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OBESITY

Obesity but not overweight is associated with increased mortality risk

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Abstract The association between body mass index (BMI) and survival has been described in various populations. However, the results remain controversial and information from low-prevalence Western countries is sparse. Our aim was to examine this association and its public health impact in Switzerland, a country with internationally low mortality rate and obesity prevalence. We included 9,853 men and women aged 25–74 years who participated in the Swiss MONICA (MONItoring of trends and determinants in CArdiovscular disease) study (1983–1992) and could be followed up for survival until 2008 by using anonymous record linkage. Cox regression models were used to calculate mortality hazard ratios (HRs) and to estimate excess deaths. Independent variables were age, sex, survey wave, diet, physical activity, smoking, educational class. After adjustment for age and sex the association between BMI and all-cause mortality was *J* shaped (non-smokers) or *U* shaped (smokers). Compared to BMI 18.5–24.9, among those with BMI $\geq$ 30 (obesity) HR for all-cause mortality was 1.41 (95% confidence interval: 1.23–1.62), for cardiovascular disease (CVD) 2.05 (1.60–2.62), for cancer 1.29 (1.04–1.60). Further adjustment attenuated the obesity-mortality relationship but the associations remained statistically significant. No significant increase was found for overweight (BMI 25–29.9). Between 4 and 6.5% of all deaths, 8.8–13.7% of CVD deaths and 2.4–3.9% of cancer deaths could be attributed to obesity. Obesity, but not overweight was associated with excess mortality, mainly because of an increased risk of death from CVD and cancer. Public health interventions should focus on preventing normal- and overweight persons from becoming obese.

Keywords Overweight · Obesity · Mortality · Relative risk · Population attributable risk

Abbreviations

CVD	Cardiovascular disease
COPD	Chronic obstructive pulmonary disease
HR	Hazard ratio
ICD	International classification of diseases
ISCED	International standard classification of education
SNC	Swiss national cohort
WHO	World health organization

Introduction

Worldwide, the prevalence of overweight and obesity increased over the past decades and has become a major burden for societies. Excess weight is associated with an increased risk of disease and death, particularly from cardiovascular disease (CVD) and cancer [1–3]. The association between BMI and mortality substantially varies between populations and causes of death [1, 3–6] and can change over time [2, 5]. A part of this variation could be due to shortcomings originating from data assessment or induced in data analyses or interpretation. For example, in many studies, data is self-reported or does not stem from general populations but from selected groups such as physicians, [7, 8] nurses [9] or alumni [10]. Also, information from low-prevalence Western countries is sparse.

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The calculation and interpretation of relative risks could become critical in countries with high prevalence because the reference population (normal weight persons) becomes an increasingly selected minority [2]. This may be an explanation for the "obesity paradox", where individuals with excess weight were found to have longer survival and fewer CVD events [6, 11]. In many studies, the *U* shape of the association between BMI and mortality risk was more pronounced among smokers than among non-smokers [5, 12, 13]. In order to estimate the independent contribution of excess weight, one should also consider that obese persons may differ in socioeconomic status and other lifestyle behaviours, e.g., regarding diet and physical activity. It is also unclear to what extent the risk associated with excess weight measured by BMI is accounted for by intermediate CVD risk factors such as high blood pressure and cholesterol level.

We aimed at determining the risk and burden of death associated with BMI on a population level. For this purpose, our study population can be regarded as exceptional. Switzerland has lower mortality (particularly for CVD) and a lower prevalence of obesity than most other countries [14]. Obesity prevalence in Switzerland is about half of that of the European average, a third of that of the UK and a quarter of that of the US [14, 15]. BMI was based on measured weight and height, and over 90% of participants could be followed-up for up to 25 years. The database includes a large set of social, behavioural and clinical parameters thus, offering the possibility to consider potential confounders or effect modifier in the analysis and to evaluate the independent effect of excess weight.

