Exploring the Association of Shift work and Cardiovascular Disease - A Systematic Review

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Abstract: *Globally, cardiovascular diseases (CVDs) account for 17.9 million deaths annually, making them the leading cause of death. Circadian rhythm plays a big part in the sleep-wake cycle. Exposure to night shift work has been reported to increase the risk of cardiovascular disease. This review aimed to explore the relationship between shift work and cardiovascular illness comprehensively based on the literature from the last five years. We conducted a thorough search on Google Scholar and PubMed to locate clinical to identify manuscripts published between February 2018 and January 2023. Randomized controlled trials and observational studies that assessed the relationship between shift work and cardiovascular disease in patients were included. Except original articles, all other types of articles were excluded. This review comprised of 15 articles chosen from a total of 1005 articles. The study included a total of 13,37,247 cohort participants (both male and female). While compared to daytime work, night shift work was related with a marginal increase of cardiovascular disease risk. The shift employment with occupational cardiovascular disease mortality was reported mostly on female nurses. The results indicated that those working night shifts typically lead unhealthy lifestyles, behavioral issues (meal skipping), and metabolic aberrations (biochemical imbalances), but it is not yet clearly known if this increases the risk of cardiovascular disease. Circadian misalignment has been linked to an increased risk of cardiovascular illnesses in night shift than in day shift workers, where intensity, duration, and type of work are also to be considered. Alleviating traditional risk factors such as sedentary life style, high blood pressure, glycemic control and smoking requires greater attention in shift workers owing to the greater propensity to develop cardiovascular disease in this population.*

Keywords: Cardiovascular disease; shift work; circadian rhythm; sleep disorder

1. Introduction

Approximately 25% of the world's workforce works in shifts, and the number of shift workers is continuously increasing (Reinganum and Thomas 2023). The term "shift work" has various meanings in the literature, but the most extensively researched condition is shift work, especially when it involves night shifts, as it may interfere with human homeostasis and well-being on multiple levels (Costa 2010). Any work completed either regularly or permanently, outside of regular business hours ie., between midnight and 5.00 AM, is classified as night work by the International Labour Organisation (ILO). There is strong evidence that shift work harms people's health and safety by interfering with their circadian cycle. Physical, psychological, and behavioral changes that occur on a 24-hour cycle are known as circadian rhythms. Light and dark are the primary stimuli that these natural systems react to. An increasing number of epidemiological studies have suggested a possible link between shift work and a higher risk of mortality in both the general population and certain occupational groups, such as nursing workers (Eriksson et al. 2022; Barger et al. 2017). Work shifts have been demonstrated to have detrimental effects on employees, leading to the classification of shift work sleep disorder as a distinct illness. Despite having a lower incidence of CVD than men, women experience a worse prognosis and greater fatality rate following acute cardiovascular events. These days, metabolic syndromes—which include high blood pressure, elevated triglycerides (TGL) and fasting glucose, decreased High-Density Lipoprotein (HDL), cholesterol, and abdominal obesity—are among the most important risk factors for public health because of their connections to cardiovascular illnesses and type 2 diabetes (Hansen et al.2016; Eckel et al. 2005). Research has also indicated that women who work shifts experience lower fertility and higher rates of abortion compared to their day-job counterparts (McDonald et al. 1988). Therefore, it is vital to characterize and critically examine the residual effect of shift work on cardiovascular diseases on one's health. The objective of this review is to thoroughly assess the quantitative relationship between shift work and cardiovascular disease risk by performing a systemic review analysis of cohort studies.

2. Methods

This systematic review was reported in accordance with the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement guidelines 2020.

2.1 Literature search strategy

For our data collection, we conducted a thorough search of the online databases; Google Scholar and PubMed. Our search was focused on finding randomized controlled clinical trials that evaluated the relationship between cardiovascular diseases brought on by shift work. We searched for the published studies from the previous five years using the following keywords: shift work and cardiovascular diseases. In the second stage, all of the citations that were collected from the two databases were combined and duplicates were eliminated. The listed articles were analysed to determine their eligibility by reading the "abstract,", "full-text," and "title," in the third, fourth, and fifth stages, respectively. Finally, the articles are retrieved after applying inclusion/exclusion criteria. All papers were independently reviewed by two authors for eligibility (DR & MS), and any discrepancies were resolved by the other author (MG). We also manually examined the reference lists of the included studies to gather additional information.

