Working hours and incidence of metabolic syndrome and its components in a Mediterranean cohort: the SUN project

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Background: Metabolic syndrome (MetS) is an important and priority public health problem globally. Long working hours have been proposed as a modifiable risk factor for MetS, despite sparse epidemiological evidence. Thus, the aim of this study was to prospectively evaluate the associations between working hours and incidence of MetS and each of its components. Methods: We assessed 6845 participants of a Spanish dynamic prospective cohort of university graduates (the SUN project), initially free of any specific criteria of MetS, and followed-up for a median of 8.3 years. Weekly working hours were collected at baseline and grouped into four categories: >0–24, 25–39, 40–49 and ≥50 h. MetS was defined according to the updated harmonizing criteria. We estimated multivariable adjusted Relative Risks (RR) of MetS and their 95% Confidence Intervals (95% CI), using Poisson regression models. Results: The cumulative incidence of MetS was 6.0%. Working hours were not independently related to MetS (25–39 h/week = RR: 1.42, 95% CI 0.90–2.25; 40–49 h/week = RR: 1.45, 95% CI 0.91–2.30; ≥50 h/week = RR: 1.49, 95% CI 0.91–2.42, P for trend = 0.235) nor to any of its individual definition criteria. Conclusion: Our findings do not suggest that long working hours increase the risk of MetS development or each of its components. Further longitudinal studies in general population should be conducted to confirm these results.

Introduction

Metabolic syndrome (MetS) is characterized by the clustering of abdominal obesity, dyslipidemia, hyperinsulinemia, impaired fasting glucose and high blood pressure, and its prevalence is over 20% in adult populations around the world.1–3 Besides its high prevalence, MetS is strongly associated with non-communicable diseases, such as type 2 diabetes and cardiovascular diseases (CVD), which are among the main public health concerns worldwide.4–7

Therefore, the investigation on which factors are associated with the development of MetS is fundamental for the primary prevention of type 2 diabetes and CVD. Long working hours have been proposed as a modifiable risk factor for MetS, despite sparse epidemiological evidence. To the best of our knowledge, only two cross-sectional studies have assessed this relationship. In the first one, working >10 h/day was independently associated with higher prevalence of MetS in subjects with ≥40 years.8 In the second study, it was found that more overtime work pooled with midnight shift work was related to MetS.9 However, the results of both studies should be interpreted with caution because the cross-sectional design does not guarantee causality. Therefore, the association between working hours and MetS remains elusive.

Notwithstanding, some longitudinal studies pointed out a relationship between long working hours and some specific MetS components, but most of these studies were done in Japan because the topic on working conditions and health have become important since Karoshi (sudden death due to cardiovascular events, resulting from working overtime) was first recognized.10 The results from prospective observational studies reinforce this finding because they suggested an approximately 40% excess risk of coronary heart disease in employees working long hours.11,12 An investigation conducted in three companies of Japan indicated that workers whose mean overtime was ≥50 h/month had higher risk of developing obesity.13 Extensive overtime work (≥40 h/month) also was associated with increased blood pressure among assembly-line workers of Japanese manufacturing company.14 Other study developed in a Japanese local public institution showed that working >9 h/day was associated with an increased risk of hypertriglyceridemia.15 Contradictorily, longer overtime work (>11 h/day) was suggested to be inversely associated with hyperglycemia or type 2 diabetes in a study with Japanese office workers.16

Thus, our aim was to prospectively evaluate the association between working hours and incidence of MetS and each of its components in a cohort of Spanish university graduates.

Methods

Study population

The ‘Seguimiento Universidad de Navarra’ [University of Navarra Follow-up] (SUN) Project is a dynamic prospective cohort study with permanently open recruitment, conducted in Spain with university graduates since December 1999. Additional details on its objectives, design and methods have been previously published elsewhere.17,18
Information is gathered by mailed or electronic mailed questionnaires collected biennially. After baseline assessment (Q_0), participants receive follow-up questionnaires every 2 years (Q_2, Q_4, Q_6, Q_8, ..., Q_n) with important questions to evaluate changes in lifestyle and health-related behavior, anthropometric measures, moods/personality, incident diseases and medical conditions.

