The Relationship Between Shift Work and Men's Health

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ABSTRACT

Background: More than 21 million Americans and nearly 20% of the U.S. workforce are shift workers. Non-standard shift work, defined as work that falls outside of 6 AM–6 PM, can lead to poor diet, exercise, and sleep habits that lead to decreased productivity, increased workplace accidents, and a variety of negative health outcomes.

Aim: To investigate the associations between shift work exposure and chronic medical conditions such as metabolic syndromes, cardiovascular disease, gastrointestinal disturbances, and depression as well as urologic complications including hypogonadism, male infertility, lower urinary tract symptoms, and prostate cancer with a focus on the effects of shift work sleep disorder (SWSD) on the severity of these negative health outcomes.

Methods: We reviewed the literature examining effects of shift work and SWSD on general and urologic health.

Outcomes: We produced a summary of effects of shift work on health with focus on the increased risk of negative health outcomes in non-standard shift workers, particularly those with SWSD, when compared to daytime workers or workers without SWSD.

Results: Studies have associated non-standard shift work schedules and poor health outcomes, including increased risks of diabetes mellitus, dyslipidemia, hypertension, heart disease, peptic ulcer disease, and depression, in shift workers. However, few studies have focused on the role that shift work plays in men's urologic health. Current evidence supports associations between non-standard shift work and increased hypogonadal symptoms, poor semen parameters, decreased fertility, lower urinary tract symptoms, and prostate cancer. These associations are strengthened by the presence of SWSD, which affects up to 20% of shift workers. Unfortunately, interventions, such as planned naps, timed light exposure, melatonin, and sedative hypnotics, aimed at alleviating excessive nighttime sleepiness and daytime insomnia in non-standard shift workers experiencing SWSD, are limited and lack strong evidence to support their efficacy.

Conclusions: Non-standard shift work has been associated with a variety of negative health outcomes and urologic complications, especially with concurrent SWSD. Recognition of these increased risks among shift workers can potentially aid in more effective screening of chronic health and urologic conditions. Non-pharmacologic treatment of SWSD focuses on behavioral therapy and sleep hygiene while melatonin, hypnotics, and stimulants are used to alleviate insomnia and excessive sleepiness of SWSD. Further research into both pharmacologic and non-pharmacologic therapies for SWSD is needed to establish more definitive guidelines in the treatment of SWSD in order to increase productivity, minimize workplace accidents, and improve quality of life for shift workers. **Deng N, Kohn TP, Lipshultz LI, et al. The Relationship Between Shift Work and Men's Health. Sex Med Rev 2018;6:446–456.**

Key Words: Shift work; shift work sleep disorder; sperm; hypogonadism; male infertility; lower urinary tract symptoms; erectile function; male health

INTRODUCTION

It is estimated that more than 21 million Americans, or 17.7% of the U.S. labor force, are non-standard shift workers whose work schedules fall outside of the hours of 6 AM–6 PM.[1] A non-standard shift work schedule interrupts the natural sleep-wake cycle, leading to decreased duration and quality of sleep. Akerstedt and Wright[2] showed that sleep deprivation from working non-standard shifts can lead to a circadian rhythm sleep disorder, shift work sleep disorder (SWSD). SWSD is defined by the third

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edition of the *International Classification of Sleep Disorders* as insomnia or excessive sleepiness due to decreased total sleep time as a result of work schedule for a minimum of 3 months causing significant distress or impairment in mental, physical, or social functioning.[2–4] Affecting up to 20% of shift workers, SWSD has been associated with several detrimental behavioral and health outcomes including increased risk of gastric ulcers, sleep-related accidents, absenteeism, and depression.[5,6]

Shift work has also been linked to urologic health problems in men. While infertility and shift work has been extensively studied in females, there are few studies examining the effects of shift work on male reproductive health.[7] Non-standard shift workers have higher rates of lower urinary tract symptoms (LUTS), elevated prostate-specific antigen levels, hypogonadal symptoms, and sexual dysfunction.[8–10] Since urologists are often the point of entry into the health care system for men, it is important to recognize shift work as a risk factor for various urologic and non-urologic health issues. In this review, we explore the impact of shift work on general men's health and specifically urological complications. We also examine the impact of SWSD on these health issues, review current treatment options, and suggest future directions for research into the impact of shift work on men's health.

METHODS

To conduct this review, a search of MEDLINE was performed for all English-language literature published on or before November 2017 using the following search terms and their combinations: men's health, disease, urologic conditions, shift work, and SWSD. Articles were included if they assessed the impact of shift work or SWSD on men's health with a special focus placed on urologic diseases. Abstracts were excluded from this review.

