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ORIGINAL ARTICLE

Workplace stress and prescription of antidepressant medications: a prospective study on a sample of Italian workers

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Abstract
Purpose The main aim of this study was to examine prospectively the relationship between antidepressant prescriptions (ADP), as a proxy of depressive symptoms, and work-related stress, measured according to the demand–control model.
Methods A cohort of 2,046 union workers who participated in a survey on working conditions and health in 1999–2000 was followed up to 2005, through the Regional Drug Prescription Register, for an ADP. The relative risks associated with demand, control and job strain were estimated using Poisson regression, adjusting for age, sex and other workplace factors (shift work, overtime, loud noise and psychological violence).
Results In final multivariable models, high demand significantly increased the risk of depressive symptoms among blue collars (RR = 1.82), whereas among white collars, it was significantly protective (RR = 0.38). No significant relationship was found for job control or strain in either occupational class.
Conclusions The direct association observed elsewhere among blue collars between depressive symptoms and demand was confirmed, but not for job control or job strain. It cannot be ruled out that the association with demand was at least in part determined by reverse causation, due to exposure over-reporting among subjects with subclinical depressive symptoms at baseline. The protective effect of demand among white collars is not consistent with the literature and may be attributable to the particular characteristics of this sample, which included mainly workers employed in public administrative positions.

Keywords Depressive symptoms · Antidepressants · Demand–control · Work · Stress · Epidemiology

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Introduction

According to the World Mental Health Survey 2001 promoted by WHO, the 12-month prevalence for any mental health disorder in Europe ranges from 8.2 to 20.5%; anxiety and mood disorders account for over 90% of mental illness in non-institutionalized populations, with an estimated 12-month prevalence of 5.9–12.0% for anxiety and 3.6–9.1% for mood disorders (Demyttenaere et al. 2004). Depressive syndromes, in particular, are an important public health burden in the Euro Area in terms of Disability Adjusted Life Years lost (WHO 2008). In fact, depression has generally a long duration (Tylee et al. 1999), and about one-third of cases presenting with an acute episode develop chronic symptoms (Judd et al. 1998). Depression contributes to long-term sick leave (Henderson et al. 2005) and early retirement (Karpansalo et al. 2005) and is an independent risk factor for coronary heart disease (Rugulies 2002; Wulsin and Singal 2003).

Depressive syndromes are more frequent among women, middle-aged people and those of lower socio-economic status (Everson et al. 2002; Savoie et al. 2004). They have been associated with stressful life events, such as the death of a close relative (spouse or child), divorce, severe illness or injury, job loss or major financial problems (Kessler 1997), and with social isolation or poor social support (Leskela et al. 2006). Depressive syndromes have also been linked to several occupational factors, such as long working hours (Harrington 1994a; Spurgeon et al. 1997), shift work (Harrington 1994b), noise (Stansfeld 1992), job insecurity (Rugulies et al. 2006), work-related violence or threat (Eriksen et al. 2006), and to psychosocial factors related to work organization, such as low autonomy, low influence, low social support, high monotony and intense quantitative demands (Rugulies et al. 2006; Paterniti et al. 2002; Wang 2004; Shields 2006).

One of the most popular models for assessing exposure to workplace psychosocial factors is the demand–control model (Karasek 1985), according to which a work environment characterized by high psychological demand (fast pace and both high and conflicting demands) and low decision latitude (low level of both autonomy and use of skills) exposes workers to high strain. In the original model proposed by Karasek, the combination of the levels of exposure to psychological demand and decision latitude (also named "job control") would give rise to four types of jobs. High strain jobs, i.e., jobs with high demand and low decision latitude, would involve a higher risk of negative effects on mental health, compared to the other three groups, because the potential harmful effect of being exposed to high demand would not be moderated by sufficient resources of the worker, in terms of autonomy, variety of tasks and use of skills, as it would happen for "active" jobs, similarly characterized by high levels of demand, but also by high decision latitude. The last two types include jobs with low psychological demand: those with high decision latitude ("low strain" jobs) would be associated with the lowest risk of ill health, because the workers would have limited challenges and enough resources to deal with these challenges, whereas the "passive" jobs, characterized by both low levels of demand and decision latitude, would produce loss of motivation and atrophy of workers' skills, but not increased levels of psychological strain. The four job groups have been more often obtained by dividing the demand and the control scales at their median values, and the occurrence of health effects associated with exposure to high strain has been compared with that in the low strain group or in the other three groups combined; in other studies, the job strain dimension has been built as a continuous variable, dividing the value of the demand scale by that of the control one (Landsbergis et al. 1994; Choi et al. 2008).

