PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	How much of the stalled mortality trends in Scotland and England can be attributed to obesity?
AUTHORS	Walsh, David; Tod, Elaine; McCartney, Gerry; Levin, Kate Ann

VERSION 1 – REVIEW

REVIEWER	Hajo Zeeb Bremen Institute for Prevention Research and Social Medicine
REVIEW RETURNED	13-Sep-2022

GENERAL COMMENTS	This is an interesting and carefully developed paper on the contribution of obesity to the stalled mortality trends observed in England and Scotland. The methods and underlying data are well chosen and described, and particularly the use of different HR for the calculation of PAF is commended, as is the analysis of the influence of potential biases. The paper is well written, the methodology is complex but clearly described, and well documented. Comments: Among the main problems – identified by the authors – is the issue of sex-specific HRs that were not available, overall rather surprising given the large number of studies conducted. Similarly a stratification by SES would have been desirable, again not possible due to data limits. However, in particular regarding the latter issue, the discussion could be amended, e.g. by giving more details and perhaps PAFs for related diseases (e.g. Diabetes) as analogue, supporting the discussion. A strong point is the discussion of biases, with evaluation of the likely effect. What I missed is a short discussion regarding the partially substantial differences in findings regarding Scotland and the UK. Looking at the obesity proportions and time dynamics, there is little to explain this, but perhaps the authors can expand on this topic a bit.

REVIEWER	Sigrid Bjerge Gribsholt Aarhus University Hospital
REVIEW RETURNED	20-Sep-2022

GENERAL COMMENTS	The potential contribution of increasing obesity levels to the changes in overall mortality in Scotland and England is interesting and relevant. The authors find that in Scotland 10% (males) and 14% (females) of the difference between observed and predicted mortality rates in 2017-19 may be attributable to increasing prevalence of obesity and that the corresponding numbers in

	England are 20% and 35% respectively. Potential sources of bias are discussed thoroughly. Major comments. Please describe the data sources in the abstract Please provide more information on the surveys used in the paper. What are the time periods? How many participants were included? How many of the invited participants were not included? Please describe how mortality was assessed – the reader may guess that it is based on registry data – but is that correct? Did you have information on causes of deaths? Did they differ over time? Please provide the time periods for the inclusion periods and the follow up periods. How many participants were lost to follow up? Please discuss the impact of this. Minor comments: Table 1. Please provide information on the rates – is it per 100.000 population corresponding to figures 2 and 3? P 14, l 58 "…the use of age-specific (rather than age and sex specific) HRs (the latter were not available)…" It is unclear what "latter" refers to. Supplementary tables 1 and 3, please add kg/m2 to the BMI-cutoffs

VERSION 1 – AUTHOR RESPONSE

Comments to Authors	Response to reviewers
Reviewer 1: Dr. Hajo Zeeb, Bremen Institute for Prevention Research and Social Medicine	
Comments to the Author: This is an interesting and carefully developed paper on the contribution of obesity to the stalled mortality trends observed in England and Scotland. The methods and underlying data are well chosen and described, and particularly the use of different HR for the calculation of PAF is commended, as is the analysis of the influence of potential biases. The paper is well written, the methodology is complex but clearly described, and well documented.	We are extremely grateful for Dr. Zeeb's helpful and positive comments – and indeed for giving up his time to review the paper.
Comments:	
Among the main problems – identified by the authors – is the issue of sex-specific HRs that were not available, overall rather surprising given the large number of studies conducted. Similarly a stratification by SES would have been desirable, again not possible due to data limits. However, in particular regarding the latter issue, the discussion	Thanks for this helpful comment. In response, we have made an addition to the Discussion to provide more details of why we were unable to stratify the analyses by SES. This states that: "Such stratification was not possible for

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could be amended, e.g. by giving more details and perhaps PAFs for related diseases (e.g. Diabetes) as analogue, supporting the discussion.	numerous reasons including: a lack of available hazard ratios for different socioeconomic groups; lack of population denominator data for individual socioeconomic position (SEP) categories included in the surveys; the different area deprivation indices in use in Scotland and England, which would have made comparative interpretation of results problematic; and the likely small sample sizes (especially in the Scottish survey data) which would also have increased levels of analytical uncertainty." The suggestion of providing PAFS for specific relevant diseases such as diabetes is a helpful and sensible one. However, because of the fundamentally different way such PAFs would be calculated, this is unfortunately unlikely to provide a meaningful comparison. As is explained in detail in the paper, our PAFs were calculated on the basis of a comparison of BMI distribution in 2008 and 1995, with the latter (1995 values) being the counterfactual. This is because we were focussing on the role of *changes*to BMI (i.e. including increases in obesity prevalence). However, other studies are more likely to define the counterfactual in a different manner, often as 0% prevalence. For this reason, we have not discussed, nor compared, other, disease-specific, PAFS. We hope this makes sense, and is acceptable to the reviewer.
A strong point is the discussion of biases, with evaluation of the likely effect. What I missed is a short discussion regarding the partially substantial differences in findings regarding Scotland and the UK. Looking at the obesity proportions and time dynamics, there is little to explain this, but perhaps the authors can expand on this topic a bit.	Again, thanks for this helpful point, and we agree that the paper would benefit with some additional clarification regarding the issue. Thus, we have added the following text to the discussion of other relevant literature: "Some of these criticisms of PAFs, particularly that relating to the sensitivity of the definition of the counterfactual, are potentially relevant to some of the results of our study. The differences between Scotland and England relate in large part to different PAF values for the oldest age group (70-89 years): although the values of the PAFs for this group are very small, their impact is significant because of the higher numbers of deaths that are observed. As described in the results section, the differences in PAF values between countries

