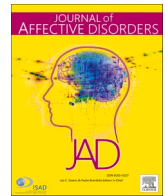


Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

## Journal of Affective Disorders

journal homepage: [www.elsevier.com/locate/jad](http://www.elsevier.com/locate/jad)

Research paper

# Work-related violence and depressive disorder among 955,573 employees followed for 6.99 million person-years. The Danish Work Life Course Cohort study

## Work-related violence and depression

Ida E.H. Madsen<sup>a,\*</sup>, Annemette Coop Svane-Petersen<sup>a</sup>, Anders Holm<sup>b,c</sup>, Hermann Burr<sup>d</sup>, Elisabeth Framke<sup>a</sup>, Maria Melchior<sup>e</sup>, Naja Hulvej Rod<sup>f</sup>, Børge Sivertsen<sup>g,h,i</sup>, Stephen Stansfeld<sup>j</sup>, Jeppe Karl Sørensen<sup>a</sup>, Marianna Virtanen<sup>k,l</sup>, Reiner Rugulies<sup>a,f,m</sup>

<sup>a</sup> National Research Centre for the Working Environment, Copenhagen, Denmark<sup>b</sup> The Rockwool Foundation, Copenhagen, Denmark<sup>c</sup> Western University, London, Canada<sup>d</sup> Unit Psychosocial Factors and Mental Health, Federal Institute for Occupational Safety and Health, Berlin, Germany<sup>e</sup> Social Epidemiology Research Group, Institut Pierre Louis d'Épidémiologie et de Santé Publique (IPLESP), INSERM UMR\_S 1136, Paris, France.<sup>f</sup> Section of Epidemiology, Department of Public Health, University of Copenhagen, Denmark<sup>g</sup> Department of Health Promotion, Norwegian Institute of Public Health, Bergen, Norway<sup>h</sup> Department of Research and Innovation, Helse Fonna HF, Haugesund, Norway<sup>i</sup> Department of Mental Health, Norwegian University of Science and Technology (NTNU), Trondheim, Norway<sup>j</sup> Centre for Psychiatry, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK<sup>k</sup> School of Educational Sciences and Psychology, University of Eastern Finland, Joensuu, Finland<sup>l</sup> Division of Insurance Medicine, Karolinska Institute, Sweden<sup>m</sup> Department of Psychology, University of Copenhagen, Denmark

## ARTICLE INFO

## Keywords:

Occupational exposure  
Workplace violence  
Offending Behaviors  
Depressive disorder  
Occupational stress

## ABSTRACT

**Background:** We examined the association between probability of work-related violence and first diagnosis of depressive disorder whilst accounting for the potential selection of individuals vulnerable to depression into occupations with high probability of work-related violence.

**Methods:** Based on a pre-published study protocol, we analysed nationwide register data from the Danish Work Life Course Cohort study, encompassing 955,573 individuals followed from their entry into the workforce, and free from depressive disorder before work-force entry. Depressive disorder was measured from psychiatric in- and outpatient admissions. We measured work-related violence throughout the worklife by the annual average occupational risk of violence exposure. Using Cox proportional hazards regression, we examined the longitudinal association between work-related violence (both past year and cumulative life-long exposure) and first depressive disorder diagnosis, whilst adjusting for numerous confounders including parental psychiatric and somatic diagnoses, childhood socioeconomic position, and health services use before workforce entry.

**Results:** The risk of depressive disorder was higher in individuals with high probability of past year work-related violence (hazard ratio: 1.11, 95% CI: 1.06-1.16) compared to employees with low probability of exposure, after adjustment for confounders. Among women, associations were robust across industries, whereas among men, associations were limited to certain industries.

**Limitations:** Violence was measured on the job group and not the individual level, likely resulting in some misclassification of the exposure.

**Conclusions:** Work-related violence may increase the risk of depressive disorder, independent of pre-existing risk factors for depressive disorder. These findings underline the importance of preventing work-related violence.

\* Corresponding author.

E-mail address: [ihm@nrcwe.dk](mailto:ihm@nrcwe.dk) (I.E.H. Madsen).<https://doi.org/10.1016/j.jad.2021.03.065>

Received 29 September 2020; Received in revised form 29 January 2021; Accepted 19 March 2021

Available online 26 March 2021

0165-0327/© 2021 The Authors.

Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license

<http://creativecommons.org/licenses/by-nc-nd/4.0/>.

## Introduction

Depressive disorders are a leading cause of disability (Hay et al., 2017) with a complex etiology involving biologic, psychological and social risk factors (Kendler and Gardner, 2016; Kendler et al., 2002, 2006; Köhler et al., 2018; Pettersson et al., 2018). Work-related risk factors for depression may provide potential targets for intervention and primary prevention. Several psychosocial working conditions, including high demands and low control at work, low social support, and bullying have been linked with the risk of depressive symptoms or clinical depression (Madsen et al., 2017; Theorell et al., 2015). One work-related risk factor, work-related violence, has been found to predict depressive symptoms (Butterworth et al., 2016), antidepressant treatment (Dement et al., 2014; Madsen et al., 2011), and affective disorders (Wieclaw et al., 2006), but studies examining risk of depressive disorders using a clinical endpoint are rare. A recent systematic review on the topic found four such studies, including two examining the risk of antidepressant treatment, and reported an association between work-related violence and depressive disorder with a hazard ratio of 1.42 (95% CI: 1.31–1.54) (Rudkjoebing et al., 2020). However, as pointed out by the systematic review, the existing evidence is limited by several methodological concerns, including a lack of studies assessing exposure non-self-reportedly and repeatedly (Rudkjoebing et al., 2020). Furthermore, previous studies have not accounted for bias by the potential selection of individuals with higher depression vulnerability into occupations with high risk of violence, which has been raised as a concern (Madsen et al., 2011). Such selection is plausible, because work-related violence occurs most frequently in person-related work, such as police- prison, or caring work (Madsen et al., 2010), and studies suggest that individuals from socially disadvantaged backgrounds or with parental illness tend to be selected into such occupations (Fussell and Bonney, 1990; Nikcević et al., 2007). Supporting this notion, a previous study found that caring professionals had higher antidepressant treatment rates years before entering care work (Madsen et al., 2012).

### Aims of the study

In the present study, we examine the longitudinal associations between work-related violence and depressive disorder in the Danish Work Life Course Cohort (DaWCo), an open cohort of employees in Denmark followed from the beginning of their working lives. The design and analyses were pre-defined in a pre-published protocol (Madsen et al., 2018b). We estimated exposure annually, as the average occupational risk of work-related violence and measured incident depressive disorder from hospital registers containing psychiatric inpatient and outpatient diagnoses. To account for selection of vulnerable individuals into high risk occupations, we adjusted for risk factors from before workforce entry, including parental psychiatric and somatic diagnoses, childhood socioeconomic position, and health services use. To distinguish between short-term and accumulating effects, we included measures of both past year exposure and exposure cumulated throughout the work life.

## Material and methods

DaWCo is an open inception cohort study of all individuals who first entered the Danish workforce during the years 1995–2009 and were 15 to 30 years old at entry (Svane-Petersen et al., 2019). DaWCo was constructed using nationwide Danish registers on employment, health, demographic- and socioeconomic factors to examine effects of working conditions on health. Working conditions are measured repeatedly throughout the work life and health endpoints are based on clinical diagnosis. Workforce entry was defined as the first year with employment as the main source of income (n=979,257). We excluded individuals with missing data on gender and ethnicity (n=5,176), and individuals who died (n=71), emigrated (n=13,087), or received disability pension (n=361) in their year of entry, leaving 960,562

individuals in the cohort. To study incident depressive disorder, we further excluded individuals with diagnosed depressive disorder before or in the year of workforce entry (n=4,989), yielding a final cohort of 955,573 individuals followed for 6,991,811 person years (mean follow up: 7.3 years).

### Measurement of work-related violence

Work-related violence was measured using a job exposure matrix (JEM) estimating the average gender- and age-specific probability of work-related violence in occupations classified according to the Danish version of the International Standard Classification of Occupations (International Labour Organization, 2004). The JEM was constructed using survey data from the Danish Work Environment Cohort Study (Burr et al., 2003). For details see the study protocol (Madsen et al., 2018b). The JEM showed good validity when compared to self-reported information using ROC-curve analysis. Within the Danish Working Environment Cohort study, the JEM showed an Area under the Curve (AUC) of 0.89, and a similar JEM showed AUCs of 0.84 and 0.86 for men and women respectively, when tested in an independent sample (Madsen et al., 2018a). The occupations with highest and lowest exposure are presented in **Supplementary Material, Table S1**.