Although the mechanisms through which exposure to stress would cause depression are largely unknown and several neurotransmitters are likely involved (McEwen 2008), a sustained activation of hypothalamus–pituitary–adrenal cortex (HPA) axis appears to play an important role (Herman and Cullinan 1997). Under physiologic conditions, exposure to different types of physical and psychological acute stressors causes the secretion from neurons in the paraventricular nucleus (PVN) of the hypothalamus of the corticotropin release hormone (CRH), which stimulates the release of the adrenocorticotropin hormone (ACTH) from the anterior pituitary; this hormone stimulates the secretion from the adrenal cortex into the bloodstream of glucocorticoids (cortisol in humans), which are pivotal hormones in the regulation of most essential physiological processes, including energy metabolism, modulation of the immune system and stress responses. Glucocorticoids also exert an inhibitory effect on the synthesis and secretion of CRH, which reduces the activity of the HPA axis when glucocorticoids levels are sufficiently high (Herman and Cullinan 1997). In chronic stress, this negative feedback mechanism would be impaired, with the consequence of oversecretion of CRH, ACTH and cortisol and disruption of the circadian pattern of cortisol secretion (McEwen 1998). Support to this model comes from observations of persistently high cortisol levels, together with changes in the circadian pattern of cortisol secretion, in both subjects exposed to different types of psychosocial stressors (Steptoe et al. 2000; Evolahti et al. 2006; Chida and Steptoe 2009) and patients affected by depression (Deuschle et al. 1997; Carroll et al. 2007).

Many of the earlier epidemiologic studies using the demand–control model, reviewed by Van der Doef and Maes (1999), found workers exposed to high strain at increased risk of psychological distress or depressive symptoms. Most of these studies, however, were cross-sectional in which a positive association could have been generated by differential reporting of workplace stressors by case status. Furthermore, because the great majority of studies in this research area relied on self-reports of psychosocial exposures, the possibility of reverse causation due to over-reporting of unfavorable working conditions among subjects with poor mental health, burnout, negative affectivity or low self-esteem has been risen by several authors (Mills and Huebner 1998; de Lange et al. 2004, 2005; Stansfeld and Candy 2006). More recent longitudinal studies have supported the demand–control model, for the most part, although several found associations with high demand or low control, but not with job strain (de Lange et al. 2003; Stansfeld and Candy 2006).

The effect of workplace stress is likely modified by the cultural and social context, and hence the necessity of studying it in diverse national and regional settings. To our

knowledge, no longitudinal studies on the relationship between depressive syndromes and work-related stress have been conducted in Italy. One reason for this is the scarcity of information systems in which medical consultations for mental health problems, and related diagnoses, are systematically recorded. This makes case ascertainment in a large cohort problematic and very labor intensive.

Given that, in recent years, antidepressants are recommended in the treatment of both depressive and anxiety disorders (Dannon et al. 2004; Hansen et al. 2008), a prescription of antidepressants appears a useful proxy indicator for the all types of depressive symptoms with psychological and/or somatic complaints. In clinical practice, the primary source of these prescriptions is general practitioners, who use symptoms rather than complex diagnostic tools for making their treatment decisions. The existence of an archive of antidepressant prescriptions supplied through the public health care system, covering the entire resident population in the Piedmont region of Italy, provided a feasible opportunity to follow up a cohort of workers for depressive symptoms, who had been assessed for exposure to psychosocial and other hazards at work.

The main aim of this study was to examine the relationship between the presence of depressive symptoms, as assessed by antidepressant prescriptions (ADP), and self-reported exposure to workplace stressors, measured according to the demand–control model, in an Italian cohort of workers.

Methods

Data collection

The study population consisted of members of the General Confederation of Italian Workers (CGIL) trade union in the Turin area of the Piedmont region. During 1999–2000, a questionnaire on working conditions and health was distributed by CGIL to about 7,000 of its members in the Turin area who were working in 206 companies that employed at least 15 workers, within a wide range of economic sectors such as power generation and distribution, textile and rubber industries, metalworking, mechanics, motor vehicle manufacturing, transportation, communication, etc. The questionnaire contained over 200 items concerning demographics, work characteristics, exposure to chemical, physical, ergonomic and psychosocial factors in the workplace, and current symptoms and diseases. The section on psychosocial hazards at work was designed specifically for this study and consisted of 28 items on perceived working conditions with a four-point Likert response scale (from zero to three): never or almost never, rarely, sometimes, often or always. A two-stage factor analysis (Marradi 1981) was performed that identified nine items as belonging to the domain of job control and four items to that of psychological demand (Table 1). Information on the job performed was collected asking participants to check one of the following categories: manual worker, clerical worker, technical employee and supervisor; or to provide a description if they felt that their job was not classifiable using these categories. Occupational class was assigned based on this information, classifying manual workers as blue collars and workers in other categories as white collars; 148 subjects, who did not recognized themselves as belonging to any predetermined job category, were classified as blue or white collars by one of the authors, on the basis of the self-reported job descriptions.

