

Comparison of methods to estimate obesity-attributable mortality and high-BMI-attributable mortality by educational level in England & Wales, Finland, and Italy



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Abstract

In this working paper, we compare different methods to estimate obesity-attributable mortality and high-BMI attributable mortality, and we show how different estimation methods lead to different levels and trends in age-standardized obesity and high-BMI mortality by educational level (low, middle, high), for those aged 30 and over in England & Wales, Finland, and Italy, from the early 1970s onwards. For the three educational groups, levels of age-standardized obesity-attributable mortality rates (SOAMR) are higher when using an all-cause prevalence approach (method M2) compared to a cause-specific prevalence approach (method M1). In addition, trends in SOAMR are increasing instead of declining for method 2 compared to method 1, except for Italian males for which the two methods reveal rather similar trends. For England & Wales and Finland, method 1 results in more convergence in SOAMR levels over time between educational groups compared to method 2. In the 3 countries analyzed, similar descending trends of age-standardized high-BMIattributable mortality (SHBAMR) are obtained with methods M1 (cause-specific prevalence approach), M2 (all-cause prevalence approach), and M3 (cause-specific GBD PAFs approach). For Method 4 (multiple cause of death approach), however, ascending trends of SHBAMR are observed in England & Wales and Finland after the year 1996. These results reveal that levels and trends in SOAMR and SHBAMR by sex and educational level clearly differ by estimation method.

Keywords: obesity; high BMI; mortality; education; socio-economic status; lifestyle epidemics

Abbreviations

CVD Cardiovascular diseases

GBD Global Burden of Disease (database)

HBAMR High-BMI-attributable mortality rates

HBAMF High-BMI-attributable mortality fractions

M1 Method 1: Cause-specific prevalence approach

M2 Method 2: All-cause prevalence approach

M3 Method 3: Cause-specific GBD PAFs approach

M4 Method 4: Multiple cause of death approach

OAMR Obesity-attributable mortality rates

OAMF Obesity-attributable mortality fractions

PAFs Population attributable fractions

RRs Relative risks

SHBAMR Age-standardized high-BMI-attributable mortality rate

SHBAMF Age-standardized high-BMI-attributable mortality fraction

SDR Age-standardized mortality rate

SMF Age-standardized mortality fractions

SOAMR Age-standardized obesity-attributable mortality rate

SOAMF Age-standardized obesity-attributable mortality fraction

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1. Introduction

Obesity in Europe presents itself as an ongoing epidemic (WHO, 2022; Haththotuwa et al., 2020; Sumińska et al., 2022). Although socio-economic differences in obesity and overweight prevalence exist (e.g. Roskam et al. 2010; Devaux & Sassi 2013) and importantly affect socio-economic mortality inequalities (e.g. Petrovic et al. 2018), much less is known about the exact progression of the obesity and overweight epidemic by socio-economic groups in Europe (see Kagenaar et al. 2022). The few existing cross-national studies for Europe focused on the study of trends in obesity prevalence by educational level (Hoffmann et al. 2017; Kagenaar et al. 2022). Cross-national studies on trends in obesity-attributable mortality by educational level for Europe are lacking.

A first step in performing such studies is the estimation of obesity-attributable mortality by educational level. This is not a straightforward task. Vidra et al. (2018) illustrated, for example, for the general population of the Netherlands that the estimates of levels and trends of obesity-attributable mortality differ depending on the method applied. Applying the available methodologies to estimate obesity-attributable mortality by educational level not only requires additional data by educational level, which is not always available, and will very likely result in important differences between methods in the estimated levels and trends of obesity attributable mortality by educational level.

Our objective is to illustrate how different methods to estimate obesity-attributable mortality and high-BMI attributable mortality led to different levels and trends in age-standardized obesity and high-BMI mortality by educational level (low, middle, high), for those aged 30 and over in England & Wales, Finland, and Italy, from the early 1970s onwards.

We will compare two methods for obesity-attributable mortality (OAM) (method 1 and method 2) and four methods for high-BMI-attributable mortality (HBAM). Method 1 up to method 3 are population-attributable fraction (PAF) approaches, which use prevalence data and (causespecific) relative risks of dying from obesity or high-BMI to obtain an estimate of the fraction of (cause-specific) deaths attributable to obesity or high-BMI. Subsequently by multiplying these (cause-specific) PAFs with (cause-specific) death counts, an estimate of OAM or HBAM is obtained. In the first method (cause-specific prevalence approach) we use prevalence data by educational level and cause-specific RRs and mortality. In the second method (all-cause prevalence approach), we use prevalence data as well by educational levels but all-cause RRs and mortality. In the third method we directly use the high-BMI PAFs calculated by the Global Burden of Disease (GBD) study which are based on prevalence data not specified by educational level and cause-specific RRs. Method 4 (M4) is a cause of death approach which uses information on both underlying and contributory causes of death that are either completely or partly attributable to high-BMI attributable mortality. Age-standardized mortality rates and age-standardized mortality fractions are calculated for each method and for both OAM and HBAM. The results reveal that levels and trends in age-standardized OAM and HBAM by sex and educational level clearly differ by estimation method. The rest of this working paper is structured as follows: Section 2 provides details about the data needed for the different estimations of OAM and HBAM. Section 3 describes the calculations underlying the four different estimation methods of OAM and HBAM. Section 4 shows the results of comparing age-standardized mortality rates with the four methods, separately for OAM and separately for HBAM. Section 5 offers concluding remarks.

2. Data

For the estimation of obesity- and high-BMI attributable mortality by educational level, we used data from England & Wales, Finland, and Italy (Turin), for the longest time series possible, for those aged 30 and over. We use a lower age limit of 30 years to ensure the validity of educational attainment as a measure of socio-economic status. Obesity refers to a body mass index (BMI) of 30 and over, whereas with high BMI we refer to overweight and obesity combined, which refers to a BMI of 25 and over. In line with previous research (e.g. de Gelder et al. 2017), we distinguished three educational attainment groups according to the International Standard Classification of Education (ISCED) 1997 (UNESCO, 1997): low (no, pre-primary, primary, and lower secondary education; ISCED-1997 0-2), middle (upper secondary and post-secondary non-tertiary education; ISCED-1997 3-4), and high (tertiary education; ISCED-1997 5-6).

Table 1 summarizes the 4 methods and the different types of data that were needed to calculate OAM and HBAM in England & Wales, Finland, and Italy. The following data was used: a) prevalence of obesity and high-BMI by educational level, b) all-cause and cause-specific death counts by educational level, c) all-cause and cause-specific relative risks (RRs) of dying from obesity or high BMI, and d) cause-specific PAFs pertaining to high-BMI obtained from the Global Burden of Disease Study (GBD).

For **Method 1**, we used the data of prevalence of obesity and high-BMI by educational level, sex, calendar year, and single-year of age, that we calculated based on the information of national surveys (see Gonzales Martinez and Janssen, 2023). We also used cause-specific relative risks, by sex and five-year age groups, and cause-specific death counts by educational level, sex, and five-year age groups. We obtained the RRs for obesity and high-BMI from the study of Hoffmann et al. (2015) and used, for high-BMI, RRs for additional causes of death from the GBD database. For **Method 2**, we used similar prevalence data compared to method 1, but combined them with all-cause relative risks, by sex and five-year age groups and all-cause death counts by educational level, sex, and five-year age groups. The all-cause RRs of dying from obesity and high-BMI were obtained from the study of Hoffmann et al. (2015). The calculations of HBAM of **Method 3** are based on cause-specific PAFs from the GBD database, and cause-specific death counts. Finally, the calculation of HBAM in **Method 4** is obtained with death counts by educational level, sex, and age for both the underlying cause of death and contributory causes of death.

2.1. Prevalence data by educational level

For method 1 (cause-specific prevalence approach) and method 2 (all-cause prevalence approach) we used information on obesity and high-BMI prevalence by educational level, sex, age (25+), and year. For this purpose, we used our database on obesity and high BMI prevalence by educational level, sex, and single year of age (25-100) for adjacent calendar years for England & Wales, Finland, and Italy, that we created earlier (see Gonzales Martinez and Janssen, 2023), based on the earlier acquired prevalence data by educational level (Kagenaar et al. 2022). Using interpolation across years and smoothing across age, we consolidated the data from available national health surveys from the 1970s onwards, into data without missing years and with similar age groups across time. Subsequently, we applied the two-dimensional Rizzi et al. (2019) smoothing algorithm to obtain prevalence data by educational level (low, middle, high), sex, five-year age groups (25-95+) and single calendar years.

Table 1. Alternative methods applied to calculate obesity-attributable mortality (OAM) and high-BMI attributable mortality (HBAM)

		Methods	ş*	
	Method 1: Cause-specific prevalence approach	Method 2: All-cause prevalence approach	Method 3: Cause-specific GBD PAFs approach	Method 4: Multiple cause of death approach
Description of the method	This population-attributable fraction (PAF) method combines our prevalence data by educational level with cause-specific relative risks of dying to calculate PAFs by cause of death, year, educational level, sex, and age. Cause-specific obesity or high-BMI attributable mortality is obtained by multiplying the PAFs with the cause-specific death counts by year, educational level, sex, and age. OAM and HBAM by year, educational level, sex and age is obtained by summing the obesity or high-BMI attributable death counts over the causes of death.	This population-attributable fraction (PAF) method combines our prevalence data by educational level with all-cause relative risks of dying to calculate PAFs for all-cause mortality, by year, educational level, sex and age. OAM and HBAM by year, educational level, sex, and age. is subsequently obtained by multiplying the all-cause PAFs with the all-cause death counts by year, educational level, sex, and age.	This population-attributable fraction (PAF) method directly uses the cause-specific PAFs from the Global Burden of Disease (GBD) database, which pertain to high-BMI and are not education-specific. Cause-specific obesity or high-BMI attributable mortality is obtained by multiplying the GBD PAFs with the cause-specific death counts by year, educational level, sex, and age. OAM and HBAM by year, educational level, sex and age is obtained by summing the obesity or high-BMI attributable death counts over the causes of death.	The multiple cause of death approach estimates the number of (cardiovascular-related) deaths due to high BMI by educational level, sex, and five-year age groups based on the mention of any (cardiovascular) disease as the underlying cause of death on the death certificate in combination with either diabetes, chronic kidney disease, obesity, lipidaemia, or hypertensive heart diseases as a contributory cause of death (Adair & Lopez 2020).
Formulas	$PAF_{c,a,t,s,e} = \frac{p_{a,t,s,e}(RR_{c,a,s} - 1)}{1 + p_{a,t,s,e}(RR_{c,a,s} - 1)}$ $AM_{c,a,t,s,e} = PAF_{c,a,t,s,e} \cdot n_{c,a,t,s,e}$ $OAM_{a,t,s,e} = \sum_{\delta=1}^{n} OAM_{\delta,a,t,s,e} + od_{a,t,s,e}$ $HBAM_{k,a,t,s,e} = \sum_{\delta=1}^{k} HBAM_{\delta,a,t,s,e} + od_{a,t,s,e}$	$PAF_{a,t,s,e} = \frac{p_{a,t,s,e} (RR_{a,s} - 1)}{1 + p_{a,t,s,e} (RR_{a,s} - 1)}$ $OAM_{,a,t,s,e} = PAF_{allcause_obesity,a,t,s,e} \cdot n_{allcause,a,t,s,e}$ $HBAM_{a,t,s,e} = PAF_{allcause_highBMI,a,t,s,e} \cdot n_{allcause,a,t,s,e}$	$AM_{c,a,t,s,e} = PAF_{c,a,t,s,e}^{(GBD)} \cdot n_{c,a,t,s,e}$ $AAM_{\delta GBD,a,t,s,e} = \sum_{\delta=1}^{k} PAF_{c,d,t,s,e}^{(GBD)} \cdot n_{c,a,t,s,e}$ $HBAM_{GBD,a,t,s,e} = \sum_{\delta=1}^{k} HBAM_{\delta,a,t,s,e} + od_{a,t,s,e}$	$n_{\delta,s,a,e} = egin{cases} 1 & if & \delta \subset \Delta \\ 0 & else \end{cases}$ $HBAM_{\Delta,s,a,e} = \sum_{\delta \subset \Delta} n_{\delta,s,a,e}$
Data needed (input)	year age groups.	e, and year. all-cause mortality, respectively), by sex and five- ectively, by educational level, sex, age and year.	 Cause-specific death counts by educational level, sex, age and year for high BMI. Cause-specific PAFs from the GBD database by country, year, sex, and age 	Death counts by educational level, sex, age, and year for both underlying causes of death and three contributory causes of death
Output	OAM and HBAM	OAM and HBAM	HBAM	(CVD-related) HBAM
Pros	The underlying data (prevalence; Both OAM and HBA For the all-cause prevalence appro	M can be obtained.	Cause-specific mortality data by educational level as input. All causes of death that are associated with high-BMI are considered.	Purely relies on cause-specific mortality data by educational level. Lag time is not an issue, because we directly capture mortality
Cons	Does not consider time lag between being o Depends on the availability and quality of the prevale less compared to those for ca RRs are not available by educational level, and – at the For obesity, cause-specific RRs are only available	nce data by educational level, which are considered use-specific mortality data. e aggregate level – we cannot add interaction terms.	Only estimates of HBAM are obtained. Cause-specific PAFs are not available by educational level. GBD PAFs only available from 1990 to 2017 (we extrapolated them). The underlying RRs are not context-specific, and the underlying prevalence data (for the national populations) is largely modelled	Only estimates of HBAM are obtained, and the method is originally purely intended for CVD-related HBAM. Long-term multiple cause of death data is not available in many countries (e.g. for Italy).

^(*) OAM: Obesity-attributable mortality. HBAM: high-BMI-attributable mortality. $PAF_{C,a,t,S,e}$ are prevalence and $RR_{c,s,a}$ are prevalence and $RR_{c,s,a}$ are risk ratios by cause of death (c), age (a), and sex (s), and educational level (e), $p_{a,t,S,e}$ are prevalence and $RR_{c,s,a}$ are risk ratios by cause of death (c), age (a), and sex (s), and $RR_{a,s}$ are all-cause relative risk by age and sex. $AM_{c,a,t,S,e}$ is cause-specific attributable mortality obtained by multiplying $PAF_{c,a,t,S,e}$ times the death counts $n_{c,a,t,S,e}$ of each cause of death (c), age (a), and sex (s), and $RR_{a,s}$ are all-cause attributable mortality obtained by multiplying $PAF_{c,a,t,S,e}$ times the all-cause death counts $n_{c,a,t,S,e}$ of each cause of death (c), age (a), which can be added to obtain an aggregate measure of attributable mortality with $AAM_{\delta GBD,a,t,S,e}$ are GBD PAFs and δ is a subset of the causes of death (c), age (a), which can be added to obtain an aggregate measure of attributable mortality with $AAM_{\delta GBD,a,t,S,e}$. $n_{c,a,t,S,e}$.

Table 2 details the characteristics of the national health surveys that were used to calculate obesity and high-BMI prevalence by educational level in England & Wales, Finland, and Italy. In all national health surveys, the level of education was measured based on the highest level of education completed or highest degree obtained, except for Finland where the level of education was based on years of schooling. Details about the conversion of the country-specific educational classification to the ISCED 1997 classification can be found in the Supplementary File II of Kagenaar et al. (2022).

Table 2. The national health surveys used to build the database on obesity and high BMI prevalence by educational level and sex, for England & Wales, Finland, and Italy

	England & Wales	Finland	Italy
Surveys	HSE (1991-2018)	AVTK (1978-2014) ATH (2013-2017) FinSote (2018-2020)	NMSS (1990) HCHS (1994, 1999, 2000, 2004, 2005, 2013) AVQ (2001-2018)
Age range	15-85+	15-75+ (1978-2014) 20-90+ (2013-2017) 10-90+ (2018-2020)	18-80+ (1990) 18-75+ (2001-2018) 15-85+ (1994, 1999, 2000, 2004, 2005, 2013)
Age interval	5 years (1991-2013, 2015-2018) 10 years (2014)	5 years (1991-2013, 5 years (1990, 1994, 1920) 5 years (2015-2018) 10 years 2012)	
Data	Unweighted	Unweighted	Weighted

HSE: Health Survey for England and Wales; AVTK: Health Behavior and Health of Adult Population; ATH: Adult Health, Welfare and Service Research; FinSote: FinSote National survey of health; NMSS: National Multipurpose Social Survey; HCHS: Health conditions and use of Health Service; AVQ: Aspects of Daily Life

As can be partly deducted from Table 2, the obstacles to build the database were that the original (raw) data of the surveys have different sources (different types of surveys with different formats) and are grouped in dissimilar age groups, with missing data for some age groups (particularly for the older age groups), and missing data for some years, plus that there were occasional strata with missing data for the years and age groups, because of low cell counts.

In our database we dealt with these obstacles by interpolating and extrapolating missing values, applying one-dimensional smoothing using the Rizzi et al. (2015) algorithm to deal with dissimilar age groups over time, and subsequently applying the two-dimensional smoothing using the Rizzi et al. (2019) algorithm. Both these algorithms are available in the R package "ungroup" (Pascariu et al., 2018). The Rizzi et al. (2019) algorithm is based on a bivariate Poisson stochastic process, in line with obesity and high BMI having a bivariate distribution of counts by age and calendar years. The Rizzi et al. (2019) algorithm maximizes a penalized likelihood of B-splines applied to the bivariate distributions of obesity and high BMI by age and calendar years. Through this maximization, the Rizzi et al. (2019) algorithm produces detailed smooth surfaces of prevalence, based on prevalence data of adjacent calendar years and age groups without missing strata. In the 2D smoothing algorithm, the optimization is based on the minimization of the Bayesian

Information Criterion (BIC), as BIC was suggested as a proper statistic to compare competing models of bivariate densities based on B-splines (Lambert, 2011).

In the end the database contains data for the adjacent years 1991-2018 for England and Wales, 1978-2020 for Finland, and 1990-2018 for Italy. On the next page some more detailed information is provided on the original data and the consolidation we did before applying the 2D smoothing procedure.

To match the prevalence data in our database with the cause-specific mortality data which we obtained by five-year age groups, we converted the prevalence data by single age to prevalence data by five-year age groups (25-29, ..., 90-94, 95+) by obtaining weighted averages using the single-year prevalence with the single-year population numbers by sex, educational level, country, and year, that we obtained through our longitudinal mortality follow-ups (see the next section).

In England & Wales, individual level data on measured height and weight for ages 15-85+, for adjacent years from 1991 to 2018, was obtained from the Health Survey for England & Wales (HSE). The age of the individuals was provided in five-year age groups for the years 1991-2013 and 2015-2018, and in 10-year age groups for the year 2014. Weights were only available from 2003 onwards. No interpolation or extrapolation was applied to the data of England and Wales, and only the information of the year 2014 received a treatment with the 1D Rizzi et al. algorithm (Rizzi et al., 2015). With the purpose of obtaining uniform age groups, we disaggregated the information of the year 2014 into single-year age groups and later we aggregated this data into five-year age groups similar to those of the years 1991-2013 and 2015-2018.

For Finland, aggregate obesity, overweight, and survey counts by educational level, sex, and age—based on self-reported height and weight—are available for adjacent years from 1978 to 2020. However, there is only information for the ages 15-55+ (every 5 years) in the years 1978 up to 1992, and in 1994, 1996, 1998, 2000, 2002, 2004, 2006, 2008, 2010, 2012, and 2014. Due to this missing information for older adults, linear regression for each age-group was used to extrapolate the information for the age groups 65-75+ between the years 1978 to 1992, on the basis of the observed information available 1993 to 2013, and interpolation with an average between years for the age groups 65-75+ in the years 1994, 1996, 1998, 2000, 2002, 2004, 2006, 2008, 2010, 2012, and 2014. The data stem from the Health Behavior and Health of Adult Population (AVTK) for the years 1978 to 2014, the Health behavior and Health among Finnish Elderly (EVTK) surveys for every two years between 1993 and 2011), the Adult Health, Welfare and Service Research (ATH) for the years 2013 to 2017, and the FinSote national survey of health for the years 2018 to 2020. Weighted data was only available for 2013-2017. We obtained the data grouped in 10-year age intervals, but the data of ATH starts at age 20 and ends at age 90+, the data of AVTK-EVTK starts at age 15 and ends at 75+, and the data of FinSote starts at age 10 and ends at age 90+.

