85/1,000), and in the recent systematic review which synthesised a rate of 4.94/1,000 for adults (Maulik et al (2011) Res. Dev. Disabil. 32, 419). We have added the latter reference on page 3. We are grateful for the reviewer in pointing out that the contentious suggestion of a hidden minority doesn't directly impact on the study implications for clinicians: we have clearly measured and reported the exact proportion of the cohort with each level of severity of intellectual disabilities, so this is transparent to readers in our paper.

Reviewer comment: b) The high% invites further scrutiny of their definition of multi-morbidity, of which there is no accepted standard. Most definitions however are based on conditions that are chronic with significant impact on patients in terms of treatment, reduced function, reduced quality of life and risk of future morbidity and mortality.

Response: We agree with the reviewer that this is important, and requires clear definition in the absence of an accepted standard, and so have added the following to the methods on page 4:

"There is no standard definition for multimorbidity. A recent NICE guideline on multimorbidity reflected that whilst multimorbidity is most commonly defined simply as having 2 or more long-term conditions, this type of definition is not necessarily helpful when providing clinical care (NICE, 14.9.16. [nice.org.uk/guidance/ng54](https://www.nice.org.uk/guidance/ng54)). Hence in the NICE guideline, the term multimorbidity refers to the presence of 2 or more long-term health conditions, which can include: defined physical and mental health conditions such as diabetes or schizophrenia; on-going conditions such as learning disability; symptom complexes such as frailty or chronic pain; sensory impairment such as sight or hearing loss and; alcohol and substance misuse. The guideline coverage was for adults with 2 or more long-term physical health conditions, and/or adults with 1 or more mental health conditions and at least 1 physical health condition. Given that the focus of this study is exclusively on adults with intellectual disabilities, we have used a tighter criteria of intellectual disabilities plus at least two physical health conditions."

Reviewer comment: Firstly, nowhere in the paper is the complete list of the eligible conditions given, and this need to be included as a supplement. Secondly, the methods fail to make clear what the timing on these are e.g. when infections (fungal, LRTI) are listed are these current or historical? The Barnett et al 2012 paper (reference #5) includes a supplement where it is clear whether the condition is based on a Read code ever recorded (e.g. Stroke) or whether for recent treatment (e.g. Constipation is for  $\geq 4$  laxative prescriptions in last year). This needs to be stated so other researchers can follow and replicate the methods.

Response: We have added that the conditions were recorded at the time of assessment on page 3. We also collected information on past history of conditions, but have not included this information within this paper. Our methodology is different to that of Barnett et al. They had to rely on secondary analysis of data extracted from primary care records, of data recorded for purposes other than the study, and hence also had to introduce proxy measures of conditions such as the one for constipation that the reviewer describes. Hence they predetermined a restricted list of conditions to include and had to predefine them e.g. in the absence of direct evidence of constipation, they concluded that  $\geq 4$  laxatives in the last 12 was a suitable proxy-measure. They were limited to the Read codes that had previously been recorded in the notes. In our study, we conducted individual assessments with each person, using a semi-structured instrument (the C21st Health Check: based around bodily systems, physical examination, phlebotomy protocol, and other investigations where indicated). We defined the conditions according to ICD-10 criteria. Our methodology is replicable. (page 3).

Reviewer comment: c) Lastly the high% does not immediately fit in with other data (also see point Q8 below) and these differences should be discussed and explained further. The most obvious of these would be the Scottish cross-sectional study of primary care data (Cooper et al 2015, reference #8) which is referred to (lines 33-34)...

Response: We have compared our finding with the previous literature, and outlined the methodological differences in the introduction. We thank the reviewer for highlighting the need for clarification. We have now also inserted the following in the opening paragraph of the discussion "A full range of physical health conditions were comprehensively assessed, rather than a shorter list of pre-selected conditions, or only conditions that had already been presented to primary care, or proxy-measures for conditions. An extremely high prevalence of multi-morbidity was reported, at 98.7%. As expected, the percentage was much higher than in previous studies due to this methodology" (page 6, first paragraph)

Reviewer comment: ...but I have to query their interpretation of these findings. They quote 68.2% from this study as having multi-morbidity, but this seems disingenuous as they've counted ID as one. The Cooper paper doesn't do this (e.g. Figure 2) and instead reports "two or more morbidities" as 40.6% (Table 1).

