Workplace bullying and workplace violence as risk factors for cardiovascular disease: a multi-cohort study

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Abstract

Aims

To assess the associations between bullying and violence at work and cardiovascular disease (CVD).

Methods and Results

Participants were 79 201 working men and women, aged 18 to 65 years and free of CVD, and were sourced from three cohort studies from Sweden and Denmark. Exposure to workplace bullying and violence was measured at baseline using self-reports. Participants were linked to nationwide health and death registers to ascertain incident CVD, including coronary heart disease and cerebrovascular disease. Study-specific results were estimated by marginal structural Cox regression and were combined using fixed-effect meta-analysis.

Nine percent reported being bullied at work and 13% recorded exposure to workplace violence during the past year. We recoded 3229 incident CVD cases with a mean follow-up of 12.4 years (765 in the first 4 years). After adjustment for age, sex, country of birth, marital status and educational level, being bullied at work versus not was associated with a hazard ratio of 1.59 (95%CI 1.28-1.98) for CVD. Experiencing workplace violence versus not was associated with a hazard ratio of 1.25 (95%CI 1.12-1.40) for CVD. The population attributable risk was 5.0% for workplace bullying and 3.1% for workplace violence. The excess risk remained similar in analyses with different follow-up lengths, cardiovascular risk stratifications and after additional adjustments. Dose-response relations were observed for both workplace bullying and violence ($P_{trend}<0.001$). There was only negligible heterogeneity in study-specific estimates.

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Conclusion

Bullying and violence are common at workplaces and those exposed to these stressors are at higher

risk of CVD.

Keywords

Workplace, bullying, violence, cardiovascular disease, psychosocial stress, occupational health

Introduction

Adverse psychosocial working conditions, including job strain, effort-reward imbalance and long working hours are associated with a higher risk of cardiovascular disease (CVD).[1] Other potentially severe workplace stressors such as bullying and violence are associated with a moderately higher risk of type 2 diabetes,[2] but their status as risk factors for CVD remains unclear.

Workplace bullying and violence constitute different social stressors. Workplace bullying is characterised by repeated or enduring psychologically aggressive behaviours at work,[3] whereas workplace violence is known as the intentional use of physical force or threats of such actions at work (definitions are provided in Supplementary Text S1).[4] As social stressors, both workplace bullying and violence may contribute to lowered self-esteem and loss of coping resources.[3] They may also elicit a range of coping-oriented behavioural changes, such as over-eating and excessive alcohol consumption,[5-7] and induce a variety of negative emotions.[8-10] For example, bullied individuals are three times more likely to report a depressed mood, whereas increased feelings of anger have been noted among people exposed to workplace violence.[8-10] In addition, both bullying and violence can lead to anxiety.[9, 10] It has been hypothesised that these coping-oriented behaviours and negative emotions increase CVD risk,[11-13] along with various stress-related physiological reactions, including elevated blood pressure, increased heart rate and systemic inflammation level.[1] They can also result in reduced insulin sensitivity, increased platelet aggregation, and hypercoagulability, endothelial dysfunction, and arrhythmias.[1]

Only a few studies have examined the risk of CVD in employees exposed to bullying at work and the results are conflicting.[14-17] Bullying was associated with a higher risk of self-reported incident CVD in 601 male and 4831 female Finnish hospital employees followed for 2 years, and in a case-control study of 7374 CVD cases and 7374 CVD-free controls from Germany.[15, 17] However, in a cross-sectional study in the U.S. based on 17 524 adults, an association was noticed with self-

reported angina pectoris but not with ischaemic heart disease or stroke.[16] These conflicting results may be due to a low number of outcome events,[15, 16] imprecise measurements of CVD endpoints,[15-17] and uncontrolled or imprecisely measured key confounders, such as employment status and educational level,[17] making the association between workplace bullying and CVD unclear. Regarding violence, most research has focused on intimate partner violence or general violence, rather than violence occurring at the workplace specifically.[18] Although both environmental threats to security (e.g., national monthly homicide counts) and incidence of physical assault have shown to be associated with higher rates of CVD death,[19, 20] the association between workplace violence and incident CVD is still inconclusive.

To address these limitations, we pooled individual-level data from three large longitudinal studies including a total of 79 201 men and women to examine the prospective associations between workplace bullying and workplace violence with incident CVD.

Methods

Study population

Four independent cohorts were utilised in this study, taken from the following three population-based studies: the Swedish Work Environment Survey (SWES) (divided into two cohorts with baseline years 1995/1997/1999/2001 and 2007/2009/2011, source population: participants of Swedish Labour Force Survey; response proportion: 79%),[21] the Swedish Longitudinal Occupational Survey of Health (SLOSH) (baseline: year 2006/2008, source population: participants of SWES; response proportion: 65%)[22] and the Danish Work Environment Cohort Study (DWECS) (baseline: year 2005, source population: random sample from Danish population register; response proportion: 63%)[23] (Figure 1). In cohorts with multiple baseline years, we only kept the first participation record. Until 2012, SLOSH collected follow-up information on a biannual basis, and 38% of all respondents of the SLOSH2006/2008 respondents answered all follow-up surveys. Detailed descriptions of each cohort can be found in the Supplementary Text S2.

Using the personal identification number assigned to all residents in Sweden and Denmark, participants were linked to national registries in each country. We included employees aged 18 to 65, with no prior CVD and with information available on workplace bullying or violence, totalling a sample of 79 201 participants.

Ethical approval was obtained from the Regional Ethical Review Board in Stockholm for SWES and SLOSH.[22] DWECS was approved by the Danish Data Protection Agency (registration number: 2007-54-0059).[24]

Assessment of baseline workplace bullying and violence

Workplace bullying was assessed via a self-administered questionnaire measuring whether the participant had been bullied within the 12 months preceding the baseline. Exposure to violence at work was defined as being exposed to violent actions or threats of violence at work within 12 months prior to the baseline. Please see Supplementary Table S1 for details. SWES and SLOSH also included information about the frequency of exposure. We constructed a dose-response variable with the categories 'frequently exposed' (exposed more than once a week), 'occasionally exposed' (less than once a week, but at least one exposure within the past 12 months) and 'not exposed'.

Ascertainment of cardiovascular disease

Incident CVD is a composite outcome including diagnoses of the first hospitalization with coronary heart disease (CHD) or cerebrovascular disease (CD). They were identified through nationwide registries based on the International Classification of Diseases (ICD) 8, 9 and 10 codes. Main diagnoses in inpatient register (in SLOSH, SWES95-01, SWES07-11, and DWECS), outpatient register (in SLOSH, SWES07-11 and DWECS) and death registers (in SLOSH, SWES95-01, SWES07-11, and DWECS) were used. The diagnostic codes for CHD were ICD-10 I20.0, I20.1, I21-I25 (excluding unspecified angina), and ICD-8/9 410-414, whereas ICD-10 I60-I69 and ICD-8/9 430-438 were used to detect CD. Definitions of specific CVD subtypes, such as myocardial

infarction (MI), ischaemic stroke (IS) and haemorrhagic stroke (HS) can be found in the Supplementary Text S3. Incident CVD cases were identified during the follow-up. Further information on standards and quality of CVD diagnosis in Denmark and Sweden can be found in Supplementary Text S4.

Covariates

We used prior knowledge and the method of directed acyclic graph method to select covariates.[25-27] In addition to age and sex, we identified country of birth, educational level, and marital status as potential confounders. This information was all register-based. Educational level was classed as '≤ 9 years', '10 to 12 years' and '≥ 13 years'. Baseline marital status was categorised as unmarried, married/cohabiting, divorced/separated or widowed. Country of birth was categorised into 'Nordic countries', 'other European countries' and 'other continents'.

Body mass index (BMI), alcohol consumption, current smoking status and mental disorders were considered both as potential confounders and mediators, and they were thus only adjusted for in the sensitivity analysis. We also considered the impact from other stressors at workplace, private life and other health conditions, which might be related to both the onset of exposure and the outcome. These included shift work occupations (e.g. health care professionals), occupational grade, having young children at home (<5 years of age), family-work conflict, workplace role stressors, pre-existing diabetes and other comorbidities (Charlson Comorbidity Index [CCI]) at or prior to the baseline examination. The measurements for these variables are described in Supplementary Texts S5 and S6 and Table S2.