Each individual was assigned an annual probability of work-related violence exposure, with a probability of 0 in years of non-employment. We measured cumulated exposure by summing these annual probabilities. After applying logarithmic transformation ( $\log_2$ ), the measures for past year and cumulated work-related violence exposure were included as continuous variables in the main analysis to estimate the risk of depressive disorder associated with a doubling of exposure. To avoid logarithmic transformation of 0 we added a small constant before log-transformation.

For comparability to previous research, we also constructed a categorical measure for past year risk of work-related violence defined as low (0 to <1% probability of work-related violence), medium (1 to 2% probability), and high (>2% probability). The categories were constructed using the quartiles of exposure probability but collapsing the first two quartiles. We further constructed a categorical measure for the proportion of previous annual measures with high risk of work-related violence categorized into 0 to 5%, 6% to 25%, 26% to 75%, and 76% or more. The Pearson's correlation between past year and cumulated work-related violence risk was 0.74 and the relation between past year and cumulated high probability of violence is illustrated in **Supplementary Material, Table S1**.

### Measurement of depressive disorder

Information on depressive disorder was obtained from The Psychiatric Central Research Register (Mors et al., 2011) during 1969–1994 and The National Patient Register during 1995–2010 (Lynge et al., 2011). The registers encompass all inpatient psychiatric admissions in Denmark since 1969, and from 1995 onwards also outpatient admissions (Mors et al., 2011). We defined depressive disorder as a main diagnosis of F32 or F33 from ICD-10 (for years 1994 to 2010), and 296.0, 296.2, 298.0, 300.4 from ICD-8 (for years 1969 to 1993). ICD-9 was never used in Denmark. To exclude individuals with depressive disorder prior to workforce entry, we also used the codes F92.0 (ICD-10) and 308.02 (ICD-8) for depressive disorder in childhood or adolescence.

### Measurement of covariates

As covariates, we included calendar year, gender, age, cohabitation, ethnicity, number of children, employment status, education, years of non-employment, years of work experience, income, number of health services used in the year before workforce entry, childhood socioeconomic position, and maternal and paternal psychiatric and somatic diagnoses before the cohort member entered the workforce. All covariates

were included from National Danish Registers (Andersen et al., 2011; Baadsgaard and Quitzau, 2011; Jensen and Rasmussen, 2011; Lyngge et al., 2011; Mors et al., 2011; Pedersen, 2011). Childhood socioeconomic position was measured by maternal and paternal educational level and labour market status when the cohort member was 15 years. Linkage to parental data was available from 1980 onwards and only for individuals with parents residing in Denmark and 11.3% of individuals had missing maternal data and 12.6% had missing paternal data. To ensure cohort completeness, we retained these individuals in the analysis but adjusted for missing data. Data on number of health services used was included from the Danish National Health services register, encompassing mainly primary health care services (Andersen et al., 2011). Age, cohabitation, number of children, education, income, employment status, years of non-employment, and years of work experience were included as annual time-varying variables, while remaining covariates were considered time-invariant.

### Statistical modeling

We analyzed data using Cox regression with time-to-first diagnosis of depressive disorder as the outcome, modelling past year and cumulated exposures concurrently. We used calendar time as the time-axis to account for period effects on psychiatric treatment (Mors et al., 2011) and analyzed data longitudinally with a one year time-lag, relating exposure during year  $t$  to events during year  $t+1$ . Individuals were followed from workforce entry until first depressive disorder diagnosis, death, emigration, receipt of disability pension, or end of follow-up 31 December 2010, whichever came first. We limited follow-up to 2010 because exposures could not be updated after 2009 due to changes in the occupational classification.

The main analysis (model 1) adjusted for gender, age, cohabitation, ethnicity, number of children, employment status (employed vs. non-employed with studying and self-employment included as dummies), years of non-employment, years of work experience, income, childhood socioeconomic position, and maternal and paternal psychiatric and somatic diagnoses. In model 2, we further adjusted for the number of health services used in the year before workforce entry to account for non-specific health-related selection into high risk occupations. Fulfillment of the proportional hazards assumption were assessed by visual inspection of the log-log hazard plots.

### Sensitivity analyses

As pre-planned (Madsen et al., 2018b), we conducted sensitivity analyses stratifying by 1) gender, 2) ethnicity, 3) educational level, 4) industry. We conducted sensitivity analyses 1, 3, and 4 to assess if associations were similar in men and women and across educational levels and industries. We conducted sensitivity analysis 2 because no data were available for migrants prior to their migration to Denmark, and thus these individuals could have worked or been diagnosed with depressive disorder in another country before cohort entry.

### Post hoc supplementary analyses

As post hoc supplementary analyses we included analyses 1) without adjustment for parental data to gauge the extent of confounding in previous studies without parental data, 2) adjusting only for gender, age and employment status (minimally adjusted), 3) stepwise adding covariates from model 1 to the minimally adjusted model, 4) excluding individuals with any psychiatric diagnoses before workforce entry, 5) adjusting for occupational level of job control, as low job control may be a risk factor for depressive disorder, 6) examining two alternate cut-off points for the categorical definition of work-related violence, based on a previous study on work-related violence and affective disorder (Wieclaw et al., 2006) (a) low: <1%, medium:  $\geq 1\%$  to <8%, and high:  $\geq 8\%$ ; b) low: <1%, medium:  $\geq 1\%$  to <14%, and high:  $\geq 14\%$ ), 7) stratifying

by both industry and gender to further examine gender-specific patterns, 8) estimating the extent of bias caused by non-differential misclassification of exposure by the JEM for work-related violence. This analysis was conducted using the methods for quantitative bias analysis proposed by Lash, Fox, & Fink (2009) applying a sensitivity of 0.85 and a specificity of 0.80 based on data from a previous JEM validation (Madsen et al., 2018a).

## RESULTS

### Cohort characteristics

Table 1 shows the characteristics of the study population in their year of cohort entry. There were 49.3 percent women and the mean age was 20.2 years. About seven percent of the population had a mother with a psychiatric diagnosis.

We identified 16,148 cases of incident hospital-treated depressive disorder during 6.99 million person-years of follow-up (23 cases per 10,000 person years). Individuals were censored due to migration ( $n=103,762$ , 10.9%), death ( $n=2,734$ , 0.3%), and disability pensioning ( $n=8,132$ , 0.9%). Table 2 shows the association between population characteristics and the risk of depressive disorder. As expected, risk of first diagnosis with depressive disorder was higher in women than men, for individuals with lower education, and individuals with a parent with a psychiatric diagnosis, especially for maternal psychiatric diagnosis.

### Work-related violence and depressive disorder

Table 3 shows the association between work-related violence and risk of depressive disorder. Higher past year probability of work-related violence was statistically significantly associated with a small elevated risk of depressive disorder with a hazard ratio of 1.01 (95%CI: 1.00-1.01) per doubling of exposure probability of work-related violence. As an example of interpretation, this estimate shows that individuals with 4% probability of work-related violence had a hazard ratio of 1.01 compared to individuals with a 2% probability of work-related violence. When quantifying the association in terms of exposure categories, the hazard ratio for high vs. low probability of work-related violence was 1.11 (95% CI: 1.06-1.17). There was no additional association with accumulated exposure to work-related violence. Results were similar without (model 1) and with (model 2) adjustment for health care services use prior to workforce entry.

### Preplanned sensitivity analyses

Table 4 shows the results of the gender and ethnicity-stratified sensitivity analyses. The association between probability of work-related violence and depressive disorder was seen in women (HR=1.14, 95%CI: 1.08-1.21 for high vs. low exposure) but not in men (HR=0.99, 95%CI: 0.90-1.08 for high vs. low exposure).

The results for high compared to low work-related violence probability within educational strata are shown in **Supplementary Material, Table S3**. High work-related violence probability was associated with depressive disorders among individuals in the strata of “Primary and lower secondary education”, “Upper secondary education” and “Bachelor education” whereas the association was absent in the strata of “Short cycle tertiary education” and “Masters’ level education”.

When stratifying analyses by industry, the association between high work-related violence probability and risk of depressive disorders was present in four industries, including industries with high risk of work-related violence such as “Public- and personal services”, with point estimates ranging from 1.11 to 1.18. The association was absent in three industries, where statistically non-significant tendencies of increased risk were seen for employees in occupations with medium risk of violence (Table S4).