Response: We thank the reviewer for noticing this error; the 68.2% refers to the Barnett et al definition of multi-morbidity which includes intellectual disabilities as a condition. We have changed the percentage to 40.6% with multi-morbidity (excluding intellectual disabilities as a condition), in keeping with the tighter criteria used in this paper submitted to BMJ Open.

Reviewer comment: Review Checklist. Q2. The Abstract results states "The pattern of multi-morbidity differs to that seen in the general population ..." While this is undoubtedly true, the authors study presents no data on the general population, so this sentence is not justified by their results.

Response: We thank the reviewer for this comment and have now made reference to this in the Results page 5 under heading: 'Top 20 most prevalent physical health conditions' and in the Discussion (first paragraph):



Results: “For both the adults with intellectual disabilities and adults with Down syndrome, these patterns differ from the general population in whom the most prevalent physical health conditions have been reported to be, in order, hypertension, painful condition, asthma, coronary heart disease, irritable bowel disease, dyspepsia and diabetes (Cooper et al. 2015).”

Discussion: “The pattern of multi-morbidity also differed from the general population, hence findings from the general population are not transferrable; multi-morbidity amongst people with intellectual disabilities requires specific study” (NICE guideline, 14.9.16. nice.org.uk/guidance/ng54)

Reviewer comment: Q4. No full list of the 30 odd conditions is given

Response: All conditions are assessed using the C21st Health Check as reported in page 3, first paragraph of Measures and procedure, and classified using ICD-10 criteria. This is not a discreet list of a limited number of conditions (unlike the lists necessarily used in published studies of secondary analysis of general practitioner data), hence we have not listed all conditions. This is a different methodology to that extracting previously recorded data, as each person was individually and systematically assessed across all bodily systems.

Reviewer comment: Q6. Their top 20 conditions was based on all ID subjects – but does this miss any key differences which may be much higher in Down syndrome subjects such as Hypothyroidism or Dementia?

Response: The reviewer is correct – we have addressed this from the experience of people with intellectual disabilities: we separated out people with Down syndrome due to their different health profiles. Our study focusses on physical conditions, hence does not include dementia. 24.2% of the participants with Down syndrome had a thyroid disorder, which is more common than several of the other conditions listed in table 2, and we have commented in the discussion that the “top 20” refers to people with intellectual disabilities, not Down syndrome (page 7). This paper is highly data–dense and already includes results from 20 regressions, and the reviewers’ comment that tables include too much data, hence we have not added an additional table on the top 20 most prevalent conditions in Down syndrome, but would be happy to do so if the editor wishes.

Reviewer comment: Q8. The authors state that “Only three studies were identified that investigated multi-morbidity amongst adults with intellectual disabilities” (Lines 29-30). I think two others could be reasonably referred to

- Emerson et al (2016), reference #4, studied adults with mild ID and only found 8% with “multiple morbidity” (their Table 1), although their list focused on more chronic long term conditions.

- Carey et al (BJGP 2016 <http://bjgp.org/content/66/645/e264> ), used primary care data on a large group of ID patients and found “22.9% having  $\geq 2$  recorded conditions”. Again the list of conditions was shorter, but could be discussed.

Response: These studies have now been included in the introduction, and paragraph 1 has been modified to:

“Only five studies were identified that investigated multi-morbidity amongst adults with intellectual disabilities. Three studies reported high rates of multi-morbidity; 71% in 695 older persons with intellectual disabilities<sup>6</sup>, 80 % in 1,047 older persons receiving paid support<sup>7</sup> and 40.6% in 8,014 adults with intellectual disabilities<sup>8</sup>.

