

## Journal Scan

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*Indian J Sleep Med 2014; 9.4, 190-199*

1. *Br J Cancer. 2013 Oct 29;109(9):2472-80.*

### **The association between different night shiftwork factors and breast cancer: A case-control study.**

**Fritschi L(1), Erren TC, Glass DC, Girschik J, Thomson AK, Saunders C, Boyle T El-Zaemey S, Rogers P, Peters S, Slevin T, D’Orsogna A de Vocht F, Vermeulen R, Heyworth JS.**

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**BACKGROUND:** Research on the possible association between shiftwork and breast cancer is complicated because there are many different shiftwork factors, which might be involved including: light at night, phase shift, sleep disruption and changes in lifestyle factors while on shiftwork (diet, physical activity, alcohol intake and low sun exposure).

**METHODS:** We conducted a population-based case-control study in Western Australia from 2009 to 2011 with 1205 incident breast cancer cases and 1789 frequency age-matched controls. A self-administered questionnaire was used to collect demographic, reproductive, and lifestyle factors and lifetime occupational history and a telephone interview was used to obtain further details about the shiftwork factors listed above.

**RESULTS:** A small increase in risk was suggested for those ever doing the graveyard shift (work between midnight and 0500 hours) and breast cancer (odds ratio (OR)=1.16, 95% confidence interval (CI)=0.97-1.39). For phase shift, we found a 22% increase in breast cancer risk (OR=1.22, 95% CI=1.01-1.47) with a statistically significant dose-response relationship (P=0.04). For the

other shiftwork factors, risks were marginally elevated and not statistically significant.

**CONCLUSION:** We found some evidence that some of the factors involved in shiftwork may be associated with breast cancer but the ORs were low and there were inconsistencies in duration and dose-response relationships.

2. *Ann Oncol. 2013 Nov;24(11):2724-32.*

### **A meta-analysis on dose-response relationship between night shift work and the risk of breast cancer.**

**Wang F(1), Yeung KL, Chan WC, Kwok CC, Leung SL, Wu C, Chan EY, Yu IT, Yang XR, Tse LA.**

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This study aimed to conduct a systematic review to sum up evidence of the associations between different aspects of night shift work and female breast cancer using a dose-response meta-analysis approach. We systematically searched all cohort and case-control studies published in English on MEDLINE, Embase, PSYCInfo, APC Journal Club and Global Health, from January 1971 to May 2013. We extracted effect measures (relative risk, RR; odd ratio, OR; or hazard ratio, HR) from individual studies to generate pooled results using meta-analysis approaches. A log-linear dose-response regression model was used to evaluate the relationship between various indicators of exposure to night shift work and breast cancer risk. Downs and Black scale was applied to assess the methodological quality of included studies. Ten studies were included in the meta-analysis. A pooled adjusted relative risk for the association between ‘ever exposed

to night shift work and breast cancer was 1.19 [95% confidence interval (CI) 1.05-1.35]. Further meta-analyses on dose-response relationship showed that every 5-year increase of exposure to night shift work would correspondingly enhance the risk of breast cancer of the female by 3% (pooled RR = 1.03, 95% CI 1.01-1.05; Pheterogeneity < 0.001). Our meta-analysis also suggested that an increase in 500-night shifts would result in a 13% (RR = 1.13, 95% CI 1.07-1.21; Pheterogeneity = 0.06) increase in breast cancer risk. This systematic review updated the evidence that a positive dose-response relationship is likely to present for breast cancer with increasing years of employment and cumulative shifts involved in the work.

3. *Occup Environ Med.* 2013 Dec;70(12):831-8.

### **Increased risk of breast cancer associated with long-term shift work in Canada.**

**Grundy A(1), Richardson H, Burstyn I, Lohrisch C, SenGupta SK, Lai AS, Lee D, Spinelli JJ, Aronson KJ.**

(1)Department of Public Health Sciences and Queen's Cancer Research Institute, Queen's University, Kingston, Ontario, Canada.

**OBJECTIVES:** Long-term night work has been suggested as a risk factor for breast cancer; however, additional studies with more comprehensive methods of exposure assessment to capture the diversity of shift patterns are needed. As well, few previous studies have considered the role of hormone receptor subtype.

