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**Indoor, outdoor, and night work and blood concentrations of vitamin D and parathyroid hormone**

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We observed lower 25OHD and higher PTH concentrations among permanent but not rotating night workers compared with indoor workers. Furthermore, that 25OHD levels increased significantly by increasing hours spent outdoors. Clinicians should be aware that vitamin D insufficiency may be more prevalent among permanent night workers and employers should consider the beneficial health effects of outdoor work.

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**Key terms:** blood concentration; cross-sectional study; diet; indoor work; night work; occupation; occupational health; outdoor work; parathyroid hormone; risk factor; season; shift work; ultraviolet radiation; vitamin D

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# Indoor, outdoor, and night work and blood concentrations of vitamin D and parathyroid hormone

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**Objectives** The aim of this study was to examine blood concentrations of 25-hydroxyvitamin D (25OHD) and parathyroid hormone (PTH) among indoor, outdoor, permanent and rotating night workers and the association with hours spent outdoors on and off work days.

**Methods** Blood samples were collected from 425 workers *(*162 indoor, 112 outdoor, 118 rotating night and 33 permanent night workers) throughout all seasons. Serum concentrations of 25-hydroxyvitamin D (25OHD) and parathyroid hormone (PTH) were analyzed by isotope dilution liquid chromatography-tandem mass spectrometry (LC MS/MS) and an automated immune analyzer, respectively. Personal light exposure levels were continuously recorded and used to estimate hours spent outdoors (all workers).

**Results** Permanent night workers had 25.3% (95% CI 11.9–36.6) lower 25OHD concentration, 4.55 (95% CI 1.39–14.94) higher odds of vitamin D insufficiency (<50 nmol/L) and 14.5% [95% confidence interval (CI) 0.1–31.1] higher PTH concentration than indoor workers. Outdoor workers had similar 25OHD concentrations but 7.5% (95% CI -0.5–14.9) lower PTH concentration compared to indoor workers. Rotating night workers 25OHD and PTH concentrations did not differ from indoor workers. Concentration of 25OHD increased by 5.2% (95% CI 1.1–9.5) per hour spent outdoor at workdays in the summer.

**Conclusion** Clinicians should be aware that vitamin D insufficiency may be more prevalent among permanent night workers and human resources should consider the positive effect of allowing workers to spend time outdoors during work hours.

**Key terms** cross-sectional study; diet; indoor work; occupation; occupational health; outdoor work; risk factor; season; shift work; ultraviolet radiation.

The importance of vitamin D in maintaining calcium homeostasis and skeletal health is well established (1). The anti-proliferative and immunomodulatory effects of vitamin D (2, 3) as well as the presence of vitamin D receptors in tissues not related to calcium metabolism (4) suggest that vitamin D has pleiotropic effects beyond calcium metabolism. Epidemiological studies have reported an association between low vitamin D and increased risks of extra skeletal diseases such as colorectal cancer (5), cardiovascular disease (6, 7), diabetes (8), multiple sclerosis (9), and allergy (10). Permanent and rotating shift work has been associated with increased risk of cancer (11), diabetes (12–14) and fractures (15). Opposing, outdoor work has been inversely associated with cancer (16–18), multiple sclerosis (19, 20) and Parkinson's disease (21–23). Though any causal relations remain to be established, vitamin D has repeatedly been suggested as a mediator of the observed associations (20, 21, 24, 25). With the exception of one study (29), previous research (26–28) have found higher 25-hydroxyvitamin D (25OHD) concentrations among outdoor than day workers. Permanent night work has been associated with lower 25OHD concentrations among female but not male night workers (30).

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Rotating night workers had lower 25OHD concentration compared to day workers in male and mixed populations (31–33). However, no difference between day and rotating night workers has also been found in male and mixed populations (29, 34, 35).

Vitamin D is a fat-soluble pro-hormone mainly derived from synthesis by the skin upon exposure to ultraviolet B radiation (UVB) from sunlight; only a minor part is obtained from foods such as milk, fish, and meat (36). In Denmark (latitude 55–56 °N), vitamin D synthesis is only induced by UVB from March till September and summer sun exposure is important for vitamin D concentration around the year (37).

Vitamin D status is defined by plasma concentrations of 25OHD. The cut-off value to define vitamin D insufficiency in terms of skeletal outcomes is 50 nmol/L (38). In terms of non-skeletal health outcomes it is suggested that a sufficient vitamin D status requires concentrations >75–80 nmol/L (39). Importantly, the optimal 25OHD concentration in non-skeletal health outcomes has not yet been clarified (40). Vitamin D insufficiency is common worldwide, also in Denmark where studies have suggested a prevalence of vitamin D insufficiency as high as 52.2% among healthy adults (41).

Parathyroid hormone (PTH) concentrations are inversely correlated with 25OHD concentrations. A rise in PTH signals that insufficient 25OHD concentrations start to negatively affect bone metabolism (42). The 25OHD concentration at which PTH concentrations start to increase has substantial inter-individual variation. Independently of 25OHD concentrations, increased PTH concentrations have been associated with increased risk of fractures (43), cardiovascular disease (44), and overall mortality (45).

