

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint



Review article

WHO/ILO work-related burden of disease and injury: Protocol for systematic reviews of exposure to long working hours and of the effect of exposure to long working hours on depression



Reiner Rugulies^{a,b,c,*}, Emiko Ando^d, Jose Luis Ayuso-Mateos^{e,f,g}, Michela Bonafede^h, Maria Cabello^{e,f}, Cristina Di Tecco^h, Nico Draganoⁱ, Quentin Durand-Moreau^{j,k}, Hisashi Eguchi^l, Junling Gao^m, Anne H. Garde^{a,b}, Sergio Iavicoli^h, Ivan D. Ivanovⁿ, Nancy Leppink^o, Ida E.H. Madsen^a, Frank Pegaⁿ, Annette M. Prüss-Üstünⁿ, Bruna M. Rondinone^h, Kathrine Sørensen^a, Kanami Tsuno^p, Yuka Ujita^o, Amy Zadow^q

^a National Research Centre for the Working Environment, Copenhagen, Denmark

^b Department of Public Health, University of Copenhagen, Copenhagen, Denmark

^c Department of Psychology, University of Copenhagen, Copenhagen, Denmark

^d Osaka University, Suita, Osaka, Japan

^e Department of Psychiatry, Universidad Autonoma de Madrid, Madrid, Spain

^f Instituto de Salud Carlos III, Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Madrid, Spain

^g Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Madrid, Spain

^h Department of Environmental and Occupational Medicine, Epidemiology and Hygiene, INAIL, Monte Porzio Catone, Rome, Italy

ⁱ Universitätsklinikum Düsseldorf, Düsseldorf, Germany

^j Occupational Diseases Center, University Hospital of Brest, Brest, France

^k LABERS EA 3149, University of Brest, Brest, France

^l Kitasato University School of Medicine, Sagami-hara, Kanagawa, Japan

^m School of Public Health, Fudan University, Shanghai, China

ⁿ Department of Public Health, Environmental and Social Determinants of Health, World Health Organization, Geneva, Switzerland

^o Labour Administration, Labour Inspection and Occupational Safety and Health Branch, International Labour Organization, Geneva, Switzerland

^p Wakayama Medical University, Wakayama-shi, Wakayama, Japan

^q University of South Australia, Adelaide, Australia

ARTICLE INFO

Keywords:

Working hours
Depression
Mental health
Systematic review
Meta-analysis
Burden of disease

ABSTRACT

Background: The World Health Organization (WHO) and the International Labour Organization (ILO) are developing a joint methodology for estimating the national and global work-related burden of disease and injury (WHO/ILO joint methodology), with contributions from a large network of experts. In this paper, we present the protocol for two systematic reviews of parameters for estimating the number of deaths and disability-adjusted life years from depression attributable to exposure to long working hours, to inform the development of the WHO/ILO joint methodology.

Objectives: We aim to systematically review studies on occupational exposure to long working hours (Systematic Review 1) and systematically review and meta-analyse estimates of the effect of long working hours on depression (Systematic Review 2), applying the Navigation Guide systematic review methodology as an organizing framework, conducting both systematic reviews in tandem and in a harmonized way.

Data sources: Separately for Systematic Reviews 1 and 2, we will search electronic academic databases for potentially relevant records from published and unpublished studies, including Medline, EMBASE, Web of Science, CISDOC and PsycINFO. We will also search electronic grey literature databases, Internet search engines and

* Corresponding author at: National Research Centre for the Working Environment, Lersø Parkallé 105, DK-2100 Copenhagen, Denmark.

E-mail addresses: rer@nrcwe.dk (R. Rugulies), andoemiko-ky@umin.ac.jp (E. Ando), jose-luis.ayuso@uam.es (J.L. Ayuso-Mateos), m.bonafede@inail.it (M. Bonafede), maria.cabello@uam.es (M. Cabello), c.ditecco@inail.it (C. Di Tecco), Dragano@med.uni-duesseldorf.de (N. Dragano), Quentin.durand-moreau@chu-brest.fr (Q. Durand-Moreau), eguchi@med.kitasato-u.ac.jp (H. Eguchi), jlgaofudan.edu.cn (J. Gao), ahg@nrcwe.dk (A.H. Garde), s.iavicoli@inail.it (S. Iavicoli), ivanovi@who.int (I.D. Ivanov), leppink@ilo.org (N. Leppink), ihm@nrcwe.dk (I.E.H. Madsen), pegaf@who.int (F. Pega), pruess@who.int (A.M. Prüss-Üstün), b.rondinone@inail.it (B.M. Rondinone), ksn@nrcwe.dk (K. Sørensen), tsuno@wakayama-med.ac.jp (K. Tsuno), ujita@ilo.org (Y. Ujita), Amy.zadow@unisa.edu.au (A. Zadow).

<https://doi.org/10.1016/j.envint.2018.11.011>

Received 18 January 2018; Received in revised form 1 November 2018; Accepted 5 November 2018

Available online 06 February 2019

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organizational websites; hand search reference list of previous systematic reviews and included study records; and consult additional experts.

Study eligibility and criteria: We will include working-age (≥ 15 years) participants in the formal and informal economy in any WHO and/or ILO Member State, but exclude child workers (< 15 years) and unpaid domestic workers. For Systematic Review 1, we will include quantitative prevalence studies of relevant levels of occupational exposure to long working hours (i.e. 35–40, 41–48, 49–54 and ≥ 55 h/week) stratified by country, sex, age and industrial sector or occupation, in the years 2005–2018. For Systematic Review 2, we will include randomized controlled trials, cohort studies, case-control studies and other non-randomized intervention studies with an estimate of the relative effect of relevant level(s) of long working hours on the incidence of or mortality due to depression, compared with the theoretical minimum risk exposure level (i.e. 35–40 h/week).

Study appraisal and synthesis methods: At least two review authors will independently screen titles and abstracts against the eligibility criteria at a first stage and full texts of potentially eligible records at a second stage, followed by extraction of data from qualifying studies. At least two review authors will assess risk of bias and the quality of evidence, using the most suited tools currently available. For Systematic Review 2, if feasible, we will combine relative risks using meta-analysis. We will report results using the guidelines for accurate and transparent health estimates reporting (GATHER) for Systematic Review 1 and the preferred reporting items for systematic reviews and meta-analyses guidelines (PRISMA) for Systematic Review 2.

PROSPERO registration number: CRD42018085729

1. Background

The World Health Organization (WHO) and the International Labour Organization (ILO) are developing a joint methodology for estimating the work-related burden of disease and injury (WIIO/ILO joint methodology) (Ryder, 2017). The organizations plan to estimate the numbers of deaths and disability-adjusted life years (DALYs) that are attributable to selected occupational risk factors for the year 2015. The WHO/ILO joint methodology will be based on already existing WHO and ILO methodologies for estimating the burden of disease for selected occupational risk factors (International Labour Organization, 2014; Prüss-Üstün et al., 2017). It will expand these existing methodologies with estimation of the burden of several prioritized additional pairs of occupational risk factors and health outcomes. For this purpose, population attributable fractions (Murray et al., 2004) – the proportional reduction in burden from the health outcome achieved by a reduction of exposure to the risk factor to zero – will be calculated for each additional risk factor-outcome pair, and these fractions will be applied to the total disease burden envelopes for the health outcome from the WHO *Global Health Estimates* (World Health Organization, 2017b).

The WHO/ILO joint methodology will include a methodology for estimating the burden of depression from occupational exposure to long working hours if feasible, as one additional prioritized risk factor-outcome pair. To optimize parameters used in estimation models, a systematic review is required of studies on the prevalence of exposure to long working hours ('Systematic Review 1'), as well as a second systematic review and meta-analysis of studies with estimates of the effect of exposure to long working hours on depression ('Systematic Review 2'). In the current paper, we present the protocol for these two systematic reviews, in parallel to presenting systematic review protocols on other additional risk factor-outcome pairs elsewhere (Descatha et al., 2018; Godderis et al., 2018; Hulshof et al., in press; Li et al., 2018; Mandrioli et al., 2018; Paulo et al., Accepted; Teixeira et al., Accepted; Tenkate et al., Accepted). To our knowledge, this is the first systematic review protocol of its kind. The WHO/ILO joint estimation methodology and the burden of disease estimates are separate from these systematic reviews, and they will be described and reported elsewhere.

We refer separately to Systematic Reviews 1 and 2, because the two systematic reviews address different objectives and therefore require different methodologies. The two systematic reviews will, however, be harmonized and conducted in tandem. This will ensure that – in the later development of the methodology for estimating the burden of disease from this risk factor-outcome pair – the parameters on the risk factor prevalence are optimally matched with the parameters from studies on the effect of the risk factor on the designated outcome. The findings from Systematic Reviews 1 and 2 will be reported in two

distinct journal articles. For all four protocols in the series with long working hours as the risk factor, one Systematic Review 1 will be published.

1.1. Rationale

WIIO ranks depression as the single largest contributor to non-fatal health loss worldwide, with 7.5% of all years lived with disability attributed to depression in 2015 (World Health Organization, 2017a). To consider the feasibility of estimating the burden of depression due to exposure to long working hours, and to ensure that potential estimates of burden of disease are reported in adherence with the guidelines for accurate and transparent health estimates reporting (GATHER) (Stevens et al., 2016), WHO and ILO require a systematic review of studies on the prevalence of relevant levels of exposure to long working hours (Systematic Review 1), as well as a systematic review and meta-analysis of studies with estimates of the relative effect of exposure to long working hours on the incidence of and mortality from depression, compared with the theoretical minimum risk exposure level (Systematic Review 2). The theoretical minimum risk exposure level is the exposure level that would result in the lowest possible population risk, even if it is not feasible to attain this exposure level in practice (Murray et al., 2004). These data and effect estimates should be tailored to serve as parameters for estimating the burden of depression from exposure to long working hours in the WHO/ILO joint methodology.

To our knowledge, this is the first systematic review that will provide this evidence base for burden of depression attributable to long working hours. Three previous reviews have estimated the association of long working hours with risk of depressive symptoms and depression (Theorell et al., 2015; Virtanen et al., 2018; Watanabe et al., 2016). Theorell et al. reported, based on six cohort studies of high or moderate quality that there was a prospective association of long working weeks with risk of onset of depressive symptoms (Theorell et al., 2015). Using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system, they assessed the evidence as “limited” for women and “very limited” for men. The authors refrained from upgrading the evidence level for long working weeks, because they found the estimates of the association of long working weeks and depression neither consistent, nor large enough for qualifying for an upgrade, and they also did not conduct a meta-analysis of the included effect estimates. In another systematic review, Watanabe et al. examined overtime work and risk of onset of depressive disorders and identified seven cohort studies (Watanabe et al., 2016). The meta-analysis conducted in this systematic review showed an increased, but not statistically significant association of overtime work with risk of depressive disorders (relative risk 1.24; 95% CI 0.88 to 1.75). Virtanen et al. included in

their meta-analysis 10 published cohort studies and 18 prospective cohort studies with individual-participant data, yielding 31 study-specific estimates (as 3 studies of the published studies had provided estimates stratified by sex) (Virtanen et al., 2018). The outcome was named “depressive symptoms” and included both measures of clinical depression and depressive symptoms and of psychological distress. The overall pooled estimate (odds ratio, OR) for the association of long working hours with risk of onset of depressive symptoms was 1.14 (95% CI 1.03 to 1.25). The association was stronger in studies from Asian countries (OR = 1.50, 95% CI 1.13 to 2.01), weaker in European studies (OR = 1.11, 95% CI 1.00 to 1.22) and absent in North American studies (OR = 0.95, 95% CI 0.70 to 1.29). When stratified by clinical depression/depressive symptoms versus psychological distress, the pooled ORs were 1.09 (0.94 to 1.26) and 1.18 (1.06 to 1.32) for clinical depression/depressive symptoms and psychological distress, respectively. Meta-regressions did not show any statistically significant differences in the estimates for clinical depression, depressive symptoms and psychological distress.

The review by Virtanen et al. was published recently (Online First, 8 February 2018) and two authors of the Virtanen et al. article are also authors of this protocol (RR and IEHM). Therefore, we want to briefly delineate the main differences between the Virtanen et al. article and this protocol. First, our search is broader, Virtanen et al. searched two academic databases whereas we will search seven academic databases and two grey literature databases. Second, Virtanen et al. searched studies published until January 2017, whereas we will search for studies published until 30 June 2018. Third, the endpoint in the Virtanen et al. review was depressive symptoms, including but not limited to measures of clinical depression, and psychological stress, whereas our endpoint is restricted to clinical depression. Fourth, Virtanen et al. used the Cochrane’s “Tool to Assess Risk of Bias in Cohort Studies” whereas our risk of bias assessment will be derived from the Navigation Guide (Woodruff and Sutton, 2014). Fifth, we aim to do a subgroup analysis stratified by industrial sector or occupation, if data allow this, an analysis not conducted by Virtanen et al. Sixth, Virtanen et al. did not assess the quality of evidence of the summarized results, whereas we aim to assess quality of evidence using the most suitable tools currently available (Guyatt et al., 2011; Higgins and Green, 2011; Morgan et al., 2016). We are not aware of a previous review of prevalence of exposure to long working hours. To the best of our knowledge, this is the first systematic review of parameters required for estimating the global and national burden of depression attributable to long working hours.

Work in the informal economy may lead to different exposures and exposure effects than does work in the formal economy. The informal economy is defined as “all economic activities by workers and economic units that are – in law or in practice – not covered or insufficiently covered by formal arrangements”, but excluding “illicit activities, in particular the provision of services or the production, sale, possession or use of goods forbidden by law, including the illicit production and trafficking of drugs, the illicit manufacturing of and trafficking in firearms, trafficking in persons, and money laundering, as defined in the relevant international treaties” (p. 4) (104th International Labour Conference, 2015). We consider the formality of the economy studied in studies included in both Systematic Reviews.

Table 1
Definitions of the risk factor, risk factor levels and the minimum risk exposure level.

	Definition
Risk factor	Long working hours (including those spent in secondary jobs), defined as working hours > 40/week hours, i.e. working hours exceeding standard working hours (35–40 h/week).
Risk factor levels	Preferable exposure categories are 35–40, 41–48, 49–54 and ≥ 55 h/week. However, whether we can use these categories will depend on the information provided in the studies. If the preferable exposure categories are not available, we will use the exposure categories provided by the studies as long as these exposure categories exceed 40 h/week.
Theoretical minimum risk exposure level	Standard working hours defined as working hours of 35–40 h/week.

1.2. Description of the risk factor

The definition of the risk factor, the risk factor levels and the theoretical minimum risk exposure level are presented in Table 1. Long working hours are defined as any working hours (both in main and secondary jobs) exceeding standard working hours, i.e. working hours of ≥ 41 h/week. Based on results from earlier studies on long working hours and health endpoints (Kivimäki et al., 2015a; Kivimäki et al., 2015b; Virtanen et al., 2015), the preferred four exposure level categories for our review are 35–40, 41–48, 49–54 and ≥ 55 h/week, allowing calculations of potential dose-response associations. If the studies provide the preferred exposure categories, we will use the preferred exposure categories, if they provide other exposure categories, we will use the other exposure categories, as long as exposure exceeds 40 h/week.

The theoretical minimum risk exposure is standard working hours defined as 35–40 h/week. We acknowledge that it is possible that the theoretical minimum risk exposure might be lower than standard working hours, but we have to exclude working hours < 35 h/week, because studies indicate that a proportion of individuals working less than standard hours do so because of existing health problems (Kivimäki et al., 2015a; Virtanen et al., 2012). In other words, poor health might have selected a certain proportion of individuals into working fewer than standard working hours and therefore a group working fewer than standard working hours cannot serve as a comparator. Consequently, if a study uses as the reference group individuals working less than standard hours, or combines individuals working standard hours and individuals working less than standard hours as the reference group, then these studies will be excluded from the review and meta-analysis. Since the theoretical minimum risk exposure level is usually set empirically based on the causal epidemiological evidence, we will change the assumed level as evidence suggests.

If several studies report exposure levels differing from the standard levels we define here, then, if possible, we will convert the reported levels to the standard levels and, if not possible, we will report analyses on these alternate exposure levels as supplementary information in the systematic reviews. In the latter case, our protocol will be updated to reflect our new analyses.

1.3. Description of the outcome

The WHO *Global Health Estimates* group outcomes into standard burden of disease categories (World Health Organization, 2017b), based on standard codes from the *International Statistical Classification of Diseases and Related Health Problems 10th Revision* (ICD-10) (World Health Organization, 2015). The relevant WHO *Global Health Estimates* category for this systematic review is “II.E.1 Major depressive disorders” (World Health Organization, 2017b). In line with the WHO *Global Health Estimates*, we define the health outcome covered in Systematic Review 2 as depression, corresponding with the ICD-10 codes F32 (depressive episode), F33 (recurrent depressive disorder) and F34.1 (dysthymia). We will consider prevalence of, incidence of and mortality from depression. Table 2 presents for each disease or health problem included in the WHO *Global Health Estimates* category the inclusion

Table 2

ICD-10 codes and disease and health problems covered by the WHO burden of disease category *II.E.1 Depressive disorders* and their inclusion in this review.

ICD-10 code	Disease or health problem	Included in this review
F32	Depressive episode	Yes
F33	Recurrent depressive disorder	Yes
F34.1	Dysthymia	Yes

criteria for this review. This review covers all the relevant WHO *Global Health Estimates* categories.

1.4. How the risk factor may impact the outcome

Fig. 1 presents the logic model for our systematic review of the causal relationship between exposure to long working hours and

depression. This logic model is an a priori, process-orientated one (Rechfuss et al., 2018) that seeks to capture complexity of the risk factor-outcome causal relationship (Anderson et al., 2011).

Based on knowledge of previous research on long working hours and depression we assume that the effect of long working hours on risk of depression may be mediated via (a) disturbance of work/life balance, (b) exhaustion, (c) emotional distress, (d) health-related behaviors, such as lack of physical activity, high alcohol consumption and reduced sleeping hours, and (e) psycho-physiological changes, such as activation of the hypothalamic-pituitary-adrenal (HPA) axis, inflammation processes, circadian disruptions, and sleep impairment (Baglioni et al., 2011; Bannai and Tamakoshi, 2014; Bergs et al., 2018; Boden and Fergusson, 2011; Fujimura et al., 2014; Gold, 2015; Kronfeld-Schor and Einat, 2012; McEwen, 2004, 2012; Pariente and Lightman, 2008; Pittenger and Duman, 2008; Virtanen et al., 2009; Virtanen et al., 2015).