**Table 1**  
Characteristics of the study population in their year of entry into the workforce.

	N	%	Mean
<b>Total sample</b>	955,573	100	
<b>Gender</b>			
Men	484,422	50.7	
Women	471,151	49.3	
<b>Age</b>			20.2
15-17	103,410	10.8	
18-19	379,211	39.7	
20-25	378,299	39.6	
25-30	94,653	9.9	
<b>Cohabitation</b>			
Yes	613,502	64.2	
No	298,507	31.2	
Unknown	43,564	4.6	
<b>Ethnicity</b>			
Danish	811,622	84.9	
Non-Danish	143,951	15.1	
<b>Children in the household</b>			
0	286,040	29.9	
≥ 1	669,533	70.1	
<b>Education</b>			
Primary or lower secondary	686,791	71.9	
Upper secondary	172,169	18.0	
Short cycle tertiary	4,319	0.5	
Bachelor or equivalent	13,319	1.4	
Master or equivalent	5,389	0.6	
Doctoral or equivalent	13	<0.1	
Not classified/unknown	73,573	7.7	
<b>Maternal psychiatric diagnosis</b>			
Yes	62,543	6.5	
No	893,030	93.5	
<b>Paternal psychiatric diagnosis</b>			
Yes	57,733	6.0	
No	897,840	94.0	
<b>Maternal somatic diagnosis</b>			
Yes	40,617	4.3	
No	821,176	85.9	
Missing	93,780	9.8	
<b>Paternal somatic diagnosis</b>			
Yes	55,373	5.8	
No	794,235	83.1	
Missing	105,965	11.1	
<b>Maternal education</b>			
Primary or lower secondary	207,277	21.7	
Upper secondary	238,304	24.9	
Short cycle tertiary	16,331	1.7	
Bachelor or equivalent	111,198	11.6	
Master or doctoral	22,624	2.4	
Not classified/unknown	359,839	37.7	
<b>Paternal education</b>			
Primary or lower secondary	123,473	12.9	
Upper secondary	258,260	27.0	
Short cycle tertiary	22,091	2.3	
Bachelor or equivalent	54,981	5.8	
Master or doctoral	45,357	4.8	
Not classified/unknown	451,411	47.2	
<b>Maternal labour market status</b>			
Employed	653,987	68.4	
Non-employed	192,581	20.2	
Unknown	109,005	11.4	
<b>Paternal labour market status</b>			
Employed	705,361	73.8	
Non-employed	122,213	12.8	
Unknown	127,999	13.4	
<b>Missing maternal data</b>			
Yes	93,780	9.8	
No	861,793	90.2	
<b>Missing paternal data</b>			
Yes	105,965	11.1	
No	849,608	88.9	
<b>Depression status</b>			
Yes	16,148	0.2	
No	7,038,803	99.8	

**Table 2**  
Characteristics of the study population throughout the study period and first depression diagnosis.

	N person years (PY)	%	Incident depressive disorder per 10 000 PY
<b>Gender</b>			
Men	3,557,929	50.9	15
Women	3,433,882	49.1	31
<b>Age</b>			
15-17	129,766	1.9	14
18-19	713,866	10.2	20
20-25	2,950,696	42.2	22
25 ≤	3,197,484	45.7	25
<b>Cohabitation</b>			
Yes	4,125,032	59.0	19
No	2,827,071	40.4	29
Unknown	39,709	0.6	12
<b>Ethnicity</b>			
Danish	6,227,382	89.1	23
Non-Danish	764,430	10.9	21
<b>Children in the household</b>			
0	3,971,528	56.8	25
≥ 1	3,020,283	43.2	21
<b>Income</b>			
Decile 1 (lowest)	695,042	9.9	28
Decile 2	696,497	10.0	27
Decile 3	697,306	10.0	24
Decile 4	696,029	10.0	27
Decile 5	695,626	9.9	31
Decile 6	698,686	10.0	27
Decile 7	701,324	10.0	23
Decile 8	703,373	10.1	17
Decile 9	704,381	10.1	14
Decile 10 (highest)	703,546	10.1	10
<b>Education</b>			
Primary or lower secondary	2,532,115	36.2	30
Upper secondary	3,234,617	46.3	20
Short cycle tertiary	194,981	2.8	14
Bachelor or equivalent	610,136	8.7	17
Master or equivalent	260,469	3.7	10
Doctoral or equivalent	8,512	0.1	11
Not classified/unknown	150,981	2.2	18
<b>Maternal psychiatric diagnosis</b>			
Yes	408,335	5.8	46
No	6,130,292	87.7	22
Missing	543,184	6.5	21
<b>Paternal psychiatric diagnosis</b>			
Yes	376,882	5.4	43
No	6,083,487	87.0	22
Missing	531,442	7.6	22
<b>Maternal somatic diagnosis</b>			
Yes	291,007	4.2	28
No	6,247,620	89.4	23
Missing	453,184	6.5	21
<b>Paternal somatic diagnosis</b>			
Yes	394,292	5.6	28
No	6,066,078	86.8	23
Missing	531,442	7.6	22
<b>Maternal education</b>			
Primary or lower secondary	1,355,122	19.4	28
Upper secondary	1,568,099	22.4	23
Short cycle tertiary	107,161	1.5	19
Bachelor or equivalent	781,177	11.2	22
Master or doctoral	146,172	2.1	21
Not classified/unknown	3,034,080	43.4	21
<b>Paternal education</b>			
Primary or lower secondary	691,532	9.9	30

(continued on next page)

Table 2 (continued)

	N person years (PY)	%	Incident depressive disorder per 10 000 PY
Upper secondary	1,707,880	24.4	23
Short cycle tertiary	153,423	2.2	21
Bachelor or equivalent	395,212	5.7	19
Master or doctoral	312,296	4.5	21
Not classified/ unknown	3,731,469	53.4	23
<b>Maternal labour market status</b>			
Employed	4,984,017	71.3	21
Non-employed	1,410,346	20.2	30
Unknown	597,448	8.5	22
<b>Paternal labour market status</b>			
Employed	5,352,716	76.6	21
Non-employed	895,407	12.8	32
Unknown	743,689	10.6	24

## Supplementary post hoc analyses

Figure 1 summarizes the results from analyses stratified by industry and gender (for detailed results see **Supplementary Material, Table S5**). We found associations or statistically non-significant tendencies towards associations between work-related violence probability and depressive disorder for women in all industries, and for men in certain industries (“Retail trade; hotels and restaurants”, “Financial intermediation, business etc.”, and “Public and personal services”).

**Supplementary Material, Table S6** shows results of the post hoc supplementary analyses. Results were similar after omitting adjustment for parental data. The minimally adjusted model showed an association which was only slightly stronger than the main analyses, with a hazard ratio of 1.21 (95% CI: 1.15-1.27) for high probability of work-related violence and 1.15 (95% CI: 1.09-1.21) for medium probability of work-related violence. When applying stepwise adjustment, the largest reduction in the hazard ratios was related to further adjustment for income, which reduced the hazard to 1.15 (95% CI: 1.10-1.21) for high probability of work-related violence and 1.09 (95% CI: 1.04-1.15) for medium probability of work-related violence. Results remained similar when excluding individuals with any psychiatric diagnosis prior to work-force entry (n=48,638). When adjusting for occupational job control, the estimate for work-related violence increased. When changing the cut-off points defining high, medium and low probability of work-related violence, the association in women became more pronounced, but still no association was seen in men. We found some

indication of accumulation when analyzing the proportion of annual measures with high probability of work-related violence, with an additionally higher risk of depressive disorder for individuals with 76% or more of measurements with high exposure probability.

Our quantitative bias analysis, accounting for measurement error in terms of exposure misclassification by the JEM, showed that the hazard ratio of 1.11 for high vs. low probability of work-related violence increased to 1.22 when accounting for exposure misclassification.

## DISCUSSION

Our study, based on an inception cohort of the entire employed population of Denmark between 1995 and 2009, found that employees in occupations risking work-related violence had a higher risk of first-time hospital diagnosed depressive disorder. This association was not explained by risk factors for depressive disorder pre-existing work-force entry, including parental psychiatric or somatic diagnoses, childhood socioeconomic position, and primary care health services use. The association between work-related violence and depressive disorder was gender- and industry-specific. While the association in women was largely robust, only men employed in certain industries had a higher risk of depressive disorder in relation to work-related violence. The association was modest in strength, but may be a conservative estimate of the underlying association, as also indicated by the quantitative bias analysis.