This study was conducted in June 2013, and to warrant a minimum follow-up of 6 years, all participants who had answered their first questionnaire before October 2006 and were free of any specific MetS criterion or diabetes at baseline were considered as eligible (n = 11 950). Out of them, we excluded those who had reported extremely low or high values for total energy intake (n = 1092) (<800 kcal/day in men and 500 kcal/day in women or >4000 kcal/day in men and 3500 kcal/day in women),19 because they were more likely to have failed to properly complete the questionnaires; those who had not answered any of the follow-up questionnaires (n = 544); and those who did not reply both 6 years (Q_6) and 8 years (Q_8) follow-up questionnaires (n = 1291), because the MetS incidence was diagnosis at these end points. In addition, we also excluded participants who had missing information on MetS components at baseline questionnaire (n = 1039), and those who were unemployed (n = 157) or did not work (n = 1002). Thus, a total of 6845 participants were included in the final analyses.

The study was conducted according to Declaration of Helsinki and all procedures involving human subjects were approved by the institutional review board of the University of Navarra. Voluntary completion of baseline questionnaire was considered to imply informed consent.

**Exposure assessment—working hours**

Information about self-reported working hours was collected at baseline questionnaire through the following question: ‘How many hours do you work per week, excluding domestic chores?’ The participants could choose among 16 categories: do not work, <20, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84 and ≥85 h/week. Thus, considering the distribution of the variable observed in our sample, and the Spanish labour law,20 working hours were recoded into four categories: (i) >0–24 h/week, (ii) 25–39 h/week, (iii) 40–49 h/week and (iv) ≥50 h/week.

**Outcome assessment—MetS and its components**

MetS was defined according to International Diabetes Federation and American Heart Association/National Heart, Lung and Blood Institute harmonizing definition,21 which requires the diagnosis of three or more of following five criteria: (i) high waist circumference (≥94 cm for men and ≥80 cm for women, cut-off points for European population); (ii) elevated triglycerides (≥150 mg/dl or presence of pharmacologic treatment for hypertriglyceridaemia); (iii) reduced HDL-cholesterol (<40 mg/dl for men and <50 mg/dl for women or presence of pharmacologic treatment for reduced HDL-cholesterol); (iv) elevated blood pressure (systolic ≥130 mmHg and/or diastolic ≥85 mmHg or presence of pharmacologic treatment for hypertension in patient with history of this disease) and (v) elevated fasting glucose (≥100 mg/dl or pharmacologic treatment for hyperglycaemia).

In Q_6 and Q_8 follow-up questionnaires, self-reported data on these MetS criteria were collected. Waist circumference was measured in a horizontal plane, midway between the inferior margin of the ribs and the superior border of the iliac crest. All participants were sent a tape measure with Q_6 and 8-year Q_8 follow-up questionnaires, and an explanation of how to measure their waist.22

The validation of the self-reported MetS components was assessed in a specific study within a subsample of 287 participants. Significant intra-class correlation coefficients (P < 0.001), ranged 0.5–0.9, between self-reported MetS components and their direct assessments by an experienced physician.23 An additional validation study conducted in another subsample of SUN project showed a good agreement between the self-reported MetS diagnosis and the MetS diagnosed by medical records of our participants [proportion of confirmed MetS = 91.2% (95% CI 80.7–92.1); proportion of non-confirmed MetS = 92.2% (95% CI 85.1–96.4); sensitivity = 66%; specificity = 98%].24

An incident case of MetS was defined when the participant, free of this condition and any of the MetS criteria at baseline, met three or more of its components in either Q_6 or Q_8 follow-up questionnaires.

