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Short Communication

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Effects of the combined exposure to chemicals and unusual working hours

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Abstract

Objective: Both exposure to occupational chemicals and to unusual working hours have well documented effects on health. Determination of occupational exposure limits is, however, usually based on chemical-only exposure and assumes an 8-h workday, 5 days/week and a 40-h work week. A significant proportion of the workforce is exposed to chemicals while working in other work schedules. This review thus aimed to synthesize and evaluate the scientific support for a combined effect of unusual working hours and chemical exposure and, if possible, give recommendations for OEL adjustments to account for unusual working hours.

Methods: The search for articles was made as part of the preparation of a report for the Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals. In this report, unusual working hours were categorized as *shift work* or *extended (>8 h) working hours*. Inclusion criteria were observational studies in the English language published up to November 2021 in peer-reviewed journals, with explicit metrics of exposure (chemicals and unusual working hours) and of health outcome, and which explicitly tested the association between exposure and outcome. Search engines of seven databases were used.

Results: Of the initially 15 400 identified papers, 9 studies published between 1985 and 2021 met the inclusion criteria, 7 of which showed significant associations. Results from a few of the studies, i.e. regarding effects of dust and endotoxin on lung function, effects of acetone on sleep quality and tiredness, effects of carbon disulphide on coronary artery disease and effects of chemicals on spontaneous abortion, suggested more pronounced effects during night shifts compared to during day shifts.

Discussion: The reviewed data is considered insufficient to conclude on recommendations for OEL adjustment for shift work. Suggested areas of future studies are mentioned.

Conclusion: Further studies about the effects of the combined exposure to unusual working hours and chemical exposure are essential for risk assessment, and for recommendation of potential OEL adjustments. What is important about this paper? Effects of chemical agents at the workplace may depend not only on exposure level and duration but also on the time of exposure in relation to the circadian rhythm. This study reviewed the scientific support for a combined effect of unusual working hours and chemical exposure and revealed an obvious need for additional studies regarding the complex interplay of the two different exposures with respect to adverse health effects.

Key words: coronary artery disease; lung function; night work; shift work; spontaneous abortion; tiredness; working time.

What is important about this paper?

Effects of chemical agents at the workplace may depend not only on exposure level and duration, but also on the time of exposure in relation to the circadian rhythm. This study reviewed the scientific support for a combined effect of unusual working hours and chemical exposure and revealed an obvious need for additional studies regarding the complex interplay of the two different exposures with respect to adverse health effects.

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Introduction

A significant proportion of the work force is employed in shift work and extended working hours.

Effects of chemical agents at the workplace may depend not only on exposure level, frequency and duration but also on the time of exposure in relation to the circadian rhythm. Knowledge on combined effects of chemicals and shift work is biologically plausible given that circadian rhythms play an important role in biotransformation of many chemicals. However, such knowledge is limited.

The objectives of this paper were to review the scientific literature regarding possible effects of occupational chemical exposure in combination with unusual working hours and, if possible, provide recommendations for adjustment of the OEL to account for unusual working hours.

Methods

Search strategy and inclusion criteria

This work is a summary of the main results in a report for the Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals (Lie et al. 2023).

Online searches for human studies in English before November 2021, were conducted in the Embase, Medline, OSH, SCOPUS, Toxicology, Web of Science, ProQuest Health and Safety databases, for all years up to November 2021, using search terms related to unusual working hours e.g. "night," "evening," "rotating," "atypical," or "compressed work/shift," and chemical exposure terms, e.g. "benzene," "BTEX," "carcinogen," "ethylbenzene," "hazardous substance," "pollutant," "polycyclic aromatic hydrocarbon," "solvent,, "toluene," "xylene," "antineoplastic agents," "anticarcinogen," and "cytostatic." Thus, for some common industrial chemicals for which biotransformation is considered to be affected by metabolization by enzymes with circadian rhythms, we used specific chemical names. For other substances, like heavy metals, we assumed that they were covered by the unspecific search terms for chemicals. For an article to be included in the study, it should have clearly defined metrics of exposures (chemicals and working hours) and of health outcome, as well as an explicit test of the association between exposures and outcome. The papers were evaluated independently by 2 of the authors.

Results

Of the initially 15 432 identified articles, 9 fulfilled the inclusion criteria, 8 articles regarding shift and night work, and one regarding extended working hours. One study was a cohort study, 2 were cross-sectional studies, and the rest were studies with repeated measures across working days and work shifts. One of the shift work studies and the study on extended working hours did not show any significant association between exposure and outcome (Table 1).