As possible confounders we included age, sex and socioeconomic

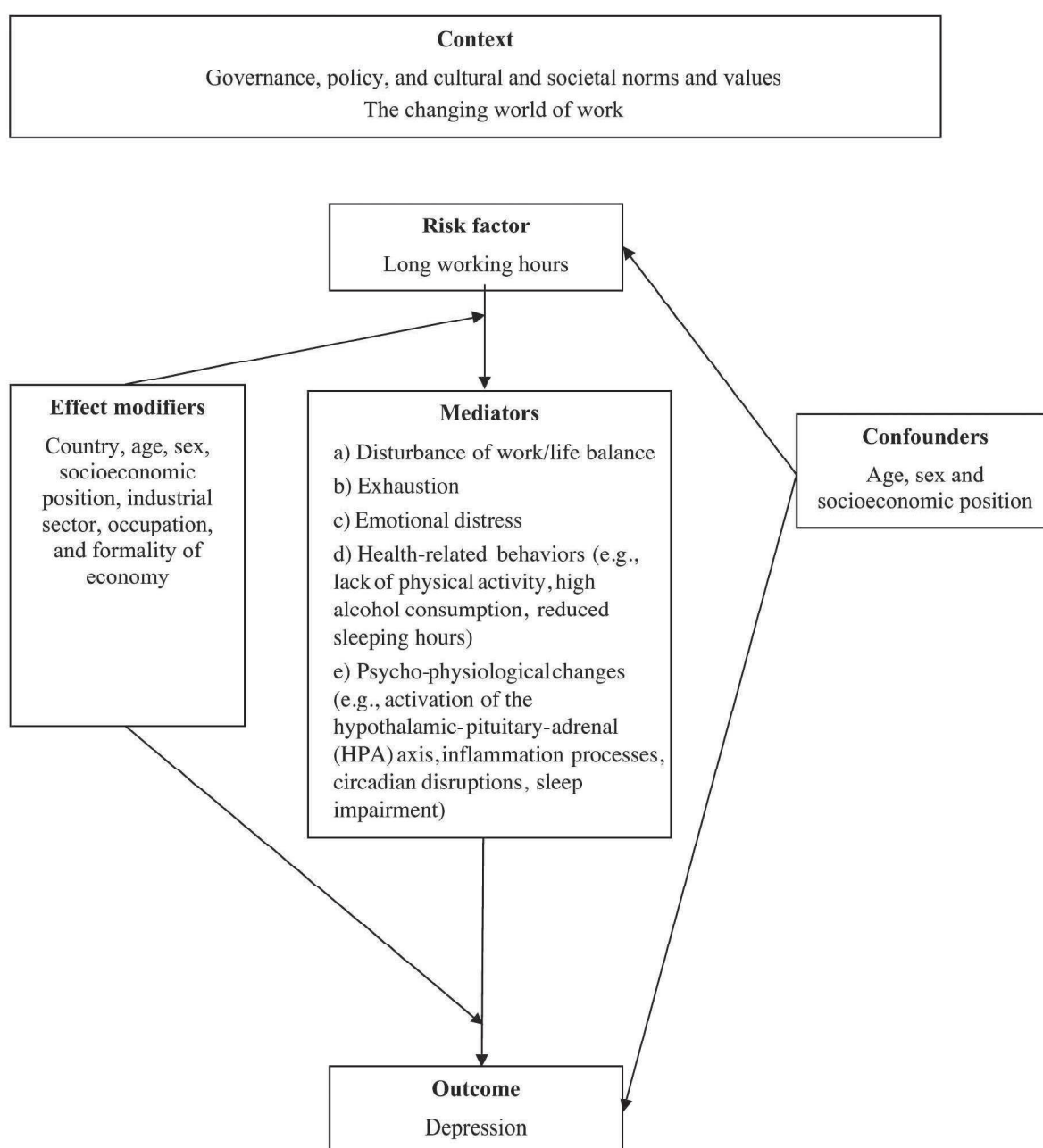


Fig. 1. Logic model of the possible causal relationship between long working hours and depression.

position, i.e. we assume that these variables may impact both long working hours and risk of depression. It is well established that women and individuals of low socioeconomic position have a higher risk of depression than men and individuals of high socioeconomic position (Kessler et al., 2003; Lorant et al., 2003; Wittchen and Jacobi, 2005). With regard to age, some studies indicate that 12-month prevalence of depression is modestly higher in young adulthood than middle adulthood (Kessler et al., 2003; Wittchen and Jacobi, 2005), although birth cohort effects may also play a role, with a higher prevalence of depression in more recent birth cohorts (Kessler et al., 2003). Age, sex and socioeconomic position may also be related to lengths of working hours, although the direction of the relations may be dependent on other variables and contextual factors (Bannai et al., 2016; Larsen et al., 2017; Lee et al., 2016; O'Reilly and Rosato, 2013; Organisation for Economic Co-operation and Development (OECD), 2018; Wirtz et al., 2012), thus, it appears reasonable to regard these three variables as potential confounders for the association of long working hours with depression. We will address this possible confounding in Systematic Review 2 by including only studies in the meta-analysis that have adjusted or stratified for age, sex and socioeconomic position.

It is possible that age, sex and socioeconomic position are not only confounders, but also effect modifiers for the association of long working hours and depression. We will address this by conducting meta-analyses stratified by age, sex and socioeconomic position, if the data allow this. We further consider as effect modifiers country, industrial sector, occupation and formality of economy and will also conduct meta-analyses stratified by these variables, if data allow this.

Fig. 1 also considers macro and meso-level context that may impact either the prevalence of long working hours or the effect of long working hours on depression, or both (Commission of Social Determinants of Health, 2008; Dahlgreen and Whitehead, 2006; Martikainen et al., 2002; Rugulies et al., 2004).

2. Objectives

1. Systematic Review 1: To systematically review quantitative studies of any design on the prevalence of relevant levels of exposure to long working hours in the years 2005–2018 among the working-age population, disaggregated by country, sex, age and industrial sector or occupation. Systematic Review 1 will be conducted in a co-ordinated fashion across all four review groups that examine long working hours with regard to health endpoints (i.e. ischaemic heart disease (Li et al., 2018), stroke (Descatha et al., 2018), alcohol use (Goderis et al., 2018) and depression (this review)) led by Grace Sembajwe from the stroke review group.
2. Systematic Review 2: To systematically review and meta-analyse randomized control trials, cohort studies, case-control studies and other non-randomized intervention studies including estimates of the relative effect of a relevant level of occupational exposure to long working hours on depression in any year among the working-age population, compared with the minimum risk exposure level of 35–40 h/week.

3. Methods

We will apply the *Navigation Guide* (Woodruff and Sutton, 2014) methodology for systematic reviews in environmental and occupational health as our guiding methodological framework, wherever feasible. The guide applies established systematic review methods from clinical medicine, including standard Cochrane Collaboration methods for systematic reviews of interventions, to the field of environmental and occupational health to ensure systematic and rigorous evidence synthesis on environmental and occupational risk factors that reduces bias and maximizes transparency (Woodruff and Sutton, 2014). The need for further methodological development and refinement of the relatively novel *Navigation Guide* has been acknowledged (Woodruff and Sutton, 2014).

Systematic Review 1 may not map well to the *Navigation Guide* framework (see Fig. 1 on page 1009 in Woodruff and Sutton, 2014), which is tailored to hazard identification and risk assessment. Nevertheless, steps 1–6 for the stream on human data can be applied to systematically review exposure to risk factors. Systematic Review 2 maps more closely to the *Navigation Guide* framework, and we will conduct steps 1–6 for the stream on human data, but not conduct any steps for the stream on non-human data, although we will briefly summarize narratively the evidence from non-human data that we are aware of.

We have registered the protocol in PROSPERO under CRD42018085729. This protocol adheres with the preferred reporting items for systematic review and meta-analysis protocols statement (PRISMA-P) (Moher et al., 2015; Shamseer et al., 2015), with the abstract adhering with the reporting items for systematic reviews in journal and conference abstracts (PRISMA-A) (Beller et al., 2013). Any modification of the methods stated in the present protocol will be registered in PROSPERO and reported in the systematic review itself. Systematic Review 1 will be reported according to the GATHER guidelines (Stevens et al., 2016), and Systematic Review 2 will be reported according to the preferred reporting items for systematic review and meta-analysis statement (PRISMA) (Liberati et al., 2009). Our reporting of the parameters for estimating the burden of depression from occupational exposure to long working hours in the systematic review will adhere with the requirements of the GATHER guidelines (Stevens et al., 2016), because the WHO/ILO burden of disease estimates that may be produced consecutive to the systematic review must also adhere to these reporting guidelines.

3.1. Systematic Review 1

3.1.1. Eligibility criteria

The population, exposure, comparator and outcome (PECO) criteria (Liberati et al., 2009) are described below.

3.1.1.1. Types of populations. We will include studies of working-age (≤ 15 years) workers in the formal and informal economy. Studies of children (aged < 15 years) and unpaid domestic workers will be excluded. Participants residing in any WHO and/or ILO Member State and any industrial setting or occupation will be included. We note that occupational exposure to long working hours may potentially have further population reach (e.g. across generations for workers of reproductive age) and acknowledge that the scope of our systematic reviews will not be able capture these populations and impacts on them. Appendix A provides a complete, but briefer overview of the PECO criteria.

3.1.1.2. Types of exposures. We will include studies that define long working hours in accordance with our standard definition (Table 1). We will prioritize measures of the total number of hours worked, including in both of: main and secondary jobs, self-employment and salaried employment and informal and formal jobs. Cumulative exposure may be the most relevant exposure metric in theory, but we will here also prioritize a non-cumulative exposure metric in practice, because we believe that global exposure data on agreed cumulative exposure measures do not currently exist. We will include all studies where long working hours were measured, whether objectively (e.g. by means of time recording technology), or subjectively, including studies that used measurements by experts (e.g. scientists with subject matter expertise) and self-reports by the worker or workplace administrator or manager. If a study presents both objective and subjective measurements, then we will prioritize objective measurements. We will include studies with measures from any data source, including registry data, in the same analyses and description.

We will include studies on the prevalence of occupational exposure to the risk factor, if it is disaggregated by country, sex (two categories:

female, male), age group (ideally in 5-year age bands, such as 20–24 years) and industrial sector (e.g. *International Standard Industrial Classification of All Economic Activities, Revision 4* [ISIC Rev. 4]) (United Nations, 2008) or occupation (as defined, for example, by the *International Standard Classification of Occupations 1988* [ISCO-88] (International Labour Organization, 1987) or 2008 [ISCO-08] (International Labour Organization, 2012)). We will also extract data on the context of risk factor exposure. Criteria may be revised in order to identify optimal data disaggregation to enable subsequent estimation of the burden of disease.

We shall include studies with exposure data for the years 2005 to 31 May 2018. For optimal modelling of exposure, WHO and ILO require exposure data up to 2018, because recent data points help better estimate time trends, especially where data points may be sparse. The additional rationale for this data collection window is that the WHO and ILO aim to estimate burden of disease in the year 2015, and we believe that the lag time from exposure to outcome will not exceed 10 years; so in their models, the organizations can use the exposure data from as early as 2005 to determine the burden of depression 10 years later in 2015. To make a conclusive judgment on the best lag time to apply in the model, we will summarize the existing body of evidence on the lag time between exposure to long working hours and depression in the review.

Both objective and subjective measures will be included. If both subjective and objective measures are presented, then we will prioritize objective ones. Studies with measures from any data source, including registries, will be eligible. The exposure parameter should match the one used in Systematic Review 2 or can be converted to match it.

3.1.1.3. Types of comparators. There will be no comparator, because we will review risk factor prevalence only.

3.1.1.4. Types of outcomes. Exposure to the occupational risk factor (i.e. long working hours).

3.1.1.5. Types of studies. This Systematic Review will include quantitative studies of any design, including cross-sectional studies. These studies must be representative of the relevant industrial sector, relevant occupational group or the national population. We will exclude qualitative, modelling, and case studies, as well as non-original studies without quantitative data (e.g. letters, commentaries and perspectives).

Study records written in any language will be included. If a study record is written in a language other than those spoken by the authors of this review or those of other reviews (Descatha et al., 2018; Godderis et al., 2018; Hulshof et al., in press; Li et al., 2018; Mandrioli et al., 2018; Paulo et al., Accepted; Teixeira et al., Accepted; Tenkate et al., Accepted) in the series (i.e. Arabic, Bulgarian, Chinese, Danish, Dutch, English, French, Finnish, German, Hungarian, Italian, Japanese, Norwegian, Portuguese, Russian, Spanish, Swedish and Thai), it will be translated into English. Published and unpublished studies will be included.

Studies conducted using unethical practices will be excluded from the review.

3.1.1.6. Types of effect measures. We will include studies with a measure of the prevalence of a relevant level of exposure to long working hours.

3.1.2. Information sources and search

3.1.2.1. Electronic academic databases. We (that is a research team formed from researchers across the four long working hour review groups, including JLAM, MB, MC, CDT, BMR, KS and KT from this review group) will, at a minimum, search the following seven electronic academic databases:

1. Ovid MEDLINE with Daily Update (1 January 2005 to 31 May 2018)
2. PubMed (1 January 2005 to 31 May 2018)
3. EMBASE (1 January 2005 to 31 May 2018)
4. Scopus (1 January 2005 to 31 May 2018)
5. Web of Science (1 January 2005 to 31 May 2018)
6. CISDOC (1 January 2005 to 31 July 2018)
7. PsycINFO (1 January 2005 to 31 July 2018)

The Ovid Medline search strategy for Systematic Review 1 is presented in Appendix B. We will perform searches in electronic databases operated in the English language using a search strategy in the English language. Consequently, study records that do not report essential information (i.e. title and abstract) in English will not be captured. We will adapt the search syntax to suit the other electronic academic and grey literature databases. When we are nearing completion of the review, we will search the PubMed database for the most recent publications (e.g., e-publications ahead of print) over the last six months. Any deviation from the proposed search strategy in the actual search strategy will be documented.

3.1.2.2. Electronic grey literature databases. We will, at a minimum, search the two following electronic grey literature databases:

1. OpenGrey (<http://www.opengrey.eu/>)
2. Grey Literature Report (<http://greylit.org/>)

3.1.2.3. Internet search engines. We will search the Google (www.google.com/) and GoogleScholar (www.google.com/scholar/) Internet search engines and screen the first 100 hits for potentially relevant records, as has been done previously in Cochrane Reviews (Pega et al., 2015; Pega et al., 2017).

3.1.2.4. Organizational websites. We will search, at a minimum, the websites of the following seven international organizations and national government departments:

1. International Labour Organization (www.ilo.org/).
2. World Health Organization (www.who.int/).
3. European Agency for Safety and Health at Work (<https://osha.europa.eu/en/>).
4. Eurostat (www.cc.europa.eu/eurostat/web/main/home).
5. China National Knowledge Infrastructure (<http://www.cnki.net/>).
6. Finnish Institute of Occupational Health (<https://www.ttl.fi/en/>).
7. National Institute of Occupational Safety and Health (NIOSH) of the United States of America, using the NIOSH data and statistics gateway (<https://www.cdc.gov/niosh/data/>).

3.1.2.5. Hand searching and expert consultation. We will hand search for potentially eligible studies in.

- Reference lists of previous systematic reviews.
- Reference lists of all study records of all included studies.
- Study records published over the past 24 months in the three peer-reviewed academic journals from which we obtain the largest number of included studies.
- Study records that have cited an included study record (identified in Web of Science citation database).
- Collections of the review authors.

Additional experts will be contacted with a list of included studies and study records, with the request to identify potentially eligible additional ones.

3.1.3. Study selection

Study selection will be carried out with Covidence (Babineau, 2014; Covidence systematic review software) and/or the Rayyan Systematic

Reviews Web App (Ouzzani et al., 2016). All study records identified in the search will be downloaded and duplicates will be identified and deleted. Afterwards, at least two review authors (from researchers across the four long working hour review groups, including JLAM, MB, MC, CDT, BMR, KS and KT from this review group), working in pairs, will independently screen against eligibility criteria titles and abstracts (step 1) and then full texts of potentially relevant records (step 2). A third review author will resolve any disagreements between the pairs of study selectors. If a study record identified in the literature search was authored by a review author assigned to study selection or if an assigned review author was involved in the study, then the record will be re-assigned to another review author for study selection. In the systematic review, we will document the study selection in a flow chart, as per GATHER guidelines (Stevens et al., 2016).

3.1.4. Data extraction and data items

A data extraction form will be developed and piloted until there is convergence and agreement among data extractors. At a minimum, two review authors (from researchers across the four long working hour review groups, including JLAM, MB, MC, CDT, BMR, KS and KT from this review group), will independently extract the data on exposure to long working hours, disaggregated by country, sex, age and industrial sector or occupation. A third review author will resolve conflicting extractions. At a minimum, we will extract data on study characteristics (including study authors, study year, study country, participants and exposure), study design (including study type), risk of bias (including missing data, as indicated by response rate and other measures) and study context. The estimates of the proportion of the population exposed to the occupational risk factor from included studies will be entered into and managed with, the Review Manager, Version 5.3 (RevMan 5.3) (2014) or DistillerSR (EvidencePartner, 2017) softwares.

We will also extract data on potential conflict of interest in included studies, including the financial disclosures and funding sources of each author and their affiliated organization. We will use a modification of a previous method to identify and assess undisclosed financial interests (Forsyth et al., 2014). Where no financial disclosure/conflict of interest is provided, we will search declarations of interest both in other records from this study published in the 36 months prior to the included study record and in other publicly available repositories (Drazen et al., 2010a; Drazen et al., 2010b).

We will request missing data from the principal study author by email or phone, using the contact details provided in the principal study record. If no response is received, we will follow up twice via email, at two and four weeks.

3.1.5. Risk of bias assessment

Generally agreed methods (i.e. framework plus tool) for assessing risk of bias do not exist for systematic reviews of input data for health estimates (The GATHER Working Group, 2016), for burden of disease studies, of prevalence studies in general (Munn et al., 2014) and those of prevalence studies of occupational and/or environmental risk factors specifically (Krauth et al., 2013; Mandrioli and Silbergeld, 2016; Vandenberg et al., 2016). None of the five standard risk of bias assessment methods in systematic reviews (Rooney et al., 2016) are applicable to assessing prevalence studies. The *Navigation Guide* does not support checklist approaches, such as Hoy et al. (2012) and Munn et al. (2014), for assessing risk of bias in prevalence studies.

We will use a modified version of the *Navigation Guide* risk of bias tool (Lam et al., 2016c) that we developed specifically for Systematic Review 1 (Appendix C). We will assess risk of bias on the levels of the individual study and the entire body of evidence. As per our preliminary tool, we will assess risk of bias along five domains: (i) selection bias; (ii) performance bias; (iii) misclassification bias; (iv) conflict of interest; and (v)

other biases. Risk of bias will be: “low”; “probably low”; “probably high”; “high” or “not applicable”. To judge the risk of bias in each domain, we will apply our a priori instructions (Appendix C).

All risk of bias assessors will trial the tool until they synchronize their understanding and application of each risk of bias domain, considerations and criteria for ratings. At least two study authors will then independently judge the risk of bias for each study by outcome, and a third author will resolve any conflicting judgments. We will present the findings of our risk of bias assessment for each eligible study in a standard ‘Risk of bias’ table (Higgins et al., 2011). Our risk of bias assessment for the entire body of evidence will be presented in a standard ‘Risk of bias summary’ figure (Higgins et al., 2011).

3.1.6. Synthesis of results

We will neither produce any summary measures, nor synthesise the evidence quantitatively. The included evidence will be presented in what could be described as an ‘evidence map’. All included data points from included studies will be presented, together with meta-data on the study design, number of participants, characteristics of population, setting, and exposure measurement of the data point.

