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Job stress and the use of antidepressant medicine: a 3.5-year follow-up study among Danish employees

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ABSTRACT

Objectives To investigate if exposure to adverse psychological job characteristics predicts incident use of antidepressants, taking into account differential misclassification and residual confounding.

Methods A prospective cohort study with a 3.5-year follow-up of 4661 Danish employees, aged 40 and 50 years, drawn from a 10% random sample of the Danish population was carried out. Job characteristics were the predictor variables and use of antidepressants was the outcome variable. Survey data on psychosocial work environment were linked with register data on dispensing of antidepressant medicine between June 2000 and December 2003. Respondents with major depression at baseline, with antidepressant use in the 5 years preceding baseline, or not employed at baseline were excluded.

Results Among men, the OR for antidepressant use was significantly increased for high quantitative demands (OR 2.12, 95% CI 1.29 to 3.48) and low social support from colleagues (OR 2.28, 95% 1.36 to 3.82) after adjustment for lifestyle factors, socio-demographic factors, co-morbidity, other work factors and depressive symptoms at baseline. Both effects were dose dependent. An interaction effect with high demands was found for high anticipated private social support and living with children. Among women, no effect of job characteristics on antidepressant use was found.

Conclusion Among men, but not among women, high quantitative demands and low social support from colleagues were predictive of incident use of antidepressants, indicating incident depressive episodes, even after taking into account differential misclassification and residual confounding. The effects were buffered for those with high anticipated private social support and for those having children.

What this paper adds

- Several prospective studies have shown that precarious psychosocial work factors may increase the risk of depression.
- Some authors argue that these associations might be seriously inflated because of misclassification and residual confounding.
- Even after adjustment for major sources of misclassification and confounding, this study confirms previous findings on the role of work factors in the aetiology of depression.
- Among men who reported high quantitative demands or low social support, the risk of depression is twice as high as for the unexposed; among women the picture remains less clear.
- At the policy and workplace level, organisational strategies should be initiated that target work overload and promote mutual support between co-workers.

INTRODUCTION

Several epidemiological studies have analysed the relationship between psychosocial factors at work and mental health. Two recent reviews conclude that high psychological job demands, low social support and high job strain (a combination of high demands and low decision latitude) in longitudinal studies are associated with depression.[1 2] Furthermore, low decision authority, low decision latitude, high job insecurity and job effort–reward imbalance are associated with common mental health problems in general.[3] Several studies have also shown that work factors might differentially affect men and women.

A major conclusion of the recent reviews is, however, that most studies on work environment and depression are limited by methodological problems—the main issues being misclassification and residual confounding—and that any conclusion regarding causality is vulnerable to these two sources of bias.

Misclassification

Most studies measure both exposure and outcome by self-administered questionnaires, which is prone to information bias. Differential misclassification is often a major problem, but even when it is non-differential for both exposure and outcome and measurements are made at different times, the errors cannot be regarded as independent.[4] This is also referred to as the 'common method bias' and might affect the associations in both directions.[5] Methods for overcoming this problem have included using job exposure matrices and/or register-based measures of outcome such as prescribed antidepressants, standardised mental health interviews or cases of in- and outpatient hospital care for depression.[4 6–11] These solutions may, however, introduce other types of misclassification.[12] Another aspect of exposure misclassification is the fact that induction and exposure time are seldom known and dealt with explicitly.

Residual confounding

Since the absolute strongest risk factor for depressive episodes in cohort studies is having had earlier episodes, it is crucial to exclude persons with earlier episodes or at least control for this variable.[13] However, information on earlier episodes is often

collected by self-report, which might leave some episodes and subclinical depression symptoms unrecorded. It has been shown that mental problems in childhood and early adulthood predict work characteristics in mid-adulthood, and therefore might be confounders.[14] Personality factors such as neuroticism, as well as current subclinical depression, may influence the way one evaluates the working environment and may be associated with new depressive episodes.[1] Most studies have controlled for socio-demographic confounders but not for other risk factors for depression, including alcohol intake, family history of depression, chronic somatic disease, private life demands or support and other psychosocial working conditions, which all also might be related to the working characteristics under study.

