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**Psychosocial work factors of the job strain model and all-cause mortality: the STRESSJEM prospective cohort study**

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We wish to dedicate this paper to the memory of our highly valued colleague, Allison Milner, who died tragically and prematurely in August 2019.

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## ABSTRACT

**Objectives:** The objectives were to examine the prospective associations between psychosocial work factors of the job strain model and all-cause mortality in a national representative cohort of French employees using various measures of time-varying exposure.

**Methods:** The study was based on a sample of 798,547 men and 697,785 women for which data on job history from 1976 to 2002 were linked to mortality data from the national death registry. Psychosocial work factors from the validated job strain model questionnaire were imputed using a job-exposure matrix. Three time-varying measures of exposure were explored: current, cumulative, and recency-weighted cumulative exposure. Cox proportional hazards models were performed to study the associations between psychosocial work factors and mortality.

**Results:** Within the 1976-2002 period, 88,521 deaths occurred among men and 28,921 among women. Low decision latitude, low social support, job strain, isostrain, high strain, and passive job were found to be risk factors for mortality. The model using current exposure was the best relative quality model. The associations of current exposure to job strain and mortality were found to be HR=1.30 (95% CI: 1.24-1.36) among men and HR=1.15 (95% CI: 1.06-1.25) among women. The population fractions of mortality attributable to job strain were 5.64% (95% CI: 4.56%-6.71%) among men and 4.13% (95% CI: 1.69%-6.71%) among women.

**Conclusions:** This study supports the role of the psychosocial work factors of the job strain model on all-cause mortality. Preventive intervention to improve the psychosocial work environment may help to prevent mortality in working populations.

### Keywords

Cumulative exposure, job strain, job stress, job-exposure matrix, mortality, psychosocial work factors

**Abbreviations**

AIC: Akaike's Information Criterion

CépiDc: Centre d'épidémiologie et de recherche sur les causes médicales de Décès

COSMOP: COhorte de Surveillance de la MOrtalité selon l'activité Professionnelle

DADS: Déclaration Annuelle des Données Sociales

DARES: Direction de l'Animation de la Recherche, des Etudes et des Statistiques (French Ministry of Labour)

HR: hazard ratio

INSEE: Institut National de la Statistique et des Etudes Economiques

INSERM: Institut National de la Santé Et de la Recherche Médicale

JCQ: Job Content Questionnaire

JEM: job-exposure matrix

PAF: population attributable fraction

SUMER: SURveillance Médicale des Expositions aux Risques professionnels

## INTRODUCTION

Psychosocial work factors have emerged over recent decades as important contributors to occupational health and safety risks. These factors are very prevalent occupational hazards among working populations in developed countries. Their associations with morbidity have been explored extensively in two main areas: mental disorders, especially depression (1-3) and cardiovascular diseases, especially coronary heart disease and stroke (4-7). Studies have underlined the morbidity burden attributable to these factors and their related costs for society (8-10). By comparison, there has been less study of their associations with mortality.

Psychosocial work factors cover a large number of factors, and their assessment has usually been focused on a limited number of factors, considered crucial, that were included in theoretical models. Among these models, the job strain model is the most widely used theoretical model in the evaluation of psychosocial work factors, as assessed through the validated Job Content Questionnaire (JCQ) by Karasek (11). This model defines three main factors: psychological demands (defined by heavy workload in terms of both amount and complexity of work), decision latitude (defined by both decision authority and skill discretion), and social support from both colleagues and supervisor. These factors may be associated with various health outcomes, when measured individually or when assessed together through job strain (the combination of high demands and low latitude) and isostrain (the combination of job strain and low social support).

A very recent systematic literature review and meta-analysis on the associations between psychosocial work factors and all-cause mortality found that the only significant association was between low job control (i.e. low decision latitude) and mortality, and that the results were inconclusive for the other studied factors (12). Indeed, among the studies exploring the associations between the job strain model factors and all-cause mortality (13-28), some of them reported the associations of low decision latitude (13, 14, 23, 24, 28) and/or job strain with all-cause mortality (13, 16, 23, 28), whereas others did not. Although the literature comprises a number of studies, some gaps remain. Few of the previous studies had samples based on national representative working populations (but rather restricted occupational or geographical samples), limiting the generalizability of findings. Few studies had a large sample size and a large number of deaths during follow-up, and consequently most had low statistical power. Almost all studies used a measure of exposure at baseline only, making the

interpretation of the association between exposure and outcome complicated, especially with mortality occurring long after baseline exposure assessment. Most of the studies did not use the validated job strain model questionnaire, making the comparison between studies difficult. Most of them used self-reported exposure assessment, known to be subject to reporting bias, and three studies only (13, 23, 24) were based on a job-exposure matrix (JEM) for exposure assessment, allowing to reduce this bias. Indeed, such a JEM provides exposure assessment at the level of groups, having the same job title, and not at individual level.

The present study contributes to research on the topic of the job strain model exposures and all-cause mortality in several ways: by using a very large and nationally representative sample of the working population of men and women who were followed up over a long period of time, evaluating exposures via the validated and recommended JCQ and a JEM from national representative data, and constructing various time-varying measures of exposure.

