BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-067310
Article Type:	Original research
Date Submitted by the Author:	10-Aug-2022
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Keywords:	PUBLIC HEALTH, SOCIAL MEDICINE, EPIDEMIOLOGY

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How much of the stalled mortality trends in Scotland and England can be attributed to obesity?

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Keywords: obesity, mortality, 'population attributable fractions', austerity, Scotland, England

Abstract

Objectives

The rate of improvement in all-cause mortality rates has slowed in the UK since around 2012. While evidence suggests that UK Government 'austerity' policies have been largely responsible, it has been proposed that rising obesity may also have contributed. The aim here was to estimate this contribution for Scotland and England.

Methods

We calculated population attributable fractions (PAFs) resulting from changes in Body Mass Index (BMI) between the mid-1990s and late 2000s for all-cause mortality among 35-89 year-olds in 2017-19. We used BMI data from national surveys, and hazard ratios (HRs) from a meta-analysis of 89 European studies. PAFs were applied to mortality data for 2017-19, enabling comparison of observed rates, BMI-adjusted rates and projected rates. Uncertainty in the estimates is dominated by the assumptions used and biases in the underlying data, rather than random variation. A series of sensitivity analyses and bias assessments were therefore undertaken to understand the certainty of the estimates.

Results

In Scotland, an estimated 10% (males) and 14% (females) of the difference between observed and predicted mortality rates in 2017-19 may be attributable to previous changes in BMI. The equivalent figures for England were notably higher: 20% and 35% respectively. The assessments of bias suggest these are more likely to be overestimates than underestimates.

Conclusions

Some of the recent stalled mortality trends in Scotland and England may be associated with earlier increases in obesity. Policies to reduce the obesogenic environment, including its structural and commercial determinants, and reverse the impacts of austerity, are needed.

(250 words)

INTRODUCTION

Deeply concerning changes to mortality rates have been observed across the UK since the early 2010s: population average mortality rates have stopped improving, whilst mortality rates among poorer populations have increased[1-5]. Such changes have been seen for many different causes of death, with cardiovascular mortality particularly affected[6,7]. Similar stalled mortality trends have been recorded in other high-income countries[2].

While the causes of these changes in the UK have been debated, a large body of evidence now suggests that UK Government 'austerity' measures, implemented in 2010 following 'the great recession' of 2008 and which have disproportionately affected the poorest in society, are largely to blame[8-14]. The impact of similar austerity measures in slowing mortality improvement in other countries has also been demonstrated[15-18].

However, it has also been proposed that these trends may have additionally been influenced by changes in levels of adult obesity prevalence: this has been suggested in relation to the UK[19], the US[20,21], Australia[21] and elsewhere[22]. This is largely because of two factors. First, there is a clear association between obesity and both cause-specific (including cardiovascular disease) and all-cause mortality, with the weight of evidence suggesting this relationship is causal[23]. Second, considerable increases in obesity prevalence have been recorded in the UK (and elsewhere) in recent decades[24], and these pre-date the more recent changes to all-cause mortality discussed above. While this hypothesis appears plausible, it has not yet been tested. The aim of this study, therefore, was to assess, and quantify, the extent to which any of the mortality changes observed in Scotland and England since the early 2010s may be attributable to prior increases in obesity levels in the population.

METHODS

Populations and data sources

We used data for the populations of Scotland and England: the change in mortality rates since 2012 has been similar in both countries[3], and trend data on adult obesity prevalence are available for both.

Mortality (and matching population denominator) data by age, sex and year were obtained from the National Records of Scotland (NRS) and the Office for National Statistics (ONS) respectively. Data on adult body mass index (BMI) distribution in the populations were accessed from the Scottish Health Survey (SHeS) and the Health Survey for England (HSE) via the UK Data Service[25-27]. Both are long-running, nationally-representative, surveys which include measured (rather than self-reported) height and weight (from which BMI is calculated) for large samples of the adult population.

Statistical analyses

Population attributable fractions (PAFs) were calculated for changes in BMI distribution (including therefore the increase in overweight and obesity) between the mid-1990s and late 2000s in relation to all-cause mortality among 35-89 year-olds. PAFs are defined as the proportion of cases (here, all-cause deaths) attributable to a particular exposure[28]: in this case the latter is defined as the change in BMI distribution over time. The 35-89 year age group was determined by the availability of age-specific hazard ratios (HRs): we used previously-published HRs from a meta-analysis of 89 European studies of BMI and all-cause mortality undertaken by the Global BMI Mortality Collaboration (GBMC)[23]. To reduce the risk of confounding and reverse causality, the GBMC meta-analysis excluded smokers, those with chronic disease at time of recruitment, and participants who died within the first five years of follow-up. HRs were available for six BMI categories and three age groups (35-49 years,

50-69 years, 70-89 years) (Supplementary Table S1), and were based on c.14 years' follow-up. The PAF calculation was based on comparison of the BMI distribution in 1995 (the earliest time point available for the Scottish data) and 2008: this covers the period of considerable increase in obesity in both Scotland and England (discussed further below), and also broadly fits with both the c.14 year follow-up period on which the HRs calculation was based, and the later period of stalling improvement in mortality in both countries. PAF was therefore calculated as:

$$PAF = \frac{[\sum(p2008\ BMI\ category\ i \times HRi)\ -\ \sum(p1995\ BMI\ category\ i\ \times HRi)]}{\sum(p2008\ BMI\ category\ i\ \times HRi)}$$

The 1995 SHeS only sampled adults aged 16-64 years; data for 65-89 years were therefore estimated from age-specific distributions in 2003 (the first survey that included all adults aged 16+ years). 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.

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): this enabled calculation and comparison of *observed* mortality rates with *BMI-adjusted* rates (i.e. excluding deaths attributable to the change in BMI distribution). These were then further compared with *projected* rates (i.e. the rates that were predicted had the stalling of improvement not occurred): the latter were calculated for 2011-2019 based on linear trends. Three sets of projections were produced: 1981-based (i.e. based on the linear trend for 1981-2010), 1991-based and 2001-based. All rates were age-standardised using the 2013 European Standard Population[29], and stratified by sex and country.

A range of sensitivity analyses were undertaken. These included the use of survey data for three-year averages instead of single year points (e.g. 1994-96 average instead of 1995), and employing different HRs for different age groups in the calculation of the PAFs: the latter HRs were approximated from a large English study of over 3.5 million adults with c.18 years follow-up, and which employed similar exclusion criteria as the GBMC study (Supplementary Table S3)[30]. Those PAFs were also applied to different age groups in the mortality analyses. Analyses of age-specific trends were undertaken to explore differences in the PAFs between Scotland and England.

An assessment of the scale and direction of any likely bias was informed by reviews of relevant PAF-based literature.

Patient and Public Involvement

Patients and the public were not involved in this study.

RESULTS

As context to the main results, Figure 1 presents trends in adult obesity prevalence in Scotland and England between 1995 and 2019. In 1995 the overall prevalence was approximately 16% in both countries; by 2019 it had increased to 28-29% (with female rates slightly higher than male rates). However, the biggest increases took place between the mid-1990s and the late 2000s, with much smaller increases seen in the later period: for example, for males in England, and males and females in Scotland, prevalence increased by only 1-2 percentage points between 2010 and 2019.

[Figure 1 about here]

The calculated PAFs by age group and country are shown in Supplementary Table S4. The age-specific values were broadly similar for both countries with the exception of the oldest

age group (70-89 years) where the PAF was small but positive for English data (0.029) and small but negative (-0.008) for the Scottish data. This is discussed further below.

Figures 2 and 3 compare the observed European age-standardised mortality rates (EASRs) for 35-89 year-olds with the BMI-adjusted EASRs and the 1991-based projected EASRs. Data are shown separately for males and females in Scotland (Figure 2) and England (Figure 3). The divergence between projected and observed rates is clear in all cases and has widened over time; it is greater for males than females. In all cases the gap in each year is reduced by the BMI-adjusted EARS, but to a greater extent in England than in Scotland.

[Figures 2 & 3 about here]

Table 1 quantifies the differences shown in Figures 2 and 3 above. It presents the three sets of EASRs (observed, projected, and BMI-adjusted) as well as a comparison of the observed-projected gap with the BMI-adjusted-projected gap: this can be interpreted as the amount of the observed-projected gap that can be potentially attributed to the change in BMI between 1995 and 2008. Data are shown annually for 2016-19, with – for simplicity – average figures for the most recent three-year period also presented.

This shows that for Scottish males, the average observed EASR for 2017-19 was 1751 (95% CIs 1729 to 1773). This reduced marginally to 1719 (95% CIs 1697 to 1741) after adjustment for the change in BMI (in effect, excluding the increase in overweight- and obesity-related deaths), but was still notably higher than the projected EASR of 1447 (95% CIs 1427 to 1467). The change in BMI therefore potentially 'explained' 10.5% of the difference between the observed and projected rates. For females, 13.6% of the difference could be attributed in this manner. However, the figures for England were notably higher: average figures of 20.1% for males and 35.1% for females.

	Males						Females				
	Year	**Observed rate**	**BMI-adjusted rate**		**Projected rate (1991)**	**% of observed-projected difference attributable to change in BMI**	**Observed rate**	**BMI-adjusted rate**		**Projected rate (1991)**	**% of observed-projected difference attributable to change in BMI**
Scotland	2016	1777.7	1744.9		1565.6	15.5%	1276.2	1257.0		1180.3	20.0%
	2017	1775.7	1744.4		1506.3	11.6%	1282.8	1263.7		1151.6	14.5%
	2018	1762.1	1729.9		1447.1	10.2%	1277.0	1257.3		1122.8	12.8%
	2019	1716.3	1684.0		1387.8	9.8%	1245.1	1224.9		1094.1	13.4%
	2017-19	*1750.7*	*1718.8*		*1447.1*	*10.5%*	*1268.0*	*1248.3*		*1122.8*	*13.6%*
England	2016	1472.1	1411.2		1252.0	27.7%	1042.1	1000.1		951.1	46.2%
	2017	1459.7	1399.2		1196.3	23.0%	1029.2	987.8		923.6	39.2%
	2018	1453.1	1392.6		1140.6	19.4%	1026.7	985.2		896.2	31.8%
	2019	1404.2	1345.7		1084.9	18.3%	985.5	945.5		868.8	34.2%
	2017-19	*1438.5*	*1378.6*		*1140.6*	*20.1%*	*1013.5*	*972.6*		*896.2*	*34.9%*

Table 1. Comparison of observed, projected and BMI-adjusted age-standardised mortality rates among 35-89 year-olds, Scotland and England, 2016-19.

The gap between the observed and projected EASRs is smaller when using 1981-based projections, and greater when using 2001-based projections. These are shown in Supplementary Figures S1 and S2, and quantified further in Supplementary Table S5.

The use of the different HRs and different age groups in sensitivity analyses resulted in lower PAFs (Supplementary Table S6). Consequently, less of the difference between observed and projected mortality rates could be attributed to changes in BMI than was the case in the main analyses. For example, the 20.1% figure for males in England shown in Table 1 was reduced to 16.4% when applied to the same 35-89 age band in the mortality analyses, to 15.1% when applied to 15-84 years, and to 13.2% when applied to 15+ years. Similar reductions of between approximately a third and a fifth were shown for females in England (Supplementary Table S7).

Additional analyses to explore the difference in the PAFs for the oldest age group in Scotland (negative) and England (positive) suggested that it was partly explained by a smaller increase in Grade I obesity in Scotland. In England, the prevalence in this age group increased by 44% from 13.6% to 19.6% between 1995 and 2008; in Scotland, the prevalence was already higher in 1995 (20.2%) and only increased marginally to 22.0% in 2008. A greater increase in Scotland would have resulted in a positive, rather than negative, PAF (data not shown). Given that the 70-89 years age group was not sampled in the 1995 SHeS, with estimates instead derived from proportions in the 2003 survey, the accuracy of these figures is uncertain. However, analyses of long-term trends for this age group showed that trends have fluctuated between approximately 20% and 24% in most years, and in that context the derived estimate for 1995 seems plausible (Supplementary Figure S3). Furthermore, comparison with English trends support the observation of higher Grade I obesity in this age group: despite considerable fluctuation in rates over time, levels were higher in Scotland in 9 of the 13 available data points between 2003 and 2019 (Supplementary Figure S4).

Despite such fluctuations in rates, only marginal differences in results were observed when using three-year averages rather than single years in the calculation of PAFs across all age groups (Supplementary Tables S8-S10).

The assessment of potential biases is shown in Table 2. Of the ten sources of potential bias listed, five suggest potential overestimation of effect size, two suggest underestimation, and the remaining three are unclear. In the majority of cases the size of any bias is either small or unclear. The implication is that the estimates produced are more likely to be overestimates of the contribution of obesity rather than underestimation, but this is uncertain.