SHIFT WORK AND OVERALL HEALTH

Shift workers more often experience insomnia, poor sleep quality, and daytime sleepiness compared to their non-shift worker colleagues.[11,12] In a study of 1,280 Italian police officers, signs of sleep disorders were linked to a greater incidence of workplace accidents among shift workers.[13] In the realm of health care, where extended work hours and shift work are a necessity to provide around-the-clock care of patients, shift work may contribute to the growing number of medical errors each year.[14] Nurses who worked shifts longer than 12.5 hours experienced decreased vigilance and were more likely to experience occupational injuries such as a needle stick.[15] Similarly, medical trainees who worked shifts longer than 24 hours were 36% more likely to commit a serious medical error and 300% more likely to commit a fatigue-related error resulting in patient death when compared with their colleagues who worked 16-hour shifts.[15] In a review of 5 studies on shift workers of various professions, the risk of accident or injury increased by 18.3% for afternoon shifts and 30.4% for night shifts when compared with morning shifts.[16] These statistics underscore the greater risk of physical injury among shift workers.

Recent research has suggested that lack of sleep due to shift work may contribute to increased work absenteeism, which can lead to loss of productivity. A study conducted on 464 police officers from the Buffalo, NY Cardio-Metabolic Occupational Police Stress cohort found that those who worked night shifts had a higher incidence of sick leave, defined as missing 3 or more consecutive workdays, compared to those who worked day or afternoon shifts with this difference being more prominent in overweight or obese officers (body mass index $\geq$25).[17] A separate study of Brazilian petroleum company employees found that workers who missed more than 5% of potential working days over a 2-year period were 2.2 times more likely to report abnormal sleep compared to workers who missed less than 5% of potential working days.[18] Natti et al[19] demonstrated a relationship between decreased work-time control and increased rates of sick days and suggested that the increased absenteeism seen in shift workers may be due to decreased work-time control inherent to shift work. In contrast, a 5-year historic cohort study examining 7,562 ground staff employees of an airline company revealed that shift work was negatively associated with more sickness absence episodes and that night shifts were not significantly associated with long-term sickness absence.[20] Interestingly, significant increase in long-term sickness absence, defined as 7 or more consecutive sickness absence days, was seen only in employees who switched into a 3-shift schedule (morning/day, evening, and night) from day work (no shift) or 2-shift schedule (morning/day and evening) with this difference being most prominent in workers whose marital statuses were single and had no children.[20] These results suggest that shift work may be just one of many factors that contribute to decreased productivity due to work absenteeism and that further work is needed to elucidate the contribution of shift work to long-term sickness absence.

While the economic impact of shift work and its associated disorders is not well studied, estimates from the economic consequences of excessive sleepiness and insomnia, 2 symptoms of SWSD, are available.[21] Estimates of financial losses from accidents as a direct result of excessive sleepiness amount to $71–93 billion annually while a worker with insomnia can add an additional $1,253 in costs compared with a worker without insomnia over a 6-month period due to hospital bills, work absenteeism, and use of disability programs.[22,23] These figures suggest that the harm of shift work is not limited to individual workers but also affects organizations on a larger scale.

CHRONIC DISEASES ASSOCIATED WITH SHIFT WORK

In addition to altered circadian rhythms, poor diet and lifestyle habits have been implicated in the increased mental and physical

health issues seen in shift workers. While definitive evidence is lacking, preliminary research has suggested that low-quality diet and irregular eating patterns as a direct result of shift work schedule, coupled with detrimental lifestyle habits such as smoking and poor sleep patterns, can lead to and exacerbate chronic metabolic diseases.[24] Furthermore, animal studies showed that mimicking exposure to shift work through repeated diurnal phase shifts can accelerate the development of cancer, glucose intolerance, and autoimmune diseases in genetically predisposed mice.[25] Despite obesity being a major risk factor for many metabolic diseases, studies have only revealed a crude relationship between shift work and increase in body weight.[26] Among chronic medical conditions, peptic ulcer disease and coronary heart disease have shown the greatest association with shift work.[27] Here, we review the evidence that supports associations between common chronic medical conditions and shift work (Table 1).