The objective of the study was to explore the prospective associations between psychosocial work factors of the job strain model and all-cause mortality. An additional objective was to examine various time-varying measures of exposure including cumulative exposure.

## **METHODS**

The details of the protocol and methods of the STRESSJEM study were published previously (29). Ethical permissions were granted by French ethics committees: Commission Nationale de l'Informatique et des Libertés (no 762430V1 and no 04-1274) and Conseil National de l'Information Statistique (no 2009X705TV).

### **Study sample**

Briefly, the study relied on a national representative prospective cohort combining the data of the national SUMER survey (DARES, French Ministry of Labour) (30-32) for exposure assessment and of the COSMOP program (Santé publique France) (33) for job history and mortality data. The sources and linkage of the data are presented in Figure 1.

The COSMOP program relied on the linkage of two sources of existing routine data, job history data and mortality data, with the objective of providing information on the associations between job characteristics (mainly occupation and economic activity) and mortality. The two following sources of data were linked:

- 1) Job history data from 1976 to 2002 from the INSEE DADS Panel, based on a random sample -1/24<sup>th</sup>- of the national French working population of employees, i.e. 1,511,456 individuals. These data included the following information about job history, for all jobs held, over the 1976-2002 period: date of start and end of job, occupation, economic activity of the company, and company size.
- 2) Mortality data over the 1976-2005 period from the national French death registry, INSERM-CépiDc, in charge of causes of death statistics in France following common recommendations and guidelines in the European Community for certification and codification) (29).

The national SUMER survey is a periodical national representative survey on working conditions that assesses occupational exposures across the national French working population of employees. The data were collected by occupational physicians and by a self-administered questionnaire that included the recommended job strain model questionnaire (JCQ) among a study sample of 24,486 employees in 2003. A JEM for the job strain model exposures was constructed using these self-reported data and three job title variables (occupation, economic activity, and company size). The validity of this JEM was studied by comparing individual self-reports and JEM-derived measures as well as the results of the associations of these two measures of exposure with self-reported health. This validity study was published previously (32). One of the major strengths of JEMs is to reduce reporting bias that may impact the reliability of the assessment of psychosocial work factors. This JEM was used to impute exposure estimates using the three job title variables of occupation, economic activity, and company size for each job held during the 1976-2002 period in the job history data of the INSEE DADS Panel. In other words, mean scores of exposure from the JEM were imputed for each time (day)  $i$  according to occupation, economic activity, and company size. Consequently, each person of the DADS Panel had as many exposure estimates as the number of days spent in follow-up.

### **Measures of psychosocial work exposures**

Using all exposure estimates within the 1976-2002 period, three time-varying measures of exposure were constructed: current exposure, cumulative exposure, and recency-weighted cumulative exposure. Current exposure provided an estimate of exposure at time (day)  $i$  (calculated from the exposure at this time only, i.e. on a given day  $i$ ). Cumulative exposure provided an estimate of exposure until time  $i$ , i.e. an average measure at time  $i$  calculated using past and current exposures and the time spent in these exposures up to and including

time  $i$ . Recency-weighted cumulative exposure at time  $i$  was also an average measure until time  $i$ , calculated using past and current exposures within the 5 last years and the time elapsed since exposure with higher weights assigned to more recent exposures. We made the assumption that psychosocial work exposure effects persisted for a period of up to 5 years after the end of exposure based on a previously published study (13) and decreased linearly over a 5-year period to be null after 5 years. This 5-year period was chosen as a balanced compromise between current exposure at time  $i$  only and cumulative exposure until time  $i$ , that used the whole study period between 1976 and 2002, i.e. a maximum of 27 years and a mean follow-up period of 17 years in the study sample.

The measures used for current exposure were the following. Binary exposures for psychological demands, decision latitude, and social support, derived from the JEM scores dichotomized at the median of the distribution of the first job held over the 1976-2002 period among the total sample of men and women. The distribution of the first job was chosen in order to have information for one job only randomly for each person of the study sample, as people may have had more than one job over the study period. The binary variables for job strain and isostrain were obtained from the binary variables of demands, latitude and support, job strain being defined by the combination of high demands and low latitude, and isostrain by the combination of job strain and low support. The 4-category variable describing the four quadrants by Karasek was created on the basis of the combination of demands and latitude: high strain (high demands and low latitude), low strain (low demands and high latitude), passive job (low levels for both demands and latitude), and active job (high levels for both demands and latitude). Two alternative reference groups were used: active job and low strain.

The measures used for the two cumulative exposures (cumulative and recency-weighted cumulative exposure) were based on time-weighted scores for demands, latitude, and support as previously defined and dichotomized. Job strain, isostrain and the 4-quadrant variable were constructed as mentioned earlier.