**Potential confounding factors**

We considered several variables as potential confounding factors and adjusted our analysis for a wide array of characteristics inquired at baseline questionnaire: sociodemographic [sex, age, educational level (technical, graduated, master/doctoral), marital status (single, married, other: widowed, divorced, cohabiting)]; lifestyle and health-related behaviour [smoking status (never, current, former), alcohol consumption (grams/day), physical activity (activity metabolic equivalent—MET hours/week), time watching television (h/day)]; dietary habits [total energy intake (kcal/day), Mediterranean diet adherence]; proxy of job strain [competitive and dependent at work (0–10 points scale, whose 0 means low and 10 means high)]; time standing at work (h/day); time in intensive tasks at work (h/day); personality [tense moods (0–10 points scale, whose 0 means low and 10 means high)]; and anthropometric data [baseline Body Mass Index (BMI)].

Alcohol consumption and dietary habits were assessed using a 136-item semi-quantitative food frequency questionnaire, previously validated in Spain.25,26 Mediterranean diet adherence was defined according to the nine points score proposed by Trichopoulou et al.,27 divided into low (0–2), intermediate (3–5) and high (6–9) adherence.

Leisure-time physical activity was collected through a validated questionnaire that included information about 17 activities such as walking, running, cycling, swimming, judo, soccer, sailing or skating. Leisure time physical activity estimated with this questionnaire was previously validated by our group using a tri-axial accelerometer as a gold standard. Physical activity during leisure time (estimated as MET-hours/week) derived from the questionnaire moderately correlated with kcal/day assessed through the accelerometer.28

BMI defined as weight (in kilograms) divided by height2 (in meters) was ascertained at the baseline questionnaire. The validity of self-reported weight was assessed in a subsample of the cohort. The mean relative error in self-reported weight was 1.5%. The correlation coefficient (r) between measured and self-reported weight was 0.99 (95% CI 0.98–0.99).29

**Statistical analysis**

To avoid substantial biases and the exclusion of a significant number of participants, because they had missing values in important variables, such as HDL-cholesterol and triglycerides levels at 6-year and/or 8-year follow-up questionnaires, we use the multiple imputation approach to handle missing values. This statistical technique tries to overcome the problem that the single imputed values are not actually observed but predicted values, and attributing the most probable value, therefore overestimates the precision and distorts the distribution of the data.30 Instead of a single (most likely) value, 20 values were sampled from an estimated uniform distribution (also taking into account some characteristics of participants at baseline, such as sex, age, working hours, educational level, marital status, smoking status, alcohol consumption, physical activity, total energy intake, Mediterranean diet adherence and BMI) and imputed for the 4899 participants who had missing values in HDL-cholesterol and/or triglycerides and/or time watching
television and/or time standing at work and/or time in intensive tasks at work, adding a random value. Hence, 20 datasets with imputed outcomes were created, generating several possible values to these variables.

Differences of baseline characteristics of participants according to working hours were evaluated with Pearson’s $\chi^2$ test or Analysis of Variance (ANOVA).

Poisson regression models were fitted to assess the relationship between working hours and incidence of MetS. Relative Risk (RR) and their 95% Confidence Interval (95% CI) were estimated using as the reference category those participants who worked >0–24 h/week. The results were pooled by using standard techniques, also taking into account the variation between multiple imputed datasets.

A first model did not include any covariate (model 1). We fit another model adjusting for sex and age (model 2). We also fit a third model additionally adjusting for other previously described potential confounding factors, except BMI at baseline (model 3). Finally, we adjusted the last model with BMI at baseline (model 4). Tests for linear trend were conducted assigning medians for the hours worked within each category, and this new variable was introduced as continuous variable in the Poisson regression models.

In addition, the Variance Inflation Factor (VIF) was calculated to account for multicollinearity across independent variables in model 4.

We also evaluated the interactions between working hours and other covariates in the final model, using the likelihood ratio test between the multiple-adjusted model and the same model including the product-term.

All analyses were performed with STATA version 12.1 (StataCorp, College Station, TX, USA) and repeated for each individual component of MetS. Statistical significance was set at 5% ($P$ values <0.05, based on 2-tailed tests).

### Results

Four hundred nine participants (259 men and 150 women) initially free of MetS were newly classified as incident cases during a median follow-up of 8.3 years. Thus, the overall cumulative incidence of MetS in this population was 6.0% (10.4% for men and 3.4% for women) and the overall incidence density was 7.4/1000 persons-year (12.9/1000 persons-year for men and 4.3/1000 persons-year for women).

