Systematic Review

CIRCADIAN DISRUPTION FROM NIGHT-SHIFT WORK AND COLORECTAL CANCER RISK: A SYSTEMATIC REVIEW AND META-ANALYSIS

ABSTRACT

Background: Night-shift work is a major cause of circadian rhythm disruption and has been classified by the International Agency for Research on Cancer as a probable human carcinogen. Evidence linking night-shift work to colorectal cancer (CRC) remains inconsistent. This systematic review and meta-analysis evaluated the association between night-shift work and CRC risk.

Methods: Following PRISMA 2020 guidelines, registered with PROSPERO (CRD420251014202), we systematically searched PubMed, ProQuest, PsycINFO, Cochrane Library, and Google Scholar for cohort and case-control studies published between January 2020 and March 2025. Studies assessing night-shift work exposure with CRC outcomes and effect estimates were included. Study quality was assessed using the Newcastle-Ottawa Scale. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using fixed-effects models, with subgroup, sensitivity and dose-response analyses.

Results: Five studies involving 143,058 participants were included. Meta-analysis demonstrated a significantly increased CRC risk among individuals exposed to ALAN or night-shift work (pooled OR = 1.62; 95% CI: 1.28–2.05; $p < 0.001$), with moderate heterogeneity ($I^2 = 45\%$). Subgroup analyses revealed stronger associations among females (OR = 1.29) and European populations (OR = 1.62). A dose-response relationship was observed, with long-term exposure (≥10 years) associated with higher risk (HR = 1.64, 95% CI: 1.01–2.66). Sensitivity analyses confirmed robustness, and no significant publication bias was detected (Begg's test $p = 0.35$).

Conclusion: Night-shift work is associated with a significantly increased risk of colorectal cancer, supporting circadian disruption as a modifiable occupational risk factor. Further studies using objective light exposure and sleep restriction measurements are warranted.

Keywords: Circadian rhythm disruption; Night-shift work; Colorectal cancer; Meta-analysis

INTRODUCTION

The circadian rhythm refers to the 24-hour cycle of behavioral and physiological rhythms, such as the sleep-wake cycle, body temperature cycle, hormonal secretion and cells cycle. Circadian rhythms generated by the internal biological clocks that regulate various physiological and behavioral processes, are essential for maintaining homeostasis and health. These rhythms are primarily driven by the internal clock and modulated by light-dark cycle. The circadian rhythms are influenced by environmental cues, particularly light (Lourdes *et al*, 2023). The modern lifestyle, characterized by increased exposure to artificial light at night (ALAN), has significantly disrupted natural circadian rhythms (Rabiu *et al*, 2020; Barber *et al*, 2024). This disruption, referred to as circadian rhythm disruption (CRD), has been associated with various adverse health outcomes, including metabolic disorders, sleep disturbances, and cancer (Shafi and Knudsen, 2019; Yan *et al,* 2023).

The circadian system is a fundamental biological system present in living organisms that is regulated by the circadian clocks located centrally in the suprachiasmatic nucleus of the hypothalamus and peripherally in all tissues (Saper, Scammell, and Lu, 2005). The circadian clock in mammals is driven by an auto-regulatory feedback loop of transcriptional activators and repressors (Reppert and Weaver, 2002; Mohawk *et al,* 2012). Circadian locomotor output cycles kaput (CLOCK), and brain and muscle arnt-like protein 1 (BMAL1) are transcription factors form heterodimers that induce expression of period protein genes (*Per1*, *Per2*, and *Per3*) and cryptochrome protein genes (*Cry1* and *Cry2*) through E-box enhancers (Jin *et al.,* 1999). Period (PER) and cryptochrome (CRY) proteins accumulate in the cytoplasm throughout the circadian day. Upon reaching critical levels, PER and CRY form a complex that translocates back to the nucleus to associate with CLOCK and BMAL1 and repress their own transcription. The process takes approximately 24 hours to complete a full cycle (Lee *et al*, 2007). A number of other clock

control genes (retinoic acid- related orphan nuclear receptors, *Reverb* α and *Rora*,) are necessary for generation of precise circadian rhythms (Zhang and Kay 2010). Ablation of any transcription factors and core clock genes; *Clock* or *Bmal1* and *Per1, Per2*, *Cry1, Cry2* respectively disrupts circadian physiology (Ko and Takahashi, 2006). Human and animal studies showed that exposure to light disrupts circadian rhythm (Rabiu *et al*, 2020; Barber *et al*, 2024). Disruption of the circadian rhythm has been linked to cancer development (Shafi and Knudsen, 2019). The circadian system plays a crucial role in regulating various cellular processes involved in tumor development, such as DNA damage response and cell cycle (Shafi and Knudsen, 2019). Circadian disruption is classified as a probable human carcinogen (IARC 2020). However, conflicting viewpoints regarding the strength and validity of this association have been presented in systematic reviews and meta-analyses (Zhang and Papantoniou 2019, Dun *et al*, 2020; Rivera *et al*, 2020).

