International Journal of Obesity (2016) **40**, 1535–1540

www.nature.com/ijo

ORIGINAL ARTICLE

Obesity in older adults and life expectancy with and without cardiovascular disease

K Dhana[1], MA Berghout[1], A Peeters[2], MA Ikram[1,3,4], H Tiemeier[1,5], A Hofman[1,6], W Nusselder[7], M Kavousi[1] and OH Franco[1]

BACKGROUND: The prevalence of overweight and obesity is increasing globally and is an established risk factor for cardiovascular disease (CVD). Our objective was to evaluate the impact of overweight and obesity on life expectancy and years lived with and without CVD in older adults.

METHODS: The study included 6636 individuals (3750 women) aged 55 years and older from the population-based Rotterdam Study. We developed multistate life tables by using prevalence, incidence rate and hazard ratios (HR) for three transitions (free-of-CVD-to-CVD, free-of-CVD-to-death and CVD-to-death), stratifying by the categories of body mass index (BMI) at baseline and adjusting for confounders.

RESULTS: During 12 years of follow-up, we observed 1035 incident CVD events and 1902 overall deaths. Obesity was associated with an increased risk of CVD among men (HR 1.57 (95% confidence interval (CI) 1.17, 2.11)) and women (HR 1.49 (95% CI 1.19, 1.86)), compared with normal weight individuals. Overweight and obesity were not associated with mortality in men and women without CVD. Among men with CVD, obesity compared with normal weight, was associated with a lower risk of mortality (HR 0.67 (95% CI 0.49, 0.90)). Overweight and obesity did not influence total life expectancy. However, obesity was associated with 2.6 fewer years (95% CI −4.8, −0.4) lived free from CVD in men and 1.9 (95% CI −3.3, −0.9) in women. Moreover, men and women with obesity lived 2.9 (95% CI 1.1, 4.8) and 1.7 (95% CI 0.6, 2.8) more years suffering from CVD compared with normal weight counterparts.

CONCLUSIONS: Obesity had no effect on total life expectancy in older individuals, but increased the risk of having CVD earlier in life and consequently extended the number of years lived with CVD. Owing to increasing prevalence of obesity and improved treatment of CVD, we might expect more individuals living with CVD and for a longer period of time.

International Journal of Obesity (2016) **40,** 1535–1540; doi:10.1038/ijo.2016.94

INTRODUCTION

Obesity is increasing globally and the association between body weight, morbidity and mortality has received widespread attention.[1] There is consensus on the association of overweight and obesity with mortality in young adults and middle aged,[2] but there is no clear consensus for the elderly.[3–5] Several studies have reported that among older individuals the longest survival is observed in the overweight and obese range.[5–7] However, older individuals with obesity are still at higher risk to develop cardiovascular disease (CVD) in their remaining lifespan.[8] Therefore, the contribution of obesity to life expectancy and in particular life expectancy with and without CVD among older individuals is still of relevance.

Previous studies investigating the impact of overweight and obesity with total life expectancy have reported that obesity in adulthood is associated with a decrease in total life expectancy of 6–7 years, and severe obesity in men aged 20–30 will shorten life expectancy by 13 years, compared with normal weight individuals.[9,10] Another study evaluating the association of obesity at the age of 45 years with total life expectancy and life expectancy with and without CVD has shown that obesity not only reduces total life expectancy, but also reduces the number of years lived free-of-CVD by 6.0 years in men and 8.4 in women.[11] However, most of studies described have evaluated the effect among young adults, whereas the effect of obesity on survival in the elderly remains controversial.[3,5] Furthermore, these studies have used data from the Framingham Heart Study using information collected during the second half of the 20th century. In recent decades, an increase of obesity prevalence[12] has been observed along with improvements in prevention and treatment of CVD.[13]

Therefore, in a population-based study of subjects 55 years and older, we aimed to evaluate the impact of overweight and obesity in the average years lived with and without CVD. We constructed multistate life tables using data collected from 1997 and with over 12 years of follow-up from the Rotterdam Study.