	Source of potential bias	Direction	Magnitude	Notes
1	BMI treated as categorical rather than continuous data	Unclear	Small	The 'proportional shift' method (the use of categorical rather than continuous data in the calculation of attributable fractions) has been shown to be associated with the potential for both underestimation and overestimation of effect size. However, the greater the number of categories, the lower the risk of such uncertainty[31]: we employ a relatively large number (six) of BMI categories.
2	Declining survey response rates	Underestimation of obesity effect	Unclear	Both surveys are large and deemed nationally representative, and both are weighted to adjust for non-response: however, in the case of the English survey, this weighting was only introduced in 2003, and therefore was not applied to the 1995 data; furthermore, despite the use of such weights, the data may still be potentially affected by a 'healthy respondent' bias[32]. The latter, however, is difficult to quantify.
3	Broad age bands with potential for residual confounding	Overestimation of obesity effect	Unclear	Some of the change in BMI between the two time periods will be due to ageing, and this may not be captured because of the large age bands employed.
4	Exclusion of those aged 16-34 and 90+ years	Underestimation of obesity effect	Small	The exclusion of these sections of the adult population would suggest potential underestimation of effect size, especially given that overweight and obesity levels increased among both age groups between 1995 and 2008[33]. However, the level of underestimation is likely to be small, given the relatively small number of deaths that occur in the younger age group overall, and the likely number of deaths *from relevant causes* for those aged 90 and above. Furthermore, sensitivity analyses using hazard ratios (HRs) approximated from the Bhaskaran et al study[30] which covered both age groups (the age bands used were 16-49, 50-69, 70-79 and 80+ years) suggested *fewer* deaths were attributable to the change in BMI than was the case using the HRs for 35-89 year-olds only. The calculated PAF for the 80+ years group was also very small in those analyses (e.g. 0.004 for English data).
5	Hazard ratios not generalisable to Scotland and England	Overestimation of obesity effect	Small	The HRs used in the analyses (from the work published by the Global BMI Mortality Collaboration (GBMC)) were calculated from a meta-analysis of 89 European studies, a considerable number of which were from the UK[23]. Assuming no effect modification from country/study-specific context, the HRs should be appropriate for use in our analyses of UK data, despite the higher levels of overweight and obesity observed in the UK. However,

	Source of potential bias	Direction	Magnitude	Notes
				sensitivity analyses using alternative HRs approximated from the study by Bhaskaran et al[30], which were calculated from data for over 3.5 million adults in England (and based on c.18 year follow-up), resulted in smaller PAFs and therefore fewer deaths attributable to BMI changes over time in England, suggesting the use of the GBMC HRs may have slightly overestimated the effect size.
6	Hazard ratios prone to confounding	Overestimation of obesity effect	Unclear	HRs from the GBMC study are not adjusted for socioeconomic deprivation, levels of physical activity or diet, and thus represent a likely overestimation of effect size, albeit one that is difficult to quantify.
7	Changes in BMI due to pre-existing ill-health	Overestimation of obesity effect	Negligible	By excluding smokers and ex-smokers, those with chronic disease at time of recruitment, and participants who died within the first five years of follow-up, the GBMC study (the HRs from which are used here) largely removed this risk.
8	Interpolated data for age 65-89 years in 1995 Scottish survey data	Unclear	Unclear	Analyses comparing the estimated figure for 1995 with observed trend data in other years of the survey do not suggest any obvious inaccuracies, and there are no other data from other Scottish surveys that can be compared. However, the PAF for the 70-89 years age group is negative in the Scottish data (-0.008) but positive in the English data (0.028) which contrasts with the other two age groups where the PAFs are very similar in the two data sets. The extent to which this may relate to the interpolation is unknown.
9	Use of single-year comparison time points in calculation of PAFs	Unclear	Small	Sensitivity analyses using three year averages (1994-96 instead of 1995, and 2007-09 instead of 2008) suggest a minimal impact.
10	Lengthy follow-up period	Overestimation of obesity effect	Unclear	The potential for overestimation of effect size has been highlighted for studies with long follow-up periods on the basis that important 'mediators' (e.g. systolic blood pressure, cholesterol) may decrease over time among those with initially recorded high BMI[34,35]. It is unclear whether – or to what extent – this may apply here.

Table 2. Assessment of potential biases in calculation of Population Attributable Fractions (PAFs).

DISCUSSION

Overall findings and implications

Our analyses suggest that changes in the BMI distribution in Scotland and England between the mid-1990s and late 2000s may have potentially contributed to the mortality changes observed in both countries since around 2012. In Scotland, an estimated 10% (males) and 14% (females) of the difference between observed and predicted mortality rates among 35-89 year-olds in 2017-19 may be attributable to previous changes in BMI. The equivalent figures for England were notably higher: 20% and 35% respectively. However, there is uncertainty around the accuracy of these estimates: sensitivity analyses and bias assessment suggest the potential for overestimation of effect size, although the degree is difficult to quantify.

Alongside the evidence of the role of UK Government austerity measures in the stalling of mortality improvement in Scotland and England[8-14,17,18], this suggests the need for a range of government policies to both reverse the damaging effects of austerity, as well as to address the negative consequences of an increased obesogenic environment in the UK[36].

Strengths and weaknesses

A number of limitations of the study are acknowledged. In relation to the survey data sources, these include: the need to derive estimates for older age bands in the 1995 SHeS (although trend analyses suggest the data are plausible); the lack of non-response weighting in the 1995 HSE, as well as the general decline over time in response rates in all such population surveys; and limited time series data (especially in the Scottish survey). Other limitations include the use of the proportional shift method in calculating the PAFS (although data constraints meant no other method was available), the use of age-specific (rather than age *and* sex specific) HRs (the latter were not available), and the lack of any socioeconomic

stratification of the analysis: the latter would have been important given that the mortality changes observed in the UK in the past decade have particularly affected more deprived populations[2,3-5]. We did not calculate 95% confidence intervals for the PAFs on the basis that this would have misrepresented the key sources of uncertainty in the analyses, which were due to a range of potential biases rather than random variation. It was also difficult to find a means of combining assessment of random variation in each of the underlying data sources (BMI distribution, mortality, projected mortality, HRs), as well as the PAF estimate, that would have adequately represented the random variation. Other weaknesses are also included within Table 2. However, the study also has a number of strengths. Despite their acknowledged limitations, both the SHeS and HSE are important data sources: they are large, nationally representative, surveys which have collected important measured (not self-reported) anthropometric data since the 1990s. The other data sources employed in the analyses were also strengths of the study: detailed mortality data for both countries' whole populations, and HRs from a comprehensive meta-analysis of a large number of European studies of BMI (and the design of which minimised the risk of confounding). We also undertook a range of sensitivity analyses and a detailed assessment of potential biases.

Relevance to other studies

The relationship between obesity and all-cause mortality has been demonstrated in numerous studies[23]. While the weight of evidence suggests that the association is causal, there has been considerable debate about both the extent of causality, and the measures such as PAFs that are used to assess it[34,37-41]. For example, limitations of PAFs (and obesity-related PAFs in particular) highlighted by Levine[37] include: the flawed nature of 'simple causal partitioning'; the overlapping nature of exposures in a population meaning that different PAFs add up to more than 100% (thus, assessing single exposures in isolation is problematic); the importance of the definition of the exposure, such that a more broadly

defined exposure will always increase the size of the PAF (meaning that a high PAF is 'not necessarily indicative of a better scientific understanding of the causes(s) of disease in the population than a low PAF'). Flegal and colleagues have echoed many of these sentiments, also cautioning against interpretations of causality: 'PAFs for obesity may be best considered as indicators of association'[34]. They supported this argument on the basis of a number of definitional and methodological issues, including: the importance of how the counterfactual is defined (with the size of the PAF varying depending on what definition is employed); potential overestimation in long follow-up studies (as alluded to in Table 2); and important differences between studies in how obesity-related PAFs are calculated which make interpretation and comparison of results difficult.

Despite these criticisms and pleas for cautious interpretation of PAFs in terms of assessing causality, obesity-related PAFs have been calculated in many studies. This includes recent work by Ho and colleagues who calculated and compared obesity and smoking related PAFs from both data sources employed here: SHeS and HSE[42]. The work suggested that deaths attributable to obesity increased from 18% to 23% between 2003 and 2017, overtaking the number of deaths attributable to smoking in the process. Other studies have demonstrated how different methodological approaches can result in different values of obesity related PAFs. For example, in the Netherlands Vidra et al generated PAFs ranging from 0.9% to 1.8% (two-fold variation) for the same population, but based on different formulae[41]. They also showed that the use of European, rather than global, HRs resulted in a higher PAF – this is relevant to our own study.

Vidra et al's estimates for the Netherlands are clearly much lower than Ho et al's for Scotland and England. Similarly, a comparative study of older (age 60+ years) English and Brazilian cohorts generated notably higher PAFs for the former compared to the latter: a PAF of 5.6% for the English cohort (broadly comparable to the PAF for those aged 50-89 years in

the HSE in our study (albeit defined quite differently)) compared to 0.9% for the Brazilian[43]. Finally, Stringhini et al calculated and compared PAFs for a range of risk factors (including obesity) from multiple cohorts across the globe[44]. There was a considerable difference between the male (-5.6%) and female (3.5%) obesity-related PAFs, highlighting a limitation of our own study in not using sex-specific HRs and PAFs.

Conclusions

Changes to BMI (including, in particular, increases in obesity) between the mid-1990s and late 2000s are likely to have made a contribution to the stalled trends in mortality observed from around 2012 in both Scotland and England. However, a number of uncertainties are associated with the available data and cautious interpretation of our results is therefore required. The results are likely to be overestimates: thus the majority of the stalled trends is explained by other factors, most likely austerity policies. Action is therefore urgently needed to address both issues: to protect the income (and therefore the health) of the poorest and most vulnerable in society, and to counter the negative consequences, and the structural and commercial determinants, of the obesogenic environment in the UK.

(3,039 words (excluding tables))

FIGURE CAPTIONS

Figure 1. Trends in the percentage of adults (aged 16+ years) classed as obese (BMI 30+), Scotland (from the Scottish Health Survey (SHeS)) and England (from the Health Survey for England), 1995-2019.

Figure 2. Observed, predicted and BMI-adjusted European age-standardised mortality rates (EASRs), Scotland 1991-2019. Note different y-axis scales for males and females.

Figure 3. Observed, predicted and BMI-adjusted European age-standardised mortality rates (EASRs), England 1991-2019. Note different y-axis scales for males and females.

What is already known on this subject?

- Concerning changes in mortality rates have been observed across the UK since the early 2010s: a stalling of improvement overall, and increasing death rates among socioeconomically deprived populations.
- While UK Government austerity measures have been shown to be the most likely explanation, prior increases in obesity levels have also been proposed as a potential contributory factor.

What this study adds?

- For the first time, we quantify the potential contribution of increasing obesity levels to the changes in overall mortality in Scotland and England.
- In Scotland 10% (males) and 14% (females) of the difference between observed and predicted mortality rates in 2017-19 may be attributable to prior increases in obesity.
- In England the figures are notably larger: 20% and 35% respectively.

ACKNOWLEDGEMENTS

We are grateful to the organisations who supplied the required data: National Records of Scotland (NRS); the Office for National Statistics (ONS); and the UK Data Service (for access to the Scottish Health Survey and Health Survey for England data). Particular thanks also to Prof. Krishnan Bhaskeran at the London School of Hygiene and Tropical Medicine for assistance in accessing the data for some of the sensitivity analyses.

DECLARATIONS

Funding: No specific funding was obtained for this work. GM has recently received funding from the WHO.

Contributions: The study was conceived jointly between GM, ET and DW. The research questions and analysis plan were agreed by all authors. DW undertook all analyses and drafted the manuscript. All authors provided substantial critical input to improve the manuscript and all authors approved the final draft.

Competing interests: None declared

Ethical approval: None required (we use secondary data sets: mortality and population counts, and published national survey data).

Data availability: No additional data available

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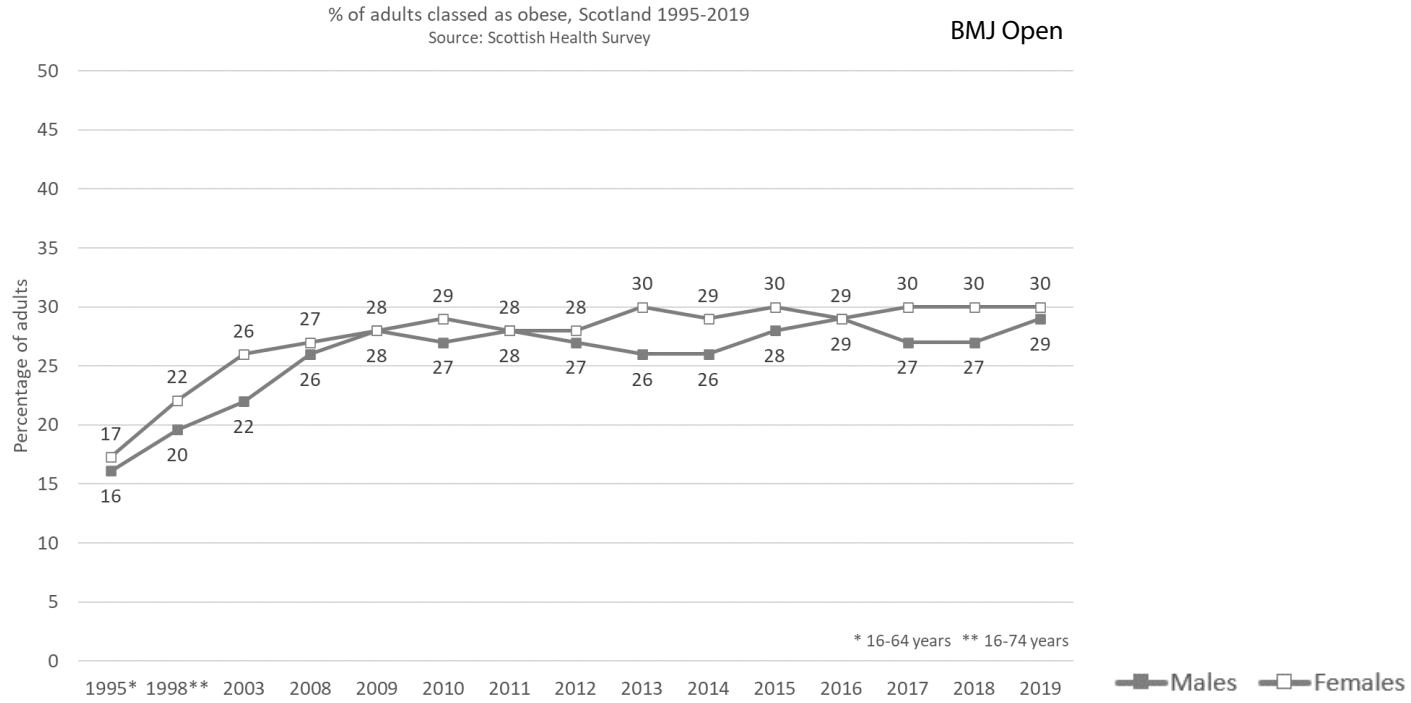
a) Scotland