**METHODS:** Relationships between night shift work and breast cancer were examined among 1134 breast cancer cases and 1179 controls, frequency-matched by age in Vancouver, British Columbia, and Kingston, Ontario. Self-reported lifetime occupational histories were assessed for night shift work, and hormone receptor status obtained from tumour pathology records.

**RESULTS:** With approximately one-third of cases and controls ever employed in night shift work, associations with duration demonstrated no relationship between either 0-14 or 15-29 years, while an association was apparent for ≥30 years (OR=2.21, 95% CI 1.14 to 4.31). This association with long-term night shift work is robust

to alternative definitions of prolonged shift work, with similar results for both health and non-health care workers.

**CONCLUSIONS:** Long-term night shift work in a diverse mix of occupations is associated with increased breast cancer risk and not limited to nurses, as in most previous studies.

4. *Neuro Endocrinol Lett.* 2013;34(4):282-6.

### **Shift work and cancer research: a thought experiment into a potential chronobiological fallacy of past and perspectives for future epidemiological studies.**

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With their 2007 classification - shift work involving "circadian disruption" is probably carcinogenic to humans (Group 2A) - the International Agency for Research on Cancer [IARC] provided a riddle for scientists and the public alike.

Thereafter, eighteen epidemiological investigations into shift work and a host of malignant endpoints (including cancers of the breast, prostate, lung, colon, rectum, pancreas, bladder, skin and non-Hodgkin lymphoma [NHL]) as well as mortality were published. Although IARC experts identified "circadian disruption" as the critical link in the "probable" chains of cancer causation, almost none of the post-IARC studies specifically considered a disturbed temporal organization of biology. This implies that epidemiological research to-date is less focused than it should be. To illustrate a potential chronobiological fallacy of past studies, we offer a thought experiment. In addition, we consider first empirical evidence from recent research which avoided such bias. Methodological perspectives for future chronobiology-driven epidemiological research are outlined.

5. *Mol Cell Biol.* 2013 Jul;33(14):2773-86.

### **Regulation of focal adhesion kinase activation, breast cancer cell motility, and amoeboid invasion by the RhoA guanine nucleotide exchange factor Net1.**

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Net1 is a RhoA guanine nucleotide exchange factor (GEF) that is overexpressed in a subset of human cancers and contributes to cancer cell motility and invasion in vitro. However, the molecular mechanism accounting for its role in cell motility and invasion has not been described. In the present work, we show that expression of both Net1 isoforms in breast cancer cells is required for efficient cell motility. Although loss of Net1 isoform expression only partially blocks RhoA activation, it inhibits lysophosphatidic acid (LPA)-stimulated migration as efficiently as knockdown of RhoA itself. However, we demonstrate that the Net1A isoform predominantly controls myosin light-chain phosphorylation and is required for trailing edge retraction during migration. Net1A interacts with focal adhesion kinase (FAK), localizes to focal adhesions, and is necessary for FAK activation and focal adhesion maturation during cell spreading. Net1A expression is also required for efficient invasion through a Matrigel matrix. Analysis of invading cells demonstrates that Net1A is required for amoeboid invasion, and loss of Net1A expression causes cells to shift to a mesenchymal phenotype characterized by high  $\alpha$ 1-integrin activity and membrane type 1 matrix metalloproteinase (MT1-MMP) expression. These results demonstrate a previously unrecognized role for the Net1A isoform in controlling FAK activation during planar cell movement and amoeboid motility during extracellular matrix (ECM) invasion.

6. *Front Endocrinol (Lausanne).* 2013 Apr 8;4:47.

### **Biological rhythms and preeclampsia.**

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The impact of impaired circadian rhythm on health has been widely studied in shift workers and trans-meridian travelers. A part from its correlation with sleep and mood disorders, biological rhythm impairment is a recognized risk factor for cardiovascular diseases and breast cancer. Preeclampsia is a major public health issue, associated with a significant maternal and fetal morbidity and mortality worldwide. While the risks factors for this condition such as obesity, diabetes, pre-existing hypertension have been identified, the underlying mechanism of this multi-factorial disease is yet not fully understood. The disruption of the light/dark cycle in pregnancy has been associated with adverse outcomes. Slightly increased risk for “small for gestational age” babies, “low birth weight” babies, and preterm deliveries has been reported in shift working women. Whether altered circadian cycle represents a risk factor for preeclampsia or preeclampsia is itself linked with an abnormal circadian cycle is less clear.

