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Infection and death by COVID-19 in a cohort of healthcare workers in Mexico

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ABSTRACT (ENGLISH)

Objective This study aimed to estimate the risk of SARS-Cov2 infection and severe COVID-19 among healthcare workers from a major social security system. **Methods** This study actively followed a cohort of social security workers from March to December 2020 to determine the number of laboratory-confirmed symptomatic cases, asymptomatic associated contacts and COVID-19-associated hospitalizations and deaths. Workers were classified into those providing direct care to infected patients (COVID teams), other active healthcare workers (OAHCW), and workers under home protection (HPW). The number of cases and rates were also estimated by job category. **Results** Among a total of 542 381 workers, 41 461 were granted stay-at-home protection due to advanced age or comorbidities. Among the 500 920 total active workers, 85 477 and 283 884 were classified into COVID teams and OAHCW, respectively. Infection rates for COVID teams, OAHCW, and HPW were 20.1% [95% confidence interval (CI) 19.8-20.4], 13.7% (95% CI 13.5-13.8), and 12.2% (95% CI 11.8-12.5), respectively. The risk of hospitalization was higher among HPW. COVID teams had lower mortality rate per 10 000 workers compared to HPW (5.0, 95% CI 4.0-7.0 versus 18.1, 95% CI 14.0-23.0). Compared to administrative workers, ambulance personnel (RR 1.20; 95% CI 1.09-1.32), social workers (RR 1.16; 95% CI 1.08-1.24), patient transporters (RR 1.15; 95% CI 1.09-1.22) and nurses (RR 1.13; 95% CI 1.10-1.15) had a higher risk of infection after adjusting for age and gender. Crude differences in mortality rates were observed according to job category, which could be explained by differences in age, sex, and comorbidity distribution. Diabetes, obesity, hypertension, hemolytic anemia, and HIV were associated with increased fatality rates. **Conclusions** COVID team workers had higher infection rates compared to the total population of active workers and HPW. Doctors had lower risk of infection than respiratory therapists, nurses, and patient transporters, among whom interventions should be reconsidered to reduce risks. The presence of comorbidities, such as diabetes, obesity, arterial hypertension, hemolytic anemia, and HIV, increased the likelihood of complications caused by COVID-19, culminating in a poor prognosis.

FULL TEXT

Headnote

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Results Among a total of 542 381 workers, 41 461 were granted stay-at-home protection due to advanced age or comorbidities. Among the 500 920 total active workers, 85 477 and 283 884 were classified into COVID teams and OAHCW, respectively. Infection rates for COVID teams, OAHCW, and HPW were 20.1% [95% confidence interval (CI) 19.8-20.4], 13.7% (95% CI 13.5-13.8), and 12.2% (95% CI 11.8-12.5), respectively. The risk of hospitalization was higher among HPW. COVID teams had lower mortality rate per 10 000 workers compared to HPW (5.0, 95% CI 4.0-7.0 versus 18.1, 95% CI 14.0-23.0). Compared to administrative workers, ambulance personnel (RR 1.20; 95% CI 1.09-1.32), social workers (RR 1.16; 95% CI 1.08-1.24), patient transporters (RR 1.15; 95% CI 1.09-1.22) and nurses (RR 1.13; 95% CI 1.10-1.15) had a higher risk of infection after adjusting for age and gender. Crude differences in mortality rates were observed according to job category, which could be explained by differences in age, sex, and comorbidity distribution. Diabetes, obesity, hypertension, hemolytic anemia, and HIV were associated with increased fatality rates.

Conclusions COVID team workers had higher infection rates compared to the total population of active workers and HPW. Doctors had lower risk of infection than respiratory therapists, nurses, and patient transporters, among whom interventions should be reconsidered to reduce risks. The presence of comorbidities, such as diabetes, obesity, arterial hypertension, hemolytic anemia, and HIV, increased the likelihood of complications caused by COVID-19, culminating in a poor prognosis.

Key terms death due to COVID-19; health worker; occupational risk; SARS-Cov2.

On 25 February 2020, the World Health Organization (WHO) (1) declared an international public health emergency due to coronavirus disease 2019 (COVID19). Given that healthcare workers are the fundamental element responsible for the care of affected patients and control of the pandemic, they may experience increased risk of infection due to contact with infected communities, relatives, friends, patients, or colleagues (2). Therefore, their protection is important for their personal safety, continuation of patient care amidst the health crisis (3), and, most importantly, ensuring that they do not become a source of infection (4-6).

Although healthcare workers account for <3% of the population in the vast majority of countries and <2% in low- and middle-income countries, approximately 14-35% of COVID-19 cases involve healthcare workers (7). This suggests a higher risk of SARS-CoV-2 infection among healthcare personnel given the lack of necessary precautions based on the disease's transmission mechanism at the beginning of the pandemic (5). Some researchers have reported that there is insufficient evidence indicating that nosocomial COVID-19 infections are the main source of infection among healthcare workers, suggesting the possibility of home environment infections (8).

Therefore, determining whether healthcare workers, especially those in the front line, are at excess risk of infection and death due to COVID-19 is of importance, particularly in developing countries given studies reporting ethnic differences in mortality due to COVID-19 (9, 10). In Mexico, the high prevalence of obesity and diabetes may increase the COVID-19 mortality, especially considering the synergy between the presence of comorbidities, age, and increased exposure.

The Mexican Social Security Institute (IMSS in Spanish) is the largest social security institution in Latin America, covering approximately half of the Mexican population. It provides social, economic, and healthcare services to workers and their families in the private sector of the economy; delivers preventive, curative, and rehabilitation services in 1521 primary-care clinics, 251 second-level hospitals, and 25 third-level hospitals; and employs almost half a million workers, a majority of whom are in healthcare, including groups of doctors and nurses organized into teams for the exclusive care of patients with COVID-19 (COVID teams). During the pandemic, the IMSS provided personal protective equipment to its workers according to the recommendations of the Pan American Health Organization while also maintaining an epidemiological surveillance system of its workers to identify those with COVID-19 symptoms and persons with whom they had come in contact. Thus, this group of workers provides us with a great opportunity to (1) estimate the risks of infection and death by COVID-19 among healthcare workers (2); compare the risks between and within job categories (3); compare healthcare workers, workers in COVID teams, and those under home protection (HPW); and (4) identify risk factors for death among infected workers.

Methods

A cohort of permanent and temporary workers hired to address the pandemic was followed from March to December 2020. The main outcome studied was RT-PCR confirmed SARS-CoV2 infection, while the secondary outcome was severe disease including hospitalization and death among these confirmed cases. Cumulative incidence rates were estimated according to job category and activity during the pandemic. The strength of selected risk factors for death was assessed in a group of cases (deaths) and controls (survivors) within this cohort.

Establishing the cohort of workers

The list of workers was obtained from the IMSS payroll. Job titles were then identified and categorized into three groups: patient care (health workers), administrative workers, and other categories. The job titles considered health workers were doctors, nurses, medical assistants, social workers, chemists/laboratory technicians, histo/cytotechnologists, food handlers, hygiene/cleaning personnel, ambulance personnel, pharmacy staff, radiologists, stomatologists, respiratory therapists, and patient transporters.

Identifying confirmed cases

Symptomatic cases within all medical units of the IMSS and preventive services for its own workers were identified. Suspected cases were registered in the Online Epidemiological Surveillance Notification System (SINOLAVE in Spanish) and identified by a unique identification number, called CURP in Mexico. In addition to the cases reported in this system, we actively looked for any additional cases reported to the Union and other absenteeism reports to the personnel administrative unit. IMSS workers have economic incentives to avoid absenteeism not related to health conditions; therefore, there is an incentive to report any medical condition that prevents them from going to work.

Workers who satisfied the operational definition of a suspected case of COVID-19 (11) underwent a nasopharyngeal swab to obtain samples for RT-PCR diagnosis and completed a questionnaire for epidemiologic surveillance. A suspected case of SARS-CoV-2 infection was defined as person who during the last seven days presented acute onset of any of two or more of the following signs or symptoms: fever, cough or headache; and one or more of the of the following signs or symptoms: dyspnea, myalgia, sore throat, coryza, diarrhea or conjunctivitis.

Similarly, samples from persons who came in contact with symptomatic workers within their work environment were obtained after four and five days despite having no symptoms. The SINOLAVE registry includes the following variables: age, sex, history of comorbidities, and RT-PCR results. This report included all confirmed cases (symptomatic and asymptomatic) from 1 March to 10 December 2020, as well as all hospitalizations and deaths identified among these cases. We searched four different data sets to look for hospitalizations and deaths among confirmed cases: intensive care unit, emergency room, hospital discharges and SINOLAVE. Emergency room visits were included as hospitalizations if the stay in this area lasted >24 hours during the pandemic.

The samples were processed in the following four reference laboratories: the Biomedical Research Center of the Northeast in Nuevo León, the Biomedical Research Center of the West in Jalisco, the Yucatan Medical Research Unit (UIMY), and the Central Laboratory of Epidemiology in Mexico City. All four laboratories have ISO 9001 certification granted by the Mexican Institute of Normalization and Certification, which is endorsed by the Mexican Accreditation Entity, with a technical capacity endorsement by the National Institute of Epidemiological Diagnosis and Reference.

Workers under home protection

During the pandemic, the Mexican Ministry of Health authorized workers to abstain from working and granted them stay-at-home protection from 24 March 2020 in the form of a paid leave of absence with benefits for those at higher risk of complications or death by COVID-19 who showed any of the following characteristics: age >65 years, pregnant or nursing women, chronic noncommunicable diseases (arterial hypertension, chronic obstructive pulmonary disease, kidney failure, lupus, cancer, diabetes, obesity, liver failure, and heart disease), or any immunosuppressive disease or treatment. This group of workers, who did not provide healthcare during the leave, were followed up using the same epidemiological surveillance criteria as active workers, representing those with non-occupational risk of infection outside medical care units. This group was used as a control when comparing the risks of infection associated with occupational exposure during medical care.

COVID team workers

To satisfy the high demand for hospitalized patient care, the IMSS organized health personnel into care teams (called COVID teams) in charge of a maximum of 24 patients. These teams consisted of medical and nursing personnel trained for the direct care of patients with COVID-19 in second- and third-level hospital units (frontline health personnel). A list of workers on these teams available in the SINOLAVE database allowed us to identify infected workers or those who died due to COVID-19.

Statistical analysis

Illness and mortality risks were estimated as the cumulative incidence rates of infection, mortality, and case-fatality according to job category. Rates were estimated by grouping the workers into the following categories (i): COVID team members (ii), other active healthcare workers (OAHCW), and (iii) workers under home protection (HPW). Excess risk according to job category was assessed using Poisson regression models with crude and adjusted rate ratios for age and sex. Rate ratios of infection and death due to COVID-19 were estimated according to job category, with administrative workers as the reference category. This evaluation excluded HPW.

The associations between age, sex, and certain comorbidities and the risk of death due to COVID-19 was assessed by comparing survivors and deceased workers using unconditional logistic regression models that compared workers with and without comorbidities with confirmatory tests. HPW were compared to OAHCW, which was the reference category. All analyses were conducted using statistical package Stata version 14.2 (IBM Corp, Armonk, NY, USA).

Results

Incidence of infection and mortality due to COVID-19

The IMSS comprised 542 381 workers at the beginning of the pandemic, of whom 41 461 were HPW. Among the remaining 500 920 active workers, 85 477 were doctors and nurses who were members of COVID teams, while 283 884 were OAHCW. The IMSS workers (56.7% female) had a mean age of 37.07 years.

The first imported case of COVID-19 in Mexico was reported on 28 February (12), while the first cases of COVID-19 among IMSS workers were reported in March 2020, with the first death recorded on 29 March.

Among the 500 920 total active workers 30.0% (149 955) reported symptoms consistent with the operational definition of suspected COVID-19, whereas 25.1% (10 414) of HPW sought medical care for similar symptoms.

Among total active symptomatic workers, 69 342 were confirmed as COVID-19 cases. Additionally, 1189 asymptomatic workers tested positive for SARS-CoV-2.

Table 1 details the infection, hospitalization, mortality, and case-fatality rates among all IMSS workers, COVID teams, and OAHCW. In general, women had higher infection rates, whereas men had higher mortality rates. The risk of being admitted to a hospital was similar between men and women, increased with age and was higher for HPW. As expected, mortality rates increased with age. Although HPW had the lowest infection rates, they had the highest mortality and case-fatality rates. COVID team members had higher infection rates but the lowest mortality and case-fatality rates.

To evaluate the influence of age, sex, and comorbidities on the risk of death among HPW, crude and adjusted (according to comorbidities, age, and sex) odds ratios (OR) were estimated. The crude OR associated with death due to COVID-19 and having remained under home protection was 2.06 [95% confidence interval (CI) 1.62-2.63] when compared to OAHCW. After adjusting for the presence of comorbidities, the OR was significantly reduced (OR 1.63, 95% CI 1.23-2.17), suggesting that this excess risk was partly due to the associated comorbidities and age that justified home protection.

Table 2 summarizes the incidence rates in the working population according to job category, age- and sex-adjusted relative risks for infection, hospitalization and death, with administrative workers as the reference group. Accordingly, respiratory therapists had the highest infection rates (19%), followed by patient transporters (17.5%) and nurses (17.1%). The relative risk for ambulance personnel, social workers, patient transporters, nurses, and hygiene and cleaning personnel remained significantly increased after adjusting for age and sex. Respiratory therapist and patient transporter had increased risk of being hospitalized. Increased mortality and case-fatality rate ratios were

observed in ambulance personnel, respiratory therapist, and pharmacy staff, although these relative risks lost statistical significance after adjusting for age and sex.

Risk factors for death

Table 3 presents the risk factors for the development of severe disease that caused death among active IMSS workers who became infected. The presence of certain comorbidities, such as diabetes (OR 2.52, 95% CI 1.94-3.29), obesity (OR 2.05, 95% CI 1.67-2.60), and arterial hypertension (OR 1.30, 95% CI 1.01-1.68, increased the risk of death, while less frequent but very high risk comorbidities included a history of hemolytic anemia (OR 10.0, 95% CI 1.20-82.75) and HIV (OR 6.97, 95% CI 1.92-25.28).

Discussion

The current study confirmed that frontline COVID-19 team workers were at excess risk of SARS-CoV-2 infection given their higher risk of exposure to increased viral loads as reported previously (13, 14). However, despite having higher rates of infection compared to other active health workers, they showed no excess risk for hospitalization or death. On the other hand, while HPW were less exposed to infection, they had a higher risk of death once infected. Considering that frontline health workers have a significantly higher risk of COVID-19 infection (14), the ability of WHO-recommended personal protective equipment in mitigating occupational transmission needs more research. The higher mortality rates among HPW than among other active health workers and COVID teams is expected given that the former had more comorbidities, whereas the latter were healthier and younger. The case-fatality rates found in the present study (0.7% and 0.2% for active health workers and COVID teams, respectively) were similar to those reported in other countries, such as the United States (0.4%) (15), China (0.3%-0.7%) (16, 17), Germany (0.2%-0.5%) (18) and Italy (1.2%) (19).

China reported that women accounted for 79% of infected workers, with the same figure being 57% in Mexico (20). Meanwhile, the current study found that older men had a higher risk of death similar to that reported in China (20, 21).

Several studies agree that health workers directly caring for patients with COVID-19, such as nursing and medical personnel, are at higher risk of infection (3, 19, 21-26). After determining the rates and risks of infection according to job category, the present study found that ambulance personnel, social workers, patient transporters, and nurses were at a high risk of infection, whereas doctors had lower infection rates. Laursen et al (27) reported that ambulance personnel were at higher risk of infection given their increased interaction with patients.

Such differences in the risk of infection according to job categories could be related to not only varying levels of exposures but also heterogeneous precautions taken during their occupational activities, with doctors being more aware of infection risks. Moreover, our results showed that ambulance personnel, respiratory therapist, and pharmacy staff had the highest mortality rates. These findings are in agreement with those presented in other studies, which suggested that while nurses had higher risks of infection, attention should be provided to workers not providing direct medical care to patients with COVID-19 given high risk of infection and death among such workers. The current study found that comorbidities were prevalent among HPW and were responsible of their greater risk of mortality from COVID-19 compared to active health workers. However, after adjusting for comorbidities, this association was considerably reduced, confirming that isolating these workers in their homes was an adequate strategy for reducing the number of deaths among susceptible workers.

Risk factors with the strongest association included history of hemolytic anemia, obesity, diabetes, HIV, and hypertension, which is in agreement with the findings published in the international literature (17, 21, 28, 29)

This observational study has several strengths and limitations that should be considered when interpreting the results. One of the advantages of the current study is the large population analyzed and the diversity of job categories included. Although an effort was made to include all clinical infections, subclinical infections were not precisely represented. However, bias related to underreporting could be similar across job categories. To assess possible bias introduced by differential testing between occupational categories, we estimated infection and mortality only for symptomatic cases. Rates did not change significantly (data not shown) due to the reduced number of asymptomatic cases; therefore, all results are presented for all confirmed cases independently of symptoms at the

time of testing (30-32). An additional limitation could be related to the identification of comorbidities given that these were reported by the worker upon COVID diagnosis.

In conclusion, COVID team workers had higher infection rates compared to the total population of active workers and those under home protection. Doctors had lower risk of infection compared to respiratory therapists, nurses, and patient transporters. As such, interventions aimed at reducing risks among these occupations should be reconsidered. The presence of comorbidities, such as diabetes, obesity, arterial hypertension, hemolytic anemia, and HIV, had been found to increase the likelihood of complications caused by COVID-19, subsequently causing a poor prognosis.

Sidebar

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DETAILS

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Efficacy of intermittent exposure to bright light for treating maladaptation to night work on a counterclockwise shift work rotation

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ABSTRACT (ENGLISH)

Objectives Rotating shift work is associated with adverse outcomes due to circadian misalignment, sleep curtailment, work-family conflicts, and other factors. We tested a bright light countermeasure to enhance circadian adaptation on a counterclockwise rotation schedule. **Methods** Twenty-nine adults (aged 20-40 years; 15 women) participated in a 4-week laboratory simulation with weekly counterclockwise transitions from day, to night, to evening, to day shifts. Each week consisted of five 8-hour workdays including psychomotor vigilance tests, two days off, designated 8-hour sleep episodes every day, and an assessment of circadian melatonin secretion. Participants were randomized to a treatment group (N=14), receiving intermittent bright light during work designed to facilitate circadian adaptation, or a control group (N=15) working in indoor light. Adaptation was measured by how much of the melatonin secretion episode overlapped with scheduled sleep timing. **Results** On the last night shift, there was a greater overlap between melatonin secretion and scheduled sleep time in the treatment group [mean 4.90, standard

deviation (SD) 2.8 hours] compared to the control group (2.62, SD 2.8 hours; $P=0.002$), with night shift adaptation strongly influenced by baseline melatonin timing ($r^2 = -0.71$, $P=0.01$). While the control group exhibited cognitive deficits on the last night shift, the treatment groups cognitive deficits on the last night and evening shifts were minimized. Conclusions In this laboratory setting, intermittent bright light during work hours enhanced adaptation to night work and subsequent readaptation to evening and day work. Light regimens scheduled to shift circadian timing should be tested in actual shift workers on counterclockwise schedules as a workplace intervention.

FULL TEXT

Headnote

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Objectives Rotating shift work is associated with adverse outcomes due to circadian misalignment, sleep curtailment, work-family conflicts, and other factors. We tested a bright light countermeasure to enhance circadian adaptation on a counterclockwise rotation schedule.

Methods Twenty-nine adults (aged 20-40 years; 15 women) participated in a 4-week laboratory simulation with weekly counterclockwise transitions from day, to night, to evening, to day shifts. Each week consisted of five 8-hour workdays including psychomotor vigilance tests, two days off, designated 8-hour sleep episodes every day, and an assessment of circadian melatonin secretion. Participants were randomized to a treatment group ($N=14$), receiving intermittent bright light during work designed to facilitate circadian adaptation, or a control group ($N=15$) working in indoor light. Adaptation was measured by how much of the melatonin secretion episode overlapped with scheduled sleep timing.

Results On the last night shift, there was a greater overlap between melatonin secretion and scheduled sleep time in the treatment group [mean 4.90, standard deviation (SD) 2.8 hours] compared to the control group (2.62, SD 2.8 hours; $P=0.002$), with night shift adaptation strongly influenced by baseline melatonin timing ($r^2 = -0.71$, $P=0.01$). While the control group exhibited cognitive deficits on the last night shift, the treatment groups cognitive deficits on the last night and evening shifts were minimized.

Conclusions In this laboratory setting, intermittent bright light during work hours enhanced adaptation to night work and subsequent readaptation to evening and day work. Light regimens scheduled to shift circadian timing should be tested in actual shift workers on counterclockwise schedules as a workplace intervention.

Key terms circadian phase; melatonin; night shift; shift worker; sustained attention.

Shift work has become increasingly common as our 24/7 global society requires more workers to do their jobs at irregular hours. According to the National Health Interview Survey (NHIS), in 2010 approximately 28.7% of the American workforce was engaged in work outside the standard 09:00-17:00 hours day shift (1). Shift workers are exposed to atypical or irregular sleep-wake schedules, which can lead to misalignment between the endogenous circadian timing system and the sleep-wake cycle. In the short term, this misalignment typically results in poor sleep, increased sleepiness, and performance decrements (2, 3). When prolonged, shift work is associated with increased risk for cardiovascular disease, metabolic syndrome, depression, certain types of cancer, and other health problems (3).

A large variety of round-the-clock work schedules exist, differing by speed and direction of rotation, length of shifts, number of consecutive shifts, and number of shifts per week (4). The magnitude of adverse outcomes varies with the characteristics of the shift work schedule. Counterclockwise shift work schedules (night to evening to day) are associated with worse sleep, lower alertness, and more negative health issues compared to clockwise (day to evening to night) rotations (5-7). While uncommon in Europe, counterclockwise shift rotation schedules are sometimes used in the US (8).

Non-pharmacologic strategies to improve adaptation to shift work based on sleep and circadian principles typically manipulate light exposure patterns and/or sleep timing (9-11). Exposure to light and darkness is the main

synchronizer of the circadian timing system, and the use of appropriately timed bright light exposure is an effective approach to enhance circadian adaptation to night shifts (12, 13).

To our knowledge, no study yet has investigated the efficacy of a bright light treatment throughout a complete counterclockwise shift rotation cycle. On such a schedule, not only is the circadian adaptation to night shifts crucial, but equally important is the readaptation back to evening and day shifts. Therefore, this laboratory simulation study, carried out between 1995-1998 but not previously reported, aimed to test the hypothesis that a bright light treatment schedule, based on the model of Kronauer and colleagues (14), could rapidly shift circadian rhythms to a night shift schedule as well as readapt them to a day-active schedule during subsequent evening and day shifts. We also tested whether greater circadian adaptation was associated with attenuated performance deficits, determined by performance on a sustained attention task at the end of each shift rotation.

Methods

Participants

A total of 29 healthy non-shift working adults, who had a mean age of 27.7 [standard deviation (SD) 6.3] years, (15 women, 14 men) participated in the study. Participants were randomized to the treatment or control group by sex. Fourteen participants (7 women; 7 men) were randomized to receive bright light treatment during work episodes, and 15 participants (8 women; 7 men) were randomized to a control group who were exposed to ordinary levels of room light during work episodes.

Participants were recruited from the community using advertisements in local newspapers and flyers posted on bulletin boards at local colleges and universities. Prior to enrollment, participants were screened, including a physical examination, clinical history, chest radiograph, electrocardiogram, clinical biochemical screening tests of blood and urine, and given either a standardized psychological questionnaire (MMPI) or a structured interview with a clinical psychologist (15). Exclusion criteria included a history of or current significant medical, psychiatric or sleep disorders; history of drug dependency; history of night work; recent (within 3 months) travel across >2 time zones; use of prescription medication. Participants were asked to refrain from using nicotine-containing products, alcohol, caffeine, and all medications for the duration of the study. Each participant had an informed consent meeting and gave written consent prior to beginning the study, which was approved by the Human Research Committee of Partners Health Care and was in accordance with the Helsinki Declaration.