Methods

Study population

Included individuals (25–74 years) were participants of the Swiss MONICA (MONItoring of trends and determinants in CArdiovscular disease) study. MONICA is an international multicentre project initiated and coordinated by the World Health Organization (WHO) [16]. In Switzerland, the study has been conducted in three waves between 1983 and 1992 [17, 18]. Sampled persons were invited to attend a health examination in their community of residence and to complete a self-administered questionnaire. The participation rate varied between 54 and 78% [19]. As in virtually all MONICA centres, no provision was made for a mortality follow-up. Recently, in Switzerland, this shortcoming could be overcome by an anonymous record linkage with the Swiss National Cohort (SNC) [20]. Details of the study population are given in Table 1. For the calculation of excess deaths attributable to obesity we used prevalence from two studies conducted in 2003 (measurement) and 2007 (self-report) [21, 22].

Record linkage procedure

In order to determine survival, data from the SNC including information on cause of death was linked to MONICA participant records. The SNC encompasses all residents of Switzerland enumerated in the national 1990 or 2000 censuses (6.8 and 7.3 million, respectively). Deterministic and probabilistic methods were used to link anonymised census, death and emigration records [23]. Also, record linkage of MONICA and the SNC based exclusively on anonymous records [20]. 97.8% of the eligible 10,160 MONICA participants could be linked to a census (1990: 9,737; 2000: 8,749), mortality (1,526, 1984–2008) and/or emigration record (320, 1990–2008). 83 participants of the last wave of MONICA could only be linked to the preceding 1990 census but not to a subsequent census, mortality or emigration record, thus, leaving 9,853 individuals for survival analysis. Linkage procedures and linkage success were described in detail [20].

Exposure variables

Education, lifestyle and clinical risk factors stem from MONICA. Measurements and blood sampling procedures have been described [17–19]. BMI was calculated from measured height (cm) and weight (kg) by dividing weight by height squared (kg/m^2). Underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2) and obesity ($\geq$30 kg/m^2) were defined according to the WHO criteria [24].

The following educational classes were used: (i) "Mandatory": compulsory schooling (corresponding to completed 8th US grade) or less (International Standard Classification of Education, ISCED 1 and 2); (ii) "Secondary": vocational training or high school (completed 12th US grade; ISCED 3); (iii) "Tertiary": technical college, upper vocational or university education (ISCED 5) [25, 26].

In order to look for the risk factor variables providing the most robust results after adjustment, we performed sensitivity analyses with smoking status (number of cigarettes smoked daily; never, former and current smokers; regular smokers, occasional smokers, non-smokers), blood cholesterol (total cholesterol, HDL-cholesterol, ratio of total cholesterol/HDL-cholesterol), blood pressure (diastolic and systolic, derived four blood pressure categories, known hypertension, hypertension treatment). We finally selected current regular and occasional smokers and non-smokers (including former smokers). Construction of diet and physical activity scores is described in the Web Annex.

Table 1 Characteristics (counts, means and proportions) of the study population, by BMI category, 9,853 participants of the Swiss MONICA study, 1983–92, 25–74 years at baseline