There are only few reports available, showing conflicting results. In this review, we will discuss recent observations concerning circadian pattern of blood pressure in normotensive and hypertensive pregnancies. We explore the hypothesis that circadian misalignments may represent a risk factor for preeclampsia.

Unraveling potential link between circadian clock gene and preeclampsia could offer a novel approach to our understanding of this multi-system disease specific to pregnancy.

7. *J Perinatol.* 2013 Apr;33 Suppl 1:S17-23.

### **Health consequences of shift work and implications for structural design.**

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The objective of the study was to perform a literature review on the health consequences of working rotating shifts and implications for structural design. A literature search was performed in June 2012 and a selection of the most relevant peer-review articles was included in the present review. Shift workers are more likely to suffer from a circadian sleep disorder characterized by sleepiness and insomnia. Shift work is associated with decreased productivity, impaired safety, diminished quality of life and adverse effects on health. Circadian disruption resulting from rotating shift work has also been associated with increased risk for metabolic syndrome, diabetes, cardiovascular disease and cancer. This article summarizes the known health effects of shift work and discusses how light can be used as a countermeasure to minimize circadian disruption at night while maintaining alertness. In the context of the lighted environment, implications for the design of newborn intensive care units are also discussed.

8. *J Biol Regul Homeost Agents.* 2013 Jan-Mar;27(1):267-74.

### **Influence of night-shift and napping at work on urinary melatonin, 17- $\beta$ -estradiol and clock gene expression in pre-menopausal nurses.**

Bracci M, Copertaro A, Manzella N, Staffolani S, Strafella E, Nocchi L, Barbaresi M, Copertaro B, Rapisarda V, Valentino M, Santarelli L.

Night-workers experience disruption of the sleep-wake cycle and light at night which may increase breast cancer risk by suppressing the nocturnal melatonin surge, resulting in higher levels of circulating estrogens. Night-work may also deregulate peripheral clock genes which have been found to be altered in breast cancer. This study investigated urinary 6-sulfatoxymelatonin (aMT6s),

serum 17-beta-estradiol levels in premenopausal shift nurses at the end of the night-shift compared to a control group of daytime nurses. Peripheral clock gene expression in lymphocytes were also investigated. All participants were sampled in the follicular phase of the menstrual cycle. The effect of nurses' ability to take a short nap during the night-shift was also explored. The shift-work group had significantly lower aMT6s levels than daytime nurses independently of a nap.

Night-shift napping significantly influences 17-beta-estradiol levels resulting in higher outcomes in nurses who do not take a nap compared to napping group and daytime workers. Peripheral clock genes expression investigated was not significantly different among the groups. Our findings suggest that shift nurses experience changes in aMT6s levels after a night-shift. Napping habits influence 17-beta-estradiol levels at the end of a night-shift. These findings might be related to the increased cancer risk reported in night-shift workers and suggest that a short nap during night-shifts may exert a positive effect.

9. *Med J Aust.* 2013 Oct 21;199(8):S11-5.

### **Sleep loss and circadian disruption in shift work: health burden and management.**

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About 1.5 million Australians are shift workers. Shift work is associated with adverse health, safety and performance outcomes. Circadian rhythm misalignment, inadequate and poor-quality sleep, and sleep disorders such as sleep apnoea, insomnia and shift work disorder (excessive sleepiness and/or insomnia temporally associated with the work schedule) contribute to these associations. Falling asleep at work at least once a week occurs in 32%-36% of shift workers. Risk of occupational accidents is at least 60% higher for non-day shift workers. Shift workers also have higher rates of cardiometabolic diseases and mood disturbances.

Road and workplace accidents related to excessive sleepiness, to which shift work is a significant contributor, are estimated to cost \$71-\$93 billion per annum in the

United States. There is growing evidence that understanding the inter individual variability in sleep-wake responses to shift work will help detect and manage workers vulnerable to the health consequences of shift work. A range of approaches can be used to enhance alertness in shift workers, including screening and treating sleep disorders, melatonin treatment to promote sleep during the daytime, and avoidance of inappropriate use of sedatives and wakefulness-promoters such as modafinil and caffeine. Short naps, which minimise sleep inertia, are generally effective. Shifting the circadian pacemaker with appropriately timed melatonin and/or bright light may be used to facilitate adjustment to a shift work schedule in some situations, such as a long sequence of night work. It is important to manage the health risk of shift workers by minimising vascular risk factors through dietary and other lifestyle approaches.