Study protocol

The 4-week protocol simulated a counterclockwise weekly shift rotation schedule of five 8-hour work days followed by two days off, beginning with day shifts (07:00-15:00 hours), night shifts (23:00-07:00 hours), evening shifts (15:00-23:00 hours), and ending with day shifts (see figure 1). During the 8-hour work episodes in the laboratory, participants remained in study rooms in the Environmental Scheduling Facility at Brigham and Women's Hospital where they performed four iterations (with rest breaks) of a 1.5-hour computer-based performance battery. After the work episodes, participants left the laboratory. Participants were instructed to adhere to an 8-hour sleep schedule at home, with sleep times specified for each shift (for day shifts, sleep was scheduled from 22:00-06:00 hours, for night shifts from 08:00 to 16:00 hours, for evening shifts from 01:00 to 09:00 hours, and for days off from 01:00 to 09:00 hours). Compliance with the at-home sleep schedule was verified by sleep diaries and wrist activity.

At the end of each work week during the transition from the 4th to the 5th work episode, a 24-32 hour constant posture (CP) regimen took place in the laboratory. After the CP, the participants left the laboratory and had two days off before their next shift type started.

The studies were carried out between 1995 and 1998 but have not been previously reported. The Environmental Scheduling Facility where the studies took place was decommissioned and no longer exists.

Light exposure

Light was administered from ceiling-mounted fixtures containing 4-foot cool white fluorescent lamps (North American Philips Lighting Corp, Bloomfield, NJ). Light levels were taken in the direction the participant was facing while sitting at the computer desk where they spent most of their shift. In the initial week of day shifts, all participants were exposed to indoor light during work episodes, which was approximately 103 lux in the direction of gaze when sitting

at the desk. Control participants worked all shifts in indoor light, whereas the treatment group was exposed to intermittent bright light on the night, evening and day shifts. As indicated in figure 1, intermittent bright light levels of -8,000, -2,500 and -1,250 lux were scheduled based on a mathematical model of the effect of light on the human circadian pacemaker, and consisted of 30 minutes of indoor light alternating with 30 minutes of bright light to initiate a phase delay during the night shifts and a phase advance on the evening and day shifts (14). Details of the timing and intensities of light exposures for the treatment group can be found in the supplementary material (www.sjweh.fi/show_abstract.php?abstract_id=3953).

During the CP, all participants were exposed to 30-60 minutes of ~2500 lux light before and after their work shifts to mimic natural light exposure while commuting during daytime hours. For CP on day shifts, these exposures occurred at 06:00 and 15:00 hours; for night shifts at 07:30 and 16:00 hours; and for evening shifts at 09:00 and 15:00 hours. These are all times at which daylight would be present outdoors in greater Boston during most of the year. In addition, during the initial part of the evening shift CP, daytime light exposure from running errands or exercising outdoors was mimicked in the laboratory by presenting 1250 lux and 2500 lux exposures between 09:30 and 15:00 hours. See figure 1 and Supplement 1. These light "commute time" exposures were not part of the treatment plan produced by the model predictions, but were added to test whether the bright light treatment could overcome light exposure during commute times, which is known to prevent adaptation.

Constant posture circadian phase assessment

CP were performed at the end of each shift rotation to assess the timing of the circadian rhythm of melatonin secretion relative to the current work and sleep schedule (16). Throughout the 24-32-hour CP, the participant was restricted to a semi-recumbent position in bed. Food and fluid intake were distributed as small hourly snacks. Lights were turned off during the scheduled sleep times, allowing participants to sleep in order to avoid confounding effects of sleep loss on performance for the final work episode of each work week.

Throughout each CP, small blood samples were obtained every 30 minutes via an intravenous forearm catheter connected to a 12-foot IV line. After collection, each blood sample was placed in a Vacutainer tube with EDTA, centrifuged at 2°C for 10 minutes at 2200-2800 rpm, and the resulting plasma was placed in an aliquot tube and frozen at -20°C. Plasma samples were assayed for melatonin shortly after each study was completed using a radioimmunoassay (lower limit of sensitivity 1.1pg/mL; DiagnosTech/Pharmasan Labs, Osceola, WI).

Sustained attention

To assess sustained vigilant attention, the Psychomotor Vigilance Task (PVT) (17) was taken every two hours beginning 30 minutes after the start of each work shift. The 10-minute PVT was the first scheduled task of a 1.5-hour cognitive test battery which took place 4 times per shift and was scheduled to always occur during times of exposure to indoor light levels in both groups. The PVT required the participant to respond to a visual stimulus appearing on a computer screen by pressing a button with their dominant thumb. The interstimulus interval varied between 2-10 seconds, resulting in ~100 trials per test. PVT performance has been shown to vary with circadian phase and to decline with duration of sustained wakefulness (18). We report the reaction time (RT) means, medians, and lapses of attention (RT>500ms), as well as reaction time percentile distributions of the PVT taken during each CP.

Statistical analyses

To examine the timing of melatonin onset, we calculated the time at which plasma melatonin levels rose to 25% of their peak (MEL25%up), an established circadian phase marker (16, 19). The peak was determined by fitting a 3-harmonic waveform to the data from the 24-hour baseline (day shift) CP, determining the amplitude of the fitted waveform (maximum-minimum of fitted waveform), and then using linear interpolation between adjacent values to calculate the time at which melatonin levels rose to 25% of this amplitude. This timing method was used to account for the wide variation in the amplitude of plasma melatonin levels between individuals (20). Plasma melatonin offset was defined as the time at which melatonin levels fell to 25% of their fitted peak (MEL25%down). The thresholds from the baseline (day shift) CP were used to determine the timing of MEL25%up/down for the remaining CP for each participant. Next, the duration of the melatonin secretory phase for each CP was defined as the interval

between MEL25%up and MEL25%down.

Under normal entrained conditions, participants sleep when their melatonin levels are high with a fitted midpoint of secretion approximately in the middle of the nocturnal sleep episode (21, 22). If the bright light treatment shifted the circadian system appropriately, melatonin should be released during the scheduled sleep time. Therefore, to assess adaptation to the shift schedule, we determined the overlap between the timing of melatonin secretion and the scheduled sleep times (in hours) for each shift schedule. Linear mixed-effects models were applied to study the effects of group (control versus treatment) CP (baseline, night, evening, and day shift), and their interaction on outcomes, with participant as random effect. For each CP, planned post hoc comparisons between the control and treatment groups were performed, where Bonferroni adjustments were used to account for multiple comparisons. Residual plots were checked for model fitting. Correlations between baseline melatonin timing and the degree of adaptation were assessed using Pearson's correlation coefficient.

PVT mean RT and median RT were recorded in milliseconds (ms). Lapses of attention were defined as RT >500 ms. To calculate reaction time distributions from the PVT, we first computed the 5th, 10th, 15th, 25th, 35th, 45th, 50th, 55th, 65th, 75th, 85th, 90th and 95th percentiles for the day, night, and evening shift CP for each participant. For each CP, these individual percentile values were then averaged across participants within each group to compute cumulative distributions for the day, night, and evening shift CP for the control and treatment group. We fitted a 4-parameter Weibull function to each average distribution using SAS PROC Reliability, which provided the overall description for each cumulative distribution (23). The CP (baseline, night, evening), group (control, treatment) and their interaction terms were included in the model. Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

Results

Twenty-nine participants completed the 27-day simulated shift work protocol, which included weekly counterclockwise shift rotations, for a total of 783 days of study. Complete data on each CP was not available for all participants, but their partial data remained included in the analysis when possible; for details see supplement 2.

Circadian adaptation

On the baseline (day shift), the melatonin amplitude was similar between the control (mean 37, SD 30 pg/ml) and the treatment group (mean 46, SD 24 pg/ml). The duration of melatonin secretion, the timing of MEL25%up, Midpoint, and MEL25%down, and the calculated overlap between melatonin secretion time and scheduled sleep time did not differ between the groups at baseline, as shown in table 1.

At the end of the week of night shifts, the MEL25%up and MEL25%down of the control group were shifted 6.4 hours and 4.7 hours later respectively, whereas the MEL25%up and MEL25%down of the treatment group had shifted by 7.2 hours and 6.5 hours. These group differences, along with differences in timing of midpoint, did not reach statistical significance due to large within-group variability (see table 1). In particular, there was a near complete absence of melatonin secretion for the entire 32-hour CP among 2 of the 12 control participants, precluding assessment of their melatonin phase (see supplementary figure S1). When we examined the phase relationship between the timing of melatonin secretion and the scheduled sleep times on the night shift, we found a longer overlap in the treatment group (mean 4.90, SD 2.8 hours) compared to the control group (mean 2.62, SD 2.8 hours; $t=-3.72$, $P=0.002$; see figure 2, panel A). The melatonin duration on the night shift was longer for the treatment group compared to the control group (7.48 vs 6.09 respectively; $t=-3.430$, $P=0.005$), as can be seen in figure 2, panel B. On both the evening shift and day shift, no significant differences between the control and treatment groups were found in the melatonin circadian phase markers, the duration of secretion, or the overlap between melatonin secretion and scheduled sleep.

On the night shift, the overlap between scheduled sleep and melatonin secretion showed significantly greater variability for both control and treatment participants compared to their overall variability at baseline (night shift SD 3 versus baseline day shift SD 0.5; repeated measures ANOVA $F=36.92$, $P<0.001$). Due to this large variability in adaptation to the night shift in both groups, we further explored individual differences in response. Overall, during the night shift the melatonin midpoint occurred during the scheduled sleep time in 8 of 12 treatment participants (67%),

whereas for the control participants, the melatonin midpoint occurred during the sleep time in only half of the participants (see figure 2, panel B). In contrast, for the evening shift and day shift, both groups showed 100% overlap between their melatonin midpoint and their scheduled sleep time. As examples, figure 3 shows melatonin profiles in relation to work and sleep times on each CP of a well-adapted treatment participant and a non-adaptive control participant on the night shift.

For the treatment group, we examined whether differences in melatonin timing at baseline (day shift) contributed to the variations in night shift adaptation. We observed a strong relationship between baseline (day shift) melatonin timing and the degree of adaptation on the night shift ($r^2 = -0.71$, $P = 0.01$) within the treatment group. The earlier a participant's melatonin timing at baseline (measured as midpoint of melatonin curve), the less adaptation (ie, hours of overlap between high melatonin secretion and sleep) was shown on the night shift (see figure 2, panel C). We also explored whether sex differences contributed to the variations in night shift adaptation within the treatment group. The 6 female participants had an average of 3.5 (SD 3.2) hours of overlap between melatonin timing and sleep timing, versus 6.3 (SD 1.6) hours among 6 male participants (Wilcoxon $S = 28$, $P = 0.09$).

Sustained attention

There were no significant differences in mean or median RT or number of lapses between the control and treatment groups at baseline or on any other shift, see supplementary table S1. There were no differences in the RT distributions between the control and treatment groups at baseline (see figure 4, presented as combined line). A significant difference in RT distribution was found between the control and treatment group during the night shift ($\chi^2 = 17.68$, $P < 0.001$) and the evening shift ($\chi^2 = 14.45$, $P < 0.001$). Within the treatment group, there were no differences in the RT distributions between the baseline, night or evening shift, showing that their response times during the night and evening shift remained similar to their response times at baseline. The control group did show a difference in response time distribution between the shift types ($\chi^2 = 8.91$, $P = 0.012$). There was a shift to the right in the entire RT distribution for the control group on the night shifts representing cognitive slowing (least mean square comparison vs baseline, $P = 0.003$), and a trend in the same direction on the evening shifts ($P = 0.07$). This is visible in the upper percentile values as shown in figure 4.

Discussion

We have demonstrated that exposure to bright light can facilitate circadian adaptation to night work and subsequent readaptation to evening and day work among participants scheduled to a counterclockwise shift rotation (ie, rotating weekly from day shift to night shift to evening shift to day shift). While counterclockwise shift rotations are currently not commonly used, they represent one of the most challenging schedules for rotating shift workers. In addition, while there have been numerous studies testing light treatments for circadian adaptation to the night shift, few studies have evaluated whether such treatments impact adaptation to subsequent shift rotations. Here we demonstrated that bright light treatment counteracted neurobehavioral response degradation not only during the night shift but also during subsequent evening work shifts.

To assess how the bright light treatment impacted the circadian system of the participants, our protocol included an assessment of the entire melatonin secretory episode at the end of each shift rotation. We did this based on prior studies showing that circadian interventions can not only shift the timing of the onset of secretion, it can independently affect the offset. Therefore, using only one circadian marker (such as the dim light melatonin onset, DLMO) can give an incomplete view of what happens to the entire melatonin secretion episode. As illustrated in figure 2 panel B, our novel method for evaluating shift work adaptation provides a more comprehensive analyses of the melatonin secretion offset, duration, and phase relationship to scheduled sleep timing.

We designed the light treatment schedule using a mathematical model of human circadian responses to light (14) and found that the light treatment, as predicted, could phase delay shift the circadian rhythm of melatonin secretion from day to night shifts to match the schedule of daytime sleep in the treatment group, despite their off-shift light exposure being uncontrolled. In contrast, participants in the control group showed more erratic responses, with 2.3 hours shorter overlap between melatonin secretion and scheduled sleep than in the treatment group. The finding that the control group still showed 2.6 hours of overlap could be due to the control group being exposed to the same

sleep/darkness times as the treatment group. Horowitz and colleagues (12) found that fixed sleep/wake times in darkness alone (without bright light exposure) induced a DLMO phase delay of ~3 hours on the night shift, whereas both fixed sleep/wake times and bright light during the night shift produced a physiological adaptation of ~7 hours on average, similar to what we observed in the treatment group in the present study.

Our results show that an individual's circadian phase prior to rotation on to the night shift accounted substantially for the variability in the circadian adaptation response to the treatment while on the night shift. This is likely due to the fact that bright light centered after an individual's body temperature nadir induces a phase advance rather than phase delay shift (24, 25), a limitation that could be overcome by restricting bright light exposure during the second half of the night shift (9, 12). Our finding that earlier melatonin timing was related to less adaptation to night work is consistent with data from field studies that show a negative association between morningness (early chronotype) and the ability to tolerate working at night (26).

Notably, two control participants exhibited no observable melatonin secretion during the entire 32-hour night shift CP, in contrast to their robust nocturnal melatonin secretion during baseline and subsequent CP (see supplementary figure S1). This finding of a loss of amplitude on the night shift was observed in a previous study after a gradual schedule inversion (27). An animal study by Filipski and colleagues (28) showed that a severe amplitude decrease in the corticosterone rhythm (23 to 6 ng/ml) was associated with accelerated tumor growth in SCN-lesioned mice. Furthermore, suppression of melatonin at night has been linked to increased risk for cancer in shift workers (29). More research is needed to understand the phenomenon of temporary loss of melatonin secretion following a schedule inversion in a subset of individuals, to examine whether this loss of melatonin amplitude might also be shown in other circadian rhythms (such as core body temperature or cortisol), and to understand what individual factors may contribute to this loss of amplitude. Much more research is needed to understand whether individuals exhibiting such a loss of melatonin secretion are more or less vulnerable to the adverse health consequences of night shift work. This research may be particularly important for older night shift workers and individuals taking melatonin-suppressing medications such as betablockers, many of whom already secrete lower amounts of melatonin at night (30).

When the participants made the transition from night to evening shifts, the treatment group had to make a larger adjustment, given the magnitude of adjustment they had made in adapting to the night shift. The finding that the treatment group showed similar melatonin phase timing as the control group on evening shifts, and that both groups showed similar overlap between melatonin secretion and scheduled sleep, demonstrates that the light treatment was successful in re-adaptation by the end of the weekly shift rotation. However, we did not assess adjustment on each individual shift, so we do not know the rate of adjustment to the evening shift that the two groups showed.

Future studies of the impact of light treatments on shiftwork adaptation should focus on sex as a potential relevant factor. Even though our sample size was small, we noticed a trend that the phase-shifting response to the bright light intervention among women was more variable than in men. There are reports that women are more adversely affected by night shifts than men (31, 32). Compelling evidence has shown that there are sex differences in both of the sleep-wake regulatory systems, the circadian system and the sleep-wake homeostat. Compared to men, women tend to be more morning types, have shorter circadian periods (33) and earlier entrained circadian phases (34). These well-defined biological sex differences may make women during the follicular phase of the menstrual cycle more vulnerable to shift work-related sleep loss and circadian misalignment compared to men (35, 36).

Besides enhancing circadian adaptation, the bright light treatment was effective in preventing the slowing of response times on both the night shift as well as on the evening shift. Participants in the treatment group who were exposed to bright light performed similarly on night and evening shifts to day shifts. In contrast, the control group showed significant slowing of their response times on the night and evening shifts, as shown in both laboratory and field studies (23, 37, 38). Our results confirm that adaptation of performance during the night shift can occur in conjunction with circadian adaptation, consistent with previous laboratory studies (39, 40).

Our study was subject to several limitations. First, the circadian phase estimation took place at the end of each work week, and we therefore could not determine the amount of overlap between melatonin secretion and sleep for the

initial shifts in each sequence. However, the advantage of our novel approach is that we assessed the entire melatonin secretion curve, including markers of secretion onset and offset (19). This allowed us to test whether there were alterations in the duration of the melatonin secretion episode, not just a change in the timing of melatonin onset (27). Second, we had no information on participants' light exposure after leaving the laboratory between shifts, and it has been reported that there are individual differences in shift workers' light exposure after work hours (41), which could have influenced their circadian adaptation. However, by allowing participants to leave the laboratory after each work shift, the bright light treatment had to be able to overcome light exposure during commuting times, a factor recognized to impede adaptation to night work. Third, we assessed circadian adaptation in response to bright light using the rhythm of plasma melatonin, a marker of the central clock located in the suprachiasmatic nucleus (SCN) of the hypothalamus, yet the human circadian system also comprises peripheral clocks found in most tissues and cells (42). While Cuesta and colleagues (43) showed that bright light exposure at night could rapidly reset both the central and peripheral clocks, we did not assess the status of any peripheral clocks. Finally, our study was carried out among non-shift working individuals who were very healthy, not taking medications, and asked to refrain from using caffeine and alcohol during the study. Thus, the generalizability of our results to actual shift workers should be taken with caution, and whether similar phase shifts and performance outcomes would be observed in actual shift workers remains to be tested. A recent field study by Bjorvatn and colleagues (44) found no effect of bright light treatment on subjective and objective sleepiness on night work and consecutive day work among nurses, which may have been due to the participants' use of medications and inappropriately-timed countermeasures or to inappropriate timing of the light intervention due to changing postures in an active work environment.

Overall though, our findings have important implications for rotating shift workers. They support the importance of acknowledging circadian principles in scheduling work hours (45) and also highlight the importance of taking into account individual circadian timing when applying a countermeasure designed to shift circadian phase. In fact, personalizing working times according to individual circadian timing (ie, chronotype) has been shown to reduce circadian disruption and improve sleep (46). Properly timed light regimens in accordance with individual circadian timing could be an effective workplace intervention for shift workers, improving their on-shift performance, health, and safety.

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Conflict of interest

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Sidebar

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Return-to-work, disabilities and occupational health in the age of COVID-19

Anonymous

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ABSTRACT (ENGLISH)

Recommendations such as physical and social distancing and wearing a facemask are highly advisable to protect against infection but may not be enough to enable some individuals to resume work. [...]decision-making requires individual comprehensive assessments of the underlying medical condition, the SARS-CoV-2 contamination risk associated with either regular work or teleworking, and vaccination opportunities. Strategies promoting return to work for these workers will need to be implemented and could be similar to programmes developed for other chronic conditions. [...]numerous more serious sequelae following critical illness suggest the need for enhanced support by rehabilitation and occupational health specialists. [...]the consequences of the epidemic must be evaluated over time for people who suffered from functional limitations before COVID-19 as their physical and mental condition may be modified by the epidemic and, specifically, the consequences of lockdown (10).

FULL TEXT

We have read with great interest the two editorials by Burdorf et al: The COVID-19 pandemic: one year later - an occupational perspective (1) and The COVID-19 (Coronavirus) pandemic: consequences for occupational health (2). The authors highlight the importance of the societal consequences of the outbreak and changes in the world of work to manage occupational health. The key points identified - such as individual socioeconomic factors, psychological effects and occupations with highest risk of contamination - modify return-to-work approaches.

It is estimated that around 800 million people of working age worldwide were living with disabilities before the SARS-CoV-2 pandemic. In early January 2021, the cumulative COVID-19 hospitalisation rate reached 207.4/100 000 (18-49-year-olds) and 505.7/100 000 (50-64-year-olds), respectively, in the United States (3). In France, the hospitalisation rate was 411.5/100 000 across all ages (4). A recent cohort study of working-age men who were hospitalised for COVID19 highlighted the long-term health consequences of such a disease (5).

The SARS-CoV-2 pandemic creates new challenges for occupational health, shifting attention away from return-to-work after health problems to resuming work during an outbreak, dealing with lockdown, and taking special account of workers with vulnerabilities (6, 7).

We recommend considering three different aspects of occupational medicine during a pandemic. Firstly, for most workers at high-risk of severe COVID-19, the issues of work disability and resuming work had never occurred before the epidemic. Recommendations such as physical and social distancing and wearing a facemask are highly advisable to protect against infection but may not be enough to enable some individuals to resume work. Therefore, decision-making requires individual comprehensive assessments of the underlying medical condition, the SARS-CoV-2 contamination risk associated with either regular work or teleworking, and vaccination opportunities. The second situation concerns workers who have suffered from COVID-19. Preliminary studies suggest that long recovery duration is related to high severity (7), but this is still a matter of debate for patients suffering from long

COVID-19 (5, 8, 9), a condition for which the long-term effects remain unknown. Any longrunning recovery must be considered to be a potential sign of long COVID-19. These long-lasting syndromes occur among patients with severe symptoms but have also been reported independently of acute phase severity, hospitalisation and receiving medical oxygen (8, 9). Researchers worldwide are currently investigating such syndromes. Strategies promoting return to work for these workers will need to be implemented and could be similar to programmes developed for other chronic conditions. Moreover, numerous more serious sequelae following critical illness suggest the need for enhanced support by rehabilitation and occupational health specialists.

Finally, the consequences of the epidemic must be evaluated over time for people who suffered from functional limitations before COVID-19 as their physical and mental condition may be modified by the epidemic and, specifically, the consequences of lockdown (10).

In all of these situations, medical, social, financial and working contexts are key elements. In addition to a medical assessment, the use of scales such as the Work Ability Index (WAI) (11) or the Work Productivity and Activity Impairment (WPAI) (12) can help perform long-term follow-up and provide information about work capacity and workload. It also gives a back to basics perspective, urging politicians to move towards a 'decent-work-for-all' policy, as advocated by the United Nation's Sustainable Development Goal (SDG) 8, which the WHO has endorsed (13).

Sidebar

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DETAILS

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Patterns of working hour characteristics and risk of sickness absence among shift-working hospital employees: a data-mining cohort study

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ABSTRACT (ENGLISH)

Objectives Data mining can complement traditional hypothesis-based approaches in characterizing unhealthy work exposures. We used it to derive a hypothesis-free characterization of working hour patterns in shift work and their associations with sickness absence (SA). **Methods** In this prospective cohort study, complete payroll-based work hours and SA dates were extracted from a shift-scheduling register from 2008 to 2019 on 6029 employees from a hospital district in Southwestern Finland. We applied permutation distribution clustering to time series of successive shift lengths, between-shift rest periods, and shift starting times to identify clusters of similar working hour patterns over time. We examined associations of clusters spanning on average 23 months with SA during the following 23 months. **Results** We identified eight distinct working hour patterns in shift work: (i) regular morning (M)/evening (E) work, weekends off; (ii) irregular M work; (iii) irregular M/E/night (N) work; (iv) regular M work, weekends off; (v) irregular, interrupted M/E/N work; (vi) variable M work, weekends off; (vii) quickly rotating M/E work, non-standard

weeks; and (viii) slowly rotating M/E work, non-standard weeks. The associations of these eight working-hour clusters with risk of future SA varied. The cluster of irregular, interrupted M/E/N work was the strongest predictor of increased SA (days per year) with an incidence rate ratio of 1.77 (95% confidence interval 1.74-1.80) compared to regular M/E work, weekends off. Conclusions This data-mining suggests that hypothesis-free approaches can contribute to scientific understanding of healthy working hour characteristics and complement traditional hypothesis-driven approaches.