2.2 Inclusion and exclusion criteria

The inclusion criteria for relevant articles (i) published in English language; (ii) published within the previous five years that assessed the link between shift work and cardiovascular disease; (iii) all are peer-reviewed; (iv) comparing a group of shift workers in the healthcare industry to a group of regular day workers; (v) with prospective/retrospective cohort, cross-sectional, case–control or randomized-control study designs; and (vi) that offer sufficient details to compute hazard risks (HRs) or odds ratios (ORs) with a

95% confidence interval (CI). Review articles, book chapters, editorials, commentaries, unpublished research, conference proceedings, and research papers written in other foreign languages were excluded.

3. Results

A total of 1005 articles written in English were taken out. Out of which 402 articles were deemed relevant and then subjected to analysis. After deleting duplicate submissions and abstract reviews, 47 articles made it to the shortlist. After applying the inclusion and exclusion criteria, 16 articles were produced. Following the full-text review, 15 articles in total were approved (Figure 1). The articles chosen consisted of the following outcomes resulted from shift work, 'mortality', 'cardiovascular disease', 'cardiovascular risks' and 'biomarkers'. Each of the chosen articles underwent quality assessment and peer review. In the study, the largest sample size of 631418 subjects was identified. A variety of professional populations, including nurses, security guards, police, and truck drivers, were involved and worked in several nations, the majority of which are in the United States, the United Kingdom, and Sweden. The study population's age (mean of means) was 47 years. We used 15 articles comprising of 13,37,247 cohort participants that were identified, and of the 15 countries chosen, 9 were in Europe/the US (60%) and 6 were in Asia (40%). The various vital signs and blood indicators linked to the CVD risk factors were evaluated (Table 1).

Only two manuscripts in this evaluation discussed shift work and mortality. The findings of both studies showed that shift work and CVD mortality were related (Table 2). According to the results of both studies, acute myocardial infarction mortality was higher in female workers, particularly in those with long-term shift work where noise exposure exceeded 90 dB (Eriksson et al.,2022) .

The prevalence of CVD in the working population was shown in three articles. A prospective cohort study by Wang et al (2021) implied there was a substantial correlation between their lifetime exposure to night shift work and their risk of developing atrial fibrillation and also elevated risk of CHD among the population, but not of HF or stroke. Similarly, a cross-sectional study by Abu mFarha et al (2021) observed a link between working night shifts and an increased risk of atherosclerosis and CVD (Table 3).

From the above-chosen articles, most of the studies concentrated on CVD risks among shift workers. The nature/type of shift work had an adverse effect on the shift employers. It was identified that night shift workers have a higher prevalence of raised SBP, DBP, and related risk factors than day shift workers (Draaijer et al. 2022; Debora et al. 2020) (Table 4).

Five studies showed an increase in blood biomarkers after night shift work. Mounting evidence has demonstrated an association between the elevation of inflammatory markers and the risk of medical conditions, including cardiovascular disease, arthritis, diabetes mellitus, and certain cancers, which are reported in shift workers too (Table 5).

4. Discussion

The investigation obtained a total of fifteen original articles that met the inclusion/exclusion criteria. The study aimed to gather data about the effects of cardiovascular disease on shift workers. As a result, studies on shift employment, especially night shifts, are widely researched because they disrupt human health and wellness on multiple fronts. Changes in lifestyle, such as irregular mealtimes, reduced physical activity, decreased sleep quality, etc., are frequently associated with working

night shifts. So, therefore, the crucial details regarding the population's working and geographic patterns are covered in this review.