10. *J R Coll Physicians Edinb.* 2013;43(3):230-5.

### **Working the night shift: a necessary time for training or a risk to health and safety?**

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The European Working Time Directive (EWTD) limits excessive night shifts and restricts the working week to no more than 48 hours. The underlying rationale is to minimise the health risks to all workers. Here we debate the impact of night rotas for doctors-in-training on patient safety and medical education; when the EWTD was agreed these topics may not have been considered, either systematically or objectively. The impacts of diurnal rhythms on human functions affect all night workers, but the nature of rostered medical and surgical work has little precedent in other industries or even in the contracts of other healthcare staff.

For example, rostered night duties need to be distinguished from permanent night shift work. On-call medical night work from training doctors is generally required for short periods and usually involves fewer patients. It is an important time in training, where clinical responsibility and decision-making can be matured in a

supervised setting. To comply with the EWTD most hospitals have adopted rota patterns that aim to cover the clinical needs, while ensuring no doctor works for more than 48 hours in an average working week. To monitor this process longterm studies are necessary to evaluate effects on a doctor's health and on patient care generally. The EWTD has also led to a loss of continuity of patient care; does this really matter?

11. *Am J Epidemiol.* 2013 Oct 15;178(8):1296-300.

### **Shift work and cognition in the Nurses' Health Study.**

Devore EE, Grodstein F, Schernhammer ES.

Rotating night-shift work, which can disrupt circadian rhythm, may adversely affect long-term health. Experimental studies indicate that circadian rhythm disruption might specifically accelerate brain aging; thus, we prospectively examined shift-work history at midlife as associated with cognitive function among older women in the Nurses' Health Study. Women reported their history of rotating night-shift work in 1988 and participated in telephone-based cognitive interviews between 1995 and 2001; interviews included 6 cognitive tests that were subsequently repeated 3 times, at 2-year intervals. We focused on shift work through midlife (here, ages 58-68 years) because cognitive decline is thought to begin during this period. Using multivariable-adjusted linear regression, we evaluated mean differences in both "average cognitive status" at older age (averaging cognitive scores from all 4 interviews) and rates of cognitive decline over time across categories of shift-work duration at midlife (none, 1-9, 10-19, or  $\geq 20$  years). There was little association between shift work and average cognition in later life or between shift work and cognitive decline. Overall, this study does not clearly support the hypothesis that shift-work history in midlife has long-term effects on cognition in older adults.

12. *Healthy Aging Clin Care Elder.* 2013 Apr 29;2013(5):9-19.

### **Polysomnographic Sleep and Circadian Temperature Rhythms as a Function of Prior Shift Work Exposure in Retired Seniors.**

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In an earlier published telephone interview study (n > 1,000) we have shown that retired shift workers subjectively report worse sleep than retired day workers. This laboratory study sought to determine whether these findings held up when objective polysomnographic (PSG) measures of sleep were taken and whether retirees' circadian temperature rhythms differed as a function of shift work exposure. All completers of the telephone interview were invited to attend a 36-hour laboratory study for which participants were paid. This involved continuous core body temperature measurement (using an ingestible pill-based system) and 2 nights of PSG. Shift work exposure (plus other measures) was collected by taking a detailed work history. The second laboratory night was scored into sleep stages. Post hoc, we divided participants into 4 shift work exposure groups: 0 years (ie, no exposure to shift work), 1 to 7 years, 7 to 20 years, and >20 years. Sample sizes were 11, 16, 15, and 15, respectively, with approximate equality in mean age (71.7 years of age, 69.1 years of age, 70.0 years of age, and 70.4 years of age, respectively) and percent male (63%, 50%, 67%, and 73%, respectively). Shift work exposure was associated with worse PSG sleep in a dose-related fashion. The percentages of participants with sleep efficiency, 80% for the 0 years, 1 to 7 years, 7 to 20 years, and >20 years groups were 36%, 63%, 67%, and 73%, respectively (P < 0.01), and the percentages with total sleep time (TST), 6 hours were 36%, 56%, 53%, and 73%, respectively (P < 0.01). From the circadian rhythm record, shift work exposure appeared to result (P = 0.06) in an increased spread of phase angles (difference between habitual bedtime and time of temperature trough). In conclusion, it appears likely that shift work may be related to a scarring of sleep and circadian rhythms. This may be associated with a change in the relationship between habitual sleep timing and the phase of the circadian pacemaker.

