David B Elliott

Editor, Opthalmic and Physiological Optics

Dear Professor Elliott,

We would like to thank Ms Cumberland and her colleagues very much for their interest and for their insightful comments on our 2014 paper[1], where we reported the prevalence of vision impairment and dual sensory problems within the UK Biobank data set of UK adults aged 40 to 69 years. Cumberland and colleagues emphasised two areas of concern; i) prevalence estimates from the UK Biobank as prevalence estimates for the general population and ii) use of 2001 census as a reference sample rather than 2011 data. Cumberland and colleagues also raised issue with our conclusion that the most common cause of visual impairment is likely to be uncorrected or sub-optimally corrected refraction. We are grateful for the opportunity to reiterate and expand on aspects of our manuscript in this response.

Prevalence estimates

We emphasised in our paper that the UK Biobank is not a population-based sample, and that prevalence estimates from the UK Biobank may be under-estimates of the prevalence in the general population (p 485-486). However, we also noted that the UK Biobank is a very large study that is reasonably demographically comparable to the general UK population, and we statistically adjusted prevalence estimates for known sampling biases (p 482).

Previous studies reported comparable values to those we reported for the UK Biobank data set. Cumberland and colleagues refer to Rahi and colleagues' [2] study of 44-year-olds from the 1958 British Birth Cohort which reported a prevalence of low vision (with habitual correction) of 1.23%. Comparable values from the UK Biobank are 0.54% (95% confidence interval 0.37-0.71) for 40-44 year-olds and 0.9% (95% CI 0.68-1.12%) for 45-49 year-olds; slightly lower than Rahi and colleagues' estimate. Given that sampling biases may apply to both the UK Biobank and the 1958 British Birth Cohort, we suggest that it is encouraging that somewhat similar prevalence estimates were obtained for the two sources.

We agree that there are rather few population-based estimates of vision impairment, particularly for younger age groups and for visual function with 'habitual' correction. Therefore we suggest that it is useful to report prevalence values from the UK Biobank data set, provided that they are interpreted bearing in mind the limitations of the UK Biobank that we outlined in the manuscript. The limitations that were specifically discussed in the manuscript include: 1) the low response rate in the UK Biobank sample may have introduced unknown biases that were not accounted for by the statistical weighting procedures used, and 2) recruitment and testing were not designed to cater for those with major vision

problems. This may have excluded people with vision impairment, and so the prevalence estimates from the UK Biobank sample may under-estimate prevalence in the general population (p 485-486). In the manuscript, we also focused on associations between demographic factors (age, sex, socioeconomic status and ethnicity). These associations may be more reliable than the prevalence estimates [3].

Use of 2001 census data

We used the 2001 census as the reference sample for the following reasons: 1) UK Biobank recruitment was carried out aiming for comparability with the 2001 census, and participants responded to demographic questions based on those from the 2001 census (see UK Biobank protocol;
http://www.ukbiobank.ac.uk/resources/?phpMyAdmin=trmKQlYdjjnQIgJ%2CfAzikMhEnx6

). 2) The UK Biobank recorded the Townsend index [4] as a measure of the area deprivation of each participant's residential area. Townsend scores are calculated based on unemployment, non-home ownership, non-car ownership and household overcrowding with reference to levels reported in the 2001 census. The area deprivation relates to 2001 and thereby is assumed to precede the outcomes of interest. This is more logical than taking 2011 deprivation and applying to study participants recruited during 2006-10. 3) At the time of writing the manuscript, descriptions of the UK population broken down by sub-groups according to age, sex, and ethnic categories that were required for the statistical weighting procedure we used were not yet available for the 2011 census. The relevant 2011 census 'Detailed Characteristics' tables (DC2101EW) were released on 16/05/2013 for England and Wales and the data for Scotland only very recently. Whilst demographic change by ethnic group was occurring during the 2000s [5], constraining the models to 2001 distributions by age, sex and ethnic group is still justifiable.