Italy has self-reported height and weight information for the years 1990, 1994, 1999/2000 (that was assigned to the year 1999) and for the years 2001 to 2018. The data from the first two sources were received grouped by five-year age groups, data from the last source was provided by five-year age groups from 2001 up to 2012 and by 10-year age groups from 2013 up to 2018. For all years, weights were available. The missing information of the years 1991-1993, 1995-1998, and the information 2000, were interpolated with an average for each age group. Additionally, 1D smoothing was applied to the information between the years 2013 to 2018 to obtain uniform age-

groups, because the age groups between the years 2013 up to 2018 (20-24, 25-34, 35-44, 45-54, 55-59, 60-64, 65-74, 75+) are different compared to the age-groups of the years 1990 to 2012 (20-85+, 5-year age intervals). The sources of the data are the National Multipurpose Social Survey (NMSS) for the year 1990 (aggregate count data), the Health Conditions and use of Health Services (HCHS) for the years 1994, 1999/2000, 2004/2005, 2013 (individual level data), and the Aspects of Daily Life (Aspetti della vita quotidiana, AVQ) for the years 2001 to 2018 (individual level data).

2.2. Cause-specific mortality data

All four methods require mortality data by educational level, sex, age, and year. Method 2 uses all-cause death counts, whereas methods 1, 3 and 4 uses cause-specific death counts. Methods 1 and 3 purely use information on the underlying cause of death, whereas method 4 uses information on both the underlying and the contributory causes of death.

We used individually linked all-cause and cause-specific mortality data by highest educational attainment (low, middle, high), sex, five-year age groups (30-34, ..., 90-94, 95+), and single calendar year for England & Wales (1972-2017), Finland (1971-2017), and Italy (Turin) (1972-2019). These data stem from longitudinal mortality follow-ups in which individual data on mortality are linked to information on their educational attainment and the population at risk either five (Finland) or ten years earlier. For Finland we obtained the data from Statistics Finland, for Italy (Turin) we used data from the Turin Longitudinal Study (Costa and Demaria, 1988), and for England & Wales we used data from the Office for National Statistics Longitudinal Study (ONS-Longitudinal Study, 2019; Shelton et al., 2019), which we adjusted to address important identified data issues (Janssen et al. submitted). The Longitudinal Study (LS) contains linked census and life events data for a 1% sample of the population of England and Wales. It contains records on over 500,000 people usually resident in England and Wales at each point in time and it is largely representative of the whole population. The LS is the largest longitudinal data resource in England and Wales. The LS has linked records at each census since the 1971 Census, for people born on one of four selected dates in a calendar year. These four dates were used to update the sample at the 1981, 1991, 2001 and 2011 Censuses. Life events data are also linked for LS members, including births to sample mothers, deaths, and cancer registrations. New LS members enter the study through birth and immigration (if they are born on one of the four selected birth dates).

Whereas underlying cause of death information is available for the years indicated above, additional contributory cause of death information (needed for method 4) was not available for Italy, only available from 1987 for Finland, and for England & Wales we dealt with the missing information on contributory causes from 1987 up to 1992, by interpolation of the cause-specific mortality rates using a three-year moving average approach. For Italy, for about 1.0% of all deaths, the cause of death was unspecified. We dealt with this by proportionally distributing the deaths (unsmoothed) with an unspecified cause of death to the different causes of death by age, sex, educational level, and year. More information on the used data can be found on https://www.futurelongevitybyeducation.com/background-information/ (Password = VICI_info).

Table 3 lists the causes of death we considered to calculate OAM and HBAM in the cause-specific prevalence approach of methods M1 and M3. We considered 6 causes of death, 10 causes of death

and 20 causes of death. The 6 causes of death are those mainly related to obesity according to Hoffmann et al. (2015). The 20 causes of death are those considered by the GBD database as related to high-BMI. The 10 causes of the death are those included in the GBD database and that were either considered by Hoffmann et al. (2015) or Gutin (2020) as relevant to calculate OAM and HBAM. **Table 4** shows the codes associated with each cause of death according to the International Classification of Diseases (ICD).

Table 3. Causes of death considered in Method 1 (cause-specific prevalence approach) and Method 3 (cause-specific GBD PAFs approach) to estimate high-BMI attributable mortality*. For obesity-attributable mortality we could purely apply method 1, and purely used the 6 causes of death.

6 causes of death		10 causes of death		20 causes of death
Colorectal cancer.	1.	Colorectal cancer.	1.	Colorectal cancer.
Breast cancer.	2.	Breast cancer.	2.	Breast cancer.
Kidney cancer.	3.	Kidney cancer.	3.	Kidney cancer.
4. Ischemic heart diseases.	4.	Ischemic heart diseases.	4.	Ischemic heart diseases.
5. CVD (Hypertensive heart	5.	Hypertensive heart disease.	5.	Hypertensive heart disease.
disease/ischemic stroke)	6.	Ischemic stroke.	6.	Ischemic stroke.
6. Diabetes mellitus type 2.	7.	Diabetes mellitus type 2.	7.	Diabetes mellitus type 2.
	8.	Gallbladder and biliary tract cancer.	8.	Gallbladder and biliary tract cancer.
	9.	Pancreatic cancer.	9.	Pancreatic cancer.
	10.	Liver cancer	10.	Liver cancer.
			11.	Esophageal cancer.
			12.	Thyroid cancer.
			13.	Non-Hodgkin lymphoma.
			14.	Multiple myeloma.
			15.	Leukemia.
			16.	Alzheimer's disease and other dementias.
			17.	Asthma.
			18.	Gallbladder and biliary diseases.
			19.	Chronic kidney disease.
			20.	Atrial fibrillation and flutter.

^(*) Note: The 6 causes of death are those mainly related to obesity according to Hoffmann et al. (2015). The 20 causes of death are those considered by the GBD database as related to high-BMI. The 10 causes of the death are those included in the GBD database and that were either considered by Hoffmann et al. (2015) or Gutin (2020).

2.3. Relative Risks

For method 1 (cause-specific prevalence approach) and method 2 (all-cause prevalence approach) we needed to use relative risks (RRs) associated with obesity and high-BMI. Ideally, we would have liked to use age-, sex- and education-specific RRs, but these proved not available in the literature. Instead, we used the available age- and sex- specific RRs.

We used two main sources for these RRs. From the supplementary material of Hoffmann et al. (2015) we used the RRs associated with obesity and with high-BMI for all-cause mortality (needed for method 2) and the six causes of death provided (see Table 2) (needed for method 1). In addition, we used RRs associated with high-BMI from the Global Burden of Disease Study (https://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks) which are available for 20 causes of death (see Table 3).

Table 4. ICD classification of the causes of death considered to calculate obesity- and high-BMI-attributable mortality in method 1

Cause of death	ICD8	ICD9	ICD10
Esophageal cancer	150	150	C15
Colon and rectum cancer	153-154	153-154	C18-C21
Liver cancer	155, 197.8	155	C22
Gallbladder and biliary tract cancer	156	156	C23-C24
Pancreatic cancer	157	157	C25
Breast cancer	174	174, 175	C50
Kidney and other urinary organs cancer	189	189	C64-66; C68
Thyroid cancer	193	193	C73
Non-Hodgkin Lymphoma	200, 202	200, 202	C82-C85, C96
Multiple Myeloma	203	203	C88-C90
Leukemia	204-207	204-208	C91-C95
Diabetes Mellitus	250	250	E10-E14
Obesity	277	278.0, 278.1	E65, E66
Alzheimer's disease + other dementias	290, 293, 331	290, 294, 331	F00-F03; G30-G31 minus G31.2.
Asthma	493	493	J45-J46
Gallbladder and biliary diseases	574-576	574-576	K80-K83
Chronic kidney disease	403-404, 581-583, 593.2,	403-404, 581-583, 585, 589	I12-I13, N02-N08, N18
<u> </u>	792, 753.0-753.3	753.0-753.3	Q61-Q62
IHD	410-414	410-414	I20-I25
Stroke	430-438	430-438	I60-I69
Hypertensive heart disease	402	402	I11
Atrial fibrillation and flutter	427.4	427.3	I48

2.3.1 All-cause RRs from Hoffmann et al. (2015)

For the RRs of dying from all-cause mortality associated with obesity and high-BMI, needed for method 2 (all-cause prevalence approach), we used the all-cause RRs from Hoffmann et al. (2015). These stem from the Dynamo-HIA project (Lobstein & Leach, 2010; Lhachimi et al., 2012). The all-cause RRs came from a review of studies mainly conducted in Western Europe and the USA. This review included RRs related to both self-reported obesity and high-BMI as well as measured obesity and high-BMI. **Table 4.1** (obesity) and **Table 4.2** (high-BMI) show in their last column the original all-cause relative risks of Hoffmann et al. (2015). The RRs for obesity (roughly around 1.5) were largely in line with the overall European RR for obesity (1.64) and high-BMI (1.39) recently estimated by the Global BMI collaboration (Di Angelantonio et al., 2016). The differences across age-groups found in that study were similar to the RRs we used to calculate OAM and high-BMI (that is, higher RRs at younger than older ages).

Table 4.1. Relative risks for obesity by sex and age group (Hoffmann et al., 2015)

Sex	Age group	Colorect al cancer	Breast Cancer	Kidney & renal pelvis cancer	Ischemic heart disease	Diabetes mellitus 2	Cerebrovascular disease / stroke	All-cause mortality
male	30-44	1.4	-	1.55	2.000	5.500	1.500	1.550
male	45-59	1.36	-	1.55	2.000	5.500	1.500	1.540
male	60-69	1.36	-	1.55	1.850	5.140	1.440	1.520
male	70-79	1.36	-	1.55	1.700	5.100	1.380	1.500
female	30-44	1.1	1.000	1.8	2.000	7.000	1.550	1.500
female	45-59	1.09	1.000	1.8	2.000	7.000	1.550	1.490
female	60-69	1.09	1.000	1.8	1.850	6.520	1.480	1.480
female	70-79	1.09	1.000	1.8	1.700	6.460	1.410	1.450

Table 4.2. Relative risks for high-BMI by sex and age group (Hoffmann et al., 2015)

Sex	Age group	Colorect al cancer	Breast Cancer	Kidney & renal pelvis cancer	Ischemic heart disease	Diabetes mellitus 2	Cerebrovascular disease / stroke	All-cause mortality
male	30-44	1.2	-	1.24	1.35	2.25	1.20	1.20
male	45-59	1.18	-	1.24	1.35	2.25	1.20	1.20
male	60-69	1.18	-	1.24	1.30	2.15	1.18	1.19
male	70-79	1.18	-	1.24	1.25	2.14	1.15	1.18
female	30-44	1.08	1	1.32	1.35	2.30	1.20	1.15
female	45-59	1.07	1.08	1.32	1.35	2.30	1.20	1.15
female	60-69	1.07	1.12	1.32	1.30	2.20	1.18	1.14
female	70-79	1.07	1.12	1.32	1.25	2.18	1.15	1.14

Because the data was only available in broad age groups, we applied interpolation to obtain the RRs by five-year age groups. For the all-cause RRs we decided to apply quadratic interpolation instead of linear interpolation, because this resulted in lower RRs for older adults, which is in line with the reduction of health risks associated with increasing body mass index (Villareal et al., 2005). In **Appendix II** we compared the effects of linear and quadratic interpolation methods on our obesity- and high-BMI attributable mortality calculations. Largely similar estimates are obtained using either a quadratic or linear interpolation for the all-cause RRs. **Table 5.1** shows (in bold) the quadratic interpolated RRs by five-year age groups and sex that we used in the end.

Table 5.1. All-cause RRs related to obesity and high-BMI by sex and five-year age groups (25+), after applying linear and quadratic interpolation to the RRs of Hoffman et al. (2015)

		Ob	esity	Higl	n BMI
Sex	Age-group	All-cause mortality (linear)	All-cause mortality (quadratic)	All-cause mortality (linear)	All-cause mortality (quadratic)
male	25-29	1.57	1.55	1.21	1.20
male	30-34	1.56	1.55	1.21	1.20
male	35-39	1.56	1.55	1.20	1.20
male	40-44	1.55	1.55	1.20	1.20
male	45-49	1.54	1.55	1.20	1.20
male	50-54	1.54	1.54	1.20	1.20
male	55-59	1.53	1.54	1.19	1.20
male	60-64	1.52	1.53	1.19	1.19
male	65-69	1.52	1.52	1.19	1.19
male	70-74	1.51	1.51	1.19	1.18
male	75-79	1.51	1.50	1.18	1.18
male	80-84	1.50	1.49	1.18	1.17
male	85-89	1.49	1.48	1.18	1.16
male	90-94	1.49	1.46	1.18	1.16
male	95-99	1.48	1.45	1.17	1.15
female	25-29	1.52	1.50	1.15	1.15
female	30-34	1.51	1.50	1.15	1.15
female	35-39	1.51	1.50	1.15	1.15
female	40-44	1.50	1.50	1.15	1.15
female	45-49	1.49	1.50	1.15	1.15
female	50-54	1.49	1.49	1.15	1.15
female	55-59	1.48	1.49	1.15	1.15
female	60-64	1.48	1.48	1.14	1.15
female	65-69	1.47	1.48	1.14	1.14
female	70-74	1.47	1.47	1.14	1.14
female	75-79	1.46	1.45	1.14	1.14
female	80-84	1.46	1.44	1.14	1.14
female	85-89	1.45	1.43	1.14	1.13
female	90-94	1.44	1.41	1.14	1.13
female	95-99	1.44	1.40	1.13	1.13

2.3.2. Cause-specific RRs from Hoffmann et al. (2015)

To estimate obesity-attributable mortality using method 1 we used the cause-specific RRs from Hoffmann et al. (2015). To estimate high-BMI-attributable mortality using method 1 we also used the cause-specific RRs from Hoffmann et al. (2015) for the six causes of death for which they are provided, but in addition we used the cause-specific RRs from the Global Burden of Disease study. The causes of death considered by Hoffmann –for both obesity and high-BMI– are kidney/renal pelvis cancer, colorectum cancer, breast cancer, diabetes mellitus, ischemic heart disease (IHD), coronary heart disease (CHD), and cerebrovascular stroke, because these are the causes of death that have an impact on overall health inequality and for which there is sufficient evidence of a causal relation with obesity (Hoffmann et al., 2015, p. 2) and high-BMI (Dai et al., 2020). The cause-specific RRs of Hoffmann et al. (2015) come from the study of Van Kreijl and Knaap (2004). This is a comprehensive study report on the impact of risk factors on mortality in the Netherlands using the best available sources for rate ratios in the international literature (see their report p. 337-

344 for all references). **Table 4a** (obesity) and **Table 4b** (high-BMI) show the original relative risks of Hoffmann et al. (2015). Because the relative risks of Hoffmann et al. (2015) are only available by sex and broad age groups (30-44 years, 45-59, 60-69 and 70-79 years), we performed interpolation to obtain the RRs by sex and five-year age groups, since RRs in uniform 5-year age intervals are needed to match the prevalence data in 5-year age intervals. We compared the results of applying both linear and quadratic interpolations. Linear interpolation of RRs was applied by Vidra et al. (2019) when calculating mortality risks. Quadratic interpolation is more in line with Zheng et al. (2021), who analyzed the obesity-mortality link and found that the hazard ratio associated with obesity decreases over time for different age groups, especially the elderly, compared to normal weight. We performed our interpolations by applying regressions, where we used central age in the linear interpolation and central age and the square of central age in the quadratic interpolation. **Appendix II** shows the results of the linear and quadratic interpolation applied to the cause-specific RRs.

The obesity RRs for 'breast cancer' and 'kidney and renal pelvis cancer' and the high BMI RRs for 'kidney and renal pelvis cancer' were not interpolated, because they are constant over age. We decided to use the linearly interpolated RRs in our calculations. That is, the quadratic interpolation of RRs produced in some cases a U-shaped form which is less in line with the theory compared to the reversed U-shape, which is the form expected to reflect higher RRs at younger than older ages. **Table 5.2** shows the cause-specific RRs related to obesity, by sex and five-year age groups (25+), that we used in the end in the calculations of obesity attributable mortality, after applying linear interpolation to the cause-specific RRs related to high-BMI, by sex and five-year age groups (25+), that we used in the end in the calculations of high-BMI attributable mortality, after applying linear interpolation to the cause-specific RRs relative to obesity in Hoffman et al. (2015).

2.3.3. Cause-specific RRs regarding high BMI from the GBD study

To estimate high-BMI attributable mortality using method 1 (cause-specific prevalence approach), we ideally would like to use RRs for the 10 high-BMI related causes of death as we identified (see Table 2-10 causes), and for comparative purposes we also would like to use RRs for the 20 high-BMI related causes of death as identified by the GBD (see Table 2-20 causes) and used for the GBD PAFs of method 3 (cause-specific GBD PAF approach). For this purpose, we used the RRs from the GBD database (https://ghdx.healthdata.org/record/ihme-data/gbd-2019-relative-risks).

The RRs from the GBD database are based on the Global Burden of Disease Study 2019 (Vos et al., 2020). The Global Burden of Disease Study 2019 (GBD 2019) is coordinated by the Institute for Health Metrics and Evaluation (IHME). In the GBD, the burden of causes of death, injuries, and risk factors is estimated for 204 countries and territories in selected subnational locations. Relative risks in the GBD are based on 81 systematic reviews and meta-regressions.