6. *Int J Occup Med Environ Health.* 2013 Aug;26(4):522-34.

### **Night shift work characteristics and occupational co-exposures in industrial plants in Łódź, Poland.**

**Pep<sup>3</sup>ońska B(1), Burdelak W, Bukowska A, Krysicka J, Konieczko K.**

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**OBJECTIVES:** Night shift work involving circadian rhythm disruption has been classified by IARC as a probably carcinogenic to humans (Group 2A). Little is known about co-exposures of the night shift work in occupational settings. The aim of our study was to characterize night shift work systems and industrial exposures occurring in the manufacturing plants in Łódź, Poland, where night shift work system operates, with particular focus on potential carcinogens.

**MATERIAL AND METHODS:** Data on the night shift work systems and hazardous agents were collected through survey performed in 44 enterprises. The identified hazardous agents were checked using the IARC carcinogen list, and the harmonized EU classification of chemical substances. We also examined databases of the Central Register of Data on exposure to substances, preparations, agents and technological processes showing carcinogenic or mutagenic properties in Poland.

**RESULTS:** The most common system of work among studied enterprises employed 3 (8-hour) shifts within a 5-day cycle. We identified as many as 153 hazards occurring in the environment of the plants, with noise, carbon monoxide and formaldehyde recorded as the most common ones. Out of these hazards, 11 agents have been classified by IARC to group 1 - carcinogenic to humans, whereas 10 agents have been classified as carcinogens by the regulation of European Classification of carcinogens. Analysis of the data from the Central Register revealed that 6 plants reported presence of carcinogens in the environment of work.

**CONCLUSIONS:** In our study we observed that in none of the workplaces the night shift work was a single exposure. Further epidemiological studies focusing on investigation of health effects of the night shift work should identify occupational co-exposures and examine them as potential confounders.

14. *J Lifestyle Med.* 2013 Sep;3(2):110-6. Epub 2013 Sep 30.

## Night Shift Work, Sleep Quality, and Obesity.

**Ko SB(1).**

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**BACKGROUND:** The aims of this study were to examine the relationship between night shift work and sleep, to investigate the correlations with various biomarkers that show the influence of sleep on obesity, and ultimately, to analyze factors that have an impact on obesity.

**METHODS:** This study used data from the National Survey of Midlife Development in the United States II (MIDUS II study) and the MIDUS II Biomarker Project. After connecting the MIDUS II study data with the MIDUS II Biomarker Project data, we analyzed data from 883 subjects to investigate the relationship between night shift work and sleep quality. We also examined the correlations with biomarkers and sleep quality. Lastly, we performed logistic regression analyses to investigate factors that had an impact on obesity.

**RESULTS:** Sleep quality was found to be low among night shift workers. Sleep quality was positively correlated with HbA1c, total cholesterol, and triglyceride levels, and inversely correlated with DHEA levels. Sleep quality was highly correlated with inflammatory markers and inversely correlated with antioxidant markers. Sleep quality was significantly associated with obesity (OR: 1.10, 95% CI: 1.03-1.18). Biomarkers that had an influence on obesity included diastolic blood pressure, HbA1c and triglyceride levels, inflammatory markers, and antioxidant values.

**CONCLUSION:** Poor sleep quality due to night shift work disturbs the circadian rhythm, causing negative changes in metabolic, inflammatory, neuroendocrine, and antioxidant biomarkers. These changes may eventually play a role in increasing the incidence of obesity.

14. *PLoS One.* 2013 Aug 16;8(8):e71107.

## The effects of shift work on sleeping quality, hypertension and diabetes in retired workers.

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**BACKGROUND:** Shift work has been associated with adverse health effects by disturbing circadian rhythms. However, its potential long-term health effects and the persistent effects after leaving shifts have not been well established.

**METHODS AND RESULTS:** We studied 26,463 workers from Tongji-Dongfeng Cohort in China. All the participants are retired employees of Dongfeng Motor Company. Information on demographics, occupational history and medical history were gathered through questionnaires. After adjusting potential confounders in the logistic regression models, shift work was associated with poor sleeping quality, diabetes and hypertension independently. We observed significant effects of shift work on poor sleeping quality, diabetes and hypertension; the ORs (95%CI) are 1.18 (1.09-1.27), 1.10 (1.03-1.17) and 1.05 (1.01-1.09) respectively. In the further analysis, we found elevated ORs (95%CI) for participants with poor sleeping quality, the ORs (95%CI) are 1.34 (1.08-1.60), 1.13 (1.05-1.21), 1.05 (1.03-1.07) and 1.05 (1.01-1.09) for 1-4, 5-9, 10-19, >20 years of shift work respectively. However, with the extension of leaving shift work duration, the effects of shift work on sleep quality gradually reduced.