Some of these possible confounders, for example alcohol intake, might be at least partially caused by the adverse work environment and may therefore be seen as intermediate steps in the causal pathway. Others, like neuroticism, may modify the effect of the work environment.

In the present paper, we set out to study in a cohort design the effect of several adverse work characteristics (high quantitative and emotional work demands, high work pace, low social support from supervisors and colleagues, low sense of workplace community, low meaning of work, low possibilities for development, low variation and high physical demands) on depression. We used register-based incident use of prescribed antidepressant medicine as the outcome measure. We specifically focused on including covariates, which might be potential confounders, mediators or effect measure modifiers, such as socio-demographic factors, lifestyle risk factors, co-morbidity, subclinical depressive symptoms, private life conflicts and private life social support as well as competing work characteristics. We hypothesised that work characteristics at baseline would predict incident antidepressant use during follow-up. We also expected that the effect of high work demands on antidepressant use would be modified by longer job tenure, using this as an indicator of exposure time. Furthermore, we expected that private life demands and resources modify the effect of work demands.[15 16] Finally, with reference to the diathesis stress theory, we expected persons with subclinical depressive symptoms to be more vulnerable to work stress.[1 17]

METHODS

Study design and population

This is a 3.5-year follow-up study of the effect of different job characteristics on incident use of antidepressant medicine. The Danish Longitudinal Study on Work, Unemployment and Health was designed to investigate the associations between psychosocial factors, unemployment, social marginalisation and health.[18] Participants were drawn from the Danish Institute of Governmental Research Longitudinal Register. This register includes data on a 10% random sample of the Danish population aged 15 years or older. From those, a random sample cohort of 11 082 Danish residents aged 40 or 50 years old on 1 October 1999, was drawn. The cohort received a postal questionnaire enquiring about psychosocial and ergonomic working conditions, health behaviours, and physical and mental health in March 2000. Overall, 7583 (68%) respondents completed the survey. The present study dataset was created by linking the baseline survey data with register data on the diagnoses of hospital in- and outpatients during 1968–2000 and on prescribed and purchased antidepressants during 1995–2003 from the Danish Medicinal Product Statistics located at Statistics Denmark and data on individual employment histories from the Institute of Governmental Research Longitudinal Register, also located at Statistics Denmark. The linkage procedure is facilitated by the unique person identification number which is assigned to every resident in Denmark.

Individuals were excluded if at baseline they (a) were not employed, (b) were current or past users (1995–2000) of antidepressants, (c) had a major depression according to the criteria of the Diagnostical and Statistical Manual Version IV (DSM-IV) during the preceding 2 weeks, as assessed by the Major Depression Inventory (MDI) in the survey, (d) had a history of hospitalisation (1968–2000) due to affective disorders or (e) had a missing value on any variable included in the multivariate analyses. The exclusion process resulted in a final sample of 4661 participants. Excluded individuals had a significantly higher likelihood of antidepressant use during follow-up (6.8%) than study participants (4.0%), as well as a higher frequency of medical histories that included hospital treated mental illness and other co-morbidity. The excluded group contained significantly more women and more people from lower social groups (34% received social benefits and were outside the labour market). Among the excluded, those defined as exposed regarding job characteristics, had generally higher use of antidepressants.

Definition and measurement of antidepressant use

Use of antidepressant medicine was defined as being dispensed an antidepressant drug at a pharmacy, which is the only legal way to purchase this type of medicine in Denmark for the non-hospitalised population. Data were retrieved from the Danish Medicinal Product Statistics that contains information on all prescribed medication purchased at pharmacies in Denmark since 1995. We identified registrations for all types of antidepressants (ATC-code N06A), coded after the Anatomical Therapeutic Chemical (ATC) classification system.[19]

'Current or past use of antidepressants' was defined by an entry of N06A in the database at any time between 1 January 1995 and 30 May 2000 (ie, the month after the baseline survey was completed). 'Incident use of antidepressants' was defined by two conditions: (a) an entry of N06A in the database during the 3.5 years of follow-up, which ran from 1 June 2000 to 31 December 2003, and (b) no current or past use of antidepressants. Furthermore, we used as an indicator of the intensity of treatment, the monthly average amount of defined daily doses (DDD) purchased. We separated cases into three groups: (a) those not using antidepressive treatment during follow-up, (b) those using less than or equal to 3.5 DDD per month, and (c) those using more than 3.5 DDD per month (with 3.5 DDD corresponding to the median usage of the sample).