We further hypothesised that employees in occupations with frequent client contact (and thus with a higher risk of exposure to workplace violence), are better trained to cope with violence.[28] Hence, occupation could be a critical modifying factor. We defined social workers, personal and protective service workers, healthcare professionals and teaching professionals as frequent-client-contact

occupations. We used comparable ISCO-88 codes from DWECS, SWES95-01, SWES07-11 and SLOSH, following a suggestion in Madsen et al.[29]

Statistical analysis

In total, 8 sub-datasets (one for bullying and one for violence per cohort) with slightly varying numbers of participants were created. We applied marginal structural Cox regression to the main analyses. This approach is based on the counterfactual framework and aims to estimate the average marginal population effect, i.e., comparing a population when everyone was exposed to when everyone was not exposed. [30]

We calculated the individual-specific stabilised inverse probability weight.[30] Different logistical models were used for calculating different weights, based on propensity score models which included the specific variables considered in each adjustment. The positivity assumption was not violated in any of the analyses, meaning that both exposure statuses were possible within each confounder strata.[30] Before fitting the weighted Cox model, the proportional hazards (PH) assumption was tested using log-log plot and interaction between time and exposure. Here, we observed an interaction between workplace bullying and follow-up length, where the hazard ratio of bullying and CVD decreased during follow-up. Thus, we restricted our analyses to the first 4 years of follow-up on workplace bullying to meet the assumption (see other motivations for choosing the 4-year follow-up limit in Supplementary Text S7). For workplace violence, full follow-up length was used as there was no violation of the PH assumption. Later, we fitted a weighted Cox proportional hazards model with age as the underlying time scale and obtained robust confidence intervals by bootstrapping 500 times.

Other main analyses included: (i) disease subtype analyses using information for MI, HS, and IS; (ii) population attributable risk (PAR) calculation, which represents the extent to which disease burden would be eliminated, had the given risk factors removed from the population, and is widely

used in the planning and prioritisation of certain public health interventions;[31] and (iii) estimation of dose-response relation. Sensitivity analysis processes are presented in Figure 2.

Due to the small number of cohorts, all cohort-specific estimates were then combined using fixed-effect meta-analysis.[32] I^2 statistic was used to test the heterogeneity of results across the cohorts. All the analyses were conducted using SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina) and R package 'meta' version 4.8-4. All tests of statistical significance were 2-sided and the significance level was set at 0.05.

Results

The mean age of the participants was 43 years across the three studies and 53% were women (see Table 1 and weighted summary in Supplementary Table S3). There were 78 955 participants with data on workplace bullying. The prevalence of bullying varied across the studies, ranging from 7% to 13% within the past 12 months. The perpetrators of workplace bullying (in DWECS) were mostly from inside the organisation (79% were colleagues, supervisors or subordinates) rather than from outside (21% were clients).

Data on workplace violence was available for 79 044 participants. The prevalence ranged from 7% to 17% across the cohorts within the past 12 months. We found that social workers (prevalence >46%), personal and protective service workers (>29%), healthcare professionals (>25%) and teaching professionals (>16%) had the highest exposure to workplace violence. The perpetrators of workplace violence (in DWECS) mainly originated from outside the organisation (91%: clients) and less often from inside (9%: colleagues, supervisors or subordinates).

Overall, only 10-14% of those exposed to at least one type of exposure was suffering from the other at the same time (Cohen's Kappa<0.20). This indicates that workplace bullying and violence are two separate concepts.

Workplace bullying and cardiovascular disease

Over a mean follow-up of 3.8 years, 760 incident CVD events were recorded, including 484 incident CHD events and 301 incident CD events, with 25 participants having both CHD and CD events as their main diagnosis during follow-up.

Figure 3 shows a forest plot of the main analyses. We observed very little heterogeneity in all analyses (I^2<0.01%). After adjusting for age, sex, educational level, marital status and country of birth, workplace bullying was associated with a 59% higher risk of incident CVD (HR=1.59; 95%CI 1.28-1.98), with the corresponding PAR being 5.0% (95%CI 2.5%-8.1%). This association was presented for both incident CHD (HR=1.56; 95%CI 1.18-2.07) and incident CD (HR=1.70; 95%CI 1.19-2.44). We further observed an association with HS (HR=2.73; 95%CI 1.16-6.45) and its excess risk was much higher than for IS (HR=1.44; 95%CI 0.93-2.23). However, the estimate of HS was based on only 42 cases, generating a relatively wide confidence interval, which overlapped with that for IS. SLOSH, SWES95-01 and SWES07-11 provided information on the frequency of workplace bullying. Of the participants who were bullied, approximately 10% were frequently bullied, whereas the remaining 90% were occasionally bullied. Dose-response relations were observed for CVD (P_{trend}<0.001). The highest risk of CVD (HR=2.22; 95%CI 1.23-4.01) was found among those being frequently bullied. The same trend was presented for CHD as well as CD.

The sensitivity analyses are summarised in Figure 4. Excluding the first year of follow-up to reduce reverse causality gave congruous results for the main analysis. There was no evidence that sex, age or smoking status influenced the results. Further variable adjustments or restriction of the population did not materially change the findings.

In SLOSH there were 4066 participants (11 707 participant-observations) who responded to all follow-up waves (2006/2008--2012). With a mean follow-up of 5.9 years, 84 incident CVD cases were recorded. Among them 21% of participants were exposed to bullying at least once (10% of

total participant-observations). Treating workplace bullying and other changeable characteristics (e.g. marital status) as time-dependent variables, we found a hazard ratio of 2.11 (95%CI 1.21-3.70) for the association between bullying and CVD.

Workplace violence and cardiovascular disease

During a mean follow-up of 12.4 years, 3226 incident CVD events were recorded, including 1971 incident CHD events and 1439 incident CD events. A total of 184 participants had both CHD and CD events as their main diagnosis during the follow-up.

Figure 5 shows that workplace violence was associated with a higher risk of incident CVD (HR=1.25; 95%CI 1.12-1.40). The corresponding PAR for workplace violence was 3.1% (95%CI 1.5%-4.9%). Looking at subtypes of CVD, the association was similar for incident CHD (HR=1.21; 95%CI 1.03-1.42) and incident CD (HR=1.25; 95%CI 1.06-1.49). HS (HR=1.31; 95%CI 0.89-1.92) and IS (HR=1.33, 95%CI 1.08-1.64) also showed similar risk estimates. There was only negligible heterogeneity across cohorts (I^2=2%). We found a dose-response relation between workplace violence and risk of CVD (P_{trend}<0.001). However, while the dose-response relation was presented for CD (P_{trend}<0.001), it was absent for CHD (P_{trend}=0.22). Frequent exposure to workplace violence was associated with 36% higher risk of incident CD (HR=1.36; 95%CI 0.99-1.86).

The sensitivity analyses are summarised in Figure 6. By limiting the follow-up length to the first four years, and excluding the first year of follow-up, the sensitivity analyses showed similar associations. No sex, age and smoking status differences were observed, and further adjustments did not change the effects. Moreover, we observed a stronger association between violence and CVD among people employed in occupations without frequent client contact (HR=1.36; 95%CI 1.07-1.73) than among those whose occupations involved frequent client contact occupations (HR=1.17; 95%CI 0.86-1.59), where the latter type of occupation shared similar results with the restricted analysis on health care professionals (night shift workers) (HR=1.06; 95%CI 0.68-1.63).

We also observed that the confidence intervals between the occupational groups had significant overlap.

Among the 4751 participants of SLOSH (11 747 participant-observations) who responded to all survey waves (2006/2008--2012), the mean follow-up was 5.9 years and 86 incident CVD were recorded. Of the participants, 17% were exposed to violence at least once (12% of total participant-observations). Treating workplace violence and other changeable statuses, e.g. marital status as time-dependent variables, we found 1.22 times (95%CI 0.61-2.45) higher risk of having CVD among those exposed to violence, which is consistent with our main analysis from the SLOSH data (HR=1.35; 95%CI 0.90-2.02).

Discussion

In this large multi-cohort analysis involving nearly 80 000 employed men and women from Denmark and Sweden, we found consistent support for our hypothesis that workplace bullying and workplace violence are associated with a higher risk of new-onset CVD. The PAR was 5.0% for workplace bullying and 3.1% for workplace violence, comparable to those for standard risk factors, e.g. diabetes (4%) and risky drinking (3-6%).[33, 34] In this case, if the association was causal, removing workplace bullying and workplace violence from the baseline population prevented 5.0% and 2.9% of the CVD cases, respectively. The dose-response relation was evident for both workplace bullying and violence, with the highest risk observed among those exposed on a weekly/daily basis. We observed no heterogeneity between study-specific estimates and there were no sex differences in the results. The results were robust for different follow-up periods, adjustments and cardiovascular risk stratifications.

