Influence of individual and combined healthy behaviours on successful aging.

Séverine Sabia, Archana Singh-Manoux, Gareth Hagger-Johnson, Emmanuelle Cambois, Eric Brunner, Mika Kivimaki

To cite this version:

Influence of individual and combined healthy behaviours on successful aging

Séverine Sabia PhD, Archana Singh-ManouxD PhD, Gareth Hagger-Johnson PhD, Emmanuelle Cambois PhD, Eric J. Brunner PhD, Mika Kivimaki PhD


Abstract

Background: Increases in life expectancy make it important to remain healthy for as long as possible. Our objective was to examine the extent to which healthy behaviours in midlife, separately and in combination, predict successful aging.

Methods: We used a prospective cohort design involving 5100 men and women aged 42–63 years. Participants were free of cancer, coronary artery disease and stroke when their health behaviours were assessed in 1991–1994 as part of the Whitehall II study. We defined healthy behaviours as never smoking, moderate alcohol consumption, physical activity (≥2.5 h/wk moderate physical activity or ≥1 h/wk vigorous physical activity), and eating fruits and vegetables daily. We defined successful aging, measured over a median 16.3-year follow-up, as good cognitive, physical, respiratory and cardiovascular functioning, in addition to the absence of disability, mental health problems and chronic disease (coronary artery disease, stroke, cancer and diabetes).

Results: At the end of follow-up, 549 participants had died and 953 qualified as aging successfully. Compared with participants who engaged in no healthy behaviours, participants engaging in all 4 healthy behaviours had 3.3 times greater odds of successful aging (95% confidence interval [CI] 2.1–5.1). The association with successful aging was linear, with the odds ratio (OR) per increment of healthy behaviour being 1.3 (95% CI 1.2–1.4; population-attributable risk for 1–4 v. 0 healthy behaviours 47%). When missing data were considered in the analysis, the results were similar to those of our main analysis.

Interpretation: Although individual healthy behaviours are moderately associated with successful aging, their combined impact is substantial. We did not investigate the mechanisms underlying these associations, but we saw clear evidence of the importance of healthy behaviours for successful aging.

In increases in life expectancy make remaining free of disease and in good functional health for as long as possible an important objective for the present and future generations.¹ Most research in this domain has focused on risk factors for single health outcomes, such as mortality, chronic diseases or functioning. However, good health at older ages is a multidimensional concept, having been defined variously with reference to absence of disease and good functional status.²,³ There is considerable research on disability outcomes at older ages,²⁶–³⁴ but less attention has been paid to successful aging combining favourable functioning outcomes with good mental health and the absence of chronic diseases and disability.⁶–¹³

Smoking, alcohol consumption, poor diet and physical inactivity are among the top 10 leading risk factors for death and disability in intermediate- and high-income countries.¹⁹ There is increasing interest in the combined effect of these behaviours on health. Studies show that people who engage in multiple unhealthy behaviours have a higher risk of death,¹⁵–²³ chronic disease²⁴–³⁰ and poor cognitive function than people who do not engage in as many unhealthy behaviours.³¹ However, whether healthy behaviours determine good functional status at older ages, combined with the absence of chronic diseases, remains unknown.

Our objective was to examine the extent to which individual and combined healthy behaviours in midlife predict successful aging about 16 years later, at 60 years of age or older. We used a comprehensive definition of successful aging that included having good mental health, having good cognitive, physical and cardiorespiratory function, and being free of disability and chronic disease (coronary artery disease, stroke, diabetes and cancer).

Competing interests: Séverine Sabia has received grant funding from the National Institute on Aging. Archana Singh-Manoux has received grant funding from the National Institutes of Health. Gareth Hagger-Johnson is supported by grants from the National Institute on Aging, the National Institutes of Health and the National Health Service Leeds Flexibility and Sustainability fund; he has received payment for lectures from the University of Leeds and the University of Ulster; and he receives royalties from Pearson International. Mika Kivimaki receives salary support from the Medical Research Council; he has received grant funding from the National Institute on Aging; and he has received a professorial fellowship from the Economic and Social Research Council. No other competing interests were declared.

This article has been peer reviewed.