	Total	Body mass index category (kg/m^2)*			
		<18.5	18.5–24.9	25–29.9	≥30
Participants (*n*)	9,853	167	4,590	3,789	1,307
Prevalence (%)	100	1.7	46.7	38.5	13.1
Women (%)	49.6	86.2	59.6	37.1	46.0
Mean age (years)	47.2	44.7 (42.6–46.8)	44.4 (44.1–44.7)	48.9 (48.6–49.3)	52.0 (51.4–52.6)
Mean follow-up time (years)	18.6	18.5 (17.7–19.3)	19.0 (18.8–19.1)	18.4 (18.3–18.6)	17.7 (17.5–18.0)
Education					
Tertiary (%)	19.3	28.9 (21.9–35.9)	23.9 (22.7–25.1)	16.2 (15.0–17.1)	10.9 (9.2–12.6)
Upper secondary (%)	48.7	51.2 (43.5–58.9)	51.5 (50.0–52.9)	47.7 (46.2–49.4)	41.5 (38.8–44.2)
Mandatory and secondary (%)	32.0	19.9 (13.7–26.0)	24.6 (23.4–25.9)	36.1 (34.5–37.6)	47.6 (44.9–50.3)
Smoking					
Current regular (%)	28.6	31.7 (24.6–38.9)	32.3 (31.0–33.7)	26.6 (25.2–28.0)	21.2 (18.9–23.4)
Current occasional (%)	4.5	3.6 (0.7–6.4)	4.8 (4.2–5.4)	4.7 (4.0–5.4)	2.8 (1.9–3.7)
Non-smokers (former and never, %)	66.9	64.7 (57.3–72.0)	62.9 (61.5–64.3)	68.7 (67.2–70.1)	76.0 (73.7–78.4)
Mean physical activity score	3.52	3.47 (3.17–3.77)	3.79 (3.74–3.84)	3.44 (3.39–3.49)	2.85 (2.76–2.94)
Mean diet score	3.51	3.51 (3.35–3.67)	3.54 (3.51–3.57)	3.51 (3.48–3.54)	3.39 (3.34–3.44)
Blood pressure (systolic/diastolic)					
Mean systolic (mmHg)	129.3	117.4 (115.0–119.9)	124.5 (124.0–125.0)	132.2 (131.6–132.8)	138.9 (137.8–139.9)
Mean diastolic (mmHg)	78.9	71.1 (69.7–72.6)	76.1 (75.8–76.4)	80.8 (80.4–81.1)	84.2 (83.7–84.8)
≥140 or ≥90 (%)	28.8	11.4 (6.5–16.2)	19.0 (17.9–20.2)	34.6 (33.1–36.1)	48.6 (45.9–51.4)
Cholesterol (C)					
Total C: HDL C (ratio)	5.06	3.79 (3.62–3.97)	4.42 (4.38–4.47)	5.52 (5.46–5.58)	6.15 (6.03–6.27)
Ratio ≥ 5 (%)	44.4	13.0 (7.8–18.3)	28.7 (27.4–30.0)	56.8 (55.2–58.4)	67.5 (64.9–70.1)
Deaths					
All causes (*n*)	1,526	24	520	634	348
Cardiovascular disease (*n*)	448	8	126	187	127
Cancer (*n*)	636	2	232	268	134

* Based on height and weight measured at baseline

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For separate analyses we used cholesterol ratio and the four blood pressure categories according to the American Heart Association [27].

Outcome variables

Causes of death were classified according to ICD (International Classification of Diseases) revisions 8 (ICD-8) and 10 (ICD-10). In Switzerland ICD-8 was used until 1994 followed by ICD-10 thereafter. Due to the relatively small number of deaths, causes of death had to be grouped into CVD (ICD-8: 410–438; ICD-10: I00–I99), cancer (ICD-8: 140–239; ICD-10: C00–C99; D00–D48), and non-cancer-non-CVD (remainder).

Statistical analyses

In a first step, we performed all analyses separately by sex. We found no significant sex differences, neither in obesity prevalence, nor in obesity related hazard ratio (HRs). In order to obtain more robust estimates, we decided to pool sexes. Kaplan–Meier curves were calculated for all-cause mortality as well as separately for CVD, cancer and non-cancer-non-CVD, using appropriate methods to account for competing risks. For the estimation of HRs, we fitted a Cox

regression model including relevant independent variables (age, sex, educational class, risk factors) and adjusting for study wave. The association between BMI and death was increasingly adjusted for additional variables using three models: (1) age, sex and survey wave; (2) + diet/physical activity scores and smoking; (3) + educational class. The proportional hazards assumption was tested and checked by visual inspection and seemed to be widely fulfilled. The methods for the calculation of population attributable fractions is described in the Web Annex. General descriptive analyses and survival estimations were performed with Stata 11 (Stata Corp, Texas, USA, 2009), Kaplan–Meier curves and attributable deaths were obtained with R 2.10.1 (The R Foundation for Statistical Computing, 2009).