### **Statistical methods**

Cox proportional hazards models were used to estimate hazard ratios (HR) of all-cause mortality according to the studied exposures, which were time-dependent variables. We checked the assumption of proportionality by graphical analysis (Supplementary Figures S1-S3). No violation of proportionality was found. However, the survival curves at older ages,

especially among women, were based on a very low number of persons and had very large confidence intervals. Age was used as the time scale. Persons entered the follow-up at the age they had at time origin (baseline age), which refers to left truncation, and exited the follow-up at the age they had at event or censoring time (which refers to right censoring). Calendar time and four occupational variables related to biomechanical, physical, chemical and biological exposures were included as adjustment variables (covariates). Calendar time was used to control for changes in the outcome over time (mortality decreased over the follow-up period). The four occupational exposures (whose assessment was performed by occupational physicians and whose definition can be found elsewhere (30)) were obtained from a JEM constructed using the same method as psychosocial work factors (32) and were used as proxies for socioeconomic status or social position, as these exposures were found to display strong social gradients (31). All results were presented with age as the time scale and adjustment for covariates. Kaplan-Meier survival curves with age as the time scale and adjustment for covariates were also used to present the results. We used a model with delayed entry. Individuals entered the cohort on the 1<sup>st</sup> January 1976 if they already had a job or when they started a first job within the 1976-2002 period.

As we had complete job history and exposure assessment during follow-up, we were able to study the associations of exposures with both mortality during time intervals with a job and mortality during the entire follow-up (including mortality after the end of last job). For the 3 exposure measures, we used mortality until the end of last job, to study mortality during time intervals with a job (called 'on-the-job' mortality); thus in this analysis, the follow-up ended at the time of death or at the end date of the last job within the 1976-2002 period, or at the end of follow-up (31st December 2002) if still working at this time, whichever came first. For the 2 measures of cumulative exposure, as delayed effects may be expected, a second analysis was performed in which the follow-up ended at the time of death or on the 31st December 2002, whichever came first. Three types of models were performed: (1) with each exposure separately, (2) with the exposures of demands, latitude, and support together, (3) with job strain, isostrain, and the 4-quadrant variable respectively. Comparisons between the models according to exposure measure were performed to identify the model with the best relative quality using Akaike's Information Criterion (AIC).

Finally, the population fractions of all-cause mortality attributable to the exposures of job strain and isostrain in France were calculated using the following formula:

$$\text{PAF} = \text{Pe}(\text{HR}-1)/[1+\text{Pe}(\text{HR}-1)]$$

with PAF being the population attributable fraction, Pe the prevalence of exposure and HR the hazard ratio for mortality associated with exposure. Pe was estimated by the weighted prevalence of exposure to job strain (19.94% among men, 28.70% among women) and iso-strain (12.72% among men, 17.44% among women) using the data of the SUMER survey. HR was estimated by the results from the present study. Simulation-modelling techniques were used to obtain confidence intervals for PAFs, as previously described (9).

As we found significant interaction terms between gender and psychosocial work factors in the total sample, suggesting gender-related differences for all exposure-outcome associations, the results were presented for each gender separately. All analyses were performed using SAS and R softwares.

### **Sensitivity analyses**

Sensitivity analyses were performed to test the robustness of the results. First, we used scores instead of binary variables for the measure of exposure. Second, we adjusted for the large groups of occupation instead of adjusting for the four occupational biomechanical, physical, chemical and biological exposures. Third, we imputed the lowest level of exposure instead of the highest level of exposure in case of multiple job-holder (only 3% of the sample had more than one job at the same time). Fourth, we extended the follow-up and studied mortality until 2005 instead of 2002. Fifth, as our measures of cumulative exposure and recency-weighted cumulative exposure may be imprecise for the first years of follow-up, we performed the analyses again after exclusion of the years of 1976-78.

## **RESULTS**

The studied sample was restricted to 1,496,332 individuals, including 798,547 men and 697,785 women because of missing values for job history among 15,214 individuals (i.e. 1%). Within the 1976-2002 period, 88,521 deaths occurred among men and 28,921 occurred among women, including 17,250 deaths among men and 4,201 among women during time intervals with a job ('on the job' mortality). A description of the job strain model factors among the study sample can be found in our previously published study protocol (29). In brief, women

were more likely to be exposed to almost all exposures: high psychological demands, low decision latitude, low social support, job strain, iso-strain, and high strain. Men were more likely to be exposed to low strain and passive job.

Tables 1-3 present the results of the associations between current, cumulative and recency-weighted cumulative exposures and mortality. Low decision latitude, low social support, job strain, isostrain, high strain, and passive job were found to be associated with mortality for almost all models and both genders. High psychological demands were a protective or non-significant factor among men and a risk factor among women, especially when on-the-job mortality was studied. The results for current exposure (Table 1) showed that psychosocial work factors increased the risk of mortality by 9-44% among men and 13-53% among women. The results for current exposure to job strain, iso-strain, and the four quadrants by Karasek are also presented using Kaplan-Meier survival curves in Supplementary Figures S1-S3. The results were very similar in the sensitivity analyses.

The study of gender-related interactions showed that all interaction terms were found to be significant, supporting gender differences in the observed associations. The most striking results were the following: the association between psychological demands and mortality was found to be significant among women only, and the associations of low decision latitude, job strain, and isostrain with mortality were in general stronger among men than among women. Furthermore, the low-risk situation was low strain among women whereas this was active job or low strain among men. The Supplementary Figures S1-S3 confirm and further illustrate these gender differences.

