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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

APPENDIX 1

Description of the cohort studies with individual-participant data

1. Americans' Changing Lives (ACL), USA

The ACL is a prospective cohort study with a multistage stratified area probability sample with oversampling of Blacks and those aged 60 and older (n=3617). The study examined participants’ activities and social relationships, how individuals adapt to acute life events and chronic stresses, and sociocultural variations in the nature of productive activities and relationships. Baseline was in 1986 and follow-up data were derived from data collections in 1989, 1994, and 2002. The 1,080 individuals who were age 35 or older, provided information on height and weight, and participated in the follow-up were included in the present analysis. The outcome questions were “Have you had a stroke during the last 12 months?”, “Have you had a heart attack or other heart trouble during the last 12 months?”, and “Have you had diabetes or high blood sugar, or have you taken medication for it?”


2. Alameda County Study (Alameda), USA

The Alameda County Study is a prospective cohort study of a stratified random sample of Alameda County (California, USA) households with non-institutionalized residents, aged 21 and older, or aged 16-21 if married. The purpose of this survey was to explore the influence of health practices and social relationships on the physical and mental health of a typical sample of the population. The study started in 1965 with a sample of 6,928 respondents (including approximately 500 women aged 65 years and older). The 1974 questionnaire, which was used as the baseline year for the current study of 1,990 participants were age 35 or older with data on BMI multimorbidity follow-up in year 1993/1994. The outcome question was “Here is a list of medical conditions chat usually last for some time. Have you EVER had any of these conditions? Please answer Yes or No for each condition.” with the items “Stroke”, “Heart trouble”, and “Diabetes”.


3. English Longitudinal Study of Ageing (ELSA), United Kingdom

The English Longitudinal Study of Ageing (ELSA) is a panel study of a representative cohort of men and women living in England aged ≥50 years. It was designed as a sister study to the Health and Retirement Study in the USA and is multidisciplinary in orientation, involving the collection of economic, social, psychological, cognitive, health, biological and genetic data. The study commenced in 2002, and the sample has been followed up every 2 years. Data are collected using computer-assisted personal interviews and self-completion questionnaires, with additional nurse visits for the assessment of biomarkers every 4 years. The original sample consisted of 11,391 members ranging in age from 50 to 100 years, but relevant data on BMI, covariates and cardiometabolic multimorbidity were available only for 4,165 with baseline data derived from wave 2 and follow-up data derived from wave 4. The outcome questions were “Has a doctor ever told you that you have (or have had) any of the conditions on this card?” with items “A heart attack (including myocardial infarction or coronary thrombosis)”, “A stroke (cerebral vascular disease)”, and “Diabetes or high blood sugar”. Funding for English Longitudinal Study of Ageing is provided by the National Institute of Aging in the United States, and a consortium of UK government departments coordinated by the Office for National Statistics. The data are available from the UK Data Service (http://ukdataservice.ac.uk). Neither the original collectors of the data nor the distributors of the data bear any responsibility for the analyses or interpretations presented here.

4. Finnish Public Sector study (FPS), Finland

The Finnish Public Sector study is a prospective cohort study comprising the entire public sector personnel of 10 towns (municipalities) and 21 hospitals in the same geographical areas. Participants, who were recruited from employers’ records in 2000-2002, were individuals who had been employed in the study organisations for at least six months prior to data collection. 48,592 individuals (9,337 men and 39,255 women aged 17 to 65) responded to the questionnaire. Of these, 37,797 were age 35 or older, had data on body mass index based on self-reported weight and height plus multimorbidity follow-up and were included in our study. Ethical approval was obtained from the ethics committee of the Finnish Institute of Occupational Health. Participants were linked to hospitalization and death registers. Coronary heart disease was defined as non-fatal myocardial infarctions, ICD-10 I21-I22 and coronary deaths, ICD-10 I20-I25; non-fatal or fatal stroke using ICD-10 codes I60, I61, I63, I64, and fatal or non-fatal type 2 diabetes using ICD-10 code E11. This cohort study is part of the IPD-Work consortium which have been supported by NordForsk (the Nordic Programme on Health and Welfare, grant #75021), the UK Medical Research Council (K013351), the UK Economic and Social Research Council (ES/J023299/1), European Union New and Emerging Risks in Occupational Safety and Health research programme, the Finnish Work Environment Fund, the Swedish Research Council for Working Life and Social Research, the German Social Accident Insurance, the Danish National Research Centre for the Working Environment, the Academy of Finland, and the Ministry of Social Affairs and Employment (Netherlands).


