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HAL Id: inserm-01165000
http://www.hal.inserm.fr/inserm-01165000
Submitted on 18 Jun 2015

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Slow walking speed and cardiovascular death in well functioning older adults: prospective cohort study

Julien Dumurgier, neurologist,1,2,3 Alexis Elbaz, epidemiologist,1,2 Pierre Ducimetière, senior epidemiologist,4,5 Béatrice Tavernier, geriatrician,6 Annick Alpérovitch, senior epidemiologist,1,2 Christophe Tzourio, head of the Inserm neuroepidemiology unit1,2

ABSTRACT
Objective To study the relation between low walking speed and the risk of death in older people, both overall and with regard to the main causes of death.
Design Prospective cohort study.
Setting Dijon centre (France) of the Three-City study.
Participants 3208 men and women aged ≥65 living in the community, recruited from 1999 to 2001, and followed for an average of 5.1 years.
Main outcome measures Mortality, overall and according to the main causes of death, by thirds of baseline walking speed (measured at maximum speed over six metres), adjusted for several potential confounders; Kaplan-Meier survival curves by thirds of baseline walking speed. Vital status during follow-up. Causes of death.
Results During 16414 person years of follow-up, 209 participants died (99 from cancer, 59 from cardiovascular disease, 51 from other causes). Participants in the lowest third of baseline walking speed had an increased risk of death (hazard ratio 1.44, 95% confidence interval 1.03 to 1.99) compared with the upper thirds. Analyses for specific causes of death showed that participants with low walking speed had about a threefold increased risk of cardiovascular death (2.92, 1.46 to 5.84) compared with participants who walked faster. There was no relation with cancer mortality (1.03, 0.65 to 1.70). In stratified analyses, cardiovascular mortality was increased across various strata defined by sex, median age, median body mass index (BMI), and level of physical activity.
Conclusion Slow walking speed in older people is strongly associated with an increased risk of cardiovascular mortality.

INTRODUCTION

There is growing interest in using walking speed in ambulatory clinics to readily assess functional status and motor performances in older people, and walking speed has been recommended as a possible “vital sign.” A few studies in well functioning older people have shown that decreased walking speed can predict adverse health related events such as falls,2,3 disability,4 admissions to hospital,14 and “persistent lower extremity limitation.” Lower walking speed has also been associated with increased all cause mortality,8 but it is unknown whether specific causes of death account for this increased mortality.

As part of a prospective cohort of well functioning older people enrolled in the Three-City (3C) study we studied the prognostic value of walking speed by investigating its relation with mortality overall and according to main causes of death. Because of recent evidence indicating that vascular risk factors might be associated with decreased motor performances,9,10 we had a special interest in the relation between walking speed and risk of cardiovascular death.

METHODS

The 3C study is an ongoing cohort study conducted in three French cities (Bordeaux, Dijon, Montpellier). Details of the study and primary outcomes have been previously reported.11 Participants aged ≥65 and living in the community were recruited from electoral rolls. The first step of the sampling procedure was to select administrative districts. Eligible inhabitants of the selected districts were invited to participate by a letter and were then contacted by phone until we reached our target number of participants; the acceptance rate was 37%. Data for the present study were obtained in Dijon (n=4931), where investigators were interested in motor function in older people. After baseline examination, follow-up examinations were performed at a mean of 1.8 years (2001-2), 3.6 years (2003-4), and 5.1 years (2005-6).

Baseline assessments

During a face-to-face interview in participants’ homes in 1999-2001 trained psychologists collected baseline demographic and medical data using standardised questionnaires. Education was defined as a four level variable (no school/primary without diploma, primary with diploma, secondary without a baccalaureate degree, baccalaureate/university degree). Participants were asked about their history of coronary artery disease (myocardial infarction, angina pectoris, coronary revascularisation), peripheral artery disease, stroke, Parkinson’s disease, and recent hip fracture (in the two preceding years). Exertional dyspnœa was self declared, based on the New York Heart Association...
defined as the ratio between distance and time. Walking speed was measured once in 1999-2001. We first considered all cause death and then defined three subgroups: cancer, cardiovascular, other causes. Cancer mortality was defined as an immediate cause of death coded by the committee between C00 and C97 and cardiovascular death as an immediate cause of death coded between I00 and I78 (including coronary heart disease, stroke, peripheral vascular disease, and other cardiovascular disease) or R960 (sudden death). Other causes of deaths included infectious diseases, digestive causes, trauma, suicide, and death of undetermined cause.