This study is the first to examine the association between work-related violence and depressive disorder whilst accounting for risk factors for depressive disorder that pre-exist workforce entry. Our findings suggest a causal effect of work-related violence on the development of depressive disorder. Such effect is plausible given the evidence concerning effects of domestic violence on risk of depressive disorder (Campbell, 2002; Weich et al., 2009). Mechanisms could include feelings of helplessness and hopelessness, which have been related to the etiology of depressive disorder (Beck and Alford, 2009). Our findings extend previous studies associating work-related violence with indicators of depressive disorder (Butterworth et al., 2016; Madsen et al., 2011; Wieclaw et al., 2006). When we omitted adjustment for potential confounders pre-existing workforce entry, results were similar to those of our main analyses, suggesting that selection of individuals vulnerable to depressive disorder into occupations with high risk of violence was probably not a major bias in previous studies on the topic.

The gender- and industry-specific patterns of the association between work-related violence and depressive disorder may be related to differences in the type of violence encountered by women and men and

Table 3

Association between work-related violence and first depression diagnosis.

	Person-years at risk (PY)	Depression cases per 10 000 PY	Model 1		P-value	Model 2		P-value
			HR	95% CI		HR	95% CI	
Past year work-related violence, per doubling	6,991,811	23	1.01	1.00-1.01	<.001	1.01	1.00-1.01	<.001
Past year work-related violence					<.001			<.001
Low	4,091,891	23	Ref.	-		Ref.	-	
Medium	1,457,375	21	1.06	1.01-1.11		1.06	1.01-1.11	
High	1,442,546	25	1.11	1.06-1.17		1.11	1.06-1.16	
Cumulated work-related violence, per doubling	6,991,811	23	1.00	1.00-1.00	0.486	1.00	1.00-1.00	0.797

PY: Person years, HR: Hazard Ratio, CI: Confidence Interval.

Associations for past year work-related violence and cumulated work-related violence are included in the same models (mutually adjusted).

Model 1 is adjusted for gender, age, cohabitation, ethnicity, number of children, employment status, years of non-employment, years of work experience, income, maternal and paternal psychiatric and somatic diagnoses, maternal and paternal education and labour market status.

Model 2 is adjusted for health services use in the year before workforce entry in addition to the covariates of model 1.

**Table 4**

Association between work-related violence and first depression diagnosis stratified by gender and ethnicity

	Person-years at risk (PY)	Depression cases per 10 000 PY	HR	95% CI	P-value
<b>Men</b>					
Past year work-related violence					0.760
Low	2,277,292	16	Ref.	-	
Medium	806,952	13	1.02	0.94-1.11	
High	473,685	14	0.99	0.90-1.08	
Cumulated work-related violence, per doubling			1.00	1.00-1.01	0.452
<b>Women</b>					
Past year work-related violence					<.001
Low	1,814,599	32	Ref.	-	
Medium	650,422	30	1.07	1.01-1.14	
High	968,860	31	1.14	1.08-1.21	
Cumulated work-related violence, per doubling			1.00	1.00-1.01	0.399
<b>Danish ethnicity</b>					
Past year work-related violence					<.001
Low	3,637,503	23	Ref.	-	
Medium	1,288,121	21	1.06	1.01-1.12	
High	1,301,758	26	1.12	1.06-1.18	
Cumulated work-related violence, per doubling			1.00	1.00-1.0	0.285
<b>Non-Danish ethnicity</b>					
Past year work-related violence					0.398
Low	454,388	23	Ref.	-	
Medium	169,254	16	0.98	0.83-1.12	
High	140,788	22	1.09	0.93-1.18	
Cumulated work-related violence, per doubling			1.00	0.99-1.00	0.565

PY: Person years, HR: Hazard Ratio, CI: Confidence Interval.

Associations for past year work-related violence and cumulated work-related violence are included in the same models (mutually adjusted). Estimates are adjusted for gender (except in the gender-stratified analysis), age, cohabitation, ethnicity (except in the ethnicity-stratified analysis), number of children, employment status, years of non-employment, years of work experience, income, maternal and paternal psychiatric and somatic diagnoses, maternal and paternal education and labour market status..

in different industries. Although there may be gender-difference in the etiology of depressive disorder (Kendler and Gardner, 2014), the association between work-related violence probability and depressive disorder was seen also for men, if they worked in industries involving person-related work, such as “Retail trade; hotels and restaurants” and “Public and personal” services. Employees in these industries are at risk of work-related violence (Madsen et al., 2010), predominantly from their clients (Wieclaw et al., 2006). The gender-difference contrasts a previous study on Danish registers, which found higher risk of affective disorders in both men and women in occupations with risk of violence (Wieclaw et al., 2006). The previous study used a nested case-control design, and it is possible that this is why the industry-specific patterns were not revealed to the same extent as in our study. Another difference is that we followed individuals from the beginning of their work lives and included only individuals aged 15-30 years at cohort entry, whereas the previously studied population included individuals aged 18-65.

Our results concerning accumulation of effects of work-related violence on depressive disorder remain inconclusive. No accumulation was seen in the main analysis, but supplementary analyses showed some indication, i.e. there was a higher risk of depressive disorder for employees with 76% or more measurements with high probability of work-related violence after accounting for past year exposure. There is a paucity of studies examining the accumulation of risks related to work-related violence, as most previous studies have measured exposure only at single time points. One study examined the cumulative effects of trauma, including violence and abuse outside the workplace, in a sample of female nurses and nursing personnel (Cavanaugh et al., 2014). The results suggested that different types of trauma accumulated, and nurses who had experienced three or more types of trauma had a two to six-fold higher risk of depression and post-traumatic stress, compared to non-exposed nurses. Further research is needed to conclude firmly regarding the potential accumulation of effects of work-related violence on depressive disorder.

Our results suggest that the association between work-related violence and depressive disorder may be causal. This finding has important implications for policy and practice as it underlines the

importance of preventive efforts targeting work-related violence. Preventive interventions may include staff training in de-escalation techniques or aggression management, and implementing a systematic approach to risk management (O'Rourke et al., 2018; Price et al., 2015; Wassell, 2009). From a clinical perspective, occupational information regarding work-related violence may be considered a risk factor in the assessment of patients possibly presenting with depressive disorder.

#### Strengths and limitations

The strengths of this study include the register-based design allowing us to follow an exhaustive cohort of employees with annual measures of work-related violence from the beginning of their work lives, without selective participation or drop out. Further strengths include the outcome measure based on clinical diagnosis, and the inclusion of potential confounders from before workforce entry. Including individuals in the study from workforce entry also means that potential underestimation of effects due to healthy worker selection was diminished.

While the register-based design entails important strengths, it also carries certain limitations. First, exposure to work-related violence was not measured at the individual level but using a JEM estimating the probability of work-related violence in relation to occupation, gender and age. Consequently, the findings should be carefully interpreted in light of previous studies showing associations at the individual level. Inherent in the JEM-measurement is a misclassification of exposure, as most persons classified as high-probability of work-related violence had not actually experienced work-related violence. This misclassification likely results in an underestimation of the effects of work-related violence on depressive disorder risk, as also suggested by the quantitative bias analysis. To further strengthen the evidence base concerning the effect of work-related violence on depression, future studies should apply individual level exposure measurement. In light of the relatively low prevalence of work-related violence in the general working population, one suggestion might be to analyse data from pooled cohort studies, such as has been conducted concerning the association between work-related violence and diabetes (Xu et al., 2018). However,