As vitamin D insufficiency is common, easily treatable and may have major health consequences for the individual, it is important to identify current risk factors for vitamin D insufficiency including the work environment. Low 25OHD concentrations in indoor and night workers may be explained by limited exposure to sunlight during work and leisure time, differences in intake of vitamin D supplement, dietary habits, or lifestyle factors. Furthermore to elucidate a possible mediation by 25OHD concentrations in epidemiological studies of night and outdoor work, knowledge of differences in 25OHD concentration by job type is crucial.

The aim of this study was to examine blood concentrations of 25OHD and PTH among indoor, outdoor, permanent and rotating night workers and the association with hours spent outdoors on work days and days off.

## Methods

### Study set up

Participants were recruited through employers and public advertisements in magazines and on webpages aimed at recruiting an equal numbers of indoor, outdoor and night workers.

A research assistant met the participants at their place of work, provided instructions, handed out a questionnaire to get data on background characteristics and collected a blood sample. For continuous measurement of light levels, participants wore a light recorder during seven days both at and off work. Data was collected from March 2012 until May 2013. All participants gave written informed consent and the Danish Data Protection Agency (J.nr. 2011-41-6850) and the Central Denmark Region Committee on Health Research Ethics (M-20110214) approved the study. Further details of the study design are presented elsewhere (46).

### Population

A total of 535 participants were recruited and 459 provided a blood sample. Samples of 8 participants could not be analyzed due to insufficient blood volume. Of the participants, 26 were excluded due to medical conditions or treatment potentially affecting calcium homeostasis and vitamin D metabolism: use of thiazide diuretics (N=10), pregnancy (N=7), suspected primary hyperparathyroidism (serum calcium and plasma PTH above normal) (N=2), anticonvulsants (N=1), systemic glucocorticoids (N=1), estimated glomerular filtration rate (eGFR) < 60 ml/min and metastasized breast cancer (N=1). The final population comprised 425 participants with complete confounder information except for 12 participants with missing information on body mass index (BMI).

*Indoor workers* were defined as those working daytime only and working ≤9 hours outdoors per week during the summer (June-August) (N=162). The majority (72.8%) of the indoor workers never worked outdoors, 12.4% worked outdoors 1-4 hours/week and 14.8% reported 5–9 outdoor work hours/week. *Outdoor workers* were defined as working daytime only and outdoors >9 hours/week during the summer (N =112). Of these, 31.3% worked outdoors 10–19 hours a week, 41.1% worked 20–29 hours/week, and 27.7% worked 30–37 hours/week. *Night workers* were defined as working >3 hours between 00:00–05:00 hours on a permanent (N=33) or rotating shift work basis (N=118) (47). Classification of participants into the above job groups was based on questionnaire data.

To define vitamin D insufficiency, we chose a cut-off value at 50 nmol/L, which is the 25OHD concentration recommended by Danish guidelines. Hyperparathyroidism was defined as PTH concentrations >6.9 pmol/L,, which is the upper reference limit used in Danish laboratories.

For analyses including hours spent outdoors, we only included workers who participated from April throughout September (N=227) where UVB exposure induces production of vitamin D. We excluded 39 workers with missing information on either BMI, hours spent outdoors on or off work, leaving 186 workers for analysis (81 indoor workers, 44 outdoor workers, 46 rotating shift workers, and 15 permanent night workers).

### Blood samples

Blood samples were drawn at participants' place of work and collected in tubes without anticoagulation for serum and EDTA tubes for plasma and stored at 5 $^{o}$C until processed to separate serum and plasma. Most samples (N=407) were processed within 8 hours (mean 3 hours 48 minutes), 30 samples were processed 10–33 hours after collection, and 4 samples were processed 94 hours after collection due to technical problems. Samples were stored at -80 $^{o}$C after processing.

### Biochemical analyses

All biochemical analyses were carried out in September 2014. Serum concentrations of 25OHD (25(OH)$D_2$ and 25O$HD_3$) were analyzed by isotope dilution liquid chromatography-tandem mass spectrometry (LC MS/MS) as described by Maunsell et al. (48). Calibrators were traceable to NIST SRM 972 (Chromsystems GmbH, Gräfeling, Germany). The coefficient of variation (CV) for 25O$HD_3$ was 6.4% at concentration 66.1 nmol/l and 9.4% at 25.3 nmol/l. Plasma PTH concentration was analyzed using an automated immune analyzer (Cobas 6000 E; Roche Diagnostics GmbH, Berlin, Germany). The CV was 3.3% and 2.7% at PTH concentrations of 7.7 and 26.6 pmol/l, respectively. Standard laboratory methods were used for measurements of total calcium, creatinine, and albumin. The estimated glomerular filtration rate (eGFR) was calculated according to the Modification of Diet in Renal Disease (MDRD) study equation (49).

