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Xin Song, Janne Pitkaniemi, Weiguo Gao, Robert Heine, Kalevi Pyörälä, S  
Soderberg, Coen D.A. Stehouwer, Björn Zethelius, Jaakko Tuomilehto, Qing  
Qiao

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**Relationship between body mass index and mortality among Europeans**

Xin Song<sup>1,2</sup>, Janne Pitkaniemi<sup>1</sup>, Weiguo Gao<sup>1,2</sup>, Robert J. Heine<sup>3,4</sup>, Kalevi Pyörälä<sup>5</sup>, Stefan Söderberg<sup>6,7</sup>, Coen D.A. Stehouwer<sup>8</sup>, Björn Zethelius<sup>9</sup>, Jaakko Tuomilehto<sup>1,2</sup>, Tiina Laatikainen<sup>2</sup>, Adam G Tabák<sup>10,11</sup>, Qing Qiao<sup>1,2</sup> for the DECODE Study Group

<sup>1</sup> Department of Public Health, Hjelt Institute, University of Helsinki, Helsinki, Finland; <sup>2</sup> Department of Chronic Disease Prevention, National Institute for Health and Welfare, Helsinki, Finland; <sup>3</sup> VU University of Medical Center, Amsterdam, The Netherlands; <sup>4</sup> Eli Lilly and Company, Indianapolis, USA; <sup>5</sup> Institute of Clinical Medicine, Faculty of Health Sciences, University of Eastern Finland, Kuopio, Finland; <sup>6</sup> Department of Public Health and Clinical Medicine, Cardiology, Umeå University Hospital, Umeå, Sweden; <sup>7</sup> Baker IDI Heart and Diabetes Institute, Melbourne, Australia; <sup>8</sup> Department of Internal Medicine and Cardiovascular Research Institute Maastricht (CARIM), Maastricht University Medical Centre, Maastricht, The Netherlands; <sup>9</sup> Department of Public Health/Geriatrics, Uppsala University Hospital, Uppsala, Sweden; <sup>10</sup> Department of Epidemiology and Public Health, University College London, London, UK; <sup>11</sup> Semmelweis University Faculty of Medicine, 1<sup>st</sup> Department of Medicine, Budapest, Hungary.

Correspondance to: Xin Song, Department of Public Health, Hjelt Institute, University of Helsinki, Helsinki, Finland; Mannerheimintie 172, KTTL, 6krs, PL 41, FIN-00014 Helsinki, Finland.

Tel. +358 9 19127320

Fax. +358 9 19127313

E-mail: xin.song@helsinki.fi

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24

25 Abstract

26 Background/Objectives: To investigate the relationship between body mass index (BMI)  
27 and mortality from various causes.

28 Subjects/Methods: Data of 72 947 European men and 62 798 women aged 24-99 years at  
29 baseline were collaboratively analyzed. Both absolute and relative mortality risks were  
30 estimated within each BMI categories. The hazard ratio (HR) was estimated using Cox  
31 regression analysis adjusting for age, cohort, and smoking status.

32 Results: Over a median follow-up of 16.8 years, 29 071 participants died, 13 502 from  
33 CVD and 8 748 from cancers of all types. All-cause and cancer mortality showed a  
34 U-shaped relationship: decreased first, leveled off, and then increased with increasing BMI  
35 with the lowest mortality risk approximately between 23.0 to 28.0 kg/m<sup>2</sup> of BMI in men  
36 and 21.0 to 28.0 kg/m<sup>2</sup> in women. The U-shaped relationship hold for all-cause mortality  
37 but disappeared for cancer mortality among non-smokers. The CVD mortality was constant  
38 until a BMI of approximately 28.0 kg/m<sup>2</sup> and then increased gradually in both men and  
39 women, which was independent of age, cohort and smoking status.

40 Conclusions: A U-shaped relationship of BMI with all-cause mortality but a graded  
41 relationship with CVD mortality at BMI greater than 28.0 kg/m<sup>2</sup> was detected. The  
42 relationship between cancer mortality and BMI largely depended on smoking status, and  
43 need to be further investigated with site-specific cancers.

44 Keywords: body mass index, cause of death, mortality, obesity

## 45 Introduction

46 Obesity had become the sixth most important risk factor contributing to the overall burden  
47 of various diseases worldwide (Ezzati *et al.*,2002) according to the World Health Organization  
48 (WHO) 2002 report. It has been well recognized that obesity defined as having a body  
49 mass index (BMI) equal or higher than 30 kg/m<sup>2</sup> is associated with many diseases that  
50 contribute to premature death, such as cardiovascular disease (CVD), diabetes and certain  
51 types of cancers (Hubert *et al.*,1983; Kurth *et al.*,2002; Nyamdorj *et al.*,2009; Colditz *et al.*,1990;  
52 Batty *et al.*,2005; Calle *et al.*,2003). However, the association of BMI with mortality of various  
53 causes is controversial: a positive(Lee *et al.*,1993), a J-shaped(Manson *et al.*,1995; Calle *et*  
54 *al.*,1999; Moore *et al.*,2008) or U-shaped(Seidell *et al.*,1996; Shaper *et al.*,1997; Rosengren *et al.*,1999;  
55 Baik *et al.*,2000; Flegal *et al.*,2005; Breeze *et al.*,2006; Pischon *et al.*,2008; Klenk *et al.*,2009) relation  
56 with all-cause mortality; a positive(Lee *et al.*,1993; Seidell *et al.*,1996; Kivimaki *et al.*,2008; Flegal  
57 *et al.*,2007), or a J-shaped(Jonsson *et al.*,2002) relation with CVD mortality; a positive(Calle *et*  
58 *al.*,1999; Calle *et al.*,2003; Hu *et al.*,2004; Berrington de Gonzalez *et al.*, 2010), a J-shaped(Reeves *et*  
59 *al.*,2007) relation, and no association(Baik *et al.*,2000; Meyer *et al.*,2002; Batty *et al.*,2005; Flegal *et*  
60 *al.*,2007) with cancer mortality have all been reported.