4.1 Direct relationship between night shift work and mortality

Long-term night shift job exposure is also linked to a higher death rate, particularly in male white-collar workers (Åkerstedt et al. 2020). There is a lower likelihood of CVD mortality among shift workers, however, Ho and his researchers found a higher risk of fatal CVD events among night workers over 50 years of age and recommended that shift workers are more likely to experience incidents and fatal cardiovascular illnesses, which can be partially mitigated by modifiable risk factors as smoking, sleep duration and quality, body weight, and metabolic status (Ho et al. 2021). The pathophysiology underlying the association between mortality and night work has not been studied but the analysis of the literature attests to the fact that working nights disrupts shift workers' circadian rhythms. An involuntary oscillation that occurs about every 24 hours, the circadian rhythm or circadian cycle regulates several bodily functions, such as body temperature, appetite, and alertness or sleepiness. When the cycle is disrupted, this results in serious illnesses and even shortening of lifespan (Leger et al. 2018). A study by Gu et al (2015) in a prospective cohort study of 74,862 registered U.S. nurses, reported that when compared to women who had never worked rotating night hours, women who had worked rotating night shifts for more than five years experienced slight increases in mortality from all causes as well as from CVD.

4.2 Night shift work and cardiovascular disease

Similarly, working night shift was linked to a higher risk of ischemic heart disease in both males and females (HR: 1.10; 95% CI: 1.05 to 1.14 and HR: 1.25; 95% CI: 1.17 to 1.34) (Wong et al. 2023). A greater risk of cardiovascular illnesses and congenital diseases is associated with circadian rhythm disturbance, which can result from at least one of the aforementioned abnormalities. A significant number of people with particular risk factor data is necessary for an examination of the connections between shift work and CVD. The median CRP levels of nurses who had worked rotating shifts for 1-5, 6-9, and ≥10 years were found to be 0.1, 0.2, and 0.2 (95% CI) mg/L higher than those of nurses who had never worked rotating night hours. Males are more likely than females to have an overactive immune system, which can raise the risk of sepsis after an untimely infection, while encouraging female shift workers to engage in physical activity may help lower their visceral adipose tissue, which in turn lowers their risk of cardiovascular disease (Vissers et al. 2013).

4.3 Duration of shift work impacts the risk of poor outcomes

According to some studies, the primary organizational elements impacting shift work sleep disorder (SWSD) are the shift's duration, intensity and type of job, and a number of consecutive nights worked in a row (Feng et al. 2021). According to Wang et al (2021) and Abu Farha et al (2021), the length of night shift employment (>10 years) had an impact on CVD in the working population. Long-hour workers were more likely to have a stroke than people with regular work schedules; there was less of a correlation between the two conditions. For consistent results, we considered the longest-held occupation to be a risk factor for CVD. In addition, rotational shift employment, while not affecting the quantity or quality of sleep, is linked to heightened risk factors for cardio-metabolic illnesses. The findings indicate that rotating shift work is bad for workers' health and well-being, and that one possible pathogenic mechanism is homeostatic desynchronization (Collins et al. 2022).

4.4.Impact of shift work on biomarkers

The elevated risks for CVD that have been noted among police cohorts may be mediated by elevated levels of inflammatory markers (CRP, IL-6) in response to shift work (Holst et al., 2019). Johnson et al. (2019) assessed that working nights has negative short and long-term impacts on selective CVD biomarkers (CRP and fibrinogen). The body uses cortisol release, which is linked to the circadian rhythm, to aid the transition from biological night to biological day. It starts increasing a few hours after sleep and peaks in the early morning and early hours of awakening (Mohd Azmi et al. 2021). Cortisol levels have a circadian rhythmicity that varies, particularly in those who work night shifts, where levels rise noticeably before and after work (Cannizzaro et al. 2020).

5. Limitations

There are some noteworthy limitations to this study. The definitions of shift and night work were imprecise. Past exposures (in the measurement of cumulative exposures) for both shift and night work, as well as intensity for night work (number of nights per year), were studied; however, no information was available regarding permanent or rotating shifts, the direction of shift rotation, the number of consecutive nights or shifts, or the start and end times of nights or shifts. Only two clinical trials from the previous five years that examined the impact of shift work on cardiac disease mortality were found, and two of them neglected to consider factors like the nature of the job or the stress associated with working a shift that might increase the effect of shift work on the risk of cardiovascular diseases in general. As a result, it was unable to assess the true mortality effect associated with shift employment.