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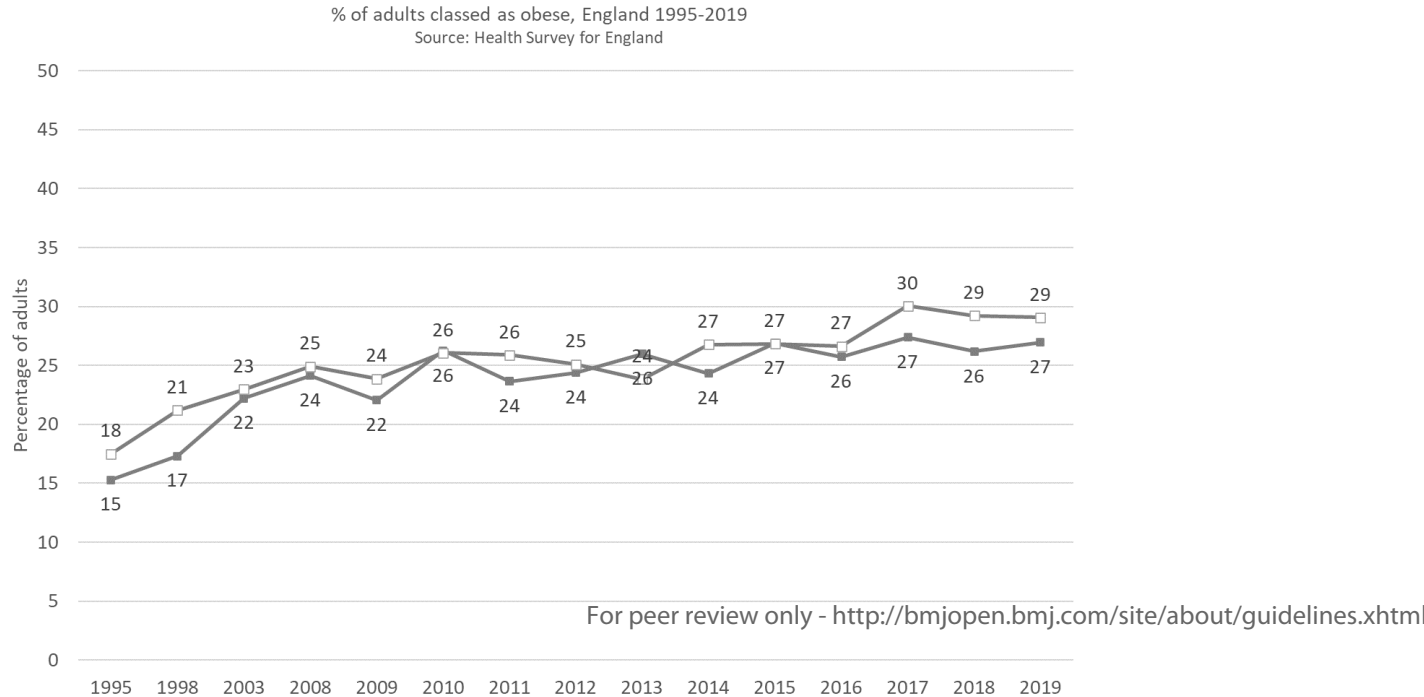
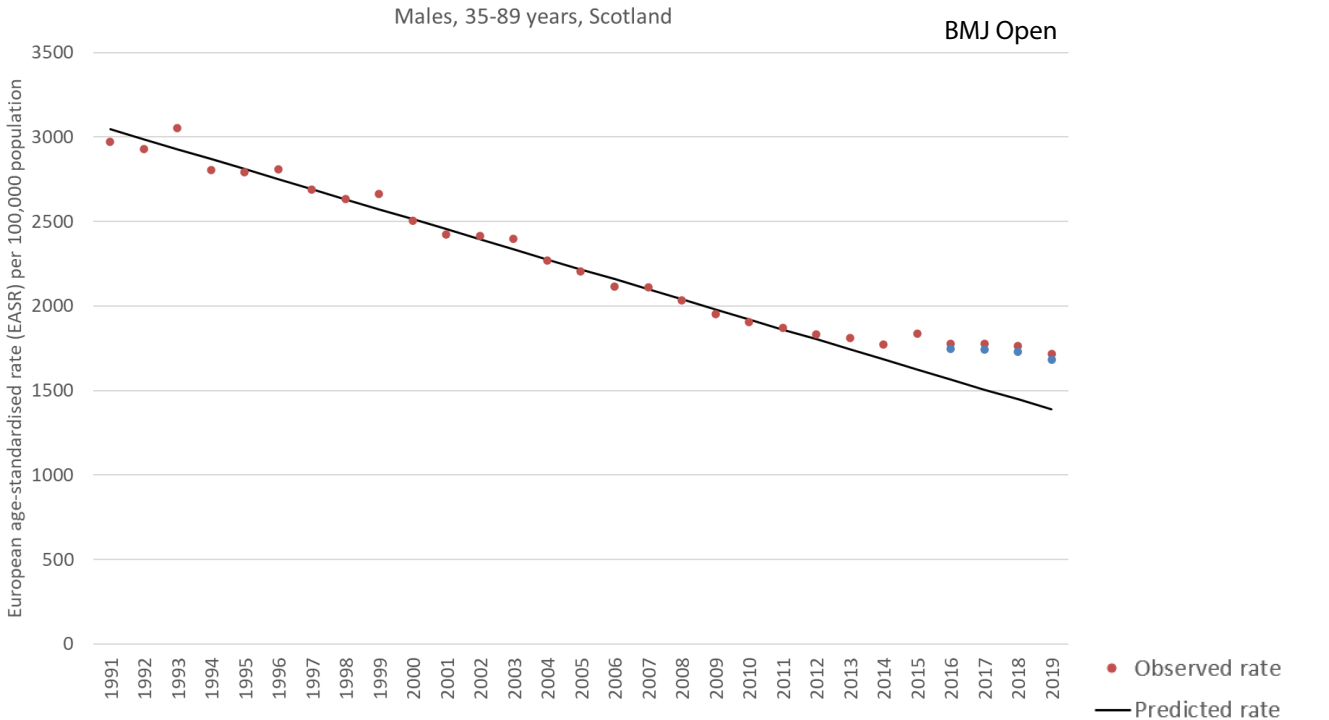


a) Males



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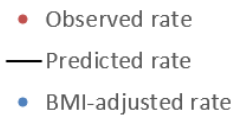
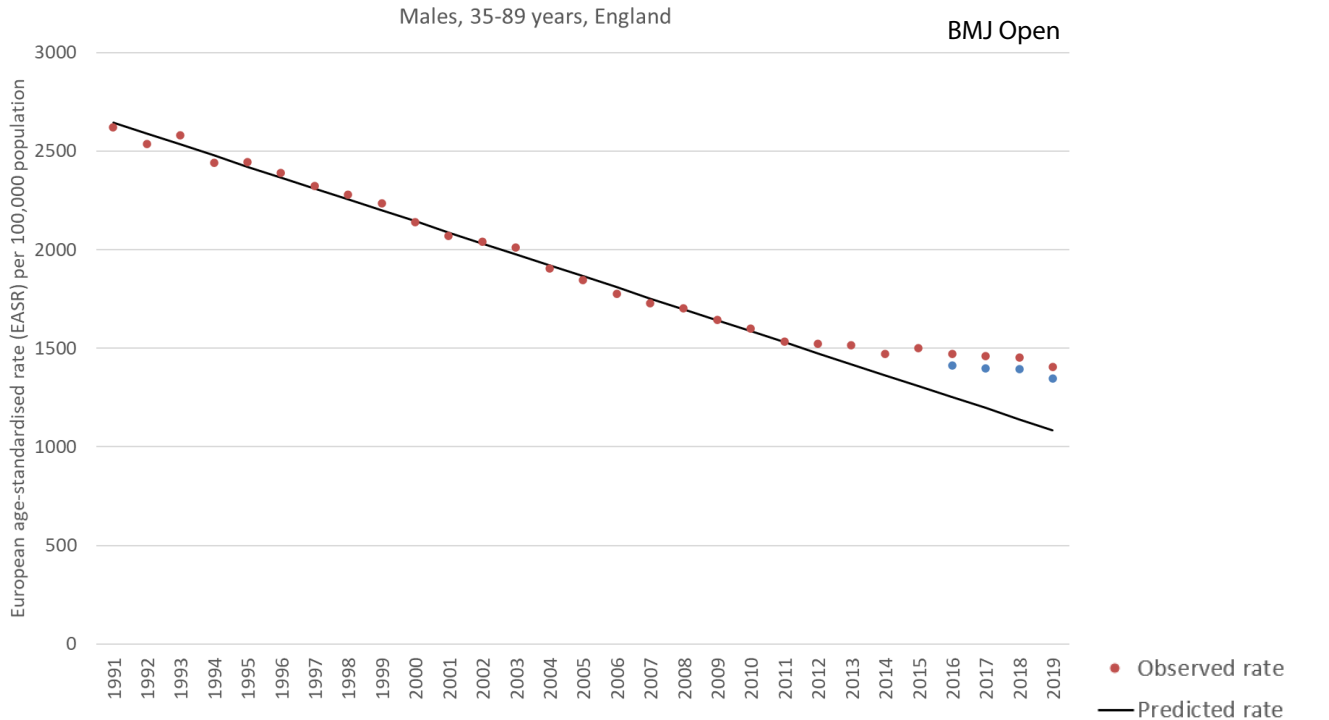


a) Males



b) Females

Online appendix

Supplementary tables

Supplementary Table S1.

Hazard ratios for BMI categories by age group from The Global BMI Mortality Collaboration (GBMC) 2016 study[1]. *Taken from eTable 11 (European studies only).*

Age group (years)	Underweight (BMI 15 to <18.5)	Normal weight (BMI 18.5 to <25)	Overweight (BMI 25 to <30)	Obesity Grade I (BMI 30 to <35)	Obesity Grade II (BMI 35 to <40)	Obesity Grade III (BMI 40 to <60)
35-49	1.86	1.00	1.17	1.90	3.01	5.34
50-69	2.25	1.00	1.11	1.60	2.23	4.04
70-89	1.65	1.00	0.98	1.12	1.56	1.91

Supplementary Table S2.

Sample sizes for 35-89 year-olds in 1995 and 2008, Scottish Health Survey (SHeS) and Health Survey for England (HSE).

Age group	SHeS 1995	SHeS 2008	HSE 1995	HSE 2008
35-49	2,381	1,532	3,918	3,547
50-69*	1,801	1,628	3,973	3,692
70-89	0†	669	1,831	1,507
Total	*4,182*	*3,829*	*9,722*	*8,746*

Methodological note: BMI category proportions for 65-69 and 70-89 years for 1995 SHeS (which only sampled 16-64 years) were derived from analysis of 2003 SHeS data (the first survey that included a sample of all adults aged 16+). Thus, for each BMI category the difference in proportions between 15-64 years and 15-69 years in 2003 were applied to 1995 data for 15-64 years to give a likely estimate for 15-69 years. Similarly, the differences in each category between 50-69 years and 70-89 years in the 2003 survey were then applied to 1995 data to provide an estimate for 70-89 years.

* 50-64 years in 1995 SHeS: in 2003 SHeS there were 1,975 in this age group, including 1,573 in the 50-64 group (as described above, these data were used to derive estimates for 1995)

† Sample size in 2003 SHeS (used to derive estimates for 1995) was 779.

Supplementary Table S3.

Hazard ratios for BMI categories by age group approximated from Bhaskaran et al[2] (sensitivity analyses).

Age group (years)	Underweight (BMI 15 to <18.5)	Normal weight (BMI 18.5 to <25)	Overweight (BMI 25 to <30)	Obesity Grade I (BMI 30 to <35)	Obesity Grade II (BMI 35 to <40)	Obesity Grade III (BMI 40 to <60)
16-49	1.73	1.00	1.27	1.65	2.31	2.84
50-69	1.79	1.00	1.12	1.43	1.89	2.54
70-79	1.88	1.00	1.03	1.27	1.63	2.34
80+	1.25	1.00	0.96	1.07	1.24	1.56

Methodological note: HRs by age group for the same BMI categories used in the GBMC paper were not available. Instead, values were approximated from the Bhaskaran et al paper's Figure 3b ('Association between BMI and all-cause mortality among never-smokers by age') using DigitizeIt software (www.digitizeit.de): the latter enabled extraction of approximate data values from the Figure. For each BMI category, the mid-point of the associated HR range was used; this was done separately for each age group‡. As the Figure presented logHR values, the extracted data were also exponentiated.

Supplementary Table S4.

Population attributable fractions (PAFs) by age group (main analyses).

Age group (years)	Scotland (SHeS)	England (HSE)
35-49	0.116	0.115
50-69	0.071	0.071
70-89	-0.008	0.028

‡Note that for the highest BMI category (Grade III obesity), the mid-point between BMI 40 and the maximum BMI value was used (as BMI values did not exceed 50 in the sample).

Supplementary Table S5.

Comparison of main analyses using 1981-, 1991- and 2001-based mortality projections (2017-19 mortality data)

	Observed rate	BMI-adjusted rate		Projected rate (1981)	% of observed-projected difference attributable to BMI change		Projected rate (1991)	% of observed-projected difference attributable to BMI change		Projected rate (2001)	% of observed-projected difference attributable to BMI change
Scotland, males	1750.7	1718.8		1503.7	12.9%		1447.1	10.5%		1423.7	9.8%
Scotland, females	1268.0	1248.3		1147.4	16.3%		1122.8	13.6%		1106.7	12.2%
England, males	1438.5	1378.6		1183.9	23.5%		1140.6	20.1%		1143.8	20.3%
England, females	1013.5	972.6		927.4	47.5%		896.2	34.9%		847.6	24.7%

Supplementary Table S6.

Population attributable fractions (PAFs) by age group using HRs approximated from Bhaskaran et al (sensitivity analyses).

Age group (years)	Scotland (SHeS)	England (HSE)
16-49	0.069	0.055
50-69	0.050	0.046
70-79	0.026	0.043
80+	-0.077	0.004

Supplementary Table S7.

Comparison of main results with sensitivity analyses using PAFs calculated from HRs approximated from Bhaskaran et al and applied to different age-specific mortality analyses, England 2017-19 (and using 1991-based mortality projections).

Methodological note: the PAFs shown in Table S6 above were applied to different age groups in the mortality analysis. For direct comparison with the main results, they were applied to the same 35-89 age band. However, as HRs were available for ages 16-80+ years, they were additionally applied to mortality data with corresponding ages (15 years+, as mortality data were accessed in five year age bands). Further sensitivity analyses restricted the age group to 15-84 years. Results are shown below for England only.

	% observed-projected difference attributable to BMI change			
	Main analyses (35-89 years using GBMC HRs)	Bhaskaran et al HRs, 35-89 years	Bhaskaran et al HRs, 15-84 years	Bhaskaran et al HRs, 15+ years
Males	20.1%	16.4%	15.1%	13.2%
Females	34.9%	28.9%	25.9%	22.9%

Supplementary Table S8.

Population attributable fractions (PAFs) by age group using three-year averages instead of single years (sensitivity analyses).