Correspondence to: Séverine Sabia, s.sabia@ucl.ac.uk

Materials and methods

Study population

The target population of our study comprised all participants of this occupational cohort for whom data on healthy behaviours in 1991–1994 were available, and who were at least 60 years old at the end of follow-up (2008–2009), with no history of stroke, myocardial infarction or cancer (n = 6,599). Our analysis included the 5,100 participants for whom data on the outcome variables were available (Figure 1).

We assessed participants’ healthy behaviours based on their responses to a questionnaire. We categorized smoking status as “current,” “former” and “never smoked.” We assessed alcohol consumption by asking for the number of alcoholic drinks consumed in the past 7 days, and categorized consumption as “abstinence from alcohol” (no alcohol in the last week), “moderate alcohol consumption” (1–14 units/wk for women; 1–21 units/wk for men) and “heavy alcohol consumption” (≥ 15 units/wk for women; ≥ 21 units/wk for men). A participant’s level of physical activity was categorized as “active” (≥ 2.5 h/wk moderate physical activity or ≥ 1 h/wk vigorous physical activity) or “inactive” (no physical activity). We assessed dietary behaviour by asking for the frequency with which fruits and vegetables were eaten.

We assessed mortality using the national mortality register kept by the National Health Services Central Registry and the National Health Service identification numbers assigned to each British citizen. Among surviving participants, we defined healthy behaviours as never smoked, moderate alcohol consumption, physically active, and eating fruits and vegetables daily. For further information on this categorization, see Appendices 1 and 2 (available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121080/-/DC1).

The sociodemographic variables in our analysis were age, sex, marital status and level of education (5-level variable), as described previously.

Figure 1: Selection of participants for the study. MI = myocardial infarction.
cose level of 7.0 mmol/L or more, a 2-hour post-load blood glucose level of 11.1 mmol/L or more, self-reported doctor-diagnosed diabetes or the use of medications for diabetes. We identified cases of cancer using the National Health Service’s cancer register.

We assessed disability based on participants’ responses to 14 questions on perceived difficulties in basic and instrumental activities of daily living. Participants with difficulties in one or more activities were considered to have a disability.

We assessed functioning during the 2007–2009 clinical examinations using standard protocols (Appendix 1). We defined poor functioning as scores in the lowest sex- and age-standardized quintile (i.e., below the 20th percentile) for each measure of functioning, with the exception of blood pressure. For blood pressure, the highest quintile (i.e., above the 80th percentile) was used. We assessed cognitive functioning using a score of global cognition calculated from 5 cognitive tests; we assessed physical functioning using walking speed measured over an 8-foot-long course; we assessed respiratory function using forced expiratory volume in 1 second; and we assessed cardiovascular function using systolic blood pressure (an average of 2 measurements in a sitting position after a 5-min rest using a sphygmomanometer [OMRON HEM 907]).

We defined good mental health as a score of more than 42 points on the mental health component of the short-form general health survey included in the 2007–2009 questionnaire.

Statistical analysis
We defined 3 categories of outcome: successful aging, death during follow-up and normal aging. The normally aging group included all participants who were alive at the end of follow-up, but who were not classified as aging successfully. We performed 2 separate logistic regressions: the first to estimate the odds ratios (ORs) for successful aging (with normal aging/death as the noncases), and the second to estimate the ORs for survival (with death as the noncases). To test whether the associations with healthy behaviours differed by sex, we tested statistical interactions between each behaviour and sex using the Wald test.

To estimate the contribution of healthy behaviours to successful aging, we calculated population-attributable risk (PAR) for individual and combined healthy behaviours. Population-attributable risk is the reduction in the rate of a disease that would be seen if the population were entirely unexposed to the risk factor, compared with the current pattern of exposure. Applied to successful aging, PAR represents the gain in cases of successful aging that would be achieved if everyone engaged in healthy behaviours, assuming that the association between healthy behaviours and successful aging is causal. The relation can be expressed by the following equation:

$$\text{PAR} = \frac{f(OR – 1)}{1 + f(OR – 1)}$$

where $f$ is the proportion of healthy behaviours in the total population at baseline, and OR is the odds ratio for successful aging for the specific healthy behaviour compared with the reference. We adjusted these estimates for covariates in a fashion similar to the corresponding logistic models for ORs.