Measurement of job characteristics

Job characteristics were measured with scales from the Copenhagen Psychosocial Questionnaire, which has been used in several Danish and international studies. A comprehensive description of the instrument and its psychometric properties has been presented elsewhere.[20]

All questions about job characteristics had the response options 'Never', 'Sometimes', 'Often' and 'Always'. Respondents who answered anything other than 'Never' or 'Sometimes' to work demand questions (work pace, quantitative demands, emotional demands, physical demands) and answered anything other than 'Often' and 'Always' to resource questions (social support from superiors, social support from colleagues, meaning of work, opportunities for development, variation of work, sense of community) were classified as being exposed to an adverse

psychosocial work environment. For quantitative job demands (three questions), physical job demands (four questions), meaning of work (three questions), possibilities for development (three questions), which were covered with more than one question, only those persons who answered at least half of the questions have been included in the analysis. We calculated average answering scores based on the number of questions answered. The midpoint of the scale was used as the threshold for classification of exposure. For the specific wording of all questions, see online supplementary appendix 1.

Definition and measurement of covariates

As covariates, we assessed gender, age, cohabitation, socio-economic position (SEP), heavy alcohol consumption, smoking, obesity, depression score at baseline, prior mental illness, co-morbidity other than mental health issues, lifestyle factors, private life conflicts and private life social support, and job tenure as well as the already described work characteristics. Moreover, we used the covariate 'employment during 2000' as a crude indicator of changed employment status during the first year of the follow-up in order to control for the effect of this.

These covariates were selected because they have been associated with risk of depression or use of antidepressants in earlier studies and are therefore possible confounders, mediators or effect modifiers. For more detailed information about the covariates, see online supplementary appendix 2.[21–34]

Statistical analysis

All analyses were conducted with the statistical program package SAS 9.0. Covariates were analysed for confounding or effect modifying effects on the exposure–outcome relationship for all work demands through single stratified analyses and Cochran–Mantel–Haenszel as well as Breslow–Day statistics. Potential effect modifiers with a significant effect on the exposure–outcome association ($p<0.05$) were used for further analysis.[35] The hypothesised roles of the variables in the analytical model are shown in online supplementary appendix 3.

The effect of work characteristics at baseline on the risk of incident use of antidepressant medicine during follow-up was measured by ORs and 95% CIs using multivariate logistic regression models separately for men and women.

Employing incident use of prescribed antidepressants as a measure of depression introduces other problems of misclassification compared to self-reported information. In an earlier study on the same cohort, we analysed the sensitivity and specificity of this misclassification for different subgroups according to age, sex and socio-economic group, using the MDI as the 'gold standard'.[12] In the present study we used this same method to check the final results for the effect of differential misclassification according to the relevant work exposure variables.

To control for the effects of the covariates, we used three models. Model 1 was adjusted for gender, age, family status, SEP, alcohol consumption, smoking, physical activity, obesity, private life conflicts and anticipated private life social support, and history of mental as well as non-mental co-morbidity at baseline. Model 2 was further adjusted for work characteristics other than the work exposure under study. Because of the high intercorrelation of the single demand and resource scales (γ coefficient 0.36–0.92), we only adjusted demand scales for resource scales and resource scales for demand scales, but not demand scales for other demand scales and not resource scales for other resource scales. Model 3 was adjusted for depressive symptoms at baseline, using the MDI score as a continuous variable. For the illustration of the effect modification/interaction effects we constructed combined variables of work exposure and the given covariate. Interaction, as departure from multiplicity, was controlled for by including interaction terms in the logistic models.

RESULTS

The frequencies of adverse work characteristics were different for men and women. The difference was significant for most factors under study, except for 'low meaning of work', 'low opportunities for development' and 'low variation of work'. The prevalence of exposed persons varied from around 5% for 'low meaning of work' to over 70% for 'low social support from superiors'. Table 1 shows all sample characteristics at baseline for men and women.