Diabetes Mellitus

Few studies have investigated the relationship between shift work and diabetes mellitus (DM) despite a high prevalence of the disease and its complications that affect multiple organ systems.[28] Questionnaire results from the Nurses' Health Study cohort including 121,700 female nurses 30−55 years old found that patients who worked longer shifts were more likely to have DM.[29] A meta-analysis of 226,652 patients demonstrated an odds ratio (OR) of 1.09 (95% CI 1.05−1.12; $P = .014$) for the association between shift work exposure and risks of DM, with this association being stronger in men (OR = 1.37, 95% CI 1.20−1.56) than women (OR = 1.09, 95% CI 1.04−1.14).[30] In a study of 475 Japanese male manufacturing workers, Ika et al[31] concluded that DM was more likely to be associated with more intense shift work (OR = 2.10, 95% CI 0.77−5.71 for continuous shift workers; OR = 0.98, 95% CI 0.28−4.81 for seasonal shift workers) compared to non-shift workers with this association being more pronounced in workers who were older than 45 years. In a longitudinal study of the Danish Nurse Cohort including 19,873 female nurses who did not have DM at initial enrollment, 837 nurses developed DM after 15 years; nurses who worked night and evening shifts were at higher risk for DM (hazard ratio = 1.58, 95% CI 1.25−1.99 for night shifts; hazard ratio = 1.29, 95% CI 1.04−1.59 for evening shifts) compared to nurses who worked day shifts.[32] These studies indicate a strong association between shift work and DM, demonstrating that shift work can have a detrimental impact on health.

Dyslipidemia

Since disruptions in sleep-wake cycles due to shift work may interfere with healthy eating and exercise habits, one might expect to see an increased risk of dyslipidemia in shift workers. A study of 140 Jordanian employees showed that shift workers had higher serum triglyceride level ($P = .012$), higher triglyceride/high-density lipoprotein cholesterol ratio ($P = .013$), and lower high-density lipoprotein cholesterol level ($P = .016$) compared to daytime workers.[33] However, a study of 360 Buffalo, NY police officers showed that lipid levels were not significantly associated with shift work alone but rather sleep quality as assessed by the Pittsburg Sleep Quality Index questionnaire.[34] Especially among female officers and officers older than 40 years, serum triglycerides and total cholesterol increased as sleep quality declined ($P < .05$).[34] This suggests that serum lipid levels may be indirectly related to shift work and more closely related to sleep disorders resulting from shift work. As other studies have concluded, a clear relationship between shift work and lipid disturbances has yet to be established.[35]

Hypertension

Like many comorbidities discussed above, the link between shift work and hypertension is not completely understood. Given that shift work schedules may predispose workers to maladaptive behaviors (ie, poor work-life balance, smoking, and weight gain) and lead to activation of the autonomic nervous system, inflammation, and other metabolic syndromes, one would expect to see a higher risk of hypertension among shift workers.[36] A study of over 25,000 German automobile workers found that hypertension was more prevalent among rotating shift and night-shift workers (11.5% and 11.0%, respectively) compared to daytime workers (7.8%, $P < .001$).[37] After adjusting for confounders such as smoking, body mass index, alcohol consumption, and lipid profiles, the authors found that rotating shift work was associated with hypertension (OR = 1.15, 95% CI 1.02−1.30) when compared to daytime workers.[37] A separate study by Guo et al[38] suggests that shift work may have long-lasting impact on blood pressure, as shift work was independently associated with hypertension in over 26,000 retired Chinese automobile plant workers (OR = 1.05, 95% CI 1.01−1.09). Data from the 2010 National Health Interview Survey of over 59,000 U.S. workers revealed that shift work was significantly associated with hypertension in blacks (OR = 1.35, 95% CI 1.06−1.72) but not in whites (OR = 1.01, 95% CI 0.85−1.20).[39] While many studies have resulted in significant but weak associations between shift work and hypertension, further research is needed to establish a true relationship considering numerous confounding variables affecting hypertension.

Cardiovascular Disease

Cardiovascular disease (CVD) is the leading cause of death in the United States and is the result of a combination of risk factors described above.[40] A meta-analysis in 1999 concluded that shift workers had a 40% increased risk of CVD compared with daytime workers.[41,42] A study of over 79,000 female nurses in the United States found that the relative risk of coronary heart disease was 1.51 (95% CI 1.12−2.03) for those who had performed rotating night shifts for 6 or more years.[29] More recently, a

Table 1. Chronic medical conditions associated with non-standard shift work exposure, reported as odds ratio or hazard ratio compared to non-shift or day workers