In table 2 in our manuscript, we reported how the demographics of the UK Biobank study compare to the general population based on 2001 census data. Cumberland and colleagues suggest that the demographics for only participants with visual acuity data should have been reported. We chose to report the demographics of the whole UK Biobank study because various subsets of the UK Biobank were utilised in our analysis (ranging from those with visual acuity data; n = 116 682, to hearing data; n = 164 770, to self-report vision data; up to n = 499 365). As there are no major differences in the demographics of these subsamples, describing the demographics of the UK Biobank study overall provides readers with a clear impression of the comparability of the UK Biobank study and provides an appropriate context with which to interpret all of the analyses we reported.

Cause of visual impairment

We suggested that the most common cause of visual impairment is likely to be uncorrected or sub-optimally corrected refraction, consistent with previous studies that came to the

same conclusion [6-8]. With the available data, we could not distinguish the proportion of impairment due to refractive error and/or use of sub-optimal correction. We were able to report better-eye visual acuity estimates with habitual correction, but 'best-corrected' visual acuity was not tested. Auto-refraction data were available, but as the participants' 'habitual' prescription was not recorded, it was not possible to establish whether a participant's 'habitual' prescription was consistent with the value obtained from auto refraction or not. Ideally, to establish whether reduction in visual acuity was due to inaccurately corrected refractive error, it would have been necessary to re-measure visual acuity whilst the participant wore the lenses given by the autorefractor result. These data were not collected by the UK Biobank.

Thank you very much for the opportunity to further explain some of the important points raised by Ms Cumberland and colleagues.

Yours sincerely

Piers Dawes[1], Christine Dickinson[2], Richard Emsley[3], Paul Bishop[4], Karen Cruickshanks[5], Mark Edmondson-Jones[6,7], Abby McCormack[6,7,8], Heather Fortnum[6,7], David R. Moore[9], Paul Norman[10], Kevin Munro[1,11]

[1] School of Psychological Sciences, University of Manchester, [2] Faculty of Life Sciences, University of Manchester, [3] Centre for Biostatistics, Institute of Population Health, University of Manchester, [4] Institute of Human Development, University of Manchester, [5] Population Health Sciences and Ophthalmology and Visual Sciences, School of Medicine and Public Health, University of Wisconsin, [6] NIHR Nottingham Hearing Biomedical Research Unit, University of Nottingham, [7] Otology and Hearing Group, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, [8]MRC Institute of Hearing Research, Nottingham, [9]Cincinnati Children's Hospital Medical Center, [10] School of Geography, University of Leeds, [11] Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre

References

1. Dawes, P., et al., *Vision impairment and dual sensory problems in middle age.* Opthalmic and Physiological Optics, 2014.
2. Rahi, J.S., P.M. Cumberland, and C.S. Peckham, *Visual impairment and vision-related quality of life in working-age adults: findings in the 1958 British birth cohort.* Opthalmology, 2009. **116**(2): p. 270-274.
3. Allen, N., et al., *UK Biobank: Current status and what it means for epidemiology.* Health Policy and Technology, 2012. **1**(123-126).

4. Norman, P., *Identifying change over time in small area socio-economic deprivation.* Applied Spatial Analysis and Policy, 2010. **3**(2): p. 107-138.
5. Rees, P., et al., *A local analysis of ethnic group population trends and projections for the UK.* Journal of Population Research, 2011. **28**(2): p. 129-148.
6. Weih, L.M., et al., *Age-specific causes of bilateral visual impairment.* Archives of ophthalmology, 2000. **118**(2): p. 264.
7. Attebo, K., P. Mitchell, and W. Smith, *Visual acuity and the causes of visual loss in Australia. The Blue Mountains Eye Study.* Ophthalmology, 1996. **103**(3): p. 357.
8. VanNewkirk, M.R., et al., *Cause-specific prevalence of bilateral visual impairment in Victoria, Australia: the Visual Impairment Project.* Ophthalmology, 2001. **108**(5): p. 960.