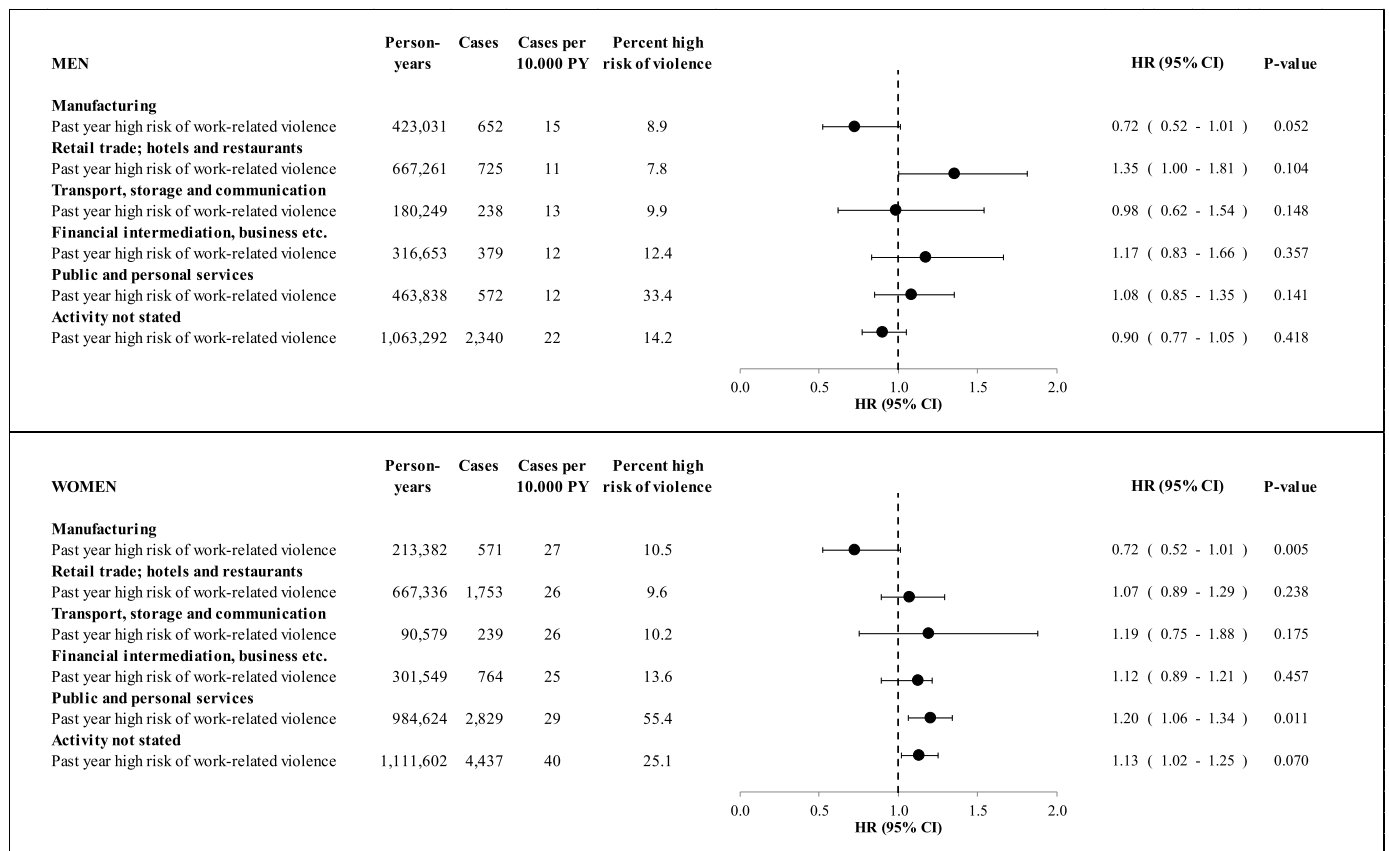


Fig. 1. Incident depressive disorder for employees with high risk of work-related violence compared to low within industries for men and women separately.

considering the already existing and mounting evidence on the adverse effects of work-related violence on (mental) health (Butterworth et al., 2016; Madsen et al., 2011; Rudkjoebing et al., 2020), the development and implementation of methods to prevent and manage violence in workplaces may be timely.

We employed a one-year time lag between exposure and outcome to avoid reverse causation. This longitudinal approach may be considered a study strength, but simultaneously it is a limitation if effects of work-related violence are acute and triggering, in which case it may have caused an underestimation. Furthermore, we could not include data on several known vulnerability factors such as life events (Kendler and Gardner, 2016) or genetics (Pettersson et al., 2018). We would argue that it is unlikely that the association found between work-related violence and depressive disorder is attributable to confounding by life events, as there is a social gradient in life events, with higher prevalence in adolescents with lower parental education and income (Glasscock et al., 2013; Masters Pedersen et al., 2015). Consequently, the association should be attenuated with adjustment for indicators of childhood socioeconomic position, if it were attributable to confounding by life events, and this was not the case in the present analysis. Furthermore, the information on parental psychiatric diagnoses could be considered a marker of biologic risk. Nevertheless, the lack of data on life events and genetics remains a limitation of our study. Finally, it should be noted that we included only cases of depressive disorder that were hospital diagnosed and associations may differ from associations with symptom-based measures (Thielen et al., 2009) as many cases of depressive disorder are untreated or treated exclusively in primary care (Alonso et al., 2004).

To conclude, we found that employees in occupations with high probability of work-related violence had a higher risk of depressive disorder, and that this association was not explained by known risk factors for depressive disorder pre-existing workforce entry, including

parental psychiatric diagnoses and childhood socioeconomic position. The association was gender- and industry-specific, possibly related to industry-specific patterns in the type of work-related violence encountered. Our findings suggest a causal role of work-related violence in the development of depressive disorder and underline the importance of preventive efforts to reduce work-related violence.

**Author contributions**

IEHM conceived the study and designed and conducted the analyses. All authors interpreted the data and discussed the results. IEHM wrote the first draft of the manuscript and all authors revised the draft critically for important intellectual content. All authors read and approved the final version for submission.

**Funding statement**

The Danish Worklife Course Cohort is funded by a grant from the Danish Working Environment Research Fund (grant number 17-2014-03). The analyses for this article were further supported by grants from the Danish Working Environment Research Fund (grant number 43-2014-03 and 27-2017-03) and NordForsk (grant number 75021).

**Conflicts of interest**

None.

**Acknowledgements**

None.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2021.03.065.