METHODS

Study population

This study was embedded within the Rotterdam Study, a prospective population-based cohort study among adults and elderly living in the Ommoord district of Rotterdam, The Netherlands. The baseline examination was completed between 1990 and 1993 by trained research assistants for 7983 participants (RS-I). In 2000–2001, the Rotterdam Study was extended with 3011 participants who had become ⩾ 55 years of age or had

[1]Department of Epidemiology, Erasmus Medical Center, University Medical Center, Rotterdam, the Netherlands; [2]Department of Obesity and Population Health, Baker IDI Heart and Diabetes Institute, Melbourne, Australia; [3]Department of Neurology, Erasmus Medical Center, Rotterdam, the Netherlands; [4]Department of Radiology, Erasmus Medical Center, Rotterdam, the Netherlands; [5]Department of Child and Adolescent Psychiatry, Erasmus Medical Center, Rotterdam, the Netherlands; [6]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA and [7]Department of Public Health, Erasmus Medical Center, Rotterdam, the Netherlands. Correspondence: Dr K Dhana, Department of Epidemiology, Erasmus Medical Center, University Medical Center, PO Box 2040, Rotterdam 3000 CA, the Netherlands.
E-mail: k.dhana@erasmusmc.nl
Received 14 February 2016; revised 20 April 2016; accepted 2 May 2016; accepted article preview online 10 May 2016; advance online publication, 14 June 2016

moved into the study district (RS-II). The objectives and design of the Rotterdam Study have been described in detail elsewhere.[14]

For the current study, we used data from the participants attending the third examination of the original cohort (RS-I-visit 3, 1997–1999; $n = 4797$) and the participants attending the first examination of the extended cohort (RS-II-visit 1, 2000–2001; $n = 3011$).

We excluded participants who did not visit the research center, did not have information on body mass index (BMI) ($n = 1051$, the baseline characteristics of this subgroup are presented in Table 1 in the supplementary material), or no information on smoking behavior ($n = 40$). In addition, we excluded participants who had BMI $\leqslant 18.5$ ($n = 51$) to account for disease-related weight loss. Finally, we excluded participants without written informed consent ($n = 30$). After exclusion, 6636 participants (3750 women) were available for the current analysis. All participants provided written informed consent to participate in the study and to obtain information from their treating physicians.

Assessment of anthropometric measurements, health behaviors and laboratory measurements

Anthropometrics were measured in the research center by trained staff. Height and weight were measured with the participants standing without shoes and heavy outer garments. We calculated BMI by dividing weight with height squared (kg m^{-2}).[15] According to the WHO cutoff criteria, we composed BMI as a categorical variable with three categories: normal weight ($18.5 \leqslant$ BMI < 25), overweight ($25 \leqslant$ BMI < 30) and obese ($30 \leqslant$ BMI).[15] Smoking status was categorized as current smoker, former smoker and never smoker, and in addition we accounted for cigarettes smoked per day. Information on education was assessed according to the standard international classification of education and was composed into four categories: elementary education, lower secondary education, higher secondary education, and tertiary education.[16] Marital status was divided in single, married, widowed or divorced/separated. Physical activity was measured by questionnaire and expressed in METhours per week. For analysis, we divided the population in 3 equal groups (tertile).[17] Alcohol consumption was categorized as <1 glass per day, 1–4 glasses per day for men and 1–2 glasses per day for women, and >4 glasses per day for men and >2 glasses per day for women. Comorbidity was considered present when 'non-obesity-related cancers other than skin cancer' or chronic obstructive pulmonary disease was prevalent at baseline. We excluded cancers that are associated with obesity,[18] or cancers that are curable and not likely to be related to weight loss or mortality, such as skin cancer.[19] Chronic obstructive pulmonary disease was defined as a type of obstructive lung disease characterized by airflow limitation not fully reversible.[20] Chronic obstructive pulmonary disease has been shown to be accompanied with weight loss.[21]

Hypertension, dyslipidemia and diabetes mellitus were considered as intermediates and not confounding variables in the association of obesity with CVD and mortality, therefore, in a sensitivity analysis, we repeated our analyses by excluding individuals with hypertension, dyslipidemia or diabetes. The presence of hypertension and dyslipidemia was based on medication information, whereas diabetes mellitus was defined as the documented use of medication or fasting plasma glucose level $\geqslant 110$ mg dl^{-1}.