The main characteristics of the participants according to categories of working hours are presented in table 1. Compared with subjects who worked between >0 and 24 h/week, those who worked ≥50 h/week were more likely to be older, men and have better educational level. Moreover, they had some positive lifestyle and health-related behaviour because they were more physically active, spent more time standing at work, more time doing intensive tasks at work, less time watching television and smoked less. On the other hand, these participants had higher total energy intake, alcohol consumption, higher BMI, and were more tense and competitive at work.

Long working hours (≥50 h/week) were associated with MetS development in the crude analysis [(RR = 1.85; 95% CI = 1.21–2.93), $P$ for trend <0.001]. However, these findings did not remain statistically significant after adjusting for age and sex [(RR = 1.30; 95% CI = 0.84–2.00), $P$ for trend = 0.21)], and were further attenuated after adjusting for other potential confounding factors [model 3 (RR = 1.33; 95% CI = 0.82–2.15), $P$ for trend = 0.188)]. These findings also did not change significantly after additional adjustment for BMI [model 4 (RR = 1.25; 95% CI = 0.81–1.94), $P$ for trend = 0.345)] (table 2).

### Table 1 Baseline characteristics of participants according to working hours

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Working hours</th>
<th>$P$-value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>&gt;0–24 h/week</td>
<td></td>
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<tr>
<td></td>
<td>25–39 h/week</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40–49 h/week</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥50 h/week</td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>Mean  SD</td>
<td>Mean  SD</td>
</tr>
<tr>
<td>Age (years)</td>
<td>35.1  11.5</td>
<td>38.1  9.7</td>
</tr>
<tr>
<td>Sex (%)</td>
<td>Male  15.9</td>
<td>22.8</td>
</tr>
<tr>
<td></td>
<td>Female  84.1</td>
<td>77.2</td>
</tr>
<tr>
<td>Educational level (%)</td>
<td>Technical/Non graduated  40.9</td>
<td>45.1</td>
</tr>
<tr>
<td></td>
<td>Graduated  49.1</td>
<td>43.9</td>
</tr>
<tr>
<td></td>
<td>Master/Doctoral  10.0</td>
<td>11.0</td>
</tr>
<tr>
<td>Marital status (%)</td>
<td>Single  48.2</td>
<td>38.5</td>
</tr>
<tr>
<td></td>
<td>Married  50.0</td>
<td>55.5</td>
</tr>
<tr>
<td></td>
<td>Other*  1.8</td>
<td>6.0</td>
</tr>
<tr>
<td>Mediterranean diet adherence score (%)</td>
<td>0–2 points  15.1</td>
<td>14.5</td>
</tr>
<tr>
<td></td>
<td>3–6 points  57.6</td>
<td>59.3</td>
</tr>
<tr>
<td></td>
<td>7–9 points  27.3</td>
<td>26.2</td>
</tr>
<tr>
<td>Total energy intake (kcal/day)</td>
<td>2355.2  596.8</td>
<td>2335.7</td>
</tr>
<tr>
<td>Alcohol consumption (g/day)</td>
<td>4.7    6.9</td>
<td>5.2</td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>29.3   22.3</td>
<td>22.3</td>
</tr>
<tr>
<td>Leisure-time physical activity (MET-h/week)</td>
<td>18.9  20.8</td>
<td>21.3</td>
</tr>
<tr>
<td>Television watching (h/day)</td>
<td>1.8    1.3</td>
<td>1.7</td>
</tr>
<tr>
<td>Competitive at work (0–10 points)</td>
<td>6.3    1.9</td>
<td>6.6</td>
</tr>
<tr>
<td>Dependent at work (0–10 points)</td>
<td>3.7    2.7</td>
<td>3.6</td>
</tr>
<tr>
<td>Tense moods (0–10 points)</td>
<td>5.8    2.3</td>
<td>5.9</td>
</tr>
<tr>
<td>Standing at work (h/day)</td>
<td>1.8    2.0</td>
<td>2.4</td>
</tr>
<tr>
<td>Intensive tasks at work (h/day)</td>
<td>0.6    1.3</td>
<td>0.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.2   2.7</td>
<td>22.5</td>
</tr>
</tbody>
</table>