3.1.7. Quality of evidence assessment

There is no agreed method for assessing quality of evidence in systematic reviews of the prevalence of occupational and/or environmental risk factors. We will adopt/adapt from the latest *Navigation Guide* instructions for grading (Lam et al., 2016c), including criteria (Appendix D). We will downgrade for the following five reasons from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach: (i) risk of bias; (ii) inconsistency; (iii) indirectness; (iv) imprecision; and (v) publication bias (Schünemann et al., 2011). We will grade the evidence, using the three *Navigation Guide* quality of evidence ratings: “high”, “moderate” and “low” (Lam et al., 2016c). Within each of the relevant reasons for downgrading, we will rate any concern per reason as “none”, “serious” or “very serious”. We will start at “high” for non-randomized studies and will downgrade for no concern by nil, for a serious concern by one grade (–1), and for a very serious concern by two grades (–2). We will not up-grade or down-grade the quality of evidence for the three other reasons normally considered in GRADE assessments (i.e. large effect, dose-response and plausible residual confounding and bias), because we consider them irrelevant for prevalence estimates.

All quality of evidence assessors will trial the application of our instructions and criteria for quality of evidence assessment until their understanding and application is synchronized. At least two review authors will independently judge the quality of evidence for the entire body of evidence by outcome. A third review author will resolve any conflicting judgments. In the systematic review, for each outcome, we will present our assessments of the risk for each GRADE domain, as well as an overall GRADE rating.

3.1.8. Strength of evidence assessment

To our knowledge, no agreed method exists for rating strength of evidence in systematic reviews of prevalence studies. We will rate the strength of the evidence for use as input data for estimating national-level exposure to the risk factor. Our rating will be based on a combination of the following four criteria: (i) quality of the entire body of evidence; (ii) population coverage of evidence (WIIO regions and countries); (iii) confidence in the entire body of evidence; and (iv) other compelling attributes of the evidence that may influence certainty. We will rate the strength of the evidence as either “potentially sufficient” or “potentially inadequate” for use as input data (Appendix E).

3.2. Systematic Review 2

3.2.1. Eligibility criteria

The PECO (Liberati et al., 2009) criteria are described below.

3.2.1.1. Types of populations. We will include studies of working-age (≤ 15 years) workers in the formal and informal economy. Studies of children (aged < 15 years) and unpaid domestic workers will be excluded. Data on the formal and informal economy that the workers work in will be extracted, if feasible. Participants residing in any WHO and/or ILO Member State and any industrial setting or occupation will be included. We note that occupational exposure to long working hours may potentially have further population reach (e.g. across generations for workers of reproductive age) and acknowledge that the scope of our systematic reviews will not be able capture these populations and impacts on them. Appendix F provides a complete, but briefer overview of the PECO criteria.

3.2.1.2. Types of exposures. We will include studies that define long working hours in accordance with our standard definition (Table 1). We will again prioritize measures of the total number of hours worked, including in both of: main and secondary jobs, self-employment and salaried employment and informal and formal jobs. We will include all studies where long working hours were measured, whether objectively (e.g. by means of time recording technology), or subjectively, including studies that used measurements by experts (e.g. scientists with subject matter expertise) and self-reports by the worker or workplace administrator or manager. If a study presents both objective and subjective measurements, then we will prioritize objective measurements. We will include studies with measures from any data source, including registry data, in the same analyses and description. Regarding years of data coverage, studies from any year will be included.

3.2.1.3. Types of comparators. The comparator will be participants exposed to the theoretical minimum risk exposure level (Table 1). We will exclude all other comparators.

3.2.1.4. Types of outcomes. We will include studies that define depression in accordance with our standard definition of this outcome (Table 2) that is depressive episode (ICD-10, F32), recurrent depressive disorder (F33) and dysthymia (F34.1). Other affective disorders, e.g., bipolar disorders, will be excluded. We expect that most studies examining long working hours and depression will not have documented ICD-10 diagnostic codes, but will have ascertained depression with methods that approximate ICD-10 criteria (e.g., a validated depression rating scale filled in by the worker). We will include both self-reported and non-self-reported measurements of the outcome, but will prioritize non-self-reported over self-reported ones.

The following measurements of depression are eligible:

- i. Psychiatric diagnostic interview.
- ii. Diagnosis by a physician, psychologist or other qualified health professional.
- iii. Hospital admission or discharge record.
- iv. Administrative data (e.g., disability pensioning with the diagnosis of depression).
- v. Register data of treatment for depression, with antidepressant medication, psychotherapy or both; will only be included if there is documentation that the treatment was for depression and not for other types of disorders.
- vi. Self-administered rating scale for depression that was previously validated against a clinical measure of depression and that dichotomized respondents into cases versus non-cases (e.g., Center of Epidemiological Studies Depression Scale (CES-D) (Radloff, 1977) or Major Depression Inventory (MDI) (Bech et al., 2001)) or other

validated self-administered rating scales.

vii. Medically certified cause of death.

Because the endpoint of our study is binary, studies exclusively reporting depression as a continuous variable (e.g., level of depressive symptoms) will be excluded, as will be all other measurements.

3.2.1.5. Types of studies. We will include studies that investigated the effect of long working hours on depression for any years. Eligible study designs will be randomized controlled trials (including parallel-group, cluster, cross-over and factorial trials) and cohort studies (both prospective and retrospective), case-control studies, and other non-randomized intervention studies (including quasi-randomized controlled trials, controlled before-after studies and interrupted time series studies). We include a broader set of observational study designs than is commonly included, because a recent augmented Cochrane Review of complex interventions identified valuable additional studies using such a broader set of study designs (Arditi et al., 2016). All other study designs, such as uncontrolled before-and-after, cross-sectional, qualitative, modelling, case and non-original studies will be excluded.

With regard to cohort studies, we will include only studies that have excluded individuals with depression at baseline (to reduce the risk of reverse causation). However, it is possible that some studies have additionally measured levels of non-clinical depressive symptoms at baseline and have included this measure as a covariate.

Records published in any year and any language will be included. Again, the search will be conducted using English language terms, so that records published in any language that present essential information (i.e. title and abstract) in English will be included. If a record is written in a language other than those spoken by the authors of this review or those of other reviews in the series (Descatha et al., 2018; Godderis et al., 2018; Hulshof et al., in press; Li et al., 2018; Mandrioli et al., 2018; Paulo et al., Accepted; Teixeira et al., Accepted; Tenkate et al., Accepted), then the record will be translated into English. Published and unpublished studies will be included.

Studies conducted using unethical practices will be excluded (e.g., studies that deliberately exposed humans to a known risk factor to human health).

3.2.1.6. Types of effect measures. We will include measures of the relative effect of a relevant level of long working hours on the risk of developing or dying from depression, compared with the theoretical minimum risk exposure level. Effect estimates of prevalence measures only will be excluded. We will include relative effect and incidence measures such as risk ratios, odds ratios and hazard ratios. Measures of absolute effects (e.g. mean differences in risks or odds) will be converted into relative effect measures, but if conversion is impossible, they will be excluded. To ensure comparability of effect estimates and facilitate meta-analysis, if a study presents an odds ratio, then we will convert it into a risk ratio, if possible, using the guidance provided in the Cochrane Collaboration's handbook for systematic reviews of interventions (Higgins and Green, 2011).

As shown in our logic framework (Fig. 1), we a priori consider the following variables to be potential effect modifiers of the effect of long working hours on depression: country, age, sex, industrial sector, occupation and formality of employment. We consider age, sex and socioeconomic position to be potential confounders. Potential mediators are: disturbance of work/life balance; exhaustion; emotional distress; health-related behaviors; and psychophysiological changes.

If a study presents estimates for the effect from two or more alternative models that have been adjusted for different variables, then we will systematically prioritize the estimate from the model that we consider best adjusted, applying the lists of confounders and mediators identified in our logic model (Fig. 1). We will prioritize estimates from models adjusted for more potential confounders over those from models adjusted for fewer. For example, if a study presents estimates from a

crude, unadjusted model (Model A), a model adjusted for one potential confounder (Model B) and a model adjusted for two potential confounders (Model C), then we will prioritize the estimate from Model C. We will prioritize estimates from models unadjusted for mediators over those from models that adjusted for mediators, because adjustment for mediators can introduce bias. For example, if Model A has been adjusted for two confounders, and Model B has been adjusted for the same two confounders and a potential mediator, then we will choose the estimate from Model A over that from Model B. We prioritize estimates from models that can adjust for time-varying confounders that are at the same time also mediators, such as marginal structural models (Pega et al., 2016) over estimates from models that can only adjust for time-varying confounders, such as fixed-effects models (Gunasekara et al., 2014), over estimates from models that cannot adjust for time-varying confounding. If a study presents effect estimates from two or more potentially eligible models, then we will explain specifically why we prioritized the selected model.

3.2.2. Information sources and search

3.2.2.1. Electronic academic databases. We (MB, CDT, BMR and KS) will, at a minimum, search the seven following electronic academic databases:

1. International Clinical Trials Register Platform (to 30 June 2018)
2. Ovid MEDLINE with Daily Update (1946 to 30 June 2018)
3. PubMed (1946 to 30 June 2018)
4. EMBASE (1947 to 30 June 2018)
5. Web of Science (1945 to 30 June 2018)
6. CISDOC (1901 to 30 June 2018)
7. PsycINFO (1880 to 30 June 2018)

The Ovid Medline search strategy for Systematic Review 2 is presented in Appendix G. We will perform searches in the electronic databases operated in the English literature using a search strategy in the English language. We will perform searches in electronic databases operated in the English language using a search strategy in the English language. We (CDT, KS and RR) will adapt the search syntax to suit the other electronic academic and grey literature databases. When we are nearing completion of the review, we will search the PubMed database for the most recent publications (e.g., e-publications ahead of print) over the last six months. Any deviation from the proposed search strategy in the actual search strategy will be documented.

3.2.2.2. Electronic grey literature databases. We (MB, CDT, BMR and KS) will, at a minimum, search the two following electronic grey literature databases:

1. OpenGrey (<http://www.opengrey.eu/>)
2. Grey Literature Report (<http://greylit.org/>)

3.2.2.3. Internet search engines. We (MB, CDT, BMR and KS) will search the Google (www.google.com/) and GoogleScholar (www.google.com/scholar/) Internet search engines and screen the first 100 hits for potentially relevant records.

3.2.2.4. Organizational websites. We (MB, CDT, BMR and KS) will search the websites of the six following international organizations and national government departments:

1. International Labour Organization (www.ilo.org/)
2. World Health Organization (www.who.int)
3. EUROSTAT (www.ec.europa.eu/eurostat/web/main/home)
4. National Institute of Occupational Safety and Health (NIOSH) of the United States of America, using the NIOSH data and statistics gateway (<https://www.cdc.gov/niosh/data/>)
5. Finnish Institute of Occupational Health (<https://www.ttl.fi/en/>)

6. International Commission of Occupational Health (ICOH) Scientific Committee on Work Organization and Psychosocial Factors (ICOH-WOPS) <http://www.ichweb.org/site/scientific-committee-detail.asp?sc=33>

3.2.2.5. Hand searching and expert consultation. We (MB, CDT, BMR, KS, SI and RR) will hand search for potentially eligible studies in.

- Reference lists of previous systematic reviews.
- Reference lists of all included study records.
- Study records published over the past 24 months in the three peer-reviewed academic journals with the largest number of included studies.
- Study records that have cited the included studies (identified in Web of Science citation database).
- Collections of the review authors.

Additional experts will be contacted with a list of included studies, with the request to identify potentially eligible additional studies.

3.2.3. Study selection

Study selection will be carried out in a reference manager database, such as Covidence (Babineau, 2014; Covidence systematic review software) or the Rayyan Systematic Reviews Web App (Ouzzani et al., 2016). All study records identified in the search will be downloaded and duplicates will be identified and deleted. Afterwards, at least two review authors (out of: RR, EA, JLAM, MB, MC, CDT, ND, QDM, HE, JG, AIG, SI, IEHM, BMR, KS, KT and AZ), working in pairs, will independently screen titles and abstracts (step 1) and then full texts (step 2) of potentially relevant records. Any disagreements between the two review authors will be resolved by discussion and the involvement of a third review author (MB, CDT, BMR or KS). If a study record identified in the literature search was authored by a review author assigned to study selection or if an assigned review author was involved the study, then the record will be re-assigned to another review author for study selection. The study selection will be documented in a flow chart in the systematic review, as per PRISMA guidelines (Liberati et al., 2009).

3.2.4. Data extraction and data items

A data extraction form will be developed and trialed until data extractors reach convergence and agreement. At a minimum, two review authors (out of: MB, CDT, BMR and KS) will extract data on study characteristics (including study authors, study year, study country, participants, exposure and outcome), study design (including summary of study design, comparator, epidemiological models used and effect estimate measure), risk of bias (including selection bias, reporting bias, confounding, and reverse causation) and study context (e.g. data on contemporaneous exposure to other occupational risk factors potentially relevant for risk of depression). A third review author (out of: MB, CDT, BMR, KS, RR) will resolve conflicts in data extraction. Data will be entered into and managed with the RevMan 5.3 software (2014).

We will also extract data on potential conflict of interest in included studies, including the financial disclosures and funding sources of each author and their affiliated organization. We will use a modification of a previous method to identify and assess undisclosed financial interests (Forsyth et al., 2014). Where no financial disclosure or conflict of interest statements are provided, we will search declarations of interest both in other records from this study published in the 36 months prior to the included study record and in other publicly available repositories (Drazen et al., 2010a; Drazen et al., 2010b).

We will request missing data from the principal study author by email or phone, using the contact details provided in the principal study record. If we do not receive a positive response from the study author, we will send follow-up emails twice, at two and four weeks.

3.2.5. Risk of bias assessment

Standard risk of bias tools do not exist for systematic reviews for hazard identification in occupational and environmental health, nor for risk assessment. The five methods specifically developed for occupational and environmental health are for either or both hazard identification and risk assessment, and they differ substantially in the types of studies (randomized, observational and/or simulation studies) and data (e.g. human, animal and/or in vitro) they seek to assess (Rooney et al., 2016). However, all five methods, including the *Navigation Guide* (Lam et al., 2016c), assess risk of bias in human studies similarly (Rooney et al., 2016).

The *Navigation Guide* was specifically developed to translate the rigor and transparency of systematic review methods applied in the clinical sciences to the evidence stream and decision context of environmental health (Woodruff and Sutton, 2014), which includes workplace environment exposures and associated health outcomes. The guide is our overall organizing framework, and we will also apply its risk of bias assessment method in Systematic Review 2. The *Navigation Guide* risk of bias assessment method builds on the standard risk of bias assessment methods of the Cochrane Collaboration (Higgins et al., 2011) and the US Agency for Healthcare Research and Quality (Viswanathan et al., 2008). Some further refinements of the *Navigation Guide* method may be warranted (Goodman et al., 2017), but it has been successfully applied in several completed and ongoing systematic reviews (Johnson et al., 2016; Johnson et al., 2014; Koustas et al., 2014; Lam et al., 2016a; Lam et al., 2014; Lam et al., 2016b; Vesterinen et al., 2014). In our application of the *Navigation Guide* method, we will draw heavily on one of its latest versions, as presented in the protocol for an ongoing systematic review (Lam et al., 2016c). Should a more suitable method become available, we may switch to it.

We will assess risk of bias on the individual study level and on the body of evidence overall. The nine risk of bias domains included in the *Navigation Guide* method for human studies are: (i) source population representation; (ii) blinding; (iii) exposure assessment; (iv) outcome assessment; (v) confounding; (vi) incomplete outcome data; (vii) selective outcome reporting; (viii) conflict of interest; and (ix) other sources of bias. While two of the earlier case studies of the *Navigation Guide* did not utilize outcome assessment as a risk of bias domain for studies of human data (Johnson et al., 2014; Koustas et al., 2014; Lam et al., 2014; Vesterinen et al., 2014) all of the subsequent reviews have included this domain (Johnson et al., 2016; Lam et al., 2016a; Lam et al., 2017; Lam et al., 2016b; Lam et al., 2016c). Risk of bias or confounding ratings will be: “low”; “probably low”; “probably high”; “high” or “not applicable” (Lam et al., 2016c). To judge the risk of bias in each domain, we will apply a priori instructions (Appendix H), which we have adopted or adapted from an ongoing *Navigation Guide* systematic review (Lam et al., 2016c). For example, a study will be assessed as carrying “low” risk of bias from source population representation, if we judge the source population to be described in sufficient detail (including eligibility criteria, recruitment, enrollment, participation and loss to follow up) and the distribution and characteristics of the study sample to indicate minimal or no risk of selection effects. The risk of bias at study level will be determined by the worst rating in any bias domain for any outcome. For example, if a study is rated as “probably high” risk of bias in one domain for one outcome and “low” risk of bias in all other domains for the outcome and in all domains for all other outcomes, the study will be rated as having a “probably high” risk of bias overall.

All risk of bias assessors (MB, CDT, BMR, KS, RR and SI) will jointly trial the application of the risk of bias criteria until they have synchronized their understanding and application of these criteria. At least two study authors (out of: MB, CDT, BMR and KS) will independently judge the risk of bias for each study by outcome. Where individual assessments differ, a third author (MB, CDT, MB, BMR, RR or SI) will resolve the conflict. In the systematic review, for each included study, we will report our study-level risk of bias assessment by domain in a

standard ‘Risk of bias’ table (Higgins et al., 2011). For the entire body of evidence, we will present the study-level risk of bias assessments in a ‘Risk of bias summary’ figure (Higgins et al., 2011).

3.2.6. Synthesis of results

We will conduct meta-analyses separately for estimates of the effect on incidence and mortality. Studies of different designs will not be combined quantitatively. If we find two or more studies with an eligible effect estimate, two or more review authors (out of: CDT, KS, RR and SI) will independently investigate the clinical heterogeneity of the studies in terms of participants (including country, sex, age, socioeconomic position and industrial sector or occupation), level of risk factor exposure, comparator and outcomes. If we find that effect estimates differ considerably by country, sex, socioeconomic position and industrial sector or occupation, or a combination of these, then we will synthesise evidence for the relevant populations defined by country, sex, age, socioeconomic position and industrial sector or occupation, or combination thereof. Differences by country could include or be expanded to include differences by country group (e.g. WHO region or World Bank income group). If we find that effect estimates are clinically homogenous across countries, sexes, age, socioeconomic position occupation and industrial sector, then we will combine studies from all of these populations into one pooled effect estimate that could be applied across all combinations of countries, sexes and age groups in the WHO/ILO joint methodology.

If we judge two or more studies for the relevant combination of country, sex and age group, or combination thereof, to be sufficiently clinically homogenous to potentially be combined quantitatively using quantitative meta-analysis, then we will test the statistical heterogeneity of the studies using the I^2 statistic (Higgins et al., 2003). If two or more clinically homogenous studies are found to be sufficiently homogenous statistically to be combined in a meta-analysis, we will pool the risk ratios of the studies in a quantitative meta-analysis, using the inverse variance method with a random effects model to account for cross-study heterogeneity (Higgins and Green, 2011). The meta-analysis will be conducted in RevMan 5.3 (2014), but the data for entry into these programmes may be prepared using another recognized statistical analysis programme, such as Stata (Stata Cooperation, 2017). We will neither quantitatively combine data from studies with different designs (e.g. combining cohort studies with case-controls studies), nor unadjusted and adjusted models. We will only combine studies that we judge to have a minimum acceptable level of adjustment for confounders. More specifically, the analyses have to be adjusted or stratified for (i) sex, (ii) age and (iii) a measure of socioeconomic position (e.g., education, income or occupational grade) to be included in the meta-analysis. If quantitative synthesis is not feasible, then we will synthesise the study findings narratively and identify the estimates that we judged to be the highest quality evidence available.