Description of the individual studies by outcome

Shift work

Reproductive effects. Attarchi et al. (2012) performed a cross-sectional study of women in reproductive age, employed in a pharmaceutical factory in Iran, to evaluate the correlation between occupational exposure to formaldehyde, phenol, *n*-hexane, and chloroform and spontaneous abortions and time to pregnancy. Odds ratios (95% CI) for spontaneous abortion were 4.10 (1.69 to 9.93) for shift work and no chemical exposure, 5.40 (2.02 to 14.4) for daytime work and chemical exposure, and 13.5 (5.28 to 34.6) for shift work and chemical exposure (all compared to daytime work and no chemical exposure). Thus, a combined effect on spontaneous abortion was found between shift work and occupational chemical exposure.

Cardiovascular disease. Carreón et al. (2014) updated the mortality data of 1874 workers employed at a chemical manufacturing plant in US 1946 to 2006. Exposures to vinyl chloride, carbon disulphide (CS_2), shift work, and categories of *o*-toluidine exposure were reassessed. The plant was operated 24/7. Internal comparisons showed increased coronary artery disease mortality among workers exposed to both CS_2 and shift work for ≥ 4 years. Internal comparisons showed increased coronary artery disease mortality among workers exposed to both CS_2 and shift work for ≥4 years (standardized rate ratio (SRR) 2.70, 95% CI 1.05 to 6.93) compared to those exposed to both CS_2 and shift work for < 4 years. Furthermore, mortality was not higher among workers with ≥4 years of just one of these exposures. The authors suggested that CS_2 and shift work may be cofactors in the presence of other risk factors. The study provides support for a combined effect of CS_2 exposure and shift work.

In a Belgian cross-sectional survey, Vanhoorne et al. (1992) investigated the cardiovascular effects among 115 male viscose rayon workers exposed to CS_2 and 76 referents not exposed to this chemical. Sixty-six percent of the CS_2 exposed workers, and 86% of the unexposed were working rotating shift work. Multiple linear regression analysis revealed an association between CS_2 cumulative exposure index and blood pressure (systolic and diastolic) and all lipoparameters except triglycerides, after adjustment for relevant confounders. However, shift work was not related to any of these outcomes, thus the study provides no

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Table 1. Studies on shift work and implication on risk assessment (health) of chemicals.

Author	Study design	Outcome (measures)	Chemical exposure	Shift work	Results
	Reproductive effects				
Attarchi et al. (2012)	*Cross-sectional study* *Cohort:* 205 female workers in 5 laboratory units (20–40 y of age) employed ≥ 1 y in a pharmaceutical factory, Tehran, Iran. *Referents:* 201 female workers employed ≥ 1 y in 2 packing units (20–40 y of age) in the same factory. Study performed 2010	Time to pregnancy, Spontaneous abortion	*Personal sampling, mean concentrations (ppm)* Formaldehyde: 0.01 phenol: 0.5 *n*-Hexane: 20.7 Chloroform: 3.2. Total exposure expressed as HI, assuming additivity and using 2008 TLVs. HIs were 0.55–0.93; in low- and high-exposed ≤0.87 and >0.87, respectively.	*Personal interviews* Daytime or shift work (fixed evening, fixed night or rotating). *Exposed* Daytime: 77.5% Shift work: 22.5%. *Referents* Daytime: 70% Shift work: 30%.	*Spontaneous abortion, OR (95% CI)* Chemically exposed versus referents 3.90 (1.54–9.85) (all, crude) 5.21 (1.95–14.12) (low-exposed, log regression) 7.70 (2.09–15.38) (high-exposed, log regression) Shift workers versus daytime workers 2.68 (1.20–5.71) (all, crude) 4.13 (1.70–10.0) (all, log regression) Chemically exposed and/or shift work versus referents 1.00 (ref. no chemical exposure, daytime work) 4.10 (1.69–9.93) shift work only 5.40 (2.02–14.4) chemical exposure only 13.5 (5.28–34.6) chemical exposure + shift work *Time to pregnancy > 12 mo, OR (95% CI)* Chemically exposed versus referents 2.20 (1.26–4.30) (all, crude) 2.76 (1.15–4.21) (low-exposed, log regression) 4.48 (1.89–8.42) (high-exposed, log regression) Shift workers versus daytime workers 2.85 (1.11–4.36) (all, log regression)