### Questionnaire

The questionnaire included information on sex, age (years), pregnancy (yes/no), current occupation, time spent working outdoors in spring, summer, autumn, and winter (never, 1–4, 5–9, 10–19, 20–29, 30–39, ≥40 hours/week), height (centimeters), weight (kilograms), smoking (current/former/never), use of medication (yes/no), vitamin pill use (yes/no), vitamin D supplement use (no/10 μg/20 μg or more or cod liver oil (yes/no), tanning bed use (weekly, monthly, never), consumption of fish and shell food (never, monthly, 1, 2–3, >4 meals/week).

### Light exposure assessment

Participants wore a Philips Respironics Actiwatch Spectrum (Actiwatch) light recorder during a 7-day study period. The Actiwatch was placed outside clothes on the upper arm and recorded white light (lux) and activity every minute. Time spent outdoors was assessed as periods where the light intensity measured by the Actiwatch was ≥1000 lux (50). Light measurements were considered invalid if the participants reported the Actiwatch was not worn or the Actiwatch recorded no physical activity for ≥20 minutes. We excluded 270 work days (26.5%) and 126 days off work (25.3%) with <80% valid light measurements between 07:00–19:00 hours. Light measurements were included from 748 work days and 373 days off work.

### Statistical analyses

Data was presented as numbers (%), means with standard deviations (SD), or medians with interquartile (25$^{th}$–75th percentiles) ranges (IQR). Concentrations of 25OHD and PTH were naturally log transformed to obtain the best approximation with normal distributions. We tested the difference of 25OHD and PTH concentrations across seasons and job groups using the Kruskal-Wallis test.

We used multivariable linear regression to estimate the relative difference of serum 25OHD and plasma PTH concentrations between outdoor, rotating night workers and permanent night workers relative to indoor workers. Models were adjusted in two steps: Model 1 included season (January-March/April-June/July-September/October-December). These differ from the traditional definitions of the seasons used in the questionnaire. Instead we classified season based on when the intensity of UVB begins (end of March) and ends (end of September) to induce vitamin D synthesis. Model 2 also included age (continuous), sex, socioeconomic status (SES) (white-collar worker / skilled blue-collar worker /unskilled blue-collar worker), current smoking (yes/no), body mass index (BMI) (continuous), vitamin D supplements or cod liver oil (yes/no), birth control or hormone replacement therapy (yes/no), fish and shell food consumption (<1 meal/week/ ≥1 meal/week), tanning bed use (ever/never), and time from blood sampling to storage. These potential confounders were identified a priori based on a review of the literature (41, 43, 51–54) (55, 56). There was no interaction between job group and month of sampling or job group and sex, and the interaction terms were thus not included.

We used logistic regression to estimate the odds ratio (OR) with 95% confidence interval (95% CI) for vitamin D insufficiency (<50 nmol/L) and hyperparathyroidism (>6.9 pmol/L). These analyses included the same covariates as in the linear regression models.

Sensitivity analyses with a reference group of only indoor workers who reported never working outdoors was also conducted. To study a possible effect of sex, sensitivity analyses of the logistic and linear regression models were carried out stratified by sex.

In linear regression analyses of the effect of time spent outdoors on 25OHD concentration, we only included the 186 workers who participated from April-September. We conducted three linear regression models (1); job group only (2) outdoor hours on work days and days off work and (3) job group and outdoor hours on work days and days off work. These analyses were adjusted for month of sampling; otherwise covariates were similar to the previous analyses.

All analyses were carried out using STATA 13.0 (StataCorp LP, College Station, TX, USA).

## *Results*

Prevalence of smoking was highest among outdoor and permanent night workers (table 1). Use of vitamin D supplements was most prevalent among rotating shift and permanent night workers and least prevalent among outdoor workers. Fish and shell food consumption was lowest among permanent night workers. Indoor workers mainly participated from April-June, rotating night workers from October to December, while no permanent