61 Recently, the WHO definition for overweight has been questioned by several studies  
62 which showed that overweight (BMI between 25.0 and 30 kg/m<sup>2</sup>) was not associated with  
63 increased risk of death (Flegal *et al.*,2005; Lenz *et al.*,2009; McGee & Diverse Populations  
64 Collaboration,2005). The controversy between previous studies may be due to differences in  
65 study design and study populations. To clarify shape of the relationship of BMI with  
66 mortality of various causes may extend our understanding on the role of underweight,

67 overweight and obesity in relation to the development of diseases and mortality of various  
68 causes, and could help to improve the definition of underweight and obesity. This is  
69 important considering the increase in the prevalence of obesity and its adverse health  
70 consequences worldwide. In the current study, the BMI-mortality relationship is  
71 investigated based on the data of the large Diabetes Epidemiology: Collaborative analysis  
72 Of Diagnostic criteria in Europe (DECODE) study.

### 73 Subjects and methods

#### 74 Study population

75 Data were collected from 33 prospective studies in 11 European countries and the study  
76 population comprised 142 885 Europeans including 76 226 men and 66 659 women aged  
77 24-99 at baseline. This involved the completion of a self-reported questionnaire on  
78 smoking and participation in a medical examination to measure body weight and height,  
79 described in detail in previous DECODE publications (DECODE, 2001). Participants with  
80 missing data on body weight and height (n=2 588), and on smoking status (n=4 490) were  
81 excluded. Subjects who had emigrated but the dates of the emigration were recorded were  
82 treated as censored cases. Individuals without exact date of emigration or completely lost to  
83 follow-up were also excluded (n=50). Thus the final sample for this analysis included a  
84 total of 135 745 participants (72 947 men and 62 798 women) with a median follow-up of  
85 16.8 years.

86 Individual participant data from each cohort was sent to the Diabetes Prevention Unit of  
87 the National Institute for Health and Welfare in Helsinki, Finland for collaborative data  
88 analyses. Each study was approved by the local ethics committees and the analysis plan

89 was approved by the ethics committee of the National Institute for Health and Welfare.

#### 90 Definition of covariates

91 BMI at baseline was calculated as body weight in kilograms divided by the square of height  
92 in meters. Smoking status at baseline was classified based on responses to the questionnaire  
93 into three categories of never smokers, current smokers and former smokers in most of the  
94 studies but not in all. The mortality risk of former smokers was checked against never- and  
95 current- smokers within each BMI category, and the results showed that the mortality risk  
96 among former smokers was similar to that of never smokers within each BMI category. In  
97 addition, the mean BMI of former smokers was similar to that of never smokers, both  
98 higher than that of current smokers. Thus in the final data analysis we combined never  
99 smokers with former smokers to form a currently non-smoking category to increase  
100 statistical power and to harmonize and standardize the smoking variables received from  
101 different studies.

#### 102 Definition of fatal events

103 Vital status and cause of deaths were recorded in all of the studies included. CVD mortality  
104 was defined according to the International Classification of Disease (ICD) codes 331, 420  
105 (7<sup>th</sup> revision), 401-448 (8<sup>th</sup> or 9<sup>th</sup> revision), and codes I10-I79 (10<sup>th</sup> revision). Cancer  
106 mortality was defined as cancers of all types by ICD codes 158, 162, 181, 193, 199, 200,  
107 204 (7<sup>th</sup> revision), 140-239 (8<sup>th</sup> or 9<sup>th</sup> revision) and codes C00-C97, D00-D09 (10<sup>th</sup>  
108 revision).

#### 109 Statistical analysis

110 Participants were classified into the following 18 BMI categories of <19.0, 19.0-19.9,

111 20.0-20.9, 21.0-21.9, 22.0-22.9, 23.0-23.9, 24.0-24.9, 25.0-25.9, 26.0-26.9, 27.0-27.9,  
112 28.0-28.9, 29.0-29.9, 30.0-30.9, 31.0-31.9, 32.0-32.9, 33.0-33.9, 34.0-34.9, and  $\geq 35.0$   
113  $\text{kg/m}^2$ . Crude mortality was calculated and plotted for each BMI category. The category  
114 with the lowest mortality rate was chosen as the reference category to estimate the relative  
115 risk or hazard ratio (HR) using Cox proportional hazards models adjusting for age, cohort,  
116 and smoking status. A sensitivity analysis by excluding the participants who died in the  
117 first five-year follow-up was performed to assess the reverse causation. Because current  
118 smokers were leaner and had increased mortality compared to current non-smokers in this  
119 study, a further analysis was performed stratified by current smoking status using nine  
120 BMI categories of  $<19.0$ , 19.0-21.0, 21.0-23.0, 23.0-25.0, 25.0-27.0, 27.0-29.0, 29.0-31.0,  
121 31.0-33.0 and  $\geq 33.0$   $\text{kg/m}^2$  to explore to what extent smoking has contributed to the  
122 increased mortality in the low BMI categories. The formal interaction between smoking  
123 status and the BMI categories was also tested. In addition, we performed analyses for  
124 competing risks using STATA 11.0 to estimate the probability of the CVD mortality in the  
125 presence of competing risk of cancer mortality, or vice versa.