Table 1. Baseline characteristics of study population

Characteristics	*Men*	*Women*
Population		
n	2886 (42%)	3750 (58%)
Age at interview (years)	68.7 ± 7.9	69.7 ± 8.4
Anthropometry		
BMI (kg m^{-2})	26.6 ± 3.2	27.5 ± 4.4
Normal (BMI 18.5–25)	944 (32.7)	1201 (32.0)
Overweight (BMI 25–30)	1545 (53.5)	1613 (43.0)
Obese (BMI 30+)	397 (13.8)	936 (25.0)
Social economic status		
Marital status		
Single	84 (3.0)	261 (7.0)
Married	2284 (79.1)	2008 (53.5)
Widowed	310 (10.7)	1099 (29.3)
Divorced/separated	208 (7.2)	382 (10.2)
Education		
Elementary	274 (9.5)	632 (16.6)
Lower secondary	870 (30.1)	2003 (53.4)
Higher secondary	1122 (38.9)	879 (23.4)
Tertiary	620 (21.5)	245 (6.6)
Lifestyle variables		
Smoking		
Never smoking	913 (31.6)	2310 (61.6)
Former smoker	1448 (50.2)	812 (21.7)
Current smoker	525 (18.2)	628 (16.7)
Daily cigarettes smoked	2.8 ± 7.0	2.3 ± 6.1
Alcohol (drinks per day)		
<1 glass per day	1289 (44.7)	2674 (71.3)
1–4 glasses per day (men); 1–2 glasses per day (women)	1363 (47.2)	669 (17.8)
>4 glasses per day (men); >2 glasses per day (women)	234 (8.1)	407 (10.9)
Physical activity (METhours per week)	73.8 ± 43.9	92.1 ± 43.3
Treatment for hypertension	641 (22.2)	997 (26.2)
Treatment for dyslipidemia	415 (14.4)	473 (12.6)
Diabetes mellitus	338 (15.1)	438 (11.7)
Comorbidities (cancer[a] and chronic obstructive pulmonary disease)	274 (9.5)	216 (5.8)

Abbreviations: BMI, body mass index; MET, metabolic equivalent. Values are means (SDs) or numbers (percentages). [a]Cancer includes 'non-obesity-related cancers other than skin cancer.

Assessment of outcome

The main outcome measures under study was incident non-fatal or fatal CVD and overall mortality. In the Rotterdam Study, CVD is defined as the presence of one or more definite manifestation of coronary heart disease (coronary revascularization or non-fatal or fatal myocardial infarction or death due to coronary heart disease), stroke and heart failure. Definite and possible fatal coronary heart disease events are coded by using the definitions applied within the Cardiovascular Health Study and Atherosclerosis Risk in the Communities Study.[22] Stroke is defined as a syndrome of rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 h or longer or leading to death, with no apparent origin other than vascular.[23] Heart failure was defined using the criteria of the European Society of Cardiology as a combination of heart failure diagnosed by a medical specialist and the presence of typical symptoms of heart failure, such as breathlessness at rest or during exertion, ankle edema and pulmonary crepitation, confirmed by objective evidence of cardiac dysfunction (chest X-ray, echocardiography).[24] Data on incident CVD are collected using an automated follow-up system by gathering information from general practitioners working in the study area. Information about cause and circumstances of death was obtained from general practitioner medical records and from municipal records. Research physicians reviewed all available information and coded the events according to the International Classification of Diseases, 10th edition (ICD-10). A consensus panel, led by a physician with expertize in field, adjudicated the final cause of death according to ICD-10 codes using standardized definitions. The follow-up was complete until 1 January 2010.

Statistical analysis

We created population-based multistate life tables to calculate the differences in life expectancy and years lived with and without CVD in normal weight, overweight and obese groups.[25] We constructed three different health states: free-of-CVD, CVD and death. The possible transition directions were from free-of-CVD-to-CVD, free-of-CVD-to-death and from CVD-to-death. No backflows were allowed (for example, from CVD-to-not having CVD), and only first event into state was considered.

First, we calculated the overall age- and sex-specific rates for each transition with Poisson regression using the Gompertz distribution to obtain smoothed age- and sex-specific rates. Second, we calculated the prevalence of normal weight, overweight and obesity by sex, 10-year age groups, and separately for subjects with and without CVD. Third, we computed gender specific hazard ratios (HR) comparing overweight and obese to normal

weight individuals by using Poisson regression with 'Gompertz' distribution in two models. Model 1 was adjusted for age; and Model 2 was adjusted for age, smoking status, cigarettes smoked per day (for current smokers), alcohol consumption, education, marital status, physical activity and comorbidities ('non-obesity-related cancers other than skin cancer' or chronic obstructive pulmonary disease).

Finally, the three sets of transitions rates were calculated for each category of BMI separately using the (a) overall transition rates, the (b) adjusted HR (model 2) for CVD and mortality and the (c) prevalence. Similar calculations have been described previously.[26,27] The multistate life table started at age 55 years and closed at age 100 years.

Confidence intervals for all life expectancies and their differences were calculated using @RISK software (Anonymous 2000; MathSoft Inc, Cambridge, MA, USA), by Monte Carlo simulation (parametric bootstrapping) 10 000 runs.[28]

Although we adjusted for smoking and comorbidities, to exclude any potential bias caused by smoking or comorbidities we repeated the analysis among non-smokers and individuals without comorbidities ('non-obesity-related cancers other than skin cancer' or chronic obstructive pulmonary disease) at baseline ($n = 5117$). In addition, we estimated the life expectancy among participants without hypertension, hyperlipidemia and diabetes mellitus at baseline ($n = 3750$). Also we computed life tables for individuals who were older than 65 years at baseline ($n = 4245$). Moreover, we estimated the HR after excluding cardiovascular events ($n = 127$) or deaths ($n = 145$) during the first two years of follow-up to take in account the reverse causation.