Workplace bullying

Our findings of a higher risk of CVD among those exposed to bullying corroborate with previous studies on the topic. A smaller longitudinal study conducted by Kivimäki et al. based on a broader self-reported assessment of CVD (hypertension, CHD and CD) showed that workplace bullying

was associated with a 2.3 times higher risk of CVD (95%CI 1.2-4.6).[15] After BMI adjustment the risk estimate was similar to the one observed in the present study, but no longer statistically significant (OR=1.6; 95% CI 0.8-3.5). Jacob and Kostev, using similar CVD definitions as our study, also found similar associations (OR=1.31; 95%CI 1.01-1.77), and their findings were not affected by further adjustments for overweight.[17]

Workplace violence

We are not aware of previous studies concerning workplace violence and incident CVD. Our results are in agreement with findings from a recent case-control study from Russia based on 1750 cases and 2000 controls, concerning general violence. They found that physical assault was associated with a 2.14 times higher risk (95%CI 1.05-4.34) of ischaemic heart disease death and a 4.36 times higher risk (95%CI 1.90-10.00) of CD death.[20] As our study, to the best of our knowledge, is the first longitudinal investigation of the relation between workplace violence and incident CVD, our findings need to be replicated in other studies. Evidence of a dose-response relation for workplace violence was not as strong as for bullying and only appeared for CD, and not for CHD. It is possible that those most frequently exposed to violence are also those working in frequent-client-contact occupations, as shown in our study. They may be more capable of tackling violence at work with cognitive adaption and their organisations may be also better geared towards preventing long-term consequences of workplace violence.[8, 28] This might be demonstrated by the similar CVD risks observed between frequent- and non-frequent-client-contact occupations in our study. Another explanation is that the intensity rather than the frequency of violence is critical in triggering of CHD events. Therefore, more research is needed to clarify the dose-response relation.

Plausible mechanisms

Workplace bullying and violence are major social stressors. They are likely to induce negative emotions and stress reactions as pathways to CVD development. They may lead to conditions

such as anxiety and depression.[8, 10, 15, 28] These negative emotions may also stimulate behaviours related to passive coping, such as over-eating and excessive alcohol consumption.[5-7] Further, activation of the physiological stress response system and activation of the hypothalamic-pituitary-adrenal axis may be involved in direct and indirect mechanisms, e.g., directly causing a higher level of saliva dehydroepiandrosterone and a lower level of saliva cortisol.[2] These hormones may have a direct impact on heart rate and blood pressure, subsequently leading to hypo-perfusion and increased cerebral blood flow pulsatility.[1] Physiological stress response may be closely related to emotional distress and behavioural changes,[11, 12] indirectly contributing to the elevated level of blood pressure and a greater progressions in intima-media thickness.[13, 35] We did not observe attenuation for both workplace bullying and violence after adjusting for health-related life style factors, but they may still act as mediators. Therefore, further research is needed to investigate these emotional, behavioural and physiological pathways.

On the other hand, workplace bullying and violence may also have distinct mechanisms. For example, the effect of workplace bullying was markedly affected by follow-up length, while this was not the case for workplace violence. It is plausible that bullying can exacerbate pre-existing cardiovascular disease risk, such as high atherosclerotic plaque burden.[1] As those who were bullied at work were very likely to change their job,[36] this exacerbation might be alleviated after the change. Furthermore, the excess risk associated with bullying was noticeably higher for HS than IS. HS is more strongly associated with high blood pressure than IS.[33] Accordingly, elevated blood pressure may be more pronounced in the mechanistic pathway between workplace bullying and CVD.[16, 37] However, with the overlapping confidence intervals of HS and IS, this latter hypothesis may be a chance finding. Thus, more research is needed to confirm the underlying mechanisms.

Limitations and strengths

In our study, workplace bullying and violence were measured only once, potentially causing some degree of misclassification of long-term exposure.[3] However, the supplementary analysis using

repeated measures in SLOSH suggests that this is not a major source of bias. Our study was conducted in a Nordic setting, where the concepts of workplace bullying and violence are well-established,[38] but caution is needed when generalising the results to other cultural settings, where individuals may perceive workplace bullying and violence differently. Additionally, information on potential confounders such as tobacco use other than smoking (e.g. snus), personality, negative emotional traits, genetic factors, other stressors at private life (e.g. marital conflict) and other work-related stressors were not available in the studies. Further data to evaluate causation and mechanisms for the associations, such as the severity of the exposures and measurements of stress hormones, blood pressure, blood cholesterol or heart rate variability, were not available to us.

However, importantly, in contrast to previous studies, we were able to link survey data to nationwide registries to identify new cases of definite CVD with nearly complete follow-up. Our large sample size and long follow-up period allowed us to assess the total effects, subtype effects and dose-response relation. It also allowed us to perform relevant sensitivity analyses on different stratifications, adjustments and restrictions with sufficient statistical power.

Conclusion

Bullying and violence are common workplace stressors. Our study sheds light on their association with a higher risk of cardiovascular events. If the association is causal, eliminating workplace bullying and violence would prevent a sizable number of CVD events from happening. Further research is needed to determine whether preventive measures directed towards bullying and violence may reduce CVD risk as well as to investigate the underlying mechanistic pathways.

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Figure legends

Figure 1. Flow chart describing study populations and analytical samples.

Figure 2. Overview of sensitivity analyses.

Figure 3. Fixed-effect meta-analysis of the association between workplace bullying and cardiovascular disease, after adjustment for age, sex, educational level, marital status and country of birth, regarding a) main analysis of cardiovascular disease, b) subtype analysis of coronary heart disease and cerebrovascular disease and c) dose-response relation analysis according to different frequencies of bullying.

Figure 4. Sensitivity analysis of the association between workplace bullying and cardiovascular diseases, using fixed-effect meta-analyses excluding first year(s) of follow-up, stratifying for sex, and with different adjustments and restrictions.

Figure 5. Fixed-effect meta-analysis on the association between workplace violence and cardiovascular disease, after adjustment for age, sex, educational level, marital status and country of birth, regarding a) main analysis of cardiovascular disease, b) subtype analysis of coronary heart disease and cerebrovascular disease and c) dose-response relation analysis according to different frequencies of violence.

Figure 6. Sensitivity analysis of the association between workplace violence and cardiovascular diseases, using fixed-effect meta-analysis excluding first year(s) of follow-up, stratifying for sex, and with different adjustments.

Table 1. Summary of studies that provided individual participant data used in the analyses for cardiovascular disease, based on largest available samples with full-follow-up length (N=79 201).

Study	Country	Baseline	Full follow-up lengths (Mean years)	Women, %	Age (Mean, SD) [a]	Bullying, %	Violence, %	CVD [b]	CHD [b]	CD [b]
SLOSH	Sweden	2006/2008	7.0	55	47(10.6)	13	17	26.7	16.2	10.7
DWECS	Denmark	2005	8.9	51	43(10.4)	9	7	41.2	21.9	20.4
SWES95-01	Sweden	1995/1997/1999/2001	17.5	52	42(11.5)	8	13	34.4	21.0	15.0
SWES07-11	Sweden	2007/2009/2011	7.1	53	44(12.1)	8	14	24.4	14.7	10.1
Total		1995-2011	12.4	53	43.3	9	13	32.7	19.7	14.4

a. SD=standard deviation.

b. CVD=cardiovascular disease; CHD=coronary heart disease; CD=cerebrovascular disease; incidence rate per 10 000 person-years.

Figure 1. Flow chart describing study populations and analytical samples.

Figure 2. Overview of sensitivity analyses.

In SLOSH, SWES and DWECS	Only in SLOSH and DWECS	Only in SLOSH	Only in DWECS	Analysis purposes
Excluding cases that occurred during the first year of follow-up		Testing effects from repeatedly measured exposure		**Robustness of methodology**
Stratifying by sex				**Cardio-vascular risk factors stratification**
Stratifying by age	Stratifying by smoking or not			
Adjusting for mental disorders prior to the baseline together with the main adjustment variables	Adjusting for BMI, alcohol consumption and smoking status together with the main adjustment variables			**Additional confounders or mediators**
Adjusting for diabetes and CCI score prior to the baseline together with the main adjustment variables				**Important factors: comorbidities**
	Adjusting for having young children together with the main adjustment variables	Adjusting for family-work conflict together with the main adjustment variables	Adjusting for role stressors at work together with the main adjustment variables	**Important factors: stressors at private life or at work**
Stratifying for frequent- and non-frequent-client-contact occupations				**Important factors: stressors at work**
Restricting analysis on health professionals for the effect on shift work				
Adjusting occupational grade instead of educational level together with the variables in the main analysis				

Figure 3. Fixed-effect meta-analysis of the association between workplace bullying and

cardiovascular disease, after adjustment for age, sex, educational level, marital status and

country of birth, regarding a) main analysis of cardiovascular disease, b) subtype analysis of coronary heart disease and cerebrovascular disease and c) dose-response relation analysis according to different frequencies of bullying.