Statistical analyses
We excluded from our analyses participants who had conditions at baseline that were strongly associated with decreased walking speed (Parkinson’s disease, dementia, hip fracture in the previous two years, disabling stroke, coronary artery disease). Descriptive statistics were used to describe baseline characteristics by vital status (deceased during follow-up, yes/no) and thirds of walking speed. We compared groups using Student’s t test or analysis of variance (with linear contrasts) for continuous measures and χ² test or Cochran-Armitage trend test for proportions. Because walking speed was strongly related to sex, we categorised it into sex dependent thirds to maintain balanced sample sizes in men and women (cut-offs were defined by tertiles of the distributions in men and women: ≤1.35 m/s, 1.36-1.50 m/s, and >1.50 m/s in women).

We calculated the cumulative incidence of death according to thirds of walking speed with the Kaplan-Meier method and compared it with the log rank test. We also computed the cumulative risk of a given cause of death taking into account other causes of death (competing risk analysis) and found similar estimates to the Kaplan-Meier ones because mortality rates were low, thus showing that competing risks are not an issue for the present analyses. We used Cox proportional hazard models to estimate hazard ratios for death and their 95% confidence intervals. The proportional hazards assumption was checked by computing Schoenfeld residuals. We tested interactions between variables by including interaction terms. Unadjusted and adjusted hazard ratios are presented. Models were initially adjusted for age and sex. We then included in the models additional covariates strongly associated with walking speed (education level, mini-mental state examination, BMI, height, baseline physical activity). In the full model, we adjusted for other covariates associated with walking speed or mortality in univariate analyses (diabetes mellitus, hypertension, use of non-steroidal anti-inflammatory drugs for joint pain, use of psychotropic drugs, alcohol drinking, cigarette smoking, homocysteine concentration, dyslipidaemia, exertional dyspnoea, peripheral artery
disease, instrumental activities of daily living, depressive symptoms). In sensitivity analyses, we considered walking speed as a continuous variable or used other cut points (quartiles, quintiles) to categorise walking speed to assess whether our findings were influenced by the coding of the walking speed variable. Stratified analyses were performed to assess the relation between walking speed and cardiovascular mortality in different subgroups defined by sex, median age, median BMI, hypertension, smoking, and physical activity level. In sensitivity analyses, participants who reported coronary artery disease at baseline were retained in the analyses.

All P values were two tailed, and P≤0.05 was considered to be significant. All statistical analyses were performed with SAS version 9.1 (SAS Institute, Cary, NC, USA).

RESULTS

At baseline, 4399 participants aged 65-85 were seen at the study centre. We excluded from the analyses 722 who had one or more prevalent medical conditions strongly associated with decreased walking speed (477 with coronary artery disease, 211 with stroke, 53 with Parkinson’s disease, 38 with dementia, 12 with hip fracture). Walking speed at baseline was missing for 469 participants, who tended to be older (P<0.001) and with a higher BMI (P<0.001) than the other participants; there was no difference for other characteristics. All cause mortality during follow-up was not significantly higher (P=0.12) in participants without a measure of walking speed compared with those with a measure available. The mean (SD) age of the 3208 participants included in the study was 73.2 (4.6); 2085 (65%) were women. Vital status was determined for 3200 (99.8%) and missing for 8 (0.2%) at the end of the third follow-up (2005-6). During a mean (SD) follow-up of 5.1 (1.0) years, corresponding to 16 414 person years, 209 participants died (99 from cancer, 59 from cardiovascular disease, 51 from other causes).

Table 1 summarises participants’ baseline characteristics by vital status and thirds of walking speed. Those who died during follow-up were older, taller, more often men, and had a higher prevalence of cardiovascular risk factors (diabetes mellitus, hypertension, smoking) compared with survivors. About half of those who died were in the lowest third of walking speed, compared with one third of those who remained alive. Those in the lowest third of walking speed were older, smaller, had higher BMI, and were more likely to have depressive symptoms, less education, lower mini-mental state examination scores, and lower physical activity levels than those in the upper thirds of walking speed. They were also more likely to have hypertension or diabetes, have exertional dyspnoea or peripheral artery disease, and die during follow-up (table 1). There were no significant differences in baseline characteristics according to causes of mortality (data not shown), except for chronic use of non-steroidal anti-inflammatory drugs, which was associated with an increased cardiovascular mortality (P=0.03).