To deal with missing values ($< 5\%$) for covariates including education, marital status, physical activity, and alcohol we used single imputation with the Expectation Maximization method in SPSS (IBM SPSS Statistical for Windows, Armonk, New York, NY, USA: IBM Corp).

We used STATA version 13 for Windows (StataCorp, College Station, TX, USA) and R version 3.1.3 (R Foundation for Statistical Computing, Vienna, Austria) for our analysis.

RESULTS

In total, we observed 1035 (18.6%) incident CVD events and 1902 (28.7%) overall deaths over 12 years of follow-up. Thirty-five percent of overall death were from CVD, and 28.5% were from malignant cancers. Compared with women, men at baseline were younger and smoked more, showed lower levels of BMI and physical activity, but higher education levels (Table 1).

Cardiovascular events and death

Table 2 shows the HR of the association between categories of BMI with risk of incident CVD and mortality among men and women. In multivariable adjusted model, obesity (as classified by BMI > 30) was associated with an increased risk of incident CVD among men (HR 1.57 (95% confidence interval (CI) 1.17, 2.11)) and women (HR 1.49 (95% CI 1.19, 1.86)) compared with normal weight individuals (Table 2).

Among men and women without CVD, overweight and obesity, compared with normal weight individuals, were not associated with mortality (Table 2, Model 2).

Among men with CVD, overweight and obesity, compared with normal weight, showed a decreased risk of mortality (HR (95% CI) 0.81 (0.66, 0.98) and 0.67 (0.49, 0.90), respectively). The association between overweight and obesity with mortality among women with CVD did not reach a statistical significance.

Total life expectancy and life expectancy with and without CVD

The association between normal weight, overweight and obesity with the risk of each transition (no CVD, CVD and death) was translated into number of years lived with and without CVD (Figure 1 and Table 3). Total life expectancy for men and women with overweight and obesity were not significantly different than normal weight counterparts. Compared with normal weight men, life expectancy of 55-year-old men in the overweight group was 0.1 (95% CI − 0.8, 1.0) years longer, and in the obese group 0.3 years (95% CI − 1.1, 1.6). For women, these differences were: 0.6 (95% CI − 0.2, 1.3) and − 0.2 (-1.2, 0.7) years, respectively (Table 3). For both men and women, obesity was associated with fewer years lived without CVD and more years lived with CVD than their normal weight counterparts. Men and women with obesity lived 2.6 (95% CI − 4.8, − 0.4) and 1.9 (95% CI − 3.3, − 0.9) fewer years without CVD, respectively, than those in normal weight group. In addition, obese men and women lived more years with CVD than their normal weight counterparts; 2.9 (95% CI 1.1, 4.8) years

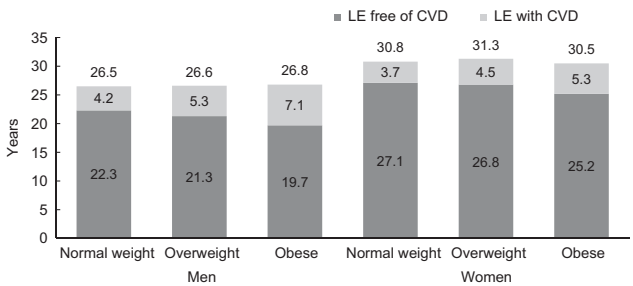

Figure 1. Effect of obesity on life expectancy with and without cardiovascular disease (CVD) at age 55 years. Body mass index (BMI) categories: normal weight BMI is < 25 kg m^{-2}; overweight BMI is 25–30 kg m^{-2}; and obese the BMI is $\geqslant 30$ kg m^{-2}. LE, life expectancy; CVD, cardiovascular disease.

Table 2. Hazard ratios for cardiovascular disease and death for overweight and obese men and women