Figure 4. Sensitivity analysis of the association between workplace bullying and cardiovascular diseases, using fixed-effect meta-analyses excluding first year(s) of follow-up, stratifying for sex, and with different adjustments and restrictions.

	Total(n)	Events(n)		HR (95% CI)
Follow-up length				
Main = first 4 years	78955	760		1.59 (1.28-1.98)
From 1 year after baseline	78741	674		1.60 (1.29-1.98)
Sex				
Male	37498	529		1.45 (1.09-1.94)
Female	41457	231		1.90 (1.30-2.76)
Age				
Yonger than 50 years	51707	181		1.18 (0.70-1.99)
50 years or older	27248	579		1.78 (1.38-2.30)
Current smoking status - in SLOSH and DWECS				
Not smoking	14563	130		1.66 (0.97-2.84)
Smoking	3984	72		1.52 (0.74-3.13)
Adjustments: Mental disorders				
Age, sex, educational level, marital status, country of birth	78955	760		1.59 (1.28-1.98)
+ Mental disorders	78955	760		1.57 (1.24-1.98)
Adjustments: Comorbidity				
+ Diabetes	78955	760		1.58 (1.27-1.96)
+ CCI score	78955	760		1.58 (1.27-1.96)
Adjustments: Life-style factors - in SLOSH and DWECS				
Age, sex	17139	180		1.41 (0.90-2.22)
Age, sex, educational level, marital status, country of birth	17139	180		1.40 (0.89-2.22)
+ Alcohol consumption	17139	180		1.37 (0.85-2.20)
+ Smoking	17139	180		1.38 (0.87-2.18)
+ BMI	17139	180		1.36 (0.86-2.14)
+ Alcohol consumption, smoking, BMI	17139	180		1.35 (0.85-2.12)
Adjustments: Stressors at private life or workplace				
+ Having young children - in SLOSH and DWECS	18121	204		1.54 (1.00-2.35)
+ Family-work conflict - in SLOSH	10553	104		1.28 (0.69-2.35)
+ Role stressors at work - in DWECS	7798	97		2.09 (1.06-4.09)
Restriction: Night shift				
Only healthcare professionals	3863	28		2.87 (1.14-7.21)
Adjustments: Occupational grade				
Age, sex, occupational grade, marital status, country of birth	66865	673		1.60 (1.26-2.04)

0.2 1 5

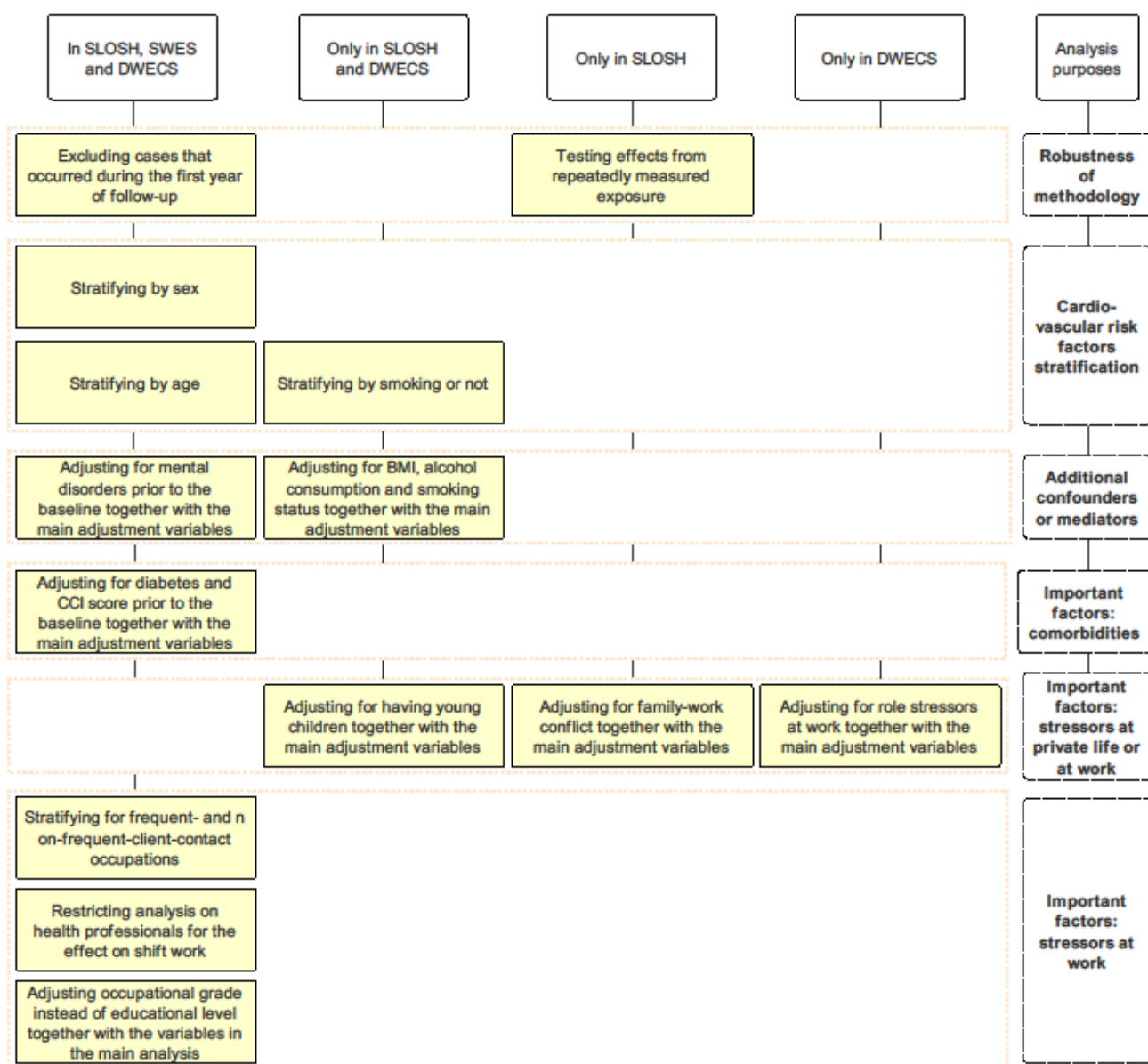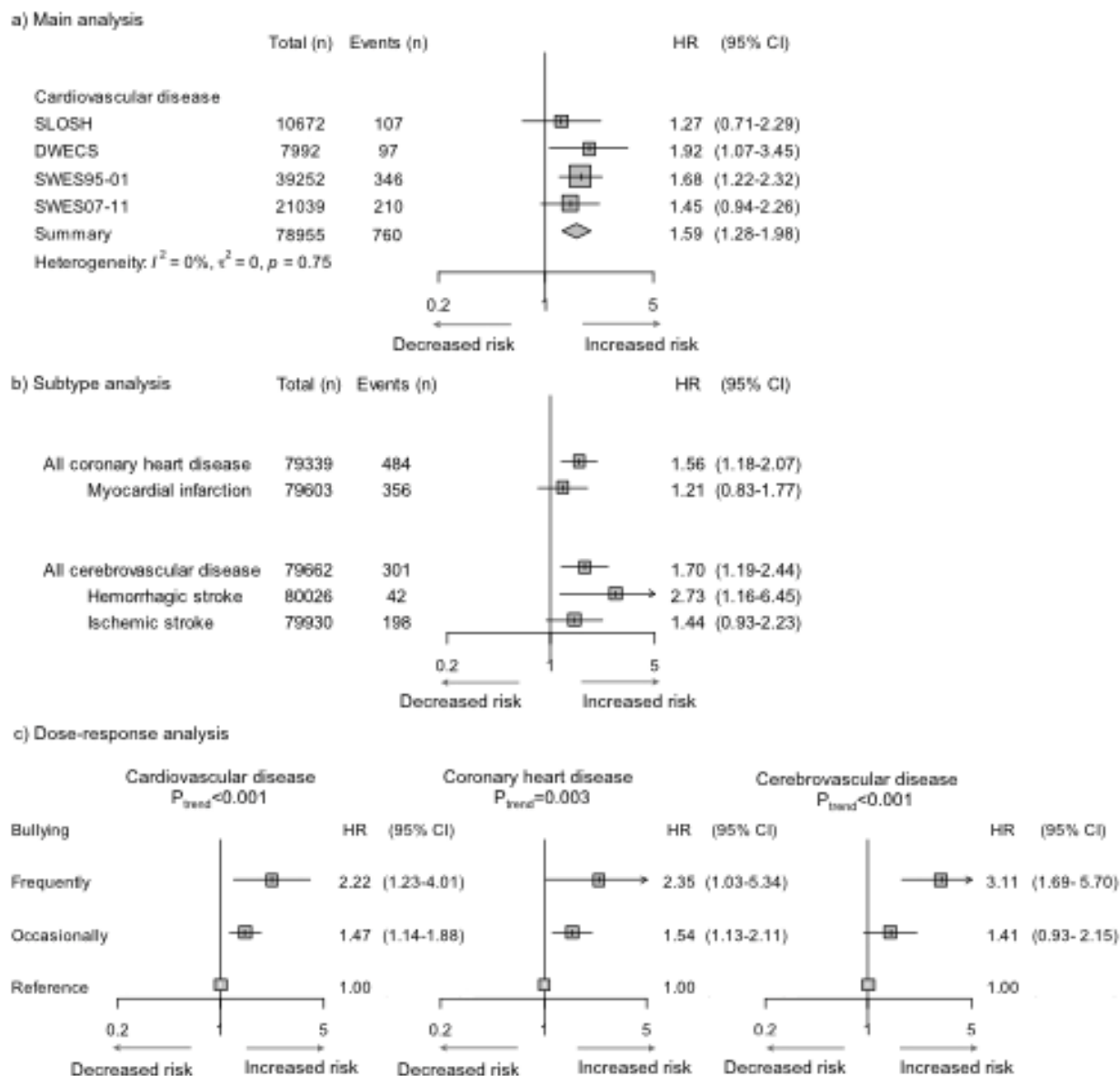Decreased risk   Increased risk