**Table 1.** Characteristics of the population. [SD=standard deviation.]

| Characteristics | Indoor workers (N=162) | | | | Outdoor workers (N=112) | | | | Rotating shift workers (N=118) | | | | Permanent night workers N = 33 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | Mean | SD | N | % | Mean | SD | N | % | Mean | SD | N | % | Mean | SD |
| Age | | | 45.3 | 11.0 | | | 40.8 | 12.6 | | | 39.3 | 9.3 | | | 44.9 | 8.6 |
| Body mass index [a] | | | 24.0 | 3.8 | | | 25.8 | 4.8 | | | 24.7 | 4.6 | | | 25.7 | 3.2 |
| Gender | | | | | | | | | | | | | | | | |
| Female | 123 | 75.9 | | | 58 | 51.8 | | | 113 | 96.3 | | | 17 | 51.5 | | |
| Male | 39 | 24.1 | | | 54 | 48.2 | | | 5 | 4.2 | | | 16 | 48.5 | | |
| Socioeconomic status | | | | | | | | | | | | | | | | |
| White-collar worker | 135 | 83.3 | | | 64 | 57.1 | | | 116 | 98.3 | | | 14 | 42.4 | | |
| Skilled blue-collar worker | 19 | 11.7 | | | 45 | 40.2 | | | 2 | 1.7 | | | 12 | 36.4 | | |
| Unskilled blue-collar worker | 8 | 5.0 | | | 3 | 2.7 | | | 0 | 0.0 | | | 7 | 21.2 | | |
| Current smoking | | | | | | | | | | | | | | | | |
| No | 141 | 87.0 | | | 82 | 73.2 | | | 105 | 89.0 | | | 24 | 72.7 | | |
| Yes | 21 | 13.0 | | | 30 | 26.8 | | | 13 | 11.0 | | | 9 | 27.3 | | |
| Supplementary vitamin D use [b] | | | | | | | | | | | | | | | | |
| No | 103 | 63.6 | | | 79 | 70.5 | | | 72 | 61.0 | | | 19 | 57.6 | | |
| Yes | 59 | 36.4 | | | 33 | 29.5 | | | 46 | 39.0 | | | 14 | 42.4 | | |
| Oestrogen use [c] | | | | | | | | | | | | | | | | |
| No | 157 | 96.9 | | | 110 | 98.2 | | | 107 | 90.7 | | | 32 | 97.0 | | |
| Yes | 5 | 3.1 | | | 2 | 1.8 | | | 11 | 9.3 | | | 1 | 3.0 | | |
| Fish and shell food | | | | | | | | | | | | | | | | |
| <1 meal/week | 60 | 37.0 | | | 42 | 37.5 | | | 48 | 40.7 | | | 18 | 54.6 | | |
| ≥1 meal/week | 102 | 63.0 | | | 70 | 62.5 | | | 70 | 59.3 | | | 15 | 45.5 | | |
| Tanning bed use | | | | | | | | | | | | | | | | |
| Never | 158 | 97.5 | | | 107 | 95.5 | | | 111 | 94.0 | | | 30 | 90.9 | | |
| Ever | 4 | 2.5 | | | 5 | 4.5 | | | 7 | 6.0 | | | 3 | 9.1 | | |
| Season | | | | | | | | | | | | | | | | |
| January-March | 45 | 27.8 | | | 32 | 28.6 | | | 15 | 12.7 | | | 7 | 21.2 | | |
| April-June | 73 | 45.1 | | | 36 | 32.1 | | | 39 | 33.1 | | | 20 | 60.6 | | |
| July-September | 20 | 12.4 | | | 23 | 20.5 | | | 16 | 13.6 | | | 0 | 0.0 | | |
| October-December | 24 | 14.8 | | | 21 | 18.8 | | | 48 | 40.6 | | | 6 | 18.2 | | |
| Hours from blood sampling to storage | | | | | | | | | | | | | | | | |
| 0–24 | 162 | 100 | | | 112 | 100 | | | 111 | 94.1 | | | 22 | 66.6 | | |
| >24 | 0 | 0 | | | 0 | 0 | | | 7 | 5.9 | | | 11 | 33.3 | | |
| Minutes outdoor/day [d, e] | | | | | | | | | | | | | | | | |
| Work days | 81 | | 147 | 89 | 44 | | 261 | 120 | 46 | | 107 | 68 | 15 | | 122 | 59 |
| Days off | 81 | | 186 | 117 | 44 | | 182 | 113 | 46 | | 190 | 105 | 15 | | 152 | 92 |

[a] 12 missing.
[b] Cod liver, multivitamin or vitamin D.
[c] Hormone replacement therapy or birth control.
[d] An outdoor minute defined as a minute with light exposure above 1000 lux between 07:00 h and 19:00 hours.
e Information only provided for the subpopulation (N=186) of workers participating from April to September.

night workers participated July-September. Outdoor workers' participation was more equally distributed across seasons. Time from blood sampling to storage >24 hours in 33% of the permanent night workers while this was not the case for any indoor or outdoor workers. In the sub-population of workers participating from April-September, permanent night workers had a higher mean BMI [26.5 (SD 3.3) kg/m$^2$] than indoor [24.1 (SD 3.8) kg/m$^2$], outdoor [25.4 (SD 4.8) kg/m$^2$], and rotating night workers [25.1 (SD 5.0) kg/m$^2$]. Otherwise, socio-demographic characteristics were equivalent to the total population. In the sub-population, outdoor workers spent the longest time and permanent night workers the shortest time outdoors on work days. Permanent night workers also spent the shortest time outdoors on days off, but exposure in the other three groups was comparable.

Table 2 shows median 25OHD and PTH concentrations and prevalence of vitamin D insufficiency and hyperparathyroidism by job group and season. Within all job groups, 25OHD concentrations were highest and prevalence of vitamin D insufficiency lowest during July-September (no measurements available from permanent night workers). The prevalence of vitamin D insufficiency was highest from January-March (56.6%) and lowest from July-September (3.6%). From July-September and October-December, indoor workers had higher median 25OHD concentrations (95.8 and 68.8 nmol/L, respectively) than outdoor workers (78.8 and 58.8 nmol/L, respectively). Otherwise indoor, outdoor and rotating night workers had comparable 25OHD concentrations. From January-March and April-June, permanent night workers had significantly lower median 25OHD concentrations than the other job groups (19.2 and 36.4 nmol/L, respectively). PTH concentrations did not vary significantly within the job groups across seasons.