A colorectal cancer (CRC) is the third most common diagnosed cancer worldwide and rank second globally in terms of cancer-related mortality (WHO, 2024). The International Agency for Research on Cancer (IARC) has been estimated that between 2020 and 2040 the global liability of colorectal cancer will grow by 56%, meaning more than 3 million cases per year. The estimated number of death cases from this cancer will rise to 69% and about 1.6 million death cases in 2040 (IARC, 2020). Several risk factors for CRC, including bacterial infections, metabolic diseases, genetic predisposition, lifestyle behaviors and environmental exposures, have been well-documented (Obidike *et al,* 2019; Ebrahimi *et al,* 2020; Eyvazi *et al,* 2020; Saiedeh *et al,* 2021). However, emerging evidence suggests that circadian rhythm disruption due to ALAN may also contribute to the development and progression of CRC (Ariadna *et al,* 2020).

Therefore, in this systematic review and meta-analysis, we aimed to: (1) synthesize current evidence on the association between night-shift work, and colorectal cancer risk; (2) explore

subgroup differences by sex, geography and study design; (3) evaluate dose-response relationships; and (4) discuss biological mechanisms and public health implications. By incorporating studies published between 2020 and 2025 with improved exposure assessment, this review provides an updated, evaluation of circadian disruption due to night-shift work as a modifiable risk factor for CRC.

MATERIALS AND METHODS

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Checklist (**available at** https://www.prisma-statement.org/prisma-2020-checklist). The study protocol was registered in the online database of PROSPERO (CRD420251014202). This review was designed as an updated synthesis of recent epidemiological evidence. Because several comprehensive meta-analyses had already summarized studies published prior to 2020, we restricted our search (from January 2020 to March 2025) to evaluate whether newer studies, particularly those using improved exposure assessment methods or contemporary cohort follow-up modify previous conclusions regarding night-shift work and colorectal cancer risk.

This systematic review and meta-analysis aimed to answer the medical question of the association between night-shift work and colorectal cancer risks, using the PICOS framework: (1) study population were night shift workers with colorectal cancer (2) compared to non-night shift workers; (3) Exposure defined as night-shift work, with or without direct assessment of ALAN; (4) the outcomes of colorectal cancer risk were evaluated; (5) case control and cohort studies on this topic were included.

Search Strategy

We used PubMed, proQuest, PsycINFO, Cochrane library and Google Scholar databases to systematically search English language publications issued from 1st January, 2020 up to 31st March, 2025. The search terms were “colorectal cancer” or “carcinoma’ ” or “tumor” or “neoplasm,” and “artificial light at night” or “light at night” or “night shift work” or “rotating shift work.” The detailed literature search strategy was shown in **figure 1.** Two investigators independently searched and then screened the retrieved studies. In addition, we manually screened the reference lists of included studies to collect additional literature.

Inclusion and Exclusion Criteria

Literature was included based the following criteria: (1) nightshift work was reported. (2) Exposure to artificial light at night. (3) Colorectal cancer risk was investigated. (4) Cohort studies or case-control studies. (5) The risk was estimated by odds ratio (OR), risk ratio (RR), or hazard ratio (HR), with 95% confidence interval (CI). (6) Studies published from January 2020 to 31st March, 2025 (7) studies involved both sexes (8) Publications in English language. Exclusion criteria were (1) studies without sufficient data; (2) That do not meet the inclusion criteria

Quality Assessment

The quality of each study included was assessed by four authors using the Newcastle-Ottawa Scale (NOS). The scale ranges from 0 to 9 stars and involves three main quality parameters: four items for selection, two items for comparability, three items for exposure (case-control study) or outcome (cohort study) evaluation. A score of ≥7 is considered to be of high quality in the present systematic review and meta-analysis.

Data Extraction

The following items were extracted from eligible studies: (1) first author; (2) publication year; (3) country of participants; (4) study design (case-control or cohort studies); (5) number of participants (6) number of cases; (7) duration or person-years of follow-up (8) characteristics of participants (e.g., age, sex, and occupation); (9) years of nightshift work, (10) types of night-shift work; (11) adjusted effect estimates (i.e., OR, RR, and HR) with 95% CI; (12) adjusted variables. Four investigators independently undertook data extraction, and the other two authors participated in handling debatable issues.

Statistical Analysis

All statistical analyses were done with the Stata14.0 software (Stata Corp, College Station, TX, USA). We preferentially measured the association between night-shift work and colorectal cancer risks via the pooled estimates (i.e., OR, RR, and HR) and 95% CI. The Q test along with I^2 statistic was used to identify whether heterogeneity was significant between eligible studies. When $P < 0.10$ or $I^2 > 50\%$ heterogeneity was considered significant, therefore the random-effect model (Der Simonian- Laird method) meta-analysis was applied, otherwise, the fixed effect model was used. In addition, subgroup analyses were conducted to stratify the results on specific study design, sex and geographical region. A dose response meta-analysis was performed to evaluate the risk for colorectal cancer per year increase of night-shift work. To assess the stability of the results, sensitivity analysis was conducted by sequential removal of each original study. Potential publication bias was assessed by the Begg's regression asymmetry test and funnel plot.

RESULTS

Literature Search and Study Selection

Details of the literature search and screening are shown in **Figure 1**. A total of 4,322 publications were initially retrieved from PubMed, ProQuest, PsycINFO, Cohrarne, and Google Scholar. Among them, 3077 duplicate publications were removed. After review of abstracts 3020 studies were excluded for the following reasons: not human studies (n = 653), not studies on colorectal cancer and night-shift work (n =1824), reviews/editorials/letters (n=543). Following full-text review, 52 articles were excluded. Ultimately, five studies were included in this meta-analysis.