5. GAZEL, France

Gazel is a prospective cohort study of 20,625 employees (15,011 men and 5,614 women) of France’s national gas and electricity company, Electricité de France-Gaz de France (EDF-GDF). Since the study baseline in 1989, when the participants were aged 35–50 years, they have been posted an annual follow-up questionnaire to collect data on health, lifestyle, individual, familial, social, and occupational factors. BMI was measured from self-reported height and weight in 1997 and 10,591 had data on BMI and follow-up for multimorbidity and were eligible for our meta-analysis. The GAZEL study received approval from the national commission overseeing ethical data collection in France (Commission Nationale Informatique et Liberté). Ascertainment of coronary heart disease, stroke and diabetes diabetes cases was based on self-report from annual questionnaires or mortality records. This cohort study is part of the IPD-Work consortium which have been supported by NordForsk (the Nordic Programme on Health and Welfare, grant #75021), the UK Medical Research Council (K013351), the UK Economic and Social Research Council (ES/J023299/1), European Union New and Emerging Risks in Occupational Safety and Health research programme, the Finnish Work Environment Fund, the Swedish Research Council for Working Life and Social Research, the German Social Accident Insurance, the Danish National Research Centre for the Working Environment, the Academy of Finland, and the Ministry of Social Affairs and Employment (Netherlands).


6. Health and Lifestyle Survey (HALS), United Kingdom

UK HALS is a nationwide sample survey of community dwelling adults in England, Scotland, and Wales. In 1984/1985, a total of 12,254 addresses were randomly chosen from Electoral Registers and one adult aged 18 years or over was selected from each household. A total of 9003 adults participated in the baseline examination. Of them, 2,963 were age 35 or older and had data on height and weight and multimorbidity follow-up questionnaire. Of these, 2,963 were age 35 or older and had data on height and weight and multimorbidity. Ethical approval for the main HALS surveys was received from the BMA Ethical Committee before the launch of survey. The outcome question was “Have you ever had ...?” with items “Any heart problems”, “Stroke”, and “Diabetes”. The data are available from the UK Data Service (http://ukdataservice.ac.uk). Neither the original collectors of the data nor the distributors of the data bear any responsibility for the analyses or interpretations presented here.

7. Health and Retirement Study (HRS), USA

The Health and Retirement Study (HRS) is a leading source for information on the health and economic well-being of adults age 50 and older in the United States. The HRS is a longitudinal project sponsored by the National Institute on Aging and the Social Security Administration. The first cohort was interviewed in 1992. Data on height, weight plus multimorbidity follow-up were available for 6,337 men and women with baseline in 1994 and follow-up up to 2012. The detailed outcome questions were “Has a doctor ever told you that you had a heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems?”, “Has a doctor ever told you that you had a stroke”, and “Has a doctor ever told you that you have diabetes or high blood sugar?” The HRS (Health and Retirement Study) is sponsored by the National Institute on Aging (grant number NIA U01AG009740) and is conducted by the University of Michigan. The Health and Retirement Study public use dataset (Ann Arbor, MI, 2016) is produced and distributed by the University of Michigan.