3.2.7. Additional analyses

If there is evidence for differences in effect estimates by country, sex, age, socioeconomic position and industrial sector or occupation, or a combination of these variables, then we will conduct subgroup analyses by these variables. If studies on workers in the informal economy and in the formal economy are included, then we will conduct subgroup analysis by formality of economy studied. Findings of these subgroup analyses, if any, will be used as parameters for estimating burden of disease specifically for relevant populations defined by these variables. We will examine the potential of these variables to be effect modification in a meta-regression, if feasible. In addition, we may conduct meta-regressions or stratified analyses for other potential effect modifiers, if allowed by the data.

If feasible, sensitivity analyses will be conducted that will include only studies judged to be of “low” or “probably low” risk of bias. If feasible, we will conduct sensitivity analyses that are stratified by whether the estimate was based on a documented ICD-10 diagnostic

code or was based on an approximation of an ICD-10 diagnostic code. We may also conduct a sensitivity analysis using an alternative meta-analytic model, namely the inverse variance heterogeneity (IVhet) model.

A recent systematic review and meta-analysis on job strain and risk of hospital treatment for depression showed that depressive symptoms are likely partly an intermediate step in the pathway linking occupational exposure and risk of depression (Madsen et al., 2017). Consequently, we regard depressive symptoms as a mediator and do not include in the main meta-analysis estimates that are adjusted for depressive symptoms, unless the analysis used a model that can adjust for this mediation (e.g. an appropriately specified marginal structural model). However, because baseline depressive symptoms may also be a confounder if they have caused both reporting of long working hours at baseline and incidence of depression at follow-up (Madsen et al., 2017), we will conduct an additional analysis with estimates that are adjusted for baseline depressive symptoms, if studies have provided such estimates.

3.2.8. Quality of evidence assessment

We will assess quality of evidence using a modified version of the *Navigation Guide* quality of evidence assessment tool (Lam et al., 2016c). The tool is based on the GRADE approach (Schünemann et al., 2011) adapted specifically to systematic reviews in occupational and environmental health (Morgan et al., 2016). Should a more suitable method become available, we may switch to it.

Working in pairs, we (MB, CDT, BMR, KS, RR and SI) will assess quality of evidence for the entire body of evidence by outcome, with any disagreements resolved by a third review author (RR or SI). We will adopt or adapt the latest *Navigation Guide* instructions (Appendix D) for grading the quality of evidence (Lam et al., 2016c). We will downgrade the quality of evidence for the following five GRADE reasons: (i) risk of bias; (ii) inconsistency; (iii) indirectness; (iv) imprecision; and (v) publication bias. If our systematic review includes ten or more studies, we will generate a funnel plot to judge concerns on publication bias. If it includes nine or fewer studies, we will judge the risk of publication bias qualitatively. To assess risk of bias from selective reporting, protocols of included studies, if any, will be screened to identify instances of selective reporting.

We will grade the evidence, using the three *Navigation Guide* standard quality of evidence ratings: “high”, “moderate” and “low” (Lam et al., 2016c). Within each of the relevant domains, we will rate the concern for the quality of evidence, using the ratings “none”, “serious” and “very serious”. As per *Navigation Guide*, we will start at “high” for randomized studies and “moderate” for observational studies. Quality will be downgraded for no concern by nil grades (0), for a serious concern by one grade (–1) and for a very serious concern by two grades (–2). We will up-grade the quality of evidence for the following other reasons: large effect, dose-response and plausible residual confounding and bias. For example, if we have a serious concern for risk of bias in a body of evidence consisting of observational studies (–1), but no other concerns, and there are no reasons for upgrading, then we will down-grade its quality of evidence by one grade from “moderate” to “low”.

3.2.9. Strength of evidence assessment

We will apply the standard *Navigation Guide* methodology (Lam et al., 2016c) to rate the strength of the evidence. The rating will be based on a combination of the following four criteria: (i) quality of the body of evidence; (ii) direction of the effect; (iii) confidence in the effect; and (iv) other compelling attributes of the data that may influence our certainty. The ratings for strength of evidence for the effect of long working hours on depression will be “sufficient evidence of toxicity/harmfulness”, “limited of toxicity/harmfulness”, “inadequate of toxicity/harmfulness” and “evidence of lack of toxicity/harmfulness” (Appendix I).

Financial support

All authors are salaried staff members of their respective institutions. The publication was prepared with financial support from the World Health Organization cooperative agreement with the Centres for Disease Control and Prevention National Institute for Occupational Safety and Health of the United States of America on implementing Resolution WHA 60.26 “Workers’ Health: Global Plan of Action” (Grant 1 E11 OH0010676-02).

Sponsors

The sponsors of this systematic review are the World Health Organization and the International Labour Organization.

Author contributions

IDI, NL, FP and APÜ had the idea for the systematic review. IDI, NL, FP and YU gathered the review team. FP led and all authors contributed to the development of the standard methodology for all systematic reviews in the series. FP led and all authors contributed to the development and writing of the standard template for all protocols in the series. RR is the lead reviewer of Systematic Review 2. RR wrote the first draft of this protocol, using the protocol template prepared by FP, and all authors made substantial contributions to the revisions of the manuscript. The search strategy was developed and piloted by KS in collaboration with a research librarian. FP coordinated all inputs from the World Health Organization, International Labour Organization and external experts and ensured consistency across the systematic reviews of this series. RR is the guarantor of Systematic Review 2.

Acknowledgments

We thank Stavroula Leka for her preliminary contribution towards the establishment of the systematic review before the review commenced and Alexis Descatha, Diana Gagliardi, Jian Li, Grace Sembajwe, Johannes Siegrist and Mark van Ommeren for their feedback on an earlier version of this protocol. We thank research librarian Elizabeth Bengtson for her assistance with developing the search strategy. We thank Frida Fischer, Anders Knutsson and Mikael Sallinen for their feedback on the search strategy. We are grateful to Lisa Bero, Rebecca Morgan, Susan Norris, Holger J. Schünemann, Patrice Sutton and Tracey Woodruff for their feedback on the methods for this protocol. We thank Paul Whaley and Tim Driscoll for their editorial guidance. The authors alone are responsible for the views expressed in this article and they do not necessarily represent the views, decisions or policies of the institutions with which they are affiliated.

Conflict of interest

CDT and SI report participation in projects granted from the Italian Ministry of Health. All other authors declare no conflict of interest.

Appendices. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envint.2018.11.011>.

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Organizational Justice and Refraining from Seeking Medical Care Among Japanese Employees: A 1-Year Prospective Cohort Study

Akiomi Inoue¹ · Akizumi Tsutsumi¹ · Hisashi Eguchi¹ · Norito Kawakami²

Published online: 27 November 2018
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Abstract

Background Using a 1-year prospective design, we examined the association of organizational justice (i.e., procedural justice and interactional justice) with refraining from seeking medical care (RSMC) among Japanese employees.

Methods We surveyed 2695 employees (1994 men and 701 women) from two factories of a manufacturing company in Japan. A self-administered questionnaire comprising scales for measuring organizational justice (Organizational Justice Questionnaire) and potential confounders (i.e., demographic and socioeconomic characteristics as well as health-related behaviors) was administered at baseline (from April to June 2011). At 1-year follow-up (from April to June 2012), a single-item question was used to measure RSMC during the follow-up period. Multiple logistic regression analysis was conducted by gender.

Results After adjusting for potential confounders, low procedural justice and low interactional justice at baseline were found to be significantly associated with higher odds of RSMC during the 1-year follow-up for male employees (odds ratio = 1.33 [95% confidence interval = 1.16–1.52], $p < 0.001$ and 1.15 [95% confidence interval = 1.02–1.29], $p = 0.019$, respectively). Similar patterns were observed for female employees (odds ratio = 1.37 [95% confidence interval = 1.08–1.74], $p = 0.009$ and 1.23 [95% confidence interval = 1.02–1.50], $p = 0.035$ for low procedural justice and low interactional justice, respectively).

Conclusions The present study provided evidence that the lack of organizational justice is positively associated with RSMC among Japanese employees, independently of demographic and socioeconomic characteristics as well as of health-related behaviors.

Keywords Access to medical care · Procedural justice · Interactional justice · Longitudinal studies

Introduction

Access to medical care is a fundamental human right and an important determinant of health [1]. The effects of delayed access to medical care on reduced quality of life, longer hospital stays, and mortality have been reported across a wide range of age groups [2–5]. In Europe and Oceania, 7–22% of adults reportedly refrain from seeking medical care (i.e., are reluctant to seek medical care) for financial reasons [6]. In Japan, where people enjoy universal health insurance coverage (the co-payment rate for the working-age population is

30%) [7], about one quarter of people have been reported to refrain from seeking medical care for the same reasons [8], which is the second-highest level among high-income countries following the USA [6]. Several studies of community residents have reported that social class (i.e., educational attainment, household income, and employment conditions) [9–14] as well as regional environmental factors (i.e., community size, having some means of transportation, non-familial support, and social capital in the neighborhood) [1, 15–18] have an effect on refraining from seeking medical care (RSMC). On the other hand, work environmental factors may play an equally important role in influencing individual's RSMC, because most of the world's population (58%) spends one third of their adult life at work [19].

Organizational justice may be one of the important factors determining RSMC among employed people. It has its origins in human rights theory and can be defined as an employee's perception of the fairness of resource allocation in the workplace organization [20, 21], which refers to management's decisions and actions that are morally right and are in

✉ Akiomi Inoue
akiomi@med.kitasato-u.ac.jp

¹ Department of Public Health, Kitasato University School of Medicine, 1-15-1 Kitasato, Minami-ku, Sagami-hara 252-0374, Japan

² Department of Mental Health, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

accordance with ethical standards and/or law [22]. In the last two decades, it has been considered as one of the psychosocial determinants of health-related behaviors and health outcomes in occupational settings [23–26]. Among others, procedural justice (i.e., the degree to which fair decision-making procedures are used to arrive at a decision [27] according to six fair process criteria, such as consistency, lack of bias, correctability, representation, accuracy, and ethicality [28]) and interactional justice (i.e., the degree to which employees are treated with respect, kindness, and dignity in interpersonal interactions with supervisor, sometimes known as interpersonal justice, and the adequacy of the explanations in terms of their timeliness, specificity, and truthfulness, sometimes known as informational justice) [29] have been viewed as primary characteristics of organizational justice within a workplace [30].

Given the definition of procedural justice and interactional justice described above [27–29], employees are less likely to be accepted as unique individuals and their fundamental human rights are less likely to be respected when organizational justice is lacking. In such a situation, employees may be mistreated just because they seek medical care and/or they may have difficulty consulting with their supervisor about re-arranging their schedules associated with seeking medical care; hence, they may refrain from seeking necessary medical care even when getting sick [20].

From the viewpoint of behavioral medicine, seeking medical care (or medical care utilization) is driven by help-seeking (or health-seeking) behavior (HSB) [31], which refers to a sequence of remedial actions that individuals undertake to rectify perceived ill-health [32]. Conceptually, the antecedents of HSB include psychosocial factors [33] as well as predisposing factors, such as workplace stress factors [34], which are postulated to influence an individual's decision to seek initial and continued care for their perceived health issue. A recent study reported that organizational justice is positively associated with employees' HSB [35]. Given such a conceptual framework and the empirical findings, employees who perceive lower levels of organizational justice may have difficulty making a decision to take help-seeking action because they are less likely to feel that they have a voice in or are respected by their workplace and/or supervisor, which may in turn lead to RSMC. To the best of our knowledge, the association of organizational justice with RSMC has not been examined.

For other work environmental factors, low job control has been reported to be associated with having less access to medical care among Japanese male employees, although it was specific to one situation (i.e., after diabetes screening in the workplace) [36]. This empirical finding also suggests that organizational justice has a potential effect on RSMC because it captures more basic elements of the social structure within which task-level job characteristics, such as job demands and job control, are operating [37].

The purpose of the present study was to examine the association of organizational justice (i.e., procedural justice and interactional justice) with RSMC among Japanese employees using a 1-year prospective design. It was hypothesized that those who perceived lower levels of organizational justice at baseline would be more likely to refrain from seeking medical care during the 1-year follow-up. In our analysis, we considered the existing evidence indicating that women experience more gender discrimination in the workplace than do men [38]. In fact, our previous study of Japanese employees revealed that female employees perceived lower levels of organizational justice than did male employees [39]. In Japan's male-dominated workplace culture, female employees may have little voice in the workplace, which may lead to gender difference in the association of organizational justice with RSMC. Therefore, the analysis was conducted separately for male and female employees.

Methods

Study Design

In the present study, we used a part of the longitudinal data collected in an occupational cohort study on social class and health in Japan (Japanese Study of Health, Occupation, and Psychosocial Factors Related Equity: J-HOPE) at baseline (from April to June 2011) and 1-year follow-up (from April to June 2012) [40].

Participants

All employees from two factories of a manufacturing company in Japan ($N = 3630$) were recruited by means of an invitation letter sent by the authors in February 2011. It should be noted that they were covered by the same corporate health insurance. Furthermore, because the two factories were located close to each other, the employees had almost equal access to medical care. All variables used in the present study, except employment status, which was obtained from the personnel records of the surveyed company, were measured using a self-administered questionnaire. Overall, 3461 employees completed the self-administered questionnaire at baseline (response rate 95.3%). During the 1-year follow-up period, 336 out of 3461 employees were transferred to other sites, took a leave of absence (i.e., sick leave, maternity leave, or childcare leave), retired, or declined to participate. Overall, 3125 employees participated at 1-year follow-up and completed the follow-up questionnaire (follow-up rate 90.3%). After excluding 430 employees who had at least one missing response for variables relevant to the present study, the data from 2695 employees (1994 men and 701 women) were analyzed. The

analysis was conducted using the J-HOPE first and second wave datasets as of December 22, 2016.

Measures

Exposure: Organizational Justice (Baseline Survey)

Organizational justice was measured using the Japanese version of the Organizational Justice Questionnaire (OJQ) [41–43], which comprises a seven-item procedural justice scale and a six-item interactional justice scale, both measured on a five-point Likert-type scale ranging from “1 = *strongly disagree*” to “5 = *strongly agree*.” The total score for each OJQ subscale was calculated by averaging item scores (score range 1–5). In this sample, Cronbach’s alpha coefficients were 0.88 for the procedural justice scale and 0.94 for the interactional justice scale for male employees; and 0.90 for the procedural justice scale and 0.95 for the interactional justice scale for female employees.

Outcome: RSMC (1-Year Follow-Up Survey)

In the follow-up questionnaire, we included a single-item question measuring RSMC, which was used in the Japanese General Social Survey conducted in 2008 (JGSS-2008) [13]. The participants were asked to respond to the question: “In the past year, have you ever refrained from visiting a hospital, clinic, acupuncturist, or dentist despite your sickness (including a slight cold or cavity) or injury?” The response options were “1 = *Yes, I have*,” “2 = *No, I have not*,” and “3 = *I did not get sick or injured*.” Participants were dichotomized into those who refrained from seeking medical care (i.e., those who answered 1) and those who did not (i.e., those who answered 2 or 3).

Potential Confounders (Baseline Survey)

Potential confounders included demographic characteristics, socioeconomic characteristics, and health-related behaviors. Demographic characteristics included age, past medical history, household size, work shift, and working hours per week. Socioeconomic characteristics included education, equivalent annual household income, occupational position, and employment status. For equivalent annual household income, the participants were asked to report their annual household income by selecting one of the following six response options: 2.99 million JPY (36,000 USD) or less, 3–4.99 million JPY (36,100–60,100 USD), 5–7.99 million JPY (60,200–96,300 USD), 8–9.99 million JPY (96,400–120,400 USD), 10–14.99 million JPY (120,500–180,600 USD), and 15 million JPY (180,700 USD) or more (USD was converted from JPY using monthly exchange rate as of April 2011 [83 JPY per USD]). Subsequently, equivalent household income was

calculated by dividing the median household income of each response option by the square root of the household size. Health-related behaviors included smoking habits (never smoker, ex-smoker, and current smoker), drinking habits (rarely, sometimes, and daily), and physical activity (none, light physical activity one or more times a week, intense physical activity once or twice a week, and intense physical activity thrice or more times a week). Categories of demographic and socioeconomic characteristics are shown in Table 1.

Sample Size

Multiple logistic regression analysis was selected as a main analysis. According to a formula proposed by Peduzzi et al. [44], we calculated the minimum required sample size for multiple logistic regression analysis while considering that the prevalence of RSMC among Japanese employees has been reported to be about 50% for both genders [45] and that the maximum number of independent variables (i.e., the number of continuous variables and dummy variables in the fully adjusted model) was 29 for male and 28 for female employees. As a result, the minimum required sample size was 580 for male and 560 for female employees; therefore, our sample size was considered to have sufficient statistical power for the main analysis.

Statistical Analysis

After descriptive analysis using Student’s *t* test or Fisher’s exact test, which aimed to compare those who did and those who did not refrain from seeking medical care in demographic and socioeconomic characteristics as well as in total score for each justice dimension, we conducted the main analysis. Prior to the main analysis, total score for each justice dimension was reverse-coded so that higher scores indicated lower justice, which allowed us to interpret the results easier. Taking reversed total score for each justice dimension as an independent variable, multiple logistic regression analysis was conducted to estimate the odds ratio (OR) and its 95% confidence interval (CI) for RSMC associated with a one-point decrease in each justice dimension. In the series of analysis, we first adjusted for demographic characteristics (Model 1). Subsequently, we incrementally adjusted for socioeconomic characteristics (Model 2) and health-related behaviors (Model 3). The level of significance was 0.05 (two-tailed). The statistical analysis was conducted using IBM® SPSS® Statistics Version 23.0 for Windows.

Results

Table 1 shows the detailed characteristics of the participants by those who did and those who did not refrain from seeking

Men ($n = 1994$) Springer

Table 2 Association of low organizational justice with refraining from seeking medical care at 1-year follow-up among Japanese employees by gender: the results of multiple logistic regression analysis

	Model 1 ^a		Model 2 ^b		Model 3 ^c	
	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value
Men (<i>n</i> = 1994)						
Procedural justice	1.34 (1.17–1.53)	< 0.001	1.35 (1.18–1.55)	< 0.001	1.33 (1.16–1.52)	< 0.001
Interactional justice	1.16 (1.03–1.30)	0.013	1.15 (1.02–1.29)	0.018	1.15 (1.02–1.29)	0.019
Women (<i>n</i> = 701)						
Procedural justice	1.39 (1.11–1.76)	0.005	1.36 (1.08–1.72)	0.010	1.37 (1.08–1.74)	0.009
Interactional justice	1.21 (1.00–1.46)	0.054	1.23 (1.02–1.50)	0.035	1.23 (1.02–1.50)	0.035

In the analysis, total scores for procedural justice and interactional justice were reverse-coded so that higher scores indicated lower justice

OR odds ratio, CI confidence interval

^a Adjusted for age, past medical history, household size, work shift, and working hours per week

^b Additionally adjusted for education, equivalent annual household income, occupational position, and employment status

^c Additionally adjusted for smoking habits, drinking habits, and physical activity

of non-significant association of low interactional justice with RSMC after adjusting for demographic characteristics.