The comparison between the models for the two cumulative exposure measures (Tables 2-3) suggested that, although the statistical power was higher, because of a larger number of deaths, the study of mortality until 31/12/2002 (i.e. after the end of the last job) led to a reduction in the magnitude of most of HRs (i.e. a dilution of the effects of exposure after end of job) compared to the study of 'on-the-job' mortality.

The results were very similar for the three measures of exposure. However, the calculation of AICs showed that the model with the highest relative quality was the model including current exposure and the model with the lowest relative quality was the model including cumulative exposure (significant difference among men, but non-significant among women), the model

with recency-weighted cumulative exposure being in between. Given these results, we calculated the population fractions of mortality attributable to current exposure to job strain and iso-strain. Regarding job strain, the PAFs were 5.64% (95% CI: 4.56%-6.71%) among men and 4.13% (95% CI: 1.69%-6.71%) among women. Regarding iso-strain, the PAFs were 3.56% (95% CI: 2.71%-4.28%) among men and 2.71% (95% CI: 1.03%-4.19%) among women.

## **DISCUSSION**

### **Summary of the results**

This study showed that low decision latitude, low social support, job strain, isostrain, high strain, and passive work were found to be risk factors for all-cause mortality in the national French working population of employees. These results were observed for current exposure but also for cumulative and recency-weighted cumulative exposures, although the model with the best relative quality was the model using current exposure. The population fractions of mortality attributable to job strain were 5.64% for men and 4.13% for women.

### **Comparison with the literature**

We compared our results to the studies that explored the associations between psychosocial work factors of the job strain model and all-cause mortality (13-28), although unlike ours, almost all of these studies used a measure of exposure at baseline only. The most robust result found in our study and in the literature is the association between low decision latitude and mortality. Indeed, low decision latitude (also called low job control) was the only significant risk factor for all-cause mortality in a recent review and meta-analysis (12), with five previous studies (13, 14, 23, 24, 28) showing a significant association between this factor and mortality. In our study, we found that low social support was a risk factor for mortality. There were very few previous studies exploring social support in association with mortality (13, 14, 19, 22, 25), and only two studies found low social support as a risk factor (22, 25). Our results appear inconclusive for high psychological demands, which were found to be either non-significant, or a protective factor, or a risk factor according to the model considered. These inconclusive results echo the results of the literature. Indeed, among the studies that explored psychological demands, most of them did not find any association for this factor (13-16, 19, 24, 27), except one study for which psychological demands were observed as a risk factor (23) and another study for which this exposure was a protective factor among women (28). It

is however noticeable in our study that psychological demands were a risk factor for on-the-job mortality among women.

Among the combined variables of job strain, isostrain, and quadrants, the most studied variables were job strain and the four quadrants in the literature. In our study, the association between job strain and mortality was significant, and the association was also significant for the high strain quadrant. Among the studies that explored job strain or the high strain quadrant, the results are mixed with a number of studies reporting significant associations between job strain or high strain and mortality (13, 16, 23, 28) and others for which the results were not significant (15, 26, 27). Regarding the results for the other quadrants, our results suggested that passive work was associated with mortality. Only two studies reported an association between passive work and mortality (13, 28), and some others did not (15, 23, 26, 27). Our results using either active job or low strain as reference group suggested that the low-risk situation might be low strain among women, and active work or low strain among men. Some studies in the literature used active work as the reference category (13, 26), whereas some others used low strain (27, 28) or high strain (15) or all other quadrants as reference for the study of each quadrant (23). This makes comparison between studies difficult due to different perspectives on the most appropriate reference category. Our study showed that isostrain was a risk factor for mortality and may thus be the first one to report such an association.

If we limit our comparison with the three studies that also used a JEM (13, 23, 24), our results for decision latitude are perfectly consistent with these three studies (13, 23, 24). Our results are in agreement with two of these studies for job or high strain (13, 23) and with the study by Amick et al. for passive job (13). Only the study by Nilsen et al. (23) reported an association between psychological demands and mortality whereas the two other studies did not. The absence of evidence for psychological demands may be related to the relatively lower performance of JEMs for this factor compared to the other factors.

Only one previous study explored a cumulative exposure measure for psychosocial work factors and all-cause mortality. In this study, Amick et al. (13) used a measure of cumulative exposure that took the time spent in each quartile of the exposure distribution into account within the study time period, i.e. 1968-1991. The study by Amick et al. was performed using an exposure lag of 5 years, that censored the exposure information after 5 years past the last

job. Consequently, the measure used by Amick et al. is close to our measure of recency-weighted cumulative exposure although there were no weights in the exposure within a 5-year period in their study whereas we assumed a linear decrease of the effects in our study. Amick et al. also performed an analysis using a 10-year lag. There was no difference in Amick's results according to the choice of the lag, and the conclusions were the same for low decision latitude, high strain, and passive work, that were found to be risk factors for mortality in the analyses using both the 5-year and 10-year lags. The absence of differences between the two exposure lags observed by Amick et al. is in agreement with our results that provided no major difference in results using cumulative exposure or recency-weighted cumulative exposure. What our study adds in this topic is that the relative quality of the models may be higher using current exposure instead of cumulative exposure, suggesting that current or more recent exposure may be more important than past exposure.