Condition	Study	*N*	Findings
DM	Gan et al[30]	Meta-analysis of 226,652	Compared to non-shift workers, shift workers were at higher risk of developing DM - OR = 1.09 (95% CI 1.05–1.12) overall - OR = 1.37 (95% CI 1.20–1.56) in men
	Ika et al[31]	475	Shift-work intensity associated with increased risk of developing DM - OR = 2.10 (95% CI 0.77–5.71) for continuous shift workers - OR = 0.98 (95% CI 0.28–4.81) for seasonal shift workers
	Hansen et al[32]	19,873	Compared to day workers, both evening and night-shift workers had higher risk of developing DM with night-shift workers having the highest risk - HR = 1.58 (95% CI 1.25–1.99) for night-shift workers - HR = 1.29 (95% CI 1.04–1.59) for evening-shift workers
Dyslipidemia	Alefishat et al[33]	140	Compared to daytime workers, shift workers had higher TG/HDL-C ratio ($P = .013$), higher serum TG levels ($P = .012$), and lower HDL-C levels ($P = .016$) - Shift workers: 30.5% had TG/HDL-C ratio >3.5 - Daytime workers: 8.6% had TG/HDL-C ratio >3.5
	Charles et al[34]	360	Officers age ≥40 y who reported poor sleep quality had higher TC levels compared to colleagues who reported good sleep quality ($P = .010$) - Poor sleep: TC level = 202.9 ± 3.7 mg/dL - Good sleep: TC level = 190.6 ± 4.0 mg/dL
Hypertension	Ohlander et al[37]	25,343	Shift work was significantly associated with hypertension compared to day workers - OR = 1.15 (95% CI 1.02–1.30) Hypertension was more prevalent among rotating shift and night-shift workers compared to day workers ($P < .001$) - Rotating shift: 11.5% had hypertension - Night shift: 11.0% had hypertension - Day worker: 7.8% had hypertension
	Guo et al[38]	26,463	Shift work was independently associated with hypertension in retired shift workers - OR = 1.05 (95% CI 1.01–1.09)
	Ceide et al[39]	59,199	Shift work was significantly associated with hypertension in blacks but not in whites - Blacks: OR = 1.35 (95% CI 1.06–1.72) - Whites: OR = 1.01 (95% CI 0.85–1.20)
Heart disease	Kawachi et al[29]	79,109	Nurses who performed rotating night shifts for ≥6 y were at higher risk of developing coronary heart disease - RR = 1.51 (95% CI 1.12–2.03)
	Vetter et al[43]	189,158	Increased duration (y) of night-shift work is associated with higher coronary heart disease risk - <5 y: HR = 1.02 (95% CI 0.97–1.08) - 5–9 y: HR = 1.12 (95% CI 1.02–1.22) - ≥10 y: HR = 1.18 (95% CI 1.10–1.26)
	Knutsson et al[42]	504	Shift workers had 40% increased risk of CVD compared with daytime workers
	Hublin et al[44]	20,142	No significant association between shift work and cardiovascular disease was found
	Frost et al[45]	1,047,698	
GI disturbances	Koller[47]	340	Prevalence of GI disease was higher in shift workers compared to day workers ($P < .01$) - Shift workers: 30.1% - Day workers: 13.2%
	Caruso et al[48]	343	Evening shift workers reported more GI symptoms than day workers - OR = 3.30 (95% CI 1.35–8.07)

(continued)

Table 1. Continued

Condition	Study	N	Findings
	Pietroiusti et al[49]	348	In subjects with *Helicobacter pylori* infections, non-standard shift workers were more likely to develop duodenal ulcers compared to day workers - OR = 3.92 (95% CI 2.13–7.21) Shift workers who performed at least 7 night shifts per month had higher risk of peptic ulcer disease compared to colleagues who worked fewer shifts - OR = 3.13 (95% CI 1.14–8.54)
Depression	Park et al[51]	50,032	Higher percentage of shift workers reported depressive symptoms compared to non-shift workers ($P < .001$) - Shift workers: 43.6% - Non-shift workers: 38.7%
	Lee et al[52]	9,789	Shift workers were more likely to report depressive symptoms than non-shift workers - OR = 1.519 (95% CI 1.380–1.674)
	Lindgren et al[53]	2,066	Shift workers reported more severe depressive symptoms as measured by scores on PHQ-9 ($P = .001$) - Shift workers: 5.022 ± 5.017 - Non-shift workers: 4.388 ± 5.006 Increased number of shifts worked per week is associated with worse depressive symptoms on PHQ-9 - Spearman rank: $\rho = 0.125$, $P = .002$

CVD = cardiovascular disease; DM = diabetes mellitus; GI = gastrointestinal; HDL-C = high-density lipoprotein cholesterol; HR = hazard ratio; OR = odds ratio; PHQ = Patient Health Questionnaire; RR = relative risk; TC = total cholesterol; TG = triglyceride.

prospective cohort study of almost 190,000 female nurses in the Nurses' Health Studies suggested that increased duration of rotating night shifts was associated with significantly higher incidences of coronary heart disease, but this risk seemed to decline with time after cessation of shift work when participants were followed up over a 24-year period.[43] Despite these convincing results, several large studies have demonstrated a lack of significant association between shift work and CVD,[44,45] although most current data suggest that shift work may play a detrimental role in CVD.