Table 1 Questions in the demand and control scales

Demand scale
My job requires that I work very fast
My job requires that I work very hard
I have enough time to get my work done
My job requires a lot of mental effort
Control scale
My job allows me to make a lot of decisions on my own
My job involves a lot of repetitive work
I have very little freedom to decide how I do my work
I have the opportunity to decide the order of my tasks
I have a lot of say about what happens in my job
I can choose the people I work with
I have flexibility in organizing my work schedule
I can choose when to take a vacation
I have a variety of different tasks in my job

In total, 4,507 self-administered questionnaires were completed and returned to CGIL by 3,305 blue-collar and 1,202 white-collar workers (response rate of about 60%). Questions related to the demand and control scales were incomplete on 441 (9.8%) and 689 (15.3%) questionnaires, respectively. This raised concern that the exclusion of these workers may distort the distribution of work-related stress measures, as they differed significantly from respondents with regard to sex, age, occupational class and job seniority. Therefore, missing data were imputed if a scale had no more than one missing value (161 for demand and 345 for control, representing 3.6 and 7.7% of respondents, respectively). Missing values were predicted using multiple regression models: through these models, the score of the missing item in each scale (i.e., demand or control) was predicted using as independent variables occupational class and the scores of non-missing items in the same scale. The overall scores on the demand and control scales were obtained by summing the values on the items belonging to

each domain, whereas the score of the job strain scale was computed as the ratio of the values of the demand and the control scales. Both scales demonstrated acceptable consistency (Cronbach's alpha: 0.64 for the demand scale, 0.82 for the control scale).

Of the 4,507 workers who participated in the baseline survey in 1999–2000, 2,295 (51%) gave their informed consent to be followed up to 31 December 2005. The follow-up of the cohort was conducted by means of record-linkage with an administrative archive of drugs prescription, without any further contact with the study participants after the baseline survey. To link workers to antidepressant prescriptions, a two-step procedure was followed. First, using their health care identification number as the record-linkage key, the archive of the study population was linked to the regional Health Care Population Register (HCPR), which includes all residents of Piedmont; 2,105 (92%) of those who had consented to be followed up were linked to the HCPR. Among these subjects, which constituted the actual study population, the mean values were 8.8 for the demand scale (SD = 2.7, median = 4.0, range = 0–12), 19.9 for control (SD = 6.2, range = 0–26, median = 11.0) and 0.52 for job strain (SD = 0.32, range = 0.05–3, median = 0.375). This archive was then linked, by means of the same identification code, to the regional Drug Prescription Register (DPR), which contains all drugs prescribed through the National Health Service (NHS) since 1997. It does not include prescriptions by private physicians or drug classes not covered by the NHS.

In Italy, antidepressants supplied through the NHS are free of charge. Nevertheless, as the price of this class of drugs is generally quite low, we cannot exclude that a small proportion of workers would not acquire their antidepressants through the NHS, but through a private physician, from whom an antidepressant prescription is valid for up to 3 months with as many as five refills of 28 pills. Antidepressants sold in Piedmont through the NHS in 2003, the only year for which this information was available, represented 88% of the total sales in the region (Testa, personal communication), indicating that the proportion of subjects who had a prescription of antidepressants, but are not present in the drug prescription archive, is expected to be quite low. Owing to this lack of completeness and the small number of workers with repeat prescriptions (53% of those with an ADP) during the follow-up period, the case definition adopted was 'at least one antidepressant prescription during the observation period'. The antidepressants were identified in the DPR by their Anatomical Therapeutic Chemical (ATC) classification code (N06A) (WHO Collaborating Centre for Drug Statistics Methodology 2004) and included monoamino-oxidase inhibitors (MAOI), selective serotonin uptake inhibitors (SSRI), tricyclic antidepressants (TCA) and others.

Statistical analysis

The relationship between ADP and previous exposure to psychosocial and other work-related factors was analyzed using Poisson regression to estimate the relative risk of depressive symptoms, in which person-years of observation were computed as the interval from the date of the baseline survey to that of the first ADP, if any, or to the end of the follow-up period. Fifty-nine participants with an antidepressant prescription between 1 January 1997 and the date of the baseline survey were considered prevalent cases and excluded (2.8% of those linked to the HCPR), leaving 2,046 workers for the follow-up analysis. It was not considered feasible examining administrative and technical white collars separately, because of their small number in the cohort (no. 289 and no. 122, respectively), so in all the analyses, they were considered as a single group.