### **Limitations and strengths of the study**

The study included a number of strengths. It was based on a very large national representative sample of men and women and gender differences were explored leading to stratified analyses on gender. Indeed, the observed gender-related interactions suggested that the exposure-outcome associations were not the same for men and women, because of differences in the significance or magnitude of the associations between genders. Psychological demands played a substantial role in mortality among women, whereas the other factors, and particularly low decision latitude, job strain, and isostrain were more strongly associated with mortality among men. Although these results may be difficult to interpret, they suggest that more attention should be given to gender differences in this topic. The study had a long follow-up for both exposure and outcome. There was no response bias (all data were routine data collected independently from the people), and there was consequently no participation or selection bias. However, a healthy worker effect could not be ruled out for the study of current exposure and on-the-job mortality which may have underestimated the exposure-outcome associations. There was no attrition bias as we had complete follow-up for the whole study sample. There was no reporting bias as both outcome (based on data from the national registry) and exposure (assessed using a JEM) were objective measures. Consequently, perception or personality factors could not impact our results. Adjustment was made for other occupational exposures that also served as reasonable proxies for socioeconomic status or social position, and led to more conservative estimates in the models. Taking these other exposures into account was thus a cautious approach. The validated and recommended questionnaire for the job strain

model (JCQ) was used to measure the exposures. The study included different measures of time-varying exposure, which is very rare in the literature. The cumulative measure of exposure using past and current exposures during follow-up implied the persistence of exposure over time. The recency-weighted cumulative measure was based on past and current exposures over a 5-year period with higher weights assigned to more recent exposures. The comparison between the three measures of exposure suggested that current or the most recent exposure may be more important than past exposure. Mortality was provided by the national French Death Registry that is in charge of national mortality data in France. The study explored two outcomes ('on-the-job' and until 31/12/2002 mortality). Using the first outcome, the persons were working and there was no distance between exposure and outcome (the exposure was still present at the time of death). Using the second outcome, the persons may have stopped working and there may have been a distance between exposure and outcome. It was a way to test the effects of exposure even after the exposure had stopped. The magnitude and significance of HRs were smaller for the second outcome compared to the first one suggesting a dilution of the effects of exposure over time, or in other words a potential reversibility of the effects of exposure, after removal of exposure. Several sensitivity analyses were performed that confirmed the robustness of the results. The literature on the effects of psychosocial work factors on morbidity, especially mental disorders and cardiovascular diseases brings support to the results we observed, as these factors may impact all-cause mortality through specific causes of death such as suicide and cardiovascular mortality. Our analyses according to specific causes of death, particularly suicide, cardiovascular mortality, and preventable mortality (including mortality related to high-risk behaviours such as smoking and alcohol use), reinforce the plausibility of the associations between psychosocial work factors of the job strain model and all-cause mortality (34-36). Finally, to our knowledge, this study is the first one to provide estimates of the population fractions of all-cause mortality attributable to job strain and iso-strain. The population attributable fractions of mortality were however related to two specific exposures (job strain and iso-strain) and may underestimate the global burden of mortality attributable to psychosocial work factors, as other exposures such as for example job insecurity or long working hours were not studied.

A number of limitations should, however, be acknowledged. There was a limited number of adjustment/stratification variables, as the study relied on routine data only. Consequently, residual confounding bias is likely. The results may be affected by the inherent limitations of JEM, leading to non-differential misclassification and bias towards the null hypothesis.

Moreover, even if the use of JEM has pros and cons, it may be underlined that the assessment of psychosocial work exposures using JEMs may differ in nature from the assessment through self-reports, as JEMs remove the individual perception and reporting of exposure, and there only remains the exposure as captured by job title (occupation for example). There was missing information for some jobs, that was treated using midcensoring. There was no evaluation of complete working life course measures of exposure, as the data were related to the 1976-2002 period only. The global impact of all these limitations on the results was difficult to assess, as they implied both under- and over-estimation of the associations.

### **Conclusion**

Our study showed that psychosocial work factors were associated with all-cause mortality. The results were found to be significant for low decision latitude, low social support and the combined exposures of job strain, isostrain, high strain, and passive work. The estimated population attributable fractions suggested that these factors may play a role on the burden of mortality, and that prevention policies oriented towards psychosocial work factors may be beneficial for mortality as well as other associated adverse effects on health.