## 126 Results

127 Baseline characteristics of the cohorts are presented in table 1. Over a median follow-up of  
128 16.8 years, 29 071 participants died, 13 502 from CVD and 8 748 from cancers. Old age  
129 was associated with both CVD and cancer mortality (table 2). Current smoking was  
130 associated with cancer mortality in both genders and with CVD mortality in men but not in  
131 women. Mean BMI was significantly higher in individuals who died of CVD but not in  
132 those who died of cancers compared with those who were still alive.



133 Crude mortality rates per 1000 person-years and HRs (95% confidence intervals) for  
134 mortality from various causes adjusted for age, cohort and further adjusted for smoking  
135 status are shown in figure 1 and online tables 1-2. All-cause and cancer mortality decreased  
136 first, leveled off, and then increased with increasing BMI levels ( $\text{kg/m}^2$ ), a U-shaped  
137 relationship with the lowest all-cause mortality in the BMI interval of 23.0 to 28.0  $\text{kg/m}^2$  in  
138 men and 21.0 to 28.0  $\text{kg/m}^2$  in women approximately. The mortality from CVD was  
139 approximately constant up to a BMI of 28  $\text{kg/m}^2$  and then increased gradually in both men  
140 and women. The relationship between BMI and mortality from various causes did not  
141 change substantially after exclusion of deaths occurring during the first five-year follow-up  
142 (online tables 1-2).

143 Adjustment for smoking status lowered the HRs in the lower BMI categories but  
144 increased the HRs associated with higher BMI levels (figure 1). Smokers tended to have  
145 low BMI (table 3). The smoking-BMI interaction was significant for mortality from various  
146 causes in both men and women. Our analysis stratified by smoking status showed that  
147 among non-smokers the U-shaped relationship between BMI and all-cause mortality held,  
148 but it disappeared for cancer mortality. CVD mortality increased gradually at the upper  
149 BMI distribution among non-smokers. Among current smokers the HRs for mortality of  
150 various causes were constantly higher across the entire range of BMI than non-smokers  
151 within the same BMI category. Because the deaths from CVD and cancers are mutually  
152 exclusive, a competing risk analysis was also performed which did not alter the observed  
153 relationship between BMI and mortality of CVD and cancers (online tables 1-2).

154 Discussion

155 In this European population, a U-shaped relationship between BMI and mortality from  
156 all-cause and from all cancers was observed, however the increased risk associated with  
157 low BMI disappeared for cancer mortality among non-smokers. Mortality from CVD  
158 increased positively with increasing BMI levels at the upper BMI distribution, which was  
159 independent of smoking status.

160 Almost all studies investigating all-cause mortality have found significantly increased  
161 risk at both the lower and the upper ends of the BMI distributions, with constant lower risk  
162 of mortality in the middle of the BMI distribution(Manson *et al.*,1995; Calle *et al.*,1999; Moore *et*  
163 *al.*,2008; Seidell *et al.*,1996; Rosengren *et al.*,1999; Flegal *et al.*,2005; Breeze *et al.*,2006; Kivimaki *et*  
164 *al.*,2008; Klenk *et al.*,2009; Prospective Studies Collaboration *et al.*,2009). Thus, these studies  
165 claimed a J- or a U-shaped relationship of BMI with all-cause mortality, but the ideal BMI  
166 range where the mortality risk was low has not been consistently defined partly due to  
167 differences in BMI classifications, methods used to estimate mortality risk and partly by  
168 different smoking rates within different populations. There was, however, one study  
169 reporting a positive relationship between all-cause mortality and BMI in men(Lee *et al.*,1993),  
170 without any excess mortality among lean individuals ( $BMI < 22.5\text{kg/m}^2$ ). It worths to  
171 mention that the BMI cut-off to define “lean” was set higher in this study compared with  
172 ours that might obscure a risk increase at low BMI levels. As shown in the table 3, more  
173 current smokers than non-smokers had a low BMI category, and smoking has largely  
174 contributed to the high mortality risk observed in the lean individuals. This is consistent  
175 with a previous study by Lawlor *et al.* (Lawlor *et al.*,2006).

176 For CVD mortality, most studies have consistently reported a positive relationship at the

177 upper BMI levels, with varying cutoff values from 22.5 to 30.0 kg/m<sup>2</sup>(Lee *et al.*,1993; Seidell  
178 *et al.*,1996; Kivimaki *et al.*,2008; Prospective Studies Collaboration,2009; Flegal *et al.*,2007). There  
179 were two studies, however, showing a U-shaped relationship with the lowest CVD  
180 mortality at the BMI interval of 20.0 to 29.9 kg/m<sup>2</sup> in Swedish men(Jonsson *et al.*,2002), and  
181 22.5 to 24.9 kg/m<sup>2</sup> in Austrian adults(Klenk *et al.*,2009). Our study with a large sample size  
182 showed a strong positive relationship between CVD mortality and BMI among  
183 non-smokers at BMI levels above approximately 28.0 kg/m<sup>2</sup> in both men and women.