In addition to demand, control and job strain, the following workplace exposures were taken into account as suspected risk factors for depressive symptoms and, therefore, potential confounders of the association with work-related stress, all of which were assessed in the baseline questionnaire: frequent overtime work, shift work, excessive noise and psychological violence in the workplace. The effects of demand, control and job strain were evaluated by dividing them into tertiles (low, intermediate, high) and treating the scales as categorical. Information on age was obtained from the HCPR, as in the survey it was collected using age classes (15–24, 25–44, 45+ years) which resulted in a strongly uneven distribution (only 2.8% of subjects in the youngest class).

In the first analysis, the effect of each work factor and of self-reported anxiety at baseline were evaluated separately, adjusted for age class (15–34, 35–49, 50+) and sex. In the baseline questionnaire, anxiety was defined based on a yes/no answer to the question "Do you suffer from any of the following health problems:", followed by a list of symptoms, among which "anxiety".

A multivariable Poisson model was fitted by entering these variables in the rank order of their significance in the previous step, together with age and sex. A variable was retained in the model if it was statistically significant at the 5% level or if its addition changed the coefficients of the other variables in the model by more than 20%. First-order interactions between occupational class (blue or white collar), work exposures, age and sex were also explored. All analyses were also stratified by occupational class, as the interaction with demand was statistically significant. The analyses were performed using Stata (version 10).

Table 2 Description of socio-demographic and work-related characteristics at baseline, by inclusion or not in the follow-up ($N = 4{,}057$)

Work and demographic characteristics	Subjects followed up % (n)	Subjects not followed up % (n)	p value[a]
All	46.7 (2,105)	53.3 (2,402)	
Blue-collar workers	79.9 (1,682)	67.6 (1,623)	<0.001
Females	23.0 (477)	22.9 (517)	0.92
Age 15–24 years	2.1 (44)	3.5 (83)	0.01
Age 25–44 years	61.6 (1,288)	59.5 (1,406)	
Age 45+ years	36.3 (760)	37.0 (874)	
Frequent shift work	50.1 (1,037)	40.2 (952)	<0.001
Frequent overtime work	14.0 (283)	15.0 (343)	0.33
Excessive noise	51.3 (994)	44.2 (942)	<0.001
Psychological violence	6.5 (137)	5.1 (122)	0.04
Anxiety	17.4 (366)	16.2 (389)	0.29
Imputed records—demand scale	3.4 (72)	3.7 (89)	0.61
Imputed records—control scale	7.0 (147)	8.2 (198)	0.11
	Mean (SD)	Mean (SD)	p value[b]
Demand	8.8 (2.7)	8.6 (2.7)	0.01
Control	19.9 (6.2)	21.3 (6.4)	<0.001
Job strain	0.52 (0.32)	0.48 (0.30)	<0.001

Inclusion in the follow-up determined by availability of informed consent plus successful record-linkage of the subjects with the health care population register (HCPR)

[a] Chi-square test

[b] Two-sample t-test

Results

In Table 2, self-reported work-related factors and socio-demographic data at the baseline survey are presented by inclusion in the follow-up. Among workers who consented to follow-up and were linked to the HCPR, there were significantly larger proportions of blue collars, frequent shift workers, reports of excessive noise or psychological violence at work and workers in the youngest age class. These workers also reported significantly lower job control, higher psychological demand and higher job strain at baseline.

The distribution of most workplace factors in the cohort was heterogeneous across occupational class and sex (Table 3). Among blue collars and women, in particular, there were larger proportions of shift workers, and workers reporting excessive noise, high psychological demand, low job control and high job strain. Women worked less overtime compared to their male counterparts, with the smallest proportion among blue-collar women. The proportion of white-collar women reporting psychological violence from co-workers or supervisors was more than twofold that in the other groups. Self-reported anxiety among women was also over twice that reported by men.

The risk of depressive symptoms among women was more than twice that observed among men (RR = 2.25, 95% CI: 1.72–2.94), whereas it was not significantly different by occupational class after adjusting for age and sex (white collars vs. blue collars: RR = 1.08, 95% CI: 0.78–1.48). The average follow-up time between the baseline survey and the first antidepressant prescription was 2.5 years.

In the analysis including all workers, adjusted for age, sex and occupational class (Table 4), previous exposure to high demand or low control significantly increased the risk of depressive symptoms, together with anxiety, which was the only other factor associated. Among blue-collar workers, the protection associated with high control was similar to that observed in the whole cohort, whereas the risk estimate for high demand almost doubled. The effect of demand was stronger among women, but the interaction between demand and sex was not significant ($p = 0.29$). Among white-collar workers, although not significant, the risk decreased with increasing demand, and no association was found with job control. Exposure to high job strain was associated with a non-significant increase in the risk of depressive symptoms among blue collars. Regarding the other factors, a significant increase in risk was found among blue collars who had reported working overtime of less than 4 h per week, psychological violence from co-workers or supervisors, or anxiety at baseline. White collars who worked any type of shift work were at twice the risk (RR = 2.06, 95% CI: 1.08–3.94) compared to those who did not.