Our results showed that low procedural justice was significantly associated with RSMC for both genders, which supported our hypothesis. In Japan, it is common to take time off (i.e., paid holiday) to seek medical care on working days because paid sick leave is not stipulated by law. In principle, it is possible for employees to take time off without explaining their reasons, while workplaces also have a right to ask employees about the reasons for taking time off to maintain normal business operations. Regardless of reasons, workplaces should not treat employees who want to take time off unfairly. However, in work settings in which decision-making styles are unfair and obscure, employees may be afraid of being mistreated just because they take time off [46], which may make them to have difficulty seeking necessary medical care. Furthermore, a significant association of low interactional justice with RSMC was observed in the fully adjusted model for both genders, which also supported our hypothesis. When employees perceive the attitude of their supervisor as irreverent, they may face difficulties consulting with him/her about taking time off to seek medical care and re-arranging their work schedules. From the viewpoint of behavioral medicine, HSB may be a key mediator of the association of organizational justice with RSMC. As introduced earlier, organizational justice has been reported to be positively associated with employees' HSB [35]. In work settings in which organizational justice is lacking, employees are less likely to perceive that they have a voice in or are respected by their workplace and/or supervisor. Such perception of injustice may repress their decision making to take help-seeking action, which may lead to

RSMC. Future research on detailed mechanisms underlying the association of organizational justice with RSMC is needed.

When we compare the strength of the association of procedural justice with RSMC with that of interactional justice, procedural justice had a greater association with RSMC. This could be attributed to the fact that procedural justice is more closely related to company regulations that stipulate employees' time off and sickness absence. Our findings suggest that procedural justice rather than interactional justice is a stronger determinant of medical care seeking behavior among employees.

Although the strength of the association of procedural justice with RSMC was similar for male and female employees, the association of interactional justice with RSMC was slightly greater for female employees than for male employees. This gender difference may be explained by the fact that all managers were men in our sample (see Table 1); hence, our female participants always had to interact with a supervisor of the opposite gender. Pelled and Xin [47] reported that employees show higher levels of trust and relationship quality in same-gender supervisory relationships than in opposite-gender ones. Therefore, in our sample, female employees may be more hesitant to discuss taking time off to seek medical care with their male supervisor, especially with regard to female-specific diseases, when they perceive him as having low interactional justice. The imbalanced male-female ratio of managers observed in our sample is common in the male-dominated workplace culture in Japan. In fact, the latest national statistics on employment in Japan have reported that the average proportion of female managers is still only about

10%, and about 45% of companies do not have any female manager [48]; therefore, our findings may be true of many other Japanese companies. However, the association of interactional justice with RSMC in the context of other types of supervisory relationships, such as female supervisor–male employee or female supervisor–female employee relationships, should be examined in future research.

Furthermore, for female employees, the association of interactional justice with RSMC was not significant after adjusting for demographic characteristics (Model 1), while it became significant after additionally adjusting for socioeconomic characteristics (Model 2). According to Table 1, female employees who refrained from seeking medical care had relatively higher socioeconomic status. Highly educated and/or permanent employees are more likely to be expected to play an important role in their workplace and therefore to be respected by supervisor. At the same time, such pressure from the workplace may make it difficult for them to seek medical care when they get sick. Such a background may be reflected in our findings of the association of interactional justice with RSMC for female employees.

Possible limitations of the present study should be considered. First, some employees dropped out at follow-up due to sick leave. These employees may have perceived lower levels of organizational justice at baseline and refrained from seeking medical care until their disease became severe, which may have underestimated the true association. Furthermore, 430 out of 3125 employees were excluded from the analysis due to missing responses. It has been reported that the lack of organizational justice is associated with poor mental health, such as psychiatric disorders and depression [24], which present with poor concentration. Therefore, those who perceived lower levels of organizational justice may have been more likely to have missing responses due to poor concentration and to be excluded from the analysis. Such excluded employees may have been highly encouraged to seek medical care due to severe psychological symptoms. Our results may thus have overestimated the true association. Second, we measured RSMC by simply asking the participants to recall their experience over the past year; therefore, recall bias may have skewed our findings. Furthermore, we focused only on refraining from seeking “therapeutic” care when individuals get sick but not on “preventive” care, such as regular dental care. Further research on RSMC should also focus on preventive care. Third, RSMC at baseline may have affected our findings, as it may have been influenced by personality traits. Recent studies have reported that neuroticism is associated with an increased number of physician visits [49] as well as with lower levels of perceived justice [50]; therefore, our findings may be underestimated. Fourth, although we conducted the gender-stratified analysis, the distribution of socioeconomic characteristics was quite different between genders. Especially for employment status, almost all men were permanent employees, while the proportion of permanent employees among women was only

40% (see Table 1). It is possible that organizational justice is maintained only among permanent employees [51]. Therefore, such a difference in the distribution of employment status across genders might have affected our findings. Fifth, our data was obtained from one particular manufacturing company in Japan from 2011 to 2012; therefore, there is a limitation to generalizability and some changes in context may have occurred for the last 6 to 7 years. Our findings should thus be interpreted with caution. Sixth, organizational justice is defined as an employee’s “perception” of the fairness in the workplace. However, perceived stress measured by self-report has been reported to be only moderately related to actual stress exposure [52]. Therefore, our findings do not completely reflect the association of actual exposure to organizational (in)justice with RSMC. Finally, although a recent study on organizational justice utilized a multilevel approach in view of its contextual effect [53], the present study could not examine such an effect.

In conclusion, the present study provided evidence that the lack of procedural justice increases the tendency to refrain from seeking medical care among Japanese employees, independently of demographic and socioeconomic characteristics as well as of health-related behaviors. Our findings suggest that establishing fair and open decision-making styles in the workplace effectively promotes medical care-seeking behaviors among employees. Although interactional justice, characterized by the fair and respectful attitude of the supervisor, may also be an important factor associated with RSMC, future studies on this topic should account for gender differences in supervisory relationships.

Funding Information The present study was supported by Ministry of Education, Culture, Sports, Science and Technology (MEXT KAKENHI: Grant Number JP21119001), Japan Society for the Promotion of Science (JSPS KAKENHI: Grant Numbers JP26253042 and JP17K09172), and Ministry of Health, Labour and Welfare (Industrial Disease Clinical Research Grants: Grant Numbers 170401-02 and 180701-01).

Compliance with Ethical Standards

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

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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Association between working hours, work engagement, and work productivity in employees: A cross-sectional study of the Japanese Study of Health, Occupation, and Psychosocial Factors Relates Equity

Emi Okazaki¹  | Daisuke Nishi^{1,2}  | Ryoko Susukida^{1,3}  | Akiomi Inoue⁴  | Akihito Shimazu⁵  | Akizumi Tsutsumi⁴ 

¹Department of Mental Health Policy, National Institute of Mental Health, National Center of Neurology and Psychiatry, Kodaira, Japan

²Department of Mental Health, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

³Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

⁴Department of Public Health, Kitasato University School of Medicine, Sagamihara, Japan

⁵Center for Human and Social Sciences, College of Liberal Arts and Sciences, Kitasato University, Sagamihara, Japan

Correspondence

Daisuke Nishi, Department of Mental Health, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan.
Email: d-nishi@umin.ac.jp

Funding information

The present study was supported by a Grant-in-Aid for Scientific Research on Innovative Areas (Research in a Proposed Research Area) 2009-2013 (No. 4102-21119001) from the Ministry of Education, Culture, Sports, Science and Technology, Japan, a KAKENHI Grant Number 26253042 from the Japan Society for the Promotion of Science, and 2016-2018 (H27-Rodo-Anzen-Eisei-Sogo) from the Ministry of Health, Labour and Welfare, Japan.

Abstract

Objectives: The aims of the study were to investigate the association between working hours, work engagement, and work productivity, and to examine if work engagement moderates the influence of working hours on work productivity.

Methods: We used cross-sectional data from the Japanese occupational cohort survey, which involved 2093 employees in a manufacturing industry. Working hours were self-reported by the study participants. Work productivity was assessed with absolute presenteeism based on the scale of the validated Japanese version of World Health Organization Health and Work Performance Questionnaire (WHO-HPQ). Work engagement was assessed with the Nine-item Utrecht work Engagement Scale (UWES-9). Univariate and multivariable regression analyses were conducted to examine the association of working hours and work engagement with work productivity. We also carried out stratified multivariable regression analysis separately for those with high-work engagement and those with low-work engagement.

Results: Working >40 to 50 hours per week and >50 hours per week were significantly positively associated with work productivity in univariate analysis. However, the significant association no longer held after adjusting for work engagement. Work engagement was positively associated with work productivity even after controlling for potential confounders. Working hours were not significantly associated with work productivity among those with high-work engagement or among those with low-work engagement.

Conclusions: Working hours did not have any significant associations with work productivity when taking work engagement into account. Work engagement did not moderate the influence of working hours on work productivity, though it attenuated the relationship between working hours and work productivity.

KEYWORDS

work engagement, work productivity, working hours

1 | INTRODUCTION

Work productivity has been increasingly gaining attention as one of the key social measures in Japan especially because Japan is experiencing rapid aging of its society and shortage of labor force.¹ The improvement in work productivity has become one of the most important goals for sustainable economic growth. As a result, there is a growing interest on what determines work productivity and how to improve it.

Working hours have been investigated as one of the predictive factors of work productivity. There are some positive aspects of long working hours on work productivity. One study using British war plant data suggested that longer working hours increased work productivity though output decreased as working hours increase above a threshold.² Another research with the data of medical-surgical nurse has reported that the positive correlation between working hours and work engagement,³ positive mind of states for work, which leads to higher work productivity. On the other hand, some studies have suggested that excessively high-level of commitment in workplace can have a negative impact on work productivity. Previous study using the data of workers in manufacturing industry, for example, have suggested that long working hours do not always improve work productivity.⁴ Another study using longitudinal Japanese firm data has shown that working more than 50 hours per week degrade the state of mental health⁵ and has also found a dose-response relationship between working hours and incident cardiovascular disease.⁶ Additionally, a meta-analysis has reported the positive correlation between working hours and both physiological and psychological health symptoms.⁷ These health symptoms in workplace could lead to lower work productivity, absenteeism, and presenteeism.⁸ Given these findings, long working hours might reduce work productivity through deterioration of health condition. However, another meta-analysis has reported that the working 50 or more hours per week was not significantly associated with the onset of depressive disorder.⁹ Therefore, it is not entirely clear how working hours and work productivity are interrelated to each other.⁴ As described above, while the concept of work productivity has been used widely and the definition is full of variety, most review articles have been defined work productivity as “absenteeism” and “presenteeism.”^{10,11} Absenteeism refers to the missed time of work because of illness. “Presenteeism” refers to the reduction in work performance due to illness in employees while at work.¹²

In recent literature, work engagement has been attracting attention as a key factor in improving work productivity.¹³ Work engagement is defined as “positive, fulfilling, work-related state of mind that is characterized by vigor, dedication, and absorption.”¹⁴ Previous studies have shown that work engagement is predictive of work performance.^{15–18} Highly engaged employees tend to perform well^{15,16} and contribute to sales.¹⁷ Another research using data of workers in the Netherlands has shown that highly engaged workers reported fewer errors compared to workers with burnout.¹⁸

Given these findings on the relationship between working hours, work engagement, and work productivity, work engagement may moderate the influence of working hours on work productivity. Long working hours may increase work productivity among those who have higher-work engagement, while it may decrease work productivity among those who have lower-work engagement. The purpose of this study was to investigate the association of work productivity with working hours and work engagement. This study also examined if work engagement moderate the influence of working hours on work productivity.

2 | MATERIALS AND METHODS

2.1 | Participants

Our data are drawn from the four survey waves of an occupational cohort study on social and health in Japan (Japanese Study of Health, Occupation, and Psychosocial Factors Relates Equity; J-HOPE). The first wave was conducted between October 2010 and December 2011, and the following waves were conducted just about 1 year after the previous ones. Data were collected from annual health checkups, which were required for all Japanese employees. The recruitment differed across study sites; the health checkups were carried out in a fixed month every year. The study population consisted of employees working for 13 companies in 12 industries and a wide variety of occupations.

We used a cross-sectional data set from the third wave which included three main variables of this study, working hours, work engagement, and work productivity. We analyzed the data of 2093 participants (participation rates: 79.0%) after excluding the missing data ($N = 101$, 4.6% out of 2194 correspondents). These participants were workers in a manufacturing company since the questionnaire about work productivity was geared exclusively to this industry. Job categories were manager, professional (eg, researcher, computer engineer), technologist (eg, electrician, nutritionist), office job, service, productive technologist to need technic (eg, architect, mechanic), productive technologist to operate machine (eg, running of machine), productive technologist with using body (eg, packaging, cleaning) and the others.

2.2 | Measures

2.2.1 | Working hours

Working hours were measured by the following question: “How long do you work on average in a week (including overtime hours)?” The survey asked respondents to choose from five working hour brackets (<30, 31 to 40, 41 to 50, 51 to 60, and >60 hours per week). Working hours were classified into 3 groups (31 to 40

hours per week, >40 to 50 hours per week, and more than 51 hours per week) based on a previous study¹⁹ after omitting <30 hours per week bracket to exclude part-time job worker in the study.

2.2.2 | Health and work performance questionnaire

World Health Organization Health and Work Performance Questionnaire (WHO-HPQ) is a self-report questionnaire for measuring job performance.²⁰ We used the validated Japanese version of the WHO-HPQ short form.²¹ WHO-HPQ consists of two aspects: absolute presenteeism and relative presenteeism. Absolute presenteeism is actual performance; and relative presenteeism is a ratio of actual performance to the performance of most workers at the same job.²² In this study, we used absolute presenteeism as a measure of work productivity. Absolute presenteeism is measured by the following question: “On a scale from 0 to 10, where 0 is the worst job performance anyone could have at your job and 10 is the performance of a top worker, how would you rate your overall job performance on the days you worked during the past four weeks?”²² The absolute presenteeism score is calculated by multiplying the respondent's answer to the question by 10. The absolute presenteeism score range from 0 (total lack of performance during working hours) to 100 (no lack of performance during working hours). Low-presenteeism score indicates poor job performance.

2.2.3 | Nine-item Japanese version of the Utrecht Work Engagement Scale

Nine-item Utrecht work Engagement Scale (UWES-9) is a self-report questionnaire for measuring work engagement.²³ It consists of three subscales; vigor (eg, “At my work, I feel bursting with energy”), dedication (“I am enthusiastic about my job”), and absorption (“I feel happy when I am working intensely”). Each subscale consists of three items which were rated on a 7-point Likert scale ranging from 0 (“never”) to 6 (“always”). Overall score for the UWES-9 was the sum of these three subscales. The validity and reliability of the Japanese versions of UWES-9 are confirmed.²⁴

2.2.4 | Demographic characteristics

The following variables were included in the analyses as potential confounders: age (continuous variable), gender (men vs women), and educational attainment (high school or below, junior college, college, graduate school).

2.3 | Statistical analysis

We conducted statistical analysis with complete cases. Univariate and multivariable regression analyses were conducted to examine the association of working hours and

work engagement with work productivity. The first model estimated a crude coefficient with univariate regression analysis. Next, we estimated multiple regression model using work productivity as a dependent variable and working hours as an independent variable while controlling for demographic characteristics (age, gender, and educational level). The third model added work engagement to model 2.

Furthermore, in order to assess if work engagement moderate the influence of working hours on work productivity, we carried out stratified multivariable regression analysis separately for those with high-work engagement and those with low-work engagement (divided into high and low based on median). This analysis was adjusted for demographic characteristics (age, gender, and educational level). Data were analyzed using IBM SPSS Statistics version 23.0 for windows (IBM Japan, Tokyo, Japan).

3 | RESULTS

The characteristics of the study participants are presented in Table 1. Approximately half of the participants were working >40 to 50 hours per week. The proportion of those who were working 31 to 40 hours per week with low-work engagement was higher than those same working hours with high-work engagement. The proportion of those who were working more than 50 hours per week with high-work engagement was higher than those same working hours with low-work engagement.

Table 2 shows the results of univariate and multivariable regression analysis. Univariate regression analysis showed that working >40 to 50 hours per week and >50 hours per week were significantly positively associated with work productivity. Multivariable regression analysis showed that work engagement was positively associated with work productivity after adjusting for demographic characteristics, whereas working hours were not significantly associated with work productivity.

Table 3 presents the results of stratified multivariable regression analysis which assessed if work engagement moderates the influence of working hours on work productivity. Working hours were not significantly associated with work productivity among those with both high-work engagement and low-work engagement.

4 | DISCUSSION

We found that working hours did not have any significant associations with work productivity after adjusting for work engagement. This finding is inconsistent with the previous study using manufacturing company data, which found that work productivity was proportional to working hours.² It is likely that work engagement has direct association with work

TABLE 1 Characteristics of participants (N = 2093)

Variables	n	%	Mean (range)	Median (range)	SD
Age			43.6 (20–65)		9.8
Gender, men	1860	88.9			
Education					
Graduate school	331	15.8			
College	894	42.8			
Junior college	190	9.1			
High school or below	678	32.4			
Working hours					
Working 31 to 40 hours/week	422	20.2			
Working >40 to 50 hours/week	1103	52.7			
Working more than 50 hours/week	568	27.1			
Working hours and work engagement					
Working 31 to 40 hours/week with low-work engagement	267	12.8			
Working 31 to 40 hours/week with high-work engagement	155	7.4			
Working >40 to 50 hours/week with low-work engagement	510	24.3			
Working >40 to 50 hours/week with high-work engagement	593	28.3			
Working more than 50 hours/week with low-work engagement	227	10.9			
Working more than 50 hours/week with high-work engagement	341	16.3			
Work engagement			2.9 (0–6)		1.0
Low	1004	48.0			
High	1089	52.0			
Occupation					
Managers	525	25.1			
Not managers	1568	74.9			
Work productivity			57.4 (0–100)		18.4

productivity, and working hours may be a proxy of the level of work engagement.

The present study demonstrated that the influence of working hours on work productivity was not moderated by work engagement. That is, our hypothesis was not supported. This insignificant finding might be due to the type II error. Since the lower confidence limit was almost 0, the relationship might be significant if the sample size was much larger. In addition, our results suggested that work engagement attenuated the relationship between working hours and work productivity. Therefore, a further study would be required to verify the relationship between working hours, work engagement, and work productivity.

While the causal relationship between work engagement and work productivity was not examined in our study, our findings suggested that not the length of working hours but the level of work engagement might be an important factor in improving work productivity. Similar findings were demonstrated that not working hours but work condition, such as high job satisfaction, high job control, was important to improve psychological health in occupational field.^{19,25} On the other hand, some studies have suggested that excessively high engagement

would not be recommended. The previous studies have shown that exceedingly high levels of work engagement could increase the level of C-reactive protein²⁶ and the risk of onset of major depressive episode.²⁷ It has been also reported that excessively high engagement to the workplace is associated with work-to-home conflict.²⁸ Therefore, excessively high engagement may not be necessarily always beneficial for increasing work productivity. Moderately high engagement would improve work productivity; however, further examination is necessary to determine optimal level of work engagement.