**CONCLUSIONS:** Shift work may be an independent risk factor for sleeping quality, diabetes and hypertension even in retired workers. Applicable intervention strategies are needed for prevention of sleep loss, diabetes, and hypertension for shift workers.

15. *Front Endocrinol (Lausanne)*. 2013 Aug 7;4:92.

### **Shift work and circadian dysregulation of reproduction.**

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Health impairments, including reproductive issues, are associated with working nights or rotating shifts. For example, shift work has been associated with an increased risk of irregular menstrual cycles, endometriosis, infertility, miscarriage, low birth weight or pre-term delivery, and reduced incidence of breastfeeding. Based on what is known about circadian regulation of endocrine rhythms in rodents (and much less in humans), the circadian clock is an integral regulatory part of the reproductive system. When this 24-h program is disordered by environmental perturbation (such as shift work) or genetic alterations, the endocrine system can be impaired. The purpose of this review is to explore the hypothesis that misalignment of reproductive hormones with the environmental light-dark cycle and/or sleep-wake rhythms can disrupt menstrual cycles, pregnancy, and parturition. We highlight the role of the circadian clock in regulating human reproductive physiology and shift work-induced pathology within each step of the reproductive axis while exploring potential mechanisms from the animal model literature. In addition to documenting the reproductive hazards of shift work, we also point out important gaps in our knowledge as critical areas for future investigation. For example, future studies should examine whether forced desynchronization disrupts gonadotropin secretion rhythms and whether there are sleep/wake schedules that are better or worse for the adaptation of the reproductive system to shift work. These studies are necessary in order to define not only whether or not shift work-induced circadian misalignment impairs reproductive capacity, but also to identify strategies for the future that can minimize this desynchronization.

17. *Coll Antropol*. 2013 Jun;37(2):379-84.

### **Shift work, quality of life and work ability among Croatian hospital nurses.**

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This paper is a report of a study of the associations of shift work with work ability and quality of life (QoL) among clinical nurses. A cross-sectional study was conducted in 2007-2008 on 1124 nurses using the Work Ability Index Questionnaire and the Quality of Life Questionnaire (WHOQOL-BREF). Lower education was a predictor for low level of work ability and low physical health domain of QoL. Older age and having no partner were statistically significantly related to lower social interaction. Predictors significantly related to low environment domain of QoL were low education and shift work. Shift workers had higher level of level of work ability, but clinically insignificant. The study provides no evidence of a significant association between shift work and work ability or quality of life. Education has a positive association with nurses' work ability and quality of life.

18. *Chronobiol Int*. 2013 Oct;30(8):1050-65.

### **Circadian time organization of professional firemen: desynchronization -tau differing from 24.0 hours- documented by longitudinal self-assessment of 16 variables.**

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We investigated the circadian synchronization/desynchronization (by field-study assessment of differences in period,  $\delta$ , of 16 coexisting and well-