Two separate multivariable models were fitted, one including both demand and control and the other with job strain. The risk estimate associated with job strain after adjusting for potential confounders was essentially the same as the age- and sex-adjusted estimate (Table 4) for the whole cohort and for both occupational classes (data not shown).

The final regression models for demand and control are shown in Table 5, adjusted (second column) and stratified

Table 3 Distribution of self-reported workplace factors at baseline for workers followed up, excluding prevalent ADP cases, stratified by sex and occupational social class ($N = 2,046$)

Work factors	Blue-collar males % ($n = 1,273$)	Blue-collar females % ($n = 362$)	White-collar males % ($n = 304$)	White-collar females % ($n = 107$)	p value[a]
Shift work					
None	44.3	32.7	80.5	87.7	<0.001
2 shifts	29.6	49.7	3.0	1.9	
3–4 shifts	21.5	14.8	8.9	0.9	
Irregular shifts	4.6	2.8	7.6	9.5	
Overtime work					
None	84.9	92.4	82.0	85.6	<0.001
≤4 h/week	3.6	2.0	7.5	5.8	
>4 h/week	11.5	5.6	10.5	8.6	
Excessive noise	58.6	58.1	24.4	24.6	<0.001
Psychological violence	6.5	5.8	4.9	12.2	0.06
Anxiety	13.7	29.8	9.9	24.3	<0.001
Demand					
Low	39.0	24.4	46.5	47.5	<0.001
Intermediate	36.1	36.1	34.2	29.7	
High	24.9	39.5	19.3	22.8	
Control					
Low	37.7	68.0	6.2	19.8	<0.001
Intermediate	39.0	28.7	34.1	40.6	
High	23.3	3.3	59.7	39.6	
Job strain					
Low	30.9	8.4	50.9	46.5	<0.001
Intermediate	32.6	25.5	37.5	29.7	
High	36.5	66.1	11.6	23.8	

[a] Chi-square test

by occupational class (third and fourth columns). In the analysis including all workers, frequent overtime work, female gender and anxiety were significantly associated with ADP risk, whereas demand and control were not. Among blue collars, the risk of depressive symptoms associated with demand did not substantially change after adjusting for the other significant predictors: overtime work, sex and anxiety; the risk related to psychological violence was not significant (RR = 1.45, 95% CI: 0.86–2.44) after accounting for anxiety. The inclusion of control in the same model as demand only slightly reduced the risk associated with high demand (RR = 1.72, 95% CI: 1.10–2.69), whereas the protective effect of job control decreased and lost significance (intermediate: RR = 0.83, 95% CI: 0.57–1.23; high: RR = 0.76, 95% CI: 0.42–1.36). When a continuous measure of demand was used, a significant direct relationship was observed ($p = 0.007$). Among white collars, the protective effect found for high demand in the age- and sex-adjusted analysis (RR = 0.50, 95% CI: 0.20–1.21) increased and became significant (RR = 0.38, 95% CI: 0.15–0.96) after accounting for any type of shift work; anxiety was retained in the final model, because its inclusion reduced the coefficient for sex by more than one quarter.

Discussion

In this cohort of Italian union workers, the risk of depressive symptoms, as assessed by ADP, was 80% higher among blue collars who had reported high work-related psychological demand at baseline, after adjusting for potential confounders. The effect of job control was not significant after accounting for psychological demand, although a moderate protection persisted for higher control. The non-significant increase in risk associated with high job strain also appears to be mainly owing to the effect of demand. These results do not support the job strain hypothesis, but appear to indicate that psychological demand is the most important work dimension associated with the risk of depressive symptoms, and that job control likely has a smaller role.