Methodological note: for English data, comparisons were made between the single year approach (i.e. the change in BMI distribution between 1995 and 2008) and three year averages around those single years (i.e. 1994-96 and 2007-09). This was not possible for Scottish data: there were no surveys run in 1994, 1996 or 2007; thus, comparisons were instead made between 1995 and 2008, and 1995 and 2008-10.

Age group (years)	Scotland (SHeS) 1995 and 2008-10	England (HSE), using 1994-96 and 2007-09
35-49	0.124	0.108
50-69	0.076	0.072
70-89	-0.006	0.023

Supplementary Table S9.

Comparison of main results with sensitivity analyses using PAFs derived from 2008-10 instead of 2008 in the Scottish Health Survey, and applied to analyses of 2017-19 Scottish mortality data (using 1991-based mortality projections).

See methodological note for Supplementary Table S8.

			Main analyses (1995 and 2008)		Sensitivity analyses (1995 and 2008-10)	
	Observed rate	**Projected rate (1991)**	**BMI-adjusted rate**	**% of observed-projected difference attributable to BMI change**	**BMI-adjusted rate**	**% of observed-projected difference attributable to BMI change**
Males	1750.7	1447.1	1718.8	10.5%	1713.1	12.4%
Females	1268.0	1122.8	1248.3	13.6%	1244.4	16.3%

Supplementary Table 10.

See methodological note for Supplementary Table S8.

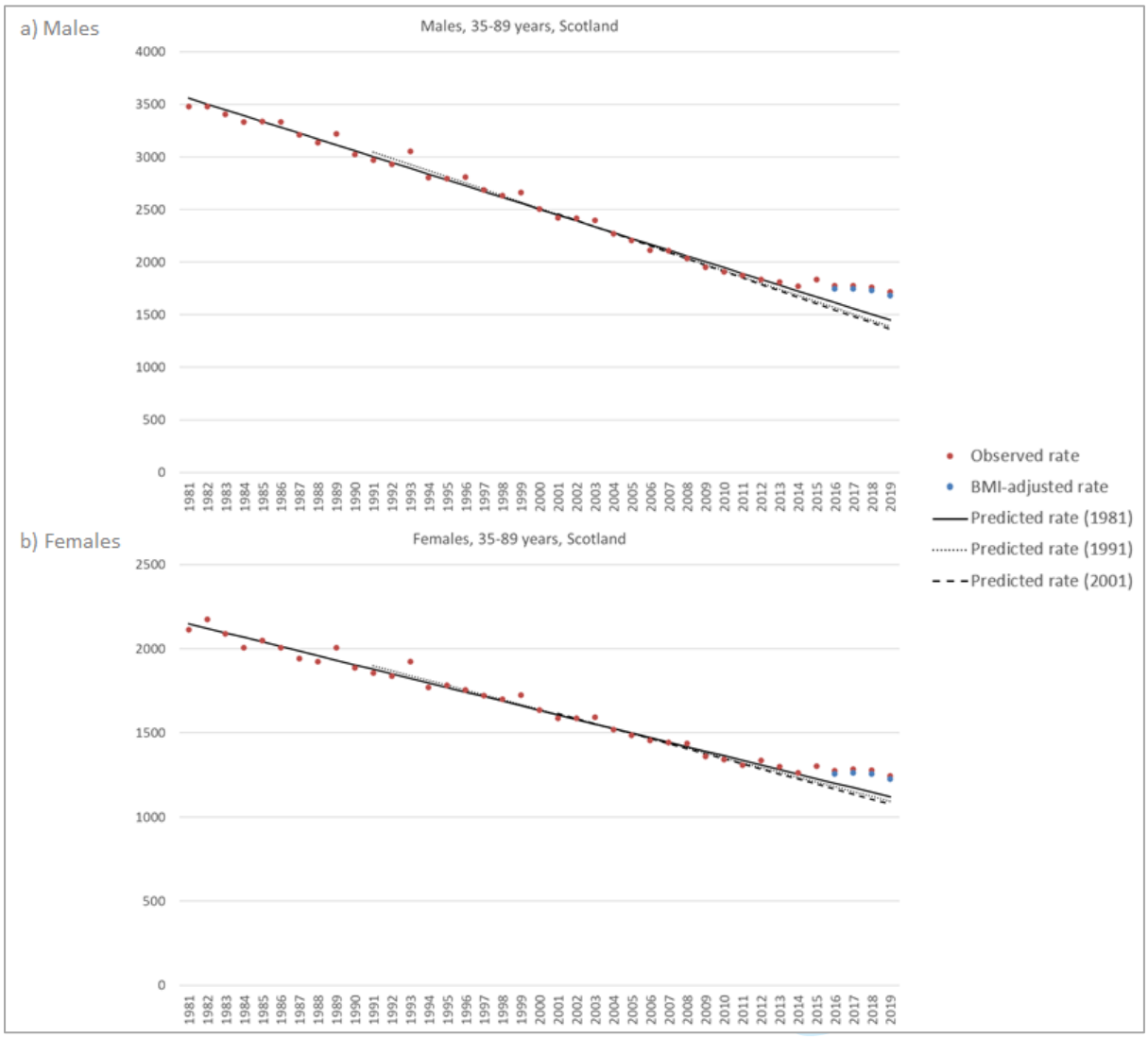
Comparison of main results with sensitivity analyses using PAFs derived from 1994-96 and 2007-09 instead of 1995 and 2008 respectively in the Health Survey for England, and applied to analyses of 2017-19 English mortality data (using 1991-based mortality projections)

			Main analyses (1995 and 2008)		Sensitivity analyses (1994-96 and 2007-09)	
	Observed rate	**Projected rate (1991)**	**BMI-adjusted rate**	**% of observed-projected difference attributable to BMI change**	**BMI-adjusted rate**	**% of observed-projected difference attributable to BMI change**
Males	1438.5	1140.6	1378.6	20.1%	1383.8	18.4%
Females	1013.5	896.2	972.6	34.9%	976.3	31.7%

Supplementary Figures

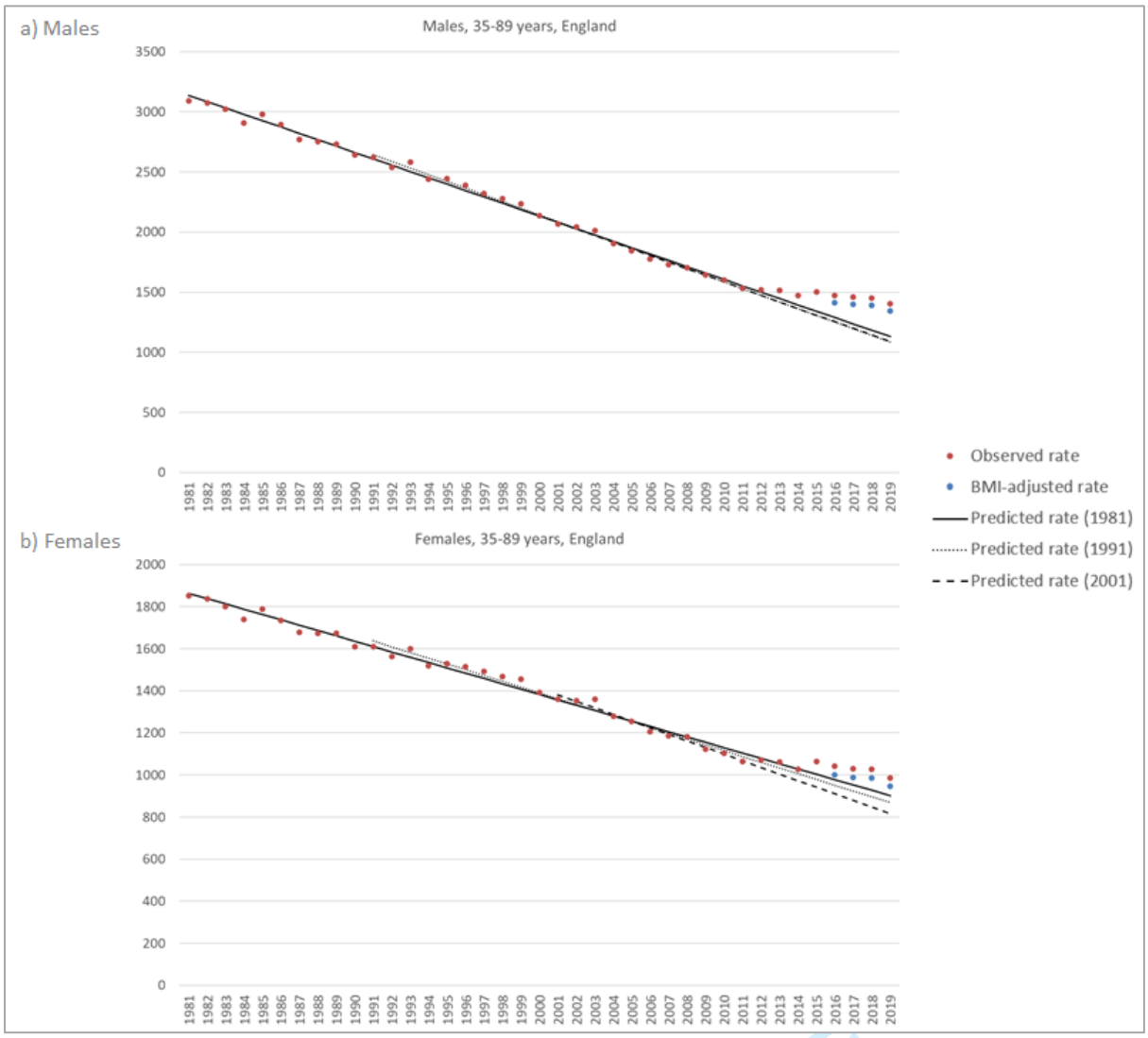
Supplementary Figure S1.

Observed, predicted and BMI-adjusted European age-standardised mortality rates (EASRs), Scotland 1981-2019 –comparing 1981-, 1991- and 2001-based predictions. Note different y-axis scales for males and females.



Supplementary Figure S2.

Observed, predicted and BMI-adjusted European age-standardised mortality rates (EASRs), Scotland 1981-2019 –comparing 1981-, 1991- and 2001-based predictions. Note different y-axis scales for males and females.

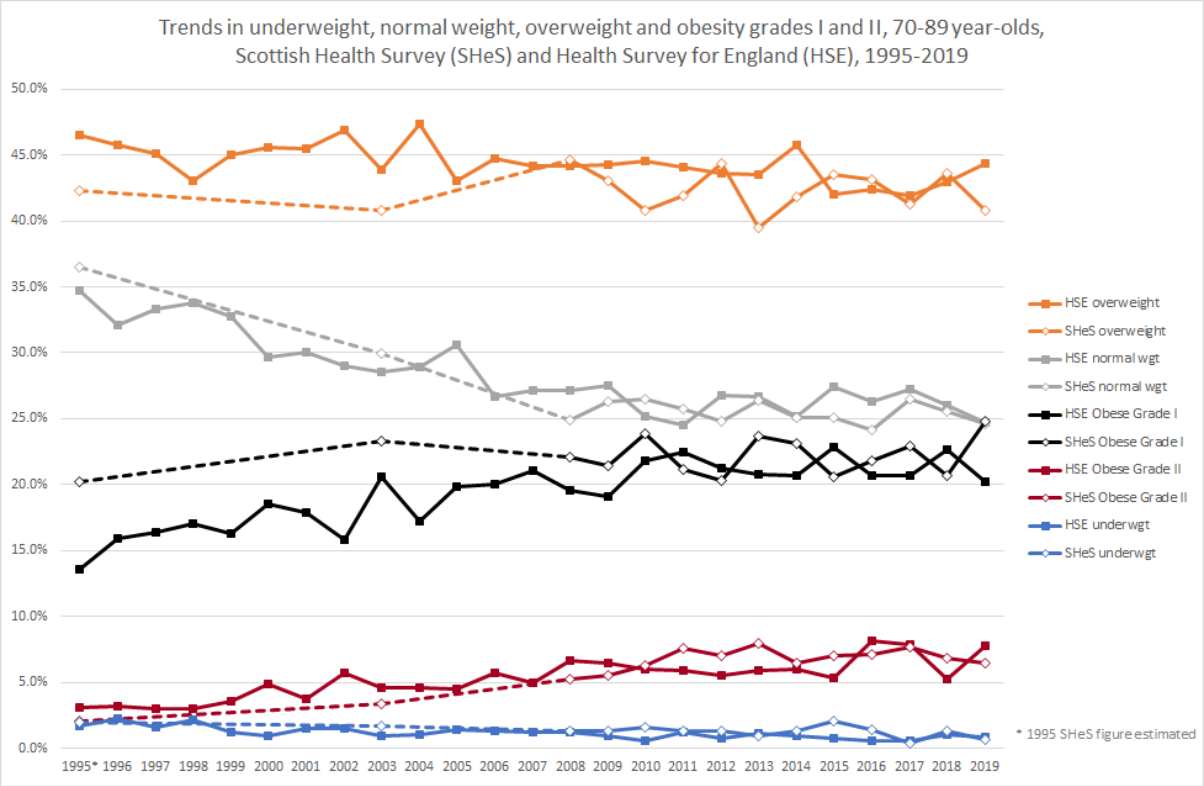


Supplementary Figure S3.

Trends in the percentage of adults aged 70-89 years classed as Obese Grade I (BMI 30 to <35), Scotland, 1995-2019

Supplementary Figure S4.

Trends in the percentage of adults aged 70-89 years in different BMI categories, Scotland and England, 1995-2019



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[1] Global BMI Mortality Collaboration. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. Lancet 2016; 388(10046): 776-86

[2] Bhaskaran K., Dos-Santos-Silva I., Leon D.A., Douglas I.J., Smeeth L. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UK. Lancet Diabetes Endocrinol. 2018; 6(12): 944-953

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5-7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-7
		(*b*) Describe any methods used to examine subgroups and interactions	5-7
		(*c*) Explain how missing data were addressed	n/a
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	7

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6 (and Supplementary Table S2)
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	n/a (total population)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	7-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-10
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at

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BMJ Open

How much of the stalled mortality trends in Scotland and England can be attributed to obesity?

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-067310.R1
Article Type:	Original research
Date Submitted by the Author:	17-Nov-2022
Complete List of Authors:	Walsh, David; Glasgow Centre for Population Health Tod, Elaine; Public Health Scotland Glasgow Office McCartney, Gerry; University of Glasgow; Public Health Scotland Glasgow Office, Clinical and Protecting Health Levin, Kate Ann; NHS Greater Glasgow and Clyde
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health
Keywords:	PUBLIC HEALTH, SOCIAL MEDICINE, EPIDEMIOLOGY

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How much of the stalled mortality trends in Scotland and England can be attributed to obesity?