Table 5.2. Cause-specific RRs related to obesity by sex and five-year age groups (25+), after applying linear interpolation to the cause-specific RRs of Hoffman et al. (2015)

		Obesity							
Sex	Age- group	Colorectal cancer	Breast Cancer	Kidney and renal pelvis cancer	Ischemic heart disease	Diabetes mellitus type 2	Cerebro- vascular disease stroke		
male	25-29	1.40		1.55	2.11	5.65	1.54		
male	30-34	1.40		1.55	2.07	5.60	1.53		
male	35-39	1.39		1.55	2.04	5.54	1.51		
male	40-44	1.39		1.55	2.00	5.49	1.50		
male	45-49	1.38		1.55	1.96	5.43	1.49		
male	50-54	1.38		1.55	1.93	5.38	1.47		
male	55-59	1.37		1.55	1.89	5.32	1.46		
male	60-64	1.36		1.55	1.86	5.26	1.44		
male	65-69	1.36		1.55	1.82	5.21	1.43		
male	70-74	1.35		1.55	1.78	5.15	1.41		
male	75-79	1.35		1.55	1.75	5.10	1.40		
male	80-84	1.34		1.55	1.71	5.04	1.39		
male	85-89	1.34		1.55	1.68	4.99	1.37		
male	90-94	1.33		1.55	1.64	4.93	1.36		
male	95-99	1.33		1.55	1.60	4.88	1.34		
female	25-29	1.10	1.00	1.80	2.11	7.21	1.60		
female	30-34	1.10	1.00	1.80	2.07	7.13	1.58		
female	35-39	1.10	1.00	1.80	2.04	7.06	1.57		
female	40-44	1.10	1.00	1.80	2.00	6.98	1.55		
female	45-49	1.10	1.00	1.80	1.96	6.91	1.53		
female	50-54	1.09	1.00	1.80	1.93	6.83	1.52		
female	55-59	1.09	1.00	1.80	1.89	6.76	1.50		
female	60-64	1.09	1.00	1.80	1.86	6.68	1.48		
female	65-69	1.09	1.00	1.80	1.82	6.61	1.47		
female	70-74	1.09	1.00	1.80	1.78	6.53	1.45		
female	75-79	1.09	1.00	1.80	1.75	6.46	1.43		
female	80-84	1.09	1.00	1.80	1.71	6.38	1.42		
female	85-89	1.09	1.00	1.80	1.68	6.31	1.40		
female	90-94	1.08	1.00	1.80	1.64	6.23	1.38		
female	95-99	1.08	1.00	1.80	1.60	6.16	1.37		

Table 5.3. Cause-specific RRs related to high-BMI by sex and five-year age groups (25+), after applying linear interpolation to the cause-specific RRs of Hoffman et al. (2015)

		High-BMI							
Sex	Age- group	Colorectal cancer	Breast Cancer	Kidney and renal pelvis cancer	Ischemic heart disease	Diabetes mellitus type 2	Cerebro- vascular disease stroke		
male	25-29	1.20		1.24	1.39	2.29	1.22		
male	30-34	1.20		1.24	1.37	2.28	1.21		
male	35-39	1.20		1.24	1.36	2.26	1.21		
male	40-44	1.19		1.24	1.35	2.25	1.20		
male	45-49	1.19		1.24	1.34	2.23	1.20		
male	50-54	1.19		1.24	1.33	2.22	1.19		
male	55-59	1.18		1.24	1.31	2.20	1.18		
male	60-64	1.18		1.24	1.30	2.18	1.18		
male	65-69	1.18		1.24	1.29	2.17	1.17		
male	70-74	1.18		1.24	1.28	2.15	1.17		
male	75-79	1.18		1.24	1.27	2.14	1.16		
male	80-84	1.17		1.24	1.25	2.12	1.15		
male	85-89	1.17		1.24	1.24	2.11	1.15		
male	90-94	1.17		1.24	1.23	2.09	1.14		
male	95-99	1.17		1.24	1.22	2.08	1.14		
female	25-29	1.08	0.99	1.32	1.39	2.35	1.22		
female	30-34	1.08	1.00	1.32	1.37	2.33	1.21		
female	35-39	1.08	1.02	1.32	1.36	2.31	1.21		
female	40-44	1.08	1.03	1.32	1.35	2.30	1.20		
female	45-49	1.08	1.05	1.32	1.34	2.28	1.20		
female	50-54	1.07	1.06	1.32	1.33	2.26	1.19		
female	55-59	1.07	1.08	1.32	1.31	2.25	1.18		
female	60-64	1.07	1.10	1.32	1.30	2.23	1.18		
female	65-69	1.07	1.11	1.32	1.29	2.21	1.17		
female	70-74	1.07	1.13	1.32	1.28	2.20	1.17		
female	75-79	1.07	1.14	1.32	1.27	2.18	1.16		
female	80-84	1.07	1.16	1.32	1.25	2.17	1.15		
female	85-89	1.07	1.18	1.32	1.24	2.15	1.15		
female	90-94	1.06	1.19	1.32	1.23	2.13	1.14		
female	95-99	1.06	1.21	1.32	1.22	2.12	1.14		

Table 6 shows the cause-specific RRs from the GBD database by sex and five-year age groups (20-24, ..., 90-94, 95+) that we used to calculate HBAM in Method 1 (cause-specific prevalence approach). For some causes of death, the GBD 2019 study did not provide an overall RR, but only RRs for more detailed causes. For leukemia, for example, the underlying causes of death related to acute lymphoid leukemia, chronic lymphoid leukemia, acute myeloid leukemia, chronic myeloid leukemia, and other leukemia had similar RRs, which we took over as the overall RR for leukemia. Similarly for liver cancer, we took the overall RR by sex based on the RRs for liver cancer due to hepatitis B, hepatitis C, and alcohol use.

In the case of chronic kidney diseases, we used the average of the RRs of chronic kidney diseases related to diabetes mellitus type 2, hypertension, glomerulonephritis, and other unspecified causes. For chronic kidney disease, RRs were only available from age 35-39 onwards, and only for both sexes combined. We therefore implemented a RR of 1 for age groups 25-29 and 30-34, and we applied the RRs for both sexes combined to both males and females.

Table 6. Relative risks for high-BMI from the GBD database

sex	age-group	Colorectal cancer	Breast Cancer	Kidney cancer	Ischaemic heart diseases	Hypertensive heart disease
male	25-29 years	1.177		1.24	2.274	3.122
male	30-34 years	1.177		1.24	2.018	3
male	35-39 years	1.177		1.24	1.724	2.769
male	40-44 years	1.177		1.24	1.599	2.573
male	45-49 years	1.177		1.24	1.567	2.407
male	50-54 years	1.177		1.24	1.52	2.281
male	55-59 years	1.177		1.24	1.466	2.159
male	60-64 years	1.177		1.24	1.414	2.035
male	65-69 years	1.177		1.24	1.364	1.955
male	70-74 years	1.177		1.24	1.319	1.86
male	75-79 years	1.177		1.24	1.274	1.792
male	80-84 years	1.177		1.24	1.17	1.697
male	85-89 years	1.177		1.24	1.17	1.697
male	90-94 years	1.177		1.24	1.17	1.697
male	95+ years	1.177		1.24	1.17	1.697
female	25-29 years	1.059	0.89	1.32	2.274	3.122
female	30-34 years	1.059	0.89	1.32	2.018	3
female	35-39 years	1.059	0.89	1.32	1.724	2.769
female	40-44 years	1.059	0.89	1.32	1.599	2.573
female	45-49 years	1.059	0.89	1.32	1.567	2.407
female	50-54 years	1.059	1.089	1.32	1.52	2.281
female	55-59 years	1.059	1.089	1.32	1.466	2.159
female	60-64 years	1.059	1.089	1.32	1.414	2.035
female	65-69 years	1.059	1.089	1.32	1.364	1.955
female	70-74 years	1.059	1.089	1.32	1.319	1.86
female	75-79 years	1.059	1.089	1.32	1.274	1.792
female	80-84 years	1.059	1.089	1.32	1.17	1.697
female	85-89 years	1.059	1.089	1.32	1.17	1.697
female	90-94 years	1.059	1.089	1.32	1.17	1.697
female	95+ years	1.059	1.089	1.32	1.17	1.697

Table 6 - continued

sex	age-group	Ischaemic stroke	Diabetes mellitus type 2	Gallbladder and biliary tract	Pancreatic cancer	Liver cancer
			,,	cancer		
male	25-29 years _	2.472	3.547	1.155	1.071	1.289
male	30-34 years	2.235	3.455	1.155	1.071	1.289
male	35-39 years _	1.979	3.349	1.155	1.071	1.289
male	40-44 years	1.826	3.16	1.155	1.071	1.289
male	45-49 years	1.733	2.864	1.155	1.071	1.289
male	50-54 years	1.635	2.624	1.155	1.071	1.289
male	55-59 years	1.543	2.417	1.155	1.071	1.289
male	60-64 years	1.455	2.215	1.155	1.071	1.289
male	65-69 years	1.38	2.046	1.155	1.071	1.289
male	70-74 years	1.304	1.896	1.155	1.071	1.289
male	75-79 years	1.228	1.74	1.155	1.071	1.289
male	80-84 years	1.068	1.461	1.155	1.071	1.289
male	85-89 years	1.068	1.461	1.155	1.071	1.289
male	90-94 years	1.068	1.461	1.155	1.071	1.289
male	95+ years	1.068	1.461	1.155	1.071	1.289
female	25-29 years	2.472	3.547	1.344	1.092	1.176
female	30-34 years	2.235	3.455	1.344	1.092	1.176
female	35-39 years	1.979	3.349	1.344	1.092	1.176
female	40-44 years	1.826	3.16	1.344	1.092	1.176
female	45-49 years	1.733	2.864	1.344	1.092	1.176
female	50-54 years	1.635	2.624	1.344	1.092	1.176
female	55-59 years	1.543	2.417	1.344	1.092	1.176
female	60-64 years	1.455	2.215	1.344	1.092	1.176
female	65-69 years	1.38	2.046	1.344	1.092	1.176
female	70-74 years	1.304	1.896	1.344	1.092	1.176
female	75-79 years	1.228	1.74	1.344	1.092	1.176
female	80-84 years	1.068	1.461	1.344	1.092	1.176
female	85-89 years	1.068	1.461	1.344	1.092	1.176
female	90-94 years	1.068	1.461	1.344	1.092	1.176
female	95+ years	1.068	1.461	1.344	1.092	1.176

Table 6 - continued

sex	age-group	Oesophageal cancer	Thyroid cancer	Non-Hodgkin Lymphoma*	Multiple myeloma	Leukemia
male	25-29 years	1.391	1.221	1.089	1.089	1.086
male	30-34 years	1.391	1.221	1.089	1.089	1.086
male	35-39 years	1.391	1.221	1.089	1.089	1.086
male	40-44 years	1.391	1.221	1.089	1.089	1.086
male	45-49 years	1.391	1.221	1.089	1.089	1.086
male	50-54 years	1.391	1.221	1.089	1.089	1.086
male	55-59 years	1.391	1.221	1.089	1.089	1.086
male	60-64 years	1.391	1.221	1.089	1.089	1.086
male	65-69 years	1.391	1.221	1.089	1.089	1.086
male	70-74 years	1.391	1.221	1.089	1.089	1.086
male	75-79 years	1.391	1.221	1.089	1.089	1.086
male	80-84 years	1.391	1.221	1.089	1.089	1.086
male	85-89 years	1.391	1.221	1.089	1.089	1.086
male	90-94 years	1.391	1.221	1.089	1.089	1.086
male	95+ years	1.391	1.221	1.089	1.089	1.086
female	25-29 years	1.351	1.136	1.068	1.092	1.131
female	30-34 years	1.351	1.136	1.068	1.092	1.131
female	35-39 years	1.351	1.136	1.068	1.092	1.131
female	40-44 years	1.351	1.136	1.068	1.092	1.131
female	45-49 years	1.351	1.136	1.068	1.092	1.131
female	50-54 years	1.351	1.136	1.068	1.092	1.131
female	55-59 years	1.351	1.136	1.068	1.092	1.131
female	60-64 years	1.351	1.136	1.068	1.092	1.131
female	65-69 years	1.351	1.136	1.068	1.092	1.131
female	70-74 years	1.351	1.136	1.068	1.092	1.131
female	75-79 years	1.351	1.136	1.068	1.092	1.131
female	80-84 years	1.351	1.136	1.068	1.092	1.131
female	85-89 years	1.351	1.136	1.068	1.092	1.131
female	90-94 years	1.351	1.136	1.068	1.092	1.131
female	95+ years	1.351	1.136	1.068	1.092	1.131

Table 6 - continued

sex	200 0000	Alzheimer's disease and other	Asthma	Gallbladder and biliary		Atrial fibrillation and flutter	
sex	age-group	dementias	Astnma diseases		Chronic kidney disease	Atrial fibriliation and flutter	
male	25-29 years	1.218	1.409	1.464	1.000	1.344	
male	30-34 years	1.218	1.409	1.464	1.000	1.344	
male	35-39 years	1.218	1.409	1.464	1.746	1.344	
male	40-44 years	1.218	1.409	1.464	1.746	1.344	
male	45-49 years	1.218	1.409	1.464	1.746	1.344	
male	50-54 years	1.218	1.409	1.464	1.746	1.344	
male	55-59 years	1.218	1.409	1.464	1.746	1.344	
male	60-64 years	1.218	1.409	1.464	2.039	1.344	
male	65-69 years	1.218	1.409	1.464	2.039	1.344	
male	70-74 years	1.218	1.409	1.464	1.614	1.344	
male	75-79 years	1.218	1.409	1.464	1.614	1.344	
male	80-84 years	1.218	1.409	1.464	1.438	1.344	
male	85-89 years	1.218	1.409	1.464	1.438	1.344	
male	90-94 years	1.218	1.409	1.464	1.438	1.344	
male	95+ years	1.218	1.409	1.464	1.438	1.344	
female	25-29 years	1.214	1.402	1.729	1.000	1.346	
female	30-34 years	1.214	1.402	1.729	1.000	1.346	
female	35-39 years	1.214	1.402	1.729	1.746	1.346	
female	40-44 years	1.214	1.402	1.729	1.746	1.346	
female	45-49 years	1.214	1.402	1.729	1.746	1.346	
female	50-54 years	1.214	1.402	1.729	1.746	1.346	
female	55-59 years	1.214	1.402	1.729	1.746	1.346	
female	60-64 years	1.214	1.402	1.729	2.039	1.346	
female	65-69 years	1.214	1.402	1.729	2.039	1.346	
female	70-74 years	1.214	1.402	1.729	1.614	1.346	
female	75-79 years	1.214	1.402	1.729	1.614	1.346	
female	80-84 years	1.214	1.402	1.729	1.438	1.346	
female	85-89 years	1.214	1.402	1.729	1.438	1.346	
female	90-94 years	1.214	1.402	1.729	1.438	1.346	
female	95+ years	1.214	1.402	1.729	1.438	1.346	

For non-Hodgkin lymphoma we used the relative risks from the supplementary material of Gakidou et al. (2017)—representing the RRs of the GBD 2017 study—because non-Hodgkin lymphoma is not included as a cause of death associated to high BMI in the GBD 2019 study. We decided to include non-Hodgkin lymphoma as a cause of death related to obesity because obesity is associated with altered immune and inflammatory responses, and it may therefore influence the risk of non-Hodgkin's lymphoma (Larsson and Wolk, 2007). For all the other causes of death the relative risks are from the GBD 2019. We compared the values of the relative risks in the GBD 2017 database against those in the GBD 2019 database and we did not observe differences between the GBD relative risks of the year 2017 compared to those of the GBD 2019 for the 20 causes of death that we considered for the calculation of HBAM.

Table 7 below shows the comparison of the cause-specific relative risks (RRs) of Hoffmann et al. (2015) against the cause-specific RRs of the GBD for high BMI. The RRs of the GBD are higher than those of Hoffmann et al. (2015) in the case of ischemic heart disease, diabetes mellitus type 2, and cerebrovascular disease/stroke. In the case of 'kidney and renal pelvis cancer', the RRs of GBD are equal to the RRs of Hoffmann et al. (2015). The GBD's RRs of breast cancer are lower than those of Hoffmann, and the GBD's RRs of colorectal cancer are similar than those of Hoffmann for males and lower in the case of females.

Table 7. Comparison of the cause-specific relative risks of dying from high BMI of Hoffmann et al. (2015) against those of the GBD

Sex	age group	Colorectal cancer		Breast Cancer		Kidney and renal pelvis cancer		Ischemic heart diseases		Diabetes mellitus type 2		Cerebrovascular disease/stroke	
		Hoffmann	GBD	Hoffmann	GBD	Hoffmann	GBD	Hoffmann	GBD	Hoffmann	GBD	Hoffmann	GBD
Male	30-44	1.20	1.18			1.24	1.24	1.35	1.78	2.25	3.32	1.20	2.01
Male	45-59	1.18	1.18			1.24	1.24	1.35	1.52	2.25	2.64	1.20	1.64
Male	60-69	1.18	1.18			1.24	1.24	1.30	1.39	2.15	2.13	1.18	1.42
Male	70-79	1.18	1.18			1.24	1.24	1.25	1.30	2.14	1.82	1.15	1.27
female	30-44	1.08	1.06	1.00	0.89	1.32	1.32	1.35	1.78	2.30	3.32	1.20	2.01
female	45-59	1.07	1.06	1.08	1.02	1.32	1.32	1.35	1.52	2.30	2.64	1.20	1.64
female	60-69	1.07	1.06	1.12	1.09	1.32	1.32	1.30	1.39	2.20	2.13	1.18	1.42
female	70-79	1.07	1.06	1.12	1.09	1.32	1.32	1.25	1.30	2.18	1.82	1.15	1.27

The differences between the GBD's RRs and the RRs of Hoffmann are the results of the fact that the GBD's RRs are based on meta-regressions applied to data of 204 countries worldwide, while in the case Hoffmann et al. (2015) the RRs are based on information from the UK, Europe, and the USA.

Because we regard the use of the RRs by Hoffmann et al. (2015) as more relevant for our study of selected European countries, compared to the use of the worldwide RRs by GBD we will –when estimating HBAM using method 1– always use the RRs by Hoffmann for the six main high-BMI attributable causes of death, and complement these— when using the 10 or 20 high-BMI related causes— with the RRs from the GBD for the remaining causes of death.

2.4 Cause-specific GBD PAFs

For method 3, we directly applied the cause-specific high-BMI PAFs from the GBD to cause-specific mortality to obtain estimates of high-BMI attributable mortality.

For this purpose, we obtained country-specific but not education-specific estimates of cause-specific population-attributable fractions (PAFs) related to high-BMI from the Global Burden of Disease (GBD) Study (IHME, 2018) by sex and five-year age group (30-34, ..., 90-94, 95+) for single calendar years from 1990 up to 2017. We obtained these PAFs for the 20 causes of death listed in Table 2. The GBD's PAFs for multiple risk factors were computed for the years 1990–2019 based on PAF_i for i = 1,2,...,n individual risk factors:

$$PAF_{1...i} = 1 - \prod_{i=1}^{n} (1 - PAF_i)$$

assuming no significant covariance between individual PAFs. In the GBD study, spatiotemporal Gaussian process regression was applied to estimate the prevalence of overweight and obesity and risk-outcome pairs were defined based on strength of available evidence supporting a causal effect. The relative risks used in the PAFs per five-unit change in BMI for each disease was obtained from meta-analyses, and where available, pooled analyses of prospective observational studies. In cases where a relative risk per five-unit change in BMI was not available, the GBD study computed their own dose-response meta-analysis using two-step generalized least squares for time trends estimation methods (GBD 2019 Risk Factors Collaborators, 2020).

In order to obtain PAF estimates for 1970-2025, we performed linear extrapolation of the absolute annual change in the cause-, sex, and age-specific PAFs between 1990 and 2017, assuming linear increases or decreases in these PAFs over time, in line with the observed trends in the PAFs. In few cases, to avoid illogical outcomes, we applied instead linear extrapolation of the logit of the cause-, sex, and age-specific PAFs, based on the 1990-1995 values to obtain the values for 1970-1989, and based on the 2012-2017 values to obtain the values after 2017.

3. Methods

3.1. Method 1: Cause-specific prevalence approach

The first method, our main method, is a population-attributable fraction (PAF) method in which we combine our prevalence data by educational level with cause-specific relative risks of dying to calculate PAFs by cause of death, year, educational level, sex, and age. Subsequently cause-specific obesity or high-BMI attributable mortality is obtained by multiplying the PAFs with the cause-specific death counts by year, educational level, sex, and age. And finally, OAM and HBAM by year, educational level, sex, and age is obtained by summing the obesity or high-BMI attributable death counts over the causes of death.

To estimate OAM, we used obesity-related RRs for the six causes of death listed in Table 3. This because we were unable to find RRs for obesity associated to other causes of death, and because using six causes is in line with the study of Hoffmann et al. (2015). Hoffmann et al. (2015) based their selection of causes of death on those most frequently associated to high-BMI and obesity-attributable mortality in previous studies.

To estimate HBAM, we selected –as our baseline– the 10 causes of death associated with high-BMI (see Table 3). The selection of these 10 causes of death as the most important associated with high-BMI mortality was based on the following rule: causes of death considered by either Hoffmann et al. (2015) or Gutin (2020) and those considered in the Global Burden of Cause of death (GBD) database as being high-BMI attributable. **Table 8** compares the causes of deaths considered by Hoffmann et al. (2015) and Gutin (2020) with those included in the GBD database. For the 6 causes of death included in Hoffmann et al. 2015 we used the RRs from Hoffmann et al., whereas for the remaining 4 causes of death we used the RRs from the GBD database.

For high BMI, the baseline for comparison is calculated with the 6 causes of death considered by Hoffmann et al. (2015), to be in line with the selection for OAM, and for the remaining causes of death based we considered those considered by the GBD.