There are some limitations to be considered in this study. First, since this study was a cross-sectional design, we could not investigate causal relationships between work productivity, working hours, and work engagement. Second, this study focused only on the samples of workers in manufacturing industry in Japan. Thus, the findings of this study may have limited generalizability to different industries. Third, response bias may have existed if non-respondents were systematically different from respondents. Particularly, the results of these findings would have been most biased if people with excessively long working hours

TABLE 2 Results of univariate and multivariate regression analysis: relationships between working hours and work engagement with work productivity

Variables	Univariate		Multivariate			
	Model 1 ^a		Model 2 ^b		Model 3 ^c	
	Unstandardized beta (95% CI)	Standardized beta	Unstandardized beta (95% CI)	Standardized beta	Unstandardized beta (95% CI)	Standardized beta
Working hours per week:						
31 to 40	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
> 40 to 50	2.63 (0.56 to 4.69) ^d	0.07 (0.02 to 0.13) ^d	2.78 (0.67 to 4.88) ^e	0.08 (0.02 to 0.13) ^e	0.49 (−1.41 to 2.39)	0.01 (−0.04 to 0.07)
> 50	4.60 (2.28 to 6.92) ^f	0.11 (0.06 to 0.17) ^f	4.38 (1.82 to 6.93) ^f	0.11 (0.04 to 0.17) ^f	2.05 (−0.24 to 4.35)	0.05 (−0.01 to 0.11)
Work engagement	8.80 (8.08 to 9.53) ^f	0.46 (0.42 to 0.50) ^f	-	-	8.62 (7.88 to 9.36) ^f	0.45 (0.41 to 0.49) ^f
Age	0.26 (0.18 to 0.34) ^f	0.14 (0.10 to 0.18) ^f	0.37 (0.28 to 0.45) ^f	0.19 (0.15 to 0.24) ^f	0.27 (0.19 to 0.35) ^f	0.14 (0.10 to 0.18) ^f
Gender	−1.85 (−4.36 to 0.67)	−0.03 (−0.07 to 0.01)	0.66 (−1.88 to 3.20)	0.01 (−0.03 to 0.06)	1.90 (−0.38 to 4.17)	0.03 (−0.01 to 0.07)
Educational level	1.12 (0.40 to 1.83) ^e	0.07 (0.02 to 0.11) ^e	1.76 (0.93 to 2.59) ^f	0.11 (0.06 to 0.15) ^f	0.28 (−0.47 to 1.03)	0.02 (−0.03 to 0.06)

Work engagement: Nine-item Utrecht work Engagement Scale.

Work productivity: World Health Organization Health and Work Performance Questionnaire.

^aUnadjusted.^bAdjusted for age, gender, educational level.^cAdded Work engagement to Model 1 and adjusted for age, gender, educational level.^d $p < 0.05$.^e $p < 0.01$.^f $p < 0.001$.

TABLE 3 Results of stratified multivariate regression analysis of work productivity: relationships between working hours and work productivity depends on the level of work engagement

Variables	High-work engagement ^a		Low-work engagement ^b	
	Unstandardized beta (95% CI) ^c	Standardized beta	Unstandardized beta (95% CI) ^c	Standardized beta
Working hours per week				
31 to 40	Ref.	Ref.	Ref.	Ref.
>40 to 50	0.60 (−2.28 to 3.48)	0.02 (−0.06 to 0.09)	1.97 (−0.82 to 4.76)	0.05 (−0.02 to 0.13)
>50	2.67 (−0.61 to 5.95)	0.08 (−0.02 to 0.14)	2.86 (−0.78 to 6.49)	0.07 (−0.02 to 0.16)

CI, confidence interval.

Work engagement: Nine-item Utrecht work Engagement Scale.

Work productivity: World Health Organization Health and Work Performance Questionnaire.

^aAbove the median of UWES-9.^bBelow the median of UWES-9.^cAdjusted for age, gender, and educational level.

have been systematically the non-respondents. Fourth, our results may be more generalizable for men since the number of female respondents was relatively small. Future research should explore if the findings of this study can be replicated with the data with more female workers. Fifth, since we examined working hours using self-reported instrument, we could not calculate working hours objectively. Hence, future study should consider how to collect them in detail. Sixth, collecting working hours data as a continuous variable which might be more clarify whether work engagement is moderator in statistical analysis in the future. Seventh, we could not control the type of employment, regular employees or part-time job workers, which might be confounded across the key variables since we did not collect the data. Finally, absolute presenteeism was the only measure available as a proxy of work productivity.²⁰ Future studies should consider another measure of work productivity, though absolute presenteeism can evaluate respondent's work performance from worst to superior.

In conclusion, working hours did not have any significant associations with work productivity when taking work engagement into account. Work engagement did not moderate the influence of working hour on work productivity, though it attenuated the relationship between working hours and work productivity. Future studies should investigate the mechanisms through which working hours and work engagement inter-relate to impact work productivity.

ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

CONFLICT OF INTEREST

The authors declare that they have no competing interests regarding this paper.

DISCLOSURES

Approval of the research protocol: The Research Ethics Committee of the Graduate School of Medicine and Faculty of Medicine, The University of Tokyo (No. 2772), Kitasato University Medical Ethics Organization (No. B-12-103), and Ethics Committee of Medical Research, University of Occupational and Environmental Health, Japan (No. 10-004), reviewed and approved the aims and procedures of this study. *Informed consent:* Informed consent was obtained from all individual participants included in the study. *Registry and the registration no. of the study/trial:* N/A. *Animal studies:* N/A.

ORCID

Emi Okazaki  <https://orcid.org/0000-0002-1720-4048>

Daisuke Nishi  <https://orcid.org/0000-0001-9349-3294>

Ryoko Susukida  <https://orcid.org/0000-0003-0444-5368>

Akiomi Inoue  <https://orcid.org/0000-0002-4079-0719>

Akihito Shimazu  <https://orcid.org/0000-0002-7172-0043>

Akizumi Tsutsumi  <https://orcid.org/0000-0003-0966-4869>

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How to cite this article: Okazaki E, Nishi D, Susukida R, Inoue A, Shimazu A, Tsutsumi A. Association between working hours, work engagement, and work productivity in employees: A cross-sectional study of the Japanese Study of Health, Occupation, and Psychosocial Factors Relates Equity. *J Occup Health*. 2019;61:182-188. <https://doi.org/10.1002/1348-9585.12023>

EDITORIAL

Preventing overwork-related deaths and disorders—needs of continuous and multi-faceted efforts

This issue of *J Occup Health* (Vol. 61, No. 3) published three relevant reviews on overwork-related disorders in Asian countries, where this health problem has drawn a large amount of attention. In these three countries (Japan, South Korea, and Taiwan), workers tend to spend long hours at work. Furthermore, these are the only countries in which official worker's compensation guidelines recognize long-term overtime hours as a work-related factor for cardiovascular diseases (CVD). The labor administration in these countries have launched several countermeasures against overwork-related disorders. In Japan, the 2014 legislation regarding the prevention of overwork-related deaths and disorders including suicide (*karoshi* and *karojisatsu*) has accelerated research in this field. Japanese studies have identified several characteristics of *karoshi* and *karojisatsu*, and implemented preventive actions based on the findings.¹ Following the Japanese legislation, South Korea developed several prevention and compensation policies in response to long working hours. These policies appear to function by improving working conditions in South Korea. However, researchers suggest that a major issue remains in small- and medium-sized companies, which is also an issue in Japan.² Chang and Lin reviewed the background, revision, and impact of policy changes regarding overwork-related CVD in Taiwan and found there were difficulties in implementing effective measures nationwide.³

Karoshi was first recognized as a social problem in Japan as early as the second half of the 1980s, however, scientific evidence regarding the prospective relationship between long working hours and CVD has only accumulate recently. Meta-analyses based on pooled data from European cohort studies, which included unpublished research, provided the most robust evidence related to the research question.⁴ This analysis showed elevated risks for CVD among those who worked long hours compared with those working standard hours. The association with long working hours was stronger when stroke was the outcome, than when coronary heart diseases were outcomes: clear dose-response patterns were observed between long working hours and stroke onset.⁴ The prospective association

between long working hours and onset of depression was also examined. One study that included 10 published cohort studies and 18 unpublished studies showed a statistically significant (albeit weak) risk elevation.⁵ The analyses found weak or non-significant risk elevation among studies from European and US/Australian cohorts, but did find a moderate risk elevation among studies from Asia, which included countries with long working hours, such as Japan and South Korea. These research questions are now about to be replicated.

The mechanisms through which long working hours lead to onset of CVD are often explained by the exposure to adverse workplace hazards induced by long working hours and the reduced time resulting from long working hours. The former mechanism includes psychosocial stress, physical (noise), and the chemical (dust and toxic chemicals) environment. The latter includes lack of sleep and physical activity.⁶ These upstream factors are thought to induce behavioral mechanisms (eg, over eating and drinking alcohol), followed by then clinical stage before manifesting CVD (eg, high blood pressure, dyslipidemia, diabetes, inflammation, atrial fibrillation, and hypercoagulability).

There is room for interventions focused on working hours. Articles in this issue of *J Occup Health* suggest several countermeasures along with legislation to regulate overtime by setting a limit.¹⁻³ One suggested measure is introducing a minimum daily rest period to facilitate recovery from occupational fatigue and ensure workers get sufficient sleep. However, *karoshi* and *karojisatsu* cannot be prevented by decreasing working hours alone. Reducing working hours may result in high intensity work or stopping the supply of necessary services, unless there are also changes in the quantity of work or ways of handling tasks. Working hours are also closely related to occupational stress. Interviews and consequent measures by occupational physicians are being implemented for workers who work beyond the overtime limits, and workers who are identified as having high stress and request to meet with physician under Japan's Stress Check Program.¹ Avoiding trauma—occupational injuries—would also help

to prevent workers from psychological damages. Creating a safe psychological environment is therefore an important strategy. In today's society, boundaries between working and private lives are ambiguous, and careful attention should be paid to immersion of exposure in the workplace into private life. In addition, some kinds of consumption behaviors are related to working hours in contemporary businesses. For example, people enjoy the convenience of overnight delivery, but this consumption behavior places a burden on the distribution system. Continuous and multifaceted efforts, including increased public understanding, are necessary to prevent overwork-related deaths and disorders.

ACKNOWLEDGMENT

This work was partly supported by Work-related Diseases Clinical Research Grant 2018 (180701) from the Ministry of Health, Labour and Welfare, Japan.

DISCLOSURE

Approval of the research protocol: N/A. Informed consent: N/A. Registry and the registration No. of the study/trial: N/A. Animal studies: N/A. Conflict of interest: N/A.

Akizumi Tsutsumi 

Department of Public Health, Kitasato University School of Medicine, Sagamihara, Japan

Correspondence

Akizumi Tsutsumi, Department of Public Health, Kitasato University School of Medicine, 1-15-1 Kitasato, Minami, Sagamihara, Kanagawa, Japan (zip code: 252-0374).
Email: akizumi@kitasato-u.ac.jp

ORCID

Akizumi Tsutsumi  <https://orcid.org/0000-0003-0966-4869>

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Review

Proposed guidelines for primary prevention for mental health at work: an update

Akizumi Tsutsumi¹  | Akihito Shimazu² | Toru Yoshikawa³

¹Department of Public Health, Kitasato University School of Medicine

²Faculty of Policy Management, Keio University

³National Institute of Occupational Safety and Health, Japan (JNIOSH)

Abstract

Objectives: To provide a range of standard evidence-informed recommendations for the primary prevention of mental health problems at work. **Methods:** Occupational health experts and practitioners evaluated systematic reviews of primary-prevention measures for occupational mental health. A series of consensus meetings were held with the intent of developing primary-prevention guidelines for mental health at work. **Results:** Three preventive strategies were developed: self-care training, supervisor training, and improving the workplace environment. The guidelines for self-care training consist of four steps that coincide with the process of formulating and implementing measures to help individuals cope with stress (self-care) in the workplace: planning and preparing, deciding what self-care entails, selecting the forms of self-care, and making subsequent efforts. Six recommendations and four tips are provided for these four steps. The guidelines for supervisor mental health training have four categories: selection of training participants, content, delivery format, and frequency. Based on recent findings, we provided recommendations for the content that should be included in training. Training has been shown to improve supervisors' knowledge, attitude, confidence, and behaviors in supporting employees with mental health problems. For improving the psychosocial work environment, 12 items were compiled, including eight recommended items and four tips in four categories: planning and organization development, implementation regarding the basic rules of procedures, proposals for effective improvement measures, and continued implementation. **Conclusions:** Based on the best evidence currently available, we propose guidelines for primary prevention for mental health at work.

Keywords: improving workplace environment, management, organizational approach, participatory approach, self-care training, stress management

(Received April 24, 2019; Accepted July 3, 2019; Published online in J-STAGE October 4, 2019)

Introduction

In a previous study, we developed guidelines for occupational practitioners regarding the primary prevention of mental health problems at work, providing three main prevention strategies: self-care training, supervisor training, and improving the workplace environment⁽¹⁾. These guidelines were based on a systematic review of studies that investigated the psychological stress responses of

employees as study outcomes. In addition, expert opinions were obtained and incorporated into the suggested guidelines. Since we published our original guidelines, several studies have provided new evidence regarding the prevention of mental health problems in the workplace. Thus, we sought to update our guidelines based on this new research.

To improve workplace mental health, international organizations, including the World Health Organization, International Labour Organization, and European Union, have adopted common strategies to disseminate useful tools, such as guidelines and manuals based on evidence and best practice^(2–4). Although the major pro-

Correspondence

Akizumi Tsutsumi: Department of Public Health, Kitasato University School of Medicine, Kanagawa, Japan
E-mail: akizumi@kitasato-u.ac.jp



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grams adopted by the organizations mentioned above are focused on risk management, similar strategies are appropriate for the development of practical measures for workplaces to improve the psychosocial work environment. The guidelines presented here were developed based on the best evidence currently available and are intended for application in the workplace. Because relevant evidence is limited in the field of occupational health, we also took consensus of experts into account.

Characteristics of guidelines

Interventions designed to reduce occupational stress can be categorized according to their focus, content, method, and duration⁵. Regarding their focus, interventions can be divided into two main categories: 1) interventions that aim to increase individual psychological resources and responses, such as coping (individual-focused interventions), or 2) interventions that aim to improve stressful work environments (organization-focused interventions)^{6,7}. The first category of intervention is usually referred to as stress management interventions or self-care training, while the second category refers to interventions like organizational development and job redesign (improving workplace environment)^{8,9} and supervisor training¹⁰. Accordingly, three preventive strategies were developed in the proposed guidelines: self-care training, supervisor training, and improving the workplace environment¹.

Suggestions in the currently proposed guidelines are classified into recommendations and tips. For each suggestion, proposed measures are presented, along with their rationale and key aspects of their implementation. The distinction in the level of a suggestion was made according to the level of evidence; items are recommended if the measures were found to be effective or feasible in the workplace in empirical studies, whereas tips are composed of items that experts' consensus suggested to be included. Occupational health practitioners can easily prioritize measures in accordance with feasibility in the workplace and adapt the measures to their workplace.

Methods

1. Literature search for the first guidelines

For the development of the first guidelines for self-care training^{1,11}, a working group including one of the authors (AS) selected studies that had been published from 1979 to 2009 from the databases of PsychARTICLE, PsychINFO, PubMed, MEDLINE, the Web of Science, and the Ichushi-Web (a Japanese medical science literature database). The following keywords were used: (worksite OR work OR workplace) AND (stress OR distress OR depression) AND (management OR reduction OR prevention) AND (training OR program OR interven-

tion) AND (clinical trial OR randomized controlled trial OR randomized controlled trial). Eligibility criteria were as follows: 1) primary prevention; 2) individual-focused intervention; 3) psychological distress, depression, or anxiety as primary outcomes; 4) conducted in the workplace; 5) randomized controlled trial or controlled trial; and 6) original article. Following these criteria, 60 studies were included in the qualitative review.

For the development of the first guidelines for supervisor training^{1,10}, one of the authors (AT) selected studies from the databases of PubMed, the Cochrane Library, MEDLINE, the Web of Science, and the Ichushi-Web, using the following keywords: (education OR training) AND (supervisor OR manager) AND (job stress OR mental health). Seven controlled studies that included outcomes of occupational stressors and stress reactions of workers were selected up to 2010.

To develop the first guidelines for improving workplace environment^{1,12}, a working group consisting of multidisciplinary members, including one of the authors (TY), referred to two major systematic reviews on job-stress reduction by means of organizational interventions^{13,14} and two intervention studies conducted in Japan after the publication of these two review articles^{15,16}. A total of 33 articles were used as basic sources for developing the guidelines. In addition, other relevant articles were also referred to for re-examining the practical use of guidelines.

2. Consensus meetings for the first guidelines

To confirm if the guideline content is applicable for practice, we held a series of consensus meeting. The meeting members included stakeholders who were representatives for management and labor (Japan Federation of Economic Organizations and Japanese Trade Union Confederation) and occupational health practitioners, a psychologist, researchers, and a lawyer with expertise in the occupational health field (listed in the Acknowledgment). The primary investigators on each preventive strategy (AS for self-care training, AT for supervisor training and TY for improving workplace environment) presented the draft of guidelines and asked the members of how to improve the draft. Based on the recommendations of these stakeholders, the draft was revised. The process was repeated twice, and then the first guidelines were completed.

3. Revision of the guidelines

In the current revised process of guidelines for self-care training, 44 newly identified studies, which had been published from 2009 to 2015, were selected, following the same procedures as those in the first guidelines. The added evidence was similar to that in the first review, but the background information was expanded.

In the current revised process of guidelines for supervi-

sor training, five newly identified studies were selected up to April 2019. While the added evidence was limited, the expression was aligned with the other guidelines and the background information was expanded. As the guideline contents were not changed substantially for self-care training and supervisor training, consensus meetings were not held for the revised processes of those sections.

As for the guidelines for improving working environment, the working group referred to the latest review¹⁷⁾. Scrutinizing the latest information confirmed that the use of the first guidelines was expected to standardize workplace environment measures as means of primary prevention for occupational mental health and to promote improvement actions, particularly at small- and medium-sized workplaces with the support of occupational health professionals. However, as the updating process clarified the importance of overcoming the practical obstacles against the implementation to facilitate the process of improving the workplace environment, 'how to implement the process', including usage of tools, has been emphasized in the current guidelines.

Results

1. Guidelines for self-care training

1.1 State of the art on self-care training

Several previous review articles^{5,18-21)} have reported that self-care training in the workplace can be effective for reducing employees' stress-related complaints. Accumulated evidence has led to the development of guidelines for self-care training in the workplace. A total of 10 suggestions (six recommendations and four tips) are presented in the guidelines¹¹⁾ (Table 1). These suggestions are arranged following the steps involved in formulating and implementing measures to help individuals cope with stress: planning and preparing to implement self-care, determining what self-care entails, selecting the forms of self-care, and carrying out subsequent efforts. Those in control of developing measures to help workers cope with stress can immediately see which actions they should take.

1.2 Content of guidelines

Category 1: Planning and preparation

Self-care training can be effective through the use of newly acquired knowledge and skills. The inclusion of at least two training sessions and one follow-up session is recommended to reduce psychological distress among participants^{22,23)} (Recommendation 1).

Self-care training may be provided by specialists in occupational mental health or occupational health professionals^{23,24)} (Recommendation 2). When a specialist outside the workplace provides care, the specialist should be provided with information regarding workplace characteristics and the needs of potential participants. If training is conducted by an occupational health staff member with

little experience in implementing self-care, they should be trained in the necessary knowledge and skills in advance.

Many workplaces use questionnaires to assess the stress levels of their workers. Simply informing workers of their results on these assessments is not appropriate to reduce their psychological distress. Self-care training in combination with feedback about a profile of stress assessment should be provided^{23,25)} (Recommendation 3).