Transition	*Categories*	*Men*		*Women*	
		Model 1 HR (95% CI)[a]	*Model 2 HR (95% CI)*[b]	*Model 1 HR (95% CI)*[a]	*Model 2 HR (95% CI)*[b]
Incident CVD	Normal weight	1.0	1.0	1.0	1.0
	Overweight	1.17 (0.95, 1.44)	1.19 (0.96, 1.47)	1.17 (0.95, 1.43)	1.20 (0.98, 1.47)
	Obese	1.56 (1.17, 2.09)	1.57 (1.17, 2.11)	1.47 (1.18, 1.83)	1.49 (1.19, 1.86)
Mortality among those without CVD	Normal weight	1.0	1.0	1.0	1.0
	Overweight	1.02 (0.85, 1.20)	1.06 (0.89, 1.27)	0.83 (0.70, 0.99)	0.86 (0.72, 1.03)
	Obese	1.03 (0.78, 1.36)	1.08 (0.81, 1.43)	1.01 (0.83, 1.22)	1.02 (0.83, 1.24)
Mortality among those with CVD	Normal weight	1.0	1.0	1.0	1.0
	Overweight	0.78 (0.65, 0.94)	0.81 (0.66, 0.98)	0.84 (0.66, 1.05)	0.92 (0.72, 1.16)
	Obese	0.64 (0.47, 0.86)	0.67 (0.49, 0.90)	0.76 (0.59, 0.98)	0.84 (0.64, 1.09)

Abbreviations: CI, confidence interval; HR, hazards ratio. [a]Adjusted for age. [b]Adjusted for age, smoking, cigarettes smoked per day, education level, marital status, physical activity, alcohol use and comorbidities ('non-obesity-related cancers other than skin cancer' or chronic obstructive pulmonary disease).

Table 3. Differences in life expectancy, in years, at age 55 for normal weight, overweight and obesity in men and women

	Total LE	*Differences in total LE*	*LE free-of-CVD*	*Differences in number of years lived free-of-CVD*	*LE with CVD*	*Differences in number of years lived with CVD*
Body mass index						
Men						
Normal weight	26.5 (26.0, 27.1)	Ref	22.3 (21.6, 23.0)	Ref	4.2 (3.8, 4.7)	Ref
Overweight	26.6 (26.1, 27.2)	0.1 (−0.8, 1.0)	21.3 (20.7, 22.0)	− 1.0 (−2.1, 0.2)	5.3 (4.8, 5.8)	1.1 (0.3, 1.9)
Obese	26.8 (25.5, 28.1)	0.3 (−1.1, 1.6)	19.7 (17.7, 21.7)	− 2.6 (−4.8, − 0.4)	7.1 (5.4, 8.9)	2.9 (1.1, 4.8)
Women						
Normal weight	30.8 (30.3, 31.3)	Ref	27.1 (26.5, 27.7)	Ref	3.7 (3.2, 4.1)	Ref
Overweight	31.3 (30.7, 32.0)	0.6 (−0.2, 1.3)	26.8 (26.0, 27.6)	− 0.3 (−1.3, 0.7)	4.5 (3.9, 5.2)	0.9 (0.1, 1.6)
Obese	30.7 (30.0, 31.5)	− 0.2 (−1.2, 0.7)	25.2 (24.1, 26.1)	− 1.9 (−3.3, − 0.9)	5.3 (4.4, 6.3)	1.7 (0.6, 2.8)

Abbreviations: CVD, cardiovascular disease; LE, life expectancy.

for men and 1.7 (95% CI 0.6, 2.8) years for women (Figure 1 and Table 3).

Total life expectancy, number of years lived with and without CVD for normal weight, overweight and obese for non-smokers and individuals without prevalent comorbidities ('non-obesity-related cancers other than skin cancer' and chronic obstructive pulmonary disease) are presented in Supplementary Figure 1, and for individuals without hypertension, dyslipidemia and diabetes are presented in Supplementary Figure 2, and for individuals older than 65 at baseline are presented in Supplementary Figure 3. As expected, total life expectancy increased for individuals who were non-smokers and without comorbidities at baseline, or for individuals without diabetes, hypertension and dyslipidemia, but all differences among normal weight, overweight and obese individuals were similar to those found in the total population. However, differences of the BMI categories in total life expectancy and life expectancy with and without CVD became smaller for individuals older than 65 at baseline. Table 1 in the Supplementary Material shows the baseline characteristics of individuals who did not visited the research center or without information of BMI. This subgroup of individuals were older than individuals included in study, and therefore, were less physically active. In addition, when we repeated the main analysis after excluding deaths during first 2 years of follow-up, we found generally similar results (Table 2 in the Supplementary Material).

DISCUSSION

Overall we found that compared with normal weight, overweight and obesity in middle age and elderly have a considerable effect on years lived with and without CVD, although they had no effect on total life expectancy. Total life expectancy for obese men and women at age 55 years was not significantly different from the normal weight individuals. However, obesity was associated with 2.6 fewer years lived without CVD for men and 1.9 years for women. Moreover, men and women with obesity spent an extra of 2.9 and 1.7 years living with CVD, respectively.