## References

- Alonso, J., Angermeyer, M.C., Bernert, S., Bruffaerts, R., Brugha, I.S., Bryson, H., de Girolamo, G., de Graaf, R., Demeyttenaere, K., Gasquet, I., Haro, J.M., Katz, S.J., Kessler, R.C., Kovess, V., Lepine, J.P., Ormel, J., Polidori, G., Russo, L.J., Vilagut, G., Almansa, J., rbazadeh-Bouchez, S., Autonell, J., Bernal, M., Buist-Bouwman, M.A., Codony, M., Domingo-Salvany, A., Ferrer, M., Joo, S.S., Martínez-Alonso, M., Matschinger, H., Mazzi, F., Morgan, Z., Morosini, P., Palacin, C., Romera, B., Taub, N., Vollebergh, W.A.M., 2004. Use of mental health services in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatrica Scandinavica* 109, 47–54.
- Andersen, J.S., Olivarius Nde, F., Krasnik, A., 2011. The Danish National Health Service Register. *Scand. J. Public Health* 39, 34–37.
- Baadsgaard, M., Quitzau, J., 2011. Danish registers on personal income and transfer payments. *Scand. J. Public Health* 39, 103–105.
- Beck, A.T., Alford, B.A., 2009. *Depression : Causes and treatment, 2, Second Edition ed.* University of Pennsylvania Press, Philadelphia, Pa. <https://doi.org/10.9783/9780812290882>.
- Burr, H., Bjorner, J.B., Kristensen, T.S., Tüchsen, F., Bach, E., 2003. Trends in the Danish work environment in 1990-2000 and their associations with labor-force changes. *Scand. J. Work. Environ. Health* 29, 270–279.
- Butterworth, P., Leach, L.S., Kiely, K.M., 2016. Why it's important for it to stop: Examining the mental health correlates of bullying and ill-treatment at work in a cohort study. *Australian & New Zealand Journal of Psychiatry* 50, 1085–1095.
- Campbell, J.C., 2002. Health consequences of intimate partner violence. *Lancet* 359, 1331–1336.
- Cavanaugh, C., Campbell, J., Messing, J.T., 2014. A Longitudinal Study of the Impact of Cumulative Violence Victimization on Comorbid Posttraumatic Stress and Depression among Female Nurses and Nursing Personnel. *Workplace Health & Safety* 62, 224–232.
- Dement, J.M., Lipscomb, H.J., Schoenfish, A.L., Pompeii, L.A., 2014. Impact of hospital type II violent events: use of psychotropic drugs and mental health services. *Am J Ind Med* 57, 627–639.
- Fussell, F.W., Bonney, W.C., 1990. A comparative study of childhood experiences of psychotherapists and physicians: Implications for clinical practice. *Psychotherapy: Theory, Research, Practice, Training* 27, 505–512.
- Glasscock, D.J., Andersen, J.H., Labriola, M., Rasmussen, K., Hansen, C.D., 2013. Can negative life events and coping style help explain socioeconomic differences in perceived stress among adolescents? A cross-sectional study based on the West Jutland cohort study. *BMC Public Health* 13, 532.
- Hay, S.I., Abajobir, A.A., Abate, K.H., Abbafati, C., Abbas, K.M., Abd-Allah, F., Abdulkader, R.S., Abdulle, A.M., Abebo, T.A., Abera, S.F., Aboyans, V., Abu-Raddad, L.J., Ackerman, I.N., Adedeji, I.A., Adetokunboh, O., Afshin, A., Aggarwal, R., Agrawal, S., Agrawal, A., Ahmed, M.B., Aichour, M.T.E., Aichour, A.N., Aichour, I., Aiyar, S., Akinyemi, T.F., Akseer, N., Al Lami, F.H., Alahdab, F., Al-Aly, Z., Alam, K., Alam, T., Alasfoor, D., Alene, K.A., Ali, R., Alizadeh-Navaei, R., Alkaabi, J.M., Alkerwi, A.a., Alla, F., Allebeck, P., Allen, C., Al-Maskari, F., Almazroa, M.A., Al-Raddadi, R., Alsharif, U., Alsowaidi, S., Althouse, B.M., Altirkawi, K.A., Alvis-Guzman, N., Amare, A.T., Amini, E., Ammar, W., Amoako, Y.A., Ansha, M.G., Antonio, C.A.T., Anwari, P., Arnlöv, J., Arora, M., Artaman, A., Aryal, K.K., Asgedom, S.W., Atey, T.M., Atafu, N.T., Avila-Burgos, L., Avokpaho, E.F.G.A., Awasthi, A., Awasthi, S., Azarpazhooh, M.R., Azzopardi, P., Babalola, T.K., Bacha, U., Badawi, A., Balakrishnan, K., Bannick, M.S., Barac, A., Barker-Collo, S.L., Bärnighausen, T., Barquera, S., Barrero, L.H., Basu, S., Battista, R., Battle, K.E., Baune, B.T., Bazargan-Hejazi, S., Beardsley, J., Bedi, N., Béjot, Y., Bekele, B.B., Bell, M.L., Bennett, D.A., Bennett, J.R., Bensenor, I.M., Benson, J., Berhane, A., Berhe, D.F., Bernabé, E., Betsu, B.D., Beuran, M., Beyene, A.S., Bhansali, A., Bhatt, S., Bhutta, Z.A., Biadgilign, S., Bicer, B.K., Bienhoff, K., Bikbov, B., Birungi, C., Biryukov, S., Bisanzio, D., Bizuayehu, H.M., Blyth, F.M., Boneya, D.J., Bose, D., Bou-Orm, I.R., Bourme, R.R.A., Brainin, M., Brayne, C., Brazinova, A., Breitborde, N.J.K., Briant, P.S., Britton, G., Brugha, T.S., Buchbinder, R., Bulto, L.N.B., Bumgarner, B.R., Butt, Z.A., Cahuana-Hurtado, L., Cameron, E., Campos-Nonato, I.R., Carabin, H., Cárdenas, R., Carpenter, D.O., Carrero, J.J., Carter, A., Carvalho, F., Casey, D., Castañeda-Orjuela, C.A., Castle, C.D., Catalá-López, F., Chang, J.-C., Charlson, F.J., Chaturvedi, P., Chen, H., Chibabala, M., Chibueze, C.E., Chisumpa, V.H., Chitheer, A.A., Chowdhury, R., Christopher, D.J., Ciobanu, L.G., Cirillo, M., Colombara, D., Cooper, L.T., Cooper, C., Cortesi, P.A., Cortinovis, M., Criqui, M.H., Cromwell, E.A., Cross, M., Crump, J.K., Dadi, A.F., Dalal, K., Damasceno, A., Dandona, L., Dandona, R., das Neves, J., Davitoiu, D.V., Davletov, K., de Courten, B., De Leo, D., De Steur, H., Defo, B.K., Degenhardt, L., Deiparine, S., Dellavalle, R.P., Deribe, K., Deribew, A., Des Jarlais, D.C., Dey, S., Dharmaratne, S.D., Dhillon, P.K., Dicker, D., Djalalinia, S., Do, H.P., Dokova, K., Doku, D.T., Dorsey, E.R., dos Santos, K.P.B., Driscoll, T.R., Dube, M., Duncan, B.B., Ebel, B.E., Echko, M., El-Khatib, Z.Z., Enayati, A., Endries, A.Y., Ermakov, S.P., Erskine, H.E., Eshetie, S., Eshrati, B., Esteghamati, A., Estep, K., Fanuel, F.B.B., Farag, T., Farinha, C.S.E.S., Faro, A., Farzadfar, F., Fazeli, M.S., Feigl, V.L., Feigl, A.B., Fereshtehnejad, S.