In our first set of analyses, healthy behaviours were entered together in a model adjusted for age, sex, level of education and marital status. We then used the same method to assess the association between the number of healthy behaviours and successful aging and survival. To test whether there was a dose–response relation between the number of healthy behaviours and each outcome, we treated the number of healthy behaviours in the logistic model as a continuous variable; the Wald test $p$ for this variable was the test for linear trend, and $p$ less than 0.05 was considered significant. Finally, we examined separately the association between the number of healthy behaviours and each measure of func-

Table 1: Baseline characteristics of participants included in the analysis in comparison with those excluded because of missing data on health outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Study participants $n=5100$</th>
<th>Excluded participants $n=1499$</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr, mean ± SD</td>
<td>51.3 ± 5.3</td>
<td>51.4 ± 5.1</td>
<td>0.5†</td>
</tr>
<tr>
<td>Female sex</td>
<td>1506 (29.5)</td>
<td>579 (38.6)</td>
<td>&lt;0.001‡</td>
</tr>
<tr>
<td>Married or living with someone</td>
<td>3963 (77.7)</td>
<td>1118 (74.6)</td>
<td>0.01†</td>
</tr>
<tr>
<td>University degree or higher</td>
<td>1274 (25.0)</td>
<td>303 (20.2)</td>
<td>0.001†</td>
</tr>
<tr>
<td>Never smoked</td>
<td>2500 (49.0)</td>
<td>722 (48.2)</td>
<td>0.6‡</td>
</tr>
<tr>
<td>Moderate consumption of alcohol</td>
<td>3271 (64.1)</td>
<td>912 (60.8)</td>
<td>0.02†</td>
</tr>
<tr>
<td>Physically active</td>
<td>2602 (51.0)</td>
<td>721 (48.1)</td>
<td>0.05†</td>
</tr>
<tr>
<td>Daily consumption of fruits and vegetables</td>
<td>3200 (62.7)</td>
<td>884 (59.0)</td>
<td>0.01†</td>
</tr>
</tbody>
</table>

Note: SD = standard deviation.
*Unless otherwise indicated.
††$t$ test.
‡‡$\chi^2$ test.
‡Adjusted for age, sex, level of education and marital status, mutually adjusted for each healthy behaviour.
†Includes successful and normal aging groups.
*The binary outcomes are successful aging versus normal aging or death, and survival to the end of follow-up versus death.

Note: CI = confidence interval, OR = odds ratio, PAR = population-attributable risk.

Yes
No (reference)

fruits and vegetables

Daily consumption of

Physically active

of alcohol

Never smoked

Moderate consumption of alcohol

Systolic blood pressure, mm Hg, mean ± SD

Forced expiratory volume, L/m², mean ± SD

Walking speed, m/s, mean ± SD

Cognitive function, z score, mean ± SD

Mental health score, mean ± SD

Table 3: Association between healthy behaviours, successful aging and survival to end of follow-up among 5100 participants

<table>
<thead>
<tr>
<th>Healthy behaviour</th>
<th>Total population</th>
<th>Successful aging*</th>
<th>Survival†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of people</td>
<td>Adjusted OR†</td>
<td>PAR, %</td>
</tr>
<tr>
<td>Never smoked</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (reference)</td>
<td>2600</td>
<td>422</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>2500</td>
<td>531</td>
<td>1.29 (1.11–1.49)</td>
</tr>
<tr>
<td>Moderate consumption of alcohol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (reference)</td>
<td>1829</td>
<td>287</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>3271</td>
<td>666</td>
<td>1.31 (1.12–1.53)</td>
</tr>
<tr>
<td>Physically active</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (reference)</td>
<td>2498</td>
<td>386</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>2602</td>
<td>567</td>
<td>1.45 (1.25–1.68)</td>
</tr>
<tr>
<td>Daily consumption of fruits and vegetables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (reference)</td>
<td>1900</td>
<td>292</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>3200</td>
<td>661</td>
<td>1.35 (1.15–1.58)</td>
</tr>
</tbody>
</table>

Note: CI = confidence interval, OR = odds ratio, PAR = population-attributable risk.