documented rhythms) of 30 healthy firemen (FM) exposed to irregular, difficult, and stressful nocturnal work hours who demonstrated excellent clinical tolerance (allochronism). Three groups of FM were studied (A = 12 FM on 24-h duty at the fire station; B = 9 FM on 24-h duty at the emergency call center; C = 9 day-shift administrative FM) of mostly comparable average age, body mass index, career duration, chronotype-morningness/eveningness, and trait of field dependence/independence. The self-assessed 16 circadian rhythms were (i) physiological ones of sleep-wake (sleep log), activity-rest (actography), body temperature (internal transmitter pill probe), right- and left-hand grip strength (hand dynamometer), systolic and diastolic blood pressure (BP) plus heart rate (ambulatory BP monitoring device); (ii) psychological ones (visual analog self-rating scales) of sleepiness, fatigue, fitness for work, and capacity to cope with aggressive social behavior; and (iii) cognitive ones of eye-hand skill and letter cancellation, entailing performance speed (tasks completed/unit time) and accuracy (errors). Data (4-6 time points/24 h; 2 591 480 values in total) were gathered continuously throughout two 8-d spans, one in winter 2010-2011 and one in summer 2011. Each of the resulting 938 unequal-interval time series was analyzed by a special power spectrum analysis to objectively determine the prominent  $\delta$ . The desynchronization ratio (DR: number of study variables with  $\delta = 24.0$  h/number of study variables  $\times 100$ ) served to ascertain the strength/weakness of each rhythm per individual, group, and season. The field study confirmed, independent of group and season, coexistence of rather strong and weak circadian oscillators. Interindividual differences in DR were detected between groups and seasons ( $\pm 2$ ), correlation tests, analysis of variance [ANOVA]. Moreover, in each group, both in winter and summer, a normal distribution was observed in the number of FM with rhythms with  $\delta = 24.0$  h, e.g., ranging from 5/16 (large desynchronization) to 16/16 (no desynchronization). Such a normal distribution with intraindividual stability over time (i.e., seasons) is consistent with the hypothesis of an inherited origin of a differential propensity to circadian desynchronization and which is supported by the distribution of  $\delta$ s in winter and summer following the Dian-Circadian Genetic Model, i.e., with  $\delta = 24.0$  h,  $\delta = 24.0$  h +  $n(0.8$  h), and  $\delta = 24.0$  h -  $n(0.8$  h).

19. *Endocr Regul.* 2013 Jul;47(3):159-70.

## Changes of physiological functions induced by shift work.

### Herichova I.

Shift work was positively associated with higher incidence of metabolic syndrome, obesity, cardiovascular disease, sleep disturbances, decreased immune functions, and cancer. Observed disorders were manifested usually after longer time of shift work (more than 10 years). On the other hand, disturbed daily profile of melatonin and cortisol during shift work were detected even in human self reporting well tolerated shift work. Similarly, changes in thyroid stimulating hormone, prolactin, growth hormone, insulin, and ghrelin were demonstrated. Changes in hormone concentrations are influenced by shift work, sleep or circadian system or combinations of above mentioned regulatory factors. The circadian system consists of the central part localized in the hypothalamus and peripheral oscillators located in all tissues of the body. The central oscillator is predominantly synchronized by light and peripheral oscillators are more responsive to metabolic signals. Under conditions of shift work, central and peripheral oscillators dissociate that causes misalignment of daily rhythms in physiological functions. Synchronization during shift work can be improved by melatonin supplementation and manipulation with light:dark cycles and food regimens. Shift work tolerance is individual. Partial positive selection can be achieved on the basis of several psychological traits. Appropriate schedule can be estimated on the basis of chronotype.

19. *J Clin Sleep Med.* 2013 Jul 15;9(7):641-6.

**The effectiveness of light/dark exposure to treat insomnia in female nurses undertaking shift work during the evening/night shift.**

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**STUDY OBJECTIVES:** The present study investigated whether bright light exposure during the first half of the evening/night shift combined with light attenuation in the morning is effective in improving sleep problems in nurses undertaking rotating shift work who suffer from clinical insomnia.

**METHODS:** This was a prospective, randomized control study. The Insomnia Severity Index (ISI) and the Hospital Anxiety Depression Scale (HADS) were used to evaluate insomnia and anxiety/depression severity, respectively. Female hospital nurses on rotating shifts during the evening or night shift with an ISI score > 14 were

enrolled. Subjects in the treatment group (n = 46) were exposed to bright light at 7,000-10,000 lux for e" 30 minutes. Exposure was continued for at least 10 days during 2 weeks, and the subjects avoided daytime outdoor sun exposure after work by wearing dark sunglasses. Subjects in the control group (n = 46) were not exposed to bright light, but also wore sunglasses after work. Statistical analyses were performed to examine group differences and differences across treatments.

**RESULTS:** After treatment, the treatment group showed significant improvements in the ISI score and the HADS total and subscale scores as compared with pre-treatment. The ISI, HADS, and subscales of the HADS scores were significantly improved across treatments in the treatment group as compared with the control group.

**CONCLUSIONS:** The design of this study is easy to put into practice in the real world. This is the first study to document that a higher intensity and briefer duration of bright light exposure during the first half of the evening/night shift with a daytime darkness procedure performed in rotating shift work female nurses suffering from clinical insomnia could improve their insomnia, anxiety, and depression severity.