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Table 1. Continued

Author	Study design	Outcome (measures)	Chemical exposure	Shift work	Results
	Cardiovascular diseases				
Carreón et al. (2014)	*Cohort:* 1 874 workers (93% males) employed ≥ 1 day 1946–2006 in a chemical manufacturing plant, New York, US, of which 67% were exposed to carbon disulphide (CS_2). *Referents:* US mortality rates (SMR) or internal comparison (SRR).	Coronary artery disease mortality	Exposure to CS_2 in the rubber chemicals department 1954–1994. No exposure estimates were given.	The plant operated 24 h/day, 7 days/wk, and numerous workers were in a forward rotating shift work schedule.	*Coronary artery disease mortality (employment ≥90 days*, SRR (95% CI) Exposure to CS_2 and shift work ≥ 4 y versus < 4 y No shift work or CS_2 1 Only CS_2 1.10 (0.57 to 2.10) Only shift work 1.41 (0.77 to 2.60) Shift work + CS_2 2.70 (1.05 to 6.93)
Vanhoorne et al. (1992)	*Cross-sectional study* *Cohort:* 115 male workers (median age 34.0 y) exposed to carbon disulphide (CS_2) and employed for ≥1 y at a viscose rayon factory in Belgium. *Referents:* 76 unexposed male workers (median age 33.5 y) in a metal-works, a plastics factory and a starch processing factory.	Angina, History of myocardial infarction, Intermittent claudication and ECG signs of ischaemia.	*Personal monitoring (17 jobs)* 4 to 112 mg/m^3. Individual CS_2 cumulative exposure indexes were calculated ("low" or "high"). Working conditions had not changed since 1932.	*Self-administered questionnaire* Rotating shift work: Exposed: 66.1% Unexposed: 85.6%.	Cardiovascular effects *CS_2-exposure* No significant effects on the prevalence of angina, history of myocardial infarction, intermittent claudication and ECG signs of ischaemia. Significant effects of the CS_2 index (multiple linear regression analysis) Systolic and diastolic blood pressure ↑ Apolipoproteins A1 and B ↑ Cholesterol, LDL-cholesterol ↑ HDL-cholesterol ↓ HDL-cholesterol/apolipoprotein A1 ratio ↓ LDL-cholesterol/apolipoprotein B ratio ↓ *Shift work* No significant impact on the associations.

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Table 1. Continued

Author	Study design	Outcome (measures)	Chemical exposure	Shift work	Results
	Respiratory diseases				
Nemery et al. (1985)	*Cohort:* 25 steelworkers (mean age 33.1 y) from a strand casting department in Belgium. *Referents:* 11 steelworkers (mean age 34.8 y) not exposed to dust, but working according to the same shift schedule.	Lung function	*Air sampling, mean total dust*, mg/m^3 Exposed: 11.8 (0.5% soluble fluoride), personal. Referents: 1.7 and 1.8 (0.05% fluoride), stationary. *Post-shift urinary fluoride* was higher among exposed, but did not vary between day and night shifts.	21 consecutive workdays, 3-shift; 7 day shifts: morning (06 to 14) → 7 days afternoon (14 to 22) → 7 days night (22 to 06) followed by 7 days without working.	*Across-shift lung function changes* Morning shift No change in lung function in either group. Afternoon shift Significant decreases in spirometric indices in the exposed group only, but interactions between exposure and time were not significant, except for VC ($P = 0.03$). Night shift Significant decreases in spirometric indices in the exposed group, only. Interactions between exposure and time were significant for: FEV_1: 3.0% versus 1.1% ($P = 0.03$) FEV_1/VC: 2.3% versus 0.8% ($P = 0.002$) $FEF_{25\text{ to }75}$: 7.7% versus 1.0% ($P = 0.02$).
Pasker et al. (1997)	*Cohort:* 57 workers (mean age 36 y) exposed to fumes containing zinc oxide in a steel plant (production or maintenance) in Belgium. *Referents:* 55 nonexposed workers (mean age 38 y) (maintenance or strand casting department).	Lung function	*Personal sampling* Total dust (prior to the study): 1.0 to 22.8 (mean 8) mg/m^3 with an average of 39% in the respirable range (<5 µm). Zinc oxide: below or close to the TLV for fumes (5 mg/m^3) at ground floor level, but exceeding that value in the upper floors (7.6 mg/m^3). Urinary zinc post-shift, mg/g creatinine: 0.33 versus 0.24 in exposed and referents ($P = 0.002$).	Most subjects worked 21 consecutive days (7 d/shift) followed by 7 d without working. Some subjects worked normal day shifts with 2 days off at the weekend.	*Across-shift lung function changes (spirometry)* Day shift Small decreases in VC and in FEV_1 in most workers. These decreases did not differ significantly between exposed and referents. Night shift VC and FEV_1 decreased significantly in exposed (−99 ± 178 ml and −140 ± 140 ml, respectively), but not in referents (−25 ± 159 ml and −51 ± 213 ml). No significant differences between exposed and referents. The decrease in FEV_1 was maintained the day after exposure. The cross-shift decrease in lung function was noticeable only across the night shift. The effects on lung function were small but likely represent a subclinical response to the inhalation of small quantities of zinc oxide.