Gastrointestinal Disturbances

Numerous studies have found an association between shift work and various gastrointestinal (GI) disturbances, including gastroduodenal ulcers and functional GI symptoms.[46] In a study of 340 oil refinery workers that included 230 shift workers, GI diseases were more prevalent in shift workers compared to daytime workers (30.1% vs 13.2%, respectively).[47] In a cross-sectional study of 343 auto factory workers, those who worked evening shifts endorsed more GI symptoms than their colleagues working day shifts (OR = 3.30, 95% CI 1.35–8.07).[48] In patients with underlying risk factors for peptic ulcer disease, including *Helicobacter pylori* infections, non-standard shift workers were more likely to develop duodenal ulcers compared with daytime workers of similar age, sex, and family history of peptic ulcer disease (OR = 3.92, 95% CI 2.13–7.21).[49] Additionally, shift workers who worked at least 7 nights per month were more likely to develop peptic ulcers compared to other shift workers with fewer night shifts (OR = 3.13, 95% CI 1.14–8.54).[49] These data suggest that shift work may be a risk factor that accelerates the development of peptic ulcer disease in susceptible individuals, with higher risks observed in those who work more non-standard shifts.

Depression

SWSD, a direct result of sleep deprivation from working non-standard shifts, has been linked to depression.[2,5] In a small pilot study by Scott et al,[50] shift workers were more likely to experience major depressive disorder. A study examining over 50,000 Korean employees found that a significantly greater proportion of shift workers reported depressive symptoms compared with non-shift workers.[51] A survey study of nearly 10,000 Korean nurses reported increased odds of experiencing depressive symptoms among nurses who worked shifts (OR = 1.519, CI = 1.380–1.674, $P < .001$).[52] Using the Patient Health Questionnaire (PHQ)-9 as a validated measure of depressive symptoms, Lindgren et al[53] showed that shift workers had significantly more severe depressive symptoms as evidenced by higher PHQ-9 scores ($P = .001$). Interestingly, among shift workers, the number of shifts performed per week positively correlated with higher PHQ-9 scores and thus more severe depressive symptoms ($\rho = 0.125$, $P = .002$).[53] These data suggest that depressive symptoms are not merely associated with shift work exposure but also the quantity of shift work performed. However, only a limited number of studies investigating the impact of shift work on depressive symptoms exist in current literature.

Obstructive Sleep Apnea

Although obstructive sleep apnea syndrome (OSAS) has been linked to negative men's health outcomes, the relationship

between shift work and OSAS is not as well studied as the other co-morbidities described above.[54,55] Paciorek et al[56] found that OSAS patients who performed shift work had significantly higher apnea-hypopnea index (AHI) and oxyhemoglobin desaturation index during daytime sleep compared to sleep-deprived controls with OSAS who did not perform shift work. In the shift work population, AHI was higher during diurnal sleep after night shift compared to nocturnal sleep, suggesting that sleep deprivation from shift work may play an acute role in worsening OSAS.[56] In a separate study by Laudencka et al[57] including 8 OSAS patients, 4 patients were found to have higher AHI during sleep after night shift compared to sleep after day shift, which suggests that only a subgroup of patients with OSAS may experience worsening symptoms from working non-standard shifts. Future studies are needed to further characterize the effect of shift work on OSAS.

UROLOGIC CONDITIONS ASSOCIATED WITH SHIFT WORK

Systemic medical diseases, such as those described above, may be related to disorders of sexual function through common inflammatory mechanisms and shared metabolic or vascular risk factors.[58] Since the association between shift work and male urologic health is only beginning to be elucidated, studies focusing on this topic are limited. Here, we review the current literature on various aspects of urologic health seen in the male shift worker (Table 2).