Table 3 presents results from the multivariable linear regression model of the relative difference in 25OHD and PTH concentrations between the four job groups. Outdoor workers had 4.5% (95% CI -6.1-14.1) lower and permanent night workers a 28.4% (95% CI 11.1–36.1%) lower 25OHD concentration than indoor workers in the season-adjusted analyses. When also adjusting for use of vitamin supplements and other expected predictors of 25OHD and PTH concentrations, outdoor workers showed a 2.5% (-74.-13.4) higher 25OHD concentration than indoor workers, while the result for permanent night workers only changed slightly. Rotating night workers 25OHD and PTH concentrations did not differ from indoor workers in either model.

Analyses of PTH concentration adjusted for season showed a 23.6% (95% CI 9.2–39.8) higher concentration among the permanent night workers. When further adjusted the difference attenuated to 14.5% (95% CI 0.1–31.1). Outdoor workers had 7.1% (95% CI -0.6–14.2) lower PTH concentrations than indoor workers adjusted for season. After adjustment for all confounders the difference was 7.5% (95% CI -0.5–14.9). However, results were not significant. Otherwise limited differences were seen between the four job groups.

Table 4 presents job groups and OR for vitamin D insufficiency and hyperparathyroidism. Permanent night workers had a four-fold [OR 4.55, 95% CI 1.39–14.94) higher odds of vitamin D insufficiency and outdoor workers tended to have lower [OR 0.30, 95% CI 0.08–1.07) odds of hyperparathyroidism and perhaps also of vitamin D insufficiency (OR 0.85, 95% CI 0.42–1.70)

**Table 2.** Median serum 25-hydroxyvitamin D (25OHD) concentration, parathyroid hormone (PTH) concentration in plasma and percentage with vitamin D insufficiency (<50 nmol/L) and hyperparathyroidism (>6.9 pmol/L) by season and job group with interquartile (25–75$^{th}$ percentile) range (IQR) (IQR) and P-values for any difference between groups and seasons among 425 indoor, outdoor and night workers. [Prev=prevalence.]

| Season | Indoor workers (N=162) | | | | Outdoor workers (N=112) | | | | Rotating night workers (N=118) | | | | Permanent night workers (N=33) | | | | P-value | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Concentration | | | Prev [a] | Concentration | | | Prev [a] | Concentration | | | Prev [a] | Concentration | | | Prev [a] | Conc. | Prev [a] |
| | N | Median | IQR | % | N | Median | IQR | % | N | Median | IQR | % | N | Median | IQR | % | | |
| 25OHD (nmol/L) | | | | | | | | | | | | | | | | | | |
| Jan-Mar | 45 | 46.9 | 28.5–64.7 | 55.6 | 32 | 48.8 | 31.7–64.5 | 56.3 | 15 | 48.0 | 37.4–62.8 | 53.3 | 7 | 19.2 | 11.3–81.7 | 71.4 | 0.575 | 0.872 |
| Apr- June | 73 | 58.6 | 43.6–77.5 | 37.0 | 25 | 58.8 | 40.3–73.9 | 36.1 | 39 | 58.1 | 46.9–80.3 | 33.3 | 20 | 36.4 | 27.8–47.6 | 80.0 | 0.008 | 0.016 |
| July-Sept | 20 | 95.8 | 78.3–105.5 | 0.0 | 26 | 78.4 | 61.9–92.4 | 8.7 | 16 | 84.7 | 72.7–94.6 | 0.0 | 0 | | | | 0.082 | 0.203 |
| Oct-Dec | 24 | 68.8 | 57.8–81.2 | 16.7 | 26 | 56.5 | 50.1–70.8 | 23.8 | 48 | 68.3 | 44.1–91.4 | 29.2 | 6 | 76.6 | 69.8–83.7 | 16.7 | 0.204 | 0.836 |
| P-value [d] | | <0.001 | | <0.001 | | <0.001 | | 0.002 | | 0.001 | | 0.012 | | 0.050 | | <0.001 | | |
| PTH (pmol/L) | | | | | | | | | | | | | | | | | | |
| Jan-Mar | 45 | 4.6 | 3.6–5.7 | 13.3 | 32 | 3.9 | 3.7–4.8 | 3.2 | 15 | 3.5 | 3.4–4.2 | 0.0 | 7 | 4.8 | 4.0–6.3 | 14.3 | 0.071 | 0.225 |
| Apr- June | 72 | 4.5 | 3.4–5.6 | 9.6 | 36 | 4.1 | 3.5–5.1 | 0.0 | 39 | 4.4 | 3.6–5.3 | 10.3 | 20 | 5.7 | 4.6–6.3 | 15.0 | 0.025 | 0.191 |
| July-Sept | 20 | 4.4 | 3.6–5.0 | 0.0 | 23 | 4.1 | 3.4–4.9 | 4.4 | 16 | 4.7 | 3.6–5.8 | 18.8 | 0 | | | | 0.513 | 0.074 |
| Oct-Dec | 24 | 4.1 | 3.4–5.5 | 4.2 | 21 | 4.5 | 3.6–6.1 | 9.5 | 48 | 4.6 | 3.5–5.6 | 8.3 | 6 | 5.5 | 4.6–7.2 | 33.3 | 0.224 | 0.175 |
| P-value [d] | | 0.726 | | 0.282 | | 0.573 | | 0.318 | | 0.201 | | 0.349 | | 0.691 | | 0.577 | | |