The SUN Project (Seguimiento Universidad de Navarra, University of Navarra Follow-up), Navarra, Spain, 1999–2013

MET, metabolic equivalent of task; Kg/m², kilograms per square meters. *Other = widowed, divorced, cohabiting. b$P$-value from ANOVA. c$P$-value from Pearson’s $\chi^2$ test.
Testing for multicollinearity across independent variables in the model 4 revealed satisfactory values of the VIF. The range for the VIF was 1.03–1.15 and the mean VIF was 1.08. Moreover, the minimum and the maximum correlations between independent variables were $r = 0.0059$ and $r = 0.6378$, respectively.

Working hours did not independently relate to any MetS individual definition criterion ($P$ for trend of central obesity $= 0.634$; $P$ for trend of hypertriglyceridemia $= 0.981$; $P$ for trend of low HDL-cholesterol $= 0.380$; $P$ for trend of hyperglycaemia $= 0.371$; $P$ for trend of high blood pressure $= 0.793$) (table 2).

No interactions terms between working hours and potential confounding factors included in the multivariate models were significant.

### Discussion

We did not find any evidence of positive associations between working hours and the incidence of MetS or each of its components. The lack of association between working hours and MetS is not consistent with the results of previous studies on this issue. In a cross-sectional study conducted over 933 men, employees at a manufacturing company in Shizuoka, Japan, long working hours (>10 h/day) increased the risk of MetS after adjusting for age, occupation, shift work, smoking status, frequency of alcohol consumption and cohabiting status. However, that result might be influenced by some type of bias: (i) no control for other relevant potential confounding factors such as lifestyle factors (e.g. time of television watching, physical activity level); (ii) overestimation of the strength of association, since OR is not the best measure when the outcome is frequent; and (iii) most importantly, the cross-sectional design of the study does not guarantee causality. A second study conducted with 98 police officers in United State found that overtime work combined with midnight shift work might be an important contributor to MetS. Those findings are compatible with our results since they do not suggest a direct association between long working hours and MetS, but that the labour during long time in night shift work might increase the risk of MetS. Longitudinal studies have reported independent associations between shift work (but not working hours) and MetS or some of its specific individual components. However, a systematic review on this topic concluded that there was insufficient evidence to support these relationships because these results were not sufficiently adjusted for potential confounders. On the other hand, the biological plausibility of the associations may be due to disturbance in the circadian rhythm, which promotes changes in the metabolic, hormonal and immunological functions rather than by the total amount of hours spent in a job. An experimental study evidenced the development of MetS in circadian clock mutant mice.

With respect to the lack of association found between working hours and each of MetS individual definition criteria, our findings are inconsistent with previously published studies. However, those previous investigations are likely to present some sources of bias, such as: (i) insufficient adjustment for potential confounders; (ii) small sample size; (iii) no description of the statistical treatment given to missing values of the dependent variables during follow-up, which also might be influencing these relationships. For example, in our study, before using multiple imputation approach, working hours were independently associated with the development of low HDL-cholesterol ($P$ for trend $= 0.008$). We were considering missing values in HDL-cholesterol as no evidence of abnormal levels of this lipoprotein, and the percentage of participants in this situation was more frequent among those who worked less time (data not shown), which might be partially explained by the fact that they had slightly lower educational level and were less knowledgeable about their own lipid profile. Thus, after the multiple imputations, which is the recommended methodological approach in this situation, the significant association between working and low HDL-cholesterol disappeared ($P$ for trend $= 0.380$).

The results of this study may be influenced by 'healthy worker effect', because, in general, to develop or to remain in a job that require long working hours may be related to a better health status. About it, our Q_4 and Q_8 follow-up questionnaires had two questions that partially allow evaluating this condition: (i) Did
you have to cut time spent on work tasks or daily activities because of your physical health? (ii) Did you have to stop some work tasks or daily activities because of your physical health? Non-significant differences were observed among participants working >0–24 h/week or ≥50 h/week after adjusting for age, sex and baseline BMI (data not shown).