However, these studies are limited as two included only older adults<sup>6,7</sup>, one of which relied on self/proxy-reporting of known health conditions out of a list of 126, the other included 20 conditions<sup>7</sup>, and the third which was across the adult lifecourse reported data extracted electronically from primary care case records on 38 conditions, therefore only included conditions that had previously been presented to the GP<sup>8</sup>. Two further studies reported lower rates of multi-morbidity (though still higher than in the general population): 22.9% in 14,751 adults with intellectual disabilities aged 18-84 years (versus 13.3% of other people)<sup>9</sup>. and 10% in 299 adults with proxy measures of mild intellectual disabilities, aged 16-49 years (versus 5% of other people)<sup>10</sup>. The former of these included just 19 long-term conditions (selected on the basis of the UK GP contract, i.e. evidenced to be of importance for the general population), and relied on extraction of information on the 19 conditions that had previously been presented to the GP. The latter reported whether people were known to have any of only 15 health conditions, and focused only on adults with mild intellectual disabilities, who are therefore less dissimilar from the general population than are people with more severe intellectual disabilities<sup>10</sup>. These sampling and methodological differences account for the lower reported rates of multi-morbidity in these two studies than in the other three. Only one of these five studies conducted individual health assessments (and only for some of the conditions included in the study)<sup>7</sup>, and all five reported on only a limited number of pre-selected conditions.”

Reviewer comment: Q10. In terms of data presentation in the Tables and figures, I have the following comments - Table 1. Since Down syndrome is in the title of the paper, and obviously of interest in the study, I think Table 1 needs expanding with extra columns to show the N and % for each of the demographics by Down syndrome. Currently I cannot ascertain whether Down subjects are older or more deprived for example. The authors may also want to consider presenting mean age by each of the demographic categories too, as there are likely to be differences.

Response: We thank the reviewer for this suggestion – Table 1 has now been updated.

Reviewer comment: - Table 1. In the results the authors quote the mean number of conditions by gender & severity. It would be a useful addition to have a table that showed these means by the demographics in Table 1. This could replace Figure 3, which is barely referred to, and whose similar means would be included in such a table. This could allow some of accompanying text (see point 8) to be shortened or simplified.

Response: The sample comprised 562 men (54.9%) and 461 women (45.1%) with a mean age of 43.9 years (range 16–83). 186 (18.2%) had a diagnosis of Down Syndrome; 91 men (48.9%) and 95 women (51.1%) with a mean age of 41.1 years.

We have added the mean number of conditions to Table 1. To add Figure 3 to Table 1 would add an additional 20 rows which we think would be unwieldy – we are happy to follow the editors advice.

Reviewer comment: - Figure 1 mentions “ICD-10 physical health conditions” but I am not clear how ICD-10 is being used or referred to here. This could easily be an e-figure.

Response: ICD-10 was used to classify all the health conditions – we have more prominently described this (page 3, last paragraph):

“They then completed a comprehensive semi-structured health interview and targeted physical examination, and followed a phlebotomy protocol, with the person with intellectual disabilities and their carer, using the C21st Health Check (<http://www.gla.ac.uk/researchinstitutes/healthwellbeing/research/mentalhealth/research/projects/ucedd/>). Findings were discussed with one of three general practitioners who specialised in intellectual disabilities, and who classified all the physical health conditions using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision”<sup>25</sup>

Reviewer comment: - Table 3 is too busy and not an effective presentation of the data. I presume from the methods that all the odds ratios are unadjusted. The question is then, should they be? What are the authors trying to achieve in Table 3? The authors suggest in the discussion there may be age differences by severity, so are some differences in the prevalence of conditions by severity explained by age for example? Presenting unadjusted ORs is OK, but the authors should make clear that any adjustment does not explain or change their findings.