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Keywords: obesity, mortality, 'population attributable fractions', austerity, Scotland, England

Abstract

Objectives

The rate of improvement in all-cause mortality rates has slowed in the UK since around 2012. While evidence suggests that UK Government 'austerity' policies have been largely responsible, it has been proposed that rising obesity may also have contributed. The aim here was to estimate this contribution for Scotland and England.

Methods

We calculated population attributable fractions (PAFs) resulting from changes in Body Mass Index (BMI) between the mid-1990s and late 2000s for all-cause mortality among 35-89 year-olds in 2017-19. We used BMI data from national surveys (the Scottish Health Survey and the Health Survey for England), and hazard ratios (HRs) from a meta-analysis of 89 European studies. PAFs were applied to mortality data for 2017-19 (obtained from national registries), enabling comparison of observed rates, BMI-adjusted rates and projected rates. Uncertainty in the estimates is dominated by the assumptions used and biases in the underlying data, rather than random variation. A series of sensitivity analyses and bias assessments were therefore undertaken to understand the certainty of the estimates.

Results

In Scotland, an estimated 10% (males) and 14% (females) of the difference between observed and predicted mortality rates in 2017-19 may be attributable to previous changes in BMI. The equivalent figures for England were notably higher: 20% and 35% respectively. The assessments of bias suggest these are more likely to be overestimates than underestimates.

Conclusions

Some of the recent stalled mortality trends in Scotland and England may be associated with earlier increases in obesity. Policies to reduce the obesogenic environment, including its structural and commercial determinants, and reverse the impacts of austerity, are needed.

(264 words)

Strengths and limitations of this study

- We calculate population attributable fractions (PAFs) for the change in body mass index (BMI) (including obesity) for the populations of Scotland and England, using measured (not self-assessed) BMI data from nationally representative health surveys.
- We compare observed mortality rates, BMI-adjusted mortality rates, and projected mortality rates in 2016-19 to estimate the proportion of recent changes in mortality that is likely to be attributable to earlier changes in BMI (including increases in obesity).
- Weaknesses include a lack of socioeconomic stratification: as recent changes in mortality rates in Scotland and England have been more profound among socioeconomically deprived populations, this would have been an important addition to the analyses.
- While the use of nationally representative survey data represents a general strength of the methodology, declining response rates also present challenges to interpretation, and introduce potential biases.

INTRODUCTION

Deeply concerning changes to mortality rates have been observed across the UK since the early 2010s: population average mortality rates have stopped improving, whilst mortality rates among poorer populations have increased [1-5]. Such changes have been seen for many different causes of death, with cardiovascular mortality particularly affected [6,7]. Similar stalled mortality trends have been recorded in other high-income countries.

While the causes of these changes in the UK have been debated, a large body of evidence now suggests that UK Government 'austerity' measures, implemented in 2010 following 'the great recession' of 2008 and which have disproportionately affected the poorest in society, are largely to blame [8-14]. The impact of similar austerity measures in slowing mortality improvement in other countries has also been demonstrated [15-18].

However, it has also been proposed that these trends may have additionally been influenced by changes in levels of adult obesity prevalence: this has been suggested in relation to the UK [19], the US [20-21, Australia [21] and elsewhere [22]. This is largely because of two factors. First, there is a clear association between obesity and both cause-specific (including cardiovascular disease) and all-cause mortality, with the weight of evidence suggesting this relationship is causal [23]. Second, considerable increases in obesity prevalence have been recorded in the UK (and elsewhere) in recent decades [24], and these pre-date the more recent changes to all-cause mortality discussed above. While this hypothesis appears plausible, it has not yet been tested. The aim of this study, therefore, was to assess, and quantify, the extent to which any of the mortality changes observed in Scotland and England since the early 2010s may be attributable to prior increases in obesity levels in the population.

METHODS

Populations and data sources

We used data for the populations of Scotland and England: the change in mortality rates since 2012 has been similar in both countries, and trend data on adult obesity prevalence are available for both.

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. Data on adult body mass index (BMI) distribution in the populations were accessed from the Scottish Health Survey (SHeS) and the Health Survey for England (HSE) via the UK Data Service [25-27]. Both are long-running (from the early-to-mid 1990s to the present day), nationally-representative, surveys which include measured (rather than self-reported) height and weight (from which BMI is calculated) for large samples of the adult population. In 2008 (the last year of data employed here), adult sample sizes were approximately 6,500 (SHeS) and 15,000 (HSE), with household response rates of 61% and 64% respectively [28,29]. 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.

Statistical analyses

Population attributable fractions (PAFs) were calculated for changes in BMI distribution (including therefore the increase in overweight and obesity) between the mid-1990s and late 2000s in relation to all-cause mortality among 35-89 year-olds. PAFs are defined as the proportion of cases (here, all-cause deaths) attributable to a particular exposure [30]: in this case the latter is defined as the change in BMI distribution over time. The 35-89 year age

group was determined by the availability of age-specific hazard ratios (HRs): we used previously-published HRs from a meta-analysis of 89 European studies of BMI and all-cause mortality undertaken by the Global BMI Mortality Collaboration (GBMC) [23]. To reduce the risk of confounding and reverse causality, the GBMC meta-analysis excluded smokers, those with chronic disease at time of recruitment, and participants who died within the first five years of follow-up. HRs were available for six BMI categories and three age groups (35-49 years, 50-69 years, 70-89 years) (Supplementary Table S1), and were based on c.14 years' follow-up. The PAF calculation was based on comparison of the BMI distribution in 1995 (the earliest time point available for the Scottish data) and 2008: this covers the period of considerable increase in obesity in both Scotland and England (discussed further below), and also broadly fits with both the c.14 year follow-up period on which the HRs calculation was based, and the later period of stalling improvement in mortality in both countries. PAF was therefore calculated as:

$$PAF = \frac{[\sum(p2008\ BMI\ category\ i \times HRi) - \sum(p1995\ BMI\ category\ i\ \times HRi)]}{\sum(p2008\ BMI\ category\ i\ \times HRi)}$$

The 1995 SHeS only sampled adults aged 16-64 years; data for 65-89 years were therefore estimated from age-specific distributions in 2003 (the first survey that included all adults aged 16+ years). 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.

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): this enabled calculation and comparison of *observed* mortality rates with *BMI-adjusted* rates (i.e. excluding deaths attributable to the change in BMI distribution).

These were then further compared with *projected* rates (i.e. the rates that were predicted had the stalling of improvement not occurred): the latter were calculated for 2011-2019 based on linear trends. Three sets of projections were produced: 1981-based (i.e. based on the linear trend for 1981-2010), 1991-based and 2001-based. All rates were age-standardised using the 2013 European Standard Population [31], and stratified by sex and country.

A range of sensitivity analyses were undertaken. These included the use of survey data for three-year averages instead of single year points (e.g. 1994-96 average instead of 1995), and employing different HRs for different age groups in the calculation of the PAFs: the latter HRs were approximated from a large English study of over 3.5 million adults with c.18 years follow-up, and which employed similar exclusion criteria as the GBMC study (Supplementary Table S3) [32]. Those PAFs were also applied to different age groups in the mortality analyses. Analyses of age-specific trends were undertaken to explore differences in the PAFs between Scotland and England.

An assessment of the scale and direction of any likely bias was informed by reviews of relevant PAF-based literature.

Patient and Public Involvement

Patients and the public were not involved in this study.

RESULTS

As context to the main results, Figure 1 presents trends in adult obesity prevalence in Scotland and England between 1995 and 2019. In 1995 the overall prevalence was approximately 16% in both countries; by 2019 it had increased to 28-29% (with female rates slightly higher than male rates). However, the biggest increases took place between the mid-

1990s and the late 2000s, with much smaller increases seen in the later period: for example, for males in England, and males and females in Scotland, prevalence increased by only 1-2 percentage points between 2010 and 2019.

[Figure 1 about here]

The calculated PAFs by age group and country are shown in Supplementary Table S4. The age-specific values were broadly similar for both countries with the exception of the oldest age group (70-89 years) where the PAF was small but positive for English data (0.029) and small but negative (-0.008) for the Scottish data. This is discussed further below.

Figures 2 and 3 compare the observed European age-standardised mortality rates (EASRs) for 35-89 year-olds with the BMI-adjusted EASRs and the 1991-based projected EASRs. Data are shown separately for males and females in Scotland (Figure 2) and England (Figure 3). The divergence between projected and observed rates is clear in all cases and has widened over time; it is greater for males than females. In all cases the gap in each year is reduced by the BMI-adjusted EARS, but to a greater extent in England than in Scotland.

[Figures 2 & 3 about here]

Table 1 quantifies the differences shown in Figures 2 and 3 above. It presents the three sets of EASRs (observed, projected, and BMI-adjusted) as well as a comparison of the observed-projected gap with the BMI-adjusted-projected gap: this can be interpreted as the amount of the observed-projected gap that can be potentially attributed to the change in BMI between 1995 and 2008. Data are shown annually for 2016-19, with – for simplicity – average figures for the most recent three-year period also presented.

This shows that for Scottish males, the average observed EASR for 2017-19 was 1751 (95% CIs 1729 to 1773). This reduced marginally to 1719 (95% CIs 1697 to 1741) after adjustment for the change in BMI (in effect, excluding the increase in overweight- and obesity-related

deaths), but was still notably higher than the projected EASR of 1447 (95% CIs 1427 to 1467). The change in BMI therefore potentially 'explained' 10.5% of the difference between the observed and projected rates. For females, 13.6% of the difference could be attributed in this manner. However, the figures for England were notably higher: average figures of 20.1% for males and 35.1% for females.

	Males						Females				
	Year	**Observed rate**	**BMI-adjusted rate**		**Projected rate (1991)**	**% of observed-projected difference attributable to change in BMI**	**Observed rate**	**BMI-adjusted rate**		**Projected rate (1991)**	**% of observed-projected difference attributable to change in BMI**
Scotland	2016	1777.7	1744.9		1565.6	15.5%	1276.2	1257.0		1180.3	20.0%
	2017	1775.7	1744.4		1506.3	11.6%	1282.8	1263.7		1151.6	14.5%
	2018	1762.1	1729.9		1447.1	10.2%	1277.0	1257.3		1122.8	12.8%
	2019	1716.3	1684.0		1387.8	9.8%	1245.1	1224.9		1094.1	13.4%
	2017-19	*1750.7*	*1718.8*		*1447.1*	*10.5%*	*1268.0*	*1248.3*		*1122.8*	*13.6%*
England	2016	1472.1	1411.2		1252.0	27.7%	1042.1	1000.1		951.1	46.2%
	2017	1459.7	1399.2		1196.3	23.0%	1029.2	987.8		923.6	39.2%
	2018	1453.1	1392.6		1140.6	19.4%	1026.7	985.2		896.2	31.8%
	2019	1404.2	1345.7		1084.9	18.3%	985.5	945.5		868.8	34.2%
	2017-19	*1438.5*	*1378.6*		*1140.6*	*20.1%*	*1013.5*	*972.6*		*896.2*	*34.9%*

Table 1. Comparison of observed, projected and BMI-adjusted age-standardised mortality rates per 100,000 population among 35-89 year-olds, Scotland and England, 2016-19.

The gap between the observed and projected EASRs is smaller when using 1981-based projections, and greater when using 2001-based projections. These are shown in Supplementary Figures S1 and S2, and quantified further in Supplementary Table S5.

The use of the different HRs and different age groups in sensitivity analyses resulted in lower PAFs (Supplementary Table S6). Consequently, less of the difference between observed and projected mortality rates could be attributed to changes in BMI than was the case in the main analyses. For example, the 20.1% figure for males in England shown in Table 1 was reduced to 16.4% when applied to the same 35-89 age band in the mortality analyses, to 15.1% when applied to 15-84 years, and to 13.2% when applied to 15+ years. Similar reductions of between approximately a third and a fifth were shown for females in England (Supplementary Table S7).

Additional analyses to explore the difference in the PAFs for the oldest age group in Scotland (negative) and England (positive) suggested that it was partly explained by a smaller increase in Grade I obesity in Scotland. In England, the prevalence in this age group increased by 44% from 13.6% to 19.6% between 1995 and 2008; in Scotland, the prevalence was already higher in 1995 (20.2%) and only increased marginally to 22.0% in 2008. A greater increase in Scotland would have resulted in a positive, rather than negative, PAF (data not shown). Given that the 70-89 years age group was not sampled in the 1995 SHeS, with estimates instead derived from proportions in the 2003 survey, the accuracy of these figures is uncertain. However, analyses of long-term trends for this age group showed that trends have fluctuated between approximately 20% and 24% in most years, and in that context the derived estimate for 1995 seems plausible (Supplementary Figure S3). Furthermore, comparison with English trends support the observation of higher Grade I obesity in this age group: despite considerable fluctuation in rates over time, levels were higher in Scotland in 9 of the 13 available data points between 2003 and 2019 (Supplementary Figure S4).

Despite such fluctuations in rates, only marginal differences in results were observed when using three-year averages rather than single years in the calculation of PAFs across all age groups (Supplementary Tables S8-S10).

The assessment of potential biases is shown in Table 2. Of the ten sources of potential bias listed, five suggest potential overestimation of effect size, two suggest underestimation, and the remaining three are unclear. In the majority of cases the size of any bias is either small or unclear. The implication is that the estimates produced are more likely to be overestimates of the contribution of obesity rather than underestimation, but this is uncertain.