Table 8. Comparison of the causes of death associated with high BMI in the GBD against those considered by Hoffmann et al. (2015) and Gutin (2020)

Cause of death	GBD	Hoffmann*	Gutin**
Colon and rectum cancer	X	X	X
Breast cancer	X	X	
Kidney cancer	X	X	~
Ischemic heart disease	X	X	~
Hypertensive heart disease	X		~
Cerebrovascular disease (ischemic stroke)	X	X	~
Diabetes mellitus type 2	X	X	X
Gallbladder and biliary tract cancer	X		~
Pancreatic cancer	X		X
Liver cancer	X		X

x: explicitly considered

We use the information of prevalence and the information of relative risks to calculate population attributable fractions $PAF_{c,a,t,s,e}$ by cause of death (c), age (a), year (t), sex (s), and educational level (e), given our own estimations of prevalence $p_{a,t,s,e}$ by age (a), year (t), sex (s), and educational level (e), and the relative risks $RR_{c,s,a}$ by cause of death (c), age (a), and sex (s). We calculated the PAFs with the Rockhill formula (Vidra et al., 2019):

$$PAF_{c,a,t,s,e} = \frac{p_{a,t,s,e} (RR_{c,a,s} - 1)}{1 + (p_{a,t,s,e} (RR_{c,a,s} - 1))}$$
(1)

We obtained each cause-specific attributable mortality $AM_{c,a,t,s,e}$ by multiplying the $PAF_{c,a,t,s,e}$ times the death counts $n_{c,a,t,s,e}$ of each cause of death considered in the study:

$$AM_{c,a,t,s,e} = PAF_{c,a,t,s,e} \times n_{c,a,t,s,e}$$
 (2)

^{~:} implicitly considered

^{*}Hoffmann et al. (2015) explicitly considers coronary heart cause of death jointly with ischemic heart cause of death

^{**}Gutin (2020) considers cardiovascular cause of deaths (CVDs) and cardiometabolic deaths, hence it is assumed that implicitly considers ischemic heart cause of death, hypertensive heart cause of death and ischemic stroke since according to WHO (2004), mortality from major cardiovascular cause of deaths (International Classification of Cause of deaths, Tenth Revision (ICD-10, I00-178) includes deaths from Cause of deaths of heart (ICD-10 codes I00-I09, I11, I13, I20-I51); Essential hypertension and hypertensive renal cause of death (I10, I12, I15) and Cerebrovascular cause of deaths (I60-169). Gutin (2020) considers kidney-related conditions and cause of deaths related to intrahepatic bile ducts; hence it is assumed that kidney cancer and gallbladder and biliary tract cancer are implicitly considered by Gutin (2020). Gutin (2020) also considers prostate cancer, which is not included in the table as it is not explicitly considered in the GBD.

Obesity-attributable mortality (OAM) and high-BMI attributable mortality (HBAM) is obtained by adding the cause-specific attributable death counts by cause of death c:

$$OAM_{a,t,s,e} = OAM_{1,a,t,s,e} + OAM_{2,a,t,s,e} + \dots + OAM_{c,a,t,s,e} = \sum_{c=1}^{\Delta} OAM_{c,a,t,s,e}$$
(3)

$$HBAM_{a,t,s,e} = HBAM_{1,a,t,s,e} + \dots + HBAM_{c,a,t,s,e} = \sum_{c=1}^{\Delta} HBAM_{c,a,t,s,e}$$
(4)

A δ -subset of causes of death $\delta \subset \Delta$ was chosen to calculate OAM and HBAM by groups of causes of death. The baseline estimation of OAM is based on the 6 causes of death considered by Hoffmann et al. (2015), in which as a final step we add the death counts of obesity ($od_{a,t,s,e}$, ICD10 E65-E66) by age, calendar year, sex and educational level:

$$OAM_{6hoffmann,a,t,s,e} = \sum_{\delta=1}^{6} OAM_{\delta,a,t,s,e} + od_{a,t,s,e}$$
(5)

Our baseline of HBAM is based on using both the RRs from Hoffmann and the RRs of the GBD database. HBAM was calculated by combining the 6 relative risks of Hoffmann et al. (2015) with the GBD's relative risks for other diseases. For the HBAM for 10 causes of death, our baseline HBAM calculation is based on 4 relative risks from Hoffmann et al. (2015) and six RRs of the GBD database, also adding the death-counts of obesity (equal to $od_{a,t,s,e}$ in the equation above and below, corresponding to the ICD10 E65-E66 classification):

$$HBAM_{10HGD.a.t.s.e} = \sum_{\delta=1}^{6} HBAM_{hoffmann.\delta.a.t.s.e} + \sum_{\delta=1}^{4} HBAM_{GBD.\delta.a.t.s.e} + od_{a.t.s.e}$$
 (6)

In the HBAM calculated with the 20 causes of death, our baseline HBAM calculation is based on 4 relative risks from Hoffmann et al. (2015) and 16 RRs of the GBD database, adding the death counts of obesity as a final step:

$$HBAM_{20HGD,a,t,s,e} = \sum_{\delta=1}^{6} HBAM_{hoffmann,\delta,a,t,s,e} + \sum_{\delta=1}^{14} HBAM_{GBD,\delta,a,t,s,e} + od_{a,t,s,e}$$
(7)

Additionally, we calculated the HBAM for 6 causes of death, 10 causes and 20 causes of death, using only the RRs from the GBD database, adding the death counts of obesity as a final step:

$$HBAM_{6GBD,a,t,s,e} = \sum_{\delta=1}^{6} HBAM_{\delta,a,t,s,e} + od_{a,t,s,e}$$
 (8)

$$HBAM_{10GBD,a,t,s,e} = \sum_{\delta=1}^{10} HBAM_{\delta,a,t,s,e} + od_{a,t,s,e}$$
 (9)

$$HBAM_{20GBD,a,t,s,e} = \sum_{\delta=1}^{20} HBAM_{\delta,a,t,s,e} + od_{a,t,s,e}$$
 (10)

In the case of Italy, about 1% of the deaths have an unspecified cause of death. We dealt with this by proportionally distributing the deaths with an unspecified cause of death to the different causes of death by age, sex, educational level, and year. For example, for $HBAM_{20GBD,a,t,s,e}$, the adjusted HBAM for Italy is equal to:

$$\widetilde{HBAM}_{20GBD,a,t,s,e} = \left(\frac{N_{a,t,s,e}}{\sum_{\delta} d_{a,t,s,e}}\right) HBAM_{20GBD,a,t,s,e}$$
(11)

where $N_{a,t,s,e}$ is the total mortality counts from the general mortality database and $\sum_{\delta} d_{a,t,s,e}$ are the total mortality obtained by aggregating all the cause-specific death counts. The ratio of $N_{a,t,s,e}$ divided by $\sum_{\delta} d_{a,t,s,e}$ is used to distribute the unspecified death counts by age (a), year

(t), sex (s), and educational level (e) to the overall aggregated HBAM. This adjustment was applied to the calculations of OAM and HBAM in methods M1, M2 and M3 only for Italy.

3.2. Method 2: All-cause prevalence approach

The second method is a population-attributable fraction (PAF) method that uses our prevalence data as well by educational level, but now combines it purely with all-cause relative risks of dying to calculate PAFs for all-cause mortality, by year, educational level, sex, and age. Subsequently, OAM and HBAM by year, educational level, sex, and age is obtained by multiplying the all-cause PAFs with the all-cause death counts by year, educational level, sex, and age.

To calculate all-cause PAFs, we used the all-cause RRs of Hoffmann et al. (2015), after first applying quadratic interpolation. We calculated the PAF with the Rockhill formula (Vidra et al., 2019):

$$PAF_{allcause_obesity,a,t,s,e} = \frac{p_{a,t,s,e} \left(RR_{allcause_obesity,a,s} - 1 \right)}{1 + \left(p_{a,t,s,e} \left(RR_{allcause_obesity,a,s} - 1 \right) \right)}$$
(12)

$$PAF_{allcause_highBMI,a,t,s,e} = \frac{p_{a,t,s,e} \left(RR_{allcause_highBMI,a,s} - 1 \right)}{1 + \left(p_{a,t,s,e} \left(RR_{allcause_highBMI,a,s} - 1 \right) \right)}$$
(13)

With the all-cause PAFs, we calculate all-cause OAM and all-cause HBAM by age (a), calendar year (t), sex (s), and educational level (e):

$$OAM_{allcause.a.t.s.e} = PAF_{allcause\ obesitv.a.t.s.e} \times n_{allcause.a.t.s.e}$$
(14)

$$HBAM_{allcause,a.t.s.e} = PAF_{allcause\ highBMI.a.t.s.e} \times n_{allcause.a.t.s.e}$$
 (15)

3.3. Method 3: Cause-specific GBD PAFs approach

The third method is as well a population-attributable fraction (PAF) method, but we now directly use the cause-specific PAFs from the Global Burden of Disease (GBD) database, which pertain to high-BMI and are not education-specific.

We obtained HBAM death counts by cause, year, educational level, sex, and age by multiplying the GBD's PAFs by the death counts of each cause of death $n_{c,a,t,s,e}$:

$$HBAM_{c,a,t,s,e} = GBDPAF_{c,a,t,s,e} \times n_{c,a,t,s,e}$$
(16)

As in method 1, in method 3 we use the GBD PAFs to calculate HBAM for 6, 10 and 20 groups of causes of death, but in method 3 we considered the calculation with the 20 groups of causes of death as our baseline:

$$HBAM_{6GBD,a,t,s,e} = \sum_{\delta=1}^{6} HBAM_{\delta,a,t,s,e} + od_{a,t,s,e}$$

$$\tag{17}$$

$$HBAM_{20GBD,a,t,s,e} = \sum_{\delta=1}^{20} HBAM_{\delta,a,t,s,e} + od_{a,t,s,e}$$
 (18)

$$HBAM_{10GBD,a,t,s,e} = \sum_{\delta=1}^{10} HBAM_{\delta,a,t,s,e} + od_{a,t,s,e}$$
 (19)

Because the GBD PAFs are only available from 1990-2017, we had to extrapolate the PAFs to obtain PAF estimates for 1970-2025. For this purpose, we performed linear extrapolation of

the absolute annual change between 1990 and 2017, assuming linear increases or decreases in the PAFs over time. In a few exceptions, however, we applied instead linear extrapolation of the logit of the PAFs, based on the 1990-1995 values to obtain the values for 1970-1989, and based on the 2012-2017 values to obtain the values after 2017.

3.4. Method 4: Multiple causes of death approach

The fourth method is not a population-attributable fraction approach, but a cause of death approach, that merely uses cause of death information, that is the method estimates high-BMI -attributable mortality for different underlying causes of death that are partly-attributable to high-BMI by assessing whether the contributory causes of death are high-BMI-attributable or not.

The method is based on the method by Adair & Lopez (2020) who estimated the number of cardiovascular-related deaths due to high BMI based on the mention of any cardiovascular disease as the underlying cause of death on the death certificate in combination with either diabetes, chronic kidney disease, obesity, lipidaemia, or hypertensive heart diseases as a contributory cause of death (Adair & Lopez, 2020).

We extended this method and used it to estimate not only the number of cardiovascular-related deaths due to high BMI, but also the number of all deaths due to high BMI based on the mention of any (cardiovascular) disease as the underlying cause of death on the death certificate in combination with either diabetes, chronic kidney disease, obesity, lipidaemia, or hypertensive heart diseases as a contributory cause of death. See **Table 9** for the official classification codes of these causes of death. For cardiovascular disease we used ICD8: 390-458, ICD9: 390-459, and ICD10: I00-I99.

Table 9. Contributory causes of death considered in the multiple causes of death approach (Method 4)

Contributory cause of death	ICD8	ICD9	ICD10
Hypertensive heart disease*	401-404	401-404	I10-I13
Diabetes	250	250	E10-E14
Chronic kidney disease*	585	585	N18
Lipidemia	272	272.0-272.5	E78
Obesity	277	278.0, 278.1	E65-E66

^{*} How we define hypertensive heart disease and chronic kidney disease here is in line with Adair & Lopez (2020), and different from the tables on the causes of death partly related to alcohol and high BMI, which were based on the GBD definitions

The main outcomes of method M4 are high-BMI-attributable CVD mortality, and high-BMI-attributable all-cause mortality. In our baseline calculation of method 4, we used information on the first three contributory causes of death on the death certificate, because for Finland only information on those three causes were available. Formally:

$$HBAM_{multiplecause,a,t,s,e}^{CVD} = \sum_{i=1}^{3} n_{i,a,t,s,e}^{CVD}$$
 (20)

where $n_{i,a,t,s,e}^{CVD}$ are death counts associated to cardiovascular disease (CVD) mortality (the underlying cause of death), by age (a), year (t), sex (s), and educational level (e), and

 $\sum_{i=1}^{3} n_{i,a,t,s,e}^{CVD}$ are the sum of deaths that have CVD as the underlying cause of death and any of contributory causes hypertensive heart disease, diabetes, chronic kidney disease, lipidaemia, or obesity as one of the first three contributory causes on the death certificate. In the case of England & Wales, information on the first 8 contributory causes of death on the death certificate are available, hence for England & Wales besides calculations for 3 contributory causes of death, additional calculations are performed for 8 contributory causes of death.

Method 4 was applied only to England & Wales and Finland, because Italy lacks long-term information on contributory causes of death by educational level. England & Wales and Finland have information of the underlying cause of death and the contributory causes of death. In the case of England & Wales, we have information of 8 contributory causes of death and hence we calculated HBAM for 3 and for 8 causes of death. In the case of Finland, we only have information of 3 causes of death, so HBAM rates and fractions in Finland are only calculated with 3 contributory causes of death.

3.5 Comparisons made with the four methods.

To enable the comparison of estimation between the four different methods, we assessed trends in age-standardized mortality rates (30-95+) and age-standardized mortality fractions (30-95+), by educational level for each relevant method, both for OAM and HBAM

To estimate age-standardized mortality rates (ASCDR, 30-95+) we applied direct age-standardization by 5-year age groups using the standard population distribution of the in 2013 revised European Standard Population (European Commission, 2013). This European Standard Population (ESP) is based on the projected total (=male + female combined) population of the European Union (EU)-27 plus the European Free Trade Association (EFTA) countries, based on the Eurostat 2010-based population projections, averaged over the period 2011-2030. To perform the age-standardization, we first calculated strata-specific mortality rates $MR_{a,t,s,e}$ (by age a, year t, sex s, and educational level e) by dividing OAM and HBAM death counts with the population counts over time $N_{a,t,s,e}$ (by age a, year t, sex s, and educational level e):

$$OAMR_{a,t,s,e} = \frac{\sum_{\delta} OAM_{\delta,a,t,s,e}}{N_{a,t,s,e}}$$
 (28)

$$HBAMR_{a,t,s,e} = \frac{\sum_{\delta} HBAM_{\delta,a,t,s,e}}{N_{a,t,s,e}}$$
 (29)

Subsequently, we calculated the age-standardized mortality rates ($ASCDR_{t,s,e}$, 30-95+) by applying the in 2013 revised European Standard Population to the strata-specific mortality rates, by means of a weighted sum, where the weights represent the ESP weights w_a^{ESP} for 5-year age groups (30-95+), detailed in **Table 10** below:

$$SOAMR_{t,s,e} = \sum_{a} w_a^{ESP} OAMR_{a,t,s,e}$$
 (30)

$$SHBAMR_{t,s,e} = \sum_{a} w_a^{ESP} HBAMR_{a,t,s,e}$$
 (31)

To calculate the age-standardized mortality fractions (ASPAF), we need a standard mortality schedule instead of a standard population distribution. For this standard mortality schedule, we used all-cause death counts for the country-specific general population by 5-year age groups

for the year 2017. We also performed a sensitivity analysis in which we applied a sex- and educational level specific mortality schedule (see **Appendix I**). For both standardizations, we first calculated strata-specific mortality fractions $MF_{a,t,s,e}$ (by age a, year t, sex s, and educational level e) by dividing OAM and HBAM death counts by all-cause death counts $D_{a,t,s,e}$ (all-cause death counts $D_{a,t,s,e}$ by age a, year t, sex s, and educational level e):

$$OAMF_{a,t,s,e} = \frac{\sum_{\delta} OAM_{\delta,a,t,s,e}}{D_{a,t,s,e}}$$
(32)

$$HBAMF_{a,t,s,e} = \frac{\sum_{\delta} HBAM_{\delta,a,t,s,e}}{D_{a,t,s,e}}$$
(33)

Subsequently, we obtained age-standardized mortality fractions ($ASPAF_{t,s,e}$) by weighing the strata-specific mortality fractions with the relevant weights (in line with the selected standard mortality schedule): either the mortality weights w_a^M by 5-year age groups (30-95+, **Table 11**), or the mortality weights $w_{a,s,e}^M$ by sex, educational level, and 5-year age groups (30-95+), for England & Wales (**Table 12.1**), Finland (**Table 12.2**), and Italy (**Table 12.3**):

$$SOAMF1_{t,s,e} = \sum_{a} w_a^M OAMF_{a,t,s,e}$$
 (34)

$$SHBAMF1_{t,s,e} = \sum_{a} w_a^M HBAMR_{a,t,s,e}$$
 (35)

$$SOAMF2_{t,s,e} = \sum_{a} w_{a,s,e}^{M} OAMF_{a,t,s,e}$$
 (36)

$$SHBAMF2_{t,s,e} = \sum_{a} w_{a,s,e}^{M} HBAMR_{a,t,s,e}$$
 (37)

Table 10. ESP 2013 weights by age group used to calculate age-standardized mortality rates of OAM and HBAM (30-95+)

Age-group	Standard population	ESP weights
[30 - 35)	6500	0.097744361
[35 - 40)	7000	0.105263158
[40 - 45)	7000	0.105263158
[45 - 50)	7000	0.105263158
[50 - 55)	7000	0.105263158
[55 - 60)	6500	0.097744361
[60 - 65)	6000	0.090225564
[65 - 70)	5500	0.082706767
[70 - 75)	5000	0.07518797
[75 - 80)	4000	0.060150376
[80 - 85)	2500	0.037593985
[85 - 90)	1500	0.022556391
[90 - 95)	800	0.012030075
[95+	200	0.003007519
Total	66500	1

Table 11. Mortality weights by age group used to calculate OAM and HBAM fractions, based on national all-cause death counts for the general population, by 5-year age groups, for the year 2017

A	Mortality weights							
Age-group	England & Wales	Finland	Italy					
[30 - 35)	0.005528131	0.0048368508	0.001230895					
[35 - 40)	0.007740079	0.0054414571	0.001948918					
[40 - 45)	0.008519925	0.0080866099	0.004923582					
[45 - 50)	0.016282641	0.0111096416	0.010462612					
[50 - 55)	0.023828753	0.0222948590	0.013847574					
[55 - 60)	0.032492458	0.0327432123	0.023489589					
[60 - 65)	0.045687514	0.0555671019	0.029541491					
[65 - 70)	0.069475657	0.0857974191	0.046876603					
[70 - 75)	0.098527233	0.1005346987	0.071904811					
[75 - 80)	0.122269757	0.1218470724	0.127397682					
[80 - 85)	0.162764132	0.1570087101	0.188019284					
[85 - 90)	0.186236846	0.1926238026	0.226382193					
[90 - 95)	0.145548659	0.1443497648	0.179403016					
[95+	0.075098215	0.0577587999	0.074571751					
Total	1	1	1					

Table 12.1. England & Wales: Mortality weights by age group, education, and sex, used to calculate OAM and HBAM fractions, based on national all-cause death counts for the general population, by 5-year age groups, for the year 2017