When self-care training is implemented in the workplace, various constraints on time, expense, and personnel can arise. In such instances, groups most in need of the training should be identified, and the training should begin with those groups²²⁾ (Tip 1). In selecting a certain group, a high level of interest in self-care, conditions in the workplace (whether conditions facilitate the use of what has been learned), and the level of stress should be considered.

Based on the conditions in the workplace, the burden placed on participants, and the associated fatigue, the duration of a training session should be kept within 2 hours²⁶⁾ (Tip 2). If a single session does not allow adequate time for training, self-care training can be implemented over multiple sessions.

Category 2: Deciding what self-care entails

Review articles on individual-focused stress management in the workplace^{5,18-21)} have indicated that the most effective stress management programs are those involving cognitive-behavioral training or cognitive-behavioral training in combination with relaxation techniques. Therefore, applying cognitive-behavioral training or cognitive-behavioral training in combination with relaxation techniques is recommended^{19,27)} (Recommendation 4). Since a range of cognitive-behavioral training and relaxation techniques exist, appropriate techniques should be chosen in accordance with the needs and circumstances of potential participants.

Category 3: Forms of self-care

An appropriate format should be chosen, taking into account the circumstances of participants, the trainer, and relative advantages and disadvantages of each program format²²⁾ (Recommendation 5). Programs can be conducted as group training, individual training, or through e-learning. There are advantages and disadvantages of each format. For instance, group training allows a large number of participants to be trained at one time, but participation tends to be more passive, and it may be challenging to meet the diverse needs of participants. Individual training involves one-on-one interaction between trainer and participant. This method allows a flexible approach to meeting the participant's needs, but is more expensive (including labor costs, as well as the allocation of a location and time). Web-based learning (e-learning) is free from the constraints of time and place that hamper individual training and group training, and allows participants to learn at their own pace. However, participants in

web-based learning programs have few opportunities to interact with other participants, and participants can only learn in places equipped with a computer.

The effectiveness of self-care training can be improved through the repeated use of learned knowledge and acquired skills in everyday life. Thus, creating conditions in the workplace that encourage workers to apply learned skills is crucial²⁸⁾ (Tip 3). In a workplace where workers are given appropriate discretion, opportunities to apply newly acquired knowledge and skills will occur, enhancing the likelihood that training will be effective. Thus, self-care training should be accompanied by measures to increase worker discretion in the workplace.

Category 4: Subsequent efforts

Self-care training can lead to reduced psychological distress by teaching both knowledge and skills and by encouraging the use of newly acquired knowledge and skills in everyday life. Following training, a follow-up session should be conducted to enable participants to reflect on what they have learned, to encourage them to remember the knowledge gained and the skills acquired, and to encourage them to apply their newly acquired knowledge and skills in everyday life²⁹⁾ (Recommendation 6). This will help participants improve the effectiveness of the training.

Even if participants understand the content of training, improvement of mental health cannot be achieved without applying what has been learned to everyday life. Thus, it is recommended to encourage workers to apply learned knowledge and acquired skills to their own problems and circumstances^{22,30)} (Tip 4) by, for instance, assigning homework to the participants.

2. Guidelines for supervisor training

2.1 State of the art on workplace mental health training for supervisors

A recent systematic review and meta-analysis revealed that supervisor mental health training improved supervisor's knowledge in terms of mental health issues and their roles and responsibilities when supporting employees with mental health problems; their attitudes towards mental health issues, such as non-stigmatizing attitudes; and their behavior in supporting employees experiencing mental health problems. However, due to the relatively small number of studies, no effect of supervisor mental health training on employees' psychological distress has been confirmed³¹⁾. Thus, as in the first guideline set¹⁾, we updated our guidelines based on the best available individual evidence showing positive effects of supervisor training on employees' health outcomes.

New evidence has accumulated since we conducted our first systematic review¹⁰⁾. A cluster randomized controlled trial revealed that a 4-hour manager mental health training program led to a significant reduction in work-related sickness absence³²⁾. A 3-hour training program designed to increase leaders' mental health literacy, with primary areas including early recognition, early action (referral for cases) and assessment, resulted in a reduction in the duration of short-term disability claims of employees in a cluster randomized controlled trial³³⁾. Another controlled trial using a wait-list design with random assignment indicated that a short (3-hour) training session for leaders increased their subordinate employees' willingness to seek out resources³⁴⁾.

2.2 Content of guidelines

Category 1: Selection of training participants

As a general rule, training should be provided to all supervisors (Recommendation 1). Evidence from one study suggested that a higher proportion of supervisors

Table 1. Guidelines for self-care training for occupational mental health*

Category 1: Planning and preparation
R-1 Include at least two training sessions and one follow-up session
R-2 Trainers may be specialists in occupational mental health or occupational health professionals
R-3 Feedback a worker profile of stress assessment in combination with stress management training
T-1 Start with groups that are most in need of that training, on the limited condition
T-2 Wrap up a session within 2 hours
Category 2: Deciding what self-care entails
R-4 Apply cognitive-behavioral techniques, combined with relaxation techniques if appropriate
Category 3: Forms of self-care
R-5 Select the training format (group training or individual training) in accordance with characteristics of and conditions in the workplace and characteristics of and circumstances faced by participants
T-3 Create conditions in the workplace to encourage participants to apply what they have learned
Category 4: Subsequent efforts
R-6 Conduct a follow-up session where workers can reflect on the program
T-4 Encourage workers to apply learned knowledge and acquired skills into daily life

* R-# stands for six recommended items, T-# stands for tip items in four categories.

participating in training sessions led to better outcomes³⁵. Identifying populations with an increased need for training is also recommended, based on the finding that cases that showed positive effects of supervisor training tended to have a background requiring mental health management³⁶. Identification of such a group can be useful for prioritizing target supervisors and planning training focused of the needs and circumstances of the target workplace (Recommendation 2).

An experts' consensus suggested the importance of stratifying the target management position according to needs in training content (Tip 1). For staff who supervise others, the main training content may include a process for dealing with employees and cooperating with occupational health staff members; for business managers, training to ensure the effectiveness of establishing a system for mental health support was thought to be important¹.

Category 2: Content of training

Our previous review focused on studies showing the effectiveness of learning content that was delivered as a package¹⁰ (Recommendation 3). Recent studies have reported the effectiveness of individual content, such as a combination of mental health knowledge and communication training³², early recognition and referral for employees (mental health awareness training)³³, and improving employee resource utilization³⁴. Training in active listening could be effective, although the detailed effects are unknown because the technique is typically incorporated in a package of several intervention components, and the effect of the individual technique has not been tested³².

A mixed-method study identified specific attitudes and behaviors of supervisors that may impact workers with mental health problems returning to work³⁷. These include knowledge about symptoms of mental health problems and administrative procedures to return to work, appropriate responses and an empathic attitude, adjustment and reallocation of job responsibilities, consideration of other workers, and cooperation with occupational health staff and external organizations. Although this content belongs to tertiary prevention, we decided to include it in the delivery package together with other contents related to secondary prevention ('early recognition and referral for employees') because providing supervisors with appropriate information and skills could be an effective means of enhancing mental health within an organization³⁵.

Category 3: Delivery format of training

Beneficial effects of training appeared to be achieved through improved knowledge and the consequent favorable behavioral changes of supervisors^{35,38}. It is important to enhance not only knowledge but also self-efficacy among supervisors. For the latter purpose, incorporating participatory training, such as role playing and interactive case studies, is recommended³³. Such trainings

can be applicable for developing listening and advising techniques (active listening and referral for employees) (Recommendations 4 and 5).

It is necessary to seek efficient ways to promote better understandings of managers. Online training is an option. It allows participants to learn at their own pace, without time and place restrictions, which are often problematic in face-to-face training. A guided e-learning program for health managers based on Health and Safety Executive Management Standards was found to be acceptable³⁹.

Expert opinions suggested that incorporating data or cases that are specific to a particular workplace into the training program may help to engage participants (Tips 2 and 3).

Category 4: Frequency

Evidence is still scarce regarding the long-term effects of training beyond 1 year. Randomized controlled studies have suggested that beneficial training effects on supervisors' knowledge last no longer than 6 months following training^{32,40}. The experts in the current study also pointed out that attempting to convey an excessive amount of information may reduce the educational effects of training. Taken together, this evidence suggests that training needs to be repeated to maintain the effects, and providing training at least once each year is recommended (Recommendations 6 and 7).

3. Guidelines for improving workplace environment

3.1 State of the art on improving workplace environment

In recent years, increasing attention has focused on the effectiveness of the organizational approach addressing the improvement of the workplace environment using primary prevention measures^{13,14,17}. This view is also adopted in psychosocial factors management in the workplace, as represented by the European Directive 89/391 – OSH³. Improving working conditions through workplace-level interventions is expected to reduce the negative impacts on health of workers. The effectiveness of preventing job stress through improving the workplace environment has been reported in several recent systematic reviews^{13,14,17}, which included a number of studies conducted in Japan^{15,16,41,42}. However, in these reviews, a lack of consistency of the intervention effects has been noted^{17,43}, and it is important to discuss methodological and practical aspects of such interventions^{44–46}. Difficulties in engaging employers⁴⁵, the role of employees in intervention activities, interference of the intervention by organizational changes and personnel turnover⁴⁴, and an inability to adjust to a variety of confounding factors^{46,47} have been identified as major factors leading to such inconsistency.

To successfully conduct workplace interventions for preventing stress at work, how the employees evaluate the intervention itself, how the employees are involved in the planning and implementation of multifaceted preven-

Table 2. Guidelines for supervisor training for occupational mental health*

Category 1: Selection of training participants
R-1 Provide mental health training to all personnel in managerial positions
R-2 Identify population with an increased need for training and prioritize their training
T-1 Stratify the target management position according to needs in training content
Category 2: Contents
R-3 Deliver the following contents
· Workplace mental health policy
· Significance of positive mental health
· Correct knowledge of mental health problems (eliminating prejudices, stigma)
· Roles of supervisors (improvements to the workplace environment / individual consultations)
· Early awareness of developing cases and how to deal with them
· Support for returning to work (administrative procedure of returning to work, arrangement of work condition)
· Self-care recommendations, including stress awareness, relaxation, and coping methods
· Information on medical institutions or liaison offices both within and outside the workplace and increasing employees' willingness to use the resources
· How to contact and consult with medical professionals or cooperate with other insiders
· Importance of protecting workers' privacy
· Major occupational stress models
· Active listening and communication training
Category 3: Delivery formats
R-4 Incorporate participatory training to develop listening and advising techniques
R-5 Present interactive case studies
T-2 Present issues and data of the workplace
T-3 Present case examples to increase motivation in training participation
Category 4: Frequency
R-6 Provide training once a year
R-7 Provide training periodically (not only once)
T-4 Plan stepwise training

* R-# stands for seven recommended items, T-# stands for four tip items.

tive measures, and how the line managers and supervisors are involved in the intervention processes are important factors to consider^{45,48)}. Meanwhile, work environment improvement tools for job-stress prevention, such as mental health action checklists, have been developed⁴⁹⁾, and a series of studies has been conducted to assess the usefulness of these tools^{2,15,16,50)}. It is important to clarify which aspects of ongoing intervention procedures and management processes are useful for overcoming the difficulties encountered in workplace-level interventions to improve the work environment.

3.2 Content of guidelines

Category 1: Planning and organizational development

Workplace improvements in which workers actively participate are generally effective in improving mental health^{14-16,48)}. The improvement process commonly follows steps involving policy setting, planning, implementation, and evaluation^{2,13,16,51)}. The usual efforts, such as redesigning work, reducing workload, and improving communication, may also be involved in meeting the needs of a system-based approach¹⁴⁾. In clarifying policy, these steps require the creation of a concrete system and role-sharing to secure an internal system for improving the work environment¹⁶⁾. In the decision-making pro-

cess for improving the work environment, interventions involving workers are essential for improving psychosocial and health indicators^{13-16,41)}. Organizing a “work committee” designed to reduce work stress under a stress reduction program, comprising supervisors, workers, and occupational health staff; setting up a work team; and improving the work procedures and command systems in varied work stages are also reported to improve depression scores and rates of sick leave^{41,52)} (Recommendation 1).

Organizations conducting work environment improvement generally focus on taking a problem-solving approach^{2-4,16,48)}. A step-by-step problem-solving process through participatory workplace improvement activities is typically realized by a group of workers engaged in the same manufacturing area, or in a work team with improved job performance¹⁶⁾ (Recommendation 2).

As one of the important steps of primary prevention measures through improvement of the workplace environment, support and policy statements of top-level management, such as the president or plant manager, have been identified^{16,51)}. Discussing the needs for work environment improvement involving a management department or a human resource department is recommended when

beginning workplace environment improvement^{15,16,53}. Effective workplace environment improvement is widely recognized as a process that operates in stages to gain the understanding of the organization and the workplace^{2,16} (Tip 1).

Category 2: Implementation regarding the basic rules of procedures

Learning from good workplace practices in the same industry is important for stress prevention through the improvement of the work environment^{2,13,14,16}. To share concrete examples of workplace environment improvement, it is useful to collect good practices that have already been implemented and utilize them in improvement activities¹⁶. Similarly, providing good examples of workplace environment improvement is proven to be useful in management supervisor training¹⁵ (Recommendation 3).

Previous studies have provided evidence for the benefits of involving worker-participation in improving the workplace environment on the health of individuals^{13-16,52,54-57}. Work environment improvement activities undertaken by committees organized by workers and mental health experts in the workplace have proven useful for improving psychosocial indicators, such as the sense of control and subjective performance, mental and physical health status, work stress reduction, absence rate decrease, and other health indicators^{52,54,55,58-60}. Creating several small groups in the workplace, meeting once every 2 weeks to identify psychosocial stressors, and proposing solutions to employees and managers have proven effective in dealing with many stress-related factors⁵⁸ (Recommendation 4).

Improvement activities that take various factors into consideration, such as work environment and working conditions related to physical and mental burden, are reported to improve health-related indices^{16,55,56,58}. Reconstruction of work tasks, such as multi-functionalization at the task level, reorganization of work teams, and changes in production lines, may worsen the health index by increasing demands and decreasing control¹⁴ (Recommendation 5).

Category 3: Effective improvement measures

The department in charge of work environment improvement sets the schedule for training and meetings in consideration of the work situation^{16,44}. Participatory improvements that are conducted when the management situation has deteriorated, such as restructuring of the workplace for improved management, is unlikely to improve health indices^{56,59,61}. There may be limitations on participatory efforts when external factors, such as business conditions, are deteriorating¹⁴. Therefore, it is useful to promote workplace environment improvement activities by utilizing worker-driven committees voluntarily planned or set by mental health experts at the workplace^{2,15,16,41,51,52,60,62}. Interventions that consider the

situation in the workplace and are tailored to the individual workplace situation, such as personnel, scheduling of work, action-oriented training, and reviewing measures for improvement by committees authorized by management, are reported to be effective¹⁶ (Recommendation 6).

The use of good practices, action checklists, and participatory group discussions as participation-type promotion tools can facilitate positive suggestions from the workplace, which can be implemented and linked to continuous improvement^{2,15,16}. In workplace discussions, such tools are used to support participatory efforts that draw on-site awareness and ideas, identify key risks in each workplace, and specifically propose effective and low-cost improvement measures^{15,16}.

An approach suited for the workplace should be considered, making use of existing workplace structures that can lead to continuous improvement in the workplace (e.g., occupational safety and health committees and quality control circle activities). A workplace system that can be used to improve the workplace environment should involve a health and safety committee^{16,41}, staff members of the health management department^{53,60}, a work committee composed of supervisors, staff members in human resource management, and medical expertise for job-stress reduction⁴¹, labor-management utilization of a liaison coordinator⁵⁷, team formation with budget authority⁵³, and launching programs tailored to workplace safety and health training and management training⁵⁴ (Recommendation 7).

Improving the program environment gradually in accordance with the acceptance and preparation of the workplace can aid program operation^{15,16}. Employee representatives can act as liaisons between the manager and employees, and team communication, job scheduling, and employee conflict may improve with improvements in related health indicators⁵⁷. An employee-led committee chaired by a mental health specialist can help improve mental health through improvement activities combining individual-level stress management and physical burden reduction⁵⁶.

Following discussions and organizational reforms via an advisory committee consisting of employees, managers, and researchers, improvements in psychosocial scales and a drop in the rate of absenteeism were observed⁵⁴. As a result of creating an action plan designed to reduce sources of stress to increase workers' autonomy and support participatory activities in small groups, the degree of discretion and physical health both improved. Thus, taking an approach tailored to a designated workplace appears to be useful (Tips 2 and 3).

Category 4: Continuous implementation

Problem-solving participatory workplace improvement activities following the stages of activities of workers engaged in the manufacturing industry line can improve the mental health of workers and job performance¹⁶. As

Table 3. Guidelines for improving workplace environment for occupational mental health*

Category 1: Planning and organizational development
R-1 Making an agreement on the purpose, policy, and promotional organization for improving workplace environment at the workplace
R-2 Applying problem-solving approach instead of problem-finding approaches
T-1 Promoting proactive involvement of management represented by the persons in charge of organizing the implementing steps of workplace environment improvement
Category 2: Implementation regarding the basic rules of procedures
R-3 Use of good practices for planning practical and feasible improvements
R-4 Planning participatory steps to make it possible for workers to participate in the discussion and implementation of improvement measures
R-5 Looking broadly into the work environment and working conditions related to both physical and mental burdens for considering improvement measures
Category 3: Effective improvement measures
R-6 Promoting locally adjusted proposals, such as practical improvement measures in consideration of the situation, timing, and resources of the workplace
R-7 Use of effective tools for workplace improvement, especially tools that can bring out worksite awareness and ideas and make suggestions that are easy to put into action
T-2 Use of existing mechanisms of the workplace
T-3 Considering an approach suited for the workplace, such as selecting the reasonable intervention way according to organization systems for acceptance and immediate implementation
Category 4: Continuous implementation
R-8 Establishing follow-up and evaluation opportunities, such as requesting the submission of an interim report, setting the reporting period, and checking the implementation status and results in order to support continuity of implementation of workplace environment improvement
T-4 Developing a PDCA cycle, by incorporating work environment improvement efforts into the planning (Plan), implementation (Do), evaluation (Check), and review (Action) cycle so that they can be implemented continuously

* R-# stands for eight recommended items, T-# stands for tip items in four categories.

part of supervisor education for effective management, workshops can aid understanding of workplace environment improvement and follow-up evaluation^{15,16,41)}. In participatory interventions based on the “health circles” model, small groups of different types of employee representatives, led by an external moderator, meet every 2 weeks to identify psychosocial stressors and recommend solutions to employees and management⁶⁰⁾. Setting the time period, implementation status, and results can confirm the effects of these recommendations. These activities can lead to continuous work environment improvement activities (Recommendation 8).

In research on organizational interventions, work environment improvement efforts are incorporated into the planning, implementation, evaluation, and review cycle^{2-4,16,48)}. This cycle and continuous implementation play key roles for the sustainability of these interventions. Various workers’ participatory programs have been implemented, including: 1) establishment of workplace consensus, 2) improvement in multiple technical areas, and 3) continuous improvement through conducting risk assessment, taking into account various workplace stress factors related to both physical and mental health. Planning, risk assessment, and reduction measures leading to implementation, recording, and process reviews may

thus be identified with an Occupational Safety and Health Management System (OSHMS)^{3,4,48)} (Tip 4).