Figure 1 shows the cumulative risk of death (all cause, cancer, cardiovascular, other causes) by thirds of walking speed. There was a significant difference in all cause mortality across thirds of walking speed (log rank, P<0.001). Kaplan-Meier curves began to separate between 20 and 30 months after baseline and continued to diverge afterwards. The difference in the cumulative risk of death was significant for

Fig 1 Kaplan-Meier estimates of cumulative incidence of death according to thirds of walking speed, overall and by cause of death. Cut offs (tertiles) for definition of thirds of walking speed were ≤1.50 m/s, 1.51-1.84 m/s, and ≥1.85 m/s for men and ≤1.35 m/s, 1.36-1.50 m/s, and >1.50 m/s for women.
Table 1 Baseline characteristics of study sample by vital status and thirds of walking speed. Figures are numbers (percentages) unless stated otherwise.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall (n=3208)</th>
<th>Missing</th>
<th>Died during follow-up*</th>
<th>Throds of walking speed†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>No (n=2991)</td>
<td>Yes (n=209)</td>
</tr>
<tr>
<td>Mean (SD) age (years)</td>
<td>73.2 (4.6)</td>
<td>0</td>
<td>73.1 (4.5)</td>
<td>75.5 (4.6)</td>
</tr>
<tr>
<td>Women</td>
<td>2070 (64.5)</td>
<td>0</td>
<td>1968 (65.8)</td>
<td>98 (46.9)</td>
</tr>
<tr>
<td>Mean (SD) BMI</td>
<td>25.6 (4.0)</td>
<td>2</td>
<td>25.6 (4.0)</td>
<td>25.9 (4.6)</td>
</tr>
<tr>
<td>Mean (SD) height (cm)</td>
<td>161.5 (8.6)</td>
<td>2</td>
<td>161.4 (8.6)</td>
<td>162.9 (8.9)</td>
</tr>
<tr>
<td>Low education level</td>
<td>651 (20.3)</td>
<td>1</td>
<td>602 (20.1)</td>
<td>48 (23.0)</td>
</tr>
<tr>
<td>Mean (SD) MMSE score</td>
<td>27.5 (1.9)</td>
<td>4</td>
<td>27.5 (1.9)</td>
<td>27.1 (2.0)</td>
</tr>
<tr>
<td>Depressive symptoms**</td>
<td>390 (12.2)</td>
<td>29</td>
<td>361 (12.1)</td>
<td>26 (12.5)</td>
</tr>
<tr>
<td>Psychotropic drugs use</td>
<td>785 (24.5)</td>
<td>0</td>
<td>723 (24.2)</td>
<td>60 (28.7)</td>
</tr>
<tr>
<td>Low physical activity‖</td>
<td>171 (5.3)</td>
<td>23</td>
<td>149 (5.0)</td>
<td>20 (9.7)</td>
</tr>
<tr>
<td>Hypertension‡§</td>
<td>2513 (78.3)</td>
<td>0</td>
<td>2326 (77.8)</td>
<td>182 (87.1)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>262 (8.2)</td>
<td>0</td>
<td>224 (7.5)</td>
<td>38 (18.2)</td>
</tr>
<tr>
<td>Hypercholesterolaemia¶¶</td>
<td>1856 (57.9)</td>
<td>1</td>
<td>1741 (58.2)</td>
<td>112 (53.9)</td>
</tr>
<tr>
<td>Mean (SD) homocysteine (µmol/l)</td>
<td>14.7 (5.2)</td>
<td>103</td>
<td>14.6 (5.2)</td>
<td>15.0 (4.89)</td>
</tr>
<tr>
<td>Former or current smokers</td>
<td>1175 (36.6)</td>
<td>0</td>
<td>1072 (35.8)</td>
<td>99 (47.4)</td>
</tr>
<tr>
<td>Current drinker</td>
<td>2532 (78.9)</td>
<td>8</td>
<td>2362 (77.8)</td>
<td>164 (87.1)</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>76 (2.4)</td>
<td>43</td>
<td>61 (20.1)</td>
<td>14 (6.7)</td>
</tr>
<tr>
<td>Exertional dyspnoea</td>
<td>381 (11.9)</td>
<td>7</td>
<td>334 (11.2)</td>
<td>45 (21.6)</td>
</tr>
<tr>
<td>NSAIDs for joint pain</td>
<td>474 (14.8)</td>
<td>37</td>
<td>443 (15.0)</td>
<td>30 (14.6)</td>
</tr>
<tr>
<td>Walking speed in lower third</td>
<td>1091 (34.0)</td>
<td>0</td>
<td>982 (32.8)</td>
<td>105 (50.2)</td>
</tr>
<tr>
<td>Died during follow-up</td>
<td>209 (6.5)</td>
<td>8</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>105 (9.7)</td>
<td>49 (4.5)</td>
<td>55 (5.4)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