Hypogonadism

Hypogonadism is a disorder of low testosterone levels with clinical symptoms of decreased libido, erectile dysfunction, lethargy, difficulties concentrating, sleep disturbances, and loss of muscle mass.[10] Endogenous testosterone production is tied to sleep, with rising levels during rapid-eye movement sleep onset and declining levels upon awakening.[59] Thus, men with decreased rapid-eye movement frequency or poor sleep quality, such as non-standard shift workers who experience SWSD, could have lower circulating testosterone levels. However, Pastuszak et al[10] found no association between self-reported sleep quality and serum testosterone levels in a cohort of 182 non-standard shift workers. In a study of 4 oil refinery operators whose serum hormone levels were sampled every 2 hours in real-time during a night shift, the peak and trough times for serum testosterone concentrations were erratic as overall serum testosterone concentrations in these shift workers were significantly reduced.[60] In a separate study involving 73 male police officers, no changes in the diurnal rhythms of testosterone were observed when officers were exposed to more consecutive night shifts.[61] A study of 26 European junior doctors showed no changes in free and total testosterone levels while subjects were on vacation (baseline), working a week of night shifts, and working a normal week.[62]

Although there has been no definitive evidence suggesting a change in serum testosterone levels after shift work exposure, studies have found that shift workers who experience SWSD endorsed more hypogonadal symptoms, as determined using the quantitative Androgen Deficiency in the Aging Male questionnaire.[10] When assessing the relationship between sleep quality and hypogonadal symptoms, Pastuszak et al[10] found a significant linear association between self-reported sleep quality and Androgen Deficiency in the Aging Male scores ($P = .008$) as respondents who were "very satisfied" with their sleep quality had higher scores than those who were "somewhat dissatisfied" with their sleep quality ($P = .02$). While there is no consensus on the effects of non-standard shift work on serum testosterone levels, there exists clear evidence supporting more severe symptoms of hypogonadism in non-standard shift workers with poor sleep quality and SWSD.

Male Infertility

A non-standard shift work schedule poses a challenge for couples who wish to achieve fertility. In couples where one or both partners work non-standard shifts, spending time together may come at a premium. Variations in work schedules may strain relationships and limit opportunities for intimacy.[63] A study of the relationship between infertility and occupation revealed that male infertility was associated with working in industry and construction, fields in which workers were more likely to work shifts (OR = 3.12, 95% CI 1.19−8.13) and endure physical exertion (OR = 3.35, 95% CI 1.44−7.80).[64] More recently, Eisenberg et al[65] found that shift work was not directly associated with semen quality but workplace exertion was. In a study of 255 infertile and 267 fertile men, male infertility was more likely to be observed in shift workers (OR = 3.60, 95% CI 1.12−11.57).[66] Similarly, Irgens et al[67] showed that reduced semen quality was more likely in shift workers, although this difference was statistically insignificant (OR = 1.46, 95% CI 0.89−2.40).

Few have theorized the mechanism of decreased fertility in shift workers. Previous studies have linked subfertility or infertility to toxic exposures in the workplace, including to electromagnetic fields, heavy metals, and chemical solvents.[66,67] Recent studies have suggested the role of circadian rhythm disturbances as a function of shift work schedules is related to disruption of the brain-gonadal axis, which can ultimately lead to infertility. Ortiz et al[68] suggested the detrimental role of serotonin on male reproductive health when the authors found higher levels of urinary 5-hydroxyindoleacetic acid (HIIA), a metabolite of serotonin, in infertile male shift workers compared to shift workers who recently fathered children; higher 5-HIIA levels were associated with decreased sperm concentration and forward motility. Serum markers such as serotonin, as indirectly measured by urinary 5-HIIA, may reflect the neuroendocrine imbalances associated with male infertility in shift workers.

Table 2. Urologic conditions associated with non-standard shift work exposure, reported as odds ratio or relative risk compared to non-shift or day workers