The findings in this study appear consistent with the results from other longitudinal studies that focused

Table 4 Relative risk of antidepressant drug prescription related to workplace factors reported at baseline

Workplace factors	All workers[a]			Blue collars			White collars		
	No. cases	Person-years	RR (95% CI)	No. cases	Person-years	RR (95% CI)	No. cases	Person-years	RR (95% CI)
Shift work									
None	101	5,380.6	1	65	3,620.6	1	36	1,760.0	1
2 shifts	77	2,993.3	1.34 (0.97–1.86)	74	2,935.2	1.21 (0.86–1.70)	3	58.1	2.85 (0.87–9.30)
3–4 shifts	35	1,869.5	1.13 (0.76–1.69)	31	1,721.9	1.01 (0.66–1.56)	4	147.6	1.78 (0.61–5.16)
Irregular shifts	12	521.3	1.30 (0.71–2.37)	6	354.1	0.98 (0.42–2.27)	6	167.2	1.79 (0.83–4.72)
Overtime									
None	181	9,039.7	1	142	7,328.4	1	39	1,711.3	1
≤4 h/week	13	401.7	1.71 (0.97–3.01)	9	268.2	2.00 (1.02–3.92)	4	142.6	1.33 (0.47–3.73)
>4 h/week	20	1,100.8	1.00 (0.63–1.60)	16	876.7	1.08 (0.64–1.82)	4	224.0	0.84 (0.30–2.35)
Excessive noise									
No	90	4,874.8	1	60	3,353.9	1	36	1,520.9	1
Yes	110	5,228.2	1.14 (0.86–1.52)	99	4,742.8	1.18 (0.86–1.63)	11	485.5	0.96 (0.49–1.89)
Psychological violence									
No	108	10,248.1	1	161	8,257.2	1	47	1,990.9	1
Yes	19	696.0	1.33 (0.83–2.13)	17	541.7	1.70 (1.03–2.80)	2	154.3	0.49 (0.12–2.02)
Anxiety									
No	159	9,238.4	1	121	7,375.1	1	38	1,863.3	1
Yes	68	1,705.7	1.99 (1.48–2.67)	57	1,423.8	2.07 (1.50–2.85)	11	281.9	1.58 (0.78–3.22)
Demand									
Low	68	3,980.3	1	42	3,037.5	1	26	942.7	1
Intermediate	74	3,719.9	1.14 (0.82–1.58)	60	3,023.9	1.34 (0.90–1.99)	14	696.1	0.73 (0.38–1.39)
High	72	2,752.7	1.40 (1.00–1.96)	66	2,322.0	1.77 (1.20–2.62)	6	430.8	0.50 (0.20–1.21)
Control									
Low	99	3,833.2	1	94	3,634.0	1	5	199.1	1
Intermediate	68	3,776.6	0.75 (0.55–1.04)	49	3,034.7	0.73 (0.51–1.04)	19	741.8	1.06 (0.39–2.90)
High	39	2,685.3	0.60 (0.39–0.91)	17	1,567.6	0.57 (0.33–0.97)	22	1,117.7	0.84 (0.31–2.29)
Job strain									
Low	55	3,073.3	1	29	2,153.4	1	26	919.9	1
Intermediate	55	3,205.4	0.95 (0.65–1.40)	41	2,394.7	1.05 (0.65–1.70)	14	810.7	0.72 (0.38–1.38)
High	95	3,547.7	1.27 (0.88–1.83)	89	3,219.6	1.41 (0.91–2.19)	6	328.1	0.70 (0.29–1.72)

Poisson regression adjusted for age class and sex

[a] Adjusted for age class, sex and occupational class

Table 5 Workplace and demographic characteristics at baseline associated with the risk of antidepressant drug prescription

Workplace and demographic characteristics	All workers[a]	Blue collars RR (95% CI)	White collars RR (95% CI)
Age			
15–34 years			1
35–49			1.76 (0.72–4.29)
50+			3.26 (1.18–8.99)
Sex			
Male	1	1	1
Female	2.07 (1.56–2.74)	2.22 (1.60–3.08)	1.78 (0.91–3.49)
Anxiety			
None	1	1	1
Yes	2.08 (1.55–2.80)	2.12 (1.51–2.98)	1.65 (0.79–3.46)
Overtime			
None	1	1	
≤4 h weekly	1.82 (1.03–3.20)	2.25 (1.14–4.43)	
>4 h weekly	1.03 (0.65–1.64)	1.13 (0.66–1.94)	
Shift work			
None			1
Any type			2.58 (1.30–5.11)
Demand			
Low		1	1
Intermediate		1.33 (0.88–2.01)	0.69 (0.36–1.33)
High		1.82 (1.21–2.74)	0.38 (0.15–0.96)

Final Poisson multivariable models, adjusted (second column) and stratified (third and fourth column) by occupational social class

[a] Adjusted for occupational class

specifically on depressive syndromes and reported significant associations with high demand, low control or both, with no interaction between them (Rugulies et al. 2006; Paterniti et al. 2002; Wang 2004; Shields 2006; Kawakami et al. 1992). Two recent reviews on the role of psychosocial work factors on the risk of depressive syndromes have reported higher and more consistent associations with demand than control (Bonde 2008; Netterstrom et al. 2008). The only other longitudinal study, to our knowledge, that has examined the risk of depressive symptoms and workplace stress, also using antidepressant prescriptions as a proxy, found an increased risk with past exposure to high demand, but only among men and with no interaction between demand and control (Virtanen et al. 2007).