Discussion

We acknowledge that the proposed guidelines involve several limitations, including the small number of previous studies (in particular on supervisor training), the relatively small effects observed, and methodological shortcomings, limiting the conclusions that can be drawn. Unlike clinical guidelines, most of the present guideline recommendations were underpinned by best available evidence in the occupational health field because of the limited evidence from effectiveness studies^{31,63)}. To develop the guidelines based on the current evidence, we decided against quality assessment of the selected studies. Thus, the guidelines should be regularly reviewed and refined through the incorporation of new evidence and good practices.

A unique feature of intervention in the workplace is that measurements are delivered as a package (a single measurement is rarely tested). This characteristic makes it difficult to interpret the effectiveness of the individual intervention measurements and to make clear recommendations on them in the guidelines. On the users’

side, it is possible that not all measures of a multimodal intervention will be accepted in the workplace. Guideline developers should provide an assessment of the strength of each individual recommendation so that practitioners can choose between the recommendations more easily⁶⁴. As the evidence underpinning workplace guidelines is scarce⁶³, we adopted two categories of suggestion — recommendations and tips — based on the best available evidence.

Conclusions

Based on the best evidence currently available, we propose guidelines for primary prevention for mental health at work. Although evidence is limited, providing recommendations about the most effective measures to take first in the workplace can be useful for promoting effective occupational health practices. We believe that a range of standardized evidence-informed recommendations is useful for occupational practice.

Funding information

The present study was supported by Ministry of Health, Labour and Welfare (Industrial Disease Clinical Research Grants: Grant Numbers 180701-01).

Conflict of interest

The authors declare no conflicts of interest.

Acknowledgments

The authors thank the following experts for their significant commitment to develop the guidelines: Seitaro Dohi, Takeshi Hayashi, Chiyo Igarashi, Tomoko Ikeda, Kotaro Imamura, Takashi Haratani, Akiomi Inoue, Norito Kawakami, Masaharu Kido, Yuka Kobayashi, Kazutaka Kogi, Takenori Mishiba, Tosiaki Miyamoto, Ippei Mori, Jiro Moriguchi, Takao Nakagiri, Satoko Nakamura, Kazuyuki Nishiyama, Yuko Odagiri, Aska Sakuraya, Yumi Sano, Satoru Shima, Yuriko Takeuchi, Teruichi Shimomitsu, Kunihiko Shinbo, Yuki Sugihara, Mitsuru Sugiyama, Misato Takada, Masao Tsuchiya, Kanami Tsuno, Rino Umanodan, Etsuko Yoshikawa, and Kazuhiro Watanabe. We thank Benjamin Knight, MSc., from Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

ORCID

Akizumi Tsutsumi  <https://orcid.org/0000-0003-0966-4869>

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Association Between Reported Long Working Hours and History of Stroke in the CONSTANCES Cohort

Marc Fadel, MD; Grace Sembajwe, ScD; Diana Gagliardi, MD; Fernando Pico, MD, PhD;
Jian Li, MD, PhD; Anna Ozguler, MD, PhD; Johannes Siegrist, PhD;

Bradley A. Evanoff, MD, MPH; Michel Baer, MD; Akizumi Tsutsumi, MD, DMS;
Sergio Iavicoli, MD, PhD; Annette Leclerc, PhD; Yves Roquelaure, MD, PhD; Alexis Descatha, MD, PhD

Background and Purpose—Long working hours (LWHs) are a potential risk factor for stroke. The aim of this study was to investigate this association in a large general population cohort.

Methods—We used the French population-based cohort, CONSTANCES (Cohorte des Consultants des Centres d'Examens de Santé), to retrieve information on age, sex, smoking, and working hours from the baseline, self-administered questionnaire. Other cardiovascular risk factors and previous occurrence of stroke were taken from a parallel medical interview. We defined LWH as working time >10 hours daily for at least 50 days per year. Participants with primarily part-time jobs were excluded as were those with stroke before LWH exposure. We used logistic models to estimate the association between LWH and stroke, stratified by age, sex, and occupation. In additional modeling, we excluded subjects whose stroke occurred within 5 years of the first reported work exposure.

Results—Among the 143 592 participants in the analyses, there were 1224 (0.9%) strokes, 42 542 (29.6%) reported LWH, and 14 481 (10.1%) reported LWH for 10 years or more. LWH was associated with an increased risk of stroke: adjusted odds ratio of 1.29 (95% CI, 1.11–1.49). Being exposed to LWH for 10 years or more was more strongly associated with stroke, adjusted odds ratio of 1.45 (95% CI, 1.21–1.74). The association showed no differences between men and women but was stronger in white-collar workers under 50 years of age.

Conclusions—This large analysis reveals a significant association between stroke and exposure to LWH for 10 years or more. The findings are relevant for individual and global prevention. (*Stroke*. 2019;50:1879-1882. DOI: 10.1161/STROKEAHA.119.025454.)

Key Words: epidemiology ■ logistic models ■ odds ratio ■ risk factors ■ work

Stroke is a devastating though largely preventable health condition.¹ Long working hours (LWH) may be a risk factor for cardiovascular diseases and stroke.² In Japan, 60% of compensated Karoshi (death from over-work) cases died of stroke.³ A meta-analysis observed a dose-response relationship between LWH and stroke but did not adjust for other modifiable risk factors of stroke.⁴ A Danish study found association with LWH only for hemorrhagic stroke.⁵

Our study investigated the association between LWH and stroke in a large general population study.

Methods

The article adheres to the American Heart Association Journals' implementation of the Transparency and Openness Promotion Guidelines. The data of the CONSTANCES cohort (Cohorte des

Consultants des Centres d'Examens de Santé) are protected by our national regulatory agency (Commission nationale de l'informatique et des libertés, number 910486). However, the CONSTANCES cohort is an open epidemiological laboratory and access to study protocols and data is available on request (http://www.constances.fr/index_EN.php#proposer).

The French CONSTANCES study is a population-based cohort started in 2012.⁶ Participants are randomly selected adults aged 18 to 69 years. Data are compiled from self-administered questionnaires and health examinations conducted at affiliated health-screening centers. All study participants gave informed consent before enrolling in the study, which obtained human studies approval.

Using baseline questionnaire data, we restricted our selection to subjects who had ever worked for >6 months and had worked predominantly in full-time jobs. Age, sex, smoking, occupation, and LWH were retrieved from the baseline questionnaires. Participants reported if they were exposed to LWH (≥10 hours daily for at least 50 days, yes/no variable), and the number of years of exposure (<1

Received March 8, 2019; final revision received April 23, 2019; accepted May 6, 2019.

From the Inserm, UMS 011/UMR-S 1168, Villejuif, France (M.F., A.L., A.D.); AP-HP UVSQ, OHU/EM92 (Samu 92), CHU Poincaré, Garches, France (M.F., A.O., M.B., A.D.); Department of Occupational Medicine, Epidemiology and Prevention, Northwell Health, New York, NY (G.S.); INAIL, Department of Occupational and Environmental Medicine, Epidemiology and Hygiene, Rome, Italy (D.G., S.I.); Neurology and Stroke Unit, Versailles Mignot Hospital, Le Chesnay, France (F.P.); Medical School, Versailles Saint Quentin en Yvelines/Paris Saclay University, France (F.P.); Institute of Occupational, Social and Environmental Medicine, Centre for Health and Society, Faculty of Medicine (J.L.) and Life Science Centre, University of Düsseldorf, Germany; Fielding School of Public Health, School of Nursing, University of California, Los Angeles (J.L.); Division of General Medical Sciences, Washington University in St. Louis, MO (B.A.E.); Department of Public Health, Kitasato University School of Medicine, Minami, Sagami-hara, Japan (A.T.); and Univ Angers, CHU Angers, Univ Rennes, Inserm, EHESP, Irset, UMR_S 1085, France (Y.R., A.D.).

The online-only Data Supplement is available with this article at <https://www.ahajournals.org/doi/suppl/10.1161/STROKEAHA.119.025454>.

Correspondence to Alexis Descatha, MD, PhD, CHU Poincaré, 104 bd Poincaré, 92380 Garches, France. Email alexis.descatha@inserm.fr

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Stroke is available at <https://www.ahajournals.org/journal/str>

DOI: 10.1161/STROKEAHA.119.025454

Table 1. Multivariable Analyses Describing Associations Between Relevant Risk Factors and History of Stroke

	Total	Stroke Cases, N (%)	Crude Odds Ratios (95% CI)	Adjusted Odds Ratios (95% CI)*	Adjusted Odds Ratios (95% CI)*	Adjusted Odds Ratios (95% CI)*
Age, y			1.07 (1.07–1.08)	1.04 (1.04–1.05)	1.04 (1.03–1.05)	1.04 (1.03–1.05)
Body mass index, kg/m ²			1.07 (1.05–1.08)	0.99 (0.97–1.01)	0.99 (0.97–1.00)	0.99 (0.97–1.01)
Sex						
Men	72 551	691 (0.95)	1	1	1	1
Women	71 041	533 (0.75)	0.79 (0.70–0.88)	1.01 (0.87–1.18)	1.02 (0.88–1.19)	1.02 (0.88–1.19)
Occupation						
Self-owner/manager/chief executive officer/professional jobs/farmer	45 903	329 (0.72)	0.85 (0.73–0.99)	0.92 (0.78–1.10)	0.93 (0.78–1.10)	0.93 (0.78–1.10)
High-skilled white-collar jobs	38 549	326 (0.85)	1	1	1	1
Low-skilled white-collar jobs	30 569	238 (0.78)	0.92 (0.78–1.09)	1.13 (0.94–1.37)	1.13 (0.94–1.37)	1.13 (0.94–1.37)
Blue-collar jobs	14 051	156 (1.11)	1.32 (1.09–1.59)	1.18 (0.94–1.49)	1.19 (0.95–1.49)	1.19 (0.95–1.49)
Long working hours						
No	95 391	763 (0.80)	1	1		
Yes	42 542	394 (0.93)	1.16 (1.03–1.31)	1.29 (1.11–1.49)		
Long working hours						
No (or 1 y)	107 602	844 (0.78)	1		1	
Yes (1–5 y)	8844	40 (0.45)	0.57 (0.42–0.79)		0.98 (0.69–1.40)	
Yes (5–10 y)	6937	52 (0.75)	0.96 (0.72–1.27)		1.05 (0.75–1.48)	
Yes (10–15 y)	4634	54 (1.17)	1.49 (1.13–1.97)		1.39 (1.00–1.93)	
Yes (15–20 y)	3185	39 (1.22)	1.57 (1.14–2.17)		1.55 (1.09–2.20)	
Yes ≥20 y	6662	128 (1.92)	2.48 (2.05–2.99)		1.45 (1.16–1.81)	
Long working hours						
No (or 1 y)	107 602	844 (0.78)	1			1
Yes (1–10 y)	15 781	92 (0.58)	0.74 (0.60–0.92)			1.02 (0.79–1.31)
Yes ≥10 y	14 481	221 (1.53)	1.96 (1.69–2.28)			1.45 (1.21–1.74)
High blood pressure diagnosed						
No	126 281	677 (0.54)	1	1	1	1
Yes	17 311	547 (3.16)	6.05 (5.40–6.78)	2.60 (2.22–3.05)	2.60 (2.22–3.05)	2.60 (2.22–3.05)
Diabetes mellitus diagnosed						
No	139 717	1130 (0.81)	1	1	1	1
Yes	3875	94 (2.43)	3.05 (2.47–3.77)	0.95 (0.73–1.25)	0.95 (0.72–1.24)	0.95 (0.72–1.24)
Dyslipidemia diagnosed						
No	130 690	722 (0.55)	1	1	1	1
Yes	12 902	502 (3.89)	7.29 (6.49–8.18)	3.09 (2.63–3.62)	3.08 (2.63–3.61)	3.08 (2.63–3.61)
Familial history of cardiovascular diseases						
No	129 106	1067 (0.83)	1	1	1	1
Yes	14 486	157 (1.08)	1.32 (1.11–1.56)	0.96 (0.79–1.18)	0.96 (0.79–1.18)	0.96 (0.79–1.18)
Smoking						
No smoker	63 218	468 (0.74)	1	1	1	1
Current/former smoker <30 pack/y	58 881	461 (0.78)	1.06 (0.93–1.20)	1.13 (0.98–1.31)	1.13 (0.98–1.31)	1.13 (0.98–1.31)
Current/former smoker ≥30 pack/y	5897	136 (2.31)	3.17 (2.61–3.84)	1.58 (1.26–1.98)	1.57 (1.25–1.97)	1.57 (1.25–1.97)

*Adjusted on age, body mass index, sex, occupations, high blood pressure, diabetes mellitus, dyslipidemia, familial history of cardiovascular diseases, and smoking habits (in addition of long working hours).

year, short [1–<10 years], and long duration of LWH [≥ 10 years]). Cumulative exposure in 5-year increments was also calculated. Subjects reporting LWH but missing data on exposure duration were included in the <1-year category.

Each participant had a medical interview completed by a physician, including history of stroke (all subtypes together) and age of occurrence, diabetes mellitus, history of high blood pressure, dyslipidemia (hypercholesterolemia or hypertriglyceridemia), family history of cardiovascular events, and body mass index.

The main outcome was having a stroke reported by a physician. Subjects missing data were considered as not having a stroke. Subjects who had a stroke before being exposed to LWH were excluded from analysis. Logistic models were used, adjusted by cardiovascular risk factors. Additional models were stratified by occupation, age, and sex. See the online-only Data Supplement for additional analyses.

All study participants gave informed consent before enrolling in the study. CONSTANCES has obtained authorization from the French National Data Protection Authority and was approved by the National Council for Statistical Information, the National Medical Council, and the Institutional Review Board of the National Institute for Medical Research (INSERM).

Results

From the 162 115 subjects with at least 6 months work experience, 18 508 (11.4%) had a history of predominantly part-time jobs, and 15 (0.01%) reported a stroke before the onset of exposure to LWH. In the final sample ($n=143\,592$), 1224 strokes were included (0.9%), 42 542 (29.6%) participants reported LWH, and 14 481 (10.1%) reported exposure to LWH for 10 years or more.

LWH were associated with stroke (Table 1), especially among those exposed to LWH for 10 years or more (adjusted odds ratio, 1.45; [95% CI, 1.21–1.74]). Younger people had a higher risk of stroke when exposed to LWH for >10 years (Table 2). Stratification by occupation revealed a lower effect for owners, managers, chief executive officers, professionals, and farmers, though no interaction between LWH/occupation was found ($P>0.05$).

Discussion

An association between LWH and stroke was found with modest increases in adjusted odds ratio for LWH exposures of 10 years or more. Results are consistent with studies elsewhere: a meta-analysis, where the meta-risk was 1.31 for work of >55 hours per week⁴ and 2 Korean case-control studies on all types of stroke and hemorrhagic stroke only.^{7,8} Our results support the temporal sequence and a dose-response relationship with exposure duration.

Various studies have postulated direct and indirect causal pathways for effects of working conditions on stroke, including those mediated by modifiable behaviors that also increase the risk of cardiac arrhythmias/hypercoagulability among patients with LWH.⁹ Irregular shifts, night work, and job strain are suspected of being responsible for unhealthy working conditions.^{10–12} Owners, executives, managers, professionals, and farmers generally have greater decision latitude than other workers, perhaps accounting for the smaller effects in these groups. The Danish studies that showed no effect did not document years of exposure; in addition, working conditions in Denmark are among the best worldwide, which might explain their difference with other studies.⁵

Table 2. Stratified Analyses by Sex, Age, and Occupation for Association Between Long Working Hours and History of Stroke

	Long Working Hours	Adjusted Odds Ratios (95% CI)*
Sex		
Men	No (or 1 y)	1
	Yes (1–10 y)	0.83 (0.58–1.19)
	Yes ≥ 10 y	1.39 (1.13–1.73)
Women	No (or 1 y)	1
	Yes (1–10 y)	1.27 (0.89–1.82)
	Yes ≥ 10 y	1.52 (1.10–2.11)
Age		
<50 y	No (or 1 y)	1
	Yes (1–10 y)	0.96 (0.61–1.50)
	Yes ≥ 10 y	2.28 (1.46–3.58)
≥ 50 y	No (or 1 y)	1
	Yes (1–10 y)	1.00 (0.74–1.36)
	Yes ≥ 10 y	1.36 (1.12–1.65)
Occupation		
Self-owner/manager/chief executive officer/professional jobs/farmer	No (or 1 y)	1
	Yes (1–10 y)	1.07 (0.71–1.63)
	Yes ≥ 10 y	1.21 (0.91–1.59)
High-skilled white-collar jobs	No (or 1 y)	1
	Yes (1–10 y)	1.25 (0.80–1.97)
	Yes ≥ 10 y	1.77 (1.28–2.43)
Low-skilled white-collar jobs	No (or 1 y)	1
	Yes (1–10 y)	0.77 (0.43–1.40)
	Yes ≥ 10 y	1.70 (1.09–2.67)
Blue-collar jobs	No (or 1 y)	1
	Yes (1–10 y)	0.79 (0.38–1.64)
	Yes ≥ 10 y	1.59 (0.97–2.61)

*Adjusted for body mass index, high blood pressure, diabetes mellitus, dyslipidemia, familial history of cardiovascular diseases, and smoking (plus age and occupation for sex, sex and occupation for age, and sex and age for occupation).

The main limitation is the stroke diagnosis. Positive predictive values for self-reported stroke were around 60% in a UK study.¹³ In our study, stroke was defined by a doctor who examined each participant following protocol guidelines to improve diagnosis accuracy. Though the clinician cannot check medical/imaging records, misclassification probably had a low impact on the association found. In this same cohort, diabetes mellitus recorded from the same examination protocol had high agreement with health claims data.¹⁴ In addition to exclusion of prior stroke, we further controlled the temporal sequence by using a 5-year lag to ensure that exposure would precede the event. Moreover, in this study, known independent risk factors for stroke (and not other types

of brain events) were found to be associated with stroke, giving additional reassurance of the diagnosis. Our study did not distinguish ischemic from hemorrhagic stroke, where effects of LWH might be different: job demand was previously related to ischemic but not hemorrhagic stroke,¹¹ whereas other analyses observed an association with LWH only for hemorrhagic stroke.⁵ Although recall and selection bias are related to death or major cognitive sequelae, it is unlikely that these would have modified the LWH association observed. Finally, subjects reporting mainly part-time work were excluded from the sample. Future studies may include job exposure matrices to better control recall bias, diagnoses separating ischemic and hemorrhagic stroke, and focus on incident stroke.

Conclusions

This large-scale analysis reveals a significant association between exposure to LWH for a period of 10 years or more and history of stroke. Future study may confirm this link with prevention strategies for reducing LWH in patients with high-risk profiles for stroke and reducing the global burden of disease.¹⁵

Sources of Funding

The authors are paid by their institutions. The CONSTANCES cohort study was supported and funded by the Caisse nationale d'assurance maladie; it is an "Infrastructure nationale en Biologie et Santé" and benefits from Agence Nationale de la Recherche (ANR-11-INBS-0002) grant funding. CONSTANCES is also partly funded by Merck Sharp Dohme, AstraZeneca, and Lundbeck.

Disclosures

None.

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