Results

Descriptive crude analyses

Characteristics of participants are summarized in Table 1. The number of underweight persons was small and mainly consisted of women. In contrast, among obese, there were about as many women as men. The prevalence of obesity was higher than that based on a survey with self-reports but in line with that based on a study with measurement of height and weight in 2003 [21, 22]. Obese persons were older, particularly when compared to normal weight participants. Between BMI categories there were also differences regarding educational class and smoking status. Variations in blood pressure and cholesterol were substantially larger than in physical activity and diet.

Kaplan–Meier curves decrease when a death occurs (Fig. 1). The curves of overweight and obese persons decrease more rapidly than the curve of normal weight persons. However, one should consider that persons in the different BMI categories also differed by sex and age: normal weight persons were younger and more often women. The curve of obese persons differs more strongly from the curve of overweight persons in CVD than in cancer deaths.

Adjusted analyses

Figure 2 shows HRs for all-cause mortality by BMI category in smokers (regular and occasional) and non-smokers (never and former). The curves have a *J* shape (non-smokers) or a *U* shape (smokers), with increased HRs at one or both extremes. Under- and normal- weight smokers had in average a higher risk than obese non-smokers. In both groups, overweight was not associated with higher risk than normal weight. The increase in HRs at BMI < 20 kg/m^2 was only due to an increase in men–in women, HRs remained fairly unchanged. However, the number of deaths was small and the confidence intervals were overlapping between sexes. In contrast, increase in HRs for BMI ≥ 30 kg/m^2 was almost identical in men and women (sex differences not shown). The curve of the entire population (smokers and non-smokers combined) is shown in Web Annex Fig. 1.

Table 2 shows all-cause and cause-specific mortality risk by BMI category. The results are adjusted with an increasing number of variables leading to three different models. For none of the cause of death groups and in none of the models, overweight was associated with increased mortality. Underweight tended to be associated with higher CVD but with lower cancer mortality. The number of cases was however, small in that group. After full adjustment, mortality from all-causes among obese persons was 36% higher than among normal weight persons. CVD mortality was more strongly associated with obesity than cancer mortality. Non-cancer-non-CVD deaths were comparably more frequent among underweight than among normal weight individuals. In underweight persons, HRs for CVD and non-cancer-non-CVD deaths were higher in men than in women but the differences did not reach statistical significance (not shown). Generally, there were no fundamental differences between age groups (Web annex Table 1). In separate analyses, adjustment for cholesterol ratio and blood pressure substantially attenuated the association of obesity with CVD mortality by about 50%. Nevertheless, this association remained statistically significant. The relationship of CVD mortality with overweight was virtually not affected by the adjustment.

Figure 3 shows deaths attributable to obesity as percentage of all deaths related to all death in the corresponding group (all-cause, CVD, cancer, non-cancer-non-CVD). Prevalence rates from studies with either self-reported (empty diamonds) or measured height and weight (filled circles) used for the calculation of attributable deaths are given in the legend. Due to the higher obesity prevalence, the proportion of attributable deaths was higher when it was based on measured height and weight: 4% (self-report) and 6.5% (measurement) of all deaths were attributable to obesity. The proportions were higher for CVD (8.8 and 13.7% of all CVD deaths) than for cancer (2.4 and 3.9% of all cancer deaths).

Discussion

Main results

In this general Swiss population, obesity but not overweight was associated with increased risk of dying from