BMI = body mass index; MMSE = mini-mental state examination; IADL = instrumental activity of daily living; NSAID = non-steroidal anti-inflammatory drug.

*Vital status not determined for eight people.

‡Cut offs (tessile): ≤1.50 m/s, 1.50-1.85 m/s, and ≥1.85 m/s for men and ≤1.35 m/s, 1.35-1.50 m/s, and ≥1.50 m/s for women.

§Assessed by Center of Epidemiological Studies Depression Scale.

¶Dependent from at least one activity of the Lawton IADL scale.

††Defined as walking less than 1 hour/day and no sport activity.

‡‡Systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg or intake of antihypertensive drugs.

§§Total cholesterol concentration ≥6.20 mmol/l or intake of lipid lowering drugs.

cardiovascular deaths (P<0.001) and other causes of death (P=0.004), while there was no significant difference for cancer deaths (P=0.26). In each of these analyses, there was no significant difference in the cumulative incidence of death between the middle and highest thirds of walking speed, and the increased risk of death mainly concerned those in the lowest third of walking speed. Our subsequent results are for the lowest third of walking speed compared with the two upper thirds.

Table 2 shows multivariable analyses of the relation between walking speed and mortality. In analyses adjusted for age and sex (table 2, model 2), participants in the lowest third of walking speed had an increased risk of dying during follow-up [hazard ratio 1.64, 95% confidence interval 1.24 to 2.17] compared with those in the upper thirds; the difference in mortality was significant for cardiovascular mortality (2.85, 1.64 to 4.94) and other causes of death (1.79, 1.00 to 3.19), while there was no association with deaths from cancer (1.13, 0.74 to 1.71). After adjustment for other covariates associated with walking speed, the association remained significant overall and for cardiovascular mortality table 2, model 3. Further adjustment for baseline vascular risk factors, psychotropic drug use, exertional dyspnoea, peripheral artery disease, being dependent in at least one instrumental activity of daily living, depressive symptoms, and use of non-steroidal anti-inflammatory drugs for joint pain led to similar results (table 2, model 4). Inclusion of walking speed as a continuous variable or using other cut points (quartiles or quintiles) led to similar conclusions (data not shown).

Figure 2 shows the results of stratified analyses; in each strata, hazard ratios are adjusted for age, sex, BMI, height, education level, mini-mental state examination, physical activity, diabetes mellitus, hypertension, use of non-steroidal anti-inflammatory drugs for joint pain, psychotropic drug use, alcohol, smoking, dyslipidaemia, exertional dyspnoea, peripheral artery disease, dependence in instrumental activities of daily living, depressive symptoms, and homocysteine level (model 4). In all strata, cardiovascular mortality was higher in the lowest third of walking speed than in the upper thirds (model 4). Interaction tests comparing the hazard ratios across the strata were not significant.

In analyses in which we excluded those who were dependent in at least one instrumental activity of daily living at baseline (171, 5.3%, table 1), the hazard ratio (model 4) was 1.50 (1.08 to 2.08) for overall...
mortality and 3.13 (1.64 to 5.99) for cardiovascular mortality, while there was no association with other causes of death (1.21, 0.62 to 2.38) and cancer mortality (1.10, 0.68 to 1.79). In sensitivity analyses, we included participants who reported coronary artery disease at baseline and had a measurement of walking speed; our findings remained unchanged. Hazard ratios (model 4) were 1.41 (1.05 to 1.89) for overall mortality, 2.48 (1.33 to 4.62) for cardiovascular mortality, 1.11 (0.72 to 1.72) for cancer mortality, and 1.34 (0.77 to 2.32) for other causes of death.