Negative results for both dimensions have been reported by other authors, such as Carayon (1993) and Ylipaavalniemi et al. (2005), which may be partly explained by differences in methodology and in the working populations investigated. For example, in the study by Ylipaavalniemi et al. (2005), participants were asked to rate the emotional distress caused by various aspects of work-related demand, whereas in most studies, demand was assessed using the Job Content Questionnaire (JCQ) (Karasek 1985) or a similar questionnaire, in which workers are asked to describe specific features of their work environment and tasks. Analogously, the absence of an effect for job control in our study may be related to the method of assessment, which was based on a set of questions that differ in part from those in the original JCQ, where more weight is given to skill variety and development than to work autonomy, compared to our questionnaire, in the construction of the decision latitude dimension. The demand scale, on the other hand, was constructed in a manner similar to that of the JCQ short version, but based on four questions instead of five. The study population in both negative studies consisted mainly of white-collar workers, whereas in the studies with positive findings, it was either blue collars or a representative sample of mainly blue collars, among which exposure to high demand is more likely to entail fast, strenuous and repetitive tasks, as in the manufacturing industry. This would suggest that the demand scale used, which was nonetheless similar to that of the JCQ short version, was not able to properly assess the 'demands' of white-collar workers.

The protective effect of demand observed among white collars, which has not been reported in other studies to our knowledge, may be related to the peculiar characteristics of our sample of white-collar workers, who were mainly employed in administrative or technical positions in public companies engaged in the supply of services (natural gas, electric power, mail and courier, and transportation). In fact, they reported low levels of psychological demand, on

average, even lower than blue collars, which is inconsistent with several studies (Schrijvers et al. 1998; Suadicani et al. 2001; Kristensen et al. 2002). Also, in a less strenuous work environment, high demand of a non-repetitive nature may protect workers from the negative impact of monotony, boredom and the meaningless of their work, all of which are only partially captured by the control dimension.

Working shifts of any kind more than doubled the risk of depressive symptoms among white collars, whereas working overtime of up to 4 h weekly had a similar effect among blue collars. The few studies that investigated the relationship between mental health and both overtime and shift work obtained conflicting results (Harrington 1994a, b; Spurgeon et al. 1997; Grosch et al. 2006). A plausible explanation for the absence of an effect for overtime in excess of 4 h weekly is the healthy worker effect: working more than a specified number of overtime hours is mainly voluntary in Italy, and blue collars less susceptible to the effects of long working hours are more likely to do it. The absence of an association with overtime work among white collars may be related to the nature of the work itself (as in the case of demand) and/or the perceived benefits of engaging in such work, resulting in less mental and physical overload. Shift work, on the other hand, may be perceived as socially undesirable among white collars, rendering them more susceptible than blue collars to the development of depressive symptoms. These hypotheses should be explored further.

There are several limitations on the interpretation of these results. First, the use of antidepressant prescriptions as a proxy of depressive symptoms was based on the assumption that a physician prescribed these drugs to a certain patient because recognized him as affected by depressive symptoms. Nonetheless, ADP may be a relatively poor surrogate of depressive symptoms, involving a substantial misclassification of the outcome, given that on one hand seeking care is possibly influenced by various social and cultural factors, while on the other hand being prescribed an antidepressant by a physician is likely characterized by a substantial variability related to physicians' attitudes. Depression is strongly underdiagnosed and undertreated, even in developed countries (Davidson and Meltzer-Brody 1999; Demyttenaere et al. 2004). From data of the European Study of the Epidemiology of Mental Disorders (ESEMeD), in Europe only 24% of patients affected by unipolar depression, diagnosed according to the standardized criteria of the DSM-IV, were treated with antidepressants during the 12 months preceding the interview (Alonso et al. 2004). According to Tylee and Jones (2005), depression follows the rule of halves: "Only half of depressed patients seek help from doctors, half are detected in primary care, half receive treatment with only half completing it", resulting in fewer than 10% who complete a therapeutic course of treatment. Therefore, we can infer that cases identified through ADP represented only a subset of those with depressive symptoms and that subjects with milder symptoms were likely under-represented in our case series. However, unless seeking care behavior or physicians' attitudes are correlated with exposure to psychosocial factors at work, which seems unlikely, the outcome misclassification is expected to be non-differential with respect to exposure status. Although it is possible that subjects with higher socioeconomic status and higher income may have been more likely to get a prescription from a private physician and therefore to be less represented in the drug prescription archive, the fact that case definition was based on only one prescription during a long observation period and that analyses were stratified by occupational social class is expected to have reduced the distortion of the risk estimates eventually produced by this bias.