Figure 5. Fixed-effect meta-analysis on the association between workplace violence and cardiovascular disease, after adjustment for age, sex, educational level, marital status and country of birth, regarding a) main analysis of cardiovascular disease, b) subtype analysis of coronary heart disease and cerebrovascular disease and c) dose-response relation analysis according to different frequencies of violence.

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Figure 6. Sensitivity analysis of the association between workplace violence and cardiovascular diseases, using fixed-effect meta-analysis excluding first year(s) of follow-up, stratifying for sex, and with different adjustments and restrictions.
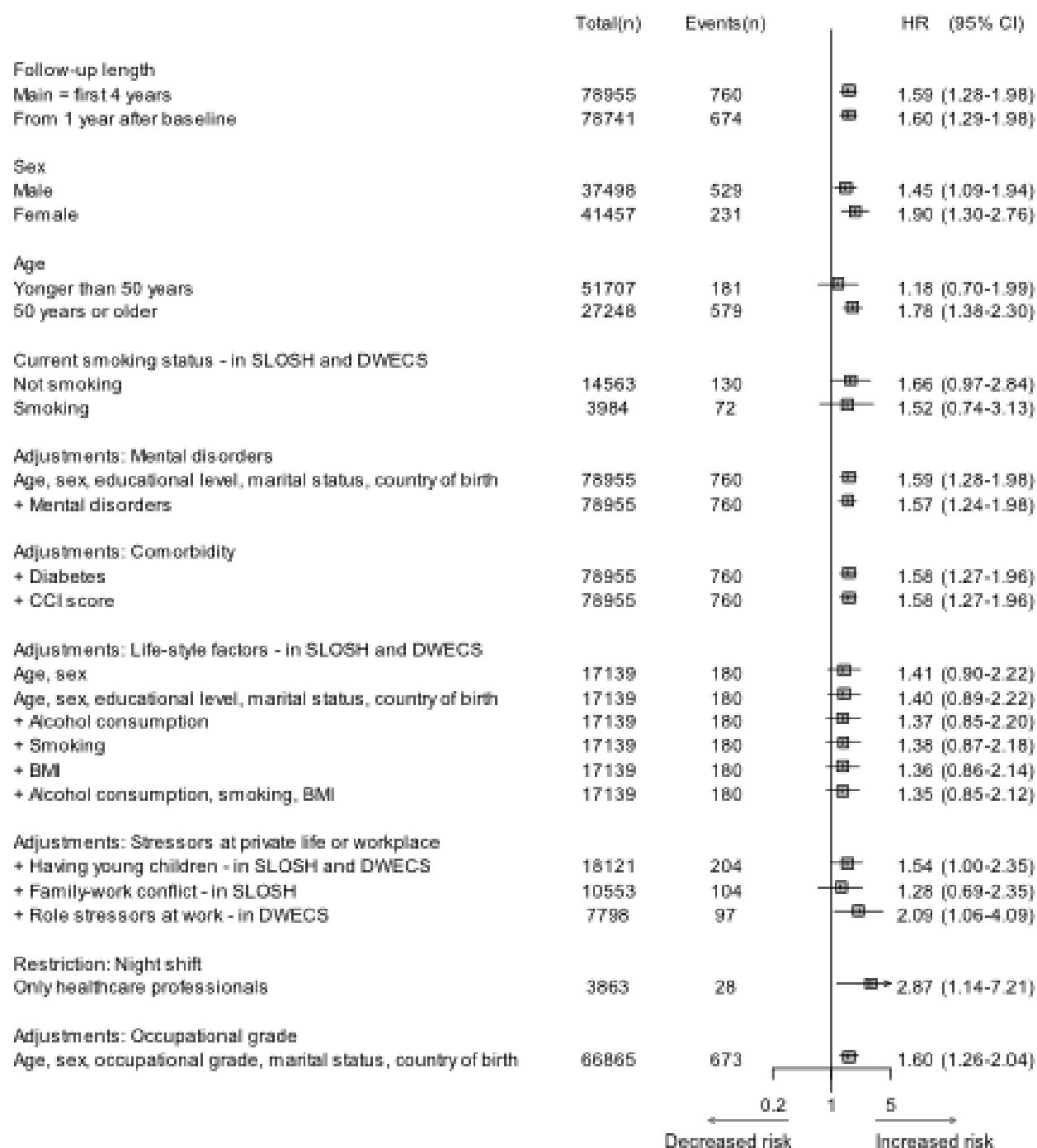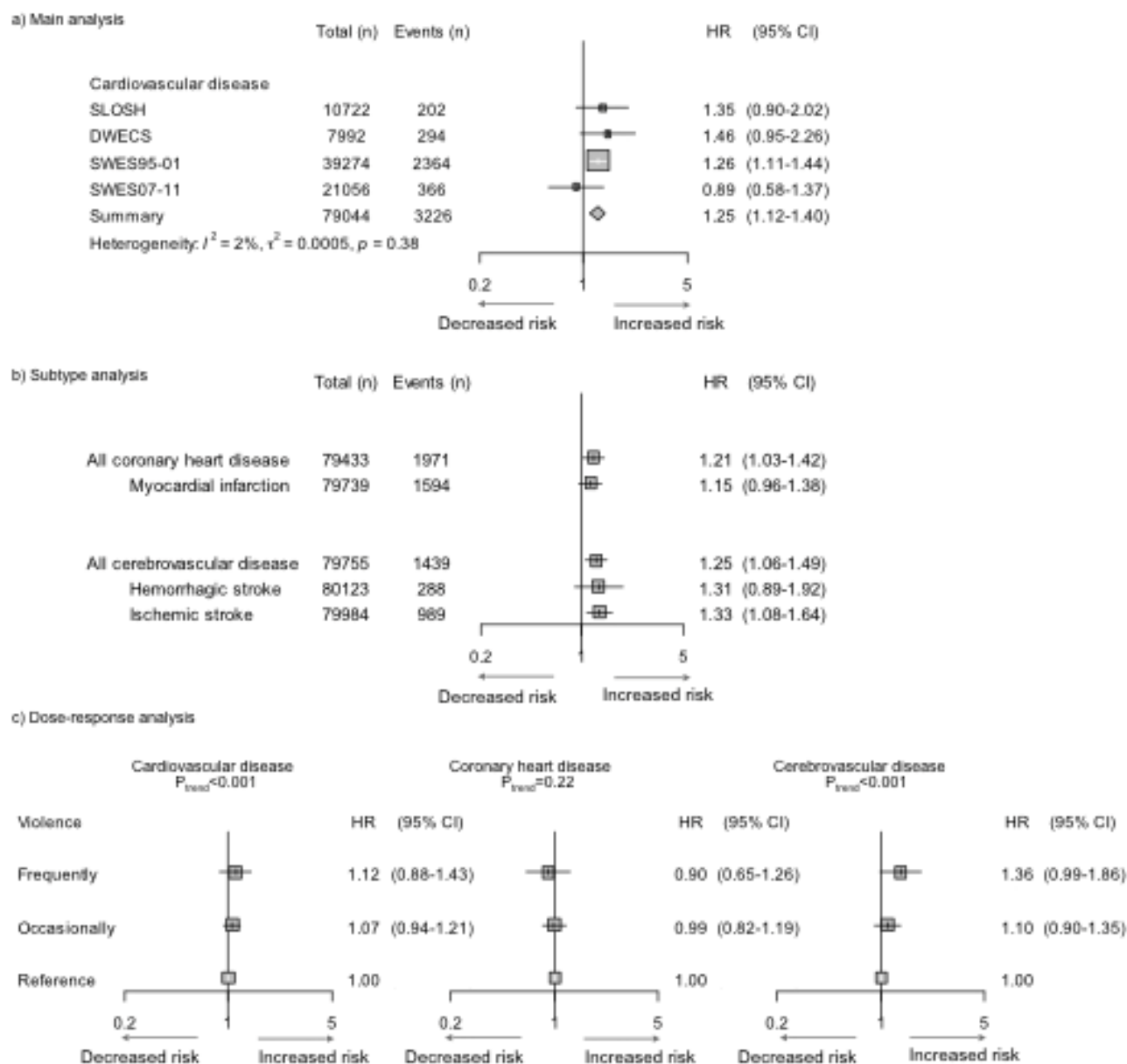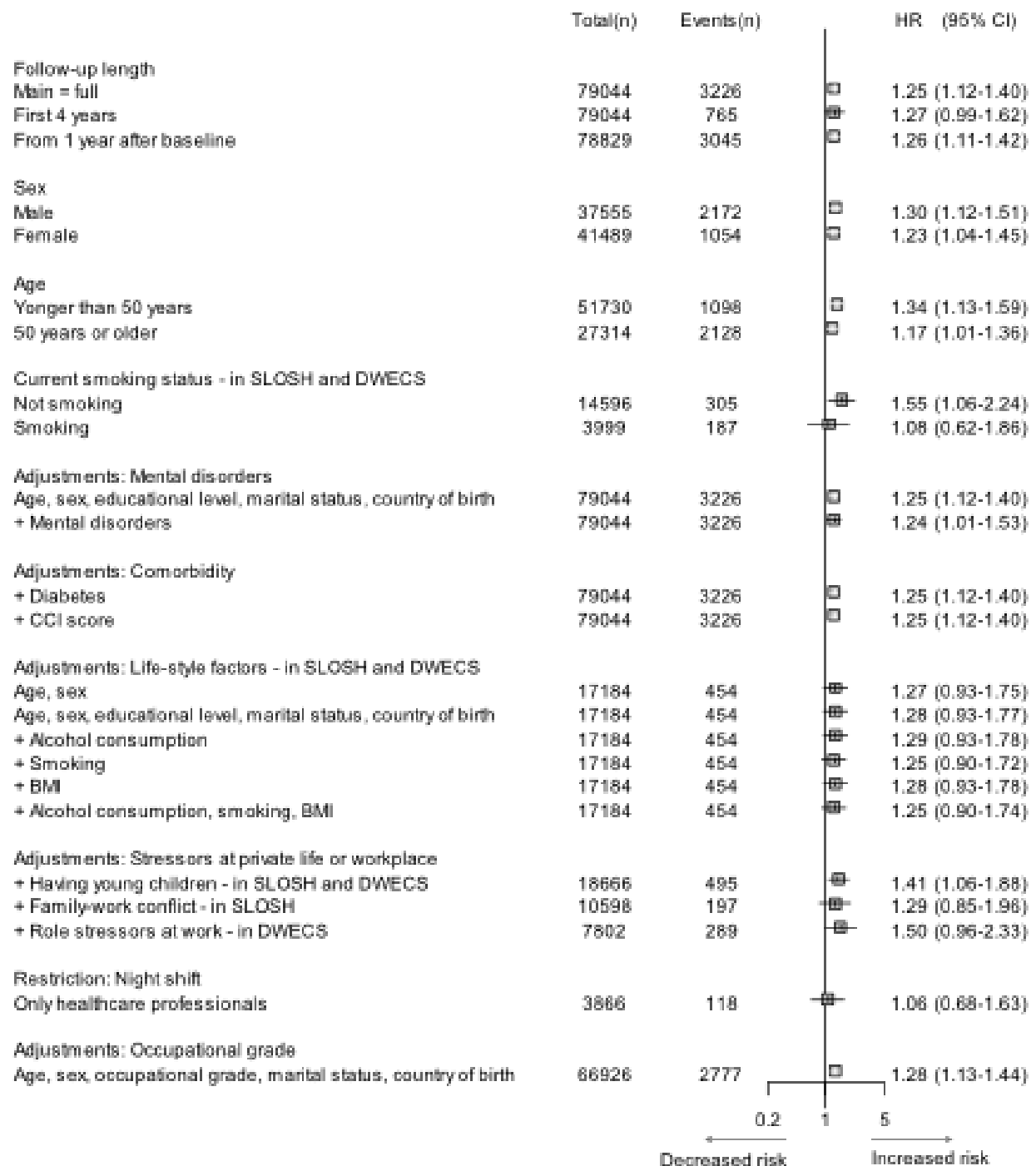
	Total(n)	Events(n)	HR (95% CI)
Follow-up length			
Main = full	79044	3226	1.25 (1.12-1.40)
First 4 years	79044	765	1.27 (0.99-1.62)
From 1 year after baseline	78829	3045	1.26 (1.11-1.42)
Sex			
Male	37555	2172	1.30 (1.12-1.51)
Female	41489	1054	1.23 (1.04-1.45)
Age			
Yonger than 50 years	51730	1098	1.34 (1.13-1.59)
50 years or older	27314	2128	1.17 (1.01-1.36)
Current smoking status - in SLOSH and DWECS			
Not smoking	14596	305	1.55 (1.06-2.24)
Smoking	3999	187	1.08 (0.62-1.86)
Adjustments: Mental disorders			
Age, sex, educational level, marital status, country of birth	79044	3226	1.25 (1.12-1.40)
+ Mental disorders	79044	3226	1.24 (1.01-1.53)
Adjustments: Comorbidity			
+ Diabetes	79044	3226	1.25 (1.12-1.40)
+ CCI score	79044	3226	1.25 (1.12-1.40)
Adjustments: Life-style factors - in SLOSH and DWECS			
Age, sex	17184	454	1.27 (0.93-1.75)
Age, sex, educational level, marital status, country of birth	17184	454	1.28 (0.93-1.77)
+ Alcohol consumption	17184	454	1.29 (0.93-1.78)
+ Smoking	17184	454	1.25 (0.90-1.72)
+ BMI	17184	454	1.28 (0.93-1.78)
+ Alcohol consumption, smoking, BMI	17184	454	1.25 (0.90-1.74)