DISCUSSION
In this large cohort of older people living in the community we found that lower walking speed at baseline was associated with increased mortality during a five year follow-up. Participants in the lowest third of walking speed had a 44% increased risk of death compared with those in the upper thirds. With regard to specific causes of death, participants in the lowest third of walking speed had about a threefold increased risk of cardiovascular death, while no relation was found with cancer mortality. This increased risk of cardiovascular death was seen in both sexes, younger as well as in older participants, those with or without a high risk vascular profile, and those with low or usual physical activity.

Findings in context and possible mechanisms
Few studies have investigated the relation between walking speed and mortality, and their methods were not uniform.13 One study found that regular walking speed below 1 m/s was associated with mortality in older people,7 and another study found that a measure of walking speed alone provided information on mortality similar to that provided by a more complex evaluation of physical performance.9 It was unknown, however, whether specific causes of death accounted for this increased mortality. Our results show that the increased mortality observed in slow walkers was mostly cardiovascular mortality. Other causes of death tended to be higher in people with lower walking speed, but the relatively low number of events did not allow detailed analyses. Additionally, after adjustment for covariates associated with walking speed or death, the association between walking speed and other causes of death was considerably attenuated. Stratified analyses showed that the excess cardiovascular mortality among people who walked more slowly was observed in different subgroups. The relation between walking speed and mortality was not explained by inclusion of participants who were dependent in at least one instrumental activity of daily living at

<table>
<thead>
<tr>
<th>Cause of death and walking speed</th>
<th>Person years</th>
<th>Events</th>
<th>Rate (%)</th>
<th>Hazard ratio (95% CI)</th>
<th>Hazard ratio (95% CI), P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All causes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper thirds§</td>
<td>10 940</td>
<td>104</td>
<td>9.5</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Lower third**</td>
<td>5474</td>
<td>105</td>
<td>19.2</td>
<td>2.07 (1.58 to 2.72), &lt;0.001</td>
<td>1.64 (1.24 to 2.17), &lt;0.001</td>
</tr>
<tr>
<td>Other causes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper thirds§</td>
<td>10 940</td>
<td>59</td>
<td>5.4</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Lower third**</td>
<td>5474</td>
<td>40</td>
<td>7.3</td>
<td>1.38 (0.93 to 2.07), 0.11</td>
<td>1.13 (0.74 to 1.71), 0.56</td>
</tr>
</tbody>
</table>

*Unadjusted model.
†Adjusted for age and sex.
‡Adjusted for variables included in previous model plus body mass index (BMI), height, education level, mini-mental state examination, and physical activity.
§Adjusted for variables included in previous model plus diabetes mellitus, hypertension, use of non-steroidal anti-inflammatory drugs for joint pain, psychotropic drug use, alcohol, smoking, dyslipidaemia, exertional dyspnoea, peripheral artery disease, dependence for at least one instrumental activity of daily living, depressive symptoms, and homocysteine concentration.
**Cut off for walking speed: ≤1.50 m/s for men; ≤1.35 m/s for women.

Fig 2 | Walking speed in lowest third and risk of cardiovascular death: stratified analyses. Hazard ratios estimate relative risk of cardiovascular death in those in lowest third of walking speed (≤1.50 m/s for men; ≤1.35 m/s for women) compared with those in two highest thirds (reference group)
WHAT IS ALREADY KNOWN ON THIS TOPIC

Walking speed is a simple and reliable measure that is considered as a surrogate for overall quality of gait and motor function in older people

Decreased walking speed has been shown to be associated with several adverse health related events, including death

WHAT THIS STUDY ADDS

Participants with a walking speed in the lower third of the distribution had about a threefold increased risk of cardiovascular death, but no increased risk of mortality from cancer or other causes of death

baseline because their proportion was low and analyses restricted to non-dependent participants were comparable with the overall analyses.