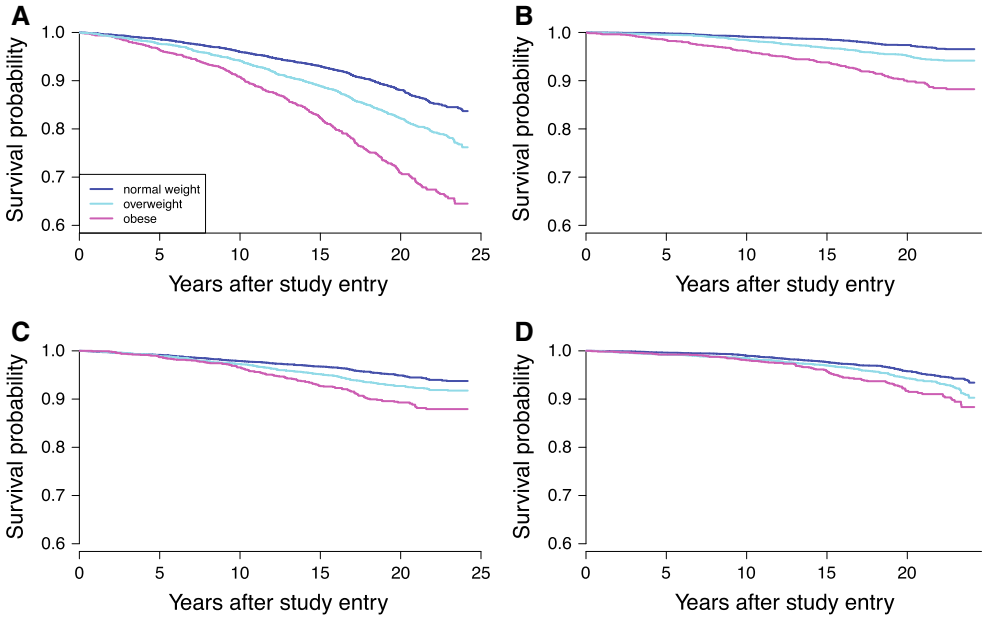

Fig. 1 Kaplan–Meier curves of normal weight, overweight and obese individuals for mortality from all causes (**A**), CVD (**B**), cancer (**C**) and non-cancer-non-CVD (**D**), 9,853 participants of the Swiss MONICA study, 1983–92, 25–74 years at baseline. *MONICA* MONItoring of trends and determinants in CArdiovscular disease. *CVD* Cardiovascular Disease. Body Mass index categories are based on height and weight measured at baseline

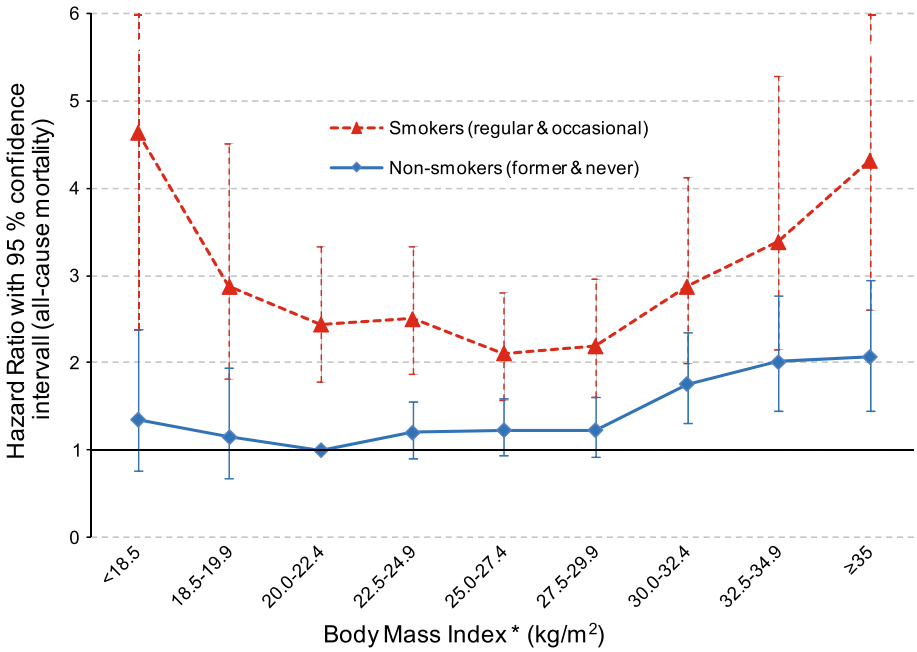

Fig. 2 All-cause mortality (hazard ratios with 95% confidence interval) by smoking status and BMI category, adjusted for age, sex and study wave, 9,853 participants of the Swiss MONICA study, 1983–92, 25–74 years at baseline. *MONICA* MONItoring of trends and determinants in CArdiovscular disease. Reference category are non-smokers with BMI 20.0–22.4 kg/m^2. *Asterisk* represents based on height and weight measured at baseline

CVD and, to a smaller extent, from cancer. The relationship between BMI and all-cause mortality followed a *J* shaped pattern in non-smokers and a *U* shape pattern in smokers (Fig. 2). Among underweight persons, the tendency to an increased risk was driven by CVD (men) and non-cancer-non-CVD (men and women). However, this relationship was confounded by smoking status. The relative risk of death associated with obesity remained significantly increased after adjustment for lifestyle factors and educational level (Table 2).