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Table 1. Continued

Author	Study design	Outcome (measures)	Chemical exposure	Shift work	Results
Zock et al. (1999)	*Cohort:* 97 male shift workers in the potato processing industry, the Netherlands.	Lung function	*JEM* based on categorization of job by plant with 27 categories. *Endotoxins* Estimated overall geometric mean exposure: 534 EU/m^3 (53 to 8167 EU/m^3).	*Sequence of shift rotation*: afternoon → morning → night → afternoon, etc. A work period lasted 3 to 4 days, with a subsequent leisure period of 2 to 3 days.	*Across-shift changes in lung function (PEF)* Work schedules Morning +2.7% Afternoon –1.3% Night –1.7% (consistent with expectations, based on the circadian rhythm). Endotoxins Change in PEF (%) associated with an increase in exposure from 249 to 1411 EU/m^3 (interquartile range) Morning –0.46% ($P < 0.05$ versus afternoon) Afternoon –1.78% Night –0.83% ($P < 0.10$ verus afternoon) A higher endotoxin exposure was associated with an increased prevalence of work-related symptoms.
Kiesswetter *et al.* 1997	*Repeated measures design* *Cohort*: 8 males from a cellulose acetate manufacturing plant, Germany. *Referents*: 8 male workers in the packing department. Mean age: 38 y.	Sleep quality	*Personal sampling* 2 × 4 *h/day* Acetone: 980 ppm (mean).	Cohort + referents 3-shift work: Morning → afternoon → night starting at 06, 14 and 22.	*Quality of sleep* Acetone exposure Less sleep recovery ($P = 0.05$) Acetone exposure × night shift Low recovery ($P = 0.005$) Easy falling asleep ($P < 0.1$) Low depth of sleep ($P < 0.1$) Dose to response relationships were found between acetone in air and urine during the 3 different work shifts and sleep quality.

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Table 1. Continued

Author	Study design	Outcome (measures)	Chemical exposure	Shift work	Results
	Other outcomes				
Kiesswetter et al. (1996)	*Repeated measures design* *Cohort A:* 8 male cleaners working in floor covering production, Germany. *Referents*: 8 male workers in the packing department in the same firm. Mean age: 44 y. *Cohort B*: 8 males from a cellulose acetate manufacturing plant, Germany. *Referents*: 8 male workers in the packing department. Mean age: 38 y.	Neurobehavioral effects studied: (a) Performance (reaction time, color word vigilance) (b) Acute symptoms (discomfort, irritations, breathing difficulties) (c) Well-being (tension, tiredness, complaints and annoyance).	*Cohort A* 15 solvents from printing colors and cleaning agents were quantified in 110 personal full-shift air samples/dosimeters. 12 of the solvents were clearly below 25% of the German MAK-value. Concentrations of 1-methoxy-propanol-2, cyclohexanone, 2-butoxyetanol exceeded 25% of MAK. *Cohort B* *Personal sampling* *2 × 4 h/days* Acetone: 980 ppm (mean)	*Rotating shift work*: Cohort A + referents 2-shift work starting at 05 and 13. Cohort B + referents 3-shift work: Morning → afternoon → night starting at 06, 14 and 22.	*Cohort A (mixed solvents + 2-shift)* Mixed solvents No effects. Shift Tiredness and annoyance: $P < 0.05$ Mixed solvents/shift Tension and tiredness: $P < 0.05$ Mixed solvents/across shift Reaction time and annoyance: $P < 0.05$ Shift/across shift Reaction time, tension and tiredness: $P < 0.05$ Mixed solvents/shift/across shift No association *Cohort B (acetone + 3-shift)* Acetone Acute symptoms: $P < 0.05$ Well-being: $P < 0.05$ (for each) Shift Performance: $P < 0.05$ (for each) Acute symptoms: $P < 0.05$ Acetone/shift No effects. Acetone/across shift Acute symptoms: $P < 0.05$ Well-being: $P < 0.05$ (for each) Shift/across shift Color word vigilance: $P < 0.05$ Acute symptoms: $P < 0.05$ Tension and tiredness: $P < 0.05$ Trends for tiredness and color word vigilance within shift, differed more from referents during the morning shift than during the other shifts, although the exposed group revealed the highest values of tiredness during the night shift. Acetone/shift/across shift Color word vigilance: $P < 0.05$. Overall Both exposure to acetone and shift work contributed to the strong adverse effects.