Ago group	low education		middle e	ducation	high education	
Age-group	men	women	men	women	men	women
[30 - 35)	0.00313724	0.00255920	0.00488205	0.00959309	0.01295431	0.02522839
[35 - 40)	0.00451530	0.00901505	0.00389284	0.01003690	0.01818252	0.02009850
[40 - 45)	0.00521561	0.01005010	0.01579918	0.00690287	0.02118230	0.01110337
[45 - 50)	0.01074309	0.01703566	0.01198522	0.01609763	0.03465054	0.05232768
[50 - 55)	0.01619011	0.02945762	0.02162005	0.02443054	0.06585795	0.03353798
[55 - 60)	0.02319854	0.03972339	0.02665467	0.03584094	0.06146639	0.04997523
[60 - 65)	0.03428367	0.05031011	0.03772966	0.05990799	0.06240373	0.07121617
[65 - 70)	0.05361429	0.07247638	0.06062950	0.09894113	0.07515601	0.10026203
[70 - 75)	0.07964255	0.10942672	0.08576303	0.13103340	0.08708473	0.11527801
[75 - 80)	0.10413712	0.13879404	0.12268935	0.14303485	0.10281788	0.11735542
[80 - 85)	0.15335113	0.17837325	0.17041831	0.17278648	0.11659575	0.12823585
[85 - 90)	0.20651571	0.17984047	0.19351483	0.16495520	0.14436580	0.13708074
[90 - 95)	0.19067304	0.11951512	0.14973362	0.09488301	0.11904831	0.09897225
[95+	0.11478260	0.04342288	0.09468768	0.03155597	0.07823377	0.03932839
Total	1	1	1	1	1	1

Table 12.2. Finland: Mortality weights by age group, education, and sex, used to calculate OAM and HBAM fractions, based on national all-cause death counts for the general population, by 5-year age groups, for the year 2017

A go group	low education		middle e	ducation	high education		
Age-group	men	women	men	women	men	women	
[30 - 35)	0.00544115	0.00134228	0.01328114	0.00590319	0.00298635	0.00285470	
[35 - 40)	0.00537227	0.00175080	0.01398015	0.00455389	0.00490614	0.00856409	
[40 - 45)	0.00674978	0.00169244	0.01929260	0.00961376	0.01343857	0.01227519	
[45 - 50)	0.00764515	0.00315144	0.02823990	0.01130039	0.01813140	0.01969740	
[50 - 55)	0.01646119	0.00595273	0.05620020	0.02799798	0.02986348	0.03739652	
[55 - 60)	0.02224671	0.00828713	0.08206347	0.04705684	0.04735495	0.05138453	
[60 - 65)	0.04903919	0.01844179	0.12721935	0.06797099	0.07572526	0.06994005	
[65 - 70)	0.08933122	0.03764225	0.15434084	0.10322145	0.11497440	0.09820154	
[70 - 75)	0.11247331	0.05608404	0.13994128	0.10575139	0.15059727	0.11218955	
[75 - 80)	0.14911495	0.09530201	0.11994967	0.12228032	0.14249147	0.11418784	
[80 - 85)	0.18975136	0.15973154	0.10596952	0.14707371	0.14910410	0.13959463	
[85 - 90)	0.20194228	0.26046104	0.08583811	0.16360263	0.14590444	0.15186983	
[90 - 95)	0.11509057	0.24038518	0.04235985	0.12868949	0.07849829	0.11875535	
[95+	0.02934086	0.10977531	0.01132392	0.05498398	0.02602389	0.06308878	
Total	1	1	1	1	1	1	

Table 12.3. Italy: Mortality weights by age group, education, and sex, used to calculate OAM and HBAM fractions, based on national all-cause death counts for the general population, by 5-year age groups, for the year 2017

A go group	low education		middle e	ducation	high education		
Age-group	men	women	men	women	men	women	
[30 - 35)	0.00000000	0.00000000	0.00269906	0.00066756	0.00343053	0.00383142	
[35 - 40)	0.00000000	0.00000000	0.00337382	0.00133511	0.00771870	0.00383142	
[40 - 45)	0.00052219	0.00103270	0.01012146	0.00400534	0.01286449	0.01021711	
[45 - 50)	0.00104439	0.00000000	0.02631579	0.01068091	0.01372213	0.03703704	
[50 - 55)	0.00208877	0.00103270	0.02631579	0.01869159	0.03173242	0.03065134	
[55 - 60)	0.00678851	0.00206540	0.05533063	0.02937250	0.03945111	0.04853129	
[60 - 65)	0.01462141	0.00929432	0.06005398	0.03471295	0.04545455	0.04980843	
[65 - 70)	0.03916449	0.01962134	0.07422402	0.05607477	0.08147513	0.04597701	
[70 - 75)	0.07832898	0.04027539	0.10053981	0.07142857	0.09948542	0.07918263	
[75 - 80)	0.15091384	0.10154905	0.16936572	0.11949266	0.13121784	0.09578544	
[80 - 85)	0.23498695	0.20447504	0.17881242	0.13818425	0.18181818	0.13409962	
[85 - 90)	0.26370757	0.26058520	0.16396761	0.23230975	0.18010292	0.18390805	
[90 - 95)	0.15195822	0.24543890	0.09919028	0.19292390	0.13550600	0.19284802	
[95+	0.05587467	0.11462995	0.02968961	0.09012016	0.03602058	0.08429119	
Total	1	1	1	1	1	1	

For obesity-attributable mortality, our main comparison is between our main method (= method 1 (= cause-specific prevalence approach with 6+1 causes) and method 2 (all-cause prevalence approach).

In addition, for obesity-attributable mortality, as sensitivity analyses, we compared for method 1 (cause-specific prevalence approach with 6+1 causes), which we regard as our baseline method, different standardizations of mortality fractions (the results can be found in **Appendix I**) and we compared for method 2 (all-cause prevalence approach) outcomes obtained using linearly interpolated RRs against outcomes obtained with a quadratic interpolation of RRs (the results can be found in **Appendix II**).

For high-BMI attributable mortality, our main comparison is between our main method and the other three methods. Our main estimation method for high-BMI-attributable mortality is the cause-specific-prevalence approach (method 1), thereby selecting 10 high-BMI-attributable causes of death plus including as well obesity-attributable deaths and using the RRs from Hoffmann et al. (2015) for the 6 causes of death they included, and the RRs from the GBD for the additional 4 causes of death.

For high-BMI attributable mortality, we —in addition— compared the results of our main method, with (a) the cause-specific prevalence approach (method 1) based on GBD's relative risks for 10 causes of death, (b) the cause-specific prevalence approach (method 1) based on GBD's relative risks for 20 causes of death, and (c) the cause-specific GBD PAF approach (method 3) based on GBD's relative risks for 20 causes of death (method 3). This to gain more insights into where the difference between the results from method 1 and method 3 stem from.

Also, for high-BMI attributable mortality we compared CVD-related high-BMI attributable mortality obtained through method 1, method 3 and method 4. This to gain more insights into the observed differences between these three cause-specific methods.

4. Results

4.1. Results for obesity-attributable mortality

Estimates of age-standardized obesity-attributable mortality (SOAMR) can only be obtained with method M1 (cause-specific prevalence approach) and method M2 (all-cause prevalence approach).

Figures 1.1, 1.2, and 1.3 compare Method 1 and Method 2 per country: England & Wales (Figures 1.1), Finland (Figures 1.2) and Italy (Figures 1.3). It can be observed that across the three educational groups, the levels of obesity-attributable mortality rates obtained with Method 2 (all cause prevalence approach) are higher than the obesity-attributable mortality rates obtained with Method 1 (cause-specific prevalence approach), both for males and females

The results by socio-economic stratum show that the difference in levels between SOAMR obtained both with Method 1 (cause-specific prevalence approach) and Method 2 (all-cause prevalence approach) has increased over the years for low- and middle- educated men and women in England & Wales. This increase in the gap between the levels of SOAMR obtained both with Method 1 (cause-specific prevalence approach) against the SOMAR calculated with Method 2 (all-cause prevalence approach) is also observed for low educated men and women

in Finland (Figure 1.2). This difference between the SOAMR obtained with methods 1 and methods 2 is observed in Italy only for women (Figure 1.3, right). At the same time, in Italy, the levels of SOAMR obtained with method 2 (all cause prevalence approach) are closer to the levels of SOAMR obtained with method 1 (cause specific prevalence approach) in the case of females (Figure 1.3).

The trends in SOAMR, for the three educational groups, are in general stable and increasing instead of declining for method 2 (all cause prevalence approach) compared to method 1 (cause specific prevalence approach), particularly among low- and middle- educated men and women in England & Wales (Figure 1.1) and for low-, middle- and high educated men and women in Finland (Figure 1.2). In Italy, similar trends of SOAMR are obtained with method 2 (all cause prevalence approach) and method 1 (cause specific prevalence approach, Figure 1.3). **Figure 2** compares the levels and trends over time in age-standardized OAM rates (SOAMR, 30-95+) by educational level and sex for England & Wales, Finland, and Italy, obtained through Method 1 (cause-specific prevalence approach with 6+1 causes) and Method 2 (all-cause-prevalence approach). Figure 2.1 for females, and Figure 2.2 for males. The left column of Figures 2.1 and 2.2 shows the results for Method 1 by educational level and the right column shows the results for Method 2 by educational level. What can be observed is that for England & Wales and Finland, for both males and females, method 1 results in more convergence in SOAMR levels over time between educational groups compared to method 2.

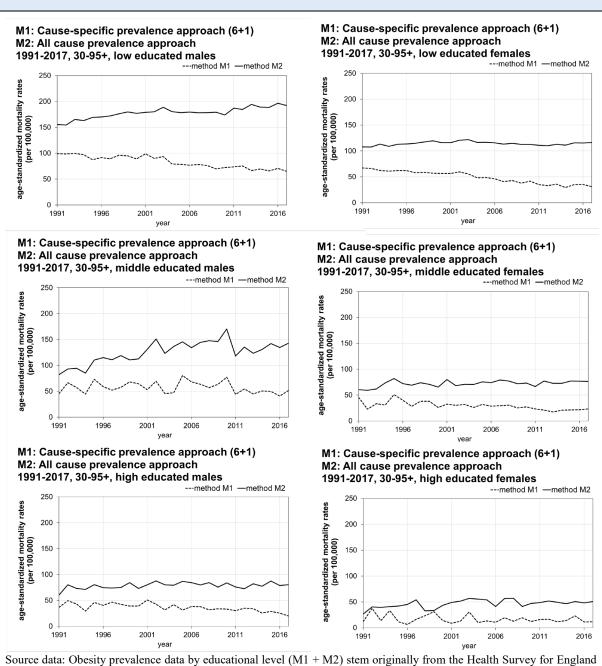
4.2. Results for high-BMI attributable mortality

Estimates of age-standardized high-BMI attributable mortality (SHBAMR) can be obtained using method M1 (cause-specific prevalence approach), method M2 (all-cause prevalence approach), method M3 (cause-specific prevalence approach based on the GBD's PAFs), and method M4 (multiple causes of death approach). The latter method could only be applied to England & Wales and Finland, based on the available data.

Figures 3.1, 3.2 and **3.3** compare the results of SHBAMR calculated with four methods, in England & Wales (Figure 3.1), Finland (Figure 3.2), and Italy (Figure 3.3), by sex and by educational level. The method M1 (cause-specific prevalence approach), M2 (all-cause prevalence approach), and M3 (cause-specific prevalence approach based on the GBD's PAFs) are based on the results of SHBAMR obtained with 10 causes of death plus obesity, combining 6 causes of death identified by Hoffmann et al. (2015) with 4 additional causes identified by the GBD. Method M4 (multiple causes of death approach) is based on the use of three contributory causes of death.

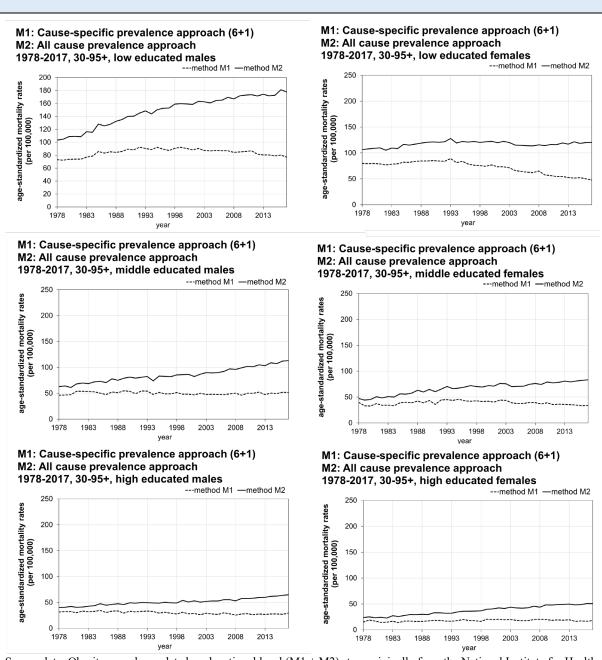
The lowest levels of age-standardized high-BMI attributable mortality rates are the ones calculated with method 1 (cause-specific prevalence approach). Stable and declining trends of SHBAMR are obtained with methods M1 (cause-specific prevalence approach), M2 (all-cause prevalence approach), and M3 (cause-specific prevalence approach based on the GBD's PAFs). In the case of M1 and M3, the trends are very similar and show a recent stagnation in the decline of trends for the three educational groups. In contrast, for Method 4 (multiple cause of death), increasing trends are observed from the year 1990 onwards. Specifically, ascending trends of SHBAMR estimated using method 4 are observed in England & Wales (Figure 3.1) after the year 1997, and in Finland (Figure 3.2) after the year 1996.

Figure 1.1. Trends in age-standardized obesity-attributable mortality rates (SOAMR), by educational level - comparing Method 1 (cause-specific prevalence approach, 6+1 causes) against Method 2 (all-cause prevalence approach), 30-95+: England & Wales



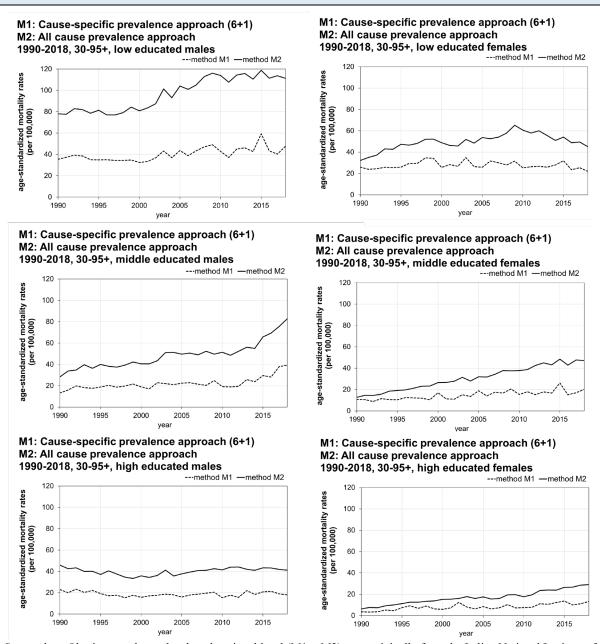
Source data: Obesity prevalence data by educational level (M1 + M2) stem originally from the Health Survey for England and were adjusted by Gonzales Martinez and Janssen (2023). All-cause (M2) and cause-specific (M1) RRs from Hoffmann et al. (2015). All-cause (M2) and cause-specific (M1) mortality data by educational level from the ONS – Longitudinal Study.

Figure 1.2. Trends in age-standardized obesity-attributable mortality rates (SOAMR), by educational level - comparing Method 1 (cause-specific prevalence approach, 6+1 causes) against Method 2 (all-cause prevalence approach), 30-95+: Finland.



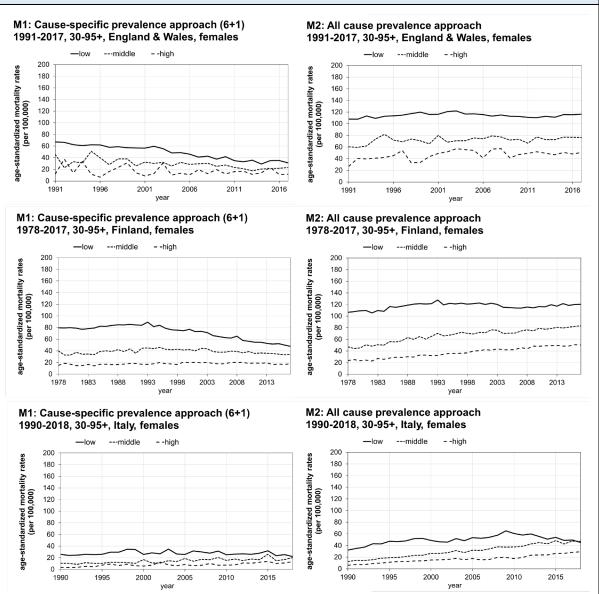
Source data: Obesity prevalence data by educational level (M1 + M2) stem originally from the National Institute for Health and Welfare and were adjusted by Gonzales Martinez and Janssen (2023). All-cause (M2) and cause-specific (M1) RRs from Hoffmann et al. (2015). All-cause (M2) and cause-specific (M1) mortality data by educational level from Statistics Finland.

Figure 1.3. Trends in age-standardized obesity-attributable mortality rates (SOAMR), by educational level - comparing Method 1 (cause-specific prevalence approach, 6+1 causes) against Method 2 (all-cause prevalence approach), 30-95+: Italy



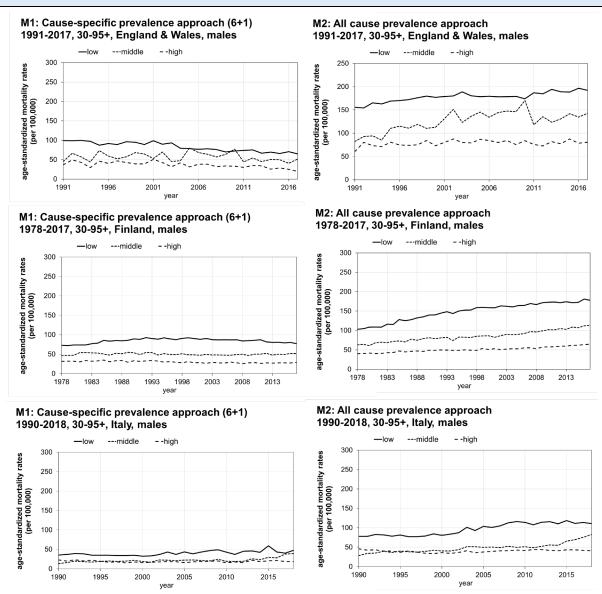
Source data: Obesity prevalence data by educational level (M1 + M2) stem originally from the Italian National Institute of Statistics (ISTAT) and were adjusted by Gonzales Martinez and Janssen (2023). All-cause (M2) and cause-specific (M1) RRs from Hoffmann et al. (2015). All-cause (M2) and cause-specific (M1) mortality data by educational level from the Turin Longitudinal Study.

Figure 2.1. Trends in age-standardized obesity-attributable mortality rates (SOAMR), by educational level - comparing Method 1 (cause-specific prevalence approach, 6+1 causes) against Method 2 (all-cause prevalence approach), England & Wales, Finland, and Italy (Turin), 30-95+, females:



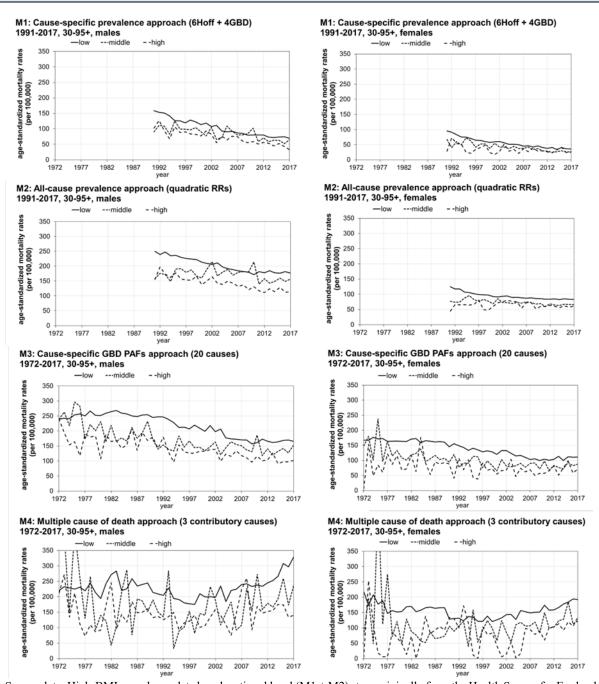
Source data: Obesity prevalence data by educational level (M1 + M2) stem originally from the Health Survey for England, the Finnish National Institute for Health and Welfare and the Italian National Institute of Statistics (ISTAT), respectively, and were adjusted by Gonzales Martinez and Janssen (2023). All-cause (M2) and cause-specific (M1) RRs from Hoffmann et al. (2015). All-cause (M2) and cause-specific (M1) mortality data by educational level from the ONS – Longitudinal Study, Statistics Finland and the Turin Longitudinal Study, respectively.