6. Conclusion

According to several studies, night shift work was associated with a marginal increase in the risk of cardiovascular disease. Shift work was also associated with a worsening of cardiovascular risk factors. This risk typically rises with increasing years of shift work. A higher BMI, less physical activity, a lower dietary quality score, frequent snoring, shorter sleep duration, frequent excessive daytime sleepiness, a high prevalence of hypertension, a high risk of diabetes, and metabolic syndrome were also linked to shift work-related sleep issues. Hence, it is imperative that shift workers take additional efforts in lowering cardiovascular risk through appropriate control of traditional risk factors.

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Authors contribution

Deepalaxmi Rathakrishnan contributed to data collection, data screening, drafted the review and wrote the manuscript. Melina I Sahay contributed to data collection, data screening, and review of manuscript. Dr.Damal Kandadai Sriram contributed to the data collection and data screening. Dr.Melvin George contributed to the study conception and design, data screening, review of data, and manuscript review. All authors approved the final version to be published.

Declaration of competing interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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Figure 1 Flow diagram showing procedure for the study selection

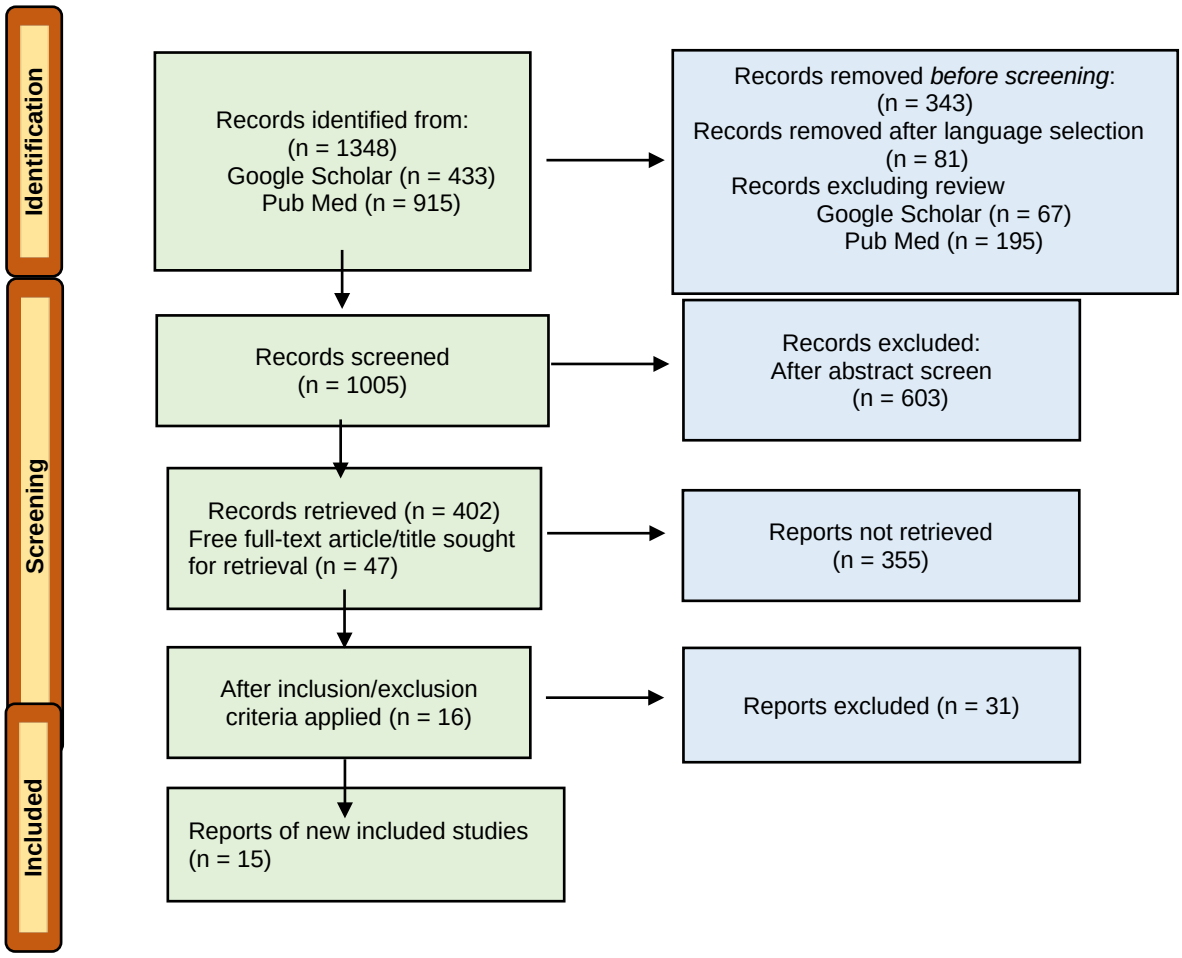

Table 1: Study population, work characteristics, and social demographic details retrieved from the selected studies

Author(s) & year of publication	Sample Size	Population	Country	Age group (Mean)	Risk factors assessed
Bigert et al., 2022	30460	Employed men and women	Stockholm	45	-
Cannizzaro et al., 2020	168	Security guards (Male)	Italy	43	Saliva cortisol, Blood Pressure (SBP, DBP)
Debora et al., 2020	137	Employed men and women	Jakarta	40	SBP, DBP, total cholesterol, fasting plasma glucose
Dicom et al., 2023	2469	Male workers	Singapore	48	BMI, Diabetes, Hypertension
Draaijer et al., 2022	607	Truck drivers (Male)	South-Africa	37	-
Eriksson et al., 2022	4496	Women	Sweden	76	Questionnaire data