-M., Fernandes, J.C., Ferrari, A.J., Feyissa, T.R., Filip, I., Fischer, F., Fitzmaurice, C., Flaxman, A.D., Foigt, N., Foreman, K.J., Franklin, R.C., Frostad, J.J., Fullman, N., Fürst, T., Furtado, J.M., Futran, N.D., Gakidou, E., Garcia-Basteiro, A.L., Gebre, T., Gebregers, G.B., Gebrehiwot, T.T., Geleijnse, J.M., Geleto, A., Gemechu, B.L., Gesesew, H.A., Gething, P.W., Ghajjar, A., Gibney, K.B., Gillum, R.F., Ginawi, I.A.M., Gishu, M.D., Giussani, G., Godwin, W.W., Goel, K., Goenka, S., Goldberg, E.M., Gona, P.N., Goodridge, A., Gopalani, S.V., Gosselin, R.A., Gotay, C.C., Goto, A., Goulart, A.C., Graetz, N., Gughani, H.C., Gupta, P.C., Gupta, R., Gupta, T., Gupta, V., Gupta, R., Gutiérrez, R.A., Hachinski, V., Hafezi-Nejad, N., Hailu, A.D., Hailu, G.B., Hamadeh, R.R., Hamidi, S., Hammami, M., Handal, A.J., Hankey, G.J., Hao, Y., Harb, H.L., Hareri, H.A., Haro, J.M., Harun, K.M., Harvey, J., Hassavand, M.S., Havmoeller, R., Hay, R.J., Hedayati, M.T., Hendrie, D., Henry, N.J., Heredia-Pi, I.B., Heydarpour, P., Hoek, H.W., Hoffman, H.J., Horino, M., Horita, N., Hosgood, H.D., Hostiu, S., Hotez, P.J., Hoy, D.G., Htet, A.S., Hu, G., Huang, J.J., Huynh, C., Iburg, K.M., Igumbor, E.U., Ikeda, C., Irvine, C.M.S., Islam, S.M.S., Jacobsen, K.H., Jahanmehr, N., Jakovljevic, M.B., James, P., Jassal, S.K., Javanbakht, M., Jayaraman, S.P., Jeemon, P., Jensen, P.N., Jha, V., Jiang, G., John, D., Johnson, C.O., Johnson, S.C., Jonas, J.B., Jürisson, M., Kabir, Z., Kadel, R., Kahsay, A., Kamal, R., Kar, C., Karam, N.E., Karch, A., Karema, C.K., Karimi, S.M., Karimkhani, C., Kasaian, A., Kassa, G.M., Kassaw, N.A., Kassebaum, N.J., Kastor, A., Katikireddi, S.V., Kaul, A., Kawakami, N., Keiyoro, P.N., Kemmer, L., Kengne, A.P., Keren, A., Kesavachandran, C.N., Khader, Y.S., Khalil, I.A., Khan, E.A., Khang, Y.-H., Khoja, A.T., Khosravi, A., Khubchandani, J., Kiadaliri, A.A., Kielling, C., Kim, Y.J., Kim, D., Kimokoti, R.W., Kinfu, Y., Kisa, A., Kissimova-Skarbek, K.A., Kissoun, N., Kivimaki, M., Knudsen, A.K., Kokubo, Y., Kolte, D., Kopec, J.A., Kosen, S., Kotsakis, G.A., Koul, P.A., Koyanagi, A., Kravchenko, M., Krohn, K.J., Kumar, G.A., Kumar, P., Kyu, H.H., Lager, A.C.J., Lal, D.K., Lalloo, R., Lallukka, T., Lambert, N., Lan, Q., Lansingh, V.C., Larsson, A., Leasher, J.L., Lee, P.H., Leigh, J., Leshargie, C.T., Leung, J., Leung, R., Levi, M., Li, Y., Li, Y., Liang, X., Lim, M.L., Lim, S.S., Linn, S., Liu, P.Y., Liu, A., Liu, S., Liu, Y., Lodha, R., Logroscino, G., Looker, K.J., Lopez, A.D., Lorkowski, S., Lotufo, P.A., Lozano, R., Lucas, T.C.D., Lunevicius, R., Lyons, R.A., Macarayan, E.R.K., Maddison, E.R., Magdy Abd El Razek, H.M.A., Magdy Abd El Razek, M., Magis-Rodriguez, C., Mahdavi, M., Majdan, M., Majdzadeh, R., Majeed, A., Malekzadeh, R., Malhotra, R., Malta, D.C., Mamun, A.A., Manguerra, H., Manhertz, T., Mantovani, L.G., Mapoma, C.C., March, L.M., Marczak, L.B., Martínez-Raga, J., Martins, P.H.V., Martins-Melo, F.R., Martopullo, I., März, W., Mathur, M.R., Mazidi, M., McAlinden, C., McGaughey, M., McGrath, J.J., McKee, M., Mehata, S., Meier, T., Meles, K.G., Memiah, P., Memish, Z.A., Mendoza, W., Mengesha, M.M., Mengistie, M.A., Mengistu, D.T., Mensah, G.A., Meretoja, T.J., Meretoja, A., Mezgebe, H.B., Michal, R., Millea, A., Miller, T.R., Minng, S., Mirarefin, M., Mirrahimov, E.M., Misganaw, A., Mishra, S.R., Mitchell, P.B., Mohammad, K.A., Mohammad, A., Mohammed, M.S.K., Mohammed, K.E., Mohammed, S., Mohan, M.B.V., Mokdad, A.H., Mollenkopf, S.K., Monasta, L., Montañez Hernandez, J.C., Montico, M., Moradi-Lakeh, M., Moraga, P., Morawska, L., Mori, R., Morrison, S.D., Moses, M., Mountjoy-Venning, C., Mruts, K. B., Mueller, U.O., Muller, K., Murdoch, M.E., Murthy, G.V.S., Murthy, S., Musa, K.I., Nachega, J.B., Nagel, G., Naghavi, M., Naheed, A., Naidoo, K.S., Nangia, V., Nasher, J.T., Natarajan, G., Negasa, D.E., Negoi, R.I., Negoi, I., Newton, C.R., Ngunjiri, J.W., Nguyen, C.T., Nguyen, Q.L., Nguyen, T.H., Nguyen, G., Nguyen, M., Nichols, E., Ningrum, D.N.A., Nong, V.M., Norheim, O.F., Norrving, B., Noubiap, J.J. N., Nyandwi, A., Obermeyer, C.M., O'Donnell, M.J., Ogbo, F.A., Oh, I.-H., Okoro, A., Oladimeji, O., Olagunju, A.T., Olagunju, T.O., Olsen, H.E., Olusanya, B.O., Olusanya, J.O., Ong, K., Opio, J.N., Oren, E., Ortiz, A., Osborne, R.H., Osgood-Zimmerman, A., Osman, M., Ota, E., Owolabi, M.O., Pa, M., Pacella, R.E., Panda, B. K., Pandian, J.D., Papachristou, C., Park, E.-K., Parry, C.D., Parsaeani, M., Patil, S.T., Patten, S.B., Patten, G.C., Paudel, D., Paulson, K., Pearce, N., Pereira, D.M., Perez, K. M., Perico, N., Pesudovs, K., Peterson, C.B., Petri, W.A., Petzold, M., Phillips, M.R., Phipps, G., Pigott, D.M., Pillay, J.D., Pinho, C., Piradov, M.A., Plass, D., Pletcher, M. A., Popova, S., Poulton, R.G., Pourmalek, F., Prabhakaran, D., Prasad, N., Purcell, C., Purwar, M., Qorbani, M., Quintanilla, B.P.A., Rabiee, R.H.S., Radfar, A., Rafay, A., Rahimi, K., Rahimi-Movaghar, A., Rahimi-Movaghar, V., Rahman, M.H.U., Rahman, M.A., Rahman, M., Rai, R.K., Rajic, S., Ram, U., Ranabhat, C.L., Rangaswamy, T., Rankin, Z., Rao, P.V., Rao, P.C., Rawaf, S., Ray, S.E., Reiner, R.C., Reinig, N., Reitsma, M., Remuzzi, G., Renzaho, A.M.N., Resnikoff, S., Rezaei, S., Ribeiro, A.L., Rivas, J.C., Roba, H.S., Robinson, S.R., Rojas-Rueda, D., Rokni, M.B., Ronfani, L., Roshandel, G., Roth, G.A., Rothenbacher, D., Roy, A., Rubagotti, E., Ruhago, G.M., Saadat, S., Safdarian, M., Safiri, S., Saghar, R., Sahathevan, R., Sahraian, M.A., Salama, J., Saleh, M.M., Salomon, J.A., Salvi, S.S., Samy, A.M., Sanabria, J.R., Sanchez-Niño, M.D., Santomauro, D., Santos, J.V., Santos, I.S., Santric Milicevic, M.M., Sartorius, B., Satpathy, M., Sawhney, M., Saxena, S., Scheltonka, K., Schmidt, M.I., Schneider, J.C., Schöttker, B., Schutte, A.E., Schwebel, D.C., Schwendicke, F., Seedat, S., Sepanlou, S.G., Servan-Mori, E.E., Shaheen, A., Shaikh, M.A., Shamsipour, M., Sharma, R., Sharma, J., She, J., Shi, P., Shihuya, K., Shields, C., Shifa, G.T., Shiferaw, M.S., Shigematsu, M., Shiri, R., Shirkoo, B., Shirude, S., Shishani, K., Shoman, H., Siabani, S., Sibai, A.M., Sigfusdottir, I.D., Silberberg, D.H., Silva, D.A.S., Silva, J.P., Silveira, D.G.A., Singh, J.A., Singh, O.P., Singh, N.P., Singh, V., Sinha, D.N., Skiadaresi, E., Slepak, E.L., Smith, D.L., Smith, M., Sobaih, B.H.A., Sobngwi, E., Soljak, M., Sorensen, R.J.D., Sousa, T.C.M., Sposato, L.A., Sreeramareddy, C.T., Srivastava, V., Stanaway, J.D., Stathopoulou, V., Steel, N., Stein, D.J., Steiner, C., Steinke, S., Stokes, M.A., Stovner, L.J., Strub, B., Subart, M., Sufiyani, M.B., Sunguya, B.F., Sur, P.J., Swaminathan, S., Sykes, B.L., Sylte, D., Szeke, C.E.I., Tabarés-Seisdedos, R., Tadakamadla, S.K., Taffere, G.R., Takala, J.S., Tandon, N., Tanne, D., Tarekgn, Y.L., Tavakkoli, M., Taveira, N., Taylor, H.R., Tegegne, T.K., Tehrani-Banihashemi, A., Tekelab, T., Terkawi, A.S., Tesfaye, D.J., Tessema, B., Thakur, J.S., Thamsuwan, O., Theadam, A.M., Theis, A. M., Thomas, K.E., Thomas, N., Thompson, R., Thrift, A.G., Tobe-Gai, R., Tobollik, M., Tonelli, M., Topor-Madry, R., Tortajada, M., Touvier, M., Traebert, J., Tran, B.X., Troeger, C., Truelsen, T., Tsoi, D., Tuzcu, E.M., Tymeson, H., Tyrovolas, S.,