Figure 2.2. Trends in age-standardized obesity-attributable mortality rates (SOAMR), by educational level - comparing Method 1 (cause-specific prevalence approach, 6+1 causes) against Method 2 (all-cause prevalence approach), England & Wales, Finland, and Italy (Turin), 30-95+, males:



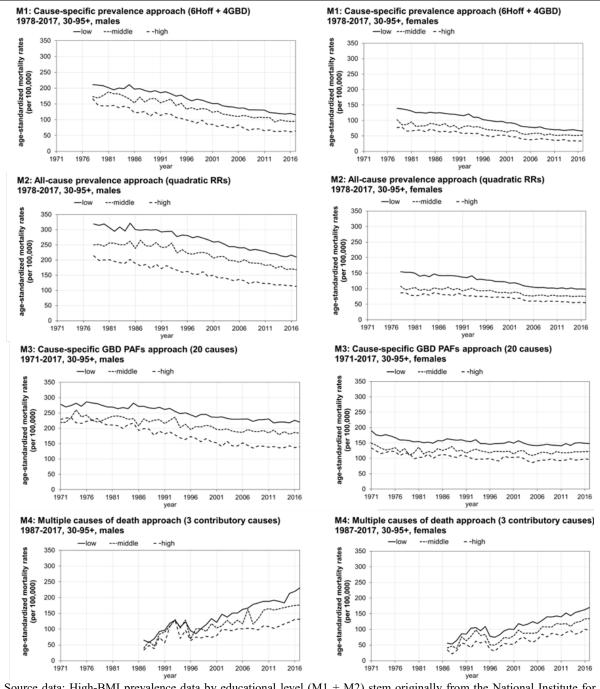
Source data: Obesity prevalence data by educational level (M1 + M2) stem originally from the Health Survey for England, the Finnish National Institute for Health and Welfare and the Italian National Institute of Statistics (ISTAT), respectively, and were adjusted by Gonzales Martinez and Janssen (2023). All-cause (M2) and cause-specific (M1) RRs from Hoffmann et al. (2015). All-cause (M2) and cause-specific (M1) mortality data by educational level from the ONS – Longitudinal Study, Statistics Finland, and the Turin Longitudinal Study, respectively.

Figure 3.1. Comparing Method 1 (M1: cause-specific prevalence approach based on our PAFs), Method 2 (M2: all-cause prevalence approach), Method 3 (M3: cause-specific prevalence approach based on GBD's PAFs), and Method 4 (M4: multiple causes of death approach): Age-standardized high-BMI-attributable mortality rates (SHBAMR), by educational level (low, middle, high), 30-95+: England & Wales



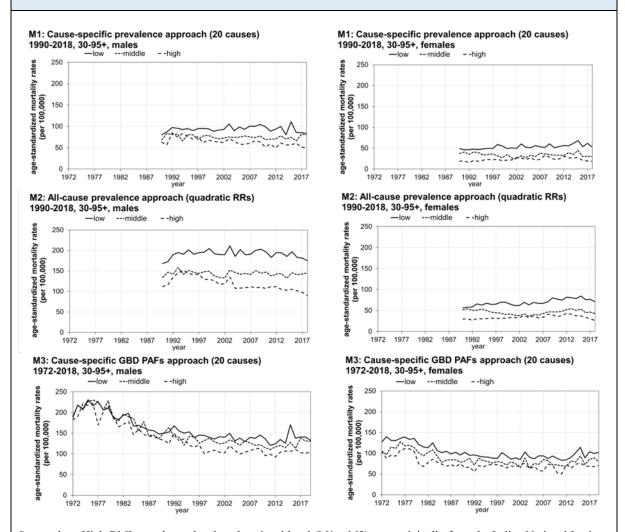
Source data: High-BMI prevalence data by educational level (M1 + M2) stem originally from the Health Survey for England and were adjusted by Gonzales Martinez and Janssen (2023). All-cause (M2) and cause-specific (M1) RRs from Hoffmann et al. (2015). All-cause (M2) and cause-specific (M1, M3, M4) mortality data by educational level from the ONS – Longitudinal Study. Cause-specific high-BMI PAFs from the Global Burden of Disease Study (2017) for M3.

Figure 3.2. Comparing Method 1 (M1: cause-specific prevalence approach based on our PAFs), Method 2 (M2: all-cause prevalence approach), Method 3 (M3: cause-specific prevalence approach based on GBD's PAFs), and Method 4 (M4: multiple causes of death approach): **Age-standardized high-BMI-attributable mortality rates (SHBAMR)**, by educational level (low, middle, high), 30-95+: **Finland.**



Source data: High-BMI prevalence data by educational level (M1 + M2) stem originally from the National Institute for Health and Welfare and were adjusted by Gonzales Martinez and Janssen (2023). All-cause (M2) and cause-specific (M1) RRs from Hoffmann et al. (2015). All-cause (M2) and cause-specific (M1, M3, M4) mortality data by educational level from Statistics Finland. Cause-specific high-BMI PAFs from the Global Burden of Disease Study (2017) for M3.

Figure 3.3. Comparing Method 1 (M1: cause-specific prevalence approach based on our PAFs), Method 2 (M2: all-cause prevalence approach), and Method 3 (M3: cause-specific prevalence approach based on GBD's PAFs): **Age-standardized high-BMI-attributable mortality rates** (SHBAMR), by educational level (low, middle, high), 30-95+: **Italy.**



Source data: High-BMI prevalence data by educational level (M1 + M2) stem originally from the Italian National Institute of Statistics (ISTAT) and were adjusted by Gonzales Martinez and Janssen (2023). All-cause (M2) and cause-specific (M1 + M3) mortality data by educational level from the Turin Longitudinal Study. Cause-specific high-BMI PAFs from the Global Burden of Disease Study (2017) for M3.

4.4. Additional comparisons

Additional comparisons were performed with the aim of assessing whether the differences between methods are the result of (i) our selection of high-BMI attributable causes of death and the use of partly using the RRs from Hoffmann et al. 2015 or not, or (ii) stem from the differences in high-BMI-attributable cardiovascular mortality.

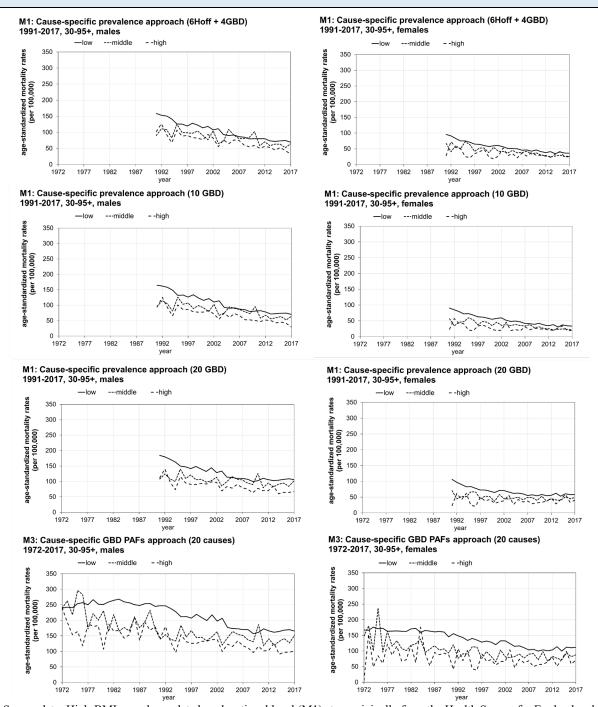
Figures 4.1, 4.2, and **4.3** compare SHBAMR for 10 and 20 causes of death, for England & Wales (Figure 4.1), Finland (Figure 4.2), and Italy (Figure 4.3). The main benchmark for comparison is the SHBAMR based on the cause-specific prevalence approach (method 1)

calculated with 10 causes of death based on Hoffmann's relative risks for 6 causes of death and the GBD's relative risks for the remaining 4 causes of death. This benchmark is compared with the SHBAMR calculated with the cause-specific prevalence approach (method 1) based on GBD's relative risks for 10 causes of death, the SHBAMR calculated with the causespecific prevalence approach (method 1) based on GBD's relative risks for 20 causes of death, and the SHBAMR calculated with the GBD's PAFs for 20 causes of death (method 3). In all the countries analyzed, the results show that similar trends and levels for all educational levels of SHBAMR are obtained when calculating SHBAMR for 10 causes of death with the GBD's relative risks and the SHBAMR for 10 causes calculated with 6 Hoffmann's relative risks and 4 GBD's relative risks. However, higher levels of SHBAMR are obtained for 20 causes of death (calculated with the GBD's relative risks), compared to SHBAMR calculated with 10 causes of death (either with the 10 GBD's relative risks or with 6 Hoffmann's relative risks and 4 GBD's relative risks). Also, the levels of SHBAMR calculated for 20 causes of death with the GBD's PAFs (method 3), is higher than the levels of SHBAMR calculated for 20 causes of death with method 1 (M1). This illustrates that the generally higher levels of HBAM for method 3 compared to method 1, is caused partly by the inclusion of HBAM from additional causes of death (M1 20 causes vs M1 10 causes), and partly by the higher –noneducation-specific- GBD PAFs compared to our PAFs (M3 vs M1 20 causes), which is probably mostly related to the different underlying prevalence data, because the different RRs used did not make a difference.

In the case of the comparisons performed to evaluate if the differences in high-BMI attributable mortality are the result of differences in high-BMI-attributable cardiovascular mortality, **Figures 5.1, 5.2,** and **5.3** compare the estimations of high-BMI-attributable cardiovascular mortality for England & Wales (Figure 5.1), Finland (Figure 5.2), and Italy (Figure 5.3). In the case high-BMI-attributable cardiovascular (CVD) mortality calculated with method 1, this CVD mortality is calculated with the Hoffmann's relative risks for ischemic heart disease and the GBD's relative risks for stroke, since there is no information of Hoffmann's relative risks for hypertension and atrial fibrillation-flutter. In method 3, based on the GBD PAFs, high-BMI CVD mortality is calculated with PAFs of mortality for ischemic heart disease, hypertension, stroke and atrial fibrillation and flutter.

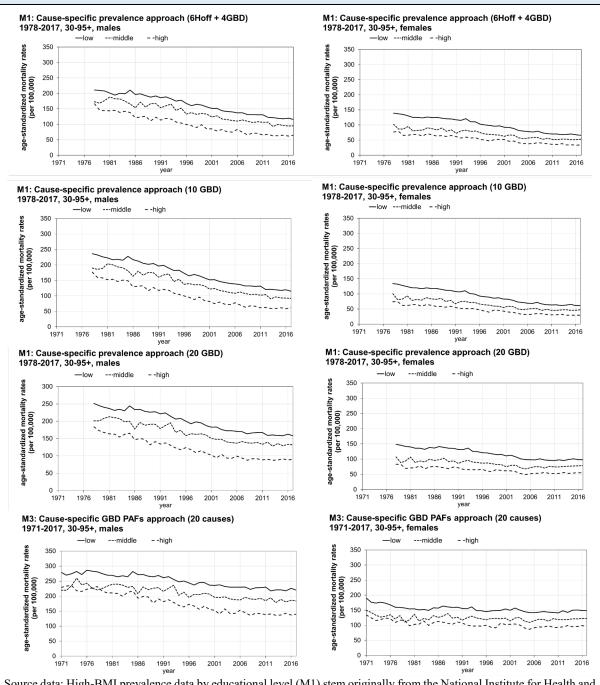
The higher CVD-related HBAM for method 3 compared to method 1 is in line with our observations for all-cause HBAM and seems to confirm that the different prevalence data behind method 3 and method 1 is the major contributor to the difference. Regarding the trends, the trends in high-BMI-attributable CVD mortality largely seem to resemble the trends in HBAM. Specifically, for high-BMI-attributable CVD mortality –for which method 4 was initially developed (Adair & Lopez 2020)— we observe a different trend in HBAM for method 4 compared to the other methods and compared to the general declining trend in CVD mortality. This might indicate that method 4 is capable to unravel the true underlying CVD-related HBAM trend, which –like the prevalence in high-BMI– showcases an increasing trend. However, on the other hand, it might also be that the tendency of high-BMI related causes to be listed as contributory causes of death on a death certificate might have increased recently because of the increased attention on the obesity epidemic.

Figure 4.1. Comparing Method 1 (M1: cause-specific prevalence approach based on our PAFs) for **10 and 20 causes of death** against Method 3 (M3: cause-specific GBD PAFs approach) for **20 causes of death**: Age-standardized high-BMI-attributable mortality rates (SHBAMR) by educational level (low, middle, high), 30-95+: **England & Wales.**



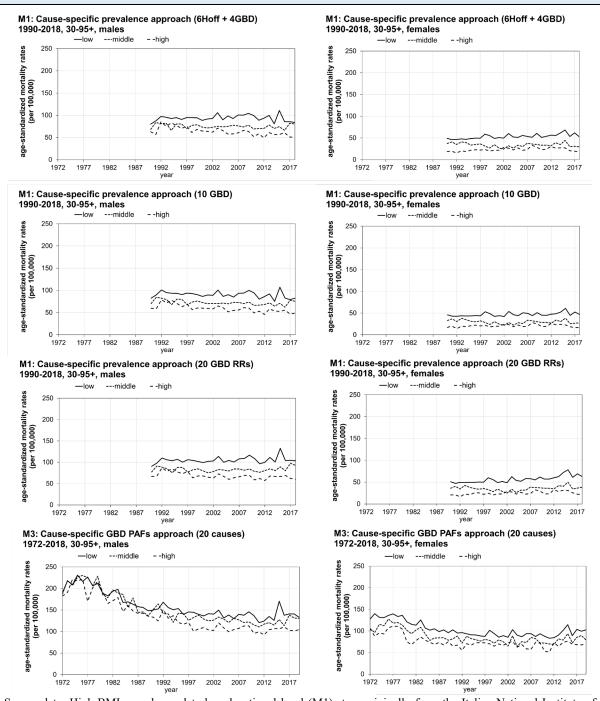
Source data: High-BMI prevalence data by educational level (M1) stem originally from the Health Survey for England and were adjusted by Gonzales Martinez and Janssen (2023). Cause-specific RRs (M1) from Hoffmann et al. (2015). Cause-specific mortality data by educational level (M1 + M3) from the ONS – Longitudinal Study. Cause-specific high-BMI PAFs from the Global Burden of Disease Study (2017) for M3.

Figure 4.2. Comparing Method 1 (M1: cause-specific prevalence approach based on our PAFs) for **10 and 20 causes of death** against Method 3 (M3: cause-specific GBD PAFs approach) for **20 causes of death**: Age-standardized high-BMI-attributable mortality rates (SHBAMR) by educational level (low, middle, high), 30-95+: **Finland.**



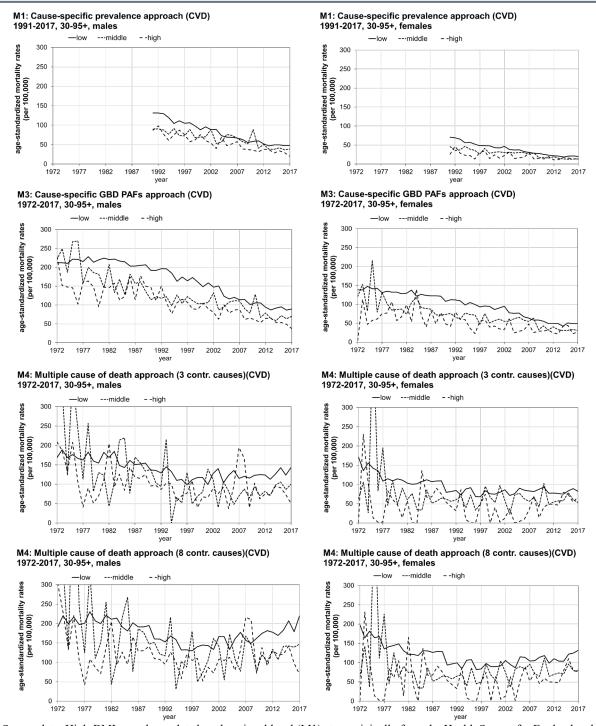
Source data: High-BMI prevalence data by educational level (M1) stem originally from the National Institute for Health and Welfare and were adjusted by Gonzales Martinez and Janssen (2023). Cause-specific RRs (M1) from Hoffmann et al. (2015). Cause-specific mortality data by educational level (M1 + M3) from Statistics Finland. Cause-specific high-BMI PAFs from the Global Burden of Disease Study (2017) for M3.

Figure 4.3. Comparing Method 1 (M1: cause-specific prevalence approach based on our PAFs) for **10 and 20 causes of death** against Method 3 (M3: cause-specific GBD PAFs approach) for **20 causes of death**: Age-standardized high-BMI-attributable mortality rates (SHBAMR) by educational level (low, middle, high), 30-95+: **Italy.**



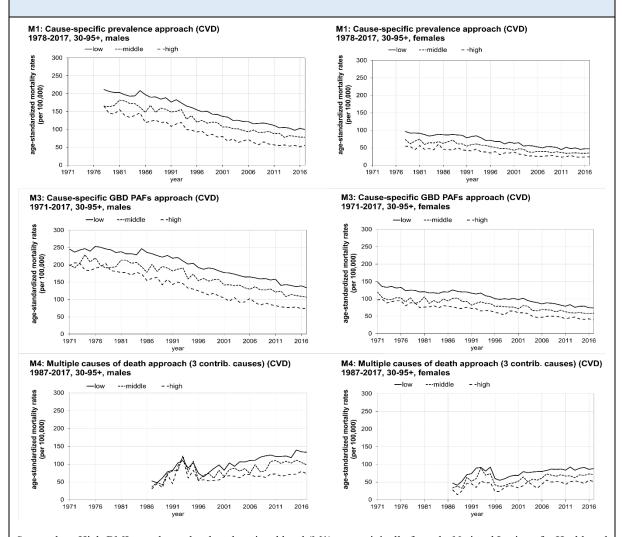
Source data: High-BMI prevalence data by educational level (M1) stem originally from the Italian National Institute of Statistics (ISTAT) and were adjusted by Gonzales Martinez and Janssen (2023). Cause-specific RRs (M1) from Hoffmann et al. (2015). Cause-specific mortality data by educational level (M1 + M3) from the Turin Longitudinal Study. Cause-specific high-BMI PAFs from the Global Burden of Disease Study (2017) for M3.