184 A limited number of studies have reported a linear(Calle *et al.*,1999; Calle *et al.*,2003; Hu *et*  
185 *al.*,2004; Berrington de Gonzalez *et al.*, 2010), or no relationship(Seidell *et al.*,1996; Baik *et al.*,2000;  
186 Meyer *et al.*,2002; Batty *et al.*,2005; Flegal *et al.*,2007) between BMI and cancer mortality. We  
187 found a vague U-shaped relationship between BMI and cancer mortality which confirmed  
188 the findings of Reeves GK *et al.*(Reeves *et al.*,2007). Stratified analysis by smoking status,  
189 however, revealed that the high cancer mortality in lean individuals was mainly attributable  
190 to smoking. As shown in our study, current smokers were more commonly found in the low  
191 BMI categories compared to non-smokers in both genders. Further investigations are  
192 required to study site-specific cancer mortality in men and women.

193 This study was based on data from large European population- or occupational-based  
194 studies and should be representative of the general population. Thus, a large number of  
195 middle-aged and elderly European men and women followed for a median 16.8 years led to  
196 a relatively large number of deaths from all causes, CVD and cancers that gave power to  
197 investigate the association between BMI and risk of mortality with small BMI intervals.

198 A relative limitation of the study is the lack of information on weight changes before the

199 study, that makes it impossible to exclude the “reverse causation” possibility which is  
200 inherently existing in any study of mortality(Willett *et al.*,1999) because the weight changes  
201 before the baseline examination could be a consequence of underlying diseases before  
202 enrolment rather than a cause of deaths. However, after excluding the deaths arisen within  
203 the first 5-year follow-up the results were not changed substantially. Another limitation of  
204 the study is that no information on physical activity (a potential confounder in our analysis)  
205 at baseline is available, furthermore physical activity and fitness is an independent  
206 predictor of death and the effect of obesity on morbidity and mortality could be largely  
207 diminished by higher levels of physical fitness(Hu *et al.*,2004). Nevertheless, the effect of  
208 physical activity on longevity is still controvesial and needs further investigation. Other  
209 potential confounders were also unavailable such as menopuse status at baseline and body  
210 composition that could be very different between men and women and changes with  
211 menopause(Poehlman *et al.*,1995; Hoover *et al.*,2000).

212 In spite of a decrease in mortality, BMI has increased slightly during the last three  
213 decades in Europe(Flegal *et al.*,2002; Hedley *et al.*,2004; Vartiainen *et al.*,2010) that might  
214 suggest that cohort effects may play a role in our findings, however the increase in BMI in  
215 the current study is too small to substantially affect the results (mean BMI 25.6 kg/m<sup>2</sup> in  
216 the 1970s, 25.6 kg/m<sup>2</sup> in the 1980s and 26.3 kg/m<sup>2</sup> in the 1990s). The shift of the BMI  
217 distribution towards the right in the general population can increase the risk of  
218 obesity-related disorders such as diabetes and CVD, but its direct impact on mortality is not  
219 straight forward, since mortality is a complex outcome of many factors including  
220 occurrence of a disease and its treatment. Therefore, obesity defined by BMI maybe a

221 useful indicator for intervention for diabetes and CVD, but a poor measure of mortality  
222 from all-causes and certain cancers. Considering the complex underlying causes of cancer  
223 deaths and the vague relationship found in our study, further investigations are required to  
224 study site-specific cancer mortality.

225 In conclusion, a U-shaped relationship between BMI and mortality from all-cause and  
226 from cancer was observed, but the relationship disappeared for cancer mortality among  
227 non-smokers. Mortality from CVD increased positively with increasing BMI levels at the  
228 upper BMI distribution, which was independent of smoking status.

229 Conflict of interest

230 There are no conflicts of interest.

231 Studies and investigators included in this collaborative study are:

232 Denmark Glostrup Study: T. Jørgensen<sup>1,2</sup>, K. Borch-Johnson<sup>3</sup>. 1. Research Centre for  
233 Prevention and Health, Glostrup University Hospital; 2. Faculty of Health Science,  
234 University of Copenhagen; 3. Steno Diabetes Center, Gentofte.

235 Finland East-West Study: A. Nissinen,<sup>1</sup> J. Pekkanen,<sup>1</sup> J. Tuomilehto<sup>1,2,3</sup>. 1. Department of  
236 Chronic Disease Prevention, National Institute for Health and Welfare, Helsinki, Finland; 2.  
237 Department of Public Health, University of Helsinki, Helsinki, Finland; 3. South  
238 Ostrobothnia Central Hospital, Seinäjoki.

239 Helsinki Policemen Study: M. Pyörälä, K. Pyörälä. Institute of Clinical Medicine,  
240 Faculty of Health Sciences, University of Eastern Finland, Kuopio.

241 National FINRISK 1972-1997 Cohorts: J. Tuomilehto<sup>1,2,3</sup>, P. Jousilahti<sup>2</sup>, J. Lindström<sup>2</sup>. 1.  
242 Department of Public Health, University of Helsinki, Helsinki; 2. Department of Chronic

243 Disease Prevention, National Institute for Health and Welfare, Helsinki; 3. South  
244 Ostrobothnia Central Hospital, Seinäjoki.