Adjustments: Stressors at private life or workplace			
+ Having young children - in SLOSH and DWECS	18666	495	1.41 (1.06-1.88)
+ Family-work conflict - in SLOSH	10598	197	1.29 (0.85-1.96)
+ Role stressors at work - in DWECS	7802	289	1.50 (0.96-2.33)
Restriction: Night shift			
Only healthcare professionals	3866	118	1.06 (0.68-1.63)
Adjustments: Occupational grade			
Age, sex, occupational grade, marital status, country of birth	66926	2777	1.28 (1.13-1.44)

0.2   1   5

Decreased risk ← → Increased risk

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Supplements

Supplementary Text S1. Definitions of workplace bullying and violence

According to the European Agency for Safety and Health at Work, as stated in their publication: *Workplace Violence and Harassment: A European Picture* in 2010,[1] a broader definition of workplace violence includes abuse, threats and assault, where abuse is defined as 'Behaviours that depart from reasonable conduct and involve the misuse of physical or psychological strength' and can be considered as an umbrella term for workplace bullying and other behaviours such as sexual harassment.

Workplace bullying includes different types of negative acts such as isolation; withholding of necessary information; assignment of tasks with unreasonable or impossible goals or deadlines; devaluation of one's rights and opinions; verbal abuse; slander; practical jokes; and ridicule. Workplace bullying is mostly of a psychological nature.[2] Most importantly, the behaviours must occur repeatedly over a long period of time with an escalation process, in order to constitute bullying.

In our study, it is important to note that in our questionnaire, people were not given a definition of workplace violence, leaving them free to interpret the term for themselves. Therefore, workplace violence includes any perceived violence that took place at the workplace.