FULL TEXT

Headnote

Objectives Data mining can complement traditional hypothesis-based approaches in characterizing unhealthy work exposures. We used it to derive a hypothesis-free characterization of working hour patterns in shift work and their associations with sickness absence (SA).

Methods In this prospective cohort study, complete payroll-based work hours and SA dates were extracted from a shift-scheduling register from 2008 to 2019 on 6029 employees from a hospital district in Southwestern Finland. We applied permutation distribution clustering to time series of successive shift lengths, between-shift rest periods, and shift starting times to identify clusters of similar working hour patterns over time. We examined associations of clusters spanning on average 23 months with SA during the following 23 months.

Results We identified eight distinct working hour patterns in shift work: (i) regular morning (M)/evening (E) work, weekends off; (ii) irregular M work; (iii) irregular M/E/night (N) work; (iv) regular M work, weekends off; (v) irregular, interrupted M/E/N work; (vi) variable M work, weekends off; (vii) quickly rotating M/E work, non-standard weeks; and (viii) slowly rotating M/E work, non-standard weeks. The associations of these eight working-hour clusters with risk of future SA varied. The cluster of irregular, interrupted M/E/N work was the strongest predictor of increased SA (days per year) with an incidence rate ratio of 1.77 (95% confidence interval 1.74-1.80) compared to regular M/E work, weekends off.

Conclusions This data-mining suggests that hypothesis-free approaches can contribute to scientific understanding of healthy working hour characteristics and complement traditional hypothesis-driven approaches.

Key terms employee scheduling; nurse rostering; occupational health; permutation distribution clustering; sick leave; shift work; shift worker.

(ProQuest: ... denotes formulae omitted.)

Shift work prevalence is 22% in the European working age population (1) and 20-25% in developed countries (2). Shift work has been linked to increased risk of sickness absence (SA), occupational injuries, depression and various chronic conditions including the metabolic syndrome, type 2 diabetes mellitus, and coronary heart disease (2-6). However, shift work captures a wide range of working hour arrangements, such as fixed night shift work; rotating eight-hour shifts (bulk shift at a.m., p.m., and night); and irregular shift work characterized by a non-standard schedule with varying start and finish times, shift lengths, and rest periods between shifts (7). Working hour characteristics in shift work can also vary in terms of the length of the working hours (eg, the length of work shifts or work shift spells), shift intensity (defined by time between the individual shifts), and time of the day (timing of work shifts) (8). It remains uncertain which specific patterns of shift work are harmful as the concept of shift work captures a wide and heterogeneous set of working hour arrangements

To date, most shift work research has been focused on one or few pre-defined shift work patterns rather than the full range of different shift work patterns. This approach does not capture interrelations between working hour characteristics, which can have different effects on health, and it may also fail to capture relevant temporal aspects of the target working hour characteristic. Wherein traditional statistical approaches often operationalize and test one confounding variable at a time, data-mining approaches can take in large quantities of data and automatically find patterns of confounding. Long work shifts, for example, are more common in hospitals during the nights and are often followed by longer time-off (9, 10). By implication, quick returns (ie, short recovery after shift) are inversely associated with long shifts, which may contribute to the unexpected findings in studies that are focused on a single

working hour characteristic only because both quick returns (11) and long working hours (3, 4) are associated with increased risk for negative health and well-being effects. An earlier study found that long work shifts were associated with less sick leaves among hospital employees working irregular shifts raising speculations that the risk estimates for long shifts were confounded by other protective effects, such as longer recovery periods after the long shifts (12). More generally, the researcher- or hypothesis-derived pre-defined shift work patterns represent only a small subset of possible patterns, whereas modern data-mining tools would allow systematic exploration through a vastly larger space of possible patterns present in the given data.

In this study, we used data-mining tools to define working hour patterns in shift work over prolonged periods based on the following shift-specific parameters: work shift length, between-shift rest period, and shift starting time. The main aims of the paper were to: (i) characterize working hour patterns in shift work by means of permutation distribution clustering as a datamining tool, and (ii) study associations between these shift work patterns and sickness absence.

Methods

Study population

We used working hour data from employees of the Hospital District of Southwest Finland. A total of 6029 hospital employees (506 men and 5523 women, mean age 39.37 years, range 18-70 years) were included in the analyses. Their work contract, or succession of contracts under the same employer, had lasted >3 years (3x365 days) basically uninterrupted (pauses of <4 days were allowed). The longest uninterrupted sequence of data per employee was used when more than one >3-year sequences were available. The included employees were also working full-time in all 1-year time windows within their longest uninterrupted data sequence. Full-time work was defined as >150x7.75 realized work hours per year (ie, in all 52-week windows; only ~8% did not satisfy the condition). We excluded physicians and, based on the work contracts, the employees having an office-hour contract so we could concentrate on hospital employees in shift work (mostly registered nurses by occupation).

Data on working hour characteristics

The records of working hours were drawn from Titania® shift-scheduling program including the final realized working hours used for payroll. For each employee, we derived work shift lengths, between-shift rest periods (time after index shift and before the next shift), and shift starting times for all available successive shifts to capture the entirety of the employees' recorded work time from 1 January 2008 to 27 August 2019 in a format conducive of time-series clustering. Therefore, the data contained the three work shift-related dimensions arranged along the dimension of work-shift succession (technically, a discrete 3-dimensional time series), and could contain up to 7845 scalar-valued observation values per employee. Work shifts starting immediately after a previous one (with 1-minute precision) were considered to be part of the previous work shift (ie, they were removed after adding their hours to the previous shift). Unreliable short entries (all <3 hours) were removed according to previously defined procedures (8).

Shift-ergonomics risk score

We also evaluated the data-driven clusters against risk scores derived from the Finnish Institute of Occupational Health (FIOH) recommendations for shift ergonomics (13). To evaluate the novel content in our cluster solution, it was preferable to compare them to the existing constructs for shift ergonomics. The FIOH recommendations have been integrated into the data-generating Titania shift-scheduling software and are used for the automatic evaluation of work shift patterns (8, 13, 14). We used three main characteristics currently considered most important by FIOH (8, 13) to derive work burden (overload) risk scores (range 0-3). The risk scores were based on (i) total work time between two days off work, (ii) number of night shifts over a 3-week period, and (iii) number of quick returns between two days off work (see supplementary material, appendix A for quantitative definitions <https://www.sjweh.fi/article/3957>).

Sickness absence data

The data on SA were derived from working hour records, which include dated indicators for absence due to sickness but no diagnosis (15, 16). SA was selected as an objective register-based outcome of high interest but was not used for deriving working hour characteristics clusters.

Statistical analysis

Time series clustering. Our first aim was to detect clusters of different patterns amongst the 3-dimensional working hour characteristics time series ... where t index successive work shifts, w working hours, r rest-hours (recovery) after the work shift, and s work shift start time in hours (ie, $x_{t,s} \in [0,24)$ o'clock; note, night shifts get implicitly represented by work shift start time and length). That is, we conducted time series clustering for data where each 3-dimensional time series represented a unique employee. We aimed at a maximally data-driven (hypothesis-free and nonparametric) approach, sensitive to patterns rather than mean levels, and robust to variation in mean levels and extreme values (for generalizability and reproducibility). Amongst the many alternatives (21, 22), we considered permutation distribution clustering (PDC) method as the most fitting starting point (23, 24).

PDC is an approach to cluster a set of time series to subsets of time series that show high within-subset 'similarities' and lower between-subset similarities. The PDC method is defined by the distance metric it gives to two distinct time series to quantify the similarity of their probability distributions. To arrive at the most suitable number of subsets, or clusters, we used the hierarchical agglomeration with complete linkage for clustering and Bayesian information criterion (BIC) to evaluate model fit per number of clusters (23, 24).

We used the default distance function of the `pdc` R package version 1.0.3, the "symmetric alpha divergence", which represents distance between two discrete probability distributions (23, 24). To map time series onto probability distributions, the PDC method embeds a time series ... sampled at equal intervals i onto a t -delayed d_a -embedding

... with a total of $f = f - (m - 1) \times d_a$ elements. Here, $d_a = 7$ and $t = 1$ were selected by an entropy heuristic (23, 24). Each element of the embedding is thus a set with d_a elements (ie, d_a successive original timeseries values) that can be sorted to ascending order by an appropriate permutation function (for instance, a function $n: \{2,3,1\} \wedge \{1,2,3\}$, if $d_a = 3$). Several elements of the embedding may get sorted by the same permutation (eg, the replacement $\{2,3,1\} \wedge \{1,2,3\}$), but many permutations are needed to sort them all and their rates depend on the original time series. An empirical permutation distribution for a time series is constructed by sorting each member of its embedding and by counting frequencies for the ensuing permutations, or codewords, $n \in S_m$, where S_m is the set of all d_a -permutations (ie, size of the set is $|S_m| = m!$ and we get T samples on it per univariate time series). These permutation distributions are called codebooks and each employee has three of them, one for each dimension of their working hour characteristic time series. The total distance between two employees is a square root of the sum of their squared symmetric alpha divergences (technical note: this "divergence" also happens to be a "distance"). After the clusters were derived, their contents were explored for interpretation by plotting specific examples and densities of probability distributions with the `ks` R package, version 1.11.7 (default kernel).

Poisson regression for predicting sickness absence. We used Pearson's chi-squared and Welch's t-tests for simple two-group comparisons, whereas Poisson regression models were used to study associations between timeseries clusters and SA days, with the unit days per year (ie, per 365 days). We modeled a count outcome with offset $\log(T/365)$, where T denotes number of days the employee was followed. Regression coefficients are reported as incidence rate ratios (IRR) and their 95% confidence intervals (CI). To improve comparability between binary and continuous regression inputs, we standardized continuous inputs by subtracting mean and dividing by 2 standard deviations (26).

We first regressed SA on independent variables over the entire follow up periods (cross-sectionally) and then (prospectively) regressed SA from latter halves of the follow up periods on independent variables defined from the first halves of the periods. That is, we defined the first half of an employee-specific time series as the past and the second half as the future. The FIOH risk scores were recomputed for the 'past' only to support prospective regression modeling. The cluster memberships were also recomputed using only the first half of the employee-specific time-series data.

To assign cluster membership based on half the original time series, we recomputed the codebooks from the selected data half and then investigated their distances from all employees' codebooks based on all of their data. The assigned 'past' cluster membership was that of the nearest neighbor in original full-data codebooks. Cluster

assignments were the same as for the full data for 99.82% of observations (altogether 99.25% of the first data half were nearest neighbors to themselves in the full data). Notice that the consecutive contract days in the data (the follow-up time) were employee-specific, meaning that the outcome of 'future' SA days per year was aggregated over periods that differed between the employees. However, the unit "per year" (achieved via the offset term) is independent of the length of the aggregation period and each employee had >1.5 years of 'future' data and at least three years of data altogether.

Tools for future research

Although we used halves of the original time series, the above-discussed algorithm for assigning cluster membership can be used to arbitrary new time series of a similar type. We release the codebooks based on our data together with our cluster-assignment algorithm to support further research. These are available online in the form of fiohpd R package: <https://bitbucket.org/rosenstroem/fiohpd>.

Results

The permutation distribution clustering favored an eight cluster solution, as characterized in table 1 (absolute BIC difference >127919 to other solutions). While some clusters had small number of employees, recall that each employee may entail up to 7845 numeric observations.

Cluster contents

In table 2, we provide our interpretations of the cluster contents for the convenience of the reader. However, this is not an exhaustive listing of their properties. The interpretations in table 2 arise from examining empirical shift-by-characteristic densities (cf. figure 1), average autocorrelations (cf. figure 2), basic descriptives (table 1), and examples of individual sequences of work shifts (the supplementary material shows more data characterizing the cluster contents). The distribution of between-shift rest periods was a long-tailed distribution containing many observations <24 hours but also occasional very long 'rests' (eg, holidays). In the figures, we therefore investigated logarithm of rest length: logtransformation retains relative order but shortens the tail (the assumption here is that eg, difference of 1 versus 2 months rest is less consequential than a difference of 1 versus 2 days).

For example, cluster #5 clearly had more variable shift lengths and shift start hours than reference cluster #1 (figure 1). Compared to the other clusters, cluster #5 contained relatively short careers within the target employee population (table 1).

To further characterize differences between the clusters, we investigated the relative contributions of the three time series dimensions to the average distances between the clusters. For example, the dimension-wise average distances between clusters #1 and #5 were 1.76, 2.23, and 1.34 for the dimensions of work shift length, between-shift rest period, and start hour, respectively. In this sense, clusters #1 and #5 differed most in their between-shift rest periods. Similarly, the distances, eg, between clusters #1 and #7, were 1.67 (shift length), 2.69 (recovery), and 2.08 (start) while those of #7 and #8 were 1.07 (shift length), 2.57 (recovery), and 1.67 (start). These patterns suggest that largest differences between clusters involve between-shift rest periods.

To understand the between-shift rest periods permutation distributions beyond cluster-average distributions, figure 2 presents the cluster-average autocorrelations of between-shift rest periods. From figure 2, we observed that employees in cluster #1 followed on average a regular pattern where every fifth rest-length was strongly positively correlated, probably representing weekends. This pattern was even more pronounced in cluster #4, which turned out to be protective against sick leaves. The pattern was less pronounced in cluster #5 and missing from cluster #7. The latter cluster fitted better with a cycle where four work shifts are followed by a longer rest and then three work shifts. Thus, some clusters (eg, #5) were associated with less predictable work-rest cycles than others (eg, #1), but not necessarily with much less between-shift rest periods or a better FIOH recovery risk score (cf. table 1).

The small clusters - #7 and #8 - also differed in their marginal distributions for rest hours. Whereas the FIOH risk scores indicated similar levels of quick returns assessed in <11-hour rests (table 1), 32.4% of shifts in cluster #7 were followed by <13 hours of rest - significantly more than the 14.48% in cluster #8.

Although clusters #4 and #6 were similar to each other in many respects, an examination of individual employees shift patterns led to a hypothesis that cluster #6 had much more variable exact work shift lengths and starting times

than cluster #4 (despite both involving morning shifts).

Associations between clusters and sickness absence

Table 3 presents the associations between the work shift patterns and SA. We chose cluster #1 as a reference cluster because it represented a comparatively large cluster of regular, a priori non-risk working hour conditions, and had no SA trend (table 1). In general, the clusters were associated with SA rates over and above (adjusting for) sex and age (Model 1, table 3). The clusters were also associated with SA when adjusting for sex, age, and the three FIOH risk scores on working hours (Model 2, table 3), and also while controlling for historical employee-specific SA rates (Model 3, table 3).

Working hour clusters #1, #4, and #8 were associated with the lowest SA rates. Cluster #7 implied an elevated risk. Cluster #5 implied the highest risk among all the covariates, followed by clusters #3 and #6.

Discussion

In this study of 6029 hospital employees in mainly fulltime shift work during a 12-year follow up, we identified eight distinct working hour patterns in a data-driven clustering analysis of the entire work-time series. These patterns ranged from relatively regular morning- and evening-oriented shift work with weekends off (cluster #1) to highly irregular working hours with night and weekend shifts under short contracts (cluster #5). The clusters associated with unpredictable or irregular working hours, short between-shift rest periods, or short contracts (clusters #2, #3, #5, #6, #7) were associated with greater risk of future SA than clusters lacking these features (clusters #1, #4, and #8). Cluster #5, which combined these features, was most strongly associated with the risk of SA.

In general, our data-driven strategy corroborated previous hypothesis-based research on the associations of working hour characteristics with SA risks. For example, quick returns, irregular working hours and night and weekend shifts were more common in clusters associated with high SA rates (11, 16). It was also clear both quantitatively and qualitatively (see below) that the comprehensive data clusters captured novel risk characteristics that are not usually identified when analyzing pre-defined working hour characteristics separately. For example, cluster effects on SA rate were comparable to predicting SA with earlier SA while also withstanding an adjustment for earlier SA. This is noteworthy as history of SA is a known strong predictor of SA rate (27, 28). Furthermore, FIOH risk scores, based on a traditional hypothesis-driven approach, offered little information on SA beyond the clusters. The next paragraph outlines other new insights.

First, both clusters #3 and #5 could be characterized by the above high-risk working hour characteristics, but cluster #5 implied even greater risk of SA than cluster #3 - even though the reverse should have happened, if anything, based on associations with the earlier risk scores (table 1). However, the employees in cluster #5 had shorter and more gapped contracts than those in #3. The career interruptions may have been caused by SA (implying reverse causation), but they may also cause job insecurity and relational injustice that might have complex effects on SA rate (29). Future studies of work hour characteristics and SA might benefit from considering contract length and form (temporary versus permanent).

Second, based on broad qualitative characterizations it might have been difficult to tell apart the employees in clusters #4 and #6, both of which were associated with morning-oriented work with free weekends (table 2). Yet, the data-driven clustering method alerted us to some difference between clusters 4 and 6 and, indeed, cluster #6 was associated with an increased risk of future SA and cluster #4 with a decreased risk. We then observed that cluster #6 contained more variation in shift length and starting time within the set of morning shifts than cluster #4. This suggests presence of either an internal or an external factor that hinders the employees settling on an accurate work routine, which may contribute to SA. Thus, future studies could be conducted on the finegrained variations in morning-oriented shift schedules and related factors. For example, employee possibility to control working hours via participatory working time scheduling can decrease SA and presumably alter working hour patterns (30).

Third, previous research has investigated quick returns (<11 hours), probably because that has been the minimum daily rest in European Working Time Directive (11) and, yet, our data-driven analysis uncovered groups (clusters #7 and #8) that had negligible difference in quick returns, while having over two-fold differences in <13-hour returns and SA risk. This suggests that 13 hours between-shift rest period (ie, rest hours) might be a threshold for recovery for

employees in hospital care. Future studies could question the typical threshold of quick returns (<11 hours) and instead consider a wider range of rest periods. These examples suggest how data-driven investigations could increase accuracy and coverage of research in the field by addressing 'unknown unknowns' (by exploration), not just 'known unknowns' (apriori hypotheses).

Our study presented an investigation of register-based working-hour time series in relation to health that was data-driven and hypothesis-free, to an unprecedented degree to our knowledge. Besides that, the strengths of the study were a large amount of reliable (objective, payroll-based) register data on the real-world working hour characteristics of shift work and SA in hospitals, a robust and general clustering procedure, and adjustments for both historical SA and previous risk scores.

Limitations of our study include it being an observational data-driven study with the associated limitations to causal inference, and possible limited generalizability due to having data from just one, albeit large, hospital district in Finland. For example, in some of our clusters, the number of men was low, although that is generally in line with female-dominated sex distribution in healthcare sector (31). As people with particular socioeconomic and health profiles may select into particular shift work schedule, future studies should address unmeasured confounders, such as having children. Those researchers who have been able to measure such variables could use our `fiohpdc` package to assess their possible relationships with our clusters (see Methods section). One might also further gauge the generalizability of clusters #7 and #8 that, while reflecting tens of thousands of sequential numeric observations, nevertheless had only few employees in our data. In addition, data-analytic approaches like the present one are frequently limited by their many degrees of freedom for the researchers. For example, besides BIC, we also tested Akaike's information criterion for selecting the appropriate number of clusters, but that would have led to very many small clusters and therefore BIC appeared to us as a principled and pragmatic choice (25). Nevertheless, there remains scope for investigating alternative cluster solutions, and alternative time series clustering methods, such as methods using autocorrelation-based or Maharaj distances (21, 22). We hope the present work inspires others through our released cluster assignment package that allows others to map their data on our cluster as closely as possible (see Methods).

In summary, our data-driven cluster analysis identified eight different clusters of working hour characteristics in shift work among hospital employees. The identified shift work clusters were associated with the rate of SA after adjusting for previous SA and previously suggested risk scores. The strongest risk of SA was associated with highly irregular working hours with night and weekend shifts and interrupted job contracts.

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Conflicts of interest

The authors declare no conflicts of interest. The funders of the study had no role in (i) study design, (ii) the collection, analysis and interpretation of the data, (iii) the writing of the report, and (iv) the decision to submit the paper for publication.

Sidebar

Rosenström T, Härmä M, Kivimäki M, Ervasti J, Virtanen M, Hakola T, Koskinen A, Ropponen A. Patterns of working hour characteristics and risk of sickness absence among shift-working hospital employees: a data-mining cohort study. *Scand J Work Environ Health*. 2021;47(5):395-403. doi:10.5271/sjweh.3957

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DETAILS

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Heart rate during work and heart rate variability during the following night: a day-by-day investigation on the physical activity paradox among blue-collar

workers

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ABSTRACT (ENGLISH)

Objectives Contrary to leisure-time physical activity, occupational physical activity (OPA) may have harmful health effects, called the physical activity paradox. A proposed mechanism is that OPA can elevate the heart rate (HR) for several hours per day. We aimed to investigate the association between the mean intensity of OPA and HR variability (HRV) indices the following night. **Methods** Three cohorts (NOMAD, DPhacto, and Physical Workload and Fitness) involving blue-collar workers from different sectors were merged in this study. HR monitors (Actiheart) recorded 24-hour inter-beat intervals (IBI) for up to four consecutive days. The relative intensity of the mean HR during work was estimated by HR reserve (%HRR), and time-domain indices of HRV were analyzed during the following night. Data were analyzed using a multilevel growth model to test the association between mean %HRR during work and HRV indices at night in a day-by-day analysis adjusted for age, BMI, alcohol consumption, smoking, and occupation. **Results** The dataset included a sample of 878 Danish blue-collar workers, with a mean %HRR during work of 31%, and 42% worked at an intensity >30%HRR. The multilevel model showed negative within- and between-subject associations between %HRR during work and HRV indices at night. **Conclusions** Our results indicate a higher %HRR during work to associate with lower HRV indices the following night and a higher HR, reflecting an imbalanced autonomic cardiac modulation. This finding supports a high mean HR during work to be a potential underlying mechanism for the harmful health effect of OPA.

FULL TEXT

Headnote

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Objectives Contrary to leisure-time physical activity, occupational physical activity (OPA) may have harmful health effects, called the physical activity paradox. A proposed mechanism is that OPA can elevate the heart rate (HR) for several hours per day. We aimed to investigate the association between the mean intensity of OPA and HR variability (HRV) indices the following night.

Methods Three cohorts (NOMAD, DPhacto, and Physical Workload and Fitness) involving blue-collar workers from different sectors were merged in this study. HR monitors (Actiheart) recorded 24-hour inter-beat intervals (IBI) for up to four consecutive days. The relative intensity of the mean HR during work was estimated by HR reserve (%HRR), and time-domain indices of HRV were analyzed during the following night. Data were analyzed using a multilevel growth model to test the association between mean %HRR during work and HRV indices at night in a day-by-day analysis adjusted for age, BMI, alcohol consumption, smoking, and occupation.

Results The dataset included a sample of 878 Danish blue-collar workers, with a mean %HRR during work of 31%, and 42% worked at an intensity >30%HRR. The multilevel model showed negative within- and between-subject associations between %HRR during work and HRV indices at night.

Conclusions Our results indicate a higher %HRR during work to associate with lower HRV indices the following night

and a higher HR, reflecting an imbalanced autonomic cardiac modulation. This finding supports a high mean HR during work to be a potential underlying mechanism for the harmful health effect of OPA.