8. Health and Social Support (HeSSup), Finland

The Health and Social Support (HeSSup) study is a prospective cohort study of a stratified random sample of the Finnish population in the following four age groups: 20–24, 30–34, 40–44, and 50–54. The participants were identified from the Finnish population register and posted an invitation to participate, along with a baseline questionnaire, in 1998. A total of 11,246 were age 35 or older, had data on BMI from self-reported height and weight, and a follow-up for multimorbidity and were thus eligible for our meta-analyses. The Turku University Central Hospital Ethics Committee approved the study. Participants were linked to hospitalization and death registers. Coronary heart disease was defined as non-fatal myocardial infarctions, ICD-10 I21-I22 and coronary deaths, ICD-10 I20-I25; non-fatal or fatal stroke using ICD-10 codes I60, I61, I63, I64, and fatal or non-fatal type 2 diabetes using ICD-10 code E11. This cohort study is part of the IPD-Work consortium which have been supported by NordForsk (the Nordic Programme on Health and Welfare, grant #75021), the UK Medical Research Council (K013351), the UK Economic and Social Research Council (ES/J023299/1), European Union New and Emerging Risks in Occupational Safety and Health research programme, the Finnish Work Environment Fund, the Swedish Research Council for Working Life and Social Research, the German Social Accident Insurance, the Danish National Research Centre for the Working Environment, the Academy of Finland, and the Ministry of Social Affairs and Employment (Netherlands).


9. National Survey of Midlife Development in the United States (MIDUS), USA

MIDUS is based on a nationally representative sample of non-institutionalized, English-speaking adults, aged 25 to 74 years in the United States, selected by random digit dialing between 1995 and 1996. The total original sample (n=7108) includes main respondents (n=3487), their siblings (n=950), a city oversample (n=757), and a twin subsample (n=1914). Data were collected in a telephone interview and with a mail questionnaire. A follow-up study of the cohort was conducted in 2004-2005. Individuals aged 35 or older, with data on BMI and multimorbidity were included in the present analysis (n=2,610). The outcome questions were “In the past twelve months, have you experienced or been treated for any of the following [stroke]”, “Have you ever had heart trouble suspected or confirmed by a doctor?”, and “In the past twelve months, have you experienced or been treated for any of the following – diabetes or high blood sugar”.

The MIDUS 1 study (Midlife in the U.S.) was supported by the John D. and Catherine T. MacArthur Foundation Research Network on Successful Midlife Development. The MIDUS 2 research was supported by a grant from the National Institute on Aging (P01-AG02166) to conduct a longitudinal follow-up of the MIDUS 1 investigation.

Repeated biomedica committee on the ethics of human research. Written informed consent was obtained at each data collection wave. For our study, the Whitehall II study protocol was approved by the University College London Medical School in 20 civil service departments in London were invited to participate in the study. Data on BMI from measured study baseline in 1985.

The Whitehall II study is a prospective cohort study set up to investigate socioeconomic determinants of health. At study baseline in 1985-1988, 10 308 civil service employees (6 895 men and 3 413 women) aged 35-55 and working in 20 civil service departments in London were invited to participate in the study. Data on BMI from measured height and weight and cardiometabolic multimorbidity were available for 7,477 men and women who were eligible for our study. The Whitehall II study protocol was approved by the University College London Medical School committee on the ethics of human research. Written informed consent was obtained at each data collection wave. Repeated biomedical examinations and event tracing was used to ascertain coronary heart disease, defined as
myocardial infarction, coded using MONICA definitions, coronary death. Non-fatal and fatal stroke was defined through linkage to national hospital admission and death registers (ICD-10 codes I60, I61, I63, I64), with additional information from self-reports in follow-up questionnaires and stroke event tracing. Type 2 diabetes was ascertained by 2-hour oral glucose tolerance test administered every five years using WHO criteria (fasting glucose >7mmol/l or 2-hour postload glucose >11.1mmol/l), and complemented by self-reports of diabetes diagnosis and medication. The Whitehall II study has been supported by grants from the British Medical Research Council; the British Heart Foundation; the British Health and Safety Executive; the British Department of Health; the National Heart, Lung, and Blood Institute (RO1HL036310); the National Institute on Aging (RO1AG03196 and RO1AG034454). This cohort study is part of the IPD-Work consortium which have been supported by NordForsk (the Nordic Programme on Health and Welfare, grant #75021), the UK Medical Research Council (K013351), the UK Economic and Social Research Council (ES/J023299/1), European Union New and Emerging Risks in Occupational Safety and Health research programme, the Finnish Work Environment Fund, the Swedish Research Council for Working Life and Social Research, the German Social Accident Insurance, the Danish National Research Centre for the Working Environment, the Academy of Finland, and the Ministry of Social Affairs and Employment (Netherlands).