*The binary outcomes are successful aging versus normal aging or death, and survival to the end of follow-up versus death.
†Includes successful and normal aging groups.
‡Adjusted for age, sex, level of education and marital status, mutually adjusted for each healthy behaviour.
at the end of follow-up. Compared with the normally aging group, participants in the successfully aging group were younger (mean age 49.7 [standard deviation (SD) 4.9] v. 51.3 [SD 5.3] yr), and were more likely to be married (81.2% v. 77.8%) and have a university education or higher (31.6% v. 24.2%) (t test for continuous variables, $\chi^2$ test for categorical variables, all $p < 0.001$) (Table 2).

Table 3 shows the association of each healthy behaviour with successful aging and staying alive for the duration of follow-up (i.e., survival). Because there was no interaction between healthy behaviours and sex (data not shown, Wald test, all $p > 0.17$), we combined men and women in the analysis. Compared with former and current smokers, participants who had never smoked had 1.3 times greater odds of meeting the criteria for successful aging (OR 1.29, 95% confidence interval [CI] 1.11–1.49; PAR 12.4%) and 1.5 times greater odds of survival (OR 1.53, 95% CI 1.27–1.85; PAR 20.6%) (Table 3). Compared with no and heavy alcohol consumption, moderate consumption was associated with greater odds of successful aging (OR 1.31, 95% CI 1.12–1.53; PAR = 16.6%) and survival (OR 1.40, 95% CI 1.16–1.68; PAR 20.4%) (Table 3). Compared with inactive participants, participants who were physically active were more likely to meet the criteria for successful aging (OR 1.45, 95% CI 1.25–1.68; PAR = 18.7%) and to be alive at the end of follow-up (OR 1.32, 95% CI 1.10–1.60; PAR 14.0%) (Table 3). Finally, consuming fruits and vegetables daily was associated with greater odds of successful aging (OR 1.35, 95% CI 1.15–1.58; PAR 18.1%) and survival (OR 1.33, 95% CI 1.10–1.60; PAR 17.2%) (Table 3).

In our study population, 4.9% of the participants engaged in no healthy behaviours (score = 0), 18.3% engaged in 1 (score = 1), 33.8% engaged in 2 (score = 2), 31.3% engaged in 3 (score = 3), and 11.8% engaged in 4 (score = 4) (data not shown). The mean change in score 5 years later was small for both the normally aging group (0.08 ± 0.95) and the successfully aging group (0.00 ± 0.95) (data not shown). By the end of follow-up, the mean score for healthy behaviours had increased in both groups (0.10 ± 1.00 for the normally aging group; 0.17 ± 0.95 for the successfully aging group) (data not shown). The correlation between repeated measurements of the score was 0.58 (Spearman correlation, $p < 0.001$, $n = 4381$) at 5 years’ follow-up and 0.53 (Spearman correlation, $p < 0.001$, $n = 4186$) at the final follow-up (data not shown).

Compared with participants who engaged in no healthy behaviours at baseline, participants who engaged in 2 or more healthy behaviours had greater odds of successful aging and survival (Figure 2). The OR for having at least 1 healthy behaviour was 1.92 for successful aging (PAR 46.6%) and 2.32 for being alive at the end of follow-up (PAR 55.6%) (Figure 2). The benefit of healthy behaviours appeared to increase linearly (Wald test, $p < 0.001$): when the score for healthy behaviours was entered in the logistic model as a continuous variable, the OR per 1 additional healthy behaviour was 1.33 (95% CI

![Figure 2: Association between the number of healthy behaviours participants showed at baseline and (A) successful aging or (B) survival. In model 1, each number of healthy behaviours is included in the model as a category, and ORs are calculated with “0 healthy behaviours” as the reference group. In model 2, the category 1–4 includes all participants with 1–4 healthy behaviours, and the ORs are calculated with “0 healthy behaviours” as the reference group. The binary outcomes are successful aging versus death or normal aging, and survival to the end of follow-up versus death. OR = odds ratio. Error bars indicate 95% confidence intervals. *Models were adjusted for age, sex, level of education and marital status, and were mutually adjusted for all health behaviours. †Reference.](image-url)
Among members of a large cohort of British men and women 42–63 years of age at baseline, all 4 healthy behaviours examined during midlife (i.e., never smoking, moderate consumption of alcohol, engaging in some physical activity and eating fruits and vegetables daily) were associated with greater odds of successful aging during a 16-year follow-up. Compared with participants who engaged in no healthy behaviours, those who engaged in all 4 healthy behaviours had greater odds of aging successfully.