245 National FINRISK 2002 Study: J. Tuomilehto<sup>1,2</sup>, T. Laatikainen<sup>2</sup>, M. Peltonen<sup>2</sup>, J.  
246 Lindström<sup>2</sup>. 1. Department of Public Health, University of Helsinki, Helsinki; 2.  
247 Department of Chronic Disease Prevention, National Institute for Health and Welfare,  
248 Helsinki.

249 Oulu Study: S Keinänen-Kiukaanniemi<sup>1,2,3</sup>, U. Rajala<sup>1</sup>, M. Laakso<sup>1,3</sup>. 1. The Institute of  
250 Health Sciences, University of Oulu, Oulu; 2. Oulu Health Centre; 3. Oulu University  
251 Hospital, Unit of General practice.

252 Vantaa Study: R. Tilvis<sup>1</sup>, J. Tuomilehto<sup>2,3</sup>. 1. Division of geriatrics, Department of  
253 medicine, University of Helsinki, Helsinki; 2. Diabetes Prevention Unit, Department of  
254 Chronic Disease Prevention, National Institute for Health and Welfare, Helsinki; 3.  
255 Department of Public Health, University of Helsinki, Helsinki.

256 Iceland Reykjavik Study: G. Sigurdsson<sup>1,2</sup>. 1. University of Iceland, Reykjavik, Iceland;  
257 Icelandic Heart Association, Kopavogur; 2. Landspítali-University Hospital, Reykjavik.

258 Israel GOH-I Study: R. Dankner<sup>1,2</sup>. 1. Unit for Cardiovascular Epidemiology, The  
259 Gertner Institute, Sheba Medical Center, Tel Hashomer, Israel; 2. Division of Epidemiology  
260 and Prevention, School of Public Health, Sackler School of Medicine, Tel Aviv University,  
261 Israel.

262 Italy Cremona Study: M.P. Garancini<sup>1</sup>, G. Calori<sup>1</sup>, G. Ruotolo<sup>1,2</sup>, S. Mannino<sup>3</sup>, M. Villa<sup>3</sup>.  
263 1. Division of Metabolic and Cardiovascular Diseases, San Raffaele Scientific Institute,  
264 Milan; 2. AstraZeneca R&D Mölndal, Sweden; 3. ASL Provincia di Cremona, Cremona.

265 Poland POLMONICA: A. Pajak, E. Kawalec. Department of Epidemiology and  
266 Population Studies, Institute of Public Health, Unit of Health Care, Collegium Medicum  
267 Jagiellonian University, Krakow.

268 Spain Catalonia Study: C. Castell. Division of Public Health, Department of Health,  
269 Generalitat of Catalonia, Barcelona.

270 Sweden Northern Sweden MONICA Survey: S. Söderberg<sup>1,2</sup>, M. Eliasson<sup>1</sup>. 1.  
271 Department of Public Health and Clinical Medicine, Cardiology, Umeå University Hospital,  
272 Umeå; 2. Baker IDI Heart and Diabetes Institute, Melbourne, Australia.

273 The Uppsala Longitudinal Study of Adult Men (ULSAM): B. Zethelius, Department of  
274 Public Health/Geriatrics, Uppsala University Hospital, Uppsala.

275 Malmo Preventive Project: PM. Nilsson and G. Berglund. Department of Clinical  
276 Sciences, Lund University, University Hospital, Malmö.

277 The Netherlands Hoorn Study: J.M. Dekker<sup>1</sup>, G. Nijpels<sup>1</sup>, C.D.A. Stehouwer<sup>2</sup>. 1.  
278 Department of Epidemiology and Biostatistics and the EMGO Institute for Health and Care  
279 Research, VU University Medical Center, Amsterdam; 2. Department of Internal Medicine  
280 and Cardiovascular Research Institute Maastricht (CARIM), Maastricht University Medical  
281 Centre, Maastricht.

282 Zutphen Study: Ed. Feskens. Department of Chronic Disease and Environmental  
283 Epidemiology, National Institute of Public Health and Environmental Protection,  
284 Bilthoven.

285 Turkey Turkish Adult Risk Factor Study: A. Onat<sup>1,2</sup>. 1. Turkish Society of Cardiology,  
286 Istanbul; 2. Department of Cardiology, Cerrahpasa Medical Faculty, Istanbul University,

287 Istanbul.

288 United Kingdom Isle of Ely Diabetes Project: N.J. Wareham, MRC Epidemiology Unit,  
289 Strangeways Research Labs, Cambridge.

290 Newcastle Heart Project: N. Unwin<sup>1</sup>, N. Ahmad<sup>1</sup>, K.G.M.M. Alberti<sup>2</sup>, L. Hayes<sup>1</sup>. 1.  
291 Department of Medicine and Epidemiology and Public Health, University of Newcastle,  
292 Newcastle; 2. Imperial College, St Mary's Campus, St Mary's Hospital, London.

293 Gooding Study: R. W. Morris, J. S. Yudkin, M. Gould, A. Haines, Department of  
294 Primary Care & Population Sciences, Royal Free and University College Medical School,  
295 London.