Figure 5.1. Comparing Method 1 (M1: cause-specific prevalence approach based on our PAFs), Method 2 (M2: all-cause prevalence approach), Method 3 (M3: cause-specific prevalence approach based on GBD's PAFs), and Method 4 (M4: multiple causes of death approach): **Age-standardized high-BMI-attributable cardiovascular mortality rates**, by educational level (low, middle, high), 30-95+: **England & Wales.**



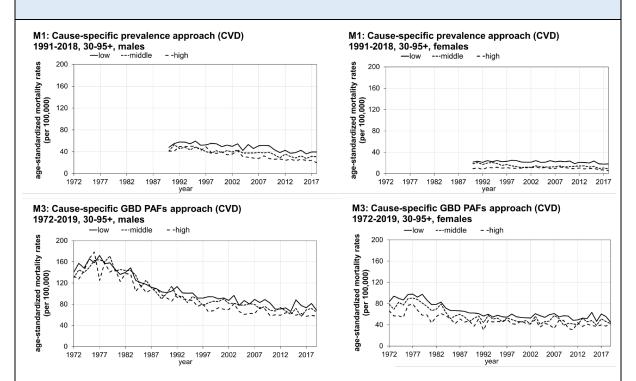
Source data: High-BMI prevalence data by educational level (M1) stem originally from the Health Survey for England and were adjusted by Gonzales Martinez and Janssen (2023). CVD-related RRs (M1) from Hoffmann et al. (2015). Cardiovascular disease mortality data by educational level (M1 + M4) from the ONS – Longitudinal Study. CVD-related high-BMI PAFs from the Global Burden of Disease Study (2017) for M3.

Figure 5.2. Comparing Method 1 (M1: cause-specific prevalence approach based on our PAFs), Method 2 (M2: all-cause prevalence approach), Method 3 (M3: cause-specific prevalence approach based on GBD's PAFs), and Method 4 (M4: multiple causes of death approach): **Age-standardized high-BMI-attributable cardiovascular mortality rates**, by educational level (low, middle, high), 30-95+: **Finland.**



Source data: High-BMI prevalence data by educational level (M1) stem originally from the National Institute for Health and Welfare and were adjusted by Gonzales Martinez and Janssen (2023). CVD-related RRs (M1) from Hoffmann et al. (2015). Cardiovascular disease mortality data by educational level (M1 \pm M4) from Statistics Finland. CVD-related high-BMI PAFs from the Global Burden of Disease Study (2017) for M3.

Figure 5.3. Comparing Method 1 (M1: cause-specific prevalence approach based on our PAFs), Method 2 (M2: all-cause prevalence approach), and Method 3 (M3: cause-specific prevalence approach based on GBD's PAFs): **Age-standardized high-BMI-attributable cardiovascular mortality rates**, by educational level (low, middle, high), 30-95+: **Italy.**



Source data: High-BMI prevalence data by educational level (M1) stem originally from the Italian National Institute of Statistics (ISTAT) and were adjusted by Gonzales Martinez and Janssen (2023). CVD-related RRs (M1) from Hoffmann et al. (2015). Cardiovascular disease mortality data by educational level (M1 + M4) from the Turin Longitudinal Study. CVD-related high-BMI PAFs from the Global Burden of Disease Study (2017) for M3.

5. Conclusions

We compared different methods to estimate obesity-attributable mortality and high-BMI attributable mortality, and how they lead to different levels and trends in age-standardized obesity and high-BMI mortality by educational level (low, middle, high), for those aged 30 and over in England & Wales, Finland, and Italy, from the early 1970s onwards. We found that the estimates of levels and trends of obesity-attributable mortality by educational level differ depending on the method applied. For the three educational groups, levels of age-standardized obesity-attributable mortality rates (SOAMR) are higher when using an all-cause prevalence approach (method M2) compared to a cause-specific prevalence approach (method M1). In addition, trends in SOAMR are increasing instead of declining for method 2 compared to method 1, except for Italian males for which the two methods reveal rather similar trends. For England & Wales and Finland, method 1 results in more convergence in SOAMR levels over time between educational groups compared to method 2. In the 3 countries analysed, similar descending trends of age-standardized high-BMI-attributable mortality (SHBAMR) are obtained with methods M1 (cause-specific prevalence approach), M2 (all-cause prevalence approach), and M3 (cause-specific GBD PAFs approach).

For Method 4 (multiple cause of death approach), however, ascending trends of SHBAMR are observed in England & Wales and Finland after the year 1996.

Our results are not surprising given that also in the study by Vidra et al. (2018) —which did not distinguish by educational level— different levels and trends in obesity-attributable mortality for the Netherlands by estimation method were observed. The generally higher levels of method 2 compared to method 1 is likely explained by the fact that the all-cause prevalence approach applies an all-cause relative risk to all causes of death, which includes many causes of death more than the 6 (or 10) causes of death included in method 1. The observed declines in obesity-attributable mortality as obtained through method 1, are in line with previous studies on obesity-attributable mortality (e.g. Vidra et al. 2018b). Apparently, the increase in obesity prevalence—and consequently in obesity-attributable mortality— is in these instances too small to counterbalance the decline in mortality from the obesity-related causes of death, and in particular the decline in CVD mortality, which constitutes the largest cause among the obesity-related causes of death considered. Indeed, for CVD-related obesity-attributable mortality the trends were largely similar compared to overall obesity-attributable mortality. The increasing trend in OAM (but not HBAM) using method 2, could imply that OAM using the all-cause method gives more weight to non-obesity-related causes of death that exhibited mortality increases over the last decades.

The generally higher levels of HBAM using method 3 compared to method 1 is –as our additional comparisons illustrate– partly due to the inclusion of HBAM from additional causes of death in method 3, and partly by the higher non-education-specific GBD PAFs compared to our PAFs, due to the higher underlying prevalence. The non-declining recent trends for HBAM when using method 4 compared to the declining trends for the other methods was also observed when purely estimating CVD-related HBAM. Our observation that the trends for CVD-related HBAM estimated by method 4 are different from the trends for CVD-related HBAM estimated through other methods, and from the overall declining trend for CVD mortality, might indicate that method 4 is capable to unravel the true underlying CVD-related HBAM trend. However, the decline in CVD-related HBAM estimated by method 4 for ENW from 1970 up to 1990 is difficult to match with this hypothesis. Moreover, the recent increase in HBAM estimated by method 4, might –at least– partly be influenced by a potentially increased recent tendency to report a high-BMI related cause of death as a contributory cause of death on the death certificate. All in all, the pros and cons of each method need to be carefully considered in making the final choice.

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In addition, the permission of the Office for National Statistics to use the Longitudinal Study is gratefully acknowledged, as is the help provided by staff of the Centre for Longitudinal Study Information & User Support (CeLSIUS). CeLSIUS is funded by the ESRC under project ES/V003488/1. The authors alone are responsible for the interpretation of the data. This work contains statistical data from ONS which is Crown Copyright. The use of the ONS statistical data in this work does not imply the endorsement of the ONS in relation to the interpretation or analysis of the statistical data. This work uses research datasets which may not exactly reproduce National Statistics aggregates.

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Appendix I: Sensitivity analysis regarding the standard mortality schedule used to obtain the age-standardized mortality fractions.

Standardized obesity-attributable mortality fractions (SOAMF) and standardized high-BMI attributable mortality fractions (SHBAMF) were calculated using all-cause death counts by age and sex alone, and using standardization by age, sex, and education. Figure AI.1 compares the results of SOAMF obtained with age and sex against those obtained with age, sex, and education, for method M1 (cause-specific prevalence approach based on our own calculations of PAFs), and Figure AI.2 makes the same comparison for all-cause SOAMF. Figure AI.3 compares the results of cause-specific SHBAMF obtained with age and sex against those obtained with age, sex, and education. Figure AI.4 makes the same comparison for all-cause SHBAMF (method M2), and Figure AI.5 compares the SHBAM fractions obtained with method M3 (cause-specific prevalence approach based on the GBD PAFs). Finally, Figure A6.1 shows SHBAM fractions obtained with the multiple causes of death approach (method M4).

Tables AI.1 and AI.2 below shows the correlation of SOAMF/SHBAMF obtained with age and sex standardization against SOAMF/SHBAMF obtained with standardization by age, sex, and education, in method M1 (cause-specific prevalence approach, Table AI.1) and method M2 (all cause prevalence approach, Table AI.2). There is a strong correlation between SOAM fractions obtained with age and sex standardization and those obtained with a standardization with age, sex, and education, for all strata and in all countries, hence indicating that there no significative differences in mortality fractions calculated with standardization based on age and sex strata, compared to mortality fractions calculated with standardization based on age, sex, and education.

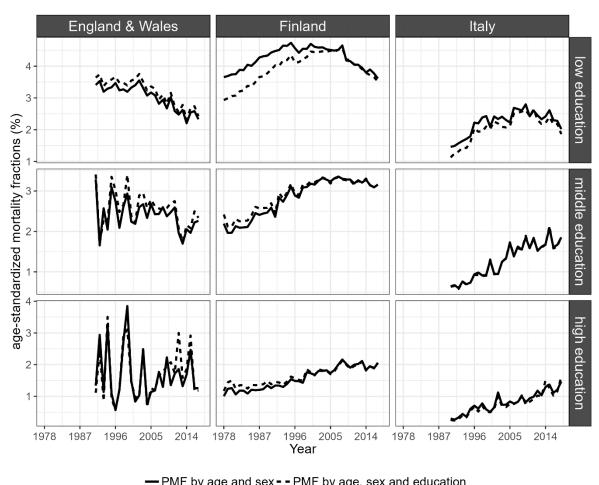
Table AI.1. Correlation between mortality fractions calculated by age group only against mortality fractions calculated by age, sex, and education: cause-specific mortality (M1)

Rates	stratum			country		
	sex	education	Correlation -	England & Wales	Finland	Italy
Obesity (SOAMR)	men	low	Correlation between SOAM fractions calculated by age group only against SOAM fractions calculated by age, sex, and education	0.979708	0.999660	0.995607
	men	middle		0.992793	0.971105	0.992578
	men	high		0.930457	0.996708	0.969800
	women	low		0.998638	0.848144	0.972871
	women	middle		0.946680	0.997343	0.998855
	women	high		0.900001	0.991634	0.979213
	men	low	Correlation between SHBAM fractions calculated by age group only against SHBAM fractions calculated by age, sex, and education	0.997629	0.997014	0.971158
	men	middle		0.986896	0.947602	0.934177
High-BMI	men	high		0.964825	0.993059	0.922638
(SHBAMR)	women	low		0.999414	0.928629	0.901779
	women	middle		0.978889	0.996302	0.992867
	women	high		0.909905	0.994128	0.860591

Table AI.2. Correlation between mortality fractions calculated by age group only against mortality fractions calculated by age, sex, and education: all-cause mortality (M2)

Rates	stratum		Completion	country		
	sex	education	Correlation -	England & Wales	Finland	Italy
Obesity	men	low	Correlation between SOAM fractions calculated by age group only against SOAM fractions calculated by age, sex, and education	0.999684	0.999942	0.999779
	men	middle		0.999957	0.999375	0.990940
	men	high		0.999903	0.999541	0.997486
(SOAMR)	women	low		0.999929	0.999074	0.998735
	women	middle		0.999909	0.999992	0.999958
	women	high		0.999997	0.999832	0.999386
	men	low	Correlation between SHBAM fractions calculated by age group only against SHBAM fractions calculated by age, sex, and education	0.999264	0.999965	0.998253
	men	middle		0.999669	0.994533	0.998958
High-BMI	men	high		0.988276	0.999649	0.946076
(SHBAMR)	women	low		0.997072	0.864151	0.999310
	women	middle		0.996720	0.999878	0.999213
	women	high		0.999199	0.999246	0.999169

Figure AI.1.1. Comparing age-standardized mortality fractions obtained through Method 1 (cause-specific prevalence approach), calculated by merely using an age-sex-specific standard mortality schedule, against using an age-, sex- and education-specific standard mortality schedule, by educational level (low, middle, high): SOAMF - females.



- PMF by age and sex - - PMF by age, sex and education

Source data: ONS Longitudinal Study (England & Wales), Statistics Finland, Turin Longitudinal Study (Italy)

Figure AI.1.2. Comparing age-standardized mortality fractions obtained through **Method 1** (cause-specific prevalence approach), calculated by merely using an age-sex-specific standard mortality schedule, against using an age-, sex- and education-specific standard mortality schedule, by educational level (low, middle, high): **SOAMF - males.**

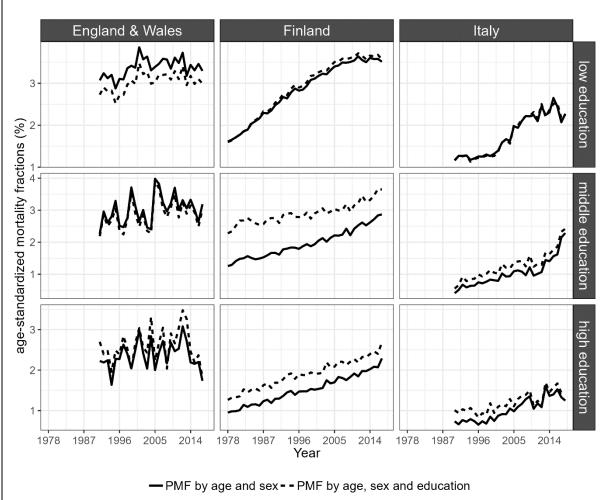


Figure AI.2.1. Comparing age-standardized mortality fractions obtained through **Method 2** (all cause prevalence approach), calculated by merely using an age-sex-specific standard mortality schedule, against using an age-, sex- and education-specific standard mortality schedule, by educational level (low, middle, high): **SOAMF - females.**



Figure AI.2.2. Comparing age-standardized mortality fractions obtained through **Method 2** (all cause prevalence approach), calculated by merely using an age-sex-specific standard mortality schedule, against using an age-, sex- and education-specific standard mortality schedule, by educational level (low, middle, high): **SOAMF - males.**

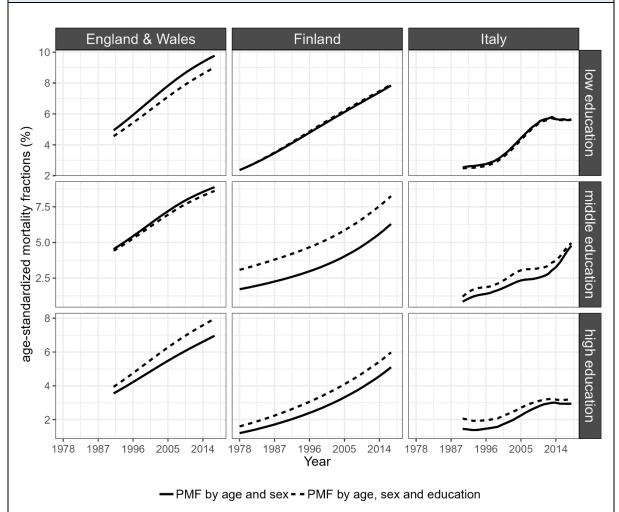


Figure AI.3.1. Comparing age-standardized mortality fractions obtained through **Method 1** (cause-specific prevalence approach), calculated by merely using an age-sex-specific standard mortality schedule, against using an age-, sex- and education-specific standard mortality schedule, by educational level (low, middle, high): **SHBAMF - females.**

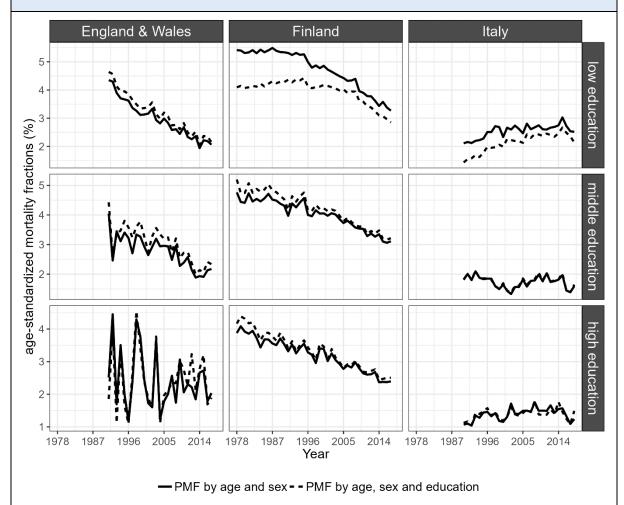


Figure AI.3.2. Comparing age-standardized mortality fractions obtained through **Method 1** (cause-specific prevalence approach), calculated by merely using an age-sex-specific standard mortality schedule, against using an age-, sex- and education-specific standard mortality schedule, by educational level (low, middle, high): **SHBAMF - males.**

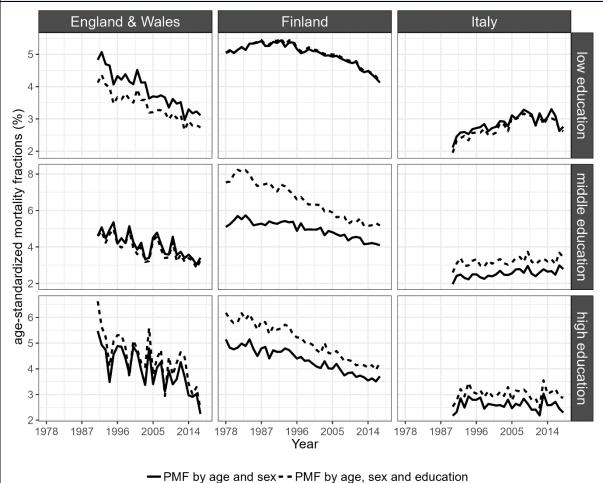


Figure AI.4.1. Comparing age-standardized mortality fractions obtained through **Method 2** (all cause prevalence approach), calculated by merely using an age-sex-specific standard mortality schedule, against using an age-, sex- and education-specific standard mortality schedule, by educational level (low, middle, high): **SHBAMF - females.**

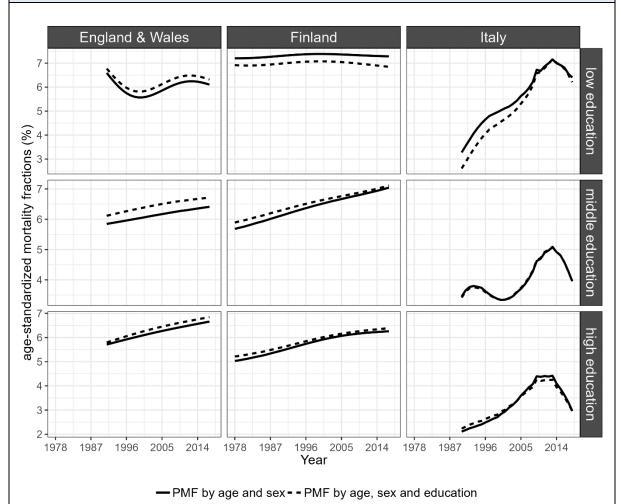


Figure AI.4.2. Comparing age-standardized mortality fractions obtained through **Method 2** (all cause prevalence approach), calculated by merely using an age-sex-specific standard mortality schedule, against using an age-, sex- and education-specific standard mortality schedule, by educational level (low, middle, high): **SHBAMF - males.**

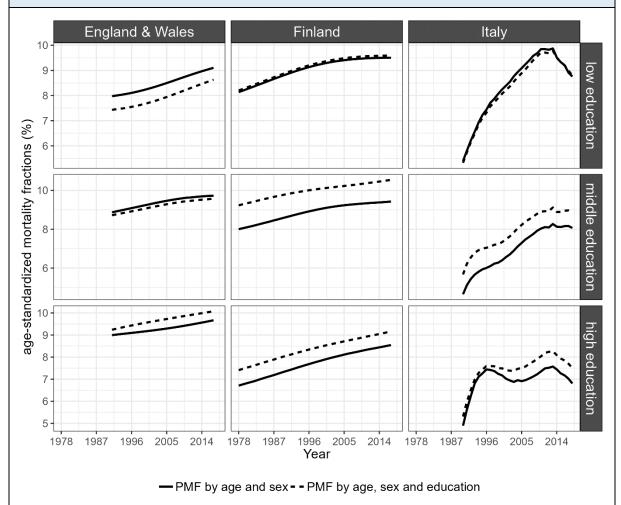


Figure AI.5.1. Comparing age-standardized mortality fractions obtained through **Method 3** (cause specific prevalence approach- GBD's PAFs), calculated by merely using an age-sex-specific standard mortality schedule, against using an age-, sex- and education-specific standard mortality schedule, by educational level (low, middle, high): **SHBAMF - males.**