Farha et al., 2018	140	Employed men and women	Jordan	40	FBG, HDL-C, TGL
Feng et al., 2021	23064	Retired workers	China	52	TC, HDL-C, SBP
Hermannson et al., 2019	4648	Men & Women	Sweden	58	Type II DM, HTN, TC, TGL
Ho et al., 2021	238661	UK Biobank participants	UK	52	LDL, TC, LP, Glycated Hb, Cystatin C, GGT
Holst et al., 2019	360	Police	USA	41	D-dimer, TNF, ICAM-1
Johnson et al., 2019	116429	Nurses (Female)	Boston, U.S	34	Fibrinogen, CRP, TC, LDL, HDL, TGL
Park et al., 2019	631418	Night Shift workers	Korea	43	Blood Pressure (SBP, DBP), FBG, BMI, Obesity
Skogstad et al., 2019	94	Industry-employed men and wor	Norway	43	LDL, HDL, CRP, TC, HbA1C
Wang et al., 2021	283657	Employed men and women	USA	55	TC, Glycates Hb

BMI-Body Mass Index; *CRP*-C-Reactive Protein; *DBP*-Diastolic Blood Pressure; *DM*-Diabetes Mellitus; *FBG*-Fasting Blood Glucose; *GGT*-Gamma-Glutamyl Transferase; *HDL*-High Density Lipoprotein; *HTN*-Hypertension; *ICAM-1*-Intercellular Adhesion Molecule-1; *LDL*-Low Density Lipoprotein; *LP*-Lipoprotein; *SBP*-Systolic Blood Pressure; *TC*-Total Cholesterol; *TGL*-Triglycerides; *TNF*-Tumour Necrosis Factor

Table 2: Studies showing mortality associated with shift work

Author(s) & year of publication	**Type of study**	**Purpose of the study**	**Main results/ conclusion**
Eriksson et al., 2022	Prospective cohort study	Investigated the relationship between shift work and occupational noise as well as the overall death rate among female industrial workers related to CVD.	NSW >10 years:AMI mortality SMR 1.33 (0.91-1.89) NSW and noise ≥ 90 dB:AMI mortality SMR 1.31 (0.97-1.73) The night shift work and AMI mortality identified using SMR are found to have a weak significant correlation.
Ho et al., 2021	Prospective cohort study	Determined whether shift work and incident or fatal cardiovascular diseases are related.	SW:CVD event HR 1.1 (1.06-1.19) SW:CVD mortality HR 1.25 (1.08-1.44) SW:IHD HR 1.95 (1.03-1.75) SW:Heart Failure HR 1.15 (1.03-1.28) SW:Stroke HR 1.09 (0.99-1.20) SW:Fatal CVD [women HR 1.16 (1.07-1.27)] SW:Fatal CVD [aged >50 years HR 1.41 (1.20-1.65)] While considering the above variables, the calculated HR shows significant IHD among workers.