296 Whitehall II Study: M.G.Marmot<sup>1</sup>, A.G. Tabák<sup>1,2</sup>, M. Kivimäki<sup>1,3</sup>, E.J. Brunner<sup>1</sup>, D.R.  
297 Witte<sup>1,4</sup>. 1. Department of Epidemiology and Public Health, University College London,  
298 London; 2. Semmelweis University Faculty of Medicine, 1<sup>st</sup> Department of Medicine,  
299 Budapest; 3. Finnish Institute of Occupational Health, Helsinki; 4. Steno Diabetes Center,  
300 Gentofte.

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**403 Figure legends**

404 Figure 1 Crude mortality rate per 1000 PY (person-years) (open circles), age- and cohort-  
405 adjusted hazard ratios (open triangles), and age-, cohort- and smoking- adjusted hazard  
406 ratios (solid circles) with their 95% confidence intervals (vertical bars) for mortality  
407 corresponding to a one unit increase in body mass index (BMI, kg/m<sup>2</sup>). In men, the BMI  
408 reference category was 23.0-23.9 kg/m<sup>2</sup> for all-cause mortality, 20.0-20.9 kg/m<sup>2</sup> for CVD  
409 mortality and 25.0-25.9 kg/m<sup>2</sup> for cancer mortality. In women, the BMI reference category  
410 for all these three was 20.0-20.9 kg/m<sup>2</sup>.

## Body mass index and mortality among Europeans

Table 1 Baseline characteristics of the cohorts and the data of follow-up

Study	Number		Age (years)	Body mass index(kg/m <sup>2</sup> )		Current smokers (%)	Non-smokers (%)	Median of follow-up (maximum)	Number of deaths		
	Men	Women		Men	Women				CVD	Cancer	All-cause
Denmark,											
Glostrup-1897	229	208	70.0(-)	24.5(3.4)	23.7(4.9)	58.1	41.9	12.5(27.0)	212	101	424
Glostrup-1914	360	306	60.2(0.4)	24.6(3.4)	23.6(4.7)	60.5	39.5	19.0(19.8)	132	89	290
Glostrup-1936	504	548	40.4(0.4)	25.4(3.3)	24.1(3.8)	54.8	45.2	17.1(17.7)	17	29	71
Finland,											
East-west men	437	0	76.4(4.6)	24.8(3.9)	-	14.0	86.0	7.8(17.1)	172	73	390
FINRISK-1972	5341	5616	41.3(9.9)	26.0(3.3)	27.0(4.6)	31.4	68.6	36.7(36.9)	2630	1242	4903
FINRISK-1977	5376	5763	44.0(11.0)	26.2(3.5)	26.7(4.7)	27.4	72.6	31.8(32)	2409	1048	4359
FINRISK-1982	4179	4326	43.9(11.4)	26.5(3.7)	26.4(4.7)	28.8	71.2	26.8(27)	1158	709	2344
FINRISK-1987	2638	2936	44.0(11.4)	26.9(3.8)	26.8(5.0)	26.7	73.3	21.8(22)	458	288	955
FINRISK-1992	2578	2831	44.2(11.4)	26.8(3.9)	26.3(4.9)	28.4	71.6	16.9(17)	208	182	531
FINRISK-1997	3848	3902	47.6(13.3)	26.9(3.9)	26.5(5.0)	24.1	75.9	11.8(12)	292	233	634
FINRISK-2002	3891	4518	47.4(13.1)	27.3(4.1)	26.7(5.1)	26.5	73.5	6.8(7.0)	96	84	239
Helsinki Policemen	1136	0	44.7(8.0)	25.9(2.8)	-	48.6	51.4	32.8(36.8)	327	178	668
Oulu-55	328	415	55.0(-)	26.4(3.4)	25.7(4.3)	23.4	76.6	16.8(17.3)	42	39	115
Vantaa	272	339	65.1(0.4)	26.0(3.7)	25.3(4.6)	16.5	83.5	17.2(17.9)	105	41	204
Iceland,											
Reykjavik	8975	9437	52.5(8.5)	25.6(3.5)	24.5(4.2)	47.0	53.0	17.7(27.1)	1941	1482	4274
Israel,											
GOH-I	2324	2370	43.6(8.4)	25.1(3.7)	26.1(4.7)	35.6	64.4	27.9(27.9)	474	283	1331
Italy,											
Cremona	909	1153	58.7(10.8)	26.2(3.8)	24.9(4.8)	22.2	77.8	15.0(15.8)	203	204	511
The Netherlands,											
Hoorn study	1137	1340	61.7(7.4)	25.5(3.0)	25.1(4.0)	33.5	66.5	8.9(10.2)	114	117	330
Zutphen study	480	0	75.8(4.6)	24.1(3.1)	-	22.9	77.1	4.7(4.8)	53	21	119