Response: The odds ratios are all adjusted – this has been clarified in the Analysis section (page 4), and additionally, table 3 has been renamed to improve clarity, and the description of the results improved (page 6):

“Twenty binary logistic regressions were conducted to determine if there were any associations between each of the 20 dependent variables (each of the twenty most prevalent physical health conditions) and the independent variables of age group, gender, level of ability, and Down syndrome”  
“Table 3 shows the results of the 20 regressions with the top 20 most prevalent physical health conditions as the dependant variables. It presents the odds ratios for gender, age, level of intellectual disabilities, and presence of Down syndrome in independently predicting each of the 20 conditions.”

Reviewer comment: - Additionally in Table 3 there are insufficient frequencies for them to present age in this way (e.g. there are only N=16 in the 75+ groups). If age is to be presented, fewer larger groups would be more effective. Similarly, combining severity (Severe or Profound vs Mild or Moderate) might be more effective to summarise their results.

Response: We agree and have re-run the 20 regressions and now present the oldest age group as 65+ years (Table 1). We prefer to retain the ability levels as, for example, there are differences between severe and profound intellectual disabilities.

Reviewer comment: - Figure 2. In the text the authors say “For women, mean number of physical health conditions was higher for individuals with severe (M = 12.02, SD = 3.91) and profound intellectual disabilities (M = 12.55, SD = 4.35) than for individuals with mild (M = 11.64, SD = 5.27) and moderate intellectual disabilities (M = 11.46, SD = 4.97).” But in Figure 2 all the lines intersect across different ages, so this seems a rather strong interpretation (and is not based on any statistical test). The accompanying text for men is confusing as it compared mild and profound versus moderate and severe.

Response: We have removed this text to avoid confusion, and retained the Figures.

Reviewer comment: The lack of visual associations in Figure 2 also don't at first glance match up with some of the odds ratios in Table 3. For example, the ORs for Severe or Profound vs. Mild are all much greater than 1 for Vision/Epilepsy/Constipation/Gait Disorder which are the top 4 conditions. The authors need to expand and explain whether there is an association with severity (either before or after adjustment for age).

Response: The difference is due to on the one hand considering the total number of conditions, and on the other, specific conditions. The logistic regressions are adjusted, we have clarified this for the methods and we discuss this in the discussion (page 6-7)

Reviewer comment: - Figure 4 could again be an e-figure as I don't think it adds much. The presentation would be better if it was using percentages rather than percentages.

Response: We are happy with this suggestion if it is keeping with the journal style and the editors preference.

Reviewer comment: Q12. The limitations section should be extended light of some other comments above. Was there a reason the authors focussed on physical conditions, and excluded mental health from their study and/or definition of multi-morbidity? Both the Cooper et al (2015) and Carey et al (2016) studies referred to above, I believe counted these in their definitions of multi-morbidity, and showed high recorded prevalence in patients with ID compared to the general population.

Response: The mental health conditions from the cohort have been previously published. The five existing intellectual disabilities papers on this topic varied in terms of whether/the extent to which they included mental health. We have added this to the discussion (Page 7 – Strengths and limitations):

“We did not include mental health conditions in this study, as this information has been previously published elsewhere (Cooper et al. 2007). Previously published intellectual disabilities papers on multi-morbidity varied in terms of whether/the extent to which they included mental health.”

**Reviewer: 2**

Reviewer Name: Dr Eilish Burke

Institution and Country: Ussher Assistant Professor in Ageing and Intellectual Disability, Trinity College Dublin, Ireland Competing Interests: none declared

Comment: Thank you for the opportunity to review this pertinent and interesting paper. The authors are to be commended on their investigation of the epidemiology of multi-morbidity among people with intellectual disability as garnering a greater understanding of this complex area will lend to raising awareness of the multi-layered complexity among people with intellectual disability and go in some way to improving healthcare provision alignment to the needs of this vulnerable population.

Response: We thank the reviewer for the positive comments

Comment: That said there are some issues the authors should consider and bring more clarity. The authors highlight a strength of their paper as the inclusion of a targeted physical exam, however do not identify what physical measures that were used and how these contributed to identifying the particular health conditions reported in the paper, clarity on this point would improve the methods.