13. Wisconsin Longitudinal Study, graduate sample (WLSG), USA

The Wisconsin Longitudinal Study is a prospective cohort study of a random sample of 10,317 participants (5326 women, 4991 men) who were born between 1937 and 1940 and who graduated from Wisconsin high schools in 1957. The present study used data from the 1992–1993 data collection as the baseline, and 2003-2005 as the follow-up. The WLS sample is broadly representative of white, non-Hispanic American men and women who have completed at least a high school education. Individuals with data on BMI and cardiometabolic multimorbidity were included, a total of 5,336 men and women aged 35 or older. The outcome questions were “Has a doctor ever told you that you had a stroke?”, “Has a doctor ever told you that you have heart trouble?”, and “Has a doctor ever told you that you have diabetes?” Since 1991, the WLS has been supported principally by the National Institute on Aging (AG-9775 and AG-21079), with additional support from the Vilas Estate Trust, the National Science Foundation, the Spencer Foundation, and the Graduate School of the University of Wisconsin-Madison. A public use file of data from the Wisconsin Longitudinal Study is available from the Wisconsin Longitudinal Study, University of Wisconsin-Madison, 1180 Observatory Drive, Madison, Wisconsin 53706 and at http://www.ssc.wisc.edu/wlsresearch/data/. The interpretations, opinions, and inferences based on the data are solely the responsibility of the authors.

14. Wisconsin Longitudinal Study, sibling sample (WLSS), USA

In addition to the main sample of the 1957 high school graduates, the Wisconsin Longitudinal Study has also collected data on a selected sibling of a sample of the graduates since 1977 (n=8778). The data collection in adulthood has been very similar although not entirely identical for the siblings as for the graduates. For the present purposes, the sibling sample was analyzed separately from the graduate sample, because the sampling frame for the individuals in the graduate cohort and sibling cohort was considered to be sufficiently different to justify not combining the samples. Baseline data collection for the siblings in the present study was 1993-1994, and follow-up was in 2004-2007. Individuals who provided information on height and weight and who participated in the follow-up of multimorbidity were included in the present analysis (n=2,626). Since 1991, the WLS has been supported principally by the National Institute on Aging (AG-9775 and AG-21079), with additional support from the Vilas Estate Trust, the National Science Foundation, the Spencer Foundation, and the Graduate School of the University of Wisconsin-Madison. A public use file of data from the Wisconsin Longitudinal Study is available from the Wisconsin Longitudinal Study, University of Wisconsin-Madison, 1180 Observatory Drive, Madison, Wisconsin 53706 and at http://www.ssc.wisc.edu/wlsresearch/data/. The interpretations, opinions, and inferences based on the data are solely the responsibility of the authors.

15. and 16. WOLF (Work, Lipids, and Fibrinogen) Stockholm and Norrland studies, Sweden