The shorter life expectancy without CVD among men and women with obesity was due to increased CVD and mortality risk. Higher risk for CVD is reflected by an earlier occurrence of CVD over the lifespan and therefore, a shorter life expectancy without CVD. Furthermore, higher risk of mortality among individuals without history of CVD follows a decrease in the total life expectancy and consequently, a shorter life expectancy without CVD could be expected. We also found that compared with normal weight, individuals with obesity spent more years living with CVD. Years spent with CVD is a consequence of CVD risk in those without history of CVD, and mortality risk in those with history of CVD. In our study, obese individuals without history of CVD had an increased risk for CVD, whereas obese individuals with history of CVD had lower risk of mortality. Taken together, this indicate that individuals with obesity will spend more years living with CVD.

Our analysis indicated that obesity increased the risk of CVD in men and women, and the HR were comparable with other studies.[29,30] The relation between obesity and mortality is well documented among younger and middle-aged populations.[31] However, among the late middle aged as well as elderly, higher BMI has not been consistently associated with higher mortality risk.[3,5] In addition, a previous meta-analysis by Flegal *et al.*[4] reported that overweight individuals are at lower risk of mortality, compared with normal weight individuals. Our study do not report a protective associations of an increased BMI in individuals without CVD. However, among overweight and obese men with CVD at baseline, after adjusting for possible confounders, we found that the risk of mortality decreased by 33% in obese individuals, compared with normal weight individuals. Although, the role of obesity among the older adults is still a topic of debate, some studies have suggested that being overweight and obese could serve as a nutritional deposit in hardship conditions such as inflammation and disease.[32,33] In contrast, some studies have rejected this paradigm, attributing the lower risk of mortality to the fact that BMI becomes less sensitive to fat mass and body fat distribution in older individuals.[34] To reduce the potential effect of underlying disease, we performed a series of sensitivity analysis in individuals without hypertension, dyslipidemia and diabetes; in non-smokers and without comorbidities at baseline. Restricting the analyses to these subgroups did not generally modify the life expectancies associated with obesity.

In our study, we found that the effect of overweight and obesity in total life expectancy is minimal. Earlier studies comprising the participants from the Framingham Heart Study showed larger differences in life expectancy between obese and normal weight.[9,11] Peeters *et al.*[9] showed that at age of 40 years life expectancy differences for obese and normal weight men is 5.8 years in nonsmoker and 6.7 in smokers. Another study by Pardo Silva *et al.*[11] noted that men with obesity lived 3.3 years and women 6.9 years shorter from age 45 than those who were normal weight. In addition, this study showed that obese men and women aged 45 years live 6.0 and 8.4 years fewer free-of-CVD, whereas in our study the difference was smaller; 2.6 and 1.9 years for men and women, respectively.[11] The differences between our findings and those of previous studies from Framingham Heart Study could be explained by two factors. First, our participants were 10–15 years older at baseline, and the association of obesity on mortality might change with increasing age.[5] Second, the calendar time when the studies were conducted is different. Although the Framingham Heart Study included participants from 1948–1950 and followed them up during the second half of the 20th century, our study included participants from 1997–2001 with follow-up until 2010. There have been reports of progressive improvements in the treatment for cardiovascular risk factors after 1990, which resulted in the reduction of cardiovascular incidence and mortality rates.[13] Our analysis is comparable to the

Health and Retirement Survey, a US prospective longitudinal study.[35] Similar to ours findings they reported that total life expectancy at age 55 in men and women was not affected by overweight and obesity. Nevertheless, they did not evaluate the impact of obesity on life expectancy with and without CVD.[35] In addition, our findings on the influence of obesity on total life expectancy are consistent with earlier analyses within Rotterdam Study by Walter *et al.*[36] in 2009 (conduced in RS-I, with baseline measures from 1990–1993). Walter *et al.*[36] evaluated the impact of overweight and obesity on disability and mortality by using a different approach from ours to calculate the total life expectancy, which took into account the recovery from disability. However, in line with our findings Walter *et al.*[36] concluded that obesity was not associated with a reduction in total life expectancy, but was associated with a higher risk of becoming and remaining disabled. In the current analyses we found that obese individuals tend to have CVD earlier in life and will spend more time living with CVD.

The strengths of our study include availability of a long follow-up time with detailed and validated information on anthropometrics, CVD and mortality. Anthropometrics such as height and weight were measured in the research center by trained staff and do not depend on self-reported information. Nevertheless, the studies that evaluate the association of obesity with mortality could be prone to incorrect adjustment for confounders such as smoking or weight loss related to diseases and comorbidities. In our study, we adjusted for smoking status and the cigarettes smoked per day. Also, we adjusted and in addition excluded participants that had 'non-obesity-related cancers other than skin cancer' or chronic obstructive pulmonary disease. Sensitivity analysis was also performed in individuals who did not died during the first 2 years of follow-up. We did not adjust for hypertension, dyslipidemia or diabetes as those factors could be considered intermediates and not confounders. However, we repeated the analysis among participants without hypertension and diabetes at the baseline.