## Body mass index and mortality among Europeans

Poland,												
MONICA-Krakow	166	192	58.0(8.4)	25.8(4.0)	28.2(4.9)	25.1	74.9	6.5(6.6)	16	6	29	
Spain,												
Catalonia	912	1184	55.3(13.9)	25.9(3.4)	25.4(4.4)	21.3	78.7	5.0(5.0)	31	29	91	
Sweden,												
Northern Swedish- MONICA 1986	815	789	45.2(11.2)	25.8(3.5)	25.5(4.4)	24.4	75.6	20.5(20.6)	80	70	256	
Northern Swedish- MONICA 1990	767	799	45.3(11.4)	26.0(3.3)	25.5(4.4)	24.5	75.5	16.5(16.6)	45	33	134	
Northern Swedish MONICA 1994	924	954	49.9(14.0)	26.1(3.6)	25.6(4.6)	21.2	78.8	12.5(14.5)	60	59	207	
Northern Swedish MONICA 1999	1070	1104	50.8(13.9)	26.7(3.5)	26.1(4.7)	16.7	83.3	7.4(13.5)	22	27	99	
Northern Swedish MONICA 2004	882	923	50.8(14.1)	27.1(4.0)	26.4(5.1)	13.9	86.1	2.5(2.6)	0	0	13	
MPP	13016	5277	49.5(4.9)	25.1(3.3)	24.5(4.4)	44.2	55.8	23.9(30.3)	1816	1739	4582	
Uppsala study	1181	0	71.0(0.6)	25.1(3.4)	-	20.7	79.3	10.0(12.4)	142	127	333	
Turkey,												
TARFS	1588	1630	53.0(12.4)	26.2(4.0)	28.3(5.6)	11.8	88.2	7.9(8.0)	91	NA	167	
UK,												
Ely	451	624	54.0(7.8)	25.8(3.2)	25.3(5.0)	17.2	82.8	14.5(15.7)	28	49	99	
Goodinge	452	582	54.7(10.3)	25.2(4.1)	25.1(5.2)	37.4	62.6	8.7(9.7)	42	47	114	
Newcastle	402	378	54.9(12.5)	26.0(3.9)	25.7(5.0)	27.7	72.3	8.9(10.6)	36	34	97	
Whitehall II	5379	2354	49.6(6.1)	25.1(3.2)	25.5(4.7)	13.8	86.2	5.9(7.9)	50	85	158	
Total	72947	62798	48.6(11.5)	25.6(3.6)	25.9(4.8)	31.5	68.5	16.8(36.9)	13502	8748	29071	

CVD, cardiovascular diseases; NA, not available.

Data are means (standard deviation) or as noted.

Table 2 Baseline characteristics of participants by mortality from all-cause, cardiovascular diseases and cancer

	Men						Women					
	All-cause		Cardiovascular diseases		Cancer		All-cause		Cardiovascular diseases		Cancer	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Number (%)	19170 (26.3)	53777 (73.7)	9175 (12.6)	63772 (87.4)	5536 (7.8)	65823 (92.2)	9901 (15.8)	52897 (84.2)	4327 (6.9)	58471 (93.1)	3212 (5.3)	57956 (94.7)
Age (years)	53 (0.08) <sup>a</sup>	47 (0.05)	54 (0.11) <sup>a</sup>	48 (0.05)	53 (0.13) <sup>a</sup>	48 (0.04)	54 (0.10) <sup>a</sup>	48 (0.05)	56 (0.13) <sup>a</sup>	48 (0.05)	53 (0.17) <sup>a</sup>	48 (0.05)
Current smokers (%)	10222 (53.3) <sup>a</sup>	18170 (33.8)	4793 (52.2) <sup>a</sup>	23599 (37.0)	3104 (56.1) <sup>a</sup>	24968 (37.9)	2613 (26.4) <sup>a</sup>	11782 (22.3)	978 (22.6)	13417 (22.9) <sup>a</sup>	985 (30.7) <sup>a</sup>	13349 (23.0)
Non-smokers (%)	8948 (46.7)	35607 (66.2)	4382 (47.8)	40173 (63.0)	2432 (43.9)	40855 (62.1)	7288 (73.6)	41115 (77.7)	3349 (77.4)	45054 (77.1)	2227 (69.3)	44607 (77.0)
Body mass index (kg/m <sup>2</sup> )	25.8 (0.07)	25.9 (0.03)	26.2 (0.09) <sup>a</sup>	25.8 (0.03)	25.2 (0.12)	25.8 (0.03) <sup>a</sup>	25.6 (0.13)	25.8 (0.05)	26.4 (0.23) <sup>a</sup>	25.7 (0.03)	25.5 (0.18)	25.6 (0.04)

<sup>a</sup> $P < 0.05$  for differences between Yes and No.

Data are cohort- and age- adjusted mean (standard error) or as noted.

Table 3 Hazard ratios (95% confidence interval) of mortality of various causes in relation to body mass index categories in non-smokers (NS) and current smokers (CS)\*