Approximately 4% of the study population had at least one incident registration for antidepressants during the 3.5 years of follow-up, with higher incidence for women than for men (tables 2 and 3). The logistic regression analysis of the female subsample showed that only low 'meaning of work' was a significant predictor in the crude model, but not after having controlled for further covariates in the other models (table 2). For men, there were significant associations for 'quantitative demands', 'social support from colleagues' and 'low meaning or variation of work' in the crude model. Similar to that observed for women, the association between 'low meaning' and co-morbidity and social position was no longer significant when the variables in model 1 were controlled for. On the other hand, in men, the OR for 'quantitative demands' and 'social support from colleagues' increased as an effect of social position (which

Table 1 Sample characteristics at baseline

	Men (n=2439)		Women (n=2222)	
Sample characteristics	**n**	**%**	**n**	**%**
Group aged 40 years	1243	51.0	1224	55.1
Group aged 50 years	1196	49.0	998	44.9
Executive managers, leading managers	817	33.5	574	25.8
Non-manual salaried employees	632	25.9	713	32.1
Manual skilled and unskilled workers	990	40.6	935	42.1
Heavy alcohol consumption	604	24.8	511	23.0
Smokers	910	37.3	751	33.8
High physical activity	645	26.5	383	17.2
Obesity	270	11.1	178	8.0
Non-mental health morbidity	1049	43.0	1046	47.1
Muscular-skeletal pain	383	15.7	471	21.2
Living alone without children	323	13.2	252	11.3
Partnership without children	637	26.1	603	27.1
Living alone with children	42	1.7	161	7.3
Partnership with children	1437	58.9	1206	54.3
Low private life social conflicts	198	8.1	204	9.2
Low private life social support	245	10.1	190	8.6
Job tenure less than 1 year	394	16.2	243	10.9
High quantitative demands	642	26.3	489	22.0
High work pace	1022	41.9	1012	45.5
High emotional demands	282	11.6	410	18.5
Low social support from colleagues	1065	56.3	1166	47.5
Low social support from superiors	624	74.4	812	63.5
Low sense of community	379	15.5	252	11.3
Low meaning of work	130	5.3	93	4.2
High physical demands	185	7.6	110	5.0
Low opportunity for development	269	11.0	265	11.9
Low variation of work	492	20.2	465	20.9

Table 2 ORs (95% CIs) of works factors in 2000 for incident use of antidepressants between 2000 and 2003, women

Work characteristic	Antidepressant (%)	Crude	Model 1*	Model 2†	Model 3‡
High quantitative demands	25 (5.1)	1.23 (0.77 to 1.95)	1.08 (0.66 to 1.75)	1.06 (0.65 to 1.73)	0.95 (0.57 to 1.56)
High work pace	47 (4.6)	1.11 (0.74 to 1.66)	1.03 (0.68 to 1.55)	0.99 (0.65 to 1.51)	0.91 (0.60 to 1.39)
High emotional demands	24 (5.9)	1.46 (0.91 to 2.34)	1.36 (0.83 to 2.22)	1.30 (0.79 to 2.16)	1.10 (0.65 to 1.85)
Low social support from colleagues	47 (4.5)	1.02 (0.68 to 1.53)	1.02 (0.68 to 1.55)	1.06 (0.70 to 1.60)	1.00 (0.66 to 1.52)
Low social support from superiors	69 (4.9)	1.39 (0.89 to 2.16)	1.40 (0.89 to 2.19)	1.40 (0.89 to 2.18)	1.27 (0.80 to 1.99)
Low sense of community	16 (6.4)	1.56 (0.90 to 2.71)	1.48 (0.84 to 2.61)	1.43 (0.81 to 2.52)	1.18 (0.66 to 2.11)
Low meaning of work	8 (8.6)	2.13 (1.00 to 4.54)	1.97 (0.90 to 4.30)	1.98 (0.90 to 4.33)	1.61 (0.73 to 3.59)
High physical demands	7 (6.4)	1.51 (0.68 to 3.34)	1.52 (0.67 to 3.46)	1.46 (0.64 to 3.36)	1.38 (0.59 to 3.23)
Low opportunity for development	14 (5.3)	1.24 (0.70 to 2.22)	1.31 (0.71 to 2.43)	1.32 (0.71 to 2.46)	1.14 (0.61 to 2.15)
Low variation of work	27 (5.8)	1.46 (0.93 to 2.31)	1.53 (0.93 to 2.51)	1.54 (0.93 to 2.55)	1.39 (0.84 to 2.31)