Key terms aerobic workload; autonomic nervous system; heart rate reserve.

High levels of leisure-time physical activity (LTPA) has consistently been associated with better health (1, 2). In contrast, high levels of occupational physical activity (OPA) have recently been linked to increased risk for cardiovascular disease and mortality (3, 4), constituting the physical activity health paradox (5).

The mechanisms behind the potential detrimental health effect of OPA remain to be disentangled, as highlighted in the WHO guidelines for physical activity (6). A conceptual framework providing hypotheses of the characteristics of physical activity and physiological responses that can explain the physical activity health paradox has recently been proposed (5). One of the proposed explanations is that a raised heart rate (HR) during work, for several hours per day, can cause an imbalanced autonomic cardiac activation (7). Imbalanced autonomic cardiac activation is well documented to increase the risk for cardiovascular disease and mortality (8-10). However, this proposed mechanism for the physical activity paradox has not previously been investigated.

The relative intensity of OPA can be assessed by device-worn HR sensors and estimated as percent HR reserve (%HRR), calculated from HR at rest, during working hours, and age-predicted maximum HR (11). The autonomic cardiac activity can also be measured by device-worn HR sensors using HR variability (HRV) analysis. Although some previous studies suggest that higher OPA is related to reduced resting or sleeping HRV (7, 12), studies have not addressed the temporal association between daily changes in the relative intensity of OPA and HRV indices at night. Such analysis should aim to be without confounding from individual factors such as age, sex, cardiorespiratory fitness, and could therefore be performed in an analysis of the day-to-day effect on HRV indices at night from the %HRR during work. No previous studies have investigated the day-to-day effects of the relative intensity of OPA on HRV indices at night using relative aerobic workload (%HRR) as the exposure measure among blue-collar workers, being occupational groups with no or short educations and exposed to manual work.

Thus, this study aimed to investigate the association between the daily mean intensity of OPA and HRV indices the following night among blue-collar workers. We hypothesized a negative association between %HRR and HRV indices the following night.

Methods

Study design

This study is based on harmonized data from three occupational field cohorts using continuous sampling of physiological parameters.

Study population and exclusion criteria

Data from blue-collar workers from the "New method for Objective Measurements of physical Activity in Daily Life" (NOMAD) (13) and "Danish Physical activity cohort with objective measurements" (DPhacto) cohorts (14), and baseline data from a cluster-randomized worksite intervention among cleaners "Physical Workload and Fitness" (15) were merged in this study.

The NOMAD, DPhacto, and Physical Workload and Fitness studies were conducted on workers recruited in Denmark. The inclusion criteria for the three studies were to be (i) allowed to participate during paid working time, (ii) employed for >20 hours per week, and (iii) aged >18-<65 years. Exclusion criteria were: (i) declining to sign the informed consent, (ii) pregnancy, (iii) fever on the testing day, and (iv) an allergy to adhesives. Population and recruitment were described in detail elsewhere (13-15).

Inclusion in the present analysis was based on the following criteria: availability of data on diurnal and nocturnal HR from the 24-hour ECG recordings with a minimum duration of >4 hours per day during work time, and a minimum duration of >4 hours per night during sleep time.

The Ethics Committee for the Capital Region of Denmark approved the NOMAD, DPhacto, and Physical Workload and Fitness studies (journal number H-22011-047, H-2-2012-011 and H-2-2011-116, respectively) and all three studies were conducted following the Helsinki Declaration. Informed consent was obtained from all participants included in the study.

Data collection

The technical measurements and questionnaires were similar across studies to enable harmonization of the data. A questionnaire was administered to the workers including age, sex, ethnicity, tobacco use, alcohol consumption, use of anti-hypertensive, anti-depressive, and heart medications. Occupational factors were also collected by the questionnaire and included present occupation (sector), job seniority, and occupational lifting/carrying.

Height (cm) was measured using a scale (Seca, model 123) and weight (kg) was measured by a digital scale (Tanita model BC 418 MA). Body mass index (BMI) was calculated according to the formulae $BMI = \text{weight (kg)}/\text{height (m)}^2$. A submaximal fitness test on a cycle ergometer (16) or a submaximal step test (17) was performed to indirectly estimate $VO_{2\max}$ as a parameter of cardiorespiratory fitness ($\text{mlO}_2/\text{min}/\text{kg}$).

A HR monitor (Actiheart system, CamNtech Ltd., Cambridge, UK) was mounted for 24-hour measurements of RR intervals (RRI). The workers were instructed to wear the device continuously for up to four consecutive days, and only to remove it in case of skin irritation. The electrodes were attached to the chest, according to previous recommendations (18). The respiratory rate was not controlled during data collection. Data were sampled at 128 Hz and processed using a band-pass filter (10-35 Hz). The participants also received a diary, in which they were asked to write the time they went out of bed in the morning, started to work, finished work, went to bed in the evening, and periods of non-wear time.

The data were downloaded using the Actiheart software and processed in the Acti4 software (The National Research Centre for the Working Environment, Copenhagen, Denmark and Federal Institute for Occupational Safety and Health, Berlin, Germany) (19). The inter-beat intervals (IBI) were used to calculate the relative aerobic workload during work and leisure and HRV indices.

The relative aerobic workload was estimated by the %HRR, which was calculated using the equation:

$\%HRR = [\text{HR}_{\text{work}} - (\text{HR}_{\text{max}} - \text{HR}_{\text{min}})] / (\text{HR}_{\text{max}} - \text{HR}_{\text{min}}) \times 100$ (20). The minimum HR (HR_{min}) was defined as the 10th lowest HR for 24 hours including sleep time (21) and the maximal HR (HR_{max}) was estimated as $\text{HR}_{\text{max}} = 208 - 0.7 \times \text{age}$ (11).

Based on the RRI series, HRV indices were analyzed from 5-minute windows with <5% erroneous RRI, both in the time and frequency domains. Abnormal beats were automatically removed before analyzing parameters of HRV. Besides the time-domain mean inter-beat interval (IBI) (ms), the HRV indices analyzed were the square root of the mean squared differences of successive IBI (RMSSD), and the standard deviation of IBI (SDNN). Mean IBI and SDNN both reflect parasympathetic as well as sympathetic modulation of the cardiac rhythm, but RMSSD is only an indicator of the parasympathetic modulation of cardiac rhythm (22, 23).

Data analysis

A day-by-day analysis was conducted using a multilevel growth model (ie, linear mixed model), with random intercept and slope, which enabled multiple measurements for each participant. %HRR during work was paired with parameters of HRV during the following night. An unstructured covariance structure was applied. The analysis was performed using unadjusted and adjusted models. In models, the workday was entered as a level-1 predictor. Moreover, weekly mean %HRR during work and the difference between daily and weekly mean %HRR during work were entered as level-2 predictors. This way, weekly mean %HRR during work enabled estimation of the between-subject effect whereas the difference between daily and weekly mean %HRR enabled estimation of the within-subject effect. Moreover, an interaction between weekly mean %HRR during work and workday was entered. In case the interaction term was non-significant ($P > 0.05$), it was excluded from the fully adjusted model. In the adjusted models, age, sex, BMI, alcohol consumption, smoking status, and present occupation (sector) were considered as potential confounders and entered as level-2 predictors. IBI, SDNN, and RMSSD values were considered as outcomes in both crude and adjusted models separately for each outcome. As the SDNN and RMSSD values were not normally distributed, the values were log-transformed. A total of 878 individuals and 1253 observations were included. The statistical models were built with a repeated statement taking the clustering of observations from the same participant into account.

A secondary analysis stratified on mean occupational aerobic workload (</>30% HRR) across all included workdays

was performed to investigate differences in associations between occupational aerobic workload and HRV indices at night. This cut-point of occupational aerobic workload was based on the recommendations from the International Labor Organization (24, 25).

A sensitivity analysis was conducted by stratifying on groups of users versus non-users of anti-hypertensive, anti-depressive, and heart medications. This was done as the effect on HRV may be reversed, concealed, or distorted by the use of these medications (26). Additionally, as the elevation in HR is relative to the individual cardiorespiratory fitness and age, and therefore may identical OPA tasks employ higher strain among less fit/older than more fit/younger workers (27). Thus, interaction terms between mean %HRR during work and cardiorespiratory fitness and age were entered. In the case of a significant interaction term ($P < 0.05$), the fully adjusted model was stratified. By occurrence of extreme values sensitivity analysis excluding those values was performed to investigate whether these results are similar to those not excluding the extreme values.

Results

From the three cohorts, there were a total of 2748 potentially eligible workers, 1297 of whom were considered eligible; 959 workers fulfilled the inclusion criteria for the current analysis, and 878 workers with complete data were included in the analysis (figure 1).

The included population of 878 participants had a median age of 46.0 years (IQR 39.0-53.0), 46% were female, and the median level of cardiorespiratory fitness was 30.1 mlO₂/min/kg (IQR 13.6-66.9) (table 1). The median level of self-reported physical demand were 6.0, on a 1-10 scale where 10 was very strenuous, and 77% reported to be exposed to occupational lifting >25% of work time. The median %HRR during work was 31%, indicating moderate to high physical work demands and 52% of the included workers had a mean work HRR >30% (24). The majority of the included population were employed in manufacturing, but all of the included participants were classified as blue-collar.

The main effect of the weekday in the crude models was non-significant (IBI -2.14, $P = 0.24$; RMSSD 0.004, $P = 0.54$; SDNN -0.002, $P = 0.75$), indicating no effect of the weekday on the HRV variables. Moreover, the interaction between the weekly mean %HRR at work and weekday was non-significant (IBI $P = 0.92$; RMSSD $P = 0.97$; SDNN $P = 0.93$), indicating that %HRR at work was not associated with the change in nighttime HRV indices over the week.

Therefore, these interactions were not included in further analysis.

The multilevel models adjusted for age, BMI, alcohol consumption, smoking status, and the occupational group showed negative associations between weekly mean %HRR during work and HRV indices during the following night, i.e., the between-subject effect (table 2). Workers with higher %HRR at work showed significantly reduced IBI (i.e., elevated HR) and decreased RMSSD. Also, negative associations were seen between %HRR and HRV indices at the worker level, i.e., the within-subject effects (table 2). Specifically, a day with higher %HRR was associated with significantly lower IBI, RMSSD and SDNN the following night.

Thus, by converting the IBI to HR in beats per minute (bpm), from the between-subject effect, this negative association implies that per one percent higher mean %HRR during work the night-time HR would increase by 0.4 bpm, and 10% higher mean %HRR during work would imply an increase in night-time HR by 4.4 bpm, as the relation between IBI and HR are reciprocal (28).

Stratifying on high (>30% HRR) and low (<30% HRR) mean %HRR across all measured workdays showed similar associations as for the main analysis (data are now shown). The sensitivity analyses stratified by use of anti-hypertensive medication also showed similar associations' direction and magnitude as the main analysis. Moreover, the data included some (16 observations among 4 participants) extreme values of IBI, SDNN and RMSSD which could be considered as outliers, although the corresponding HR estimated from the extreme IBI showed plausible HR values (ranging from 40-93 bpm). Sensitivity analysis excluding the extreme values showed results similar to the reported (table 2), except for the between-subject effects on RMSSD turning non-significant ($P = 0.07$), although the estimate and SE were similar to those reported (table 2).

Discussion

To investigate both the within- and between-subjects association between the %HRR during work and HRV indices

at night among blue-collar workers, we conducted a day-by-day analysis of %HRR during work and HRV indices the following night. Our main findings indicate that a higher %HRR during work is associated with elevated HR (from the lower IBI) and reduced HRV variables the following night. This association was observed both between workers and between days within the worker. This finding suggests that higher %HRR during work is associated with an impaired autonomic cardiac modulation during sleep, and thus indicating a potential underlying mechanism for the hazardous effects of OPA (3, 4), as described in the physical activity paradox (5).

Our main finding of a higher %HRR during work being associated with elevated HR and reduced HRV variables the following night corroborates previous cross-sectional studies indicating that high levels of OPA are associated with autonomic imbalance at rest (29) and during sleep (7). While the previous studies (7) used accelerometer measurements for estimating OPA, we used device-worn HR measurements 24 hours a day, split into work and leisure time to estimate the %HRR during work. The observed reductions in nighttime parameters of HRV (SDNN and RMSSD) indicate a decrease in vagal modulation of the HR (30), being a pre-clinical marker of cardiovascular disease and mortality (8-10). Hence, the autonomic imbalance is a possible pathway for the detrimental effect of OPA on cardiovascular health (7, 29, 31, 32). Thus, the current investigation of the relationship between the %HRR during work and autonomic activity during the following sleep time may help to understand one of the proposed mechanisms in the physical activity paradox, being that high levels of OPA, causing many hours of work per day with elevated HR, which can lead to impaired autonomic cardiac modulation (5).

The explanation for why high levels of OPA can lead to impaired autonomic cardiac modulation is suggested to be the constrained nature of OPA, where the physical activity is determined by the performance of productive work tasks with less individual control over intensity, type and rest breaks (33). Moreover, OPA often occurs over several hours (e.g., 7-8 hours per workday or more) for >5 consecutive days per week limiting the possibility for sufficient recovery (33). This is both in line with the allostatic load theory (34), where prolonged exposure to physical stressors with limited recovery could lead to an elevated allostatic load, as reflected in attenuated vagal cardiac modulation. The observation that the workers included in this cohort generally have a low cardiorespiratory fitness will likely further strengthen the association between OPA and impaired autonomic cardiac modulation. This is because workers with low cardiorespiratory fitness will both have an increased relative physiological intensity of OPA (27, 35) as well as a lower capacity to recover from OPA.

Overall, the observed effect sizes from the day-to-day analysis were rather small, which could limit the clinical relevance of our findings. However, the between-subject effects indicated that a 10% increment in weekly mean %HRR was associated with an elevation of the HR during the following night with about 4 bpm. An increase in sleeping HR of 4 bpm is shown to increase the risk of cardiovascular disease (36), and mortality (37, 38).

Practical implications

The findings of the study support that high mean intensity of OPA is harmfully related to autonomic cardiac modulation the following night. This extends on previous studies finding a similar harmful association when estimating OPA based on accelerometer measurements (7, 39), and studies finding harmful associations between high OPA and cardiovascular disease mortality and all-cause mortality (3, 4). Our study indicates that workplaces ought to make interventions for reducing the mean intensity of OPA among blue-collar workers to prevent negative influences on the cardiovascular system and future health risks. This can be achieved either by (i) reducing the total amount of physical work tasks during the working hours putting a too high load on the cardiovascular system, (ii) implementing sufficient breaks or work tasks which can be performed in a sitting posture, or (iii) workplace initiatives improving the cardiorespiratory fitness of the workers which will reduce the relative cardiovascular load of performing the manual work task and improve the capacity of the workers to recover from the manual work (33).

Strengths and limitations

The main strength of our study is the day-by-day analysis addressing the temporal association between intensity of OPA and changes in HRV indices the following night, which provides further credibility to the observed association. To our knowledge, no previous study has addressed the effect of daily changes in the intensity of OPA and HRV indices the following night. The homogeneous sample of blue-collar workers minimizes the potential

socioeconomic confounding. Furthermore, the 24-hour HR measurements assessments providing both the valid information of the relative physical intensity of OPA and parameters of HRV is an important strength of the study (40). Finally, the sensitivity analysis excluding the extreme values showed results similar to the reported, indicating robust results.

A limitation of the study is the limited measurement duration of one week, which may not be sufficient to capture slow adaptive changes in autonomic activity during sleep related to allostatic load. Furthermore, would future investigations of this association benefit from additional measurement of ambulatory blood pressure to be able to investigate whether increased blood pressures could contribute with a possible explanation of a pathogenic path of high levels of OPA to change HRV parameters. Thus, it is a risk that our study underestimated the observed associations. Moreover, would the estimation of the %HRR benefit from measurement of HRmax being more accurate than by general formula estimation. Also, one might speculate that the participating companies providing workers for recruitment in the merged studies, maybe more observant of the work environment, health, and wellbeing than the companies not providing workers for recruitment. This could introduce a selection towards participants being healthier, and working in better environments and thus a risk for our study to underestimate the observed associations. Finally, this study does not hold prospective information and thus causal conclusions cannot be drawn.

Concluding remarks

The main finding of our study was that higher mean intensity of OPA is associated with elevated HR and reduced HRV indices the following night among bluecollar workers. This association was observed both between workers and between days within the worker. This finding suggests that higher mean intensity of OPA is associated with an impaired autonomic cardiac modulation during sleep. This supports that the high mean intensity of OPA can be an underlying mechanism for the physical activity paradox.

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Conflict of interest

There is no conflict of interest associated with this publication.

Sidebar

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Monitoring trends in psychosocial and physical working conditions: Challenges and suggestions for the 21st century

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ABSTRACT (ENGLISH)

In work and health research, there is a lack of studies on prevalence of psychosocial (eg, quantitative demands, social relations) and physical (eg, physical activity, heavy lifting) working conditions among national employee populations - and their trends. Monitoring trends versus investigating risk factors It is striking that monitoring data in general are collected in organizational settings other than those where data are used for research on associations between work, health and labor market participation (20, 21). Researchers who, on the other hand, are looking at work as a possible predictor of health or labor market participation, tend to improve measurements and introduce new risk factors [therefore, the IPD-Work consortium approach of pooling data to overcome limited power of a majority of research datasets is challenged by deviating measurements of risk factors (23, 24)]. [...]when interviews are carried out, language barriers could hamper survey participation.

FULL TEXT

In work and health research, there is a lack of studies on prevalence of psychosocial (eg, quantitative demands, social relations) and physical (eg, physical activity, heavy lifting) working conditions among national employee populations - and their trends. [In the following, I shall not discuss the issue of trends of other exposures, such as chemical and dust exposures (1).] To my knowledge, in the recent decade, only a few studies have investigated this topic (2-8), and, in this issue of the Scandinavian Journal of Work, Environment and Health, such a rare study is published (9).

Trends

This issue of the journal includes a new Swedish study, which not only aims to distinguish between different types of macro trends in working conditions (going beyond the assumption of simple linear trends) but also examines whether the gap between good and bad - in terms of working environment - jobs has widened. The reason why it makes sense to go beyond trends in working conditions is obvious. Regarding the industrialized countries, some findings indicate that working conditions are largely deteriorating (3, 5, 8). Other findings indicate that inequalities in distributions of working conditions are increasing (10, 11). A third group of findings suggest that no uniform trends

exist; trends, if any, are different from country to country (7) . It has been suggested that the reason for these trends (deterioration of or increased inequality in exposure to working conditions) might be found in the last four decades of liberalization of labor markets accompanied by globalization and digitalization (10-12). Corin et al's study (9) in this issue of the journal, however, neither shows a downward uniform trend nor an increased inequality in quality of working conditions in Sweden. However, the question remains, if monitoring data in other countries were analyzed in the same manner as in this new Swedish study, what trends would we see in these countries?

Reasons for lack of scientific research focus

One can wonder why there are comparably few studies on trends in working conditions. In his first edition of *Modern Epidemiology*, Rothman claims that researchers of health risk factors tend to jump directly to advanced regression analyses skipping a thorough inspection of their data, including which groups in the analysed population are exposed to what exposures (13). Simple intercorrelation tables, or even the traditional 'Table 1' showing independent variables broken down by gender or socioeconomic status might be insufficient. Regarding a range of work environment factors, prevalences by occupation can give rich information on what a given exposure actually means for the worker. Let me just give an example from Denmark, a labor market with working hour restrictions especially among blue-collar workers negotiated by the social partners (14, 15). If we take the dimension 'work-family conflict', many would immediately think of the overworked white-collar worker with deadlines, eg, journalists, managers, or academics. But the occupational groups reporting the highest level of this conflict in Denmark are not these groups but rather truck drivers (an occupation directly subject to competition from peers from less regulated labor markets), health workers (including only one sole group of academics, namely medical doctors) and other workers subjected to night work (16). In order to understand what a variable really measures, inspection of occupational patterns can be invaluable for both practitioners and researchers. Even a lack of variation due to occupation can widen the understanding of what a variable measures. This applies, for example, to quality of leadership or social support (17, 18). These variables are assumed to rather reflect traits of organizations and departments than traits of occupations (19). So, even if research data in most cases serve purposes other than monitoring, it is worthwhile collecting and classifying data on occupation (even if it is costly) - or at least consulting local monitoring data - in order to understand better what working conditions measure.

Working conditions: Monitoring trends versus investigating risk factors

It is striking that monitoring data in general are collected in organizational settings other than those where data are used for research on associations between work, health and labor market participation (20, 21). Also, requirements of monitoring data are quite different from requirements of research data. In order to measure long-term trends, monitoring data should collect the same data over time. Only if new issues arise, old issues disappear, or profound methodological issues emerge, should changes in monitoring be introduced. One such methodological issue is the decreasing trend in participation in surveys (22). Researchers who, on the other hand, are looking at work as a possible predictor of health or labor market participation, tend to improve measurements and introduce new risk factors [therefore, the IPD-Work consortium approach of pooling data to overcome limited power of a majority of research datasets is challenged by deviating measurements of risk factors (23, 24)]. However, this does not mean that monitoring data are more conservative and research data more innovative. A comparison of psychosocial content of European monitoring questionnaires reveals a much wider focus on psychosocial factors than the one employed in longitudinal research of cardiovascular disease, burnout or depressive symptoms (25, 26). Note that the distinction of the labels 'monitoring' and 'research' assumes that dealing with prevalence and trends in working conditions is not research, an assumption which Corin et al's paper in this issue of the journal refutes.

Two challenges: Precariousness and border crossing

In industrialized countries, most data on work and health are collected among workers employed as wage earners working in workplaces in their country of permanent residence. This restriction is challenged by (i) various types of precarious employment contracts and (ii) work arrangements crossing borders, ie, involving a dislocation of work from place of residence.

Precarious employment contracts have been on the rise in recent decades and comprise, for example, temporary

contracts (some very short term), no contract (including illegal schemes), self-employed one person employment and crowd work (27-30). Note that the prevalence of types of precarious work contracts differs very much from country to country (31). Workers on such contracts might be harder to reach in surveys. In some cases, they might be excluded from sampling frame definitions if the data provider (eg, the state or the company) does not register them as employees. Of course this problem does not arise in studies where the sample frame is based on resident populations allowing also for inclusion of workers not classified as such in registers (2-9). If however precarious workers are contacted in surveys, their uncertain or temporary (or even illegal) situation could make it difficult for them to consider themselves as employees and describe their work situation.

Work arrangements crossing borders have also increased over the last decades (32, 33). This can involve - in its more simple form - border crossers, ie, workers living in one country working in another crossing borders on a daily basis (34). Such arrangements comprise among other things also posted workers [ie, those being sent by their company to work in another country on a temporary basis; this applies to workers in construction companies who are brought from the companies' country of location to the country where construction takes place (32, 35, 36)]. Another arrangement includes temporary migrant workers who work for a short period of time in agriculture, eg, harvest seasons or those who are employed as nannies, nurses or truck drivers in periods of several years (37, 38). Such temporary workers might seek work in another country on their own, they might be hired by the company they work for in their home country, or a third party might organize the work arrangement, which again can be formal, informal or illegal (39). Also workers crossing borders might be difficult to reach in surveys. They might not be part of sampling frames in the country - or company - where work is carried out (39). Moreover, when interviews are carried out, language barriers could hamper survey participation. To complicate things further aspects of precariousness and border crossing can flow together (eg, illegal work arrangements and residence), further complicating data collection.

In some countries and sectors, these challenges (precariousness and border crossing) might play a role for the coverage of existing monitoring systems or research in work and health. Appropriate data collection and analytical methods exist and should be applied to meet these two challenges (40, 41).

Concluding remarks

After this, two important questions remain: (i) Do macro trends in working conditions show continuous improvements or deteriorations over time? (ii) Is there is a widening of inequalities in unfavourable working conditions, both within and between occupations?