Our study showed that among late middle age and elderly individuals overweight and obesity do not seem to have an impact on total life expectancy, but are associated with earlier and extended periods lived with CVD. The impact of obesity on life expectancy with and without CVD was larger in men than in women. Owing to the increasing prevalence of obesity and the improved treatment of CVD, we might expect more individuals living with CVD and for a longer period of time. This will result in increasing costs of healthcare and poorer levels of quality of life.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

The dedication, commitment and contribution of inhabitants, general practitioners and pharmacists of the Ommoord district to the Rotterdam Study are gratefully acknowledged. The Rotterdam Study is funded by Erasmus MC and Erasmus University, Rotterdam, the Netherlands; the Netherlands Organization for Scientific Research (NWO); the Netherlands Organization for the Health Research and Development (ZonMw); the Research Institute for Diseases in the Elderly (RIDE); the Ministry of Education, Culture and Science; the Ministry for Health, Welfare and Sports; the European Commission (DG XII); and the Municipality of Rotterdam. KD is supported Erasmus Mundus Western Balkans (ERAWEB), a project funded by the European Commission. MK is supported by AXA Research Fund. MAI is supported by the Netherlands Heart Foundation (2012T008). OHF works in ErasmusAGE, a center for aging research across the life course funded by Nestlé Nutrition (Nestec Ltd.) and Metagenics Inc. Nestlé Nutrition (Nestec Ltd.) and Metagenics Inc. had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review or approval of the manuscript. The Rotterdam Study has been approved by the institutional review board (medical ethics committee) of the Erasmus Medical Center and by the medical ethics committee according to the Wet Bevolkingsonderzoek ERGO (Population Study Act Rotterdam Study), executed by the Ministry of Health, Welfare and Sports of The Netherlands.

AUTHOR CONTRIBUTIONS

The contribution of the authors were as follows: KD and OHF had the original idea for the study. OHF supervised analyses of study data. MB, AP, MAI, HT, AH, WN, MK and OHF revised the manuscript critically for important intellectual content and gave final approval of the version to be published.

REFERENCES

1 Haslam DW, James WP. Obesity. *Lancet* 2005; **366**: 1197–1209.
2 Berrington de Gonzalez A, Hartge P, Cerhan JR, Flint AJ, Hannan L, MacInnis RJ *et al.* Body-mass index and mortality among 1.46 million white adults. *N Engl J Med* 2010; **363**: 2211–2219.
3 Grabowski DC, Ellis JE. High body mass index does not predict mortality in older people: analysis of the Longitudinal Study of Aging. *J Am Geriatri Soc* 2001; **49**: 968–979.
4 Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. *JAMA* 2013; **309**: 71–82.
5 Stevens J, Cai J, Pamuk ER, Williamson DF, Thun MJ, Wood JL. The effect of age on the association between body-mass index and mortality. *N Engl J Med* 1998; **338**: 1–7.
6 Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess deaths associated with underweight, overweight, and obesity. *JAMA* 2005; **293**: 1861–1867.
7 Bender R, Jockel KH, Trautner C, Spraul M, Berger M. Effect of age on excess mortality in obesity. *JAMA* 1999; **281**: 1498–1504.
8 Harris TB, Ballardbarbasch R, Madans J, Makuc DM, Feldman JJ. Overweight, weight-Loss, and risk of coronary heart-disease in older women - the Nhanes-I epidemiologic follow-up-study. *Am J Epidemiol* 1993; **137**: 1318–1327.
9 Peeters A, Barendregt JJ, Willekens F, Mackenbach JP, Al Mamun A, Bonneux L. Obesity in adulthood and its consequences for life expectancy: a life-table analysis. *Ann Int Med* 2003; **138**: 24–32.
10 Fontaine KR, Redden DT, Wang C, Westfall AO, Allison DB. Years of life lost due to obesity. *JAMA* 2003; **289**: 187–193.
11 Pardo Silva MC, De Laet C, Nusselder WJ, Mamun AA, Peeters A. Adult obesity and number of years lived with and without cardiovascular disease. *Obesity (Silver Spring)* 2006; **14**: 1264–1273.
12 Collaboration NCDRF. Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. *Lancet* 2016; **387**: 1377–1396.
13 Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM *et al.* Secular trends in cardiovascular disease risk factors according to body mass index in US adults. *JAMA* 2005; **293**: 1868–1874.
14 Hofman A, Brusselle GG, Darwish Murad S, van Duijn CM, Franco OH, Goedegebure A *et al.* The Rotterdam Study: 2016 objectives and design update. *Eur J Epidemiol* 2015; **30**: 661–708.
15 Eveleth PB. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. *Am J Hum Biol* 1996; **8**: 786–787.
16 Unesco. *International Standard Classification of Education-ISCED 1997: November 1997*. Unesco, 1997.
17 Koolhaas CM, Dhana K, Golubic R, Schoufour JD, Hofman A, van Rooij FJ *et al.* Physical Activity Types and Coronary Heart Disease Risk in Middle-Aged and Elderly Persons: The Rotterdam Study. *Am J Epidemiol* 2016; **183**: 729-738.
18 World Cancer Research Fund/American Institute for Cancer Research. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. *AICR* 2008.
19 Leiter U, Eigentler T, Garbe C. Epidemiology of skin cancer. *Adv Exp Med Biol* 2014; **810**: 120–140.
20 van Durme YM, Verhamme KM, Stijnen T, van Rooij FJ, Van Pottelberge GR, Hofman A *et al.* Prevalence, incidence, and lifetime risk for the development of COPD in the elderly: the Rotterdam study. *Chest* 2009; **135**: 368–377.
21 Agusti AG, Sauleda J, Miralles C, Gomez C, Togores B, Sala E *et al.* Skeletal muscle apoptosis and weight loss in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2002; **166**: 485–489.
22 Kavousi M, Elias-Smale S, Rutten JH, Leening MJ, Vliegenthart R, Verwoert GC *et al.* Evaluation of newer risk markers for coronary heart disease risk classification: a cohort study. *Ann Intern Med* 2012; **156**: 438–444.
23 Bos MJ, Koudstaal PJ, Hofman A, Ikram MA. Modifiable etiological factors and the burden of stroke from the Rotterdam study: a population-based cohort study. *PLoS Med* 2014; **11**: e1001634.
24 Alberts VP, Bos MJ, Koudstaal PJ, Hofman A, Witteman JCM, Stricker BHC *et al.* Heart failure and the risk of stroke: the Rotterdam Study. *Eur J Epidemiol* 2010; **25**: 807–812.
25 Schoen R. *Modeling Multigroup Populations*. Springer Science & Business Media, 2013.