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Table 1. Continued

Author	Study design	Outcome (measures)	Chemical exposure	Shift work	Results
	Biomarkers of disease				
Shih TS *et al.* 2003	*Cohort:* 13 workers of which 6 with 8-h shift (mean age 40.0 y) and 7 with 12-h shift (mean age 28.9 y), exposed to carbon disulphide (CS_2) in the spinning department in the viscose rayon industry, Taiwan.	Thiothiazolidine-4-carboxylic acid levels in the urine (U-TTCA)	*Average CS_2 exposure (personal), 5 consecutive days* Air levels (TWA) and urinary TTCA collected pre and postshift	8-h or 12-h work shifts	*Carbon disulphide in air (ppm)* 12-h shift: 11.3 ± 1.47 8-h shift: 6.3 ± 0.64 $P < 0.001$ *TTCA in urine (mg/g creatinine)* Preshift 12-h shift: 1.78 ± 1.04 8-h shift: 0.76 ± 0.63 $P < 0.001$ Post-shift 12-h shift: 5.88 ± 2.04 8-h shift: 3.24 ± 1.21 $P < 0.001$ *Ratio (preshift urinary TTCA)/(airborne CS_2 levels on the preceding day)* Significant linear accumulation trend across the workdays for the 12-h shift ($r = 0.98$, $P = 0.02$).

BMI: body mass index, CI: confidence interval, DL: detection limit, ECG: electrocardiogram, EU: endotoxin unit, $FEF_{25\text{to}75}$: forced expiratory flow between. 25% and 75% of VC, FEV_1: forced expiratory volume in 1 s, HDL: high density lipoprotein, HI: hazard index, JEM: job exposure matrix, LDL: low density lipoprotein. MAK: Maximale Arbeitsplatz-konzentration (maximum workplace concentration), OR: odds ratio, PEF: peak expiratory flow, RR: relative risk, SGA: small for gestational age, SLE: systemic lupus erythematosus, SMR: standardized mortality ratio, SRR: standardized rate ratio, TLV: threshold limit value, TWA: time-weighted average, US: United States, VC: vital capacity. From the report by Lie *et al.*, (2023).

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support for a combined effect of shift work and CS_2 exposure on the cardiovascular outcomes.

Respiratory diseases. Nemery et al. (1985) investigated across-shift lung function indices in 25 steelworkers from a dusty strandcasting department and in 11 comparable steelworkers exposed to considerably lower dust levels, over an almost uninterrupted 21-days working period and over three different work shifts. Results indicate that the more pronounced decrease in spirometry indices, found over the night shift in the strandcasting workers, suggestive of slight airway obstruction, was due to the work environment. The study provides support for a combined effect of night shift work and dust exposure on lung function.

In a cohort-study of steel plant workers in Belgium, Pasker et al. (1997) examined the lung function of the workers. Fifty-seven workers were exposed to zinc oxide fumes and 55 were nonexposed. Lung function measurements were performed at the beginning and near the end of a work shift (day or night) and were repeated one day later. During the night shift, VC, FEV_1 and the slope of respiratory resistance decreased significantly in exposed, but not in controls, thus the study provides some support for a combined effect of (night) shift work and zinc oxide exposure on lung function.

Zock et al. (1999) investigated the association between endotoxin exposure, work-related respiratory symptoms, and acute peak flow changes, in a cohort study of 97 shift workers from 4 potato-processing plants in the Netherlands, during a 23-day period. A higher endotoxin exposure was associated with a smaller peak expiratory flow (PEF) increase across the morning shift and a larger PEF decrease across afternoon and night shifts as well as with an increased prevalence of work-related symptoms. The effect related to endotoxin exposure was significantly higher for the afternoon shift than for the morning and night shifts. The study indicates a combined effect of shift work and endotoxin exposure on lung function.