Overweight and obesity

A J- or U-shaped relationship between BMI and all-cause mortality has been documented in most but not all cohort studies [1, 3, 13, 15, 28–32]. A more pronounced *U* shape

Table 2 Adjusted hazard ratios for all-cause and cause specific mortality, by BMI category, 9,853 participants of the MONICA study, 1983–92, 25–74 years at baseline

	Body mass index category (kg/m^2)*						
	<18.5		18.5–24.9	25–29.9		≥30	
	HR (95% CI)	*P*	HR	HR (95% CI)	*P*	HR (95% CI)	*P*
All cause							
Model 1	1.32 (0.87–1.99)	0.187	1.00	0.96 (0.85–1.08)	0.455	1.41 (1.23–1.62)	<0.001
Model 2	1.18 (0.78–1.80)	0.431	1.00	0.95 (0.85–1.07)	0.438	1.37 (1.19–1.58)	<0.001
Model 3	1.21 (0.80–1.85)	0.367	1.00	0.94 (0.84–1.06)	0.329	1.36 (1.18–1.56)	<0.001
Cardiovascular disease (CVD)							
Model 1	1.62 (0.79–3.33)	0.189	1.00	1.10 (088–1.38)	0.407	2.05 (1.60–2.63	<0.001
Model 2	1.52 (0.74–3.13)	0.259	1.00	1.08 (0.86–1.35)	0.535	1.95 (1.52–2.51)	<0.001
Model 3	1.60 (0.77–3.29)	0.206	1.00	1.07 (0.85–1.35)	0.551	1.92 (1.49–2.47)	<0.001
Cancer							
Model 1	0.26 (0.06–1.04)	0.056	1.00	0.96 (0.80–1.15)	0.647	1.29 (1.04–1.60)	0.021
Model 2	0.24 (0.06–0.98)	0.047	1.00	0.97 (0.81–1.16)	0.711	1.28 (1.03–1.60)	0.027
Model 3	0.25 (0.06–1.01)	0.051	1.00	0.94 (0.79–1.13)	0.519	1.25 (1.00–1.56)	0.050
Non-cancer-non-CVD							
Model 1	2.54 (1.46–4.42)	0.001	1.00	0.86 (0.69–1.06)	0.158	1.10 (0.84–1.44)	0.488
Model 2	2.18 (1.23–3.88)	0.008	1.00	0.86 (0.69–1.07)	0.174	1.08 (0.82–1.42)	0.576
Model 3	2.22 (1.25–4.0)	0.006	1.00	0.86 (0.69–1.06)	0.162	1.08 (0.82–1.42)	0.585

* Based on height and weight measured at baseline

Model 1 (*basic*) adjusted for age, sex and survey wave

Model 2 (*lifestyle*) additionally adjusted for diet, physical activity and smoking