*Controlled for lifestyle, social relationships, co-morbidity and socio-demographic factors.
†Controlled for lifestyle, social relationships, co-morbidity and socio-demographic factors plus all other work environment factors.
‡Controlled for lifestyle, social relationships, co-morbidity, socio-demographic factors and all other work environment factors plus Major Depression Inventory score.

is the only co-variate in model 1) with a confounding effect of around 10%. Controlling for other work factors also raised the ORs for 'quantitative demands', 'social support', 'low variation', 'low meaning' and 'low opportunity for development' (table 3). In the fully adjusted model 3, only high 'quantitative demands' and low 'social support from colleagues' significantly increased the odds of antidepressant use for men (OR≈2), although not for women. The interaction between gender and work characteristics, tested as departure from multiplicity, was significant ($p<0.05$) for both variables. All OR estimates decreased compared to model 2 as an effect of the supplemental adjustment for subclinical depressive symptoms.

For 'quantitative demands', the OR increased with increasing exposure quartiles from 1.03 (95% CI 0.42 to 2.53) at the first quartile, to 2.38 (95% CI 1.46 to 4.91) at the second quartile and finally to 3.35 (95% CI 1.60 to 7.03) at the fourth quartile, compared to the first quartile as reference. For 'low social support from colleagues', which had a prevalence of 56%, the dose–effect gradient was less visible with similar ORs for the third (OR 5.00; 95% CI 1.19 to 21.03) and fourth (OR 5.01; 95% CI 0.96 to 26.23) exposure categories. Testing for trend showed that trends were significant ($p<0.05$) in the fully controlled model for both job characteristics. We did not find any differential effect of the highest exposure category of high work pace and social support from superiors.

Dividing the use of antidepressants into low and high average DDD during follow-up, showed that for respondents with a higher than average use, the only statistically significant association was with high 'quantitative demands' (OR 3.06; 95% CI 1.53 to 6.11). On the other hand, we found significantly increased odds for low 'social support from colleagues' for respondents taking a lower than average monthly dose (OR 3.29; 95% CI 1.31 to 8.29).

Only the covariates 'anticipated private life social support' and 'living together with children' significantly modified the effect of high quantitative demands on subsequent antidepressant use, although they had no effect on the associations with emotional demands or work pace. Neither job tenure nor subclinical depression symptoms significantly modified the effect of job demands. The combination of high 'quantitative demands' and low 'private life social support' increased the OR for antidepressant use to 2.31 (95% CI 1.15 to 4.20), whereas the combination with 'high private life social support' did not (OR 1.18; 95% CI 0.82 to 1.71). The test for interaction as departure from multiplicity was significant ($p<0.05$) in the controlled logistic regression model. Furthermore, the effect of high 'quantitative demands' was modified by 'living together with children'. For those 'living with children', there was no effect of 'quantitative demands' (OR 1.05; 95% CI 0.67 to 1.63), whereas for those not 'living with children' and experiencing work demands, the OR was increased to 1.48 (95% CI 0.92 to 2.40). Testing for interaction again showed a significant effect ($p<0.05$).

DISCUSSION

In men but not women, self-reported high 'quantitative demands' and 'low social support from colleagues' increased the OR of incident use of antidepressants during the 3.5 years of follow-up. After controlling for a variety of possible residual confounders, including subclinical depressive symptoms, the ORs remained significant. Both effects were dose dependent. The effect of 'quantitative demands' was attenuated for those

Table 3 ORs (95% CIs) of works factors in 2000 for incident use of antidepressants between 2000 and 2003, men