AMI-Acute Myocardial Infarction: *CVD*-Cardiovascular Disease; *IHD*-Ischemic Heart Disease: *NSW*-Night Shift Work: *SMR*-Standard Mortality Ratio: *SW*-Shift Work

Table 3: Incidence of cardiovascular disease among shift workers

Author(s) & year of publication	Type of study	Purpose of the study	Main results/ conclusion
Dicom et al., 2023	Retrospective Cohort study	The correlation between shift work patterns (morning, evening, night mixed schedules) and cardiometabolic risk factors (obesity, smoking, and hyperter as well as the link between these factors and cardiometabolic diseases (diabetes and CVD), in a population with a variety of ethnic backgrounds.	Non-SW:CVD event-5.8% EM-SW:CVD event- 2.1% Evening:CVD event-6.3% Night:CVD event-14.1% Mixed:CVD event-4.5% Night shift workers had a considerably higher prevalence of CVD event among the shift and non-shift workers.
Farha et al., 2018	Cross-sectional study	Examined the night shift affected the likelihood of acquiring CVD based on several predictors.	The 30-year Framingham risk score for night shift workers was marginally h (17.5%) than for day shift workers (13.2%), even though the differences a statistically significant. The length of time spent working nights and the num nights worked each month were other contributing factors.
Wang et al., 2021	Prospective cohort study	Working nights and having a genetic predisposition to AF affected the risk of illness and the correlation between working night shift cardiovascular conditions such as heart failure, stroke, and coronary heart disease (CHD) was assessed.	Usual SW:CHD HR 1.22 (1.11-1.35) ≥10 years:CHD HR 1.37 (1.20-1.58) 3-8 nights/month:CHD HR 1.35 (1.18-1.55)

CHD-Coronary Heart Disease; *CVD*-Cardiovascular Disease; *EM*-Early Morning; *HR*-Hazardous Risk score; *SW*-Shift Work;

Table 4: Incidence of cardiovascular disease among shift workers

Author(s) & year of publication	**Type of study**	**Purpose of the study**	**Main results/ conclusion**
Bigert et al., 2022		Intended to look into different aspects of working at night and throughout shifts affected the incidence of cerebrovascular disease.	Only NSW:CVD HR 1.46 (0.96-2.21) Only DSW:CVD HR 1.39 (0.88-2.21) >30 times/year:CVD HR 1.44 (1.04-1.99) >15 times/year and ≥ 3 consecutive NSW:CVD HR 1.69 (1.18-2.42) 5 years NSW:CVD HR 1.083 (1.031-1.139) >5 years NSW:CVD HR 1.87 (1.27-2.77) When compared to other shift work, employees who have worked nights for a long time (>5 years) are at a higher risk.
Debora et al., 2020	Cross-sectional study	Incidence of hypertension and other associated risk factors among night shift employees in a Jakartan construction company.	NSW:SBP OR 137.58 (134.58-141.32) DSW:SBP OR 122.14 (117.01-127.07) NSW:DBP OR 84.90 (82.53-87.27) DSW:DBP OR 76.54 (72.33-80.74) The prevalence of mean hypertension among night shift workers was found to be significantly higher than that of day shift workers.
Draaijer et al., 2022	Cross-sectional study	The relationship between night shift employment and CVD risk among long-distance truck drivers in South Africa.	Atherosclerotic CVD (ASCVD) risk score was calculated for day shift workers (5.16 (3.64–6.66)) and night shift workers (5.12 (3.57–7.63) where (p=0.94). However, the results showed that shift work was not associated with CVD.