Model 3 (*socio-economic status*) additionally adjusted for education

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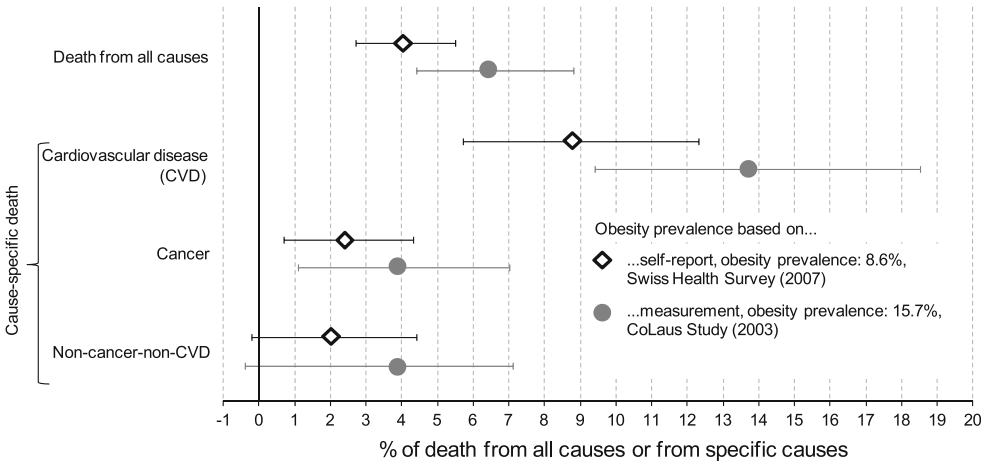

Fig. 3 Estimated excess deaths in Switzerland attributable to obesity, in percent of all causes and cause-specific deaths, 9,853 participants of the Swiss MONICA study, 1983–92, 25–74 years at baseline. *MONICA* MONItoring of trends and determinants in CArdiovscular disease. Analyses were adjusted for age and sex

comparable to ours was found in a MONICA-population from Poland and in several other studies [1, 5, 12, 13, 29, 30]. The fact that we found no increased risk in overweight persons was at variance with reports from Korea, Europe and North America and China (in persons ages <65 years) [1, 13, 29, 31], but in line with other European studies, reports from India, the US and with results from older populations [6, 12, 15, 29, 32–34]. In contrast to overweight, obesity was associated with increased risk of death in almost all available studies.

As shown by most others and by our study, the increased mortality risk was mainly due to CVD [1, 3, 13, 15, 29, 31, 35]: the HRs of obese versus normal weight persons were very similar to ours [1, 13, 15, 29, 31, 35]. In accordance with our results, no or only a marginal increase in relative CVD mortality risk in overweight persons was found in

Poland and the US [29, 35] while a small but significant increase was reported in Europe and North America, China and Korea [1, 13, 29, 31]. Our relative risks for cancer mortality associated with obesity were somewhat higher than those found in a large Asian-Pacific sample [36]. This and two other samples showed a small but significant relative cancer risk in overweight persons, which was at odds with our finding [3, 31, 36]. In a study including participants from Europe and North America, the increased risk associated with higher BMI was substantially lower for cancer than for CVD (HR per 5 kg/m^2 of increase in BMI: 1.10 vs. 1.41) [1, 3]. In contrast, in a large Korean population cancer and CVD mortality were similarly associated with obesity [31].

In our study, lifestyle factors and educational level only moderately attenuated excess risk of obese individuals. Thus, there is little evidence for uncontrolled confounding. However, in line with most literature a part of the CVD risk associated with obesity was apparently mediated by high blood pressure and cholesterol ratio [29, 31, 35]. In a meta-analysis of 21 cohort studies, almost half of the increased risk of fatal and nonfatal CHD events in overweight and obese persons was explained by higher blood pressure and cholesterol levels [37].

Others showed that fatal and non-fatal CVD events were similarly associated with overweight and obesity [35]. Analogously, cancer incidence and morbidity were associated with excess weight in a similar manner [4]. It is therefore possible that, in Switzerland, corresponding to mortality figures, there is also no increased relative risk for CVD and cancer morbidity among overweight persons.

Underweight

Persons with underweight only contributed a small number of deaths and results should therefore be interpreted cautiously. In accordance with others, the relative risk of death of underweight persons was higher in smokers than in non-smokers (Fig. 2) [1, 3, 13, 31]. The tendency to higher mortality risk of underweight persons was driven by death from non-cancer to non-CVD. Our data did not offer sufficient statistical power to assess which specific causes were responsible for excess mortality in smokers and non-smokers. Other studies showed that respiratory mortality (e.g., COPD) substantially contributed [1, 13, 31, 38]. Most but not all studies showed an increased CVD mortality at BMI below 18.5 [1, 3, 13, 29–31].