In many industrialized countries, monitoring data are available that can help answer these questions (20). For some working conditions, monitoring data over time are readily available in population and workforce- based surveys, whereas, for other work-related risk factors, data on trends over time are lacking. At least regarding European surveys, it seems that psychosocial factors are covered more broadly than physical factors (26, 42). Knowledge on trends are of paramount importance for (i) identification of new risk factors, (ii) determining whether occupational health interventions on the national level are successful, and (iii) the quantification of the health impact of various hazards. I hope that the present issue's paper by Corin et al will lead to more contributions within this field of research.

Sidebar

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Intensive longitudinal study of newly graduated nurses' quick returns and self-rated stress

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ABSTRACT (ENGLISH)

Objective Little is known about the relationship between quick returns (QR) - shift combinations that result in inter-shift rest periods <11 hours) and stress. The current study examined whether variations in the frequency of QR, both between and within individuals, were associated with changes in self-rated stress. Methods A questionnaire was sent weekly to newly graduated nurses during the first 12 weeks of work. Stress was measured with four items from the Stress-Energy Questionnaire on a scale from 1 not at all to 5 very much [mean 2.65, standard deviation (SD) 1.08]. Shifts worked in the past week were reported and QR were identified by evening-morning shift combinations (mean 0.98, SD 0.90 per week). In total, 350 persons were included in the analysis (3556 observations). Data were analyzed with a multilevel residual dynamic structural equation model (RDSEM) using Bayesian estimation procedures. Results There was no between-person effect of QR on stress averaged across measurement occasions (0.181, 95% CI -0.060-0.415). However, there was a small within-person effect of QR (0.031, 95% CI 0.001-0.062), meaning that more QR during a given week, compared to that persons average, was associated with an increase in their level of stress during that week. Conclusions Nurses were likely to report increased stress during weeks in which they worked more QR. Intervention studies are needed to determine whether the relationship is causal.

FULL TEXT

Headnote

Objective Little is known about the relationship between quick returns (QR) - shift combinations that result in inter-shift rest periods <11 hours) and stress. The current study examined whether variations in the frequency of QR, both between and within individuals, were associated with changes in self-rated stress. Methods A questionnaire was sent weekly to newly graduated nurses during the first 12 weeks of work. Stress was measured with four items from the Stress-Energy Questionnaire on a scale from 1 not at all to 5 very much [mean 2.65, standard deviation (SD)

1.08]. Shifts worked in the past week were reported and QR were identified by evening-morning shift combinations (mean 0.98, SD 0.90 per week). In total, 350 persons were included in the analysis (3556 observations). Data were analyzed with a multilevel residual dynamic structural equation model (RDSEM) using Bayesian estimation procedures. Results There was no between-person effect of QR on stress averaged across measurement occasions (0.181, 95% CI -0.060-0.415). However, there was a small within-person effect of QR (0.031, 95% CI 0.001-0.062), meaning that more QR during a given week, compared to that persons average, was associated with an increase in their level of stress during that week. Conclusions Nurses were likely to report increased stress during weeks in which they worked more QR. Intervention studies are needed to determine whether the relationship is causal. Key terms diary study; recovery; rotating shift; shift work.

Quick returns (QR) - shift combinations resulting in rest periods <11 hours - are widespread throughout Swedish healthcare with nurses commonly finishing afternoon shifts at 21:30 hours followed by a morning shift at 06:45 hours, allowing just over 9 hours to manage travel, food intake, hygiene, social obligations and sleep. Anecdotally, QR contribute to continuity of care since nurses are already acquainted with their patients when they return to start their morning shift. This, in turn, may reduce workload as less time is needed to read patient records. QR also allow nurses to compress their work weeks, allowing longer times off. However, QR also seem to be associated with insufficient recovery due to short sleeps, impaired sleep quality, insomnia, longer sleep latencies and greater levels of fatigue, which in turn may increase risk for sickness absence and injuries (1-3).

Lack of recovery contributes to sustained activation of the stress system, ie, allostatic load (4). Thus, QR are a potential cause of stress due to the limited opportunities they afford for recovery. However, there is limited evidence of a relationship between QR and stress. A study of midwives found that an intervention involving a reduction of QR led to decreased reports of mental strain and stress, although the results were hard to interpret as multiple aspects of the scheduling arrangements were changed simultaneously (5). More recently, a cross sectional study of doctors found a positive association between frequency of QR and reported stress (6). However, in contrast to these findings, a diary study of nurses found no within-person differences in stress levels between morning shifts that were preceded by either a QR or no QR (7).

Newly graduated nurses experience high levels of stress due, in part, to being new to the profession. As many as 20% of newly graduated nurses experience high levels of burnout symptoms during their first five years in the profession (8). Thus, early career nurses may be especially vulnerable to occupational factors that impair the ability to deal with stress, including QR. We have shown that newly graduated nurses can have difficulties unwinding after work during a QR, especially during periods of high workload (9). Rumination was thought to play a key role, contributing to sustained activation of the nurses' stress systems and impaired recovery during QR.

The aim of the present study was to use an intensive longitudinal design to determine whether variation in QR, both within and between individuals, was associated with self-rated stress in newly graduated nurses.

Method

An intensive longitudinal study design with weekly data collections over 12 consecutive weeks was used. Participants were recruited in four rounds between 2015-2018. Eligible participants were nursing students who were about to graduate and commence their first position as registered nurses. In 2015 and 2016, information was emailed via all universities holding nursing programmes to all nursing students and presented on digital study platforms. In 2018, information was emailed and presented verbally by the researchers at 12 universities. In addition, on all occasions, an advertisement was posted on the research group's Facebook page. We do not know how many received the information and fulfilled the inclusion criteria. However, 4099 students were enrolled at the final semester at the time of data collection. In total 409 students chose to participate, 365 completed the baseline questionnaire and 350 participated with longitudinal data during workdays. All participants gave informed consent to join the study, which had ethical approval (2014/1531-31/5, 2017/543-31/5).

A digital survey-tool (Artologik) was used for collecting data weekly during 12 consecutive weeks, starting in the first or second week of employment. Surveys were sent via email to participants on the same day and time of the week. Approximately 83-95% (across the different rounds of recruitment) answered before reminders were sent to

participants who had not responded to the survey within four days. Each survey was active for one week until the next survey was sent out. On average the participants answered ten surveys (SD 1.63).

Stress was measured with three items from the Stress-Energy Questionnaire (10). Participants answered the questions "During the past week when you have been working, how often have you felt... tense?, stressed?, and pressured?". The answers were given on a scale ranging from never=1 to always=5. The scale had high internal consistency, $\alpha=0.87$, mean 2.65, SD 1.08. QR were identified from shift combinations with evening shifts followed by a morning shift. Range was 0-4 QR shifts per week (mean 0.98, SD 0.90).

Data were analyzed with a multilevel residual dynamic structural equation model (RDSEM) using Bayesian estimation procedures in Mplus version 8.4 (11). The method integrates time-series analysis (modeling the lagged relations in repeated measures), multilevel modelling (allowing for simultaneous modelling of individual processes and differences between individuals), and structural equation modelling (allowing for latent variables modelling). Moreover, the use of Bayesian estimation provides credibility intervals based on a posterior distribution that are more intuitive to interpret (11). The effects of QR on stress were modelled on both between-person (averaged across measurement occasions) and within-person (between measurement occasions) levels. Both predictor and outcome variables were partitioned into within-between components using latent mean centering (12). Time-invariant covariates (gender, age, and cohort) were included to control for between-person variability in stress intercepts. Additionally, a linear development trend over time was modelled, accounting for autoregressive correlation of residuals.

Results

The analytical sample consisted of 350 participants (mean age 28.52, SD 6.67 years; 88.3% women) and 3556 measurement occasions. Table 1 highlights the effects estimated in the model relevant to the aim of the study. Stress levels differed between persons when averaged across measurement occasions, such that participants in the more recent cohorts reported higher stress. The general trend over time was negative, meaning that stress decreased over the first 12 weeks of employment. No between-persons effect of QR on stress levels averaged across measurement occasions was detected (0.181, 95% CI -0.060-0.415). This means that those nurses who worked more QR on average over the 12 weeks period did not report significantly higher stress levels. The within-persons effect of QR on stress at a given measurement occasion was (0.031, 95% CI 0.001-0.062), indicating that more QR during a given week, compared to a person's average, increased the stress level during that week. Model based variances of QR for the between- and within-persons were 0.212 and 0.571, respectively; residual model based variances of stress were 0.356 and 0.474, respectively. The within-level R-square was 0.282 (95% CI 0.245-0.316), which suggests that about one third of the within-person variance of stress was explained by within-person QR variability (on average across subjects), together with a time trend.

Discussion

Nurses reported increased stress during weeks in which they worked more QR. One possibility is that the relationship between QR and stress is mediated by impaired recovery. Quick returns limit the opportunity for recovery between work shifts. Insufficient recovery between work shifts results in the worker returning to work the next day in a sub-optimal state, such that they need to invest additional compensatory effort in order to perform adequately at work (13). The additional compensatory effort that accompanies QR may provoke a stress response. Epstein et al (9) reported that nurses experienced little fatigue during shifts following QR but intense fatigue after those shifts, indicating that stress activation may be masking the underlying fatigue at work. At the same time, the stress response may further inhibit recovery. A sustained stress activation and an inability to unwind after work (eg, due to rumination about the day's experiences and anticipation of the day to come) can lead to longer sleep latency and more fragmented, poorer quality sleep (9, 13). A vicious circle then ensues whereby stress increases the need for recovery, while at the same time high stress leads to impaired recovery, also referred to as the recovery paradox. Cutting down on recovery behaviors such as social life, hobbies, physical exercise etc. has been reported among newly graduated nurses (9, 14), which might fortify such a vicious circle.

An alternative explanation of the association between QR and stress is that nurses may be more likely to work QR

during periods with high demands, for example, as a result of being required to work additional shifts. Thus, high demands on the service may be an underlying cause of both increased frequency of QR and increased stress among nurses. This scenario could account for the observed pattern of results, without the need to invoke a causal relationship between QR and stress. However, in additional analyses (not shown), we found only weak correlations between self-rated workload and frequency of QR ($r < 0.10$ for within and between subjects). Thus, an arguably more likely scenario is that QR do increase stress, and that this effect is intensified during periods of high demand on the healthcare service.

It is also possible that the association between QR and stress is mediated by work-family interference, especially if the QR are associated with schedule changes at short notice. We lacked the information to examine this possibility, but future research in this area should include measures that capture stress stemming from work-home interference, as well as indicators of short notice changes to work schedules.

The observed within-subject effects of QR on stress were significant, with the model accounting for about one third of the observed variance in reported stress. Nevertheless, the effects were relatively small, which may indicate that the impact of a QR on acute stress is relatively short lived. If so, our measure of stress experienced over the course of the entire week may be somewhat insensitive to such acute effects. Future research should employ even more intensive (eg, daily) measurements of stress and work hours, so that effects in the immediate aftermath of a QR can be studied. The lack of between-persons effect was not expected but may have been due to the insensitivity of the comparison, relative to the within-persons effect. As well as the potential for unmeasured confounds, the sensitivity to the acute effects of QR may have been diluted by relying on measurement over a 12-week period (see above). Strengths of current study included the low levels of missing responses to the weekly questionnaires (on average participants answered 10 of 12 questionnaires) and the use of an intensive longitudinal design with a large sample, resulting in a large number of measurement points. Moreover, studying nurses at the beginning of their career reduces the risk of 'healthy worker' selection effects, ie, when study samples become biased as a result of vulnerable workers quitting positions that involve demanding shift combinations. The frequency of quick returns was similar to a previous study of nurses (7), suggesting that the current findings are generalizable to other healthcare systems where QR are present (eg, in Scandinavia). However, the findings may be less generalizable to other groups, especially outside healthcare settings, as newly graduated nurses experience a unique work situation and demands. While there is some uncertainty regarding the response rate to the invitation to the study, this is unlikely to have had a significant impact on the veracity of the observed within-person changes over time.

In conclusion, nurses were likely to report increased stress during weeks in which they worked more QR.

Intervention studies are needed to determine whether the relationship is causal.

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Sidebar

Dahlgren A, Tucker P, Bujaczk A, Frögéli E, Rudman A, Gustavsson P. Intensive longitudinal study of newly graduated nurses' quick returns and self-rated stress. *Scand J Work Environ Health*. 2021;47(5):404-407.

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Occupational trajectories of working conditions in Sweden: Development trends in the workforce, 1997-2015

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ABSTRACT (ENGLISH)

Objective This study aimed to explore the development of working conditions within and between occupations in the Swedish labor market from 1997 to 2015 and whether any polarization in working conditions concurrently occurred between occupations. **Methods** Cross-sectional data from ten waves of the Swedish Work Environment Surveys (1997-2015) were used and an aggregated occupational-level dataset was created using the Swedish Standard Classification of Occupations. To capture the patterns of change in working conditions over time (ie, growth), growth curve modeling was used to identify the starting points for 89 occupations (intercepts) as well as both the shape (functional form) and rate of growth (slope) over time. **Results** The Swedish labor market was stable overall, with some small, mainly positive, changes in job demands and resources. Different occupations developed in divergent directions, but there was no evidence of polarization. **Conclusions** The findings indicate that macro-level stability can hide highly heterogeneous patterns of change among different occupational groups. This type of analysis, taking context into account, could be valuable for decision makers intending to improve the work environment.

FULL TEXT

Headnote

Objective This study aimed to explore the development of working conditions within and between occupations in the Swedish labor market from 1997 to 2015 and whether any polarization in working conditions concurrently occurred between occupations.

Methods Cross-sectional data from ten waves of the Swedish Work Environment Surveys (1997-2015) were used and an aggregated occupational-level dataset was created using the Swedish Standard Classification of Occupations. To capture the patterns of change in working conditions over time (ie, growth), growth curve modeling was used to identify the starting points for 89 occupations (intercepts) as well as both the shape (functional form) and rate of growth (slope) over time.

Results The Swedish labor market was stable overall, with some small, mainly positive, changes in job demands and resources. Different occupations developed in divergent directions, but there was no evidence of polarization. **Conclusions** The findings indicate that macro-level stability can hide highly heterogeneous patterns of change among different occupational groups. This type of analysis, taking context into account, could be valuable for decision makers intending to improve the work environment.

Key terms job demand; job resource; macro trend; meso trend; official statistic; polarization; work environment. (ProQuest: ... denotes formulae omitted.)

The work environment is very important for employee health and productivity. Thanks to decades of extensive occupational health and safety research, the physical and psychosocial working conditions that constitute risks and resources are well known in Europe (1, 2). These conditions can theoretically be sorted into demands and resources and applied in the job demand-resources (JD-R) model (3), a well-recognized framework for capturing working conditions. Many studies relate job demands and resources to health and motivational outcomes, using both the JD-R and other preceding models (for an overview, see for example 4, 5). However, it is less common to use the JD-R model in a macro-level (for example, labor market) setting to investigate the broad development of working conditions in different occupations over time. With a focus on patterns and directions in the development of important job demands and resources in different occupations, this study sets out to examine working conditions within and between occupations from 1997 to 2015.

In the 1970s and 1980s, Sweden took important steps in improving the work environment, for example, implementing regulations governing working conditions, passing legislation regarding the occupational health service, and starting several national institutes of occupational safety and health. The economic crisis of the early 1990s changed the labor market and working conditions in many respects (6). Swedish national financial policy

changed its main priority from ensuring high employment to combating inflation and, at the same time, the conditions for international trade changed. The unemployment rates rose rapidly and almost tripled in size. Discussions on making the private and especially public sector more efficient intensified. Major restructuring of the private and public sectors followed, with eg, slimmed-down organizations, creating significant turbulence. In addition, the legal obligations of the occupational health service were removed. Taken together, a series of extensive changes on the labor market, like other similar countries implemented over a long period, were concentrated in a very short time in Sweden. Many employees consequently experienced deteriorated work environments (6-13). Guided by Sweden's official work environment statistics, the greatest deteriorations were found in psychosocial working conditions (6, 14), with general work intensification and substantial increases in job demands. The work intensification was later on accompanied by decreases in job control (6, 9, 15). The number of Swedish employees in high-strain work thus increased during the 1990s. Those working within the public sector were hit the hardest. In Swedish healthcare, for example, the proportion who answered that they had "too high job demands" increased by as much as 25% between 1991-1999, and job control decreased by >10% between 1995-1999 (6).

By following the same official Swedish work environment statistics - but over a longer period - Gellerstedt (16) found both positive and negative developments for manual workers between 1991-2014. In line with this, Cerdas et al (17) demonstrated that job demands, decision authority, and social support developed in different directions between 1991-2013. For example, a trend toward increasing demands and decreasing decision authority was more salient in female-dominated sectors. These findings indicate that overall macro trends might conceal different meso-level trends and that occupations might develop in divergent directions.

Other indications of concealed work environment heterogeneity are the recent findings of polarized occupational structure (18, 19). Polarization refers to a pattern of occupational change in which employees in both high- and low-skilled occupations are growing in numbers, while medium-skilled employment is being hollowed out. Technological change, in particular digitalization, is believed to be the main cause of this due to its potential to replace routine work tasks. Such occupations are found in the middle of the skill structure (for example, assemblers and office clerks). Non-routine jobs are mainly high-skilled, with digital technology instead tending to complement the work and increase productivity. However, there is also a tail of low-skilled manual jobs with non-routine characteristics (for example, waiters) that are not easy to replace with digital devices. This tail is tending to grow in relative numbers. In the Swedish case, some scholars have found that the upgrading that previously characterizing the labor market has given way to polarization in recent decades (20-22). Upgrading refers to a process in which lowskilled and often low-quality jobs are replaced with more and better high-skilled jobs (23). However, in recent decades, the low-skilled tail of the occupational structure has not continued to shrink; instead, these the number of these jobs has increased. Changes in the occupational structure have been measured using wages as a proxy for skills. This approach has been criticized, as wages do not straightforwardly mirror skill requirements (24). Using individuals' own assessments of job requirements, Tåhlin (24) found no polarization, but rather continuing upgrading on the Swedish labor market. Oesch & Piccitto (25) expanded the analysis to encompass measures of job quality besides wages - such as educational level, prestige, and job satisfaction - and did not find any evidence of polarization.

The direction of changes in the occupational structure are important since polarization may have consequences for work environments. Kalleberg (26) argued that the polarization process entails a divide between "good" and "bad" jobs, suggesting a trend towards greater inequality, while Peugny (27) showed that precarious employment conditions have become more common in the low-skilled segment over the last 20 years.

In this study, we take a comprehensive approach to the question of how working conditions have evolved within and between occupations in recent decades, focusing on central dimensions of the JD-R model. Is the Swedish occupational structure moving in the direction of polarization, or has there been a positive trend of upgrading with a decrease in unsatisfying and hazardous working conditions?

Our aim was to explore the development of working conditions among occupations on the Swedish labor market during the 1997-2015 period. Specifically, this study investigates: (i) the overall trends in both physical and psychosocial job demands and resources, ie, the macro trends; (ii) the divergent trends in the development of

working conditions between occupational groups, ie, the meso trends; and (iii) whether the variation between occupations has increased in a polarized manner over time.

Method

Study population and data collection

The Swedish Work Environment Survey (SWES), conducted biannually since 1989 by the Swedish Work Environment Authority (SWEA) and Statistics Sweden (SCB), consists of a random, stratified representative subsample of gainfully employed Swedes (~4-4,5 million individuals during the study period). The gainfully employed includes all individuals aged 16-64 years who have worked for >1 hour during the measurement week in salaried work, as self-employed, or in a family business. Hence, the sample also includes those who take on shorter assignments and thus have atypical employments.

The SWES subsample is drawn from the regular Labor Force Survey (LFS) conducted by SCB and varying between approximately 10 000-15 000 individuals (depending on the number of gainfully employed in a given year). The LFS is in turn drawn from the Register of the Total Population (RTB) as selection frame and consists of a representative sample of the whole Swedish population stratified by county, sex, and age group. The LFS is conducted by means of telephone interviews, and those who are chosen to participate in the SWES are asked additional questions during these interviews and to complete a supplementary postal or web questionnaire. The survey has been conducted using a similar methodology from its launch in 1989. In total, approximately 130 questions about physical and psychosocial working conditions are asked.

Dropout occurs at each step, first in the LFS and then in SWES, due to, for example, problems related to health, language, and available time. Prior to 2002, the dropout rate in the LFS was low and relatively stable. However, since then, the dropout has steadily increased, with the greatest increases occurring since 2009 and especially since 2013. Therefore, in 2015, LFS dropout was thoroughly assessed for 2002-2014 (28). The analysis showed that dropout has consistently been slightly higher among men, although this difference between the sexes has diminished over time. The dropout for the foreign-born and those living in densely populated areas has consistently been higher during this period. The dropout between different age categories has increased over time, with the highest dropout among 15-24-year-olds. Similarly, dropout has increased more among those with a lower educational level. Taken together, dropout has roughly doubled in the LFS since 2002. However, there is no information in the LFS on how large the dropout rate is for the subgroups employed versus not employed (29). Therefore, SWEA states that there are no prerequisites with reasonable certainty estimating how large the dropout rate was among those employed between 1997-2015 and, thus, how large the error can be assumed to be in SWES (30).

Even so, we know that the number of participants in the SWES has decreased over time (table 1); an attempt to conduct a more solid dropout analysis of SWES was made in 1999 (30). Similar to the dropout analysis of the LFS, the analysis revealed lower response rates among men, the young, and employees with low education and foreign background. Participation was also lower among those with low income, contract or part-time employment or with own businesses. Still, the response rate in SWES remains relatively high (table 1) and constitutes the best available official statistics and data source in Sweden concerning working conditions over time.

Aggregation to occupational level

We created a dataset of longitudinal occupational data for the Swedish labor market between 1997-2015 (in some cases 2013) using the Swedish Standard Classification of Occupations (SSYK). Similar to international standard classification systems (for example, ISCO by ILO), SSYK covers type of work and qualifications required. A new version of SSYK was introduced in SWES in 2012 and, by using translation keys between the older SSYK96 and the current SSYK12, ten survey rounds of the SWES could be created for this study. Observations from these rounds were compiled, generating a dataset with data for the years 1997-2015 (N=111 828 individual observations). The three-digit level of SSYK comprises 113 occupations. However, 21 small occupational groups (eg, senior officials of special interest organizations, models, religious professionals, ships deck's crew and street vendors) with few observations (N<15 for more than 50% of survey rounds) were excluded (N=1388), and four occupations in the

process industry were merged into one (see supplementary material, www.sjweh.fi/show_abstract.php?abstract_id=3955, table S1). Thus, observations from 89 occupations provided the basis for the final dataset, containing 110 440 individual observations (table 1). The data were aggregated to the occupational level, rendering a set of longitudinal data with ten waves of 89 occupations for the years 1997-2015.

Measures

Changes were made to SWES in 1995, 2005, and 2013, resulting in the rewording of some questions (31). Even so, 43 working conditions could be compared over the full study period (1997-2015) and an additional 5 over almost the full study period (1997-2013). Of these 48 dimensions, 24 were chosen to gain broad representation of physical and psychosocial working conditions. Questions with yes/no response alternatives and questions capturing very specific physical demands were not included. To facilitate interpretation, these 24 individual dimensions were categorized into four job resources and four job demands (table 2) using the JD-R model as a conceptual framework (32). To facilitate interpretation, all dimensions were normatively coded so that a high value implies a favorable work condition, thus a positive regression estimate of the slope coefficient implies improvement over time.

Analytic strategy

To capture patterns of occupational change in working conditions over time (ie, growth), growth curve modeling (GCM), a subset of hierarchical linear modeling specifically designed for longitudinal analyses, was used. GCM enables us to analyze the central tendency and variation in initial status (or starting point) of the growth (in the analyzed time frame) of occupations (intercepts) as well as both the shape (functional form) and rate (average slope and variation in slope) of growth over time. By using GCM, we consider the possibility that different occupations might have different intercepts defining their growth trajectories as well as different slopes. Before the GCM analyzes described below, the residuals were analyzed. The assumptions of constant variance, normality and linearity of the residuals were met for all of domains except Emotional demands, where the dimensions "Emotionally demanding contacts" and "Violence and threats" were found to be highly skewed, with most occupations not experience such demands at work.