	Source of potential bias	Direction	Magnitude	Notes
1	BMI treated as categorical rather than continuous data	Unclear	Small	The 'proportional shift' method (the use of categorical rather than continuous data in the calculation of attributable fractions) has been shown to be associated with the potential for both underestimation and overestimation of effect size. However, the greater the number of categories, the lower the risk of such uncertainty [33]: we employ a relatively large number (six) of BMI categories.
2	Declining survey response rates	Underestimation of obesity effect	Unclear	Both surveys are large and deemed nationally representative, and both are weighted to adjust for non-response: however, in the case of the English survey, this weighting was only introduced in 2003, and therefore was not applied to the 1995 data; furthermore, despite the use of such weights, the data may still be potentially affected by a 'healthy respondent' bias [34]. The latter, however, is difficult to quantify.
3	Broad age bands with potential for residual confounding	Overestimation of obesity effect	Unclear	Some of the change in BMI between the two time periods will be due to ageing, and this may not be captured because of the large age bands employed.
4	Exclusion of those aged 16-34 and 90+ years	Underestimation of obesity effect	Small	The exclusion of these sections of the adult population would suggest potential underestimation of effect size, especially given that overweight and obesity levels increased among both age groups between 1995 and 2008 [35]. However, the level of underestimation is likely to be small, given the relatively small number of deaths that occur in the younger age group overall, and the likely number of deaths *from relevant causes* for those aged 90 and above. Furthermore, sensitivity analyses using hazard ratios (HRs) approximated from the Bhaskaran et al study [32] which covered both age groups (the age bands used were 16-49, 50-69, 70-79 and 80+ years) suggested *fewer* deaths were attributable to the change in BMI than was the case using the HRs for 35-89 year-olds only. The calculated PAF for the 80+ years group was also very small in those analyses (e.g. 0.004 for English data).
5	Hazard ratios not generalisable to Scotland and England	Overestimation of obesity effect	Small	The HRs used in the analyses (from the work published by the Global BMI Mortality Collaboration (GBMC)) were calculated from a meta-analysis of 89 European studies, a considerable number of which were from the UK [23]. Assuming no effect modification from country/study-specific context, the HRs should be appropriate for use in our analyses of UK data, despite the higher levels of overweight and obesity observed in the UK.

	Source of potential bias	Direction	Magnitude	Notes
				However, sensitivity analyses using alternative HRs approximated from the study by Bhaskaran et al [32], which were calculated from data for over 3.5 million adults in England (and based on c.18 year follow-up), resulted in smaller PAFs and therefore fewer deaths attributable to BMI changes over time in England, suggesting the use of the GBMC HRs may have slightly overestimated the effect size.
6	Hazard ratios prone to confounding	Overestimation of obesity effect	Unclear	HRs from the GBMC study are not adjusted for socioeconomic deprivation, levels of physical activity or diet, and thus represent a likely overestimation of effect size, albeit one that is difficult to quantify.
7	Changes in BMI due to pre-existing ill-health	Overestimation of obesity effect	Negligible	By excluding smokers and ex-smokers, those with chronic disease at time of recruitment, and participants who died within the first five years of follow-up, the GBMC study (the HRs from which are used here) largely removed this risk.
8	Interpolated data for age 65-89 years in 1995 Scottish survey data	Unclear	Unclear	Analyses comparing the estimated figure for 1995 with observed trend data in other years of the survey do not suggest any obvious inaccuracies, and there are no other data from other Scottish surveys that can be compared. However, the PAF for the 70-89 years age group is negative in the Scottish data (-0.008) but positive in the English data (0.028) which contrasts with the other two age groups where the PAFs are very similar in the two data sets. The extent to which this may relate to the interpolation is unknown.
9	Use of single-year comparison time points in calculation of PAFs	Unclear	Small	Sensitivity analyses using three year averages (1994-96 instead of 1995, and 2007-09 instead of 2008) suggest a minimal impact.
10	Lengthy follow-up period	Overestimation of obesity effect	Unclear	The potential for overestimation of effect size has been highlighted for studies with long follow-up periods on the basis that important 'mediators' (e.g. systolic blood pressure, cholesterol) may decrease over time among those with initially recorded high BMI [36, 37]. It is unclear whether – or to what extent – this may apply here.

Table 2. Assessment of potential biases in calculation of Population Attributable Fractions (PAFs).

DISCUSSION

Overall findings and implications

Our analyses suggest that changes in the BMI distribution in Scotland and England between the mid-1990s and late 2000s may have potentially contributed to the mortality changes observed in both countries since around 2012. In Scotland, an estimated 10% (males) and 14% (females) of the difference between observed and predicted mortality rates among 35-89 year-olds in 2017-19 may be attributable to previous changes in BMI. The equivalent figures for England were notably higher: 20% and 35% respectively. However, there is uncertainty around the accuracy of these estimates: sensitivity analyses and bias assessment suggest the potential for overestimation of effect size, although the degree is difficult to quantify.

Alongside the evidence of the role of UK Government austerity measures in the stalling of mortality improvement in Scotland and England [8-14, 17, 18], this suggests the need for a range of government policies to both reverse the damaging effects of austerity, as well as to address the negative consequences of an increased obesogenic environment in the UK [38].

Strengths and weaknesses

A number of limitations of the study are acknowledged. In relation to the survey data sources, these include: the need to derive estimates for older age bands in the 1995 SHeS (although trend analyses suggest the data are plausible); the lack of non-response weighting in the 1995 HSE, as well as the general decline over time in response rates in all such population surveys; and limited time series data (especially in the Scottish survey). Other limitations include the use of the proportional shift method in calculating the PAFS (although data constraints meant no other method was available), the use of age-specific (rather than age *and* sex specific) HRs (age/sex-specific HRs were not available), and the lack of any

socioeconomic stratification of the analysis: the latter would have been important given that the mortality changes observed in the UK in the past decade have particularly affected more deprived populations [2, 3-5]. Such stratification was not possible for 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. We did not calculate 95% confidence intervals for the PAFs on the basis that this would have misrepresented the key sources of uncertainty in the analyses, which were due to a range of potential biases rather than random variation. It was also difficult to find a means of combining assessment of random variation in each of the underlying data sources (BMI distribution, mortality, projected mortality, HRs), as well as the PAF estimate, that would have adequately represented the random variation. Other weaknesses are also included within Table 2. However, the study also has a number of strengths. Despite their acknowledged limitations, both the SHeS and HSE are important data sources: they are large, nationally representative, surveys which have collected important measured (not self-reported) anthropometric data since the 1990s. The other data sources employed in the analyses were also strengths of the study: detailed mortality data for both countries' whole populations, and HRs from a comprehensive meta-analysis of a large number of European studies of BMI (and the design of which minimised the risk of confounding). We also undertook a range of sensitivity analyses and a detailed assessment of potential biases.

Relevance to other studies

The relationship between obesity and all-cause mortality has been demonstrated in numerous studies [23]. While the weight of evidence suggests that the association is causal, there has been considerable debate about both the extent of causality, and the measures such as PAFs that are used to assess it [36, 39-43]. For example, limitations of PAFs (and obesity-related PAFs in particular) highlighted by Levine [39] include: the flawed nature of 'simple causal partitioning'; the overlapping nature of exposures in a population meaning that different PAFs add up to more than 100% (thus, assessing single exposures in isolation is problematic); the importance of the definition of the exposure, such that a more broadly defined exposure will always increase the size of the PAF (meaning that a high PAF is 'not necessarily indicative of a better scientific understanding of the causes(s) of disease in the population than a low PAF'). Flegal and colleagues have echoed many of these sentiments, also cautioning against interpretations of causality: 'PAFs for obesity may be best considered as indicators of association' [36]. They supported this argument on the basis of a number of definitional and methodological issues, including: the importance of how the counterfactual is defined (with the size of the PAF varying depending on what definition is employed); potential overestimation in long follow-up studies (as alluded to in Table 2); and important differences between studies in how obesity-related PAFs are calculated which make interpretation and comparison of results difficult.

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 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.

Despite these criticisms and pleas for cautious interpretation of PAFs in terms of assessing causality, obesity-related PAFs have been calculated in many studies. This includes recent work by Ho and colleagues who calculated and compared obesity and smoking related PAFs from both data sources employed here: SHeS and HSE [44]. The work suggested that deaths attributable to obesity increased from 18% to 23% between 2003 and 2017, overtaking the number of deaths attributable to smoking in the process. Other studies have demonstrated how different methodological approaches can result in different values of obesity related PAFs. For example, in the Netherlands Vidra et al generated PAFs ranging from 0.9% to 1.8% (two-fold variation) for the same population, but based on different formulae [43]. They also showed that the use of European, rather than global, HRs resulted in a higher PAF – this is relevant to our own study.

Vidra et al's estimates for the Netherlands are clearly much lower than Ho et al's for Scotland and England. Similarly, a comparative study of older (age 60+ years) English and Brazilian cohorts generated notably higher PAFs for the former compared to the latter: a PAF of 5.6% for the English cohort (broadly comparable to the PAF for those aged 50-89 years in the HSE in our study (albeit defined quite differently)) compared to 0.9% for the Brazilian [45]. Finally, Stringhini et al calculated and compared PAFs for a range of risk factors (including obesity) from multiple cohorts across the globe [46]. There was a considerable difference between the male (-5.6%) and female (3.5%) obesity-related PAFs, highlighting a limitation of our own study in not using sex-specific HRs and PAFs.

Conclusions

Changes to BMI (including, in particular, increases in obesity) between the mid-1990s and late 2000s are likely to have made a contribution to the stalled trends in mortality observed from around 2012 in both Scotland and England. However, a number of uncertainties are associated with the available data and cautious interpretation of our results is therefore required. The results are likely to be overestimates: thus the majority of the stalled trends is explained by other factors, most likely austerity policies. Action is therefore urgently needed to address both issues: to protect the income (and therefore the health) of the poorest and most vulnerable in society, and to counter the negative consequences, and the structural and commercial determinants, of the obesogenic environment in the UK.

(3,403 words (excluding tables))

FIGURE CAPTIONS

Figure 1. Trends in the percentage of adults (aged 16+ years) classed as obese (BMI 30+), Scotland (from the Scottish Health Survey (SHeS)) and England (from the Health Survey for England), 1995-2019.

Figure 2. Observed, predicted and BMI-adjusted European age-standardised mortality rates (EASRs), Scotland 1991-2019. Note different y-axis scales for males and females.

Figure 3. Observed, predicted and BMI-adjusted European age-standardised mortality rates (EASRs), England 1991-2019. Note different y-axis scales for males and females.

ACKNOWLEDGEMENTS

We are grateful to the organisations who supplied the required data: National Records of Scotland (NRS); the Office for National Statistics (ONS); and the UK Data Service (for access to the Scottish Health Survey and Health Survey for England data). Particular thanks also to Prof. Krishnan Bhaskeran at the London School of Hygiene and Tropical Medicine for assistance in accessing the data for some of the sensitivity analyses.

DECLARATIONS

Funding: No specific funding was obtained for this work. GM has recently received funding from the WHO.

Contributions: The study was conceived jointly between GM, ET, DW and KAL. The research questions and analysis plan were agreed by all authors. DW undertook all analyses and drafted the manuscript. All authors provided substantial critical input to improve the manuscript and all authors approved the final draft.

Competing interests: None declared

Ethical approval: None required (we use secondary data sets: mortality and population counts, and published national survey data).

Data availability: Data may be obtained from a third party and are not publicly available.

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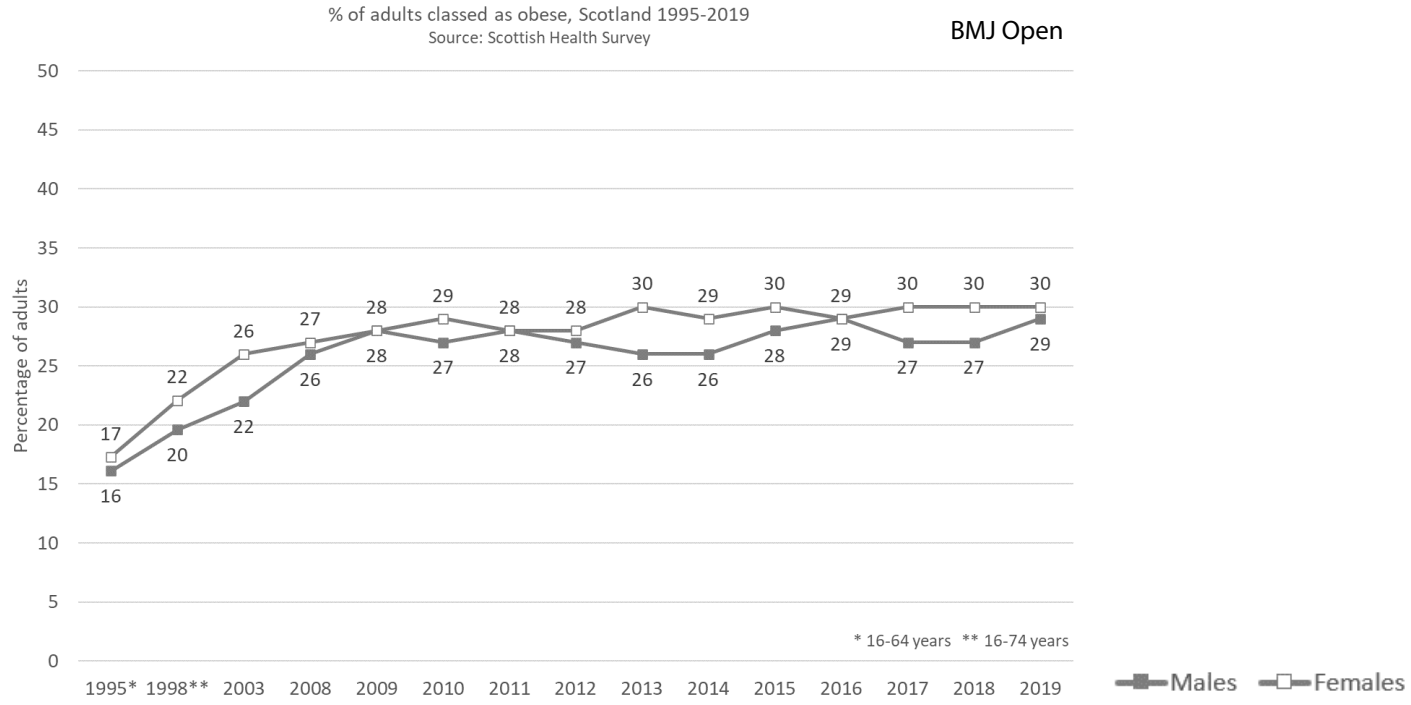
a) Scotland