The benefits of healthy behaviours appeared to increase linearly as a function of the number of healthy behaviours present. In addition, the effect of healthy behaviours does not appear to be confined to any particular domain of successful aging. Associations were evident for each of the functional domains we measured: cognitive, mental, respiratory and cardiovascular.

Our findings advance current knowledge on successful aging.2,7,9–13,27,48–51 Few previous studies have examined the impact of multiple healthy behaviours on successful aging, with most studies focusing on single behaviours or combinations of two or three behaviours.

Interpretation

Table 4: Associations between the number of healthy behaviours and measures of functioning used to define successful aging

<table>
<thead>
<tr>
<th>No. of healthy behaviours</th>
<th>Good lung function†</th>
<th>Good cognitive function†</th>
<th>Good physical function†</th>
<th>No disability‡</th>
<th>Good mental health§</th>
<th>Good systolic BP¶</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (reference)</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1</td>
<td>1.69 (1.12–2.55)</td>
<td>0.85 (0.58–1.26)</td>
<td>1.34 (0.93–1.91)</td>
<td>1.19 (0.81–1.74)</td>
<td>1.18 (0.75–1.83)</td>
<td>0.78 (0.50–1.22)</td>
</tr>
<tr>
<td>2</td>
<td>2.08 (1.41–3.07)</td>
<td>1.12 (0.77–1.63)</td>
<td>1.82 (1.29–2.56)</td>
<td>1.60 (1.11–2.31)</td>
<td>1.81 (1.17–2.79)</td>
<td>0.79 (0.55–1.15)</td>
</tr>
<tr>
<td>3</td>
<td>2.84 (1.91–4.22)</td>
<td>1.62 (1.10–2.37)</td>
<td>2.17 (1.54–3.08)</td>
<td>1.82 (1.25–2.63)</td>
<td>2.33 (1.50–3.62)</td>
<td>0.98 (0.71–1.39)</td>
</tr>
<tr>
<td>4</td>
<td>3.63 (2.31–5.71)</td>
<td>2.15 (1.39–3.33)</td>
<td>2.97 (1.99–4.45)</td>
<td>2.27 (1.49–3.47)</td>
<td>3.12 (1.83–5.29)</td>
<td>1.05 (0.80–1.71)</td>
</tr>
</tbody>
</table>

Note: BP = blood pressure; CI = confidence interval; OR = odds ratio.

*Adjusted for age, sex, level of education and marital status. Numbers of participants vary from 3487 to 4455, depending on the measure of functioning (see Appendix 3 for further details).
†Defined as no self-reported difficulties in basic and instrumental activities of daily living.
‡Defined as no use of antihypertensive drugs.
§Defined as score > 42 on mental component of the 2007–2009 questionnaire.
¶Defined as not being in the lowest age- and sex-standardized quintile.

As the number of healthy behaviours increased, so did the odds of absence of disability; good lung, cognitive and physical functioning; and mental health (Table 4, all p for trend < 0.001; Appendix 3, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121080/-/DC1).

We saw no corresponding association for systolic blood pressure before taking into account antihypertensive drugs; repeating the analysis using medication data and good systolic blood pressure to define good functioning showed a clear association with the number of healthy behaviours (Table 4, all p for trend < 0.001).