Feng et al., 2021	Retrospective Cohort study	Evaluated the duration of shift work on 10 year CVD risk.	1-<10 years SW:10-year CVD OR 1.027 (0.900-1.173) 10-<20 years SW:10 year CVD OR 1.058 (0.927-1.206) ≥20 years SW:10 year CVD OR 1.191 (1.036-1.368) Shift work was relatively a significant risk between long-duration shift work and 10-year CVD.
Hermannson et al., 2019	Case-Control study	Examined the relationship between recognized coronary artery disease risk factors and work schedules in relation to myocardial infarction risk.	WHR:DSW OR (1.75 (1.41 to 2.17)) WHR:NSW OR (1.47 (0.97 to 2.24)) PI:DSW OR (1.52 (1.30 to 1.78)) PI:NSW OR (2.74 (2.03 to 3.71)) ETGL:DSW OR (2.32 (1.85 to 2.90)) ETGL:NSW OR (3.22 (1.97 to 5.25)) Night shift workers are more likely to experience the joint effect of shift work and physical inactivity on the risk of myocardial infarction, meanwhile, they also experience the effect of higher triglycerides and a high waist-hip ratio when compared to day-shift workers.

CVD-Cardiovascular disease; *DSW*-Day Shift Work; *ETGL*-Elevated Triglyceride; *NSW*-Night Shift Work; *OR*-Odds Ratio; *PI*-Physical Inactivity; *WHR*-Waist Hip Ratio

Table 5: Biomarkers assessed for the prevalence of cardiovascular disease risk among shift workers

Author(s) & year of publication	**Type of study**	**Purpose of the study**	**Main results/ conclusion**
Cannizzaro et al., 2020	Randomized Control group	Examined blood pressure and salivary cortisol levels to determine	Salivary cortisol evaluations at Time 14.00 hrs in NWM compared to DW and NWO (q = 1.364, p > 0.05; q = 1.752, p > 0.05) and in NWO

		the association between three distinct security guard work duties and stress-related responses.	(q = 0.3882, p > 0.05) compared to DW did not show any substantial differences.
Holst et al., 2019	Cross-sectional study	The moderating effect of body mass index (BMI) in the police cohort and the relationship between shift work and biomarkers of subc CVD was evaluated.	DSW:CRP OR 1.55 (1.35-1.79) NSW:CRP OR 1.67 (1.38-2.04) DSW:Fibrinogen OR 299 (289-310) NSW:Fibrinogen OR 306 (291-322)
Johnson et al., 2019	Prospective cohort study	Assessed the relationship between night shift working and biomarkers (CRP, fibrinogen) for CVD in female nurses.	1-5 years SW:CRP 0.1 (0.0, 0.2) 1-5 years SW:Fibrinogen 1.7 (-1.6, 10.0) ≥10 years SW:CRP 0.2 (-0.0, 0.4) ≥10 years SW:Fibrinogen 3.2 (-2.7, 30.1) The regression analysis shows no association between night shift work and CRP and fibrinogen levels among the studied population.
Park et al., 2019	Cross-sectional study	The impact of working night shifts on the management of hypertension and diabetes.	DSW:AHM OR 1 (95% CI) NSW:AHM OR 0.74 (0.68-0.80) DSW:DM OR 1 (95% CI) NSW:DM OR 0.99 (0.89-1.10)
Skogstad et al., 2019	Prospective cohort study	Identified early CVD symptoms are more likely to appear in shift workers, especially those with lengthy workdays and nights.	The number of years spent working shifts was linked to early CVD symptoms in this cross-sectional research of industry workers, as evidenced by rising CRP B=0.06, p=0.03 and an elevated IMT (B=0.015, p=0.009) in the carotid artery. This may indicate that these employees are more susceptible to heart attacks and strokes.

AHM-Anti-Hypersensitive Medication; *CRP*-C-Reactive Protein; *DM*-Diabetes Mellitus; *DSW*-Day Shift Work; *DW*-Daily Workers; *NWM*-Night-time Monitoring Workers; *NWO*-Night-time Operative Workers; *NSW*-Night Shift Work; *OR*-Odds Ratio; *SW*-Shift Work