Moreover, our findings should be interpreted considering the following aspects: (i) working hours were assessed only at a single time point, not allowing adjustment of the results for exposure changes over time; (ii) both working hours and MetS components were self-reported. On the other hand, this cohort is composed of university graduates, a population with a high educational level, decreasing the risk of misclassification. Furthermore, self-reported diagnosis of MetS was previously validated in our cohort;3,24 (iii) the participants of this study are relatively young, slim and physically active, and the associations between working hours and MetS or its components would be influenced by these factors since previous studies with different profiles samples have evidenced positive relationships.8,13–16 Lastly, caution is necessary regarding the generalizability of our findings to the general population because our cohort is composed by highly educated participants, and they might not have the same pressure to perform longer labour days than manual workers.

Some strengths of this study are its prospective design, the inclusion of a high number of participants, and a long-term follow-up enabling us to assume a sufficiently large induction period and to avoid reverse causation bias. In summary, we found that the working hours are not associated with MetS or any of its components. It is conceivable that other factors related to the work situation or what individuals do during their leisure time are more relevant than working hours to predict MetS or each of its individual criteria.

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Conflicts of interest: None declared.

Key points

- Working hours were not a risk factor for MetS or its components.
- Non-adherence of healthy lifestyle and other elements of the workplace, such as shift work and job strain, might be more important than working hours to predict MetS and its components, and should be considered in public health policies for workers.
- Further longitudinal studies in general population should be conducted to revaluate these associations.

References

Sickness absence at a young age and later sickness absence, disability pension, death, unemployment and income in native Swedes and immigrants

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Background: Sickness absence with cash benefits from the sickness insurance gives an opportunity to be relieved from work without losing financial security. There are, however, downsides to taking sickness absence. Periods of sickness absence, even short ones, can increase the risk for future spells of sickness absence and unemployment. The sickness period may in itself have a detrimental effect on health. The aim of the study was to investigate if there is an association between exposure to sickness absence at a young age and later sickness absence, disability pension, death, unemployment and income from work. Methods: Our cohort consisted of all immigrants aged 21–25 years in Sweden in 1993 (N= 38 207) and a control group of native Swedes in the same age group (N= 225 977). We measured exposure to sickness absence in 1993 with a follow-up period of 15 years. We conducted separate analyses for men and women, and for immigrants and native Swedes. Results: Exposure to ≥60 days of sickness absence in 1993 increased the risk of sickness absence [hazard ratio (HR) 1.6–11.4], unemployment (HR 1.1–1.2), disability pension (HR 1.2–5.3) and death (HR 1.2–3.5). The income from work, during the follow-up period, among individuals with spells of sick leave for ≥60 days in 1993 was around two-thirds of that of the working population who did not take sick leave. Conclusions: Individuals on sickness absence had an increased risk for work absence, death and lower future income.

Introduction

Sickness absence is a common and widely used treatment, intended to give patients time to recover without losing their financial security when ill. The sickness absence rate in Sweden has fluctuated much and regulations and benefit rates have changed relatively often compared with other European countries.1 The short-term economic consequences of sickness have been very low in Sweden as well in the other Nordic countries, with low barriers to access and a high compensation grade. It has been debated whether generous and easy accessible sickness benefits will increase the propensity to take sickness absence. Ill-health is an important factor for exclusion from labour market but the sickness period itself maybe a risk factor for illness and later exclusion from labour market.2–4 Illness is required in order to have sickness benefit, but the sickness period in itself may hamper later employability. A Swedish study concludes that sickness absence also has an impact for later sickness which goes beyond the effect of ill-health.2 In a qualitative study from Sweden, sick-listed persons regarded sickness absence to be a relief in the beginning. As time went by, however, the isolation and inactivity created emotional problems and alienation.5 Some individuals also believed that they were losing their independence when much of the decision making about their life was transferred to professionals.5 Long-term sickness