[a] Prevalence of vitamin vitamin D insufficiency (<50 nmol/L) and hyperparathyroidism (>6.9 pmol/L).
[b] Kruskal-Wallis test of any difference in concentrations between job groups.
[c] Kruskal-Wallis test of any difference in prevalence of vitamin D insufficiency/hyperthyroidism between job groups.
[d] Kruskal-Wallis test of any difference between seasons.

**Table 3.** Relative differences (%) in serum 25-hydroxyvitamin D (25OHD) and parathyroid hormone (PTH) concentrations in plasma between 425 outdoor, rotating night, permanent night and indoor workers. [95% CI=95% confidence interval.]

| Typeof worker group | N | Model 1 [a] | | Model 2 [b] | |
|---|---|---|---|---|---|
| | | % Difference | 95% CI | % Difference | 95% CI |
| 25OHD | | | | | |
| Indoor workers | 162 | 0.0 | Reference | 0.0 | Reference |
| Outdoor workers | 112 | -4.5 | -14.1–6.1 | 2.5 | -7.4–13.4 |
| Rotating night workers | 118 | -1.9 | -11.8–9.1 | -5.6 | -14.8–4.4 |
| Permanent night workers | 33 | -28.4 | -39.2– -15.7 | -25.3 | -36.6– -11.9 |
| PTH | | | | | |
| Indoor workers | 161 | 0.0 | Reference | 0.0 | Reference |
| Outdoor workers | 112 | -7.1 | -14.2–0.6 | -7.5 | -14.9–0.5 |
| Rotating night workers | 118 | -1.3 | -8.9–7.0 | 0.7 | -7.3–9.4 |
| Permanent night workers | 33 | 23.6 | 9.2–39.8 | 14.5 | 0.1–31.1 |

[a] Adjusted for season.
[b] Adjusted for season, sex, age, socioeconomic status, use of vitamin D supplements, use of birth control or hormone replacement therapy, body mass index, current smoking, fish and shell food consumption, use of sunbed and hours from blood sampling to freezing.

**Table 4.** Risk of vitamin D insufficiency (<50 nmol/L) or hyperparathyroidism (>6.9 pmol/L) in outdoor and night workers relative to indoor workers among 425 workers. [OR=odds ratio; CI=confidence interval]

| Type of worker group | N | Model 1 [a] | | Model 2 [b] | |
|---|---|---|---|---|---|
| | | OR | 95% CI | OR | 95% CI |
| Vitamin D insufficiency | | | | | |
| Indoor | 162 | 1.00 | Reference | 1.00 | Reference |
| Outdoor | 112 | 1.15 | 0.66–1.99 | 0.85 | 0.42–1.70 |
| Rotating night | 118 | 1.11 | 0.63–1.95 | 1.25 | 0.61–2.56 |
| Permanent night | 33 | 3.61 | 1.59–8.20 | 4.55 | 1.39–14.94 |
| Hyperparathyroidism | | | | | |
| Indoor | 161 | 1.00 | Reference | 1.00 | Reference |
| Outdoor | 112 | 0.39 | 0.12–1.21 | 0.30 | 0.08–1.07 |
| Rotating night | 118 | 1.06 | 0.45–2.51 | 1.30 | 0.49–3.48 |
| Permanent night | 33 | 2.37 | 0.83–6.81 | 2.25 | 0.61–8.22 |

[a] Adjusted for season.
[b] Adjusted for season, sex, age, socioeconomic status, use of vitamin D supplements, use of birth control or hormone replacement therapy, body mass index, current smoking, fish and shell food consumption, use of sunbed and hours from blood sampling to freezing.

compared with indoor workers.

Table 5 presents the relative difference (%) in 25OHD concentrations between job groups and per hour spent outdoors in the sub-population (workers participating from April throughout September). The adjusted model of job groups not including variables for outdoor hours showed 8.5% % (95% CI -5.6–24.6) higher concentration of 25OHD among outdoor workers and 6.6% (95% CI -18.4–6.9) and 15.6% (95% CI -33.6–7.4) lower concentrations among rotating and permanent night workers compared with indoor workers. The adjusted model of hours spent outdoor showed a 5.2% (95% CI 1.1–9.5) increase in 25OHD concentrations per hour spent outdoors on work days but only a limited increase by hours spent outdoors on days off. The final model that included outdoor hours and job group showed attenuated estimates for outdoor and permanent night workers compared with the model that did not include outdoor hours, while the effect for rotating night workers was limited.

PTH concentrations did not change by number of outdoor hours/day (data not shown).

Sensitivity analyses with indoor worker who never worked outdoors and analyses stratified by sex supported the main results.