Condition	Study	*N*	Findings
	Touitou et al[60]	4	During a night shift, peak and trough times for serum testosterone concentrations in non-standard shift workers were erratic as overall mean serum testosterone concentration in non-standard shift workers was significantly lower compared to non-shift workers ($P < .001$) - Shift worker: 400 ± 150 ng/dL - Non-shift worker: 800 ± 400 ng/dL
	Pastuszak et al[10]	182	Significant linear association existed between sleep quality and higher qADAM scores in non-standard shift workers ($P = .008$) - "Very satisfied": qADAM score 38.0 - "Somewhat satisfied": qADAM score 35.9 - "Somewhat dissatisfied": qADAM score 34.4 - "Very dissatisfied": qADAM score 32.4 - qADAM scores were higher in workers who were "very satisfied" with sleep quality than those who were "somewhat dissatisfied" ($P = .02$)
Male infertility	Sheiner et al[64]	106	Male infertility was associated with working in industry and construction - OR = 3.12 (95% CI 1.19–8.13) Male infertility was associated with occupations requiring physical exertion - OR = 3.35 (95% CI 1.44–7.80)
	El-Helaly et al[66]	522	Male infertility was more likely in shift workers - OR = 3.60 (95% CI 1.12–11.57)
	Irgens et al[67]	365	Although statistically insignificant, reduced semen quality was more likely in shift workers - OR = 1.46 (95% CI 0.89–2.40)
LUTS	Kim[71]	1,741	Shift workers reported more nocturia frequency than non-shift workers ($P < .01$) - Shift workers: 2.38 ± 1.44 times per sleep period - Non-shift workers: 2.18 ± 1.04 times per sleep period
	Scovell et al[8]	228	In non-standard shift workers, sleep difficulties were associated with more severe LUTS as assessed by the IPSS questionnaire Difficulty falling asleep: $P < .001$ - No difficulty falling asleep: IPSS score 6 - Difficulty falling asleep: IPSS score 9 Difficulty staying asleep: $P = .004$ - No difficulty staying asleep: IPSS score 6 - Difficulty staying asleep: IPSS score 13 Difficulty falling back asleep after awakening: $P < .001$ - No difficulty falling back asleep: IPSS score 5 - Difficulty falling back asleep: IPSS score 13
Prostate cancer	Flynn-Evans et al[9]	2,017	Shift workers were more likely to have elevated PSA ≥4.0 ng/mL compared to non-shift workers aged 40–65 y - OR = 2.48 (95% CI 1.08–5.70)
	Parent et al[74]	3,649	Night-shift workers had higher risk of developing prostate cancer compared to day workers - OR = 2.77 (95% CI 1.96–3.92)
	Rao et al[75]	Meta-analysis of 2,459,845	Night-shift exposure led to an increased risk of prostate cancer - RR = 1.24 (95% CI 1.05–1.46)

IPSS = International Prostate Symptom Score; LUTS = lower urinary tract symptoms; OR = odds ratio; PSA = prostate-specific antigen; qADAM = Androgen Deficiency in the Aging Male; RR = relative risk.

Lower Urinary Tract Symptoms

In addition to sexual dysfunction and infertility, shift workers also experience LUTS, which include urinary frequency, urgency, weak stream, and nocturia.[69,70] A study of 1,741 patients found that shift workers reported nocturia more frequently than non-shift workers (2.38 ± 1.44 vs 2.18 ± 1.04 times, $P < .01$).[71] In a study of 228 non-standard shift workers, worse LUTS, as assessed by the validated International Prostate Symptom Score questionnaire, were observed in men with difficulty falling asleep, difficulty staying asleep, or difficulty falling back asleep after awakening ($P < .001$, $P = .004$, $P < .001$, respectively) compared to non-standard shift workers who did not report these sleep difficulties.[8,72] Given the relationship between poor sleep quality and LUTS, future research is needed to investigate the role that SWSD plays in LUTS severity.

Prostate Cancer

Circadian disruptions resulting from shift work have been associated with an increased risk of hormone-related cancers, particularly prostate cancer in men.[73] Analysis of the National Health and Nutrition Examination Survey study revealed that shift workers were more likely to have prostate-specific antigen levels above 4.0 ng/mL compared to non-shift workers 40−65 years old (OR = 2.48, 95% CI 1.08−5.70, $P = .03$).[9] A case-control study of over 3,500 males found that the OR of having prostate cancer among men who worked at night was 2.77 (95% CI 1.96−3.92).[74] Furthermore, a meta-analysis of nearly 2.5 million individuals showed a significantly increased risk of prostate cancer in night-shift workers (relative risk = 1.24, 95% CI 1.05−1.46, $P = .011$).[75] In addition, a dose-response meta-analysis suggested a 2.8% increased risk of prostate cancer (95% CI 0.3−5.4%, $P = .03$) for every 5-year duration of night-shift work performed.[75] Similarly, Papantoniou et al[76] observed an increased but statistically insignificant risk of prostate cancer in men who had ever worked night shifts (OR = 1.14, 95% CI 0.94−1.37) compared to those who never worked at night. However, this relationship became statistically significant in shift workers with over 28 years of experience working night shifts (OR = 1.38, 95% CI 1.05−1.81).[76]

The exact mechanism contributing to increased risk of prostate cancer in shift workers has yet to be understood. In vitro studies have suggested a role for melatonin, whose release is altered by circadian disruptions and exposure to light at night, as an anti-tumorigenic agent in prostate cancer.[9,77−79] In addition, urinary levels of androgens and their metabolites (eg, testosterone, dehydroepiandrosterone, androsterone, 11β-hydroxyl-androsterone, and 6α-hydroxyl-androstenedione) were found to be elevated in male night-shift workers compared with day workers.[80] While this difference was not statistically significant, it represents a potential mechanism for the increased incidence of prostate cancer in shift workers.