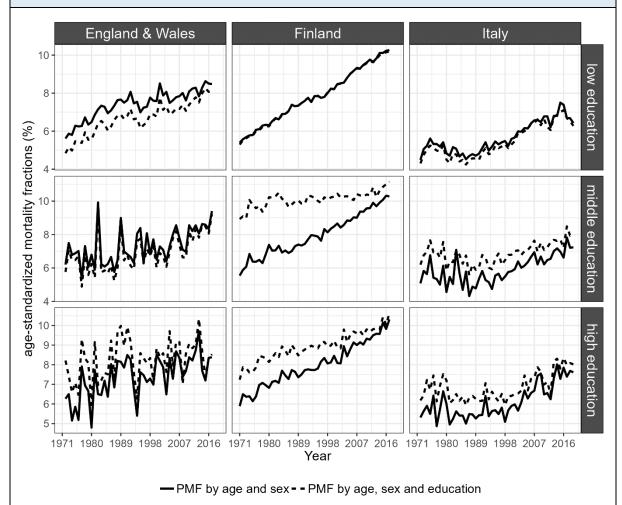


Figure AI.5.2. Comparing age-standardized mortality fractions obtained through **Method 3** (cause specific prevalence approach- GBD's PAFs), calculated by merely using an age-sex-specific standard mortality schedule, against using an age-, sex- and education-specific standard mortality schedule, by educational level (low, middle, high): **SHBAMF - females.**

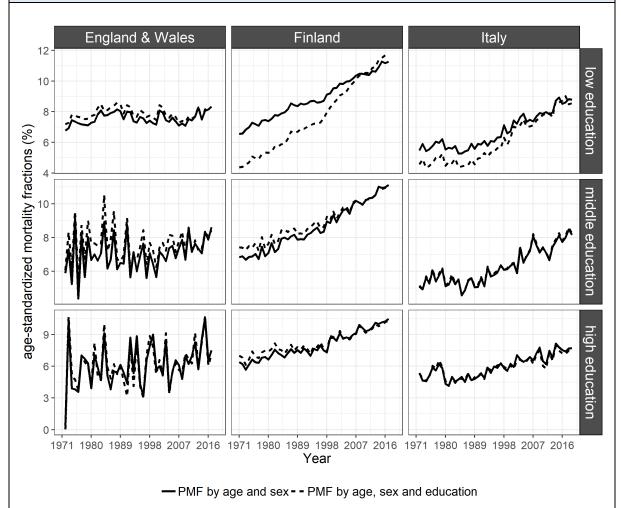
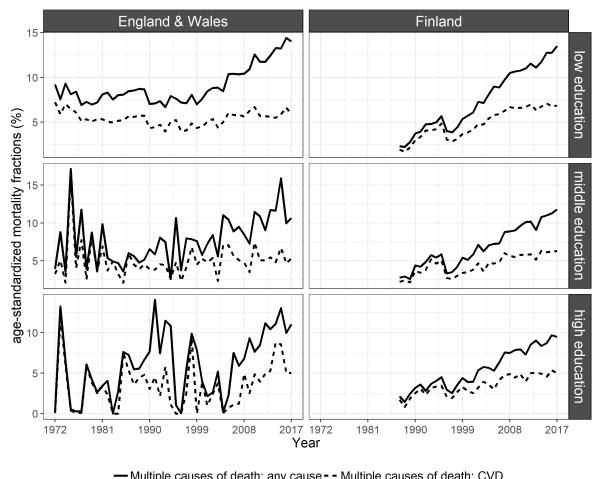


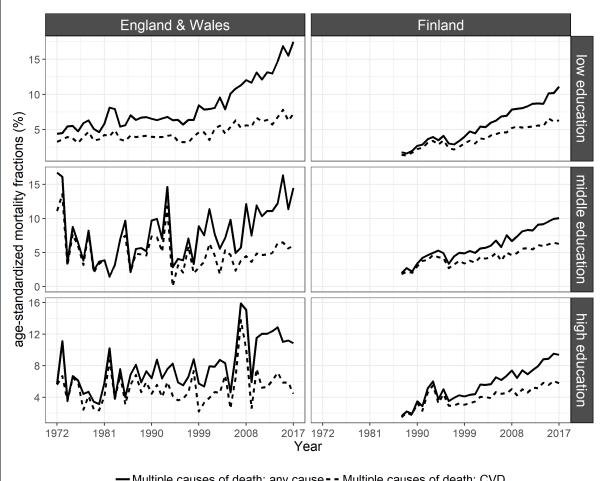
Figure AI.6.1. Comparing age-standardized mortality fractions obtained through Method 4 (multiple causes of death approach), calculated by merely using an age-sex-specific standard mortality schedule, against using an age-, sex- and education-specific standard mortality schedule, by educational level (low, middle, high): SHBAMF - females.



— Multiple causes of death: any cause - - Multiple causes of death: CVD

Source data: ONS Longitudinal Study (England & Wales), Statistics Finland, Turin Longitudinal Study (Italy)

Figure AI.6.2. Comparing age-standardized mortality fractions obtained through **Method 4** (multiple causes of death approach), calculated by merely using an age-sex-specific standard mortality schedule, against using an age-, sex- and education-specific standard mortality schedule, by educational level (low, middle, high): **SHBAMF - males.**



Multiple causes of death: any cause - Multiple causes of death: CVD
 Source data: ONS Longitudinal Study (England & Wales), Statistics Finland, Turin Longitudinal Study (Italy)

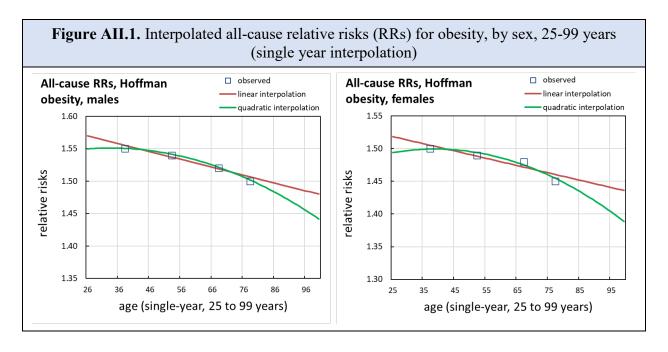
Appendix II: Sensitivity analysis of linear interpolation against quadratic interpolation of all-cause relative risks

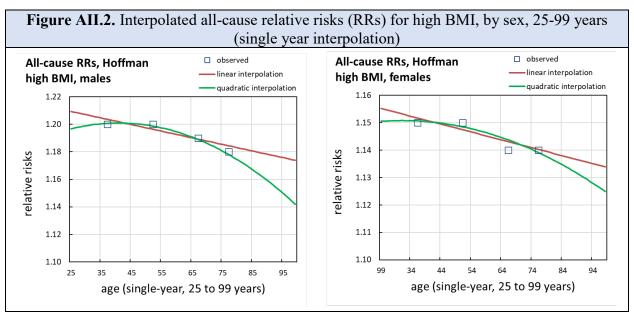
In method M2 (all-cause prevalence), we compare the results of linear and quadratic interpolation of all-cause relative risks (RRs). Linear interpolation of RRs was applied by Vidra et al. (2019) when calculating mortality risks. Quadratic interpolation is more in line with Zheng et al. (2021), who analyzed the obesity-mortality link and found that the hazard ratio associated with obesity decreases over time for different age groups, especially the elderly, compared to normal weight. This decrease is influenced by factors such as the age of obesity onset and mortality selection effects. Consequently, relative risks associated with obesity can be lower for older adults (≥ 65 years old). Obesity can be considered "protective" for older adults because it provides a metabolic reserve against diseases and is associated with increased bone mineral density, decreased osteoporosis, and a lower risk of hip fracture in older adults. This phenomenon is referred to as the 'obesity paradox.' While obesity in the general adult population is associated with a higher likelihood of early death, epidemiological findings indicate a beneficial or neutral effect of obesity on length of life after the age of 65 years (Decaria et al., 2012). See Figures AII.1, AII.2, AII.3, and AII.4.

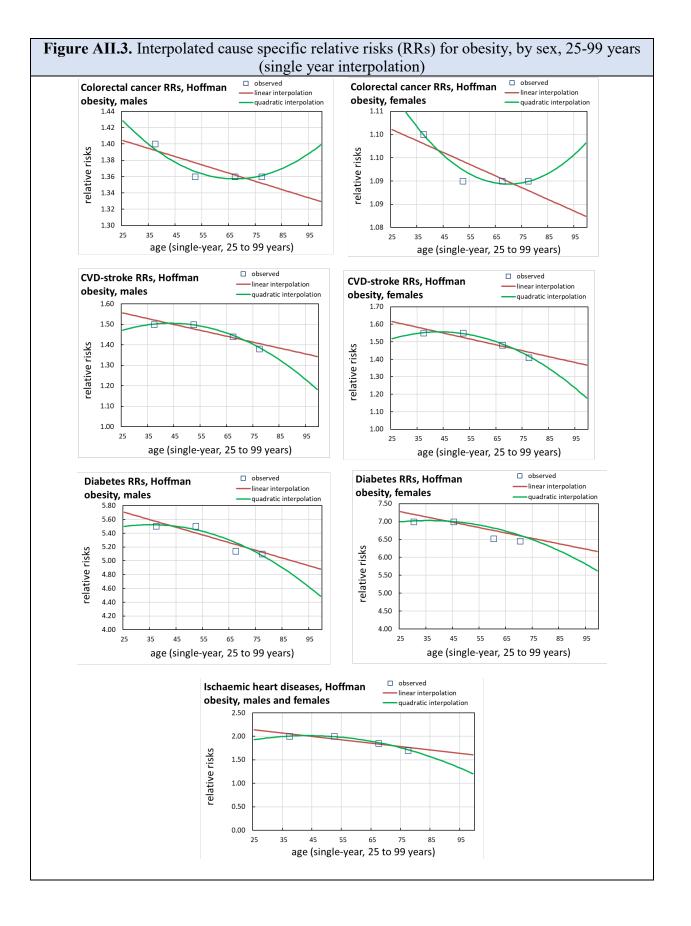
Tables AII.1 and Figures AII.5 and AII.6 present the results of comparing all-cause SOAMR and SHBAMR calculated with linear interpolation of RRs and quadratic interpolation of RRs. Figures AII.5 and AII.5 indicate that similar results are obtained when using linear interpolation compared to quadratic interpolation, with the differences being nearly indistinguishable. The trends of all-cause mortality overlap for both SOAMR (Figure AII.5) and SHBAMR (Figures AII.6). The correlation coefficients between the results obtained with linear interpolation and those obtained with quadratic interpolation are close to 1, specifically 0.99 for all countries and strata. This suggests that there is no significant difference between the results of SOAMR and HBAMR obtained with linear interpolation and those obtained with quadratic interpolation of all-cause relative risks.

Table All.1. Correlation between mortality rates calculated with linear interpolation of RRs and mortality rates calculated with quadratic interpolation of RRs

Rates	Stratum		Correlation -	country		
	sex	education	Correlation	England	Finland	Italy
Obesity (SOAMR)	men	low	correlation between all- cause SOAMR obtained with linear interpolation of RRs and all-cause SOAMR obtained with quadratic interpolation of RRs	0.999980	0.999995	0.999971
	men	middle		0.999926	0.999981	0.999965
	men	high		0.999826	0.999957	0.996115
	women	low		0.999539	0.999524	0.999948
	women	middle		0.999612	0.999921	0.999985
	women	high		0.999905	0.999953	0.999869
High-BMI (SHBAMR)	men	low	correlation between all- cause SHBAMR obtained with linear interpolation of RRs and all-cause SHBAMR obtained with quadratic interpolation of RRs	0.999981	0.999926	0.995788
	men	middle		0.998846	0.999772	0.992359
	men	high		0.999870	0.999920	0.999866
	women	low		0.999980	0.999986	0.999847
	women	middle		0.999915	0.999952	0.999757
	women	high		0.999937	0.999968	0.999817







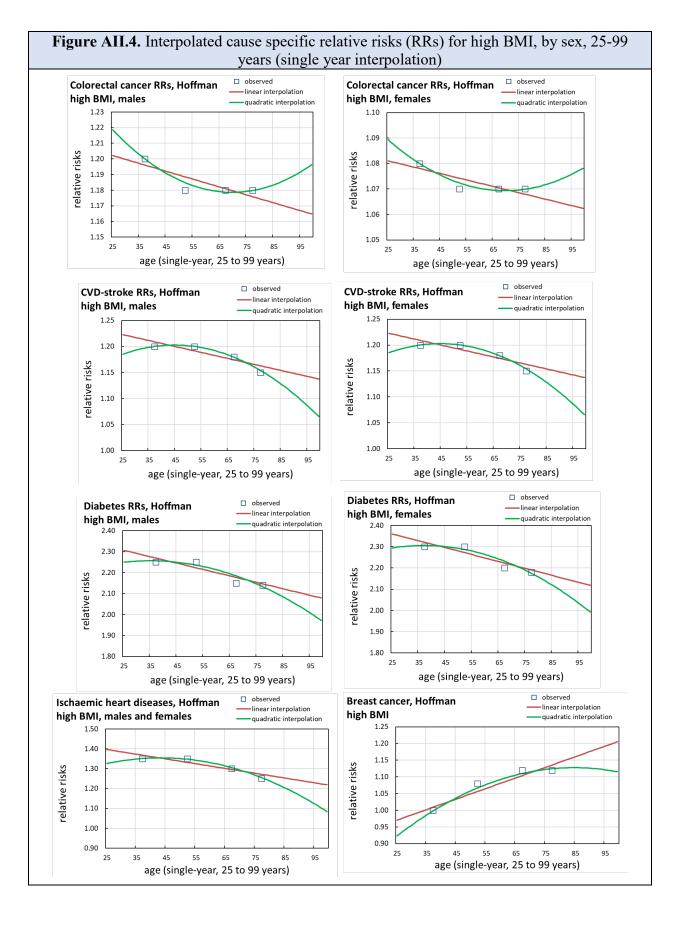
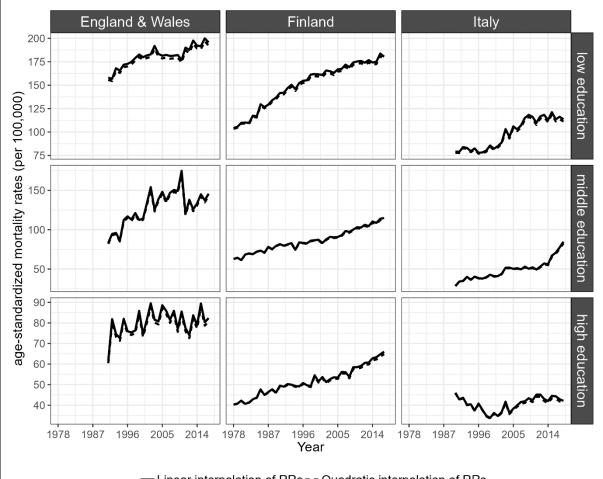


Figure AII.5.1. Comparing age-standardized mortality rates obtained through **Method 2** (all cause prevalence approach), calculated with linear interpolation of relative risks, against mortality rates calculated with quadratic interpolation of relative risks, by educational level (low, middle, high): **SOAMR – females.**



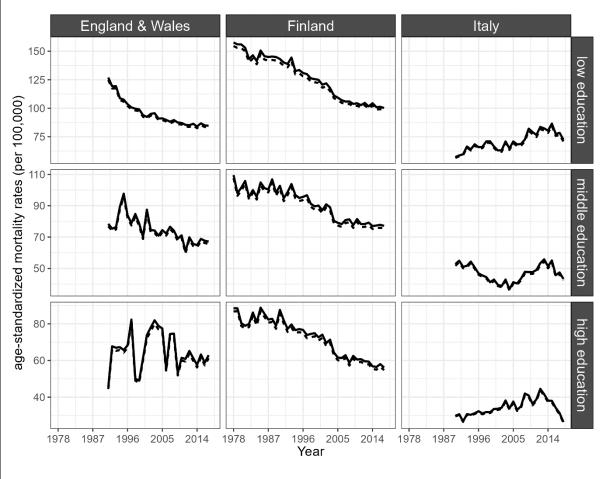
Figure AII.5.2. Comparing age-standardized mortality rates obtained through **Method 2** (all cause prevalence approach), calculated with linear interpolation of relative risks, against mortality rates calculated with quadratic interpolation of relative risks, by educational level (low, middle, high): **SOAMR – males.**



- Linear interpolation of RRs - - Quadratic interpolation of RRs

Source data: ONS Longitudinal Study (England & Wales), Statistics Finland, Turin Longitudinal Study (Italy)

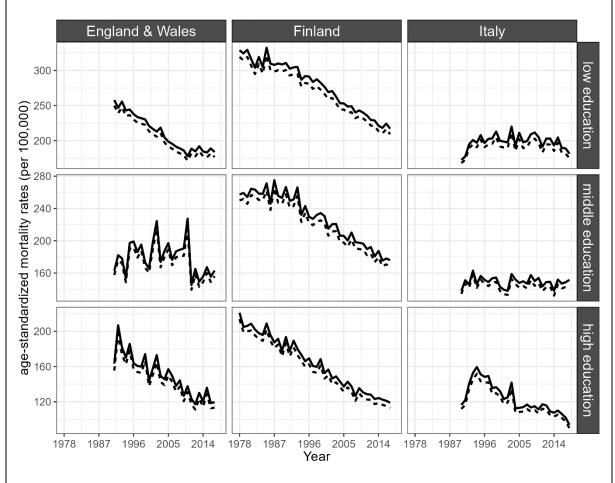
Figure AII.6.1. Comparing age-standardized mortality rates obtained through **Method 2** (all cause prevalence approach), calculated with linear interpolation of relative risks, against mortality rates calculated with quadratic interpolation of relative risks, by educational level (low, middle, high): **SHBAMR – females.**



- Linear interpolation of RRs - - Quadratic interpolation of RRs

Source data: ONS Longitudinal Study (England & Wales), Statistics Finland, Turin Longitudinal Study (Italy)

Figure AII.6.2. Comparing age-standardized mortality rates obtained through **Method 2** (all cause prevalence approach), calculated with linear interpolation of relative risks, against mortality rates calculated with quadratic interpolation of relative risks, by educational level (low, middle, high): **SHBAMR – males.**



- Linear interpolation of RRs - - Quadratic interpolation of RRs

Source data: ONS Longitudinal Study (England & Wales), Statistics Finland, Turin Longitudinal Study (Italy)

In this working paper, we compare different methods to estimate obesity-attributable mortality and high-BMI attributable mortality, and we show how different estimation methods lead to different levels and trends in age-standardized obesity and high-BMI mortality by educational level (low, middle, high), for those aged 30 and over in England & Wales, Finland, and Italy, from the early 1970s onwards. For the three educational groups, levels of age-standardized obesity-attributable mortality rates (SOAMR) are higher when using an all-cause prevalence approach (method M2) compared to a cause-specific prevalence approach (method M1). In addition, trends in SOAMR are increasing instead of declining for method 2 compared to method 1, except for Italian males for which the two methods reveal rather similar trends. For England & Wales and Finland, method 1 results in more convergence in SOAMR levels over time between educational groups compared to method 2. In the 3 countries analyzed, similar descending trends of age-standardized high-BMI-attributable mortality (SHBAMR) are obtained with methods M1 (cause-specific prevalence approach), M2 (all-cause prevalence approach), and M3 (cause-specific GBD PAFs approach). For Method 4 (multiple cause of death approach), however, ascending trends of SHBAMR are observed in England & Wales and Finland after the year 1996. These results reveal that levels and trends in SOAMR and SHBAMR by sex and educational level clearly differ by estimation method.

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