Comments to Authors	Response to reviewers
	for this age group (small but negative for Scotland, small but positive in England) are in part explained by a smaller increase in levels of Grade I obesity in the Scottish data between the two time periods; a larger increase would have resulted in a positive PAF value. With the value of the counterfactual here being derived from survey data with smaller, age-specific, sample sizes and annually fluctuating rates, this therefore both emphasises the need for caution in interpreting the precise values of the results, and also supports some of the criticisms of PAFs that have been made by Flegal and others."
Reviewer 2: Dr. Sigrid Bjerge Gribsholt , Aarhus University Hospital	
Comments to the Author: The potential contribution of increasing obesity levels to the changes in overall mortality in Scotland and England is interesting and relevant. The authors find that in Scotland 10% (males) and 14% (females) of the difference between observed and predicted mortality rates in 2017-19 may be attributable to increasing prevalence of obesity and that the corresponding numbers in England are 20% and 35% respectively. Potential sources of bias are discussed thoroughly.	Again, we are most grateful to Dr. Gribsholt for both her time and helpful comments.
Major comments.	
Please describe the data sources in the abstract	These have been added.
Please provide more information on the surveys used in the paper. What are the time periods? How many participants were included? How many of the invited participants were not included?	Some (but not all) of these details are already supplied in the second section of the Methods ('statistical analyses') and in the supplementary material. We agree, however, that this could have been both more comprehensive and better 'signposted'. Thus we have added the following text to the first section of the Methods: "In 2008 (the last year of data employed here), adult sample sizes were approximately 6,500

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	(SHeS) and 15,000 (HSE), with household response rates of 61% and 64% respectively. More precise details of the survey years employed in the analyses, and the size of the age-specific sample sizes, are provided below and in the supplementary material". The relevant later section of the Methods still reads as: "The PAF calculation was based on comparison of the BMI distribution in 1995 (the earliest time point available for the Scottish data) and 2008… Sample sizes for the 35-89 age band were approximately 4,000 in SHeS in both years, and c.9,700 (1995) and c.8,750 (2008) in HSE. Full details of sample sizes and methods employed to derive data for the older age groups in 1995 are provided in Supplementary Table S2.". We hope this is acceptable to the reviewer.
Please describe how mortality was assessed – the reader may guess that it is based on registry data – but is that correct? Did you have information on causes of deaths? Did they differ over time?	The second paragraph of the Methods section has been altered slightly and now reads as follows: "Mortality (and matching population denominator) data by age, sex and year were obtained from national registries, the National Records of Scotland (NRS) and the Office for National Statistics (ONS) respectively. Data were for all causes of death combined (rather than specific individual causes) as that was the focus of the study.".
Please provide the time periods for the inclusion periods and the follow up periods.	The three relevant time periods for the main analyses are already stated in the Methods section (bold added here): "The PAF calculation was based on comparison of the BMI distribution **in 1995** (the earliest time point available for the Scottish data) **and 2008**… PAFs were applied to observed counts of deaths by five-year age band, sex, year, and country **for the period 2016-19** (i.e. the most recent period of the stalling prior to the COVID-19 pandemic)". We are not absolutely clear as regards what additional information would be helpful with regard to this?

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How many participants were lost to follow up? Please discuss the impact of this.	We are slightly confused by this question as we have not used longitudinal data in our calculations. We use whole population level data from nationally-representative health surveys from two points in time (1995 and 2008), and we apply the PAF (derived from data for those two time points) to mortality data for the whole population for the years 2016-19. Thus no participants are lost to follow-up in that sense. However, the reduction in response rates in all population surveys is relevant to the reviewer's question – and this is already highlighted (and discussed) in Table 2 as a potential source of bias for the calculations, as well as referred to in the 'strengths and weaknesses' section of the Discussion. We hope this response clarifies the issue for the reviewer.
Minor comments:	
Table 1. Please provide information on the rates – is it per 100.000 population corresponding to figures 2 and 3?	Apologies for this oversight. We have amended the Table's description accordingly.
P 14, l 58 "…the use of age-specific (rather than age and sex specific) HRs (the latter were not available)…" It is unclear what "latter" refers to.	Again, apologies for the lack of clarity. "Latter" was referring to age/sex-specific hazard ratios. We have amended the text to make this clearer.
Supplementary tables 1 and 3, please add kg/m2 to the BMI-cutoffs	The tables have been duly amended.

VERSION 2 – REVIEW

REVIEWER	Hajo Zeeb Bremen Institute for Prevention Research and Social Medicine
REVIEW RETURNED	27-Nov-2022

GENERAL COMMENTS	Thank you for carefully revising the manuscript. The PAF discussion is now clear, and your approach not to include other specific calculations sensible given the differences pointed out.