	Body mass index (kg/m <sup>2</sup> )									P value for interaction
	<19.0	19.0-20.9	21.0-22.9	23.0-24.9	25.0-26.9	27.0-28.9	29.0-30.9	31.0-32.9	≥33.0	
Men										
Number (%)										
NS	365 (39.4)	1785 (46.4)	5385 (53.3)	10080 (60.1)	10694 (63.6)	7772 (65.4)	4572 (67.4)	2121 (66.1)	1781 (68.5)	
CS	562 (60.6)	2062 (53.6)	4713 (46.7)	6684 (39.9)	6129 (36.4)	4117 (34.6)	2215 (32.6)	1090 (33.9)	820 (31.5)	
Cardiovascular disease										
No. of deaths (NS/CS)	17/79	101/283	332/705	749/998	1007/1041	877/803	653/467	345/214	301/203	
Hazard ratios (95% CI)										
NS	0.85 (0.51-1.43)	1.00 (Reference)	0.95 (0.76-1.18)	1.02 (0.83-1.25)	1.15 (0.94-1.42)	1.25 (1.02-1.54)	1.60 (1.30-1.98)	2.05 (1.64-2.57)	2.56 (2.04-3.20)	
CS	2.27 (1.69-3.05)	1.97 (1.57-2.47)	2.11 (1.71-2.60)	1.97 (1.61-2.42)	2.27 (1.85-2.78)	2.59 (2.10-3.18)	3.09 (2.49-3.84)	2.98 (2.35-3.78)	4.18 (3.29-5.31)	P<0.001
Cancer										
No. of deaths (NS/CS)	17/84	73/258	261/581	511/718	554/609	477/441	287/228	152/109	100/76	
Hazard ratios (95% CI)										
NS	1.17 (0.69-1.98)	1.00 (Reference)	1.09 (0.79-1.34)	0.98 (0.76-1.25)	0.91 (0.71-1.16)	1.00 (0.78-1.28)	1.05 (0.81-1.36)	1.32 (0.99-1.74)	1.21 (0.90-1.64)	
CS	3.26 (2.38-4.47)	2.53 (1.95-3.28)	2.48 (1.94-3.16)	2.03 (1.59-2.59)	1.90 (1.49-2.42)	2.08 (1.62-2.66)	2.21 (1.69-2.87)	2.23 (1.66-3.00)	2.35 (1.70-3.24)	P<0.001
All-cause										
No. of deaths (NS/CS)	75/262	301/796	827/1683	1691/2270	2010/2086	1724/1512	1183/859	634/418	503/336	
Hazard ratios (95% CI)										



## Body mass index and mortality among Europeans

NS	1.52 (1.20-1.93)	1.25 (1.09-1.42)	1.00 (Reference)	0.99 (0.91-1.08)	1.01 (0.93-1.09)	1.09 (1.01-1.19)	1.30 (1.19-1.42)	1.66 (1.49-1.84)	1.86 (1.67-2.08)	
CS	3.09 (2.69-3.55)	2.37 (2.15-2.61)	2.16 (1.99-2.35)	1.93 (1.78-2.09)	1.96 (1.80-2.12)	2.12 (1.95-2.31)	2.47 (2.25-2.72)	2.54 (2.25-2.72)	3.00 (2.64-3.41)	P<0.001
Women										
Number (%)										
NS	966 (58.3)	3967 (67.5)	7969 (72.0)	9515 (76.5)	8142 (78.7)	6206 (81.5)	4381 (83.2)	2930 (84.7)	4327 (85.3)	
CS	692 (41.7)	1910 (32.5)	3095 (28.0)	2922 (23.5)	2210 (21.3)	1405 (18.5)	885 (16.8)	529 (15.3)	747 (14.7)	
Cardiovascular disease										
No. of deaths (NS/CS)	29/44	104/106	264/162	433/194	503/147	532/116	482/88	376/49	626/72	
Hazard ratios (95% CI)										
NS	1.15 (0.77-1.74)	1.00 (Reference)	0.88 (0.70-1.11)	0.97 (0.79-1.21)	1.00 (0.81-1.24)	1.23 (1.00-1.52)	1.32 (1.06-1.63)	1.58 (1.27-1.96)	2.16 (1.75-2.66)	
CS	2.57 (1.81-3.67)	2.39 (1.82-3.13)	2.23 (1.74-2.86)	2.43 (1.91-3.09)	2.26 (1.76-2.91)	2.26 (1.74-2.95)	3.04 (2.29-4.04)	2.56 (1.82-3.60)	3.55 (2.63-4.80)	P<0.001
Cancer										
No. of deaths (NS/CS)	30/75	115/116	264/222	398/186	403/151	325/94	232/67	178/27	282/47	
Hazard ratios (95% CI)										
NS	1.14 (0.77-1.71)	1.00 (Reference)	0.95 (0.76-1.18)	1.06 (0.86-1.30)	1.09 (0.88-1.34)	1.10 (0.89-1.36)	1.02 (0.81-1.28)	1.23 (0.97-1.56)	1.47 (1.18-1.83)	
CS	3.29 (2.46-4.41)	1.90 (1.47-2.47)	2.24 (1.79-2.81)	1.87 (1.48-2.36)	1.96 (1.54-2.50)	1.77 (1.35-2.33)	2.25 (1.66-3.04)	1.48 (0.97-2.25)	2.15 (1.53-3.01)	P<0.001
All-cause										
No. of deaths (NS/CS)	102/171	330/324	739/507	1114/494	1180/387	1097/277	887/195	691/97	1154/161	
Hazard ratios (95% CI)										

Body mass index and mortality among Europeans

NS	1.30 (1.04-1.63)	1.00 (Reference)	0.86 (0.76-0.98)	0.91 (0.80-1.03)	0.91 (0.81-1.03)	1.01 (0.89-1.15)	1.02 (0.89-1.16)	1.23 (1.08-1.41)	1.61 (1.42-1.82)	
CS	2.91 (2.42-3.51)	2.10 (1.80-2.45)	2.02 (1.75-2.32)	1.88 (1.63-2.16)	1.82 (1.57-2.11)	1.78 (1.51-2.08)	2.21 (1.85-2.64)	1.73 (1.38-2.17)	2.50 (2.07-3.03)	P<0.001

\*Adjusted for age and cohort.