Sleep disorders. Kiesswetter et al. (1997) investigated if organic solvent exposure alone (experimental chamber study) or combined solvent exposure and shift work (field study) influence sleep. Workers were on a rapidly rotating shift system. Measurements were undertaken for three weeks. During the shifts, acetone concentration was monitored in the air of the breathing zone and in the urine. Sleep quality was recorded via a questionnaire. The exposed shift workers reported a reduced sleep recovery, mainly in connection with daytime sleep, in comparison with nonexposed shift workers. Interaction effects between night shift and acetone exposure were found for recovery ($P = 0.005$) and trends were found both for falling asleep and depth of sleep ($P < 0.1$) The study indicates some support for a combined effect of acetone exposure and night shift work on sleep quality.

Other health outcomes. Kiesswetter et al. (1996) also studied neurobehavioral effects of shift work and organic solvent exposure among healthy males in a 2-shift and a 3-shift study, respectively. Ratings of well-being (tension, tiredness, complaints, and annoyance) and acute symptoms (discomfort, irritation, and difficulties in breathing) and scoring of performance (simple reaction time, and color word vigilance) were made at the beginning, middle, and end of each shift. The 2-shift study included 8 subjects exposed to mixed solvents from printing colors and cleaning agents and 8 matched unexposed controls from the same company. The 3-shift study included 8 subjects exposed to acetone-soaked filters and 8 matched controls who worked in a "clean air" area in the packing department. The study indicates some support for neurobehavioral effects of the combined exposure to shift work and solvents.

Extended working hours

Biomarkers of disease. Shih et al. (2003) investigated if carbon disulphide (CS_2) accumulates after a 1-week exposure period, and how the duration and exposure magnitude of 2 different work shifts affects the accumulation among workers in viscose rayon industry at Taiwan. The study included 6 CS_2-exposed subjects on 8-h shift, 7 CS_2-exposed subjects on 12-h shift and 7 unexposed control subjects. Personal air monitoring in the breathing zone covered full work shifts. Urine was collected pre and postshift every day for 5 consecutive days. Accumulation of 2-thiothiazolidine-4-carboxylic acid levels occurs for prolonged shifts (12-h), but not for the normal, 8-h shift. Further analyses indicated that the difference in preshift as well as postshift workers is well explained by differences in exposure level (magnitude) and exposure duration, thus the study provides no support for a combined effect of CS_2 exposure and extended working hours on renal function.

Discussion

Seven of the 9 included studies suggest more pronounced effects during night shifts compared to day shift exposure, i.e. regarding effects of dust and endotoxin on lung function, effects of acetone on sleep quality and tiredness, effects of carbon disulphide on coronary artery disease, and effects of chemicals on spontaneous abortion. The nonpositive findings of a combined effect of shift work and chemicals in 2 studies are not likely to be the result of limitations of the study design and analysis. The reviewed studies were insufficient to conclude on recommendations for OEL adjustment for shift work.

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Considering the vast number of evaluated articles, and the limited number that were finally included in this review, there is an obvious need for further research in this field, including

- Studies of occupations and industries in which employees are exposed to both chemicals and unusual working hours.
- Studies focusing on classes of chemicals metabolized by enzymes that are likely to be regulated by circadian rhythms and further development of pharmacokinetic modeling of body burden.
- Epidemiological studies related to chronotoxicity.
- Animal studies of the most relevant exposure route (e.g. inhalation), to improve understanding of mechanisms of the combined effects of shift work and chemicals.
- Studies of individual susceptibility to shift work in ways that might affect interactions with chemical exposure, for example of the effects on immune system, lung function or metabolic rates.

Conclusion

This review underscores the need for knowledge on the complex interplay of occupational chemical exposures and unusual working hours with respect to adverse health effects. Combined effects of chemicals and shift work are biologically plausible, given that circadian rhythms play an important role in biotransformation of many chemicals. For example, some animal data from chronopharmacological studies suggest that the time of exposure (day-night) may affect the biotransformation and toxicity of chemicals.

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Conflict of interest

The authors declare no conflict of interest relating to the material presented in this article.

Data availability

No new data were generated or analyzed in this research.

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