Response: Further detail on this has been added (page 3-4):

Physical examination included measurement of height and weight, waist circumference, three recordings of blood pressure, pulse rate, pulse rhythm, communication assessment, oral examination, vision, hearing, peak flow, inhaler technique (if used), and feet and nail assessments, followed by urinalysis, a phlebotomy protocol, and referral protocol. Most of the physical examination was protocolled, e.g: vision was assessed by first asking a series of nine questions to help detect any possible problems (e.g. for persons unable to self-report, carers were asked whether the person screws up his/her eyes when in bright sunlight), then measuring vision using Kay's pictures at 33 cm and 3 m, and referring persons with possible visual impairment to the University Visual Sciences Department for more detailed, specialist assessment; hearing, likewise, was assessed through a series of questions, then otoscopy, and if the tympanic membrane could be visualized, examination using Warblers at 1/2 m at the level of 30 db/500 Hz, 0 db/1,000 Hz, 30 db/2,000 Hz, and 30 db/4,000 Hz, with referral for specialist assessment if there was any suggestion of possible hearing impairment. If the tympanic membrane could not be visualized because of impacted cerumen, drops were first used, to clear it.

Reviewer comment: The authors use a comprehensive health assessment tool which identifies a broad range of conditions however one major drawback of this approach is that it is true the more conditions you look for the more conditions you will identify. The authors should consider highlighting this as not only a strength but also a weakness which contributed to such a high prevalence of multimorbidity. However in doing so the authors highlight the level of morbidity and perhaps conditions like 'ingrown toe nail' whilst considered minor and perhaps frequently overlooked are painful and debilitating however conditions that are easily remedied. This highlights the need for a standardised approach to health assessment among people with intellectual disability across all health settings.

Response: The sentence underlined has now been added (page 8): "Strengths of the study are the systematic and detailed health assessments by trained health professionals, the comprehensive ascertainment of the population with intellectual disabilities, large sample size, and high participation rate..... One drawback of detailed health assessments is that looking for more conditions will result in more conditions being identified. This is both a strength – as conditions are frequently overlooked in this population – but also contributes to the high prevalence of multi-morbidity that was identified".

Reviewer comment: With regards the discussion greater exploration of the main finding, the high prevalence of multimorbidity is needed, drawing out the impact and contribution this can make on the lives of people with intellectual disability.

Response: We have made this clearer in the following sentence: "It is important to note that the top 20 physical health conditions reported are known to be painful, disabling and/or life threatening and can significantly impact on quality of life; in the main these are also conditions that are amenable to treatment, if high quality care is provided". (page 7)

Reviewer comment: The authors fail to strongly highlight how their findings can challenge the single disease approach to medical training, education and care, the findings have the potential to support policy and practice change to ensure comprehensive continuity of care in the lives of people with intellectual disability especially as more and more begin to live to old age. Improving healthcare provision can only contribute to making the lives of people with intellectual disability better.

Response: We thank the reviewer for highlighting this important point and have inserted the following into the discussion: "The findings have the potential to support policy and practice change to ensure comprehensive continuity of care in the lives of people with intellectual disability especially as more and more begin to live to old age. Improving healthcare provision can only contribute to making the lives of people with intellectual disability better" (page 8, last paragraph)

Reviewer comment: The authors present the conditions identified in rank order however discuss them randomly with no systematic or orderly approach. The reader would have expected consistency in the approach to the discussion which would improve the overall flow.

Response: The discussion of conditions have been re-ordered (top 3 conditions discussed) (page 6, second paragraph):

"With regards to single conditions, visual impairment was the most prevalent condition. Previous research has highlighted that sensory impairments are often missed by carers' or health professionals, are often misattributed to the individual's intellectual disabilities (diagnostic overshadowing), and that people with intellectual disabilities are often unable to communicate that they have a problem<sup>32</sup>.