Second, the study population was not a representative sample of the working population in the Turin area. The CGIL union is the largest in Italy with about three million members; membership is widespread among blue-collar workers, but less common among white collars, especially in the private sector, for whom the sample is expected to be the least representative. In Italy, union membership is not mandatory in any workplace; thus, this survey of union members would not have systematically excluded entire workplaces in which there is no union presence. It is reasonable, therefore, to expect that a broad range of workplaces were represented, and that the bias introduced by surveying only union members is less likely to be related to systematic differences between unionized and non-unionized workplaces. Suggestion of a possible limited generalizability of the results to the general population comes also from the comparison of the study participants with the employed subjects resident in Turin at 2001 census, showing that the study population was different with respect to several characteristics: it was slightly older (mean age: 41 vs. 39 years) and included a higher proportion of men (77% vs. 54%) and manual workers (80% vs. 35%), together with a lower percentage of subjects with temporary (2% vs. 12%) and part-time jobs (2% vs. 11%).

Third, the sampled population was to a considerable extent self-selected: the response rate to the baseline survey was relatively low (60%), and a large percentage of respondents did not consent to be followed up (49%). Furthermore, workers who were followed up differed significantly from those who were not on some important socio-demographic and work characteristics. However, given that the study was longitudinal and prevalent cases were excluded, it seems unlikely that this potential bias has seriously affected its internal validity. On the other hand, it cannot be excluded that the observed association between

depressive symptoms and demand may be partly attributable to reverse causality, the extent of which would be directly related to the number of workers with depressive symptoms at baseline, and not yet on treatment with antidepressants, or who had been prescribed antidepressants before 1997 (not excluded as prevalent cases). These workers would be more likely to perceive their work conditions as psychologically demanding owing to their symptoms and, therefore, to overestimate their exposure to psychosocial factors compared to non-cases (de Lange et al. 2004).

Fourth, exposure to workplace factors was assessed only once, which may not accurately characterize exposure to hazards occurring over several years of follow-up, considering that many subjects have likely changed job or exposure category after the baseline survey. However, given the prospective design of the study, this limitation would result in a non-differential misclassification of exposure. Even assuming that there were subjects at baseline with mental symptoms, but not yet treated with antidepressant, or with prescriptions before 1997, while it is possible that these subjects have decreased their exposure to psychological stressors in a differential way compared to non-cases because of their symptoms, this would have led to an underestimation of the risk of depressive symptoms.

Anxiety is complex construct, for which there is agreement that a valid diagnostic assessment should be based on semistructured clinical interviews, such as the Anxiety Disorders Interview Schedule or the Structured Clinical Interview for DSM-IV (Shear and Maser 1994; Summerfeldt and Antony 2002). Use of these tools is, however, very time-consuming, since almost 2 h are needed to administer this kind of interviews, so that they are not commonly used in epidemiological research. Therefore, the risk of ADP estimated for anxiety, together with the expulsion of psychological violence from the final model on blue collars when anxiety was introduced, should be interpreted with caution, given that the assessment of anxiety was rather crude in this study, being based on only one question, and likely led to a low specificity of this definition.

Another limitation of this study is the lack of information on potential non-occupational confounders, such as negative life events, lack of social support, family conflicts, financial difficulties and alcohol consumption. These factors, many of which are more prevalent in low socioeconomic strata, may tend to cluster together with poor psychosocial working conditions (van Oort et al. 2005; Pearlin et al. 2005). Among workers with these characteristics, self-reported exposure to work stress may be affected by reporting bias, owing to the fact that they would tend to overestimate their occupational exposure because of their problems outside work, with a consequent distortion of the relative risk away from the null. Nevertheless, in various studies on mental health, high demand remained a significant risk factor after adjusting for negative or stressful life events (Paterniti et al. 2002; Wang 2004; Marchand et al. 2005). Similarly, controlling for the effect of personality traits, such as negative affectivity, hostility and low self-esteem, only marginally changed the strength of the association with demand or control in several longitudinal studies (Paterniti et al. 2002; Stansfeld et al. 1999; Kivimaki et al. 2003).

Last, the small number of cases in several exposure categories limited the possibility of identifying significant associations with exposure to various work characteristics, especially among white collars, such as psychological violence, overtime and job control.

Conclusions

In this prospective study, the first on this topic conducted in Italy, exposure to high psychological demand at work was a significant predictor of depressive symptoms, as assessed through ADP, among blue collars, whereas job control and high strain were not associated with an increased risk. Among white collars, a protective effect of high demand was found, which may be owing to the particular characteristics of this sample.

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Conflict of interest The authors declare that they have no conflict of interest.

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