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Supplementary Text S2. Study populations

The Swedish Work Environment Study (SWES)[1] is derived from participants of the Swedish Labour Force Survey, containing more than 20 000 persons randomly drawn from the entire Swedish population. SWES started in 1989 as a biannual survey. The dataset used in this study was taken from SWES 1995, 1997, 1999 and 2001 and SWES 2007, 2009 and 2011, based on the data availability of information on workplace bullying and violence. We excluded year 2003 and 2005, as they were used as the source population of SLOSH 2006 and 2008, which are included in this study. We further divided SWES into SWES95-01 and SWES07-11 based on whether or not data was accessible in the Swedish out-patient register.

The Swedish Longitudinal Occupational Survey of Health (SLOSH)[2] was set up to research psychosocial work environment and life course perspective on social causes of disease. It was initiated in March 2006 based on the respondents from SWES 2003, with a response proportion of 65%. In 2008 all eligible respondents to the SWES 2003 were contacted again and the survey was further extended by inviting participants from SWES 2005, with response proportion of 61%. In SLOSH, people who had been engaged in paid work for at least 30% of full time during the past 3 months were defined as 'gainfully employed'. Both participants who were gainfully employed and those who were not were followed-up in SLOSH, but with different versions of questionnaire. In this study, we used data for those participating in SLOSH in 2006 or newly recruited in 2008, who were gainfully employed.

The Danish Work Environment Cohort Study (DWECS)[3] is a cohort study with a total of 5 waves since 1990. In 1990 it drew a random sample from the Central Population Register of Denmark. Participants were aged between 18 and 69 years and were contacted every 5 years together with some extension of the population. Our baseline was established at the 4th wave of the study, in 2005, which offered comparable information on negative interpersonal relationships at work. The overall response proportion was 63% in 2005.

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Supplementary Table S1. Measurements of workplace bullying and violence

	SLOSH (2006/2008)	SWES (1995/1997/1999/2001)	SWES (2007/2009/2011)	DWECS (2005)
Bullying Question	Have you been subjected to personal persecution in the form of unkind words or behaviour from your superiors or fellow workers?	Have you been subjected to personal persecution in the form of unkind words or behaviour from your superiors or fellow workers?	Have you been subjected to personal persecution in the form of unkind words or behaviour from your superiors or fellow workers?	In the last 12 months, have you been subjected to uncomfortable bullying at your work place?
Definition	In the last 12 months: Frequently exposed: More than once a week Occasionally exposed: More than once a year, less than once a week. No exposure: answering 'no'.	In the last 12 months: Frequently exposed: More than once a week Occasionally exposed: More than once a year, less than once a week. No exposure: answering 'no'.	In the last 12 months: Frequently exposed: More than once a week Occasionally exposed: More than once a year, less than once a week. No exposure: answering 'no'.	Answering 'yes'.
Violence Question	Are you exposed to violence or threats of violence in your work?	Are you exposed to violence or threats of violence in your work?	Are you exposed to violence or threats of violence in your work?	In the last 12 months, have you been subjected to threats of violence at your work place? In the last 12 months, have you been subjected to physical violence at your work place?
Definition	In the last 12 months: Frequently exposed: More than once a week Occasionally exposed: More than once a year, less than once a week. No exposure: answering 'no'.	In the last 12 months: Frequently exposed: More than once a week Occasionally exposed: More than once a year, less than once a week. No exposure: answering 'no'.	In the last 12 months: Frequently exposed: More than once a week Occasionally exposed: More than once a year, less than once a week. No exposure: answering 'no'.	Answering 'yes' to at least one question.

Supplementary Text S3. Definitions for myocardial infarction, ischaemic stroke and haemorrhagic stroke

Myocardial infarction:

Hospital registers: using main diagnosis of ICD-10 I21-22, or 410 in ICD-9 or ICD8 41.

Death register: using any main cause of death in acute coronary death of ICD-10 I20-25, or 410–414 in ICD-9, or ICD 8 410-414.

Ischaemic stroke:

Hospital registers and death register: using main diagnosis of ICD-10 I63 or ICD-9 433-434, or ICD8 433-434.

Haemorrhagic stroke:

Hospital registers and death register: using main diagnosis of codes ICD-10 I61, I62 or ICD-9 431 or ICD8 431.

Supplementary Text S4. CVD diagnosis standard and quality of using Swedish and Danish registries

Sweden and Denmark have high and similar official standards of care. Both Sweden and Denmark follow the diagnosis standard suggested by WHO and European guidelines. In Denmark, ICD-8 was used before year 2004 and ICD10 has been used since 2004. In Sweden, ICD-8 was used before 1987 and ICD-9 was used between 1987 and 1997. ICD-10 in Sweden has been applied since 1997. Comparable ICD-8, -9 and -10 codes have been used in the study.

Several studies evaluating the quality of national patient registers have been published. In our study, CVD was only identified using main diagnoses. Using the same criteria, electronic records on CVD taken from the Swedish register have been validated since 1992 and the

most recent publication was in 2011.[1] The Positive Predicted Value (PPV) for CVD was 95% or above for myocardial infarction, angina pectoris, atrial fibrillation and stroke/transient ischaemic attack, and 88% or above for heart failure. The Negative Predicted Value (NPV) was almost 100%. Therefore, the quality of patient register diagnosis of CVD is high and valid. In Denmark, the PPV for CVD was over 95% for myocardial infarction and cerebrovascular disease.[2]

In the study, the Swedish outpatient information was distinguished from the Swedish inpatient information, as the outpatient register was only introduced since 2001 in Sweden. This register consists of information on unplanned/planned admissions, acute care data (e.g. Emergency Department care) and compulsory admission and detention under the Swedish Mental Health Act and Forensic Psyciatric Care, but does not include information from primary care.[3] Treatments for e.g. dyslipidaemia are common in primary care as a prevention strategy for cardiovascular disease,[4] but were not included in our outcome measurement.

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Supplementary Text S5. Measurement of BMI, alcohol consumption, current smoking status and mental disorders

Self-reported weight and height were used to calculate BMI (in SLOSH and DWECS), further grouped into underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2) and obese ($\geqslant$30 kg/m^2). Information on alcohol consumption (in DWECS and SLOSH) was divided into 'excessive' or 'non-excessive' alcohol consumption. 'Excessive' means more than 14-unit drinks for women or 21-unit drinks for men per week (in DWECS and SLOSH), or weekly consumption of 6 or more units per occasion (in SLOSH). Current smoking status was defined as smoker or non-smoker (in SLOSH and DWECS). Mental disorders before baseline (in SLOSH, SWES95-01, SWES07-11 and DWECS) were detected using national registers.

Any kind of mental disorder:

Hospital registers: using main and secondary diagnosis of ICD 8/9 code 290-315 and ICD 10 code F01-F99.

Supplementary Text S6. Measurement of shift work occupations (e.g. doctors and nurses), occupational grade, having young children at home (<5 years), family-work conflict and workplace role stressors

Shift work occupations were identified using ISCO-88 codes: 222, 223, 322, 323

Occupational grade was categorised according to ISCO-88 codes into high (1, 2), medium (3, 4) and low (5, 6, 7, 8, 9).

Information on having children at home was self-reported (in DWECS) and register-based (in SLOSH) and grouped into yes vs. no.

Information on family-work conflict (whether family life affected work in a negative way) was only available in SLOSH. We assumed an existence of family-work conflict if participants answered 'yes, sometimes', 'yes, quite often' and 'yes, all the time' to the question.

Workplace role stressors in DWECS were measured using two questions, one on workplace role conflict and the other on workplace role ambiguity. We constructed a 3-level variable including categories of 'having at least one role stressors frequently', 'having both/only one of the role stressors only now and then', and 'having no role stressors'.