A high index of suspicion is, therefore, needed with regards to visual impairments, particularly as these can be detected by optometrists even in people with profound intellectual disabilities. Epilepsy was the second most prevalent condition. Epilepsy amongst people with intellectual disabilities has previously been reported as much higher than for the general population, with seizures commonly multiple and resistant to drug treatment<sup>26,37</sup>. Uncontrolled epilepsy can be disabling and have serious negative consequences on both quality of life and mortality<sup>2</sup>. It is therefore essential for all health care practitioners to be aware of the prevalence and management of a complex and potentially life threatening condition in the intellectual disabilities population. Constipation was the third most prevalent physical health condition. This has been reported as common in adults with intellectual disabilities in institutional settings<sup>28</sup>, but has received little research attention in population-based cohorts. Evenhuis<sup>29</sup>, reported on the occurrence of constipation in 70 individuals over a 10-year period (mean age 70 years, range 60–92) in a Dutch residential care centre and found that 57% suffered from chronic constipation and 56% were permanently taking laxative treatment. Eight people with chronic constipation had serious side effects (rectal prolapse, diverticula of colon, intestinal obstruction, megacolon and haemorrhoids) and four eventually died of intestinal obstruction. Thus, as well as being painful, constipation may remain undetected for a long time and can cause death due to missed clinical symptoms <sup>29,30</sup>. Many factors can contribute to constipation including immobility, cerebral palsy, neurological disease, certain drugs, poor diet and lack of exercise<sup>31, 32</sup>. The high rate reported highlights the importance of this condition. Our study also adds to UK based data by providing prevalence rates on musculoskeletal impairments, constipation and gastro-oesophageal reflux disease among people with intellectual disabilities, conditions previously unreported in the UK research literature<sup>23</sup>.”

Reviewer comment: The focus is very much on constipation, which is a life threatening condition and requires increased awareness among health providers and health care workers, however there is no mention of epilepsy which is the second more common condition reported and whilst epilepsy is common within the intellectual disability field it is not within the general field. This is critical to highlight as many primary health professionals are not familiar or knowledgeable of the field of intellectual disability a point which contributes greatly to conditions being missed or misdiagnosed.

Response: We agree with the reviewer’s comments and have now included text on epilepsy (see comment above)

Reviewer comment: Table 1: The authors present the accommodation type, a deprivation category index and ethnicity for the participants however do not refer to this data within the body of the paper or do not appear to utilise the data within the analysis. Why collect and present data if it is not used or investigated? The deprivation scale scoring used is not explained therefore utility it redundant. However deprivation has been highlighted within the general population as having an impact on health and wellbeing with reports of associations between higher morbidity consistent with lower socioeconomic status. Considering that people with intellectual disability are more likely to be socially and economically impoverished it would be interesting to identify if the same social gradient applies. Which would have indications for health budget distribution.

Response: For ethnicity the majority of participants (96.4%) were white so further analysis was not possible. For deprivation we have now included the following:

Methods: “Social deprivation category was based on quintiles of Carstairs deprivation score. This ranges from 1 (most affluent) to 5 (least affluent) (Carstairs & Morris 1990)” (page 4)

Results: “A gradient across the extent of neighbourhood deprivation was not seen for multi-morbidity (figure 4)” (page 5) [New figure included].

Discussion: “Unlike the general population, a gradient across the extent of neighbourhood deprivation was not seen for multi-morbidity, as found in previous studies with adults with intellectual disabilities (Cooper et al. 2011; Cooper et al. 2015), hence focussed services are needed in all neighbourhoods.” (page 6, first paragraph).

Reviewer comment: Table 3: This is a very crowded table and does not lend itself to easy interpretation, with no measurement guide. There is no clear indication of the reference group for Down syndrome whilst it can be assumed it's those without Down syndrome however with convention the authors ought to indicate this. The authors should consider splitting this table or reducing the number of items included. It is also questionable using the youngest age group as reference for all other age groups, it is well known that there is an associated age gradient with the presence of chronic health conditions. Therefore comparing 75 year olds with teenagers is problematic.