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Figure 1. Diagram of the sources and linkage of the data (illustration of the following references: (29, 32), see abbreviations at the beginning of the present study)

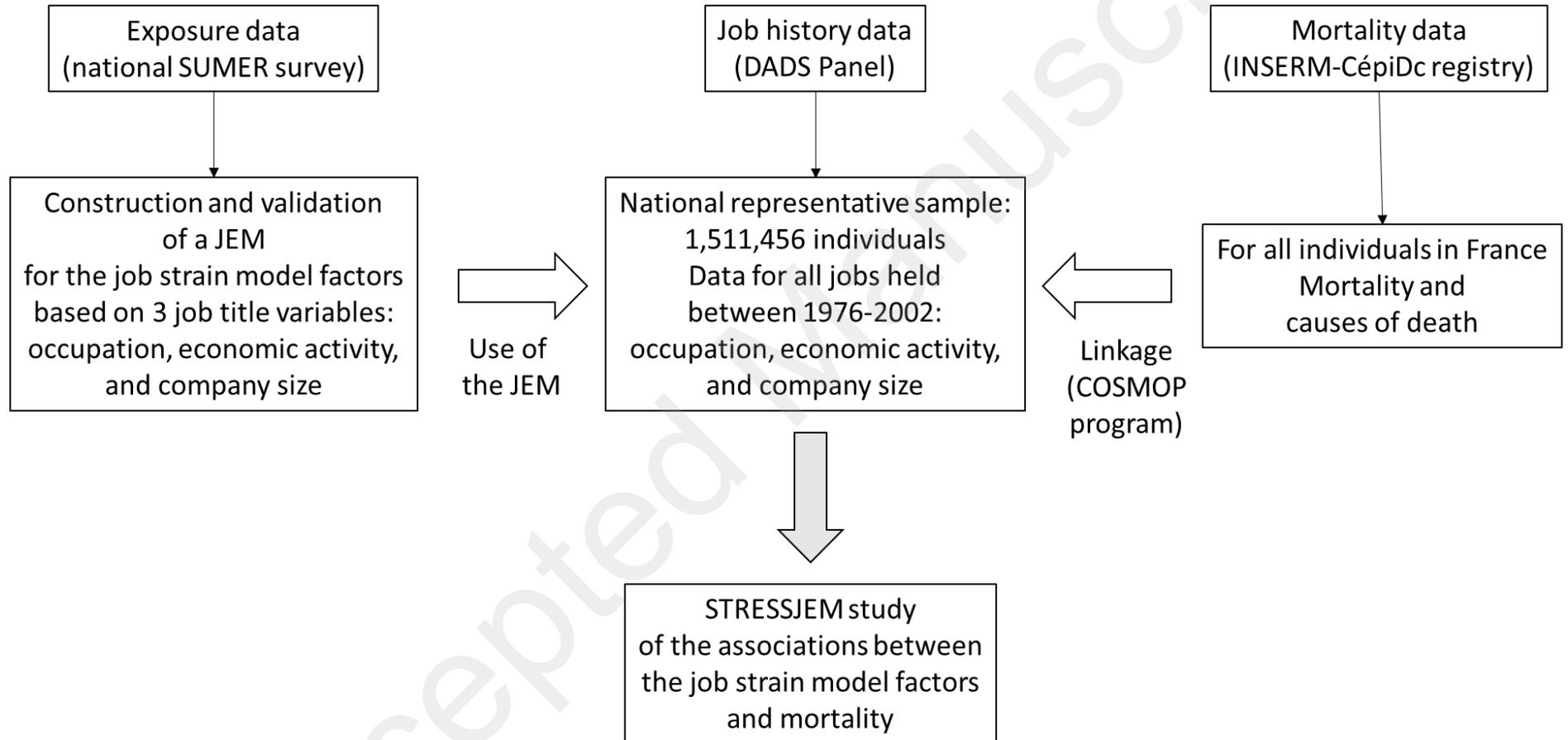


Table 1. Associations between current exposure and all-cause mortality among men and women

	MEN (N=798,547)	WOMEN (N=697,785)
	HR (95% CI)	HR (95% CI)
	(Deaths=17,250)	(Deaths=4,201)
High psychological demands <sup>a</sup>	<b>0.90 [0.86-0.94] ***</b>	<b>1.16 [1.08-1.24] ***</b>
Low decision latitude <sup>a</sup>	<b>1.37 [1.32-1.42] ***</b>	<b>1.17 [1.07-1.28] ***</b>
Low social support <sup>a</sup>	<b>1.32 [1.28-1.37] ***</b>	<b>1.20 [1.12-1.29] ***</b>
High psychological demands <sup>b</sup>	1.01 [0.97-1.06] ns	<b>1.15 [1.07-1.25] ***</b>
Low decision latitude <sup>b</sup>	<b>1.28 [1.22-1.36] ***</b>	1.10 [0.99-1.23] ns
Low social support <sup>b</sup>	<b>1.09 [1.03-1.15] **</b>	<b>1.13 [1.04-1.23] **</b>
Job strain <sup>a</sup>	<b>1.30 [1.24-1.36] ***</b>	<b>1.15 [1.06-1.25] ***</b>
Isostrain <sup>a</sup>	<b>1.29 [1.22-1.35] ***</b>	<b>1.16 [1.06-1.25] ***</b>
<b>Quadrants by Karasek<sup>a</sup></b>		
Active job (ref)	1	1
Low strain	1.05 [0.99-1.11] ns	<b>0.74 [0.65-0.83] ***</b>
Passive job	<b>1.37 [1.31-1.44] ***</b>	1.03 [0.93-1.14] ns
High strain	<b>1.44 [1.37-1.52] ***</b>	<b>1.13 [1.02-1.25] *</b>
<b>Quadrants by Karasek<sup>a</sup></b>		
Active job	0.95 [0.90-1.01] ns	<b>1.36 [1.20-1.53] ***</b>
Low strain (ref)	1	1
Passive job	<b>1.31 [1.25-1.37] ***</b>	<b>1.40 [1.22-1.60] ***</b>
High strain	<b>1.37 [1.29-1.46] ***</b>	<b>1.53 [1.34-1.75] ***</b>