Assessing macro and meso trends: specifying and fitting the growth curve model

The analyses were performed using the mixed models unit in SPSS version 24 (IBM Corp, Armonk, NY, USA). Time (ie, intra-occupational growth over time) was set as Level 1 of the hierarchy. Observations over time were nested within occupations (Level 2) constituting the inter-occupational growth. The final sample consisted of ten time waves at Level 1 and 89 occupations at Level 2. The maximum likelihood (ML) method was used to estimate the statistical parameters in order to permit likelihood ratio testing. Both linear and nonlinear changes over time were examined. By using the "unstructured" covariance type, estimation of both the variance and covariance of the random effects was allowed (33).

A series of analytical steps was performed for each dimension. In the first step, an unconditional mean model (Model I) was estimated to serve as a baseline model for examining occupational variation in the work condition at hand, without regard to time. In Model I, (i) the mean of the outcome dimension and (ii) the amount of outcome variation existing within and between occupations were assessed. In the second step, an unconditional fixed linear growth curve model (Model II) was estimated to capture the linear development over time (ie, linear macro trends, the test of the first research question). Time was scaled as years divided by ten, implying that the slope coefficient should be interpreted as the change over a 10-year period. In the third step, an unconditional random linear growth curve model (Model III) was estimated to capture the variation in occupational development trends over time (ie, the meso trends, the test of the second research question). In the fourth step (Model IV), quadratic and cubic growth curve models were estimated to identify parabolic or S-shaped (ie, nonlinear) growth curves (the test of functional form of the macro trends, related to the first research question) (34).

Calculation of effect sizes

The effect size for overall change in occupations over a 10-year period was calculated using the following procedure:

...

the fixed estimate of the slope coefficient was divided by the standard deviation of the intercept (ie, the variation between occupations) according to the following formula:

...

The effect size for trajectories of occupations was calculated as the range of change for 95% of the occupations over a 10-year period using the following formulas:

All calculations of effect sizes were based on Model III, with the linear slope only.

Polarization analysis

To detect a trend towards polarization, the covariance between the intercepts and the slope in the multilevel models for each dimension was estimated. A positive covariance indicates a "fanning out" pattern of the trajectories, and thus greater differences between the occupations over time. A positive covariance would thus give support for polarization between the occupations.

Results

Table 3 shows the lowest and highest observed means and standard deviations (SD) (based on occupational level data) between 1997-2015 for the 24 included working conditions.

Table 3 also includes calculations of the intraclass correlation coefficient [ICC (1, 1)] based on individual-level data and with occupations as the grouping variable, ie, the amount of variance attributable to the occupational (meso) level (35). Roughly 2-39% of the variance in the 24 studied working conditions could be attributed to the occupational meso level. The remaining variance may thus be explained by aspects associated with workplace, employee-specific characteristics, and measurement error. Based on low occupational-level variance, ie, ICC (1,1) values <5%, three dimensions were omitted from the final analysis: supervisor support ICC (1,1)=3%, supervisor appreciation ICC (1,1) =3%, and autonomy ICC (1,1)=4%. Thus, a total of 21 working conditions with enough variance attributable to the occupational level was used for the main analysis.

The results of the growth curve models estimating the occupational trajectories of working conditions are presented in table 4 (fixed parameters) and table 5 (random parameters).

Macro trends in development of job demands and resources

Of the 21 working conditions, 10 displayed an overall macro-level development trend, shown as a significant linear, quadratic and/or cubic slope coefficient in Table 4. Two of the job demands (difficulty of work tasks and emotionally demanding contacts) displayed linear development, suggesting that the rate of growth remained constant over time, and eight dimensions had more complex macro trends (figure 1).

In one case (work postures), the trajectory was quadratic, ie, it first decelerated and then accelerated over time. In another case (workload), the trajectory was instead cubic (S-shaped), with one peak and one trough. However, the remaining working conditions displayed even more complex macro trends with several simultaneous trends. While psychological pressure and appreciation displayed quadratic and cubic trends, decision authority: when; overtime; time pressure; and bend and twist displayed a combination of linear, cubic, and quadratic trends.

The macro trends were particularly salient among the various aspects of job demands (table 4 and figure 1).

Workload showed a clearly positive development (standardized change, 0.47), with a slight decline in later years. Overtime and time pressure were S-shaped with no clear direction over time. These quantitative demands were thus fluctuating over time. Difficulty of work tasks improved linearly (standardized change, 0.19), meaning less difficult work. Psychological pressure first clearly improved (standardized change, 0.49), but then slightly declined. A favorable development took place in the physical job demands, with work postures (standardized change, 0.16) and bend and twist (standardized change, 0.20) displaying mainly positive development after initial deterioration. Emotionally demanding contacts displayed linear negative development (standardized change, -0.08), suggesting slight deterioration in emotional demands.

Only two of eight job resources displayed a significant macro development trend. Decision authority over when to do work displayed S-shaped development with no clear direction over time, while appreciation (from workmates, patients, and/or clients) also displayed S-shaped development but with an improvement in recent years (standardized change, 0.16).

Meso trends in development of job demands and resources

Significant variation in slopes was found for 15 of the 21 working conditions investigated (table 5). The analyses showed that the occupations developed differently over time for most working conditions, revealing substantial occupational trends, ie, meso trends, within the labor market. Among the job demands, the following 8 (of 13) conditions displayed significant variation in development across occupations (the variations in slope calculated as the low and high standardized change are given after each dimension): concentration (low=-0.90, high=0.66); psychological pressure (low= 0.11, high=0.88); work-leisure spillover (low=-0.47, high=0.37); time pressure (low=-0.28, high=0.76); emotionally demanding contacts (low=-0.33, high=0.18); violence and threats (low=-0.31, high=0.34); work postures (low=-0.11, high=0.44); and bend and twist (low=-0.01, high=0.40). The following demand dimensions did not display any significant meso trends: difficulty of work tasks, monotony, workload, overtime, and physical workload.

The meso trends were noticeable among job resources, with all except one resource dimension (social support from colleagues) displaying a significant meso trend. The following seven (out of eight) dimensions displayed significant variation in development across occupations (the variations in slope calculated as the low and high standardized change are given after each dimension): decision authority: pace (low=-0.58, high=0.42); decision authority: when (low=-0.33, high=0.37); decision authority: what, how (low=-0.31, high=0.38); unbound and free (low=-0.58, high=0.60); appreciation (low=-0.43, high=0.74); pause opportunities (low=-0.59, high=0.51); meaningfulness (low=-0.37, high=0.41).

An illustration of what the meso-level observations for occupations look like for the job resource Decision authority; when is presented in figure 2. The left-hand panel shows the observed data for occupations. The right-hand panel shows the low and high estimated trajectories for selected starting points, i.e., an occupation that starts at a certain point is estimated to decrease or increase within the lines shown.

Polarization trends in development of job demands and resources

The random intercept was significant in all the working conditions measured, showing that different occupations had different "starting points" for their occupational trajectories of working conditions within the study period (table 4). To detect a trend towards polarization, the covariances between the intercepts and slopes in the multilevel models were inspected. All covariances were either not significantly different from zero or were significantly negative; no covariances were significantly positive. Thus, no support was found for polarization trends in working conditions.

Discussion

The main findings were a stable overall level of working conditions across occupations, divergent developments at the occupational level, and no conclusive support for a polarization trend. This study supported neither the ongoing upgrading nor polarization of work environments and working conditions in the occupational structure. The most important finding is that macro-level trends comprise a large variety of heterogeneous meso trends across occupational groups.

Accounts of an increase in stressful work environments are common in Swedish public debate (36, 37). The current study thus points to a more complicated picture. Its findings reveal that no clear improvement trend has occurred for most job demands and resources. This could mean that the deterioration in working conditions, with substantial increases in job demands as well as decreases in job control, that took place in Sweden in the 1990s is still present (eg, 6, 9, 14, 15.). But foremost, it discloses great heterogeneity of development between occupations.

Consequently, experiences of change in the Swedish work environment vary greatly between workers in different occupational groups.

Overall development of job demands and resources

At the macro level, most indicators of job demands and resources displayed no clear improvement trend.

Concerning job demands, 13 indicators were included in the analysis and significant macro trends were evident in eight of them. Five displayed a positive trend, one a negative trend, and two nonlinear trends. Workload was the only quantitative demand that displayed a clear improvement trend. Two of four cognitive demands (difficulty of work tasks and psychological pressure) displayed deteriorating trends of lower levels, while two of three physical job

demands (work postures and bend and twist) displayed improving trends. Only emotionally demanding contacts displayed a clear negative trend. On the resource side, only one job resource displayed a significant change at the macro-level, with increasing levels of appreciation from workmates, patients, and/ or clients. The remaining 12 indicators of job demands, and resources displayed no clear macro-level changes between 1997-2015.

Thus, at the macro level, no radical changes in the working conditions of occupations were found over time; most working conditions remained fairly stable. This result both corresponds to (38, 39), and contrasts findings from other countries, where both positive (6, 39, 40) and negative (6, 40-44) overall trends have been observed, depending on exposure and time period. Concerning the trends detected, the study showed that job resources vary less over time at the occupational level than do job demands. This may indicate that job resources are more closely related to factors on other levels than the occupational, for example, the industry or workplace level (cf. 6).

Variation across occupational groups

While the macro analysis of the work environment of occupations revealed few changes over time, the working conditions within different occupations were definitely changing. For all 21 included dimensions of working condition, the 89 included occupations had different starting points, and most of the dimensions displayed occupational variation in trajectories over time. Compared with the relatively modest changes at the macro level, these changes were quite substantial.

As illustrated in figure 2, the observed occupational developments in job demands and resources resemble a haystack with a jumble of development trends heading in different directions. While this haystack is difficult to interpret, the analytical framework presented here summarizes the occupational developments in a manageable number of statistical parameters. The most important conclusions of this analysis are that, first, for a few of the studied job demands and resources, the trends in all occupations are similar. Non-significant differences in slopes are only found for 6 of the 21 working conditions. Second, the differences in trends are in no cases unequivocally in the direction of improvement. However, there are cases in which the upper bound is clearly positive, while the lower bound is approaching zero, for example, in the cases of psychological pressure and bend and twist. Third, regarding some working conditions, the developments are strongly divergent between occupations (ie, the variations in coefficients), for example, in the cases of unbound and free, decision authority, concentration, and meaningfulness. This heterogeneity of trends may explain the non-trends in the above macro analysis results.

Previous studies have commonly looked for differences between subgroups based on, for example, gender, age, and level of education (see, for example 39, 40, 43-45.). The present findings suggest that it is equally important to consider differences in development between occupations and occupational groups (cf. 17, 41-42). The results support adding a labor market perspective taking the overall occupational structure into account.

Consequently, from an interventionist point of view, knowledge of how the job demands and resources vary between occupations that, for example, are female or male dominated, could add knowledge about contextual factors besides general gender differences (46). Policies on health and safety interventions might in this way be better targeted towards specific industries and occupations.

Do work conditions develop in a polarized manner over time?

This study has revealed strong heterogeneity in the occupational trends of working condition indicators. However, when directly testing whether the job demands and resources for different occupations tend to diverge over time - a tendency that may indicate polarization of working conditions - no clear evidence was found. This is in line with earlier findings. For example, narrowing rather than increasing disparities in job security by occupational skill level were found for working Australian between 2000 and 2008 (39). Consequently, future research could attempt to identify other patterns. Furthermore, the distribution of individuals across these occupations needs to be introduced to determine how the workforce is distributed among occupations with different trends in working conditions. In addition, attention should be paid to labor market changes, such as employment conditions, that could explain these diverging development trends (cf. 47).

Strengths and limitations

The main strength of this study is its representative sample of the Swedish labor market and working conditions over

a fairly long period that has rarely been studied, despite changes in occupational health and safety conditions. A limitation is the decreasing response rates on the SWES along with a lower response rate among men, employees with low education, low income, and foreign background as well as among those with contract or part-time employment or with own businesses (30). Since several of these groups are concentrated in occupations at the "lowest end" of the occupational structure, - for example, in the platform or gig economy - employees with atypical employment and possibly more unregulated working conditions might not be captured to the same extent in the data. If this means that entire occupations fall out of the analysis this in turn might contribute to overestimation of the positive development of working conditions. However, even though there are no official statistics available on differences in dropout between different occupations in SWES our own compilations (see supplementary table S1) shows that the 21 occupations that were omitted from the analysis due to too few respondents are represented in almost all of the main occupational groups at the Swedish labor market. Thus, since all the occupations are given the same weight in GCM analysis our judgment is that the exclusion of very small occupations will not bias the data to any troublesome extent.

The SWES relies on self-reported measures, so measurement problems could affect the levels of reported exposure; however, as the present interest is in development over time and differences between groups, the risks of wrong conclusions should be smaller (48).

A prerequisite to adopt aggregation to the occupational level is that the individual level reports contain information that could be attributed to the occupational level. Thus, the individual level ICC (1,1) values are important to judge if the aggregates contain reliable information. As stated in the results section, we found that roughly 2-39% of the variance in the 24 studied working conditions could be attributed to the occupational meso level, meaning that the remaining variance may thus be explained by aspects associated with workplace, employee-specific characteristics, and measurement error. We judged that ICC (1,1) values $>5\%$ constituted a low occupational-level variance, and therefore omitted three dimensions which fell below this limit. We conclude that not all working conditions are suitable to study at the occupational level. However, the range of variance in our 21 studied working conditions that could be attributed to the occupational meso level is still large. Similarly, to ICC (1,1) values reported by eg, Madsen et al (49), and as can be seen in table 3, the ICC is consistently high for the physical demands in our study which makes them particularly suitable for studying with our choice of method. On the other hand, the ICC values on the dimensions covering social support are the lowest in our study and additional social support dimensions were left out of the final analysis due to even lower ICC. This means that these types of working conditions are probably more closely knitted to a specific workplace, employeespecific characteristics which has also been found in other studies (eg, 6.). Most dimensions studied, however, fall in the middle of these extremes often with a mixture of lower and higher ICCs within the same domain. Aggregated level reliability is however determined not only by the individual level intraclass correlation ICC (1,1) but also by the number of responses in each occupation (50). Accordingly, we considered both these parameters when deciding which variables and occupations to include. We decided to exclude occupations with few observations ($N < 15$ for more than 50% of survey rounds). This decision was based on a trade-off between occupation level aggregated variable reliability versus the importance of retaining representability to the labor market as a whole. In order to follow the trajectories in small occupations there is a need for sampling more employees in those occupations.

The chosen time period starts after the major negative restructurings of the work environment during the 1990s. If the series had started before the crises of that time, these restructurings would have been taken into account, and what here appear to be improvements in the work environment might instead be regarded as partial recoveries at the end of a longer period of deterioration. In this study, we wanted to consider a broad range of job demands and resources, but only a few of these were available in the pre-crisis waves of the SWES.

Concluding remarks

Based on self-report surveys, fairly high overall stability was found in the physical and psychosocial working conditions at the macro level of the Swedish labor market. However, this macro-level stability hides highly heterogeneous patterns of change among different occupational groups. The study gives no clear-cut support for the

occupational structure moving in either an upgrading or polarizing direction concerning job demands and resources. The results emphasize that policy-makers, employer organizations, and other decision-makers aiming to improve the work environment of employees need to take the contexts of industries, sectors, and occupations into account to have adequate information. We see tendencies toward such a contextual approach on the European level. Eurofound has defined different types of jobs based on job quality and identified how these are distributed across different industries on the European labor markets (51). The findings of our study clearly support this endeavor as a way forward for bodies that generate work environment statistics.

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Ethics standards

The regional ethics committee in Gothenburg (Dnr 96217) approved this study.

Competing interests

The authors declare no competing interests.

Sidebar

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DETAILS

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Dysuria, heat stress, and muscle injury among Nicaraguan sugarcane workers at risk for Mesoamerican nephropathy

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ABSTRACT (ENGLISH)

Objectives Nicaraguan sugarcane workers, particularly cane cutters, have an elevated prevalence of chronic kidney disease of unknown origin, also referred to as Mesoamerican nephropathy (MeN). The pathogenesis of MeN may include recurrent heat stress, crystalluria, and muscle injury with subsequent kidney injury. Yet, studies examining the frequency of such events in long-term, longitudinal studies are limited. **Methods** Using employment and medical data for male workers at a Nicaraguan sugarcane company, we classified months of active work as either work as a cane cutter or other sugarcane job and determined occurrence of dysuria, heat events and muscle events. Work months and events occurred January 1997 to June 2010. Associations between cane cutting and each outcome were analyzed using logistic regression based on generalized estimating equations for repeated events, controlling for age. **Results** Among 242 workers with 7257 active work months, 19.5% of person-months were as a cane cutter. There were 160, 21, and 16 episodes of dysuria, heat events, and muscle events, respectively. Compared with work months in other jobs, cane cutting was associated with an elevated odds of dysuria [odds ratio 2.40 (95% confidence interval 1.56-3.68)]. The number of heat and muscle events by cane cutter and other job were limited. **Conclusions** Working as a cane cutter compared with other jobs in the sugarcane industry was associated with increased dysuria, supporting the hypothesis that cane cutters are at increased risk of events suspected of inducing or presaging clinically evident kidney injury.

FULL TEXT

Headnote

Stallings TL, Riefkohl Lisci A, McCray NL, Weiner DE, Kaufman JS, Aschengrau A, Ma Y, LaValley MR, Ramírez-Rubio O, Amador JJ, López-Rilarte D, Laws RL, Winter M, McSorley VE, Brooks DR, Applebaum KM. Dysuria, heat stress, and muscle injury among Nicaraguan sugarcane workers at risk for Mesoamerican nephropathy. *Scand J Work Environ Health*. 2021;47(5):377-386. doi:10.5271/sjweh.3963

Objectives Nicaraguan sugarcane workers, particularly cane cutters, have an elevated prevalence of chronic kidney disease of unknown origin, also referred to as Mesoamerican nephropathy (MeN). The pathogenesis of MeN may include recurrent heat stress, crystalluria, and muscle injury with subsequent kidney injury. Yet, studies examining the frequency of such events in long-term, longitudinal studies are limited.

Methods Using employment and medical data for male workers at a Nicaraguan sugarcane company, we classified months of active work as either work as a cane cutter or other sugarcane job and determined occurrence of dysuria, heat events and muscle events. Work months and events occurred January 1997 to June 2010. Associations between cane cutting and each outcome were analyzed using logistic regression based on generalized estimating equations for repeated events, controlling for age.

Results Among 242 workers with 7257 active work months, 19.5% of person-months were as a cane cutter. There were 160, 21, and 16 episodes of dysuria, heat events, and muscle events, respectively. Compared with work months in other jobs, cane cutting was associated with an elevated odds of dysuria [odds ratio 2.40 (95% confidence interval 1.56-3.68)]. The number of heat and muscle events by cane cutter and other job were limited.

Conclusions Working as a cane cutter compared with other jobs in the sugarcane industry was associated with increased dysuria, supporting the hypothesis that cane cutters are at increased risk of events suspected of inducing or presaging clinically evident kidney injury.

Key terms chronic kidney disease of unknown origin; CKDu; crystalluria; chronic kidney disease; rhabdomyolysis. Chronic kidney disease (CKD) not explained by typical CKD risk factors is exceedingly common along the Pacific coast of countries in Central America, including Nicaragua, El Salvador, Guatemala, and Costa Rica (1). This region includes the location of our present study in northwestern Nicaragua, where CKD prevalence is particularly high among young (age 30-40 years) male agricultural laborers, principally sugarcane industry workers (2-8). This distinct regional pattern of CKD is referred to as Mesoamerican nephropathy (MeN).

Among sugarcane workers, cane cutters appear at greatest risk of MeN (6, 9-12). One of the main proposed causal hypotheses has focused on the potential physical challenges faced by cane cutters, including strenuous physical exertion in extreme heat (3, 13-18), such that volume depletion in conjunction with other factors, such as muscle injury, results in recurrent episodes of subclinical kidney injury that eventually manifest with clinically apparent CKD (13-19).

Dysuria, defined as pain with urination and called "chistata" in Nicaragua, appears common among male sugarcane workers, and affected male workers may be misdiagnosed as having urinary tract infections (UTI) (20, 21).

Urinalyses of cane cutters demonstrate crystalluria (10, 14, 20, 22), with increasing crystal burden over a work shift (22). One hypothesis is that dysuria reflects mechanical trauma from crystalluria, influenced in part by work-related heat stress and volume depletion with resultant highly concentrated urine (14, 15, 20, 22, 23).

With demanding physical exertion, cane cutters may also be at risk of muscle damage with release of nephrotoxic proteins from muscle, including myoglobin (13, 14, 17-19, 24-26). Elevated concentrations of muscle injury biomarkers, myoglobin and creatinine kinase (CK), are associated with muscle damage-related illness and acute kidney injury (AKI) (24-27). Two studies reported that cane cutters experienced an increase in serum CK across a workday (19, 28), suggesting a possible role for muscle injury in MeN. Importantly, although cane cutters have been the focus of much of the MeN research, data are lacking on whether workers holding other jobs in the sugarcane industry may also experience events of dysuria, heat events, or muscle injury.

Prior research in populations at risk of MeN is limited by short-term study designs and reliance on self-report of work and medical events. In the current study, we combined employment history and medical records to create a 13-year

longitudinal retrospective cohort to examine whether cane cutters compared with workers in other jobs in the sugarcane industry sought medical care for dysuria and conditions related to heat stress and muscle injury.

Methods

Study population

Data were collected from a sugarcane plantation in northwestern Nicaragua, Department of Chinandega for a feasibility study of sugarcane workers to evaluate the potential for conducting multi-year retrospective studies in the region using employment and medical records [detailed in (29)]. Briefly, employment records were used to identify men who actively worked between 1 January 1997 and 30 June 2010. For each calendar year, workers were randomly sampled within specific job types (cane cutter, irrigator, pesticide applicator, field machine operator, factory worker, and cane gatherer), with larger sampling of cane cutters (sampled 7 cane cutters per year and 2-3 workers in the other job categories per year, approximately), yielding a total of 243 workers. Workers' complete medical records were then abstracted and medical events through 30 June 2010 were determined. For the present analysis, we excluded one worker whose data indicated he did not work during the study period, leaving 242 male workers. Below, we describe our analysis by person-month, examining whether workers received medical care for dysuria, heat events, or muscle events, and whether these were more likely to occur while working as a cane cutter or other job in the sugarcane industry.

Work classification

For these workers, employment and payroll records provided work history, including date of initial hire and dates held different jobs. For each calendar month from each workers' date sampled for the study until the end of follow-up 30 June 2010, we determined whether the worker was actively working. Only active work months were used in this analysis and each person-month was classified as time worked as a cane cutter or other job in the sugarcane industry, providing time-varying classification of job type.

Medical records

Prior data collection involved locating medical records from the onsite medical clinic, where workers receive their healthcare while working on the plantation. Data abstracted from medical records included symptoms, physician diagnoses, prescriptions, vital signs, and blood and urine laboratory results, including serum creatinine. In the medical records, information on lifestyle behaviors such as alcohol consumption and smoking were limited to 33 workers (17.4%). Medical records were abstracted in Spanish. For the present work, two native Spanish-speaking physicians translated the data to English - one a member of our team (ARL), the other at a translation service company.

Because this analysis was not focused on development of CKD but rather incidence of potential CKD precursor events by job type, we excluded person-time after a worker developed CKD (N=8 workers). For the eight workers, a total of 55 work months starting with the month of CKD diagnosis and later were excluded from the study followup period. We considered a worker to have CKD during the observation period if there was a physician diagnosis, which was confirmed with two creatinine-based estimated glomerular filtration rate (eGFR) values <60 mL/min per 1.73 m² at least three months apart estimated using the CKD-EPI equation for non-black men (30, 31).