## Discussion

In the present cross-sectional study, permanent night workers had lower 25OHD and higher PTH concentrations than indoor workers. Outdoor workers tended to have a higher 25OHD concentration during summer and a lower PTH concentration irrespective of season than indoor workers. Workers with rotating night work had comparable 25OHD and PTH concentrations with indoor workers. 25OHD concentrations increased significantly by hours spent outdoors on workdays from April to September. The observed differences between permanent night workers, outdoor workers and indoor workers were significantly reduced in models that included time spent outdoors. This indicates that it was a significant predictor for the differences observed between the job groups.

In total, 151 (35.5%) participants had vitamin D insufficiency in terms of 25OHD concentrations <50 nmol/L. As expected, prevalence was highest from January-March (56.6%), lowest from July-September 3.6% and comparable to previous findings among healthy Danes (41, 42, 57). Among indoor workers, the prevalence of vitamin D insufficiency was lower than in previous studies (29, 33, 58), but 25OHD concentrations were comparable with most previous studies (27–29, 31, 33, 58, 59) though mean 25OHD concentrations during the summer were lower in some of the studies (27, 29, 35, 58).

**Table 5.** Relative difference (%) in 25-hydroxyvitamin D concentrations with and without adjustment for hours spent outdoor/day [a] among 186 workers participating from April to September. [CI=confidence interval.]

| Variables (% difference) | N | Model with job group only [b] | | Model with outdoor hours only [b] | | Model with job group and outdoor hours [b] | |
|---|---|---|---|---|---|---|---|
| | | Estimate | 95% CI | Estimate | 95% CI | Estimate | 95% CI |
| Type of worker group | | | | | | | |
| Indoor | 81 | 0.0 | Reference | | | 0.0 | Reference |
| Outdoor | 44 | 8.5 | -5.6–24.6 | | | 0.3 | -13.5–16.3 |
| Rotating night | 46 | -6.6 | -18.4–6.9 | | | -4.0 | -16.1–9.9 |
| Permanent night | 15 | -15.6 | -33.6–7.4 | | | -11.2 | -30.0–12.7 |
| Outdoor hours [a]/day (% difference per hour/day) | | | | | | | |
| Work days | 186 | | | 5.8 | 2.3–9.5 | 5.2 | 1.1–9.5 |
| Days off | 186 | | | 0.9 | -2.1–4.0 | 1.0 | -2.1–4.1 |

[a] Defined as light measurements >1000 lux.

[b] Adjusted for month, sex, age, socioeconomic status, use of vitamin D supplements, use of birth control or hormone replacement therapy, body mass index, current smoking, fish and shell food consumption, use of sunbed and hours from blood sampling to storage.

In contrast to most previous findings, the outdoor workers in the present study did not have higher 25OHD concentrations than indoor workers all year round but only during the summer (26–28). One explanation for this may be that outdoor workers in our study spent shorter time outdoors during summer (4.5 hours on work days according to the light recordings). Our findings are, however, in line with a recent Danish study (29) reporting similar 25OHD concentrations in outdoor working farmers and their indoor working spouses.

In accordance with our results, 25OHD concentrations did not differ between indoor and rotating night workers in some previous studies (34, 35), but 25OHD concentrations were lower among rotating night workers in other studies (31, 33). In contrast to our findings the only previous study on permanent night workers of both sexes found similar 25OHD concentrations among day and night workers (34). However this study was carried out in South Korea, where lifestyle and UVB intensity differs from Denmark.

Average PTH concentrations were higher among permanent night workers and lower among outdoor workers compared to indoor workers; this underpins both the adverse and positive effects of 25OHD seen for these two job groups. To our knowledge, the association between PTH concentrations and day and night work has not previously been studied.

Despite spending more time outdoors, outdoor workers had similar 25OHD concentrations as indoor workers around the year. However, the effect estimate was higher in the summer, though not statistically significant. Outdoor workers had higher BMI, were more likely to be smokers, fewer used vitamin D supplements, and had lower socioeconomic status. Before adjustment for co-variates outdoor workers had lower 25OHD concentrations and higher odds of vitamin D insufficiency than indoor workers. After adjustment outdoor workers had higher 25OHD concentrations and lower risk of vitamin D insufficiency. Though all results were non-significant, this indicates that a poorer lifestyle among outdoor workers is counteracted by outdoor work. This is further supported by the significant association between hours spent outdoor on work days and 25OHD concentrations. However, we were not able to demonstrate the hypothesized difference in 25OHD concentration between indoor and outdoor workers. During the past decade a lot of focus has been put on skin cancer, and this may have resulted in outdoor workers protecting themselves against the sun with cloth and sunscreen resulting in less vitamin D production during work hours. Child care workers comprised a large percentage of the outdoor workers, and those working with the youngest kids are likely to work in the shade, as most playgrounds are placed to protect the children against the sun. Another industry represented in the outdoor work group is craftsmen, who tend to start work around 5–6 am during the summer and get off work early in the afternoon. During early morning hours, UVB is not intense enough to induce vitamin D production and the temperature is still low and less skin is exposed. This may cause lower total occupational UVB exposure and contribute to the lack of a difference. Another possible explanation is that high UVB exposure can degrade newly produced vitamin D present in the skin, and exposure to UVB therefore not results in 25OHD production (60). The outdoor workers reported working between 10–39 hours of outdoor/week and were compared to indoor workers who reported 0-9 hour's outdoor work/week. Lack of exposure contrast could also explain the similar 25OHD concentrations; however sensitivity analyses where only indoor workers never working outdoors were included were in line with main results.