26 Franco OH, Steyerberg EW, Hu FB, Mackenbach J, Nusselder W. Associations of diabetes mellitus with total life expectancy and life expectancy with and without cardiovascular disease. *Arch Int Med* 2007; **167**: 1145–1151.
27 Franco OH, de Laet C, Peeters A, Jonker J, Mackenbach J, Nusselder W. Effects of physical activity on life expectancy with cardiovascular disease. *Arch Int Med* 2005; **165**: 2355–2360.
28 Efron BT, R. *An Introduction to the Bootstrap*. vol. 184-188. Chapman & Hall: New York, NY, USA, 1993.
29 Wilson PWF, D'Agostino RB, Sullivan L, Parise H, Kannel WB. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. *Arch Int Med* 2002; **162**: 1867–1872.
30 Manson JE, Colditz GA, Stampfer MJ, Willett WC, Rosner B, Monson RR *et al*. A prospective study of obesity and risk of coronary heart disease in women. *N Engl J Med* 1990; **322**: 882–889.
31 Olshansky SJ, Passaro DJ, Hershow RC, Layden J, Carnes BA, Brody J *et al*. A potential decline in life expectancy in the United States in the 21st century. *N Engl J Med* 2005; **352**: 1138–1145.
32 Baik I, Ascherio A, Rimm EB, Giovannucci E, Spiegelman D, Stampfer MJ *et al*. Adiposity and mortality in men. *Am J Epidemiol* 2000; **152**: 264–271.
33 Hedlund J, Hansson L-O, örtqvist Å. Short-and long-term prognosis for middle-aged and elderly patients hospitalized with community-acquired pneumonia: impact of nutritional and inflammatory factors. *Scand J Infect Dis* 1995; **27**: 32–37.
34 Visscher TL, Seidell JC, Molarius A, van der Kuip D, Hofman A, Witteman JC. A comparison of body mass index, waist-hip ratio and waist circumference as predictors of all-cause mortality among the elderly: the Rotterdam study. *Int J Obes Relat Metab Disord* 2001; **25**: 1730–1735.
35 Reuser M, Bonneux L, Willekens F. The burden of mortality of obesity at middle and old age is small. A life table analysis of the US Health and Retirement Survey. *Eur J Epidemiol* 2008; **23**: 601–607.
36 Walter S, Kunst A, Mackenbach J, Hofman A, Tiemeier H. Mortality and disability: the effect of overweight and obesity. *Int J Obes (Lond)* 2009; **33**: 1410–1418.

Supplementary Information accompanies this paper on International Journal of Obesity website (http://www.nature.com/ijo)