<sup>a</sup> Each exposure was studied separately

<sup>b</sup> Demands, latitude and support were studied simultaneously

High strain (high demands and low latitude), low strain (low demands and high latitude), passive job (low demands and low latitude), and active job, the reference group (high demands and high latitude)

All models were adjusted for calendar time, biomechanical, physical, chemical and biological exposures

\*p<0.05, \*\*p<0.01, \*\*\*p<0.001

Bold black: significant risk factor (p<0.05)

Bold grey: significant protective factor (p<0.05)

Table 2. Associations between cumulative exposure and all-cause mortality among men and women

Follow-up	MEN (N=798,547)		WOMEN (N=697,785)	
	<b>On-the-job</b> HR (95% CI) (Deaths=17,250)	<b>Until 31/12/2002</b> HR (95% CI) (Deaths=88,521)	<b>On-the-job</b> HR (95% CI) (Deaths=4,201)	<b>Until 31/12/2002</b> HR (95% CI) (Deaths=28,921)
High psychological demands <sup>a</sup>	<b>0.94 [0.90-0.97]</b> **	<b>0.86 [0.85-0.88]</b> ***	<b>1.29 [1.19-1.39]</b> ***	<b>0.92 [0.90-0.95]</b> ***
Low decision latitude <sup>a</sup>	<b>1.35 [1.31-1.40]</b> ***	<b>1.22 [1.20-1.24]</b> ***	<b>1.09 [1.01-1.17]</b> *	<b>1.19 [1.16-1.23]</b> ***
Low social support <sup>a</sup>	<b>1.29 [1.24-1.33]</b> ***	<b>1.09 [1.07-1.11]</b> ***	<b>1.24 [1.16-1.33]</b> ***	<b>1.09 [1.06-1.12]</b> ***
High psychological demands <sup>b</sup>	1.01 [0.96-1.05] ns	<b>0.90 [0.88-0.92]</b> ***	<b>1.26 [1.16-1.37]</b> ***	<b>0.92 [0.90-0.95]</b> ***
Low decision latitude <sup>b</sup>	<b>1.27 [1.22-1.32]</b> ***	<b>1.19 [1.17-1.21]</b> ***	1.06 [0.97-1.15] ns	<b>1.15 [1.11-1.19]</b> ***
Low social support <sup>b</sup>	<b>1.16 [1.12-1.20]</b> ***	1.00 [0.99-1.02] ns	<b>1.17 [1.08-1.26]</b> ***	<b>1.06 [1.03-1.10]</b> ***
Job strain <sup>a</sup>	<b>1.28 [1.21-1.34]</b> ***	<b>1.17 [1.14-1.20]</b> ***	<b>1.18 [1.10-1.27]</b> ***	1.02 [0.99-1.05] ns
Isostrain <sup>a</sup>	<b>1.30 [1.23-1.37]</b> ***	<b>1.15 [1.12-1.18]</b> ***	<b>1.20 [1.12-1.29]</b> ***	1.02 [0.99-1.05] ns
<b>Quadrants by Karasek<sup>a</sup></b>				
Active job (ref)	1	1	1	1
Low strain	1.00 [0.95-1.05] ns	<b>1.18 [1.16-1.21]</b> ***	<b>0.61 [0.53-0.72]</b> ***	0.99 [0.95-1.04] ns
Passive job	<b>1.34 [1.28-1.40]</b> ***	<b>1.34 [1.31-1.37]</b> ***	<b>0.88 [0.80-0.97]</b> *	<b>1.25 [1.20-1.30]</b> ***
High strain	<b>1.39 [1.32-1.47]</b> ***	<b>1.32 [1.29-1.35]</b> ***	1.07 [0.98-1.16] ns	<b>1.15 [1.10-1.19]</b> ***
<b>Quadrants by Karasek<sup>a</sup></b>				
Active job	1.00 [0.95-1.05] ns	<b>0.84 [0.83-0.86]</b> ***	<b>1.63 [1.40-1.90]</b> ***	1.01 [0.96-1.06] ns
Low strain (ref)	1	1	1	1
Passive job	<b>1.34 [1.28-1.40]</b> ***	<b>1.13 [1.11-1.15]</b> ***	<b>1.43 [1.22-1.68]</b> ***	<b>1.26 [1.19-1.32]</b> ***
High strain	<b>1.39 [1.31-1.48]</b> ***	<b>1.11 [1.09-1.14]</b> ***	<b>1.74 [1.49-2.03]</b> ***	<b>1.15 [1.10-1.21]</b> ***