In a previous study, performance of long distance walking in a corridor was associated with cardiovascular events.\(^\text{14}\) Measures of walking speed over a short distance and long distance corridor walking tests are not readily comparable. Long distance walking tests measure features such as endurance, fatigability, and cardiovascular fitness that are not assessed through short distance measures of walking speed.\(^\text{15}\)

Our results are also in line with previous studies reporting an association between increased cardiovascular mortality and low cardiorespiratory fitness\(^\text{16}\) or low physical activity.\(^\text{17}\) Measures of walking speed over a distance of six metres are easier to implement in routine clinical practice and represent objective measures that can be assessed repeatedly; they can be performed in a few seconds in nearly all older people living in the community, while tests of long distance walking require around eight minutes and cannot be performed by a sizeable proportion of older people.

A possible explanation for the association between low walking speed and cardiovascular mortality is that chronic exposure to vascular risk factors is associated with both increased cardiovascular mortality and decreased walking speed. Until recently, the relation between vascular risk factors and motor performances received little attention, but there is some evidence in favour of an association. Increased thickness of the carotid artery intima media\(^\text{19}\) and raised homocysteine concentrations\(^\text{18}\) have been reported to be associated with low walking speed, while raised high density lipoprotein cholesterol concentrations have been reported to be associated with higher walking speed.\(^\text{19}\)

Recent studies have shown an association between performance measures and inflammatory markers,\(^\text{20}\) and inflammation is suspected to play a role in cardiovascular disease.\(^\text{21}\) Diabetes mellitus has been associated with symptoms of mild parkinsonism in older people,\(^\text{22}\) suggesting the involvement of deep cerebral lesions. These associations might be mediated by subclinical cerebrovascular disease in patients with vascular risk factors.\(^\text{23-27}\)

Alternative explanations are possible. Low walking speed might result from the peripheral effect of vascular risk factors—for example, heart failure or peripheral artery disease.\(^\text{28}\)

Conclusion

In summary, lower walking speed was strongly associated with cardiovascular mortality in a population of well functioning older people. These findings show that assessment of motor performances in older people with simple measures such as walking speed can be performed easily and that the role of fitness in preserving life and function in older age is important.

Strengths and limitations

The low proportion of participants who were lost to follow-up (eight out of 3208) is one of the main strengths of this study. Other strengths include the large number of person years and an automated measure of walking speed using photoelectric cells, which ensures high reproducibility of the measure.

There are limitations to consider. The 3C cohort was volunteer based and not representative of the general population. Participants were community dwelling, well functioning older people who were able to come by themselves to the study centre. Although this is likely to lead to an underestimation of the incidence of events such as death, it has been shown that, in this setting, the relation between baseline exposure and incidence of disease during follow-up is not biased.\(^\text{31}\)

Increased cardiovascular mortality was present only for participants in the lowest third of walking speed, suggesting a threshold effect. The number of cardiovascular deaths, however, did not allow us to determine a more precise cut off.

Contributors: JD conducted the statistical analyses under the supervision of AE. All authors participated in designing the analyses, interpreting the results, and writing the manuscript. All authors had full access to the data and are guarantors for the study.

Funding: The 3C study is conducted under a partnership agreement between the Institut National de la Santé et de la Recherche Médicale (INSERM), the Victor Segalen-Bordeaux II University, and the Sanofi-Synthélabo Company. The Fondation pour la Recherche Médicale funded the preparation and initiation of the study. The 3C study is also supported by the Caisse Nationale Maladie des Travailleurs Salariés, Direction Générale de la Santé, Haute Autorité de la Santé, Institut National de Prévention et d’Éducation pour la Santé (INPES), Conseils Régionaux de Bourgogne, Fondation de France, Ministry of Research-INSERM Program, “Cohortes et collections de données biologiques,” Mutuelle Générale de l’Education Nationale, Institut de la Longévité, Conseil Général de la Côte d’Or. JD was supported by a PhD scholarship from the Fondation pour la Recherche Médicale. The funding organisations played no role in the design and conduct of the study, in the collection, management, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.

Competing interests: None declared.

Ethical approval: The study was approved by the ethical committee of the University Kremlin-Bicêtre Hospital; each participant signed an informed consent form.

Data sharing: No additional data available.

Accepted: 28 August 2009