Hypertension was defined by physician diagnosis accompanied by a prescription for antihypertensive medication or elevated systolic or diastolic blood pressure (>140 and/or >90 mmHg, respectively) and diabetes by physician diagnosis accompanied by prescription for diabetic medication or serum glucose >200 mg/dl (assumed to be non-fasting).

The Institutional Review Boards at George Washington University and Boston University Medical Center and the Nicaraguan Ministry of Health [Ministerio de Salud de Nicaragua (MINSAL)] approved this study.

Classification of medical outcomes

Our classification of the three study outcomes (dysuria, heat events, and muscle events) entailed compiling symptoms and/or diagnoses that described the potential occurrence of each event. For dysuria, we identified events of pain upon urination. If a medical visit mentioned pain with urination, dysuria, chistata, cystitis, or UTI (a common misdiagnosis with later evidence supporting these were likely crystalluria, discussed in the introduction), then the

visit was reviewed as a potential dysuria event. For both heat and muscle events, we describe events meeting primary and secondary definitions of these outcomes. The primary definition of heat events focused on medical visits in which a worker was noted to have overheated. If a medical visit specifically mentioned heat stress, heat stroke, overheated, hyperthermia, dehydration, or dizziness, then the visit was reviewed as a potential primary heat event. Also, we reviewed the visit as a potential primary heat event if it indicated physical exhaustion or fatigue combined with at least one heat symptom (headache, muscle cramp or spasm, nausea, vomiting, asthenia/weakness, tiredness). For the secondary definition of a heat event, we considered as a potential event those visits with terms indicating physical exhaustion or fatigue (without accompanying heat symptoms), electrolyte imbalance, or experiencing >2 heat symptoms. We note that medical visits were reviewed in full if any one of the heat symptoms was indicated, though one heat symptom alone was considered insufficient to meet even the secondary definition. The primary definition of muscle event focused on identifying symptoms possibly related to rhabdomyolysis, a type of serious muscle injury often due to high physical exertion. Visits indicating myalgia or diffuse, non-specific muscle injury/pain or discomfort were reviewed as a potential event. The secondary definition described body pain or difficulty moving, or reddish/ tea-colored urine, a potential indicator of myoglobinuria due to rhabdomyolysis. We then applied exclusion criteria. The main reasons for excluding events were follow-up visits to check the status of the worker's health after the initial visit or cooccurred with an illness during the same visit (eg, for dysuria specifically, excluded if a sexually transmitted disease was indicated at visit; for heat or muscle event, excluded if an accompanying viral or gastrointestinal illness). A worker could experience each outcome more than once; however, only one event of each type could be counted within a calendar month. Also, another incident event of the same type could only be included after a 28-day window had passed (eg, if an incident dysuria occurred on 31 October that meant that another incident dysuria event could only be included if it occurred after 28 November). Follow-up visits for a prior event (eg, rather than a new event) were also excluded. Information on the identification of events and exclusion criteria are shown in Figure 1. Two study team members conducted an independent review of the records and were blinded to employment history. They met to resolve discrepancies.

There were 1174 medical visits during working months in total during the observation period, representing 924 person-months. All visits were reviewed for potential indicators of each of the events of interest. Of these visits, 416 (occurring in 359 person-months) had terms or phrases related to one or more of the events and these visits were examined further to determine whether they met the definition for the event(s) and if they had any exclusion criteria (the remaining 758 medical visits had no terms or phrases related to the events). Through the review of medical records, 218 (181 person-months), 221 (209 person-months), and 62 (60 person-months) medical visits were determined to have conditions identifying potential dysuria events, heat events, and muscle events, respectively. Note that there were 334 visits evaluated for only one potential type of event and 82 visits evaluated for more than one potential event type. After applying exclusion criteria, there were determined to be 160 dysuria, 44 heat events (21 primary definition), and 22 muscle events (16 primary definition), which occurred during 209 work months. Our analysis structure was based on calendar month and with only one event of each type allowed to occur during a calendar month, the number of events dropped for muscle events only, leaving 160 dysuria, 44 heat events, and 21 muscle events occurring during 209 person-months. We also note that in our examination of heat event specifically, we identified a large number of potential events, yet many of these had only one potential symptom of heat event which was determined to be insufficient to meet the definition of a heat event in our analysis and were excluded.

Statistical analyses

Demographic, occupational, and medical characteristics were described using frequencies for categorical variables and medians [interquartile range (IQR)] for continuous variables. We multiply imputed baseline age (N=10 imputations) using PROC MI in SAS when missing (N=27 workers), conditional on years since hired, cumulative months worked at baseline, and whether working as a cane cutter at baseline. Characteristics of ever and never cane cutters during study follow-up were compared using Chi-square tests/Fisher's exact tests (if an expected cell count <5), and Wilcoxon rank sum tests for categorical and continuous variables, respectively.

As described earlier, workers who worked between 1 January 1997 and 30 June 2010 were randomly selected

within job and year and only calendar months actively worked from the date sampled until they were no longer employed or until 30 June 2010 were included in the analysis. Therefore, for the follow-up period of January 1997 through June 2010, start of follow-up for each worker began with the first month of work on or after sampling date. Each at-risk person-month was classified by our exposure of interest, working as a cane cutter or working in another job in the sugarcane industry; individual workers could contribute person-time to both categories depending on their work history. Dysuria, heat events, and muscle events were treated as individual outcomes.

We compared the frequency of dysuria, heat events, or muscle events by months worked as a cane cutter or other job in the sugarcane industry, using Chi-square tests/Fisher's Exact tests. We calculated the proportion of person-months in which one of the event types occurred for cane cutters and other jobs. To examine potential associations between working as a cane cutter and odds of each binary outcome, we performed a set of logistic regression analyses based on the generalized estimating equations (GEE) method (32) to account for correlation of repeated occurrences. We estimated odds ratios (OR) and 95% confidence intervals (CI). Younger workers were more likely to work as a cane cutter than other job and more likely to experience dysuria, heat, and muscle events. We generated models with and without controlling for age (continuous). In models controlling for age, we used PROC MIANALYZE to account for imputed age. Hypertension and diabetes were considered potential confounders, but few workers were diagnosed with these conditions and adjustment did not change the associations, therefore they were not included in final models.

The analytical dataset (N=242) contained 199 workers who had available medical records, of which 160 workers had a medical visit during follow-up (eg, working month between date of sampling through June 30, 2010). There were 43 workers who had no medical record over their entire time of employment. This was assumed to be due to those workers not seeking medical attention for any reason (including not experiencing any of the events of interest) and therefore included in the analysis. We compared characteristics of workers who did and did not have medical records to identify any differences. We repeated the analyses of the events of interest and working as a cane cutter, restricting to subjects who had a medical record to see if this influenced the results.

We also examined whether workers held the job of seed cutter at any point during the work months included in this analysis. Seed cutter is a job that involves climatic heat exposure and heavy physical exertion, similar to cane cutter, conditions that may place workers at increased risk of CKD or potential CKD precursors (11). Although the initial data collection did not sample for the job of seed cutter, a review of work history data identified that a limited number of workers held this job during study follow-up (eg, due to job changes). Therefore, we examined the proportion of work months in which dysuria was experienced among seed cutters to see how that may have influenced our results. All analyses were generated in SAS version 9.4 (SAS Institute, Cary, NC).

Results

Over 13.5 calendar years, workers accrued 1417 months as cane cutters and 5840 months in other jobs. During follow-up, workers worked a median of 23 months and typically held one job (table 1). There were 93 workers who ever worked as a cane cutter during the follow-up period and their median time worked was lower than those who never worked as a cane cutter during followup (16 and 29 months, respectively).

During follow-up, there were 924 active work months with medical visits, and 66% of workers had at least one medical visit (table 2). Never cane cutters were more likely than ever cane cutters to seek medical care ($P<0.001$). There were a total of 160 dysuria events, 21 heat events, and 16 muscle events based on primary definitions. One-third of workers sought care for dysuria at least once. Workers who ever cut cane during follow-up experienced a higher median number of dysuria events compared with the never cane cutters ($P=0.04$). Based on primary definitions, 7% of workers experienced heat events and almost 6% experienced muscle events. Inclusion of secondary definitions more than doubled the number of heat events and modestly increased the number of muscle events (table 2).

The proportion of months in which dysuria and heat events (primary definition) occurred were higher for cane cutters compared with those working in other sugarcane jobs (table 3). No differences in proportion of months experienced muscle events were apparent between the job categories. In logistic regression models, the odds of dysuria among

cane cutter months were elevated compared with months worked in other jobs [adjusted OR 2.40 (95% CI 1.56-3.68)]. There were low numbers for primary heat and muscle events when grouped by cane cutter or other job and confidence intervals around the measures of association were wide, though the association with heat events did suggest that cane cutters were at elevated odds of experiencing these events. We noted earlier that not all workers had medical records and they were assumed to not have sought medical attention and therefore did not experience the events of interest. We compared characteristics for workers who did (N=199) and did not (N=43) have a medical record (supplementary material, www.sjweh.fi/article/3963, table S1). Those with a medical record were older, worked more total work months during follow-up (25 versus 11 median months), and were less likely to have ever been a cane cutter during follow-up compared with workers who did not have a medical record. In sensitivity analyses restricted to the 199 workers who had medical records, the point estimates for each type of event were somewhat strengthened relative to the results with all subjects included, and the CI largely overlapped those from our main analyses (see supplementary table S2).

In table 4, we present medical events, personmonths, and proportion of months in which events were experienced by job title. Although cane cutters experienced the highest proportion of months with dysuria, we note that nonetheless dysuria occurred in all job types. There were only 35 (0.4%) person-months contributed while working as a seed cutter and only one dysuria event, preventing meaningful interpretation of the occurrence among seed cutters in our study.

Discussion

We found that the odds of dysuria were elevated for cane cutters compared with other jobs in the sugarcane industry. While observing that cane cutters experienced dysuria was not surprising, we also observed that 30% of those holding other jobs in the sugarcane industry experienced dysuria. These results support the hypothesis that cane cutters experience more events of dysuria, potential precursors to MeN, but also highlight that workers holding other jobs in sugarcane may experience dysuria. The odds of heat events were also elevated among cane cutters compared with other jobs in the sugarcane industry, though event numbers were only one-tenth of the number of dysuria events and therefore produced wide confidence intervals.

Dysuria may occur in the setting of volume depletion (15, 23) and may reflect mechanical trauma from possible crystalluria stemming from work-related heat stress (20). Dehydration and volume depletion result in very concentrated urine with supersaturated minerals in an acidic environment promoting crystal formation (14, 33). Urinary crystalline structures may damage kidney tubules and induce an inflammatory response (14, 33) as well as result in dysuria (34). It is also possible that dysuria does not play a direct role in the eventual development of MeN but rather represents a marker of heat stress, which causes kidney damage through other pathways. Critically, existing evidence outside the specific context of MeN suggests that acute injury to the kidney can affect risk of CKD over time. For example, AKI has been found to increase risk of advanced CKD 3- to 8-fold, even in the absence of preexisting CKD (35-37).

The present study provides a view of how frequently workers seek medical care for dysuria. Dysuria (or chistata) has been reported as a common symptom among sugarcane workers (5, 23, 38, 39). A cross-sectional study that relied on self-report also found that more cane cutters (25.8%) than non-cane cutters (12.7%) reported experiencing dysuria (23). Another approach to examining potential for dysuria has involved identifying crystalluria through the use of urine samples collected at defined time points. For example, urine samples collected from cane cutters near the end of the harvest season revealed crystalluria, primarily uric acid crystals (10, 14, 22), and urinary kidney injury biomarkers were elevated compared with pre-harvest measures (9).

For each of the three outcomes investigated in the present study, several factors may have influenced our ability to observe associations. Workers needed to seek medical care for the condition, and if the condition was not severe enough to seek treatment, we would have missed those events. However, our review of medical records did identify lesser symptoms reflective of our outcomes, suggesting that workers sought care for conditions of varying severity. Among those who sought care, misclassification was also possible, meaning that we classified some individuals with and without each outcome incorrectly. Dysuria is distinct in its presentation and perhaps the least likely to

misclassify. For heat events, more events were based on symptoms rather than specific diagnosis of a heat condition. Similarly, muscle events indicative of rhabdomyolysis proved the most challenging to classify. Understandably, muscle injuries are common in this physical work environment. It is not clear whether the generalized muscle tenderness that is most prominent in rhabdomyolysis would be sufficiently severe to cause workers to seek medical care. For both heat and muscle events, our medical records review resulted in a large potential number of events, though many of these were excluded due to insufficient information from the visit that the event of interest occurred, or any indication that events may be caused by another factor such as viral illness, trauma, or specific muscle injury. In our classification of outcomes, we limited our probability of including false negatives. It is possible that our exclusion criteria resulted in leaving off events that were true events of interest, though loosening these criteria would also have resulted in increasing the opportunity for non-events to be counted as events. Inclusion of events meeting the secondary definition weakened results for heat and muscle events. In addition, it is feasible that the symptoms and diagnoses in the medical records are not distinct enough for characterizing these events of interest retrospectively. For each outcome, non-differential misclassification potentially biased results towards the null as we have no reason to think that clinic staff would treat the conditions differently by job title.

Our analyses included 43 workers who did not have a medical record, and we assumed they did not seek medical attention at the clinic nor did they experience any outcome of interest. Supporting that possibility is that workers without medical visits had shorter work durations and may not have needed medical attention during that more limited period of work. However, another possibility is that medical records for some workers were misplaced. We note that sensitivity analyses excluding the workers without medical visits did not change the results. Alternatively, given that cane cutters made up a higher percentage of those without a medical record, if we are missing events of interest in those without medical records, it is possible that our analyses may be underestimating the associations with cane cutters.

This study was comprised of active workers. These workers were prevalent hires, a phrase used in occupational epidemiology to describe workers who worked prior to the start of follow-up. We did not capture incident hires - those followed from the time of hire, which occurs during the study observation period. Prevalent hires represent a potential source of left truncated data, as they may not be representative of all those who worked prior to the start of follow-up. In prior research on occupational cohorts, prevalent hires were found to induce a downward bias on the observed association (40). However, much of the previous literature was focused on industries where there was more potential for longer work tenures and analyses focused on long-term exposure and chronic diseases. In the present analysis, both our exposure and outcomes were short-term - occurring within a month window (eg, whether experienced dysuria during a month worked as cane cutter or other job). Also, unlike a chronic disease, dysuria is a transient event from which there is short-term recovery. It is unclear if these conditions would lessen a potential impact of left truncation. Ideally, future studies of dysuria among workers would include incident hires, which would facilitate understanding the impact of left truncation.

There are other potential sources of bias. Because sampling was conducted on those actively working at the company, workers with a longer duration of work had more opportunities to be sampled and be represented in the study population. This strategy may result in length-biased sampling which may bias estimates if the occurrence of dysuria differed by length of time worked (41). In addition, the healthy worker survivor effect may have occurred, where less healthy workers stopped working or changed jobs. We observed that those who ever worked as a cane cutter during follow-up worked fewer months compared with those who did not work as a cane cutter during follow-up. This may have resulted in an underestimation of the association between dysuria and working as a cane cutter. Our study, spanning up to 13.5 years of follow-up represents the longest analytical time period for a study of urinary tract events among workers at elevated risk of MeN, to our knowledge. Additionally, few longitudinal studies have examined whether sugarcane workers experience repeated symptoms of dysuria, heat stress, and muscle injury (19, 23, 38). Quantifying the occurrence of these events across time and examining their relationship with cane cutting sheds light on one of the leading hypotheses of MeN, in which recurrent subclinical kidney injury may result in

kidney damage, eventually leading to clinically recognized kidney dysfunction (13, 14, 16, 17, 19). Our study is also unique in that it chronicles medical visits during the calendar years 1997-2010. This captures, in part, the experience prior to larger scale prevention efforts by sugarcane companies. It was only towards the end of this time period that some sugarcane companies in this region of Nicaragua began to make a series of changes in work practices aimed at decreasing the occurrence of heat stress among cane cutters. Future studies could compare event rates of dysuria by job type before and after the implementation of such heat stress prevention measures.

Concluding remarks

These findings provide quantitative estimates over an extended period of time that cane cutters were more likely to experience events suspected of placing them at increased risk of developing MeN. More research involving populations at risk of MeN should examine other jobs in the sugarcane industry more closely, including potential prevention strategies (11).

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Conflict of interest

For the present study, lead author and data analyst (TLS), senior author (KMA), and other co-investigators (ARL, NLM, DEW, JSK, AA, YM, MPL, RLL, MW, VEM) have no conflicts of interest.

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Sidebar

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DETAILS

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Effectiveness of training in guideline-oriented biopsychosocial management of lowback pain in occupational health services - a cluster randomized controlled trial

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ABSTRACT (ENGLISH)

Objective This study aimed to investigate the effectiveness of brief training in the guideline-oriented biopsychosocial management of low-back pain (LBP) in occupational health services using a cluster-randomized design. A small sample of physiotherapists and physicians from the intervention units (N=12) were given three- to seven-day training focusing on the biopsychosocial management of LBP, while professionals in the control units (N=15) received no such training. **Methods** Eligible patients with LBP, with or without radicular pain, aged 18-65, were invited to participate. A web-based questionnaire was sent to all recruited patients at baseline, three months and one year. The primary outcome measure was disability (Oswestry Disability Index, ODI) over one year. Between-group differences were analyzed using linear and generalized linear mixed models adjusted for baseline-response delay as well as variables showing between-group imbalance at baseline. **Results** The final study sample comprised 234 and 81 patients in the intervention and control groups, respectively at baseline, and 137 and 47 patients, respectively, at one year. At baseline, the mean duration of pain was longer in the intervention group (P=0.017), and

pain-related fear concerning physical activity was lower ($P=0.012$). We observed no significant difference between the groups' primary outcome measure (adjusted one-year mean difference in the ODI: 2.3; 95% confidence interval -1.0-5.7; $P=0.175$) or most secondary outcomes. Conclusions Brief training in guideline-oriented biopsychosocial management of LBP for occupational health professionals did not appear to be effective in reducing patients' symptom over one-year follow-up compared to treatment as usual.

FULL TEXT

Headnote

Ryynänen K, Oura P, Simula A-S, Holopainen R, Paukkunen M, Lausmaa M, Remes J, Booth N, Malmivaara A, Karppinen J. Effectiveness of training in guideline-oriented biopsychosocial management of low-back pain in occupational health services - a cluster randomized controlled trial. *Scand J Work Environ Health*. 2021;47(5):367-376. doi:10.5271/sjweh.3959

Objective This study aimed to investigate the effectiveness of brief training in the guideline-oriented biopsychosocial management of low-back pain (LBP) in occupational health services using a cluster-randomized design. A small sample of physiotherapists and physicians from the intervention units ($N=12$) were given three- to seven-day training focusing on the biopsychosocial management of LBP, while professionals in the control units ($N=15$) received no such training.

Methods Eligible patients with LBP, with or without radicular pain, aged 18-65, were invited to participate. A web-based questionnaire was sent to all recruited patients at baseline, three months and one year. The primary outcome measure was disability (Oswestry Disability Index, ODI) over one year. Between-group differences were analyzed using linear and generalized linear mixed models adjusted for baseline-response delay as well as variables showing between-group imbalance at baseline.

Results The final study sample comprised 234 and 81 patients in the intervention and control groups, respectively at baseline, and 137 and 47 patients, respectively, at one year. At baseline, the mean duration of pain was longer in the intervention group ($P=0.017$), and pain-related fear concerning physical activity was lower ($P=0.012$). We observed no significant difference between the groups' primary outcome measure (adjusted one-year mean difference in the ODI: 2.3; 95% confidence interval -1.0-5.7; $P=0.175$) or most secondary outcomes.

Conclusions Brief training in guideline-oriented biopsychosocial management of LBP for occupational health professionals did not appear to be effective in reducing patients' symptom over one-year follow-up compared to treatment as usual.

Key terms implementation research; risk stratification; STarT Back Tool; Örebro Musculoskeletal Pain Screening Questionnaire.

Current clinical practice fails to effectively manage low-back pain (LBP) and despite increasing healthcare resources being devoted to it, disability due to LBP has risen by over 50% since 1990 (1). The biopsychosocial model is increasingly accepted for understanding and managing pain (2). Attention should be drawn to the complex contributors to LBP such as psychological, social and biophysical factors (3). For routine use with persistent LBP, interventions that consist of non-pharmacological treatments such as exercise therapy and cognitive-behavioral therapy (CBT) should be considered (4). As best practice, a systematic review of high-quality clinical practice guidelines for musculoskeletal pain recommended the following: ensure that care is patient-centered, screen for red flags, assess the psychosocial factors, use imaging selectively, undertake a physical examination, monitor patient progress, provide education/information, address physical activity/ exercise, use manual therapy only as an adjunct to other treatments, offer high-quality non-surgical care prior to surgery, and try to enable patients to remain at work (5).

A recent review showed moderate-quality evidence that biopsychosocial interventions are more effective than education/advice for reducing disability and pain in the short-, medium- and long-term in patients with LBP, and interventions with a clear focus on psychosocial factors seem the most promising (6). However, these interventions are still in early development and their implementation in clinical practice has encountered some challenges (2, 7).

The results of different training interventions have varied widely and the optimal way to train healthcare professionals (HCP) and support the implementation process is not yet clear (8-11).

Early assessment and tailored interventions in primary healthcare seem to promote a more efficient approach for preventing the development of prolonged and disabling LBP (12, 13). The recent National Institute for Health and Care Excellence (NICE) guidelines also recommend risk-based stratification and targeted interventions for different risk groups (14). The STarT Back Tool (SBT) is a brief questionnaire, which has been developed to identify patients at a higher risk of developing persistent disabling LBP in order to provide treatments according to the risk group (15). The Örebro Musculoskeletal Pain Questionnaire (ÖMPSQ) has been developed to identify biopsychosocial factors that are known predictors of work disability (16) and the short version (ÖMPSQ-short) has shown to be valid in both clinical use and research interventions (17).

Previously, the effectiveness of patient education booklets (18, 19), and return-to-work interventions (20) have been evaluated among patients with LBP in Finnish occupational health services (OHS), but no studies have been conducted on the effectiveness of biopsychosocial pain management. Using a cluster randomized design, the objective of this study was to assess the effectiveness of brief training in the guideline-oriented biopsychosocial management of LBP for OHS providers who manage patients with LBP.

Methods

Trial design

The study design was a two-arm cluster randomized controlled trial. Units of major Finnish private and public OHS providers were invited to participate. The Ethics Committee of the University Hospital of Oulu, Finland, approved the study (79/2017, 19.9.2017), which was performed in accordance with the Helsinki Declaration.

Participants

Figure 1 is a flowchart illustrating the progression of the study. From each unit allocated to the intervention group, at least one physician and one physiotherapist were encouraged to participate in the training. All the physiotherapists and occupational health physicians in all the study units were invited to recruit eligible patients. Inclusion criteria for patients with LBP included 18-65 years of age and the possible presence of radicular pain in addition to axial pain. Exclusion criteria included suspicion of a serious underlying cause for LBP or need for urgent care. All the participants completed written informed-consent forms, participation was voluntary, and they were not reimbursed for participating in the study. No information was collected on the patients who were invited to participate but who did not sign the consent form.