The WOLF (Work, Lipids, and Fibrinogen) Stockholm study is a prospective cohort study of people aged 19-70 in companies in Stockholm county. A total of 3,846 men and women aged 35 years or older had data on height and weight and a follow-up for cardiometabolic multimorbidity.
WOLF Norrland is a prospective cohort of people working in companies in Jämtland and Västernorrland counties. At study baseline, 3,540 participants aged 35 or older underwent a clinical examination including anthropometric measurements and had a multimorbidity follow-up. The Regional Research Ethics Board in Stockholm, and the ethics committee at Karolinska Institutet, Stockholm, Sweden approved the study. Participants were linked to hospitalization and death registers. Coronary heart disease was defined as non-fatal myocardial infarctions, ICD-10 I21-I22 and coronary deaths, ICD-10 I20-I25; non-fatal or fatal stroke using ICD-10 codes I60, I61, I63, I64, and fatal or non-fatal type 2 diabetes using ICD-10 code E11. These two cohort studies are part of the IPD-Work consortium which have been supported by NordForsk (the Nordic Programme on Health and Welfare, grant #75021), the UK Medical Research Council (K013351), the UK Economic and Social Research Council (ES/J023299/1), European Union New and Emerging Risks in Occupational Safety and Health research programme, the Finnish Work Environment Fund, the Swedish Research Council for Working Life and Social Research, the German Social Accident Insurance, the Danish National Research Centre for the Working Environment, the Academy of Finland, and the Ministry of Social Affairs and Employment (Netherlands).

**APPENDIX 2**

<table>
<thead>
<tr>
<th>BMI category</th>
<th>N(total)</th>
<th>N(cases)</th>
<th>OR (95% CI)</th>
<th>Weight %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal weight</td>
<td>433</td>
<td>1</td>
<td>2.25 (0.78-6.77)</td>
<td>4.79</td>
</tr>
<tr>
<td>Overweight</td>
<td>38</td>
<td>1</td>
<td>1.13 (0.51-2.53)</td>
<td>4.80</td>
</tr>
<tr>
<td>Obese</td>
<td>516</td>
<td>1</td>
<td>1.13 (0.57-2.18)</td>
<td>5.38</td>
</tr>
<tr>
<td>Severe obesity</td>
<td>187</td>
<td>2</td>
<td>1.43 (0.72-2.85)</td>
<td>9.04</td>
</tr>
<tr>
<td>Morbid obesity</td>
<td>1878</td>
<td>2</td>
<td>1.57 (0.86-2.88)</td>
<td>9.64</td>
</tr>
<tr>
<td>Whitehall II</td>
<td>310</td>
<td>2</td>
<td>0.93 (0.29-3.04)</td>
<td>58.78</td>
</tr>
<tr>
<td>HRS</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (I-squared = 0.38%, p=0.42)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1.** Study-specific associations of BMI categories with cardiometabolic multimorbidity (odds ratios are adjusted for age, sex, ethnicity)
eFigure 2. Meta-regression: Comparison of study-specific point estimates for BMI as a predictor of multimorbidity between men and women, younger and older participants, and white and non-white participants. P-values are for differences between the groups.
APPENDIX 4

eTable 1. Summary odds ratios* and hazard ratios* for the association of BMI by category with incident multimorbidity in 6 studies with linkage to electronic health records

<table>
<thead>
<tr>
<th>BMI category, kg/m²</th>
<th>Ratio</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>Odds ratio</td>
<td>1.30</td>
</tr>
<tr>
<td></td>
<td>Hazard ratio</td>
<td>1.31</td>
</tr>
<tr>
<td>20-24.9</td>
<td>Odds ratio</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Hazard ratio</td>
<td>1.00</td>
</tr>
<tr>
<td>25-29.9</td>
<td>Odds ratio</td>
<td>2.25</td>
</tr>
<tr>
<td></td>
<td>Hazard ratio</td>
<td>2.24</td>
</tr>
<tr>
<td>30-34.9</td>
<td>Odds ratio</td>
<td>5.07</td>
</tr>
<tr>
<td></td>
<td>Hazard ratio</td>
<td>5.12</td>
</tr>
<tr>
<td>≥35</td>
<td>Odds ratio</td>
<td>20.66</td>
</tr>
<tr>
<td></td>
<td>Hazard ratio</td>
<td>19.97</td>
</tr>
</tbody>
</table>

*Odds ratios were obtained from logistic regression and hazard ratios form Cox regression analyses adjusted for sex, age, study, ethnicity, and lifestyle factors.