Our sensitivity analyses showed that excluding deaths from the main analysis did not change the association between healthy behaviours and successful aging (OR per 1 additional healthy behaviour was 1.29, 95% CI 1.20–1.38; Appendix 4, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121080/-/DC1). We found similar results when alternative cut-offs for good mental health were used (OR per 1 additional healthy behaviour 1.37, 95% CI 1.27–1.47; Appendix 5, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121080/-/DC1). In addition, the results were little changed with inverse probability weighting to account for missing data (OR per 1 additional healthy behaviour 1.35, 95% CI 1.25–1.45 for successful aging; OR 1.40, 95% CI 1.29–1.53 for survival; Appendix 6, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121080/-/DC1).
have examined the importance of healthy behaviours for successful aging, with successful aging defined using both good functioning and the absence of disease.11-12 The associations we saw were similar to those from previous studies,10-12 with the exception of physical activity. The association between physical activity and successful aging has shown heterogeneity across studies. In addition, our study shows the cumulative impact of healthy behaviours on successful aging — the greater the number of healthy behaviours, the greater the benefit. Furthermore, our sensitivity analyses show that the increased risk of death associated with unhealthy behaviours does not explain our results.

Strengths and limitations

Our study’s strengths include its comprehensive definition of successful aging based on a large set of objective functioning measures, its prospective design and long follow-up, and its large sample size.

We did not examine the mechanisms underlying the associations we saw in this study. Because our results are from a study involving an occupational cohort, the participants are healthier than the general population.5 Few of the participants engaged in very unhealthy behaviours, such as heavy alcohol consumption. For this reason, it is possible that some of the associations we report are underestimated.

We were not able to determine health status for some of the participants owing to missing data on functional outcomes. Because participants who dropped-out were more likely to have health problems,13-14 the associations we report may be underestimated. However, sensitivity analyses using inverse probability weighting suggested that any bias due to missing data is likely to be small.

Because we assessed health behaviours using self-reports, our data could be subject to potential measurement errors.

The variables used to construct the outcomes were available at different times — chronic diseases throughout follow-up, and functioning measures at the end of the follow-up. Thus, it was not possible to examine the association between the duration of exposure and the outcomes. Such analyses may have been biased by reverse causation.

The sample population did not include anyone older than 80 years, so we were unable to examine whether our results extend to older age groups.

Conclusion

Although individual healthy behaviours are moderately associated with successful aging, their combined impact is quite substantial. Multiple healthy behaviours appear to increase the chance of reaching old age disease-free and fully functional in an additive manner. Our results should motivate lifestyle changes that not only reduce mortality and morbidity, but also improve quality of life at older ages.

References


47. Afiliations: From the Department of Epidemiology and Public Health (Sabia, Singh-Manoux, Hagger-Johnson, Brunner, Kivimaki), University College London, London, UK; Inserm U1018 (Singh-Manoux), Institut national de la santé et de la recherche médicale, Villejuif Cedex, France; the Centre de Gérontologie (Singh-Manoux), Hôpital Ste Périne, AP-HP, France; and the Institut national d’études démographiques INED (Cambois), Paris, France.

Contributors: Séréine Sabia drafted and wrote the manuscript and performed the statistical analyses. All of the authors contributed to the design of the study, interpreted the results, revised the manuscript and approved the final version submitted for publication.

Funding: Data collection was funded by the UK Medical Research Council (G0902037), the British Heart Foundation and the US National Institute on Aging (R01AG013196). Salary support received by the investigators was obtained from the Medical Research Council (G0902037 for Eric Brunner and Mika Kivimaki), the National Institute on Aging (R01AG013196 and R01AG034454 for Séréine Sabia, Archana Singh-Manoux, Gareth Hagger-Johnson, Mika Kivi- makki), a European Young Investigator Award from the Euro- pean Science Foundation (Archana Singh-Manoux) and an Economic and Social Research Council professorial fellowship (Mika Kivimaki). The funders had no role in the design or conduct of the study; in the collection, analysis and interpretation of data; in the preparation or approval of the manuscript; and in the decision to submit it for publication.

Acknowledgements: The authors thank all of the participating civil service departments and their welfare, personnel, and establishment officers; the British Occupational Health and Safety Agency; the British Council of Civil Service Unions; all of the Whitehall II study participants; and all members of the Whitehall II study team. The Whitehall II study team comprises research scientists, statisticians, study coordinators, nurses, data managers, administrative assistants and data-entry staff, who make the study possible.