Work characteristic	Antidepressant (%)	Crude	Model 1*	Model 2†	Model 3‡
High quantitative demands	35 (5.5)	2.06 (1.32 to 3.21)	2.36 (1.47 to 3.81)	2.46 (1.51 to 4.01)	2.12 (1.29 to 3.48)
High work pace	40 (3.9)	1.27 (0.82 to 1.97)	1.18 (0.75 to 1.86)	1.16 (0.74 to 1.84)	1.11 (0.70 to 1.77)
High emotional demands	11 (3.9)	1.16 (0.61 to 2.21)	1.04 (0.53 to 2.03)	1.07 (0.54 to 2.13)	0.88 (0.43 to 1.77)
Low social support from colleagues	63 (4.6)	2.39 (1.45 to 3.94)	2.48 (1.49 to 4.12)	2.51 (1.50 to 4.18)	2.28 (1.36 to 3.82)
Low social support from superiors	69 (3.8)	1.60 (0.91 to 2.83)	1.66 (0.93 to 2.94)	1.66 (0.93 to 2.95)	1.48 (0.83 to 2.65)
Low sense of community	19 (5.0)	1.62 (0.96 to 2.73)	1.66 (0.96 to 2.86)	1.60 (0.92 to 2.79)	1.28 (0.72 to 2.26)
Low meaning of work	9 (6.9)	2.22 (1.08 to 4.53)	2.02 (0.97 to 4.22)	2.16 (1.02 to 4.56)	1.46 (0.66 to 3.21)
High physical demands	7 (3.8)	1.11 (0.51 to 2.45)	0.89 (0.39 to 2.03)	0.85 (0.37 to 1.99)	0.66 (0.28 to 1.61)
Low opportunity for development	14 (5.2)	1.65 (0.91 to 2.97)	1.58 (0.84 to 2.97)	1.76 (0.93 to 3.33)	1.48 (0.77 to 2.84)
Low variation of work	25 (5.1)	1.71 (1.06 to 2.76)	1.55 (0.94 to 2.56)	1.67 (1.00 to 2.78)	1.55 (0.92 to 2.62)

*Controlled for lifestyle, social relationships, co-morbidity and socio-demographic factors.
†Controlled for lifestyle, social relationships, co-morbidity and socio-demographic factors plus all other work environment factors.
‡Controlled for lifestyle, social relationships, co-morbidity, socio-demographic factors and all other work environment factors plus Major Depression Inventory score.

experiencing a lack of 'anticipated private life social support' and for those not 'living with children'. Analysis of the exposure–outcome timing indicated a stronger effect for those with shorter exposure length before baseline measurement.

Virtanen *et al* find the same increase in antidepressant use for high job demands in men.[11] The two reviews on work environment and depression that mainly include studies using indicators for depression other than antidepressant use, similarly find high job demands to be a risk factor, but without any clear gender difference.[1 2] Sinokki *et al* in a Finnish cohort study also find low social support from colleagues and supervisors to be risk factors for subsequent antidepressant use for both genders.[10] These results, however, have to be viewed with caution, because they were neither adjusted for baseline depressive symptoms nor for prior antidepressant use. Bonde *et al* in a Danish cohort study measure adverse work characteristics at the work unit level.[36] Municipality work units with low social support are predictive of new prescriptions of antidepressants. The result is weakened by the fact that it is not consistent with findings in the county work units. In our study 'quantitative demands' but not 'work pace' predicted antidepressant use. This result might indicate that it is the perceived imbalance between the allocated working time and the time required to complete work tasks that affects mental health rather than high 'work pace' only.

The effects were gender specific with regard to use of antidepressants, in contrast to studies using depression rating scales as the measure of outcome. An explanation might be that women cope differently with work stress or seek help at an earlier stage. This might result in treatment other than pharmaceutical medication for those with depressive symptoms. It is also possible that health professionals evaluate and respond to stressful work characteristics differently for men and for women. In both cases, the real associations would be underestimated or overlooked because exposed cases would be misclassified. Furthermore, men and women might evaluate the severity of adverse work characteristics differently, something we cannot control for in this study. If we accept average use of antidepressants as a crude indicator of the intensity of treatment, low social support from colleagues is predictive of low intensity treatment only. Keeping in mind that in accordance with international guidelines, antidepressant treatment for depression needs to last for about 3 months, this association might be the result of a lack of treatment efficacy, adverse effects or medical treatment inadequate in other ways.[37] The analysis of the modifying effect of private life factors showed that a lack of 'anticipated private life social support' increased the effect of high 'quantitative demands'. This underscores the importance of taking into account the interplay between private and work life demands and resources and is in line with the results of other studies.[15 16 38] Interestingly, 'living together with children' reduced the effect of high work demands in our sample, which may have indicated a buffer effect, rather than children being an additional source of demands, which has been more commonly discussed.[15]