Supplementary Table S2. Calculation for Charlson Comorbidity Index from both in- and outpatient registers using primary diagnosis (information for pre-existing diabetes was also taken from the ICD code mentioned in this table)

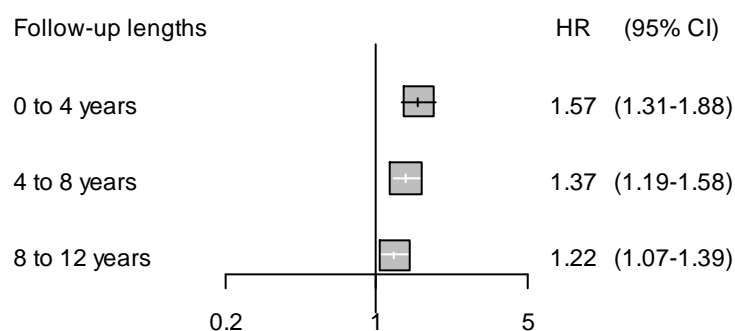| Condition	Weights	ICD-8	ICD-9	ICD-10
Acute myocardial infarction	1	410	410, 412	I21, I22, I252
Congestive heart failure	1	427.09; 427.10; 427.11; 427.19; 428.99; 782.49	428	I50
Peripheral vascular disease	1	440; 441; 442; 443; 444; 445	441, 4439, 7854, V434	I71, I790, I739, R02, Z958, Z959
Cerebral vascular accident	1	430–438	430–438	I60, I61, I62, I63, I65, I66, G450, G451, G452, G458, G459, G46, I64, G454, I670, I671, I672, I674, I675, I676, I677, I678, I679, I681, I682, I688, I69
Dementia	1	290.09–290.19; 293.09	290	F00, F01, F02, F051
Pulmonary disease	1	490–493; 515–518	490, 491, 492, 493, 494, 495, 496, 500, 501, 502, 503, 504, 505	J40, J41, J42, J44, J43, J45, J46, J47, J67, J44, J60, J61, J62, J63, J66, J64, J65
Connective tissue disorder	1	712; 716; 734; 446; 135.99	7100, 7101, 7104, 7140, 7141, 7142, 71481(now 5171), 725	M32, M34, M332, M053, M058, M059, M060, M063, M069, M050, M052, M051, M353
Peptic ulcer	1	530.91; 530.98; 531–534	531, 532, 533, 534	K25, K26, K27, K28
Liver disease	1	571; 573.01; 573.04	5712, 5714, 5715, 5716	K702, K703, K73, K717, K740, K742, K746, K743, K744, K745
Diabetes	1	249.00; 249.06; 249.07; 249.09 250.00; 250.06; 250.07; 250.09	2500,2501, 2502, 2503, 2507	E109, E119, E139, E149, E101, E111, E131, E141, E105, E115, E135, E145
Diabetes complications	2	249.01–249.05; 249.08 250.01–250.05; 250.08	2504, 2505, 2506	E102, E112, E132, E142 E103, E113, E133, E143 E104, E114, E134, E144
Paraplegia	2	344	342, 3441	G81 G041, G820, G821, G822
Renal disease	2	403; 404; 580–583; 584; 590.09; 593.19; 753.10–753.19; 792	582, 5830, 5831, 5832, 5833, 5835, 5836, 5837, 5834, 585, 586, 588	N03, N052, N053, N054, N055, N056, N072, N073, N074, N01, N18, N19, N25
Cancer	2	140–194 204–207 200–203; 275.59	14, 15, 16, 18, 170, 171, 172, 174, 175, 176, 179, 190, 191, 192, 193, 194, 1950, 1951, 1952, 1953, 1954, 1955, 1958, 200, 201, 202, 203, 204, 205, 206, 207, 208	C0, C1, C2, C3, C40, C41, C43, C45, C46, C47, C48, C49, C5, C6, C70, C71, C72, C73, C74, C75, C76, C80, C81, C82, C83, C84, C85, C883, C887, C889, C900, C901, C91, C92, C93, C940, C941, C942, C943, C9451, C947, C95, C96
Metastatic cancer	6	195–198; 199	196, 197, 198, 1990, 1991	C77, C78, C79, C80
Severe liver disease	3	070.00; 070.02; 070.04; 070.06; 070.08; 573.00; 456.00–456.09	5722, 5723, 5724, 5728	K729, K766, K767, K721
HIV	6	79.83	042, 043, 044	B20, B21, B22, B23, B24

Supplementary Text S7. Motivation for choosing 4 years follow-up time for workplace bullying

Follow-up for CVD was limited to 4 years because (1) the mechanisms linking bullying to CVD were assumed to involve triggering rather than atherosclerosis[1] and (2) to avoid effect dilution from exposure misclassification as a result of changes in work during extended follow-up periods. Our preliminary analyses support the use of a 4-year follow-up period for workplace bullying (Supplement Text S7):

    a. Log-log plot for SWES95-01 on workplace bullying (red line: being bullied)
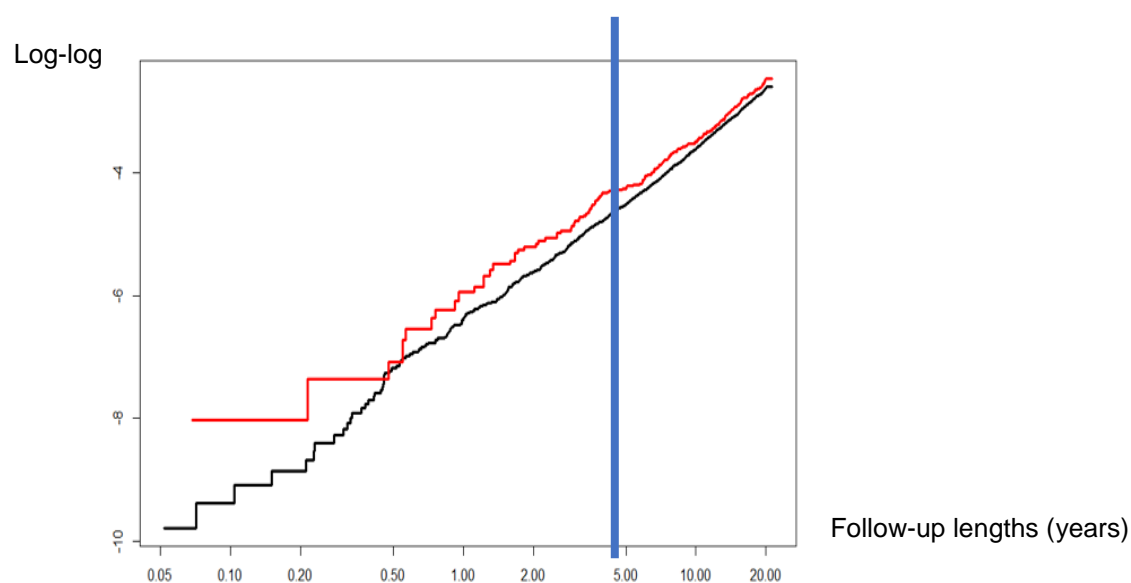
    b. Hazard ratios of workplace bullying on cardiovascular disease, stratifying by follow-up lengths.

Follow-up lengths		HR	(95% CI)
0 to 4 years		1.57	(1.31-1.88)
4 to 8 years		1.37	(1.19-1.58)
8 to 12 years		1.22	(1.07-1.39)

References:

1. Kivimäki M, Steptoe A. Effects of stress on the development and progression of cardiovascular disease. Nature Reviews Cardiology 2018;15(4):215.

Supplementary Table S3. Descriptive table to show the balance of covariates after being weighted for a) workplace bullying and b) workplace violence

a) Workplace bullying

	SLOSH (N = 10 672)				DWECS (N = 7992)				SWES95-01 (N = 39 252)				SWES07-11 (N = 21 039)			
Before or after weighting	Before		After		Before		After		Before		After		Before		After	
Exposure to bullying	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Age at baseline, mean (SD)	46 (10.2)	47 (10.7)	47 (10.7)	47 (10.1)	43 (10.7)	43 (10.5)	43 (10.7)	43 (10.5)	42 (10.9)	42 (11.6)	42 (10.9)	42 (11.6)	45 (11.3)	44 (12.0)	44 (11.4)	44 (12.0)
Women, %	56	54	55	55	62	50	52	51	52	52	51	52	55	53	53	53
≤ 9 years' education, %	10	10	10	10	18	18	18	18	17	18	18	18	9	9	9	9
From Nordic countries, %	94	97	97	97	94	97	97	97	93	96	96	96	92	95	94	94
Married, %	48	55	54	54	60	64	63	63	50	53	53	53	45	50	50	50

b) Workplace violence

	SLOSH (N = 10 722)				DWECS (N = 7992)				SWES95-01 (N = 39 274)				SWES07-11 (N = 21 056)			
Before or after weighting	Before		After		Before		After		Before		After		Before		After	
Exposure to violence	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Age at baseline, mean (SD)	46 (10.7)	47 (10.6)	47 (10.6)	47 (10.6)	43 (10.5)	43 (10.5)	43 (10.6)	43 (10.5)	41 (10.9)	42 (11.6)	42 (11.1)	42 (11.6)	43 (11.9)	44 (12.0)	44 (11.9)	44 (12.0)
Women, %	70	51	54	55	61	50	51	51	67	49	52	52	68	51	53	53
≤ 9 years' education, %	6	11	11	10	14	18	18	18	10	20	19	18	5	10	9	9
From Nordic countries, %	96	97	96	97	96	97	97	97	96	96	96	96	94	94	94	94
Married, %	49	55	54	54	56	64	63	63	50	53	52	53	46	50	50	50