Response: The table includes the results of 20 regressions. The only way we could therefore split the table is to reduce the number of regressions included (e.g. only reporting on 10 conditions). This would remove data from the paper: we will follow the editor's advice. We have classified the Down syndrome reference group. Regarding age, we prefer to retain the youngest adults (16-24 years) as the reference groups, in part to address the point made by the reviewer – whether there is a gradient across age. This is complex with this population, as the population ability level varies with age, due to earlier death of those with more severe disabilities.

Other specific areas to address

Reviewer comment: Page 2 line 21 - Make it clear and explicit what definition you are using for your study - you mention 2 or more health conditions in the introduction but do not state that this is the definition adopted for your study.

Response: We have incorporated the definition we use in the methods on page 4 to make this clear: “Given that the focus of this study is exclusively on adults with intellectual disabilities, we have used a tighter criteria for multi-morbidity, of intellectual disability plus at least two physical health conditions”.

Reviewer comment: Page 3 Methods – Clarify what measures were in place to support the individual to say no, make it clear how the rights of the individual were upheld especially as objective measures were conducted and the likelihood of acquiescence among people with intellectual disability is high.

Response: We have added the following information: “Additionally, for individuals who did not have decision-making capacity to consent, the study was explained to them in keeping with their communicative abilities, and their views sought and respected.” (page 3, first paragraph in Methods)

Reviewer comment: Page 6 line 15 – rephrase ‘not picked up’

Response: this has been changed to: “...visual impairment was the most prevalent condition. Previous research has highlighted that carers’ or health professionals are often not aware of sensory impairments”

Reviewer comment: Page 7 line 3 – rephrase ‘but they can make visual ....-worse’

Response: this has now been changed to: “but their side effects include visual disturbance, lowered seizure threshold, constipation and ataxia – the top four conditions”.

Some interesting areas the authors may consider highlighting

Reviewer comment: On examination of figure 2 Women – it is interesting that those females with moderate level of intellectual disability in the younger age group had an equal number of physical health conditions to those with profound intellectual disability, however within the next category the number falls – did the authors consider why this is, is there something particular here? Similarly for those with mild level of intellectual disability in the middle age group (45-54) there is a peak which tapers out as the age groups range increases. Again have the authors considered why this is?

Response: We thank the reviewer for raising this interesting point, which we agree is difficult to interpret: we have added a comment about this on page 7.

Reviewer comment: Overall this is an interesting paper highlighting the complex issue of multimorbidity among people with intellectual disability. As people with intellectual disability now live well into old age addressing the emerging challenges and improving healthcare delivery where multimorbidity is becoming the norm can only improve the lives of adults as they grow older.

Response: We thank the reviewer for highlighting the importance of this paper

#### VERSION 2 – REVIEW

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|------------------------|---|
| <b>REVIEWER</b>        | Iain Carey<br>St George's, University of London |
| <b>REVIEW RETURNED</b> | 31-Aug-2017                                     |

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| <b>GENERAL COMMENTS</b> | The authors have done a thorough job of responding to many queries raised by both reviewers, and the paper has significantly improved. My only remaining comment would be whether some of the data presentation can be simplified/reduced, especially if the journal limit is "five figures and tables" (e.g. many of the figures could be provided as supplementary material). However, I am happy to recommend the paper to be accepted. |
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| <b>REVIEWER</b>        | Dr Eilish Burke<br>University of Dublin, Trinity College Dublin |
| <b>REVIEW RETURNED</b> | 21-Sep-2017   |

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|-------------------------|---|
| <b>GENERAL COMMENTS</b> | Thank you for attending carefully to the review and addressing the issues highlighted. The only issue that continues to appear cumbersome is Table 3. It remains difficult to read, perhaps present the most pertinent significant results and have your full table as supplemental material. Congratulations again on the thorough investigations of multi morbidity among this complex population and whilst the figures identified are extraordinarily high they are not surprising. |
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