Interventions

A small sample of physiotherapists and physicians (N=28 in the initial training and N=21 in the booster with 17 HCP participating in both sessions) from all the intervention OHS units assigned to receive training in the guideline-orientated biopsychosocial management of LBP were simultaneously given a four-day initial training course and a three-day booster course at a conference venue near the city of Oulu. The first part of the training took place 21-24 September 2017 and the second part 3-5 June 2018. A senior pain psychologist and a physiotherapist with extensive experience in the biopsychosocial management of LBP delivered the training, assisted by other members of the research team. The training consisted of lectures on the theoretical basis of the biopsychosocial approach to LBP management, pain education, psychological risk factors, physical factors and behavioral responses to pain, interview and assessment, communication skills and individualized management of LBP. Demonstrations using real patients were followed by practice of clinical reasoning skills and discussions, and clinical case problem-solving. Role plays were also used to enhance learning. The use of stratification questionnaires (SBT and ÖMPSQ-short) was also practiced. The HCP who participated in the workshops were given access to an online platform with additional resources (research articles, videos etc.) and to a discussion forum. They were also able to consult the research team.

The participating physiotherapists and physicians were advised to share the information in their workplace and were provided with a printed educational package for this purpose. To support this, after the initial workshop, a member of the research team visited all the active units, with the aim of further introducing the research project to the whole

workplace beyond those who participated in the training. The project was described and a short introduction to the principles of the biopsychosocial approach to the management of LBP was given. The procedure of data collection was described, and related unit-specific practical instructions were given.

The intervention units were advised to use SBT (ÖMPSQ-short only for physiotherapists) during the appointments to facilitate the individualization of care plans. The patients who consented to the trial received a patient education booklet called Understanding Low Back Pain [static-content.springer.com/esm/art%3A10.1186%2Fs12913-018-3526-7/MediaObjects/12913_2018_3526_MOESM3_ESM.pdf], which has been translated into Finnish and undergone preliminary evaluation in Finnish primary healthcare (21). Based on risk classification using SBT, low-risk patients were presumed to receive education on the biopsychosocial nature of pain, advice to stay active and advice on pain medication (if needed). Moderate-risk patients were supposed to receive a treatment protocol similar to low-risk patients and in addition, active physiotherapy including evaluation and guidance of the patients' pain-related fears, functional limitations and lifestyle behaviors, such as regular physical activity, sleep, etc. High-risk patients were supposed to receive a treatment protocol similar to moderate-risk patients, but with an emphasis on exploring and integrating the management of psychosocial factors by a physiotherapist who participated in the full 7-day training. Patients could be referred to an occupational health psychologist if needed (22). The control units provided treatment as usual.

Patient-reported outcome measures

The primary outcome measure was patient-reported backrelated disability score based on the Oswestry Disability Index (ODI; 23) over 12 months. Secondary patient-reported outcome measures (PROM) - evaluated at baseline, 3 months and 12 months - included PROMIS-PF20 (PROM information system-physical function-20; 24, 25), back and leg pain intensity using a 0-10 numerical rating scale (NRS), health-related quality of life (QoL) using the EuroQol (EQ)-5D-3L (26), self-rated health (EQ-5D VAS, 0-100 scale), and work ability (0-10 NRS; 27). The Back Belief Questionnaire (BBQ; 28) was evaluated only at baseline and 3 months, whereas the Roland-Morris Disability Questionnaire (RMDQ-24; 29), the SBT (30, 31), ÖMPSQ-short (17, 32), fear of physical activity or work (Fear-Avoidance Beliefs Questionnaire, FABQ-pa and FABQ-work; 33), and self-efficacy (Pain Self-Efficacy Questionnaire, PSEQ; 34) were evaluated at baseline and 12 months. In addition, we asked the patients at all timepoints to report the use of any pain medication used at least three days per week (separate reporting for paracetamol, non-steroidal anti-inflammatory drugs, mild opioids and strong opioids). Finally, we used custommade questions to evaluate patient satisfaction with information related to pain explanation, self-efficacy, HCP skills, and being heard and understood in terms of symptoms (0-10 NRS for all items) at all timepoints.

Sample size

Power calculations for the trial were performed according to the primary outcome measure at 12 months. A total of 162 patients from 27 clusters (units), with an average of 6 participants (patients) each, and a conservative estimate for the intraclass coefficient of 0.05, has 80% power to detect at least a 4-point difference in ODI between the groups at $\alpha=0.05$, assuming a standard deviation in the ODI of 8 out of 50 points (35). This equates to a 20% difference in groups at one year if the mean ODI in the control group is projected to be 20 points (Stata version 16, StataCorp LLC, College Station TX, USA). Towards the end of the recruitment, we used the accumulated data to estimate the true intraclass coefficient in our data (36) which was 0.011, suggesting that a sample size of 135 with an average of five participants per unit would have been sufficient for the assumed effect size. With an expected drop-out rate of 30%, the adjusted sample-size requirement was 192 patients.

Randomization

The units that agreed to participate were randomized into the intervention or control groups using a random number generator, as performed by a statistician who was not aware of the characteristics of the units. Randomization was stratified by the service provider (public companies together) in an attempt to minimize selection bias. Not being involved in patient recruitment or data analysis, the last author notified the OHS providers of their allocation.

Statistical methods

Baseline characteristics at the unit and patient levels were summarized using means and standard deviations (SD),

medians and interquartile ranges (IQR), or percentages (%) and frequencies (n). The effects of the intervention on the primary and secondary outcomes at the patient level were estimated using 3-level linear or generalized linear mixed models with random effects for unit and time to allow for intraclass correlation at the unit and patient level, incorporating terms for intervention group, time and intervention by time interaction. The models were adjusted for delay in all variables, which showed between-group imbalance at baseline. The primary analysis used a full intention-to-treat (ITT) approach, using all available data at baseline, 3 and 12 months. As linear mixed models are a likelihood-based estimation procedure, and thus produce non-biased estimates under the assumption of data missing at random, the likely values for the missing data were estimated on the basis of the observed data. Estimates were reported with accompanying 95% confidence intervals (CI) and associated P-values, using bootstrapped standard errors to account for departures from normality. SPSS Statistics (version 26, IBM Corp, Armonk, NY, USA) and Stata were used for the statistical analyses. A Stata syntax demonstrating the primary analysis for ODI is presented in the supplementary material (www.sjweh.fi/article/3959) table S1.

Results

Baseline data

Figure 1 is a flowchart illustrating the progression of the study. Ten OHS providers were originally contacted, of which four declined to participate. The six participating OHS providers consented to assign 27 units in total to the trial. Two units allocated to the intervention group declined placement because they had no HCP who could participate in the training. These two units, however, agreed to participate in the control group. Finally, 12 units participated in training and 15 in the control group. Of these, 5 control units did not recruit any patients (figure 1). Patients were recruited between 25 September 2017 and 29 November 2018. The median duration from consent to the baseline response was 24 (range 5-291) days in the intervention group and 17 (range 3-115) days in the control group. The final study population comprised 315 participants (42.5% male, mean age 45 years), with 234 and 81 patients in the intervention and control groups, respectively, at baseline. At one year, the figures were 137 and 47 patients, respectively. There were no statistically significant differences between the groups at baseline in terms of demographic characteristics, general health or work-related factors (table 1). However, 34.6% of the intervention group and 17.3% of the control group reported that their pain had lasted for >12 months ($P=0.017$). Pain-related fear of physical activity was lower in the intervention than control group ($P=0.012$; table 2).

Patient-reported outcome measures

We observed no significant difference between the groups' ODI, the primary outcome at 3 and 12 months [adjusted mean difference in scores +2.3 index point of the ODI score; 95% confidence interval (CI) -1.0-5.7; $P=0.175$ at 12 months; table 3]. There were no consistent or clinically important differences between the groups' secondary outcome measures, except in self-rated health at 12 months ($P=0.032$; higher among the controls) and SBT risk-group distribution at 12 months ($P=0.028$; lower prevalence of high risk among the controls) (tables 3 and 4). We performed additional sensitivity analyses for the main outcomes (ie, ODI, back and leg pain intensity, self-rated health and work ability) by including only those with symptom duration of >2 weeks but <12 months ($N=178$; sensitivity analysis 1), patients belonging to the high-risk group based on SBT ($N=41$; sensitivity analysis 2), or patients belonging to the SBT low-risk group ($N=149$; sensitivity analysis 3), and compared these subgroups to the respective control groups. The sensitivity analyses showed similar results to those of the main analysis (supplementary tables S2-4).

Discussion

We observed no clinically relevant differences between the patient-reported outcome measures of the patients recruited by the HCP trained in biopsychosocial management of LBP and those of the patients recruited through usual OHS over one-year follow-up. Somewhat unexpectedly, the individuals in the control group reported higher self-rated health and, in the intervention group, a higher proportion of individuals were allocated to the high-risk SBT group at one-year follow-up. This may be due to several underlying factors. Firstly, the intervention group included a significantly higher percentage of individuals with pain duration of >12 months at baseline (35% versus 17%). Although pain duration was used as a covariate in all subsequent treatment effect analyses, we cannot rule out

residual confounding. Secondly, it may be that the offered training encouraged professionals in the intervention units to recruit patients with more difficult symptoms overall. In contrast, professionals may have overlooked patients with demanding symptoms in the control units or these patients may have had a higher tendency to decline to participate. Possible selection biases may also relate to the study design of a cluster randomized trial: there was no subsequent randomization of patients; they were invited to participate within the randomized units. Finally, it should be acknowledged that professional competency and treatment fidelity were not assessed. In the intervention units, an HCP who was not trained by the research team may have first contacted the patient. Such HCP may have assessed psychosocial factors using SBT and given the patient the education booklet as recommended. However, the HCP who did not participate in the training may not have been able to explain pain properly and given unclear or even contradictory messages, ie, 'mixed messages'. A previous randomized Finnish study found that a 'Back Book' information booklet combined with an occupational nurse appointment was no more effective than the booklet alone among patients with mild LBP symptoms, and this discrepancy could only be explained by unclear messages from the nurse (18).

The longer pain duration in the intervention group may have resulted in poorer recovery, as observed earlier among patients with LBP (37). Therefore, patients in the intervention group may have been more demanding at the start of the study, although their pain symptoms and SBT and ÖMPSQ-short risk-group distribution were similar. Moreover, there was on average a 1-week longer delay in baseline responses among the patients recruited into the training versus control group, which may have attenuated 'true' baseline symptom levels in the intervention group, considering the normal clinical course of LBP (38). On the other hand, the imbalance between the severity of the pain among the recruited patients in the intervention and control groups may be considered a positive phenomenon, as the physiotherapists in the intervention units seem to have been better prepared to address severe pain patients and invite the 'more challenging' patients to participate.

The use of relatively brief training of HCP without mentoring and long-term support means that the expectations of change in clinical practice, and especially in the patient outcomes, are limited. Previous studies have observed that often the beliefs and attitudes of the HCP change, but no change in practice and patient outcomes is achieved (39, 40). On the other hand, the training might have led to the desired change in biopsychosocial pain-management but not improved patient outcomes. Berube et al (9) reported that studies with positive patient outcomes tend to use face-to-face workshops of longer duration and include case studies and practical tools, allowing the practice of the new skills in clinical work and feedback from trainers to the participants. More intensive training and tutoring might have helped improve the transfer of the acquired knowledge into practice. Future interventions should consider supporting individual learning and problems arising during the course of learning.

It has also been suggested that changing individuals' beliefs and competences is not enough, and successful implementation of new knowledge requires complex changes in beliefs, attitudes and clinical routines at the individual, group and organizational levels (41, 42). More research is needed to explain the ways in which implementation design should be changed to overcome clinician and organizational barriers to improve care, and in addition, to address the facilitators of practices in implementing and sustaining the change. Analysis of the facilitators and barriers will be evaluated qualitatively in order to explain what factors have influenced the implementation outcomes.

The possible effectiveness of the intervention in reducing sick leaves, imaging and visits to HCP will be evaluated later in separate analyses based on the registry data on the patients who gave consent to the use of their healthcare records. The registry-based data may be valuable for comparing the training and control groups, as the number of patients who consented to the use of their records was higher than the number of patients who responded to the baseline questionnaire, and there were no delays in the baseline responses in that data set. Relatively simple workplace educational LBP interventions have had a positive effect on work disability in earlier studies (19, 43). We acknowledge several limitations in the current study. First, there is a strong likelihood of recruitment and selection biases. Professionals in both groups were asked to identify and recruit patients but did not keep a record of who was invited, ie, who refused to participate. Thus, a number of factors may have thwarted the ability of the trial to

include similar participants in each group, with respect to their background or baseline characteristics. This is likely reflected in the higher percentage of chronic LBP cases among the patients recruited into the training group. Second, in our trial randomized units, the OHS providers asked representatives to participate in the training, and finally the representatives were advised to disseminate the information and knowledge that they had acquired during the training. This may have resulted in weaker training intervention for most of the HCP or contamination between professionals in the control versus intervention groups within the same organization. Third, there seems to have been an uneven distribution of units between the intervention and control groups. Fourth, a total of five units, all in the control group, did not recruit any patients for the study. The intervention group contained a higher number of patients than the control group, following an approximate ratio of 3:1 at baseline. Fifth, we had a relatively high dropout rate although it appeared to be similar in both groups. Furthermore, dropout during follow-up was taken into account by the statistical approach (full ITT) in the mixed model procedures. Importantly, we adjusted for any observed imbalance in baseline characteristics between the intervention and control groups at baseline in the models. Finally, we did not evaluate the biopsychosocial knowledge of HCP before the training. Thus, we are not able to document to what extent training improved their skills and knowledge.

This study also had several strengths. Few exclusion criteria can enhance generalizability in OHS. Moreover, the extensiveness of the training resembled usual training courses and was feasible. Another strength of the current study is that we included validated patient-related outcome measures for the patient sample. For example, RMDQ and ODI have good construct validity and reliability, and responsiveness over short intervals (44). The planning of this research intervention took into account the multidimensional nature of LBP and the study was designed to enhance a new approach to pain management in the OHS setting. Assessment included physical (disability), psychological (fear of physical activity, fear-avoidance, pain catastrophizing, pain self-efficacy, depression), social (work absenteeism), and health-related quality of life measures, as recommended (45).

The value of this study stems from the fact that, for the first time, we brought to Finnish OHS a multidimensional and -professional training intervention, in which physicians and physiotherapists were trained together for LBP patients. OHS provide an excellent context for actions at an early stage: identifying individuals at increased risk of developing prolonged pain and work disability and targeting early-stage interventions. This study provides information for both primary health care interventions and the development of HCP training within health care services in general. In conclusion, this cluster-randomized controlled trial did not reveal reductions in LBP-related symptoms during a one-year follow-up among patients recruited by professionals trained in the guideline-oriented biopsychosocial management of LBP or among patients recruited through usual OHS. More research is required on the specific targets of the training in the clinical practice as well as the content and length of the biopsychosocial training intervention to improve patient-related outcomes. In addition, organizational level aspects should be evaluated when implementing evidence-based practice in OHS.

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Trial registration

The trial is registered as ISRCTN11875357.

Sidebar

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DETAILS

Subject:	Back pain; Exercise; Physical fitness; Physical activity; Occupational health care services; Clinical medicine; Occupational health; Intervention; Physicians; Questionnaires; Low back pain; Training; Clusters; Pain; Psychologists; Confidence intervals; Clinical trials; Patients; Psychological aspects; Statistical models; Patient education; Health services; Control equipment; Medical personnel
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Robles-Pérez, Eduardo, MD, PhD, González-Díaz, Belinda, MD, PhD, Miranda-García, M., MD, & Borja-Aburto, V. (2021). Infection and death by COVID-19 in a cohort of healthcare workers in Mexico. *Scandinavian Journal of Work, Environment & Health*, 47(5), 349-355. doi:<https://doi.org/10.5271/sjweh.3970>

Objective This study aimed to estimate the risk of SARS-Cov2 infection and severe COVID-19 among healthcare workers from a major social security system. **Methods** This study actively followed a cohort of social security workers from March to December 2020 to determine the number of laboratory-confirmed symptomatic cases, asymptomatic associated contacts and COVID-19-associated hospitalizations and deaths. Workers were classified into those providing direct care to infected patients (COVID teams), other active healthcare workers (OAHCW), and workers under home protection (HPW). The number of cases and rates were also estimated by job category. **Results** Among a total of 542 381 workers, 41 461 were granted stay-at-home protection due to advanced age or comorbidities. Among the 500 920 total active workers, 85 477 and 283 884 were classified into COVID teams and OAHCW, respectively. Infection rates for COVID teams, OAHCW, and HPW were 20.1% [95% confidence interval (CI) 19.8-20.4], 13.7% (95% CI 13.5-13.8), and 12.2% (95% CI 11.8-12.5), respectively. The risk of hospitalization was higher among HPW. COVID teams had lower mortality rate per 10 000 workers compared to HPW (5.0, 95% CI 4.0-7.0 versus 18.1, 95% CI 14.0-23.0). Compared to administrative workers, ambulance personnel (RR 1.20; 95% CI 1.09-1.32), social workers (RR 1.16; 95% CI 1.08-1.24), patient transporters (RR 1.15; 95% CI 1.09-1.22) and nurses (RR 1.13; 95% CI 1.10-1.15) had a higher risk of infection after adjusting for age and gender. Crude differences in mortality rates were observed according to job category, which could be explained by differences in age, sex, and comorbidity distribution. Diabetes, obesity, hypertension, hemolytic anemia, and HIV were associated with increased fatality rates. **Conclusions** COVID team workers had higher infection rates compared to the total population of active workers and HPW. Doctors had lower risk of infection than respiratory therapists, nurses, and patient transporters, among whom interventions should be reconsidered to reduce risks. The presence of comorbidities, such as diabetes, obesity, arterial hypertension, hemolytic anemia, and HIV, increased the likelihood of complications caused by COVID-19, culminating in a poor prognosis.

Lammers-van der Holst, H., M., Wyatt, J. K., Horowitz, T. S., Wise, J. C., M.S., Wang, W., Ronda, J. M., M.S., . . . Czeisler, C. A., PhD. (2021). Efficacy of intermittent exposure to bright light for treating maladaptation to night work on a counterclockwise shift work rotation. *Scandinavian Journal of Work, Environment & Health*, 47(5), 356-366. doi:<https://doi.org/10.5271/sjweh.3953>

Objectives Rotating shift work is associated with adverse outcomes due to circadian misalignment, sleep curtailment, work-family conflicts, and other factors. We tested a bright light countermeasure to enhance circadian adaptation on a counterclockwise rotation schedule. **Methods** Twenty-nine adults (aged 20-40 years; 15 women) participated in a 4-week laboratory simulation with weekly counterclockwise transitions from day, to night, to evening, to day shifts. Each week consisted of five 8-hour workdays including psychomotor vigilance tests, two days off, designated 8-hour sleep episodes every day, and an assessment of circadian melatonin secretion. Participants were randomized to a treatment group (N=14), receiving intermittent bright light during work designed to facilitate circadian adaptation, or a control group (N=15) working in indoor light. Adaptation was measured by how much of the melatonin secretion episode overlapped with scheduled sleep timing. **Results** On the last night shift, there was a greater overlap between melatonin secretion and scheduled sleep time in the treatment group [mean 4.90, standard deviation (SD) 2.8 hours] compared to the control group (2.62, SD 2.8 hours; P=0.002), with night shift adaptation strongly influenced by baseline melatonin timing (r²= -0.71, P=0.01). While the control group exhibited cognitive deficits on the last night shift, the treatment groups cognitive deficits on the last night and evening shifts were minimized. **Conclusions** In this laboratory setting, intermittent bright light during work hours enhanced adaptation to night work and subsequent readaptation to evening and day work. Light regimens scheduled to shift circadian timing should be tested in actual shift workers on counterclockwise schedules as a workplace intervention.

Return-to-work, disabilities and occupational health in the age of COVID-19. (2021). *Scandinavian Journal of Work, Environment & Health*, 47(5), 408-409. doi:<https://doi.org/10.5271/sjweh.3960>

Recommendations such as physical and social distancing and wearing a facemask are highly advisable to protect against infection but may not be enough to enable some individuals to resume work. ...]decision-making requires individual comprehensive assessments of the underlying medical condition, the SARS-CoV-2 contamination risk associated with either regular work or teleworking, and vaccination opportunities. Strategies promoting return to work for these workers will need to be implemented and could be similar to programmes developed for other chronic conditions. ...]numerous more serious sequelae following critical illness suggest the need for enhanced support by rehabilitation and occupational health specialists. ...]the consequences of the epidemic must be evaluated over time for people who suffered from functional limitations before COVID-19 as their physical and mental condition may be modified by the epidemic and, specifically, the consequences of lockdown (10).

Rosenström, T., PhD, Härmä, M., MD PhD, Kivimäki, M., FMedSci, Ervasti, J., PhD., Virtanen, M., PhD., Hakola, T., M.Sc, . . . Ropponen, A., PhD. (2021). Patterns of working hour characteristics and risk of sickness absence among shift-working hospital employees: A data-mining cohort study. *Scandinavian Journal of Work, Environment & Health*, 47(5), 395-403. doi:<https://doi.org/10.5271/sjweh.3957>

Objectives Data mining can complement traditional hypothesis-based approaches in characterizing unhealthy work exposures. We used it to derive a hypothesis-free characterization of working hour patterns in shift work and their associations with sickness absence (SA). **Methods** In this prospective cohort study, complete payroll-based work hours and SA dates were extracted from a shift-scheduling register from 2008 to 2019 on 6029 employees from a hospital district in Southwestern Finland. We applied permutation distribution clustering to time series of successive shift lengths, between-shift rest periods, and shift starting times to identify clusters of similar working hour patterns over time. We examined associations of clusters spanning on average 23 months with SA during the following 23 months. **Results** We identified eight distinct working hour patterns in shift work: (i) regular morning (M)/evening (E) work, weekends off; (ii) irregular M work; (iii) irregular M/E/night (N) work; (iv) regular M work, weekends off; (v) irregular, interrupted M/E/N work; (vi) variable M work, weekends off; (vii) quickly rotating M/E work, non-standard weeks; and (viii) slowly rotating M/E work, non-standard weeks. The associations of these eight working-hour clusters with risk of future SA varied. The cluster of irregular, interrupted M/E/N work was the strongest predictor of increased SA (days per year) with an incidence rate ratio of 1.77 (95% confidence interval 1.74-1.80) compared to regular M/E work, weekends off. **Conclusions** This data-mining suggests that hypothesis-free approaches can contribute to scientific understanding of healthy working hour characteristics and complement traditional hypothesis-driven approaches.

Korshøj, M., PhD, Rasmussen, C. L., PhD., Sato, T. d. O., PhD., Holtermann, A., PhD., & Hallman, D., PhD. (2021). Heart rate during work and heart rate variability during the following night: A day-by-day investigation on the physical activity paradox among blue-collar workers. *Scandinavian Journal of Work, Environment & Health*, 47(5), 387-394. doi:<https://doi.org/10.5271/sjweh.3965>

Objectives Contrary to leisure-time physical activity, occupational physical activity (OPA) may have harmful health effects, called the physical activity paradox. A proposed mechanism is that OPA can elevate the heart rate (HR) for several hours per day. We aimed to investigate the association between the mean intensity of OPA and HR variability (HRV) indices the following night. **Methods** Three cohorts (NOMAD, DPhacto, and Physical Workload and Fitness) involving blue-collar workers from different sectors were merged in this study. HR monitors (Actiheart) recorded 24-hour inter-beat intervals (IBI) for up to four consecutive days. The relative intensity of the mean HR during work was estimated by HR reserve (%HRR), and time-domain indices of HRV were analyzed during the following night. Data were analyzed using a multilevel growth model to test the association between mean %HRR during work and HRV indices at night in a day-by-day analysis adjusted for age, BMI, alcohol consumption, smoking, and occupation. **Results** The dataset included a sample of 878 Danish blue-collar workers, with a mean %HRR during work of 31%, and 42% worked at an intensity >30%HRR. The multilevel model showed negative within- and between-subject associations between %HRR during work and HRV indices at night. **Conclusions** Our results

indicate a higher %HRR during work to associate with lower HRV indices the following night and a higher HR, reflecting an imbalanced autonomic cardiac modulation. This finding supports a high mean HR during work to be a potential underlying mechanism for the harmful health effect of OPA.

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