TREATMENT OF SWSD

Excessive sleepiness during working hours and insomnia during daytime sleeping hours are 2 major symptoms of SWSD, which affects up to 20% of shift workers.[3,6] In fact, 90% of shift workers report feeling fatigued at work, while 29−38% of shift workers are affected by insomnia.[81,82] Research on non-pharmacologic strategies for improving sleep quality in shift workers has focused mainly on behavioral therapy and sleep hygiene.[6] In a study of 24 male aircraft maintenance engineers who worked twice weekly 12-hour overnight shifts, a 20-minute nap during the first night shift improved performance on vigilance tasks while napping during both night shifts had no effect on subjective fatigue level or sleep duration and quality.[83] Similarly, an American Academy of Sleep Medicine Report in 2007 also indicated that planned pre-shift naps improved alertness and reaction times and decreased workplace accidents.[84] Additionally, timed light exposure has been proposed as a method of shifting circadian phase in nighttime shift workers.[85] By maximizing light exposure during night shifts and darkness during the daytime sleeping hours, increased performance and alertness during night shifts and sleep duration were observed.[85]

Stimulants such as modafinil, caffeine, and to a lesser extent methamphetamine have been suggested as pharmacologic agents for those with SWSD to combat sleepiness and improve psychomotor performance during night shifts.[84,86] The use of sedative hypnotics for insomnia in shift workers is risky and potentially contraindicated in hazardous working environments, depending on the drugs' pharmacokinetics.[84] However, early studies on triazolam 0.25−0.5 mg have demonstrated increased daytime sleep but conflicting results on nighttime alertness when compared to placebo.[87,88] Similarly, a placebo-controlled study of zopiclone 7.5 mg nightly in 50 adult insomniac shift workers showed improvements in sleep induction and soundness but had no effects on work performance.[89] Although taking melatonin or melatonin agonists prior to daytime sleep could theoretically help insomnia in night-shift workers, current evidence remains inconclusive on effective dosage and timing of melatonin administration.[84,90] A small study of 17 police officers who worked 7 successive night shifts found that melatonin 5 mg taken before bedtime improved quality and duration of sleep and increased alertness during shifts, but effects on cognitive performance remained inconclusive.[91] In a study of 12 night-shift nurses, melatonin 6 mg before daytime sleep improved sleep duration and total sleep times by 56 minutes compared to placebo ($P < .05$), but nocturnal alertness was only marginally improved while improvements in performance tests were not observed.[92] Given the negative consequences of SWSD, research elucidating specific pharmacologic agents and their dosing for alleviating symptoms of SWSD could potentially make a direct impact in decreasing workplace accidents and increasing productivity.

CONCLUSION

Non-standard shift workers, including emergency first responders, health care professionals, airline pilots, and plant or manufacturing operators, comprise nearly 20% of the U.S. workforce and fill indispensable roles in society.[1] Shift work exposure has been linked to poor sleep quality and insomnia, contributing to increased workplace accidents, employee absenteeism, and billions of dollars of lost productivity annually. Current evidence supports an increased risk of developing DM, hypertension, dyslipidemia, coronary heart disease, peptic ulcer disease, and depression in shift workers, although future systematic studies controlling for confounding variables are needed to more strongly establish these relationships. Non-standard shift workers who experience SWSD or report poor sleep quality are also at increased risk of developing urologic issues including hypogonadal symptoms, male subfertility or infertility, LUTS, and prostate cancer. Given these findings, it may be beneficial for health care providers to screen for shift work status and identify

this unique subgroup of patients who are at increased risk of developing chronic medical and urologic conditions. Current therapeutic strategies for treating excessive sleepiness include melatonin, stimulants, and planned naps while strategies for treating insomnia include sedative hypnotics and timed light exposure. Since a significant proportion of shift workers experience SWSD and a large majority report fatigue during shifts, therapeutic strategies for SWSD represent an area of future research capable of profound impact on improving organizational productivity, employee safety, and overall health of non-standard shift workers.

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