The association between low BMI and death could reflect insufficient consideration of early or chronic disease leading to both thinness and death. Our data, however, provide only little evidence for this: first, our population was comparably young and age did not appear to fundamentally affect the relationship between BMI and mortality risk; second, adjustment for smoking only marginally attenuated estimates; third, the number of cancer deaths was negligible among underweight persons and the pattern (non-cancer-non-CVD > CVD > cancer) was the same as in a large study considering only healthy subjects who never smoked [3]. Furthermore, only 3.6 and 11.9% of all non-injury deaths occurred during the first 2 and 5 years after study entry. Others have shown that an increased risk of death in underweight persons was still observed among healthy participants and after exclusion of the initial 5 years of follow-up [3, 29, 39].

Excess deaths attributable to obesity

In Switzerland, nationally representative data on obesity prevalence is only available from self-reports which substantially underestimate real obesity prevalence [40]. For valid figures, excess deaths should be estimated with obesity prevalence based on measured height and weight. Since more recent data was not available, we used measured BMI data from 2003 for the calculation of excess deaths. However, this should not substantially underestimate current excess deaths because in Switzerland obesity prevalence stagnated or increased only marginally since 2003 [41].

In the US, where obesity prevalence is about twice as high as in Switzerland, approximately 29% of CVD deaths and 8% of cancer deaths were attributable to BMI $\geq$ 25 kg/m^2 [1, 11]. For the UK, the corresponding proportions were 23 and 6%, respectively [1, 42]. In accordance with our figures, a calculation based on European data estimated that in Switzerland around 700 cancer cases/year could be attributed to overweight or obesity [43]. Probably, our estimates would be higher, had we used other markers than BMI for the definition of obesity (e.g., body fat percentage) [44]. However, a large European study proved BMI to remain significantly associated with the risk of death also in models that included waist circumference or waist-to-hip ratio [32].

Public health implications

Our findings do not support the concept that persons with overweight should decrease their BMI in order to reduce their risk of premature death. For this category (BMI 25–29.9) efforts aimed at avoiding weight gain and improving health behaviour may be more appropriate. Our study also implies that by controlling and treating risk factors in obese persons, excess mortality risk can be decreased but not eliminated. Because long term weight loss is unrealistic in obese persons, the only way to decrease excess deaths on a population level is to prevent persons from becoming obese. Our results also show that

the benefit of lower BMI does not counterweight the increased risk associated with smoking. Thus, under- and normal- weight smokers should be as consequently screened and motivated for smoking cessation as obese smokers.

Limitations

The MONICA participants included in our study had a lower mortality and were thus, presumably more healthy than the general Swiss population [20]. However, in a large study conducted in an immediately neighbouring Austrian region, the difference between expected and observed mortality was even larger [13], but the observed patterns were generally the same as in our study. Obese persons are less likely to participate in health surveys than normal weight persons and the "healthy participant effect" could have distorted relative risks [45]. We also had only one measurement of height and weight at study entry and could not consider change in BMI during follow-up. Our obesity marker was restricted to BMI and did not include waist circumference, visceral fat or body fat percentage. To the extent that BMI imperfectly reflects adiposity, our results would tend to underestimate the deleterious effects of obesity [44]. Our information on diet and physical activity was based on a coarse assessment. However, the derived scores were significantly associated with mortality (not shown). Our information on pre-existing disease was restricted to known hypertension. Inclusion of this variable in the model only minimally affected estimates. Also for other reasons discussed above, we have little evidence that severe disease existing before study entry played a major role in our population. We also found no evidence that age affected the obesity-mortality relationship.

Conclusion

In this study from Switzerland, obesity but not overweight was associated with an increased risk of death. Excess mortality was driven by CVD and, to a smaller extent, by cancer. After adjustment for lifestyle risk factors and for educational class, the independent effect of obesity decreased but remained significant. Our results question the targeting of overweight individuals for weight loss programs in order to decrease burden of disease. In contrast, people should be prevented from becoming obese—irrespective of their body weight. In smokers, underweight was significantly associated with premature death, mainly due to non-cancer-non-CVD causes.

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