REF 68605 – Sargeant, invited manuscript - *"Age at diagnosis of type 2 diabetes and cardiovascular risk factor profile: a pooled analysis"*

Revision 1 - Point-by-point responses to peer review and editorial comments

Comment	Response
Peer Reviewer Comments	
Were the labs obtained in the fasting state?	Thank you to Reviewer 1 for their insightful and helpful comments. In three of the included studies (EXPEDITION, DIASTOLIC and PREDICT) fasting blood samples were taken, whereas in the remaining studies (CODEC, LYDIA) non-fasting blood samples were taken. Imprtantly, however, it has been demonstrated that fasting is not necessary in order to gain accurate measurements of the clinical laboratory biomarkers examined in this analysis (HbA1c or lipids).[1] Thus we do not feel that these differences preclude pooling of data in these analyses, or the findings presented.
Since you have the 5 features of Metabolic Syndrome please report the frequency of MetS in the 3 groups by the Alberti et al global definition	We thank the reviewer for this valuable suggestion, which undoubtedly adds strength to our analyses and manuscript. We have calculated the prevalence of metabolic syndrome for each age group, as well as in the entire pooled population, and presented these data within Table 1. We have also described these data within the "Participant Characteristics" paragraph of our Results section.
Since you had Asians/Indians more commonly in the <40 group please cite the pioneering work of Jialal I et al eg Diabetes Research, 1986 since they showed that in young Indian T2D patients in South Africa they had worse cardiovascular outcomes and were predominantly female like in your study	The reviewer highlights an interesting and important paper. We have added text into the first paragraph of our Discussion section, highlighting the higher proportions of female and Asian participants observed in the younger diagnostic age group in our study, which is an important finding of our analyses. We also outline the increased prevalence of complications and co-morbidities observed among Asian participants, including the reference suggested by the reviewer.
Other Comments	
"The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text (and directly before the References)	We have added this section. Our apologies that this was missed from our initial submission.
Please prepare and arrange the figure using PowerPoint to ensure that all graphs or arrows, or text portions can be reprocessed by the editor.	We have prepared and submitted our figure as a PowerPoint file. We hope that this allows the editorial team to process the file as required. However, please let us know if anything further is needed.

Please reduce self-citations to <10%.	The reason that our manuscript has a high self-citation percentage is because we have pooled data from five previous studies/trials conducted by our group. This has meant that these previous trials are each cited in the methods section of our manuscript. In our previous submission, we cited all previous publications for these pooled trials, including both protocol and main outcomes papers (if each had been published). In this revised submission, we have condensed these to a single reference for each study/trial, to reduce the percentage of self-citation. However, this still remains above 10%. Notably, however, there is only one self-citation elsewhere in our manuscript (none in the introduction, one in the discussion) and if we exclude citations from the methods section, we have a self-citation percentage of ~5% (1 out of 19 remaining references).
Please provide the PubMed numbers (PMID) and DOI citation numbers to the reference list. Please revise throughout.	We have edited the reference list to include PMID and DOI.
Please provide the funding agency document copies	We have uploaded a PDF file containing evidence of funding for the studies included in this analysis. Please note that due to the nature of the DIASTOLIC and PREDICT funding (as part of personal fellowship awards to author GPM) these trials and/or specific acronyms are not named within funding confirmations. Similarly, the CODEC study is supported by general infrastructure funding from the NIHR Leicester Biomedical Research Centre (https://www.leicesterbrc.nihr.ac.uk/). Various authors contributing to the current analysis and manuscript are supported by infrastructure funding of the NIHR Leicester Biomedical Research Centre, the NIHR Applied Research Collaboration East Midlands (https://arc-em.nihr.ac.uk/). The lead author (MMB) is supported by NIHR Programme Grants for Applied Research funding programme (NIHR201165; confirmation contained in the uploaded PDF).
Please proved the Conflict-of-Interest Disclosure Form – download at https://www.wjgnet.com/bpg/GerInfo/236 - save as “68605-Conflict-of-Interest Disclosure Form”	We have completed and submitted the conflict of interest disclosure form. This includes all information provided during our previous submission within the “Conflict of interest statement” in the main manuscript file.
Please provide Copyright License Agreement – download at https://www.wjgnet.com/bpg/gerinfo/250 - save as “68605-Copyright License Agreement”	We have completed and submitted a PDF file containing copyright licencing agreements for all co-authors. Unfortunately, due to remote working and annual leave within the co-author team, we have been unable to obtain signatures from three co-authors (APH, ZZH, GPM) before the deadline for our re-submission. Therefore, these are currently signed “per procurationem” by the senior

	author (JAS) on behalf of these three co-authors. We hope that this is acceptable to the editorial team. Please note also that due to remote working, some of the signatures collected are electronic and not wet ink.
Please provide the Institutional Review Board Approval Form/document (upload the primary version (PDF) of the Institutional Review Board's official approval - save as "68605-Institutional Review Board Approval Form or Document")	We have uploaded a PDF file containing evidence of favourable opinion from the NHS Research Ethics Committee (REC) which reviewed each of the studies included in this pooled analysis.

1. Emerging Risk Factors C, Di Angelantonio E, Sarwar N, Perry P, Kaptoge S, Ray KK, et al. Major lipids, apolipoproteins, and risk of vascular disease. JAMA. 2009;302(18):1993-2000.