Strengths and limitations

The study used a cohort design in order to assess new disease episodes thoroughly, and excluded persons who had had an episode of major depression at baseline and as well as those who had used antidepressants during the preceding 5.5 years. Furthermore, we were able to adjust for the baseline MDI score as an indicator for subclinical depression symptoms or distress, which in fact had the strongest attenuating effect on the exposure–outcome association. In principle, depressive symptoms might also be a result of job stress occurring before the baseline measurement. In such a case, job stress would be a mediator and our analysis would have underestimated the real associations by controlling for it. Based on the available data, it is not possible to determine the exact role of job stress prior to baseline, but it is possible that both its confounding effect and its mediating effect are taking place at the same time. The resulting 'true' values would lie somewhere between those of models 2 and 3. With this in mind, it would be relevant to discuss low variation of work and low meaning of work as further potential risk factors for incident use of antidepressants in men.

The results of the final logistic regression model were additionally controlled for a variety of potential confounders. None of them substantially affected the exposure–outcome association. This variety of covariates gave an opportunity to test private life factors for their potential role as effect modifiers. The choice of antidepressant used as an indicator of depression in this study countered the 'common method bias', which otherwise threatens analysis by inflating associations. At the same time this choice introduced another misclassification problem, because not all depressed persons receive medical treatment and antidepressants are prescribed for reasons other than depression. This latter means that our measurement of depression is imprecise, but except for a limited use of antidepressants to treat somatic chronic pain, all other indications are also related to mental ill-health.[39] In another study using the same data, we analysed the degree and direction of differential misclassification that occurs when using antidepressants as an indicator of major depression and integrated an adjustment method to compensate for the bias.[12] Using this method, that is adjusting for differential misclassification across levels of exposure, did not change the direction of the two crude main effects in the present study. On the contrary, the adjusted estimates suggest that the results of this study were an underestimation of the real effects.

The study was limited by the selection and quality of work environment measures. In particular, questions about control over work were missing, which prevented us from analysing the demand–control concept. As in other studies which use survey data to measure work factors, exposure measurement is very limited. Unknown duration of exposure makes it impossible to study the dose–response association adequately. We used 'job tenure', with change of job title as indicator for length of exposure, under the assumption that exposure will increase along with 'job tenure'. We had no knowledge about the concrete exposure situation before baseline, which made this indicator quite imprecise, covering also selection processes dependent on factors other than how much time has been spent in the workplace. The study was limited to persons aged 40 and 50 years at baseline, which also confined the potential generalisability of its results to these age groups. This is a limitation because it is possible that psychosocial exposures have different effects at different stages of life. Through the exclusion process we lost approximately 38% of the sample. As there was higher use of antidepressants among the exposed portion of the excluded respondents, it seems likely that the exclusion process had the effect of weakening the studied associations.

Concluding remarks

From a public health perspective, the results of this study lead to several conclusions. In men, self-reported high 'quantitative demands' and low 'social support from colleagues' are work stressors with high prevalence in the Danish work force, and contribute to the development of depression episodes and other

manifestations of mental ill health requiring antidepressant treatment.[40] Especially at risk are men who report high 'quantitative demands' and at the same time lack a supportive social environment within their private network. To better understand gender differences pertaining to these associations, further work is necessary that can prospectively measure mental illness independently of treatment. This would make it possible to differentiate between the effect of work stressors on mental health and on health service utilisation.

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Ethics approval The study has been notified to and registered by the Danish Data Protection Agency (Datatilsynet, see http://www.datatilsynet.dk). According to Danish law, studies that include data from questionnaires and from registers only do not need approval from the Danish National Committee on Biomedical Research Ethics (Den Centrale Videnskabsetiske Komité, see http://www.cvk.sum.dk/).

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