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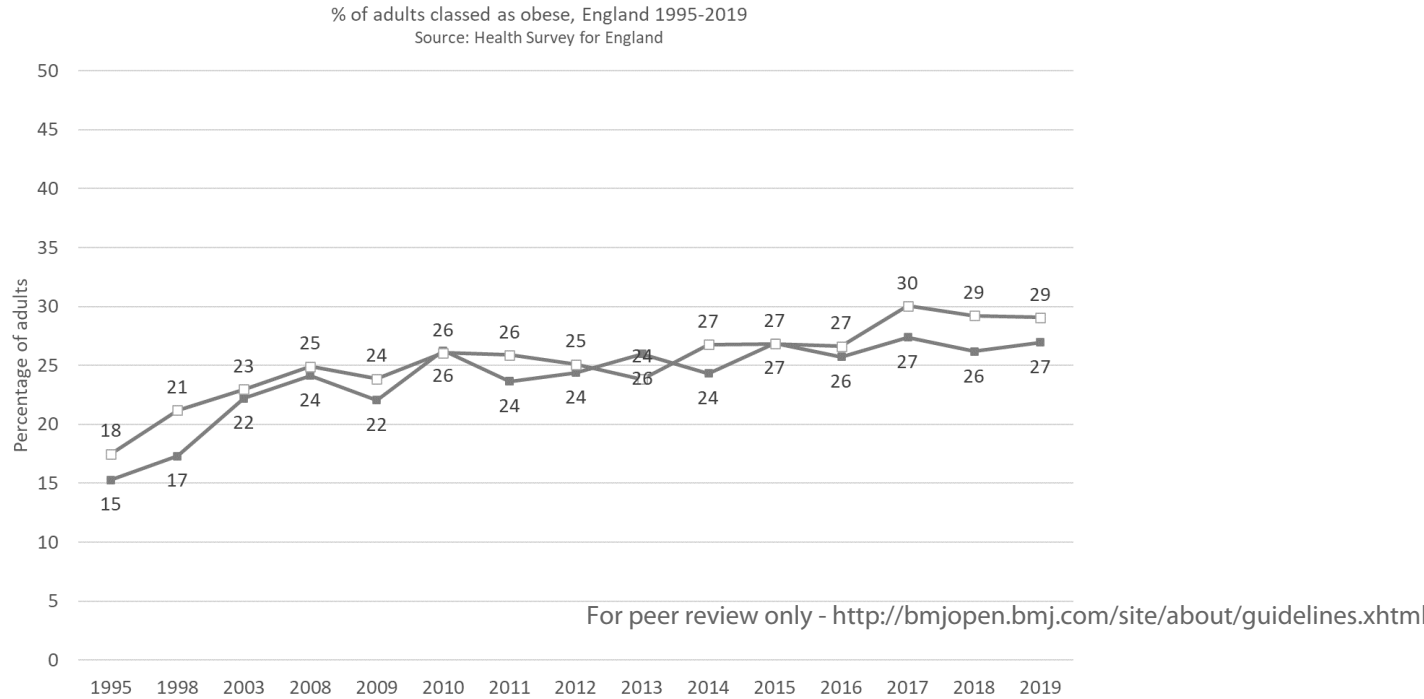
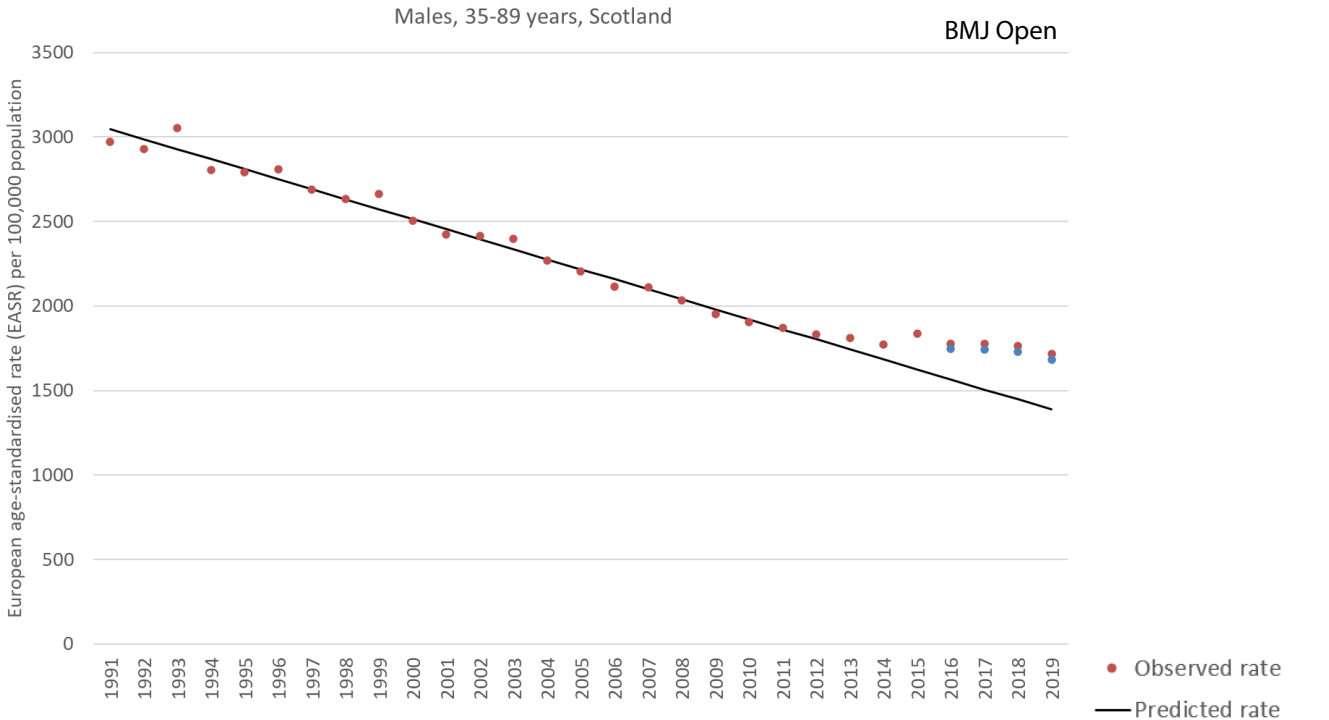


a) Males



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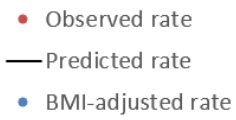
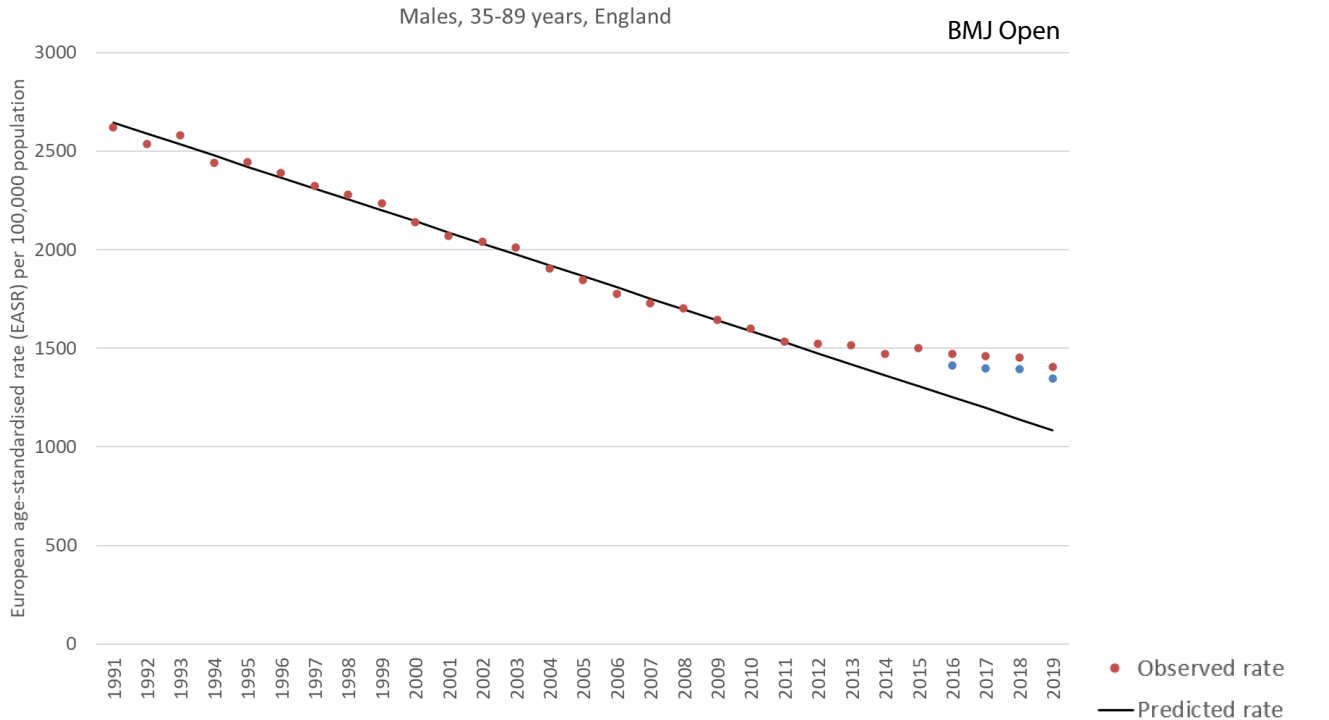


a) Males



b) Females

Online appendix

Supplementary tables

Supplementary Table S1.

Hazard ratios for BMI categories by age group from The Global BMI Mortality Collaboration (GBMC) 2016 study[1]. *Taken from eTable 11 (European studies only).*

Age group (years)	Underweight (BMI 15 to <18.5 kg/m^2)	Normal weight (BMI 18.5 to <25 kg/m^2)	Overweight (BMI 25 to <30 kg/m^2)	Obesity Grade I (BMI 30 to <35 kg/m^2)	Obesity Grade II (BMI 35 to <40 kg/m^2)	Obesity Grade III (BMI 40 to <60 kg/m^2)
35-49	1.86	1.00	1.17	1.90	3.01	5.34
50-69	2.25	1.00	1.11	1.60	2.23	4.04
70-89	1.65	1.00	0.98	1.12	1.56	1.91

Supplementary Table S2.

Sample sizes for 35-89 year-olds in 1995 and 2008, Scottish Health Survey (SHeS) and Health Survey for England (HSE).

Age group	SHeS 1995	SHeS 2008	HSE 1995	HSE 2008
35-49	2,381	1,532	3,918	3,547
50-69*	1,801	1,628	3,973	3,692
70-89	0†	669	1,831	1,507
Total	*4,182*	*3,829*	*9,722*	*8,746*

Methodological note: BMI category proportions for 65-69 and 70-89 years for 1995 SHeS (which only sampled 16-64 years) were derived from analysis of 2003 SHeS data (the first survey that included a sample of all adults aged 16+). Thus, for each BMI category the difference in proportions between 15-64 years and 15-69 years in 2003 were applied to 1995 data for 15-64 years to give a likely estimate for 15-69 years. Similarly, the differences in each category between 50-69 years and 70-89 years in the 2003 survey were then applied to 1995 data to provide an estimate for 70-89 years.

* 50-64 years in 1995 SHeS: in 2003 SHeS there were 1,975 in this age group, including 1,573 in the 50-64 group (as described above, these data were used to derive estimates for 1995)

† Sample size in 2003 SHeS (used to derive estimates for 1995) was 779.

Supplementary Table S3.

Hazard ratios for BMI categories by age group approximated from Bhaskaran et al[2] (sensitivity analyses).

Age group (years)	Underweight (BMI 15 to <18.5 kg/m^2)	Normal weight (BMI 18.5 to <25 kg/m^2)	Overweight (BMI 25 to <30 kg/m^2)	Obesity Grade I (BMI 30 to <35 kg/m^2)	Obesity Grade II (BMI 35 to <40 kg/m^2)	Obesity Grade III (BMI 40 to <60 kg/m^2)
16-49	1.73	1.00	1.27	1.65	2.31	2.84
50-69	1.79	1.00	1.12	1.43	1.89	2.54
70-79	1.88	1.00	1.03	1.27	1.63	2.34
80+	1.25	1.00	0.96	1.07	1.24	1.56

Methodological note: HRs by age group for the same BMI categories used in the GBMC paper were not available. Instead, values were approximated from the Bhaskaran et al paper's Figure 3b ('Association between BMI and all-cause mortality among never-smokers by age') using DigitizeIt software (www.digitizeit.de): the latter enabled extraction of approximate data values from the Figure. For each BMI category, the mid-point of the associated HR range was used; this was done separately for each age group[‡]. As the Figure presented logHR values, the extracted data were also exponentiated.

Supplementary Table S4.

Population attributable fractions (PAFs) by age group (main analyses).

Age group (years)	Scotland (SHeS)	England (HSE)
35-49	0.116	0.115
50-69	0.071	0.071
70-89	-0.008	0.028

[‡] Note that for the highest BMI category (Grade III obesity), the mid-point between BMI 40 and the maximum BMI value was used (as BMI values did not exceed 50 in the sample).

Supplementary Table S5.

Comparison of main analyses using 1981-, 1991- and 2001-based mortality projections (2017-19 mortality data)

	Observed rate	BMI-adjusted rate		Projected rate (1981)	% of observed-projected difference attributable to BMI change		Projected rate (1991)	% of observed-projected difference attributable to BMI change		Projected rate (2001)	% of observed-projected difference attributable to BMI change
Scotland, males	1750.7	1718.8		1503.7	12.9%		1447.1	10.5%		1423.7	9.8%
Scotland, females	1268.0	1248.3		1147.4	16.3%		1122.8	13.6%		1106.7	12.2%
England, males	1438.5	1378.6		1183.9	23.5%		1140.6	20.1%		1143.8	20.3%
England, females	1013.5	972.6		927.4	47.5%		896.2	34.9%		847.6	24.7%

Supplementary Table S6.

Population attributable fractions (PAFs) by age group using HRs approximated from Bhaskaran et al (sensitivity analyses).

Age group (years)	Scotland (SHeS)	England (HSE)
16-49	0.069	0.055
50-69	0.050	0.046
70-79	0.026	0.043
80+	-0.077	0.004

Supplementary Table S7.

Comparison of main results with sensitivity analyses using PAFs calculated from HRs approximated from Bhaskaran et al and applied to different age-specific mortality analyses, England 2017-19 (and using 1991-based mortality projections).

Methodological note: the PAFs shown in Table S6 above were applied to different age groups in the mortality analysis. For direct comparison with the main results, they were applied to the same 35-89 age band. However, as HRs were available for ages 16-80+ years, they were additionally applied to mortality data with corresponding ages (15 years+, as mortality data were accessed in five year age bands). Further sensitivity analyses restricted the age group to 15-84 years. Results are shown below for England only.