- Ukwaja, K.N., Undurraga, E.A., Uneke, C.J., Updike, R., Uthman, O.A., Uzochukwu, B.S.C., van Boven, J.F.M., Varughese, S., Vasankari, T., Veerman, L.J., Venkatesh, S., Venketasubramanian, N., Vidavalur, R., Vijayakumar, L., Violante, F. S., Vishnu, A., Vladimirov, S.K., Vlassov, V.V., Vollset, S.E., Vos, T., Wadilo, F., Wakayo, T., Wallin, M.T., Wang, Y.-P., Weichenthal, S., Weiderpass, E., Weintraub, R.G., Weiss, D.J., Werdecker, A., Westerman, R., Whiteford, H.A., Wijeratne, T., Williams, H.C., Wiyosong, C.S., Woldeyes, B.G., Wolfe, C.D.A., Woodbrook, R., Woolf, A.D., Workicho, A., Xavier, D., Xu, G., Yadgir, S., Yaghoubi, M., Yakob, B., Yan, L.L., Yano, Y., Ye, P., Yihdego, M.G., Yimam, H.H., Yip, P., Yonemoto, N., Yoon, S.-J., Yotebieng, M., Younis, M.Z., Yu, C., Zaidi, Z., Zaki, M.E.S., Zegeye, E.A., Zenebe, Z.M., Zhang, X., Zheng, Y., Zhou, M., Zipkin, B., Zodpey, S., Zocckler, L., Zuhlke, L.J., Murray, C.J.L., 2017. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet* 390, 1260–1344.
- International Labour Organization, 2004. In: *International Standard Classification of Occupations: ISCO-88*. International Labour Organization (ILO) Available from: <http://www.ilo.org/public/english/bureau/stat/isco/isco88/publ4.htm>.
- Jensen, V.M., Rasmussen, A.W., 2011. Danish Education Registers. *Scand. J. Public Health* 39, 91–94.
- Kendler, K.S., Gardner, C.O., 2014. Sex differences in the pathways to major depression: a study of opposite-sex twin pairs. *Am. J. Psychiatry* 171, 426–435.
- Kendler, K.S., Gardner, C.O., 2016. Depressive vulnerability, stressful life events and episode onset of major depression: a longitudinal model. *Psychol Med* 46, 1865–1874.
- Kendler, K.S., Gardner, C.O., Prescott, C.A., 2002. Toward a comprehensive developmental model for major depression in women. *Am. J. Psychiatry* 159, 1133–1145.
- Kendler, K.S., Gardner, C.O., Prescott, C.A., 2006. Toward a comprehensive developmental model for major depression in men. *Am. J. Psychiatry* 163, 115–124.
- Köhler, C.A., Evangelou, E., Stubbs, B., Solmi, M., Veronese, N., Belbasis, L., Bortolato, B., Melo, M.C.A., Coelho, C.A., Fernandes, B.S., Olfson, M., Ioannidis, J.P. A., Carvalho, A.F., 2018. Mapping risk factors for depression across the lifespan: An umbrella review of evidence from meta-analyses and Mendelian randomization studies. *J. Psychiatr Res* 103, 189–207.
- Lash, T.L., Fox, M.P., Fink, A.K., 2009. *Applying quantitative bias analysis to epidemiologic data*. Springer, New York.
- Lynge, E., Sandegaard, J.L., Rebolj, M., 2011. The Danish National Patient Register. *Scand. J. Public Health* 39, 30–33.
- Madsen, I.E.H., Aust, B., Burr, H., Carneiro, I.G., Diderichsen, F., Rugulies, R., 2012. Paid care work and depression: A longitudinal study of antidepressant treatment in female eldercare workers before and after entering their profession. *Depress. Anxiety* 29, 605–613.
- Madsen, I.E.H., Burr, H., Diderichsen, F., Pejtersen, J.H., Borritz, M., Bjorner, J.B., Rugulies, R., 2011. Work-related violence and incident use of psychotropics. *Am J Epidemiol* 174, 1354–1362.
- Madsen, I.E.H., Diderichsen, F., Burr, H., Rugulies, R., 2010. Person-related work and incident use of antidepressants: relations and mediating factors from the Danish work environment cohort study. *Scand. J. Work. Environ. Health* 36, 435–444.
- Madsen, I.E.H., Gupta, N., Budtz-Jørgensen, E., Bonde, J.P., Framke, E., Flachs, E.M., Petersen, S.B., Svane-Petersen, A.C., Holtermann, A., Rugulies, R., 2018a. Physical work demands and psychosocial working conditions as predictors of musculoskeletal pain: a cohort study comparing self-reported and job exposure matrix measurements. *Occup. Environ. Med.* 75, 752–758.
- Madsen, I.E.H., Nyberg, S.T., Magnusson Hanson, L.L., Ferrie, J.E., Ahola, K., Alfredsson, L., Batty, G.D., Bjorner, J.B., Borritz, M., Burr, H., Chastang, J.F., de Graaf, R., Dragano, N., Hamer, M., Jokela, M., Knutsson, A., Koskenvuo, M., Koskinen, A., Leineweber, C., Niedhammer, I., Nielsen, M.L., Nordin, M., Oksanen, T., Pejtersen, J.H., Pentti, J., Plaisier, I., Salo, P., Singh-Manoux, A., Suominen, S., Ten Have, M., Theorell, T., Toppinen-Tanner, S., Vahtera, J., Vaananen, A., Westerholm, P.J.M., Westerlund, H., Fransson, E.I., Heikkilä, K., Virtanen, M., Rugulies, R., Kivimäki, M., 2017. Job strain as a risk factor for clinical depression: systematic review and meta-analysis with additional individual participant data. *Psychol Med* 47, 1342–1356.
- Madsen, I.E.H., Svane-Petersen, A.C., Holm, A., Bonde, J.P., Burr, H., Framke, E., Melchior, M., Rod, N.H., Sivertsen, B., Stansfeld, S., Sørensen, J.K., Virtanen, M., Westerlund, H., Rugulies, R., 2018b. In: Study protocol for analyses on the prospective association of work-related violence, and decision latitude with risk of depression in The Danish Work Life Course Cohort (DAWCO).
- Masters Pedersen, J., Hulvej Rod, N., Andersen, I., Lange, T., Poulsen, G., Prescott, E., Lund, R., 2015. Accumulation of major life events in childhood and adult life and risk of type 2 diabetes mellitus. *PLoS One* 10, e0138654.
- Mors, O., Perto, G.P., Mortensen, P.B., 2011. The Danish Psychiatric Central Research Register. *Scand. J. Public Health* 39, 54–57.
- Nikčević, A.V., Kramolisova-Advani, J., Spada, M.M., 2007. Early childhood experiences and current emotional distress: what do they tell us about aspiring psychologists? *J. Psychol.* 141, 25–34.
- O'Rourke, M., Wrigley, C., Hammond, S., 2018. Violence within mental health services: how to enhance risk management. *Risk management and healthcare policy* 11, 159–167.
- Pedersen, C.B., 2011. The Danish Civil Registration System. *Scand. J. Public Health* 39, 22–25.
- Pettersson, E., Lichtenstein, P., Larsson, H., Song, J., Agrawal, A., Børglum, A.D., Bulik, C.M., Daly, M.J., Davis, L.K., Demontis, D., Edenberg, H.J., Grove, J., Gelernter, J., Neale, B.M., Pardiñas, A.F., Stahl, E., Walters, J.T.R., Walters, R., Sullivan, P.F., Posthuma, D., Polderman, T.J.C., 2018. Genetic influences on eight psychiatric disorders based on family data of 4 408 646 full and half-siblings, and genetic data of 333 748 cases and controls. *Psychol. Med.* 49, 1166–1173.
- Price, O., Baker, J., Bee, P., Lovell, K., 2015. Learning and performance outcomes of mental health staff training in de-escalation techniques for the management of violence and aggression. *Br J Psychiatry* 206, 447–455.
- Rudkjøbing, L.A., Bungum, A.B., Flachs, E.M., Eller, N.H., Borritz, M., Aust, B., Rugulies, R., Rod, N.H., Biering, K., Bonde, J.P., 2020. Work-related exposure to violence or threats and risk of mental disorders and symptoms: a systematic review and meta-analysis. *Scand. J. Work. Environ. Health* 46, 339–349.
- Svane-Petersen, A.C., Framke, E., Sørensen, J.K., Rugulies, R., Madsen, I.E.H., 2019. Cohort profile: the Danish Work Life Course Cohort study (DaWCo). *BMJ Open* 9, e029658.
- Theorell, T., Hammarström, A., Aronsson, G., Träskman Bendz, L., Grape, T., Hogstedt, C., Marteinsdóttir, I., Skoog, I., Hall, C., 2015. A systematic review including meta-analysis of work environment and depressive symptoms. *BMC Public Health* 15, 738.
- Thielen, K., Nygaard, E., Andersen, I., Rugulies, R., Heinesen, E., Bech, P., Bültmann, U., Diderichsen, F., 2009. Misclassification and the use of register-based indicators for depression. *Acta Psychiatr. Scand.* 119, 312–319.
- Wassell, J.T., 2009. Workplace violence intervention effectiveness: A systematic literature review. *Safety Science* 47, 1049–1055.
- Weich, S., Patterson, J., Shaw, R., Stewart-Brown, S., 2009. Family relationships in childhood and common psychiatric disorders in later life: systematic review of prospective studies. *British Journal of Psychiatry* 194, 392–398.
- Wieclaw, J., Agerbo, E., Mortensen, P.B., Burr, H., Tüchsen, F., Bonde, J.P., 2006. Work related violence and threats and the risk of depression and stress disorders. *J. Epidemiol. Community Health* 60, 771–775.
- Xu, T., Hanson, L.L.M., Lange, T., Starkopf, L., Westerlund, H., Madsen, I.E., Rugulies, R., Pentti, J., Stenholm, S., Vahtera, J., 2018. Workplace bullying and violence as risk factors for type 2 diabetes: a multicohort study and meta-analysis. *Diabetologia* 61, 75–83.