The higher (non-significant) 25OHD concentrations observed the sub-population of outdoor workers participating through the month where UVB induces vitamin D production may indicate a positive effect of outdoor work during summer, which did not last throughout the year. However, there was no statistical interaction between job group and season in the full population. The lack of an interaction may indicate that the higher 25OHD observed during the summer is a chance finding, but it may also owe to lack of statistical power.

Among rotating night workers, 25OHD and PTH concentrations did not differ from indoor workers; this is in line with some (34, 35) but not all previous studies (31, 33). The rotating night workers were mostly women whereas the study by Romano et al only included males (31) and Munter et al studied a mixed population (33). The rotating shift workers in this study were mainly healthcare workers, who may have a healthier vitamin D lifestyle than factory workers, which counteracts the lower exposure to daylight on work days. The majority of the permanent night workers in the present study were factory workers. Compared to the rotating night workers they had a higher BMI, lower SES, were more likely to smoke and less likely to eat fish. However the prevalence of supplementary vitamin D use were similar to rotating night worker's and the prevalence of sunbed use higher, but all over this supports a poorer lifestyle among factory workers. The lack of a difference between the rotating night workers and day workers may also owe to frequency of night shifts, an information lacking in the present study. If numbers of night shifts are few, the overall difference in UVB exposure may be too small to be reflected in 25OHD concentrations. As seen with outdoor workers, the results from the sub-population were a little different. Rotating night workers had 6.6% (95% CI -6.9–18.4) lower 25OHD than indoor workers during the light half year. This may, as suggested for outdoor workers, be due to a transient effect of hours spent outdoors during the summer, but it may also be a chance finding.

The concentration of 25OHD increased with hours spent outdoors on summer days. Studies on self-reported time outdoor have reported both similar (33, 61) and conflicting results (58, 62). In contrast to our study, a Danish study among farmers only found an association between mean daily UVR dose on days off work, but not on work days (29). This finding could perhaps be explained by farmers currently spending much of the workdays inside tractors and other vehicles, where the measured UVR mainly consists of UVA radiation, which does not induce 25OHD synthesis. No association was found between hours spent outdoors and PTH concentrations, probably because of sufficient 25OHD production during the sunny part of the year and a maximal suppression of PTH.

The threshold value of 50 nmol/l used to define vitamin D insufficiency is based on the 25OHD concentrations, where PTH start to increase in different populations (63). However, the relevant 25OHD concentrations for vitamin D insufficiency differ between individuals (43), as not all subjects with 25OHD <50 nmol/L show signs of vitamin D insufficient in terms of eg, elevated PTH concentrations. The optimal 25OHD concentration with respect to extra-skeletal diseases is unknown, but has been suggested to be 75 nmol/l (39). The implication would be a higher prevalence of participants with vitamin D concentrations that are harmful to health.

### Strengths and limitations

The study was cross-sectional and results should be interpreted cautiously regarding causality. However, it is not very likely that vitamin D concentrations influenced participants' decision on whether to work during the day or night. Hours of outdoor work was self-reported and prone to recall bias, however this is not likely related to 25OHD or PTH concentration and misclassification would cause non-differential misclassification and bias towards null. Serum 25OHD and plasma PTH concentrations were measured with the most precise laboratory methods. We excluded subjects with medical conditions or treatment with drugs potentially affecting calcium homeostasis and vitamin D metabolism. Further, we used objective measures of light to assess time spent outdoors. We adjusted for a wide range of known predictors of vitamin D concentrations, but some residual confounding cannot be excluded. Oestrogen concentrations are an important predictor of 25OHD concentrations, we adjusted for use of exogenous oestrogen, but we did not have information on postmenopausal status or menstrual cycle. However, we adjusted for age which is closely related to postmenopausal status and menstrual cycle has been shown not to affect 25OHD (64).

### Concluding remarks

Permanent night workers spent less time outdoors and had lower 25OHD and higher PTH concentrations than indoor workers. Outdoor workers spent more hours outdoors but 25OHD concentrations were similar to indoor workers. This was partly explained by a poorer lifestyle among outdoor workers. PTH and odds of hyperparathyroidism were lower among outdoor workers though not significant. Rotating night workers' 25OHD and PTH concentrations did not differ from indoor workers. The concentration of 25OHD increased by hours spent outdoor on workdays during summer, and differences between job groups were partly explained by differences in time spent outdoor. Clinicians should be aware that vitamin D insufficiency may be more prevalent among permanent night workers, and employers should consider the positive effects on 25OHD and PTH status by allowing their workers to spend time outdoors during work hours.

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### Declaration of interest

All authors declare no conflicts of interest.

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