	% observed-projected difference attributable to BMI change			
	Main analyses (35-89 years using GBMC HRs)	Bhaskaran et al HRs, 35-89 years	Bhaskaran et al HRs, 15-84 years	Bhaskaran et al HRs, 15+ years
Males	20.1%	16.4%	15.1%	13.2%
Females	34.9%	28.9%	25.9%	22.9%

Supplementary Table S8.

Population attributable fractions (PAFs) by age group using three-year averages instead of single years (sensitivity analyses).

Methodological note: for English data, comparisons were made between the single year approach (i.e. the change in BMI distribution between 1995 and 2008) and three year averages around those single years (i.e. 1994-96 and 2007-09). This was not possible for Scottish data: there were no surveys run in 1994, 1996 or 2007; thus, comparisons were instead made between 1995 and 2008, and 1995 and 2008-10.

Age group (years)	Scotland (SHeS) 1995 and 2008-10	England (HSE), using 1994-96 and 2007-09
35-49	0.124	0.108
50-69	0.076	0.072
70-89	-0.006	0.023

Supplementary Table S9.

Comparison of main results with sensitivity analyses using PAFs derived from 2008-10 instead of 2008 in the Scottish Health Survey, and applied to analyses of 2017-19 Scottish mortality data (using 1991-based mortality projections).

See methodological note for Supplementary Table S8.

			Main analyses (1995 and 2008)		Sensitivity analyses (1995 and 2008-10)	
	Observed rate	**Projected rate (1991)**	**BMI-adjusted rate**	**% of observed-projected difference attributable to BMI change**	**BMI-adjusted rate**	**% of observed-projected difference attributable to BMI change**
Males	1750.7	1447.1	1718.8	10.5%	1713.1	12.4%
Females	1268.0	1122.8	1248.3	13.6%	1244.4	16.3%

Supplementary Table 10.

See methodological note for Supplementary Table S8.

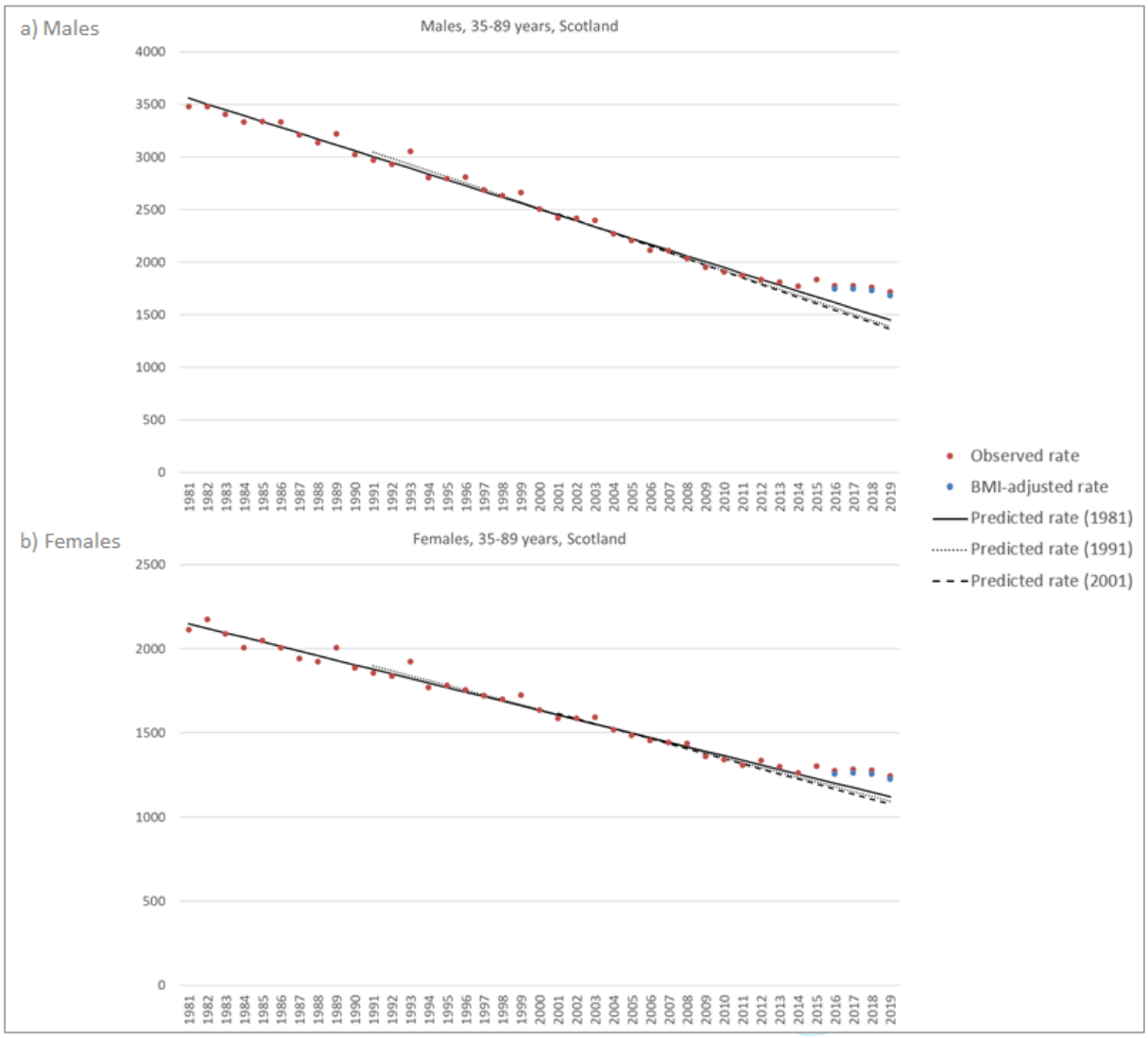
Comparison of main results with sensitivity analyses using PAFs derived from 1994-96 and 2007-09 instead of 1995 and 2008 respectively in the Health Survey for England, and applied to analyses of 2017-19 English mortality data (using 1991-based mortality projections)

			Main analyses (1995 and 2008)		Sensitivity analyses (1994-96 and 2007-09)	
	Observed rate	**Projected rate (1991)**	**BMI-adjusted rate**	**% of observed-projected difference attributable to BMI change**	**BMI-adjusted rate**	**% of observed-projected difference attributable to BMI change**
Males	1438.5	1140.6	1378.6	20.1%	1383.8	18.4%
Females	1013.5	896.2	972.6	34.9%	976.3	31.7%

Supplementary Figures

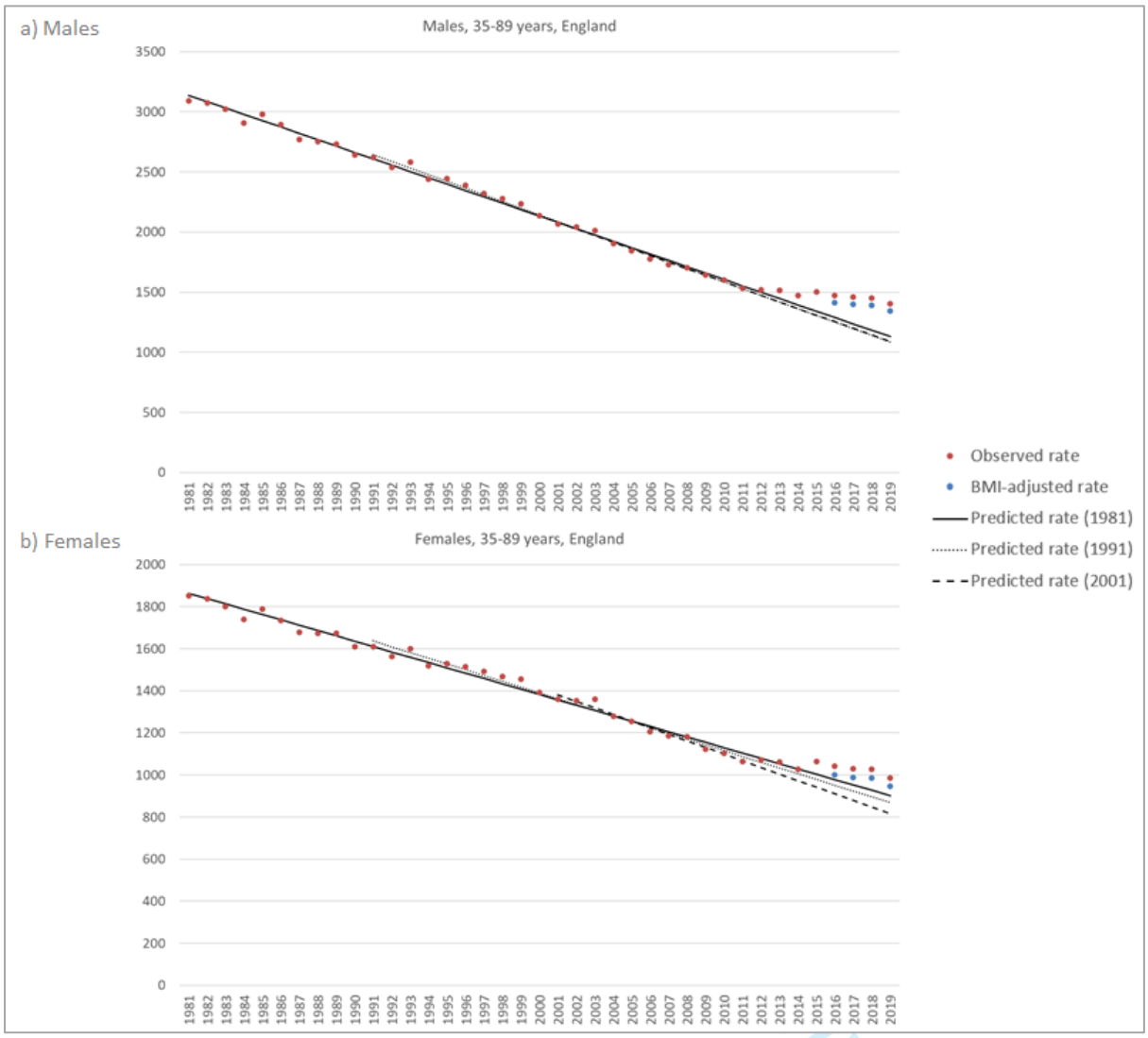
Supplementary Figure S1.

Observed, predicted and BMI-adjusted European age-standardised mortality rates (EASRs), Scotland 1981-2019 – comparing 1981-, 1991- and 2001-based predictions. Note different y-axis scales for males and females.



Supplementary Figure S2.

Observed, predicted and BMI-adjusted European age-standardised mortality rates (EASRs), Scotland 1981-2019 – comparing 1981-, 1991- and 2001-based predictions. Note different y-axis scales for males and females.

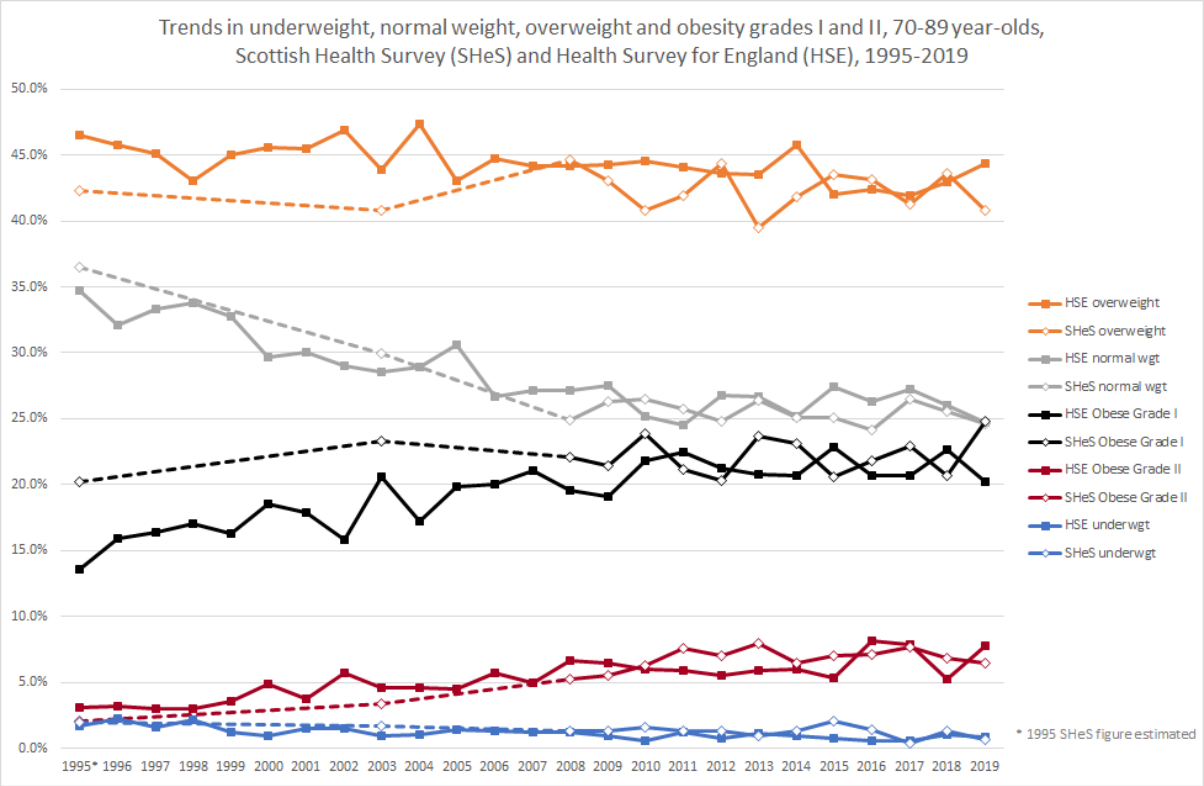


Supplementary Figure S3.

Trends in the percentage of adults aged 70-89 years classed as Obese Grade I (BMI 30 to <35), Scotland, 1995-2019

Supplementary Figure S4.

Trends in the percentage of adults aged 70-89 years in different BMI categories, Scotland and England, 1995-2019



References

[1] Global BMI Mortality Collaboration. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. Lancet 2016; 388(10046): 776-86

[2] Bhaskaran K., Dos-Santos-Silva I., Leon D.A., Douglas I.J., Smeeth L. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UK. Lancet Diabetes Endocrinol. 2018; 6(12): 944-953

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5-7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-7
		(*b*) Describe any methods used to examine subgroups and interactions	5-7
		(*c*) Explain how missing data were addressed	n/a
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	7

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6 (and Supplementary Table S2)
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	n/a (total population)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	7-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-10
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at

http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.