<sup>a</sup> Each exposure was studied separately

<sup>b</sup> Demands, latitude and support were studied simultaneously

High strain (high demands and low latitude), low strain (low demands and high latitude), passive job (low demands and low latitude), and active job, the reference group (high demands and high latitude)

All models were adjusted for calendar time, biomechanical, physical, chemical and biological exposures

\*p<0.05, \*\*p<0.01, \*\*\*p<0.001

Bold black: significant risk factor (p<0.05)

Bold grey: significant protective factor (p<0.05)

Table 3. Associations between recency-weighted cumulative exposure and all-cause mortality among men and women

Follow-up	MEN (N=798,547)		WOMEN (N=697,785)	
	<b>On-the-job</b> HR (95% CI) (Deaths=17,250)	<b>Until 31/12/2002</b> HR (95% CI) (Deaths=88,521)	<b>On-the-job</b> HR (95% CI) (Deaths=4,201)	<b>Until 31/12/2002</b> HR (95% CI) (Deaths=28,921)
High psychological demands <sup>a</sup>	<b>0.92 [0.88-0.95]</b> ***	<b>0.83 [0.81-0.85]</b> ***	<b>1.34 [1.25-1.45]</b> ***	<b>0.92 [0.88-0.96]</b> ***
Low decision latitude <sup>a</sup>	<b>1.38 [1.33-1.43]</b> ***	<b>1.23 [1.21-1.26]</b> ***	<b>1.17 [1.08-1.27]</b> ***	<b>1.25 [1.19-1.31]</b> ***
Low social support <sup>a</sup>	<b>1.43 [1.38-1.48]</b> ***	<b>1.16 [1.14-1.19]</b> ***	<b>1.30 [1.21-1.39]</b> ***	<b>1.11 [1.06-1.15]</b> ***
High psychological demands <sup>b</sup>	1.02 [0.98-1.06] ns	<b>0.88 [0.85-0.90]</b> ***	<b>1.33 [1.23-1.44]</b> ***	<b>0.93 [0.89-0.98]</b> **
Low decision latitude <sup>b</sup>	<b>1.19 [1.14-1.24]</b> ***	<b>1.18 [1.15-1.21]</b> ***	<b>1.11 [1.01-1.22]</b> *	<b>1.20 [1.13-1.28]</b> ***
Low social support <sup>b</sup>	<b>1.29 [1.24-1.35]</b> ***	<b>1.04 [1.01-1.07]</b> **	<b>1.20 [1.11-1.30]</b> ***	1.05 [1.00-1.10] ns
Job strain <sup>a</sup>	<b>1.29 [1.23-1.36]</b> ***	<b>1.21 [1.17-1.24]</b> ***	<b>1.32 [1.22-1.42]</b> ***	1.04 [0.99-1.09] ns
Isostrain <sup>a</sup>	<b>1.30 [1.24-1.37]</b> ***	<b>1.15 [1.12-1.19]</b> ***	<b>1.34 [1.25-1.45]</b> ***	1.05 [1.00-1.10] ns
<b>Quadrants by Karasek<sup>a</sup></b>				
Active job (ref)	1	1	1	1
Low strain	1.02 [0.97-1.07] ns	<b>1.27 [1.23-1.31]</b> ***	<b>0.65 [0.57-0.75]</b> ***	1.01 [0.93-1.08] ns
Passive job	<b>1.37 [1.31-1.44]</b> ***	<b>1.39 [1.35-1.44]</b> ***	<b>0.90 [0.81-1.00]</b> *	<b>1.31 [1.23-1.40]</b> ***
High strain	<b>1.43 [1.36-1.51]</b> ***	<b>1.40 [1.36-1.45]</b> ***	<b>1.20 [1.09-1.31]</b> ***	<b>1.20 [1.13-1.28]</b> ***
<b>Quadrants by Karasek<sup>a</sup></b>				
Active job	0.98 [0.93-1.03] ns	<b>0.79 [0.76-0.81]</b> ***	<b>1.53 [1.34-1.75]</b> ***	0.99 [0.92-1.07] ns
Low strain (ref)	1	1	1	1
Passive job	<b>1.35 [1.29-1.41]</b> ***	<b>1.10 [1.07-1.13]</b> ***	<b>1.38 [1.19-1.60]</b> ***	<b>1.30 [1.21-1.41]</b> ***
High strain	<b>1.40 [1.32-1.49]</b> ***	<b>1.11 [1.07-1.15]</b> ***	<b>1.83 [1.59-2.11]</b> ***	<b>1.19 [1.10-1.29]</b> ***

<sup>a</sup> Each exposure was studied separately

<sup>b</sup> Demands, latitude and support were studied simultaneously

High strain (high demands and low latitude), low strain (low demands and high latitude), passive job (low demands and low latitude), and active job, the reference group (high demands and high latitude)

All models were adjusted for calendar time, biomechanical, physical, chemical and biological exposures

\*p<0.05, \*\*p<0.01, \*\*\*p<0.001

Bold black: significant risk factor (p<0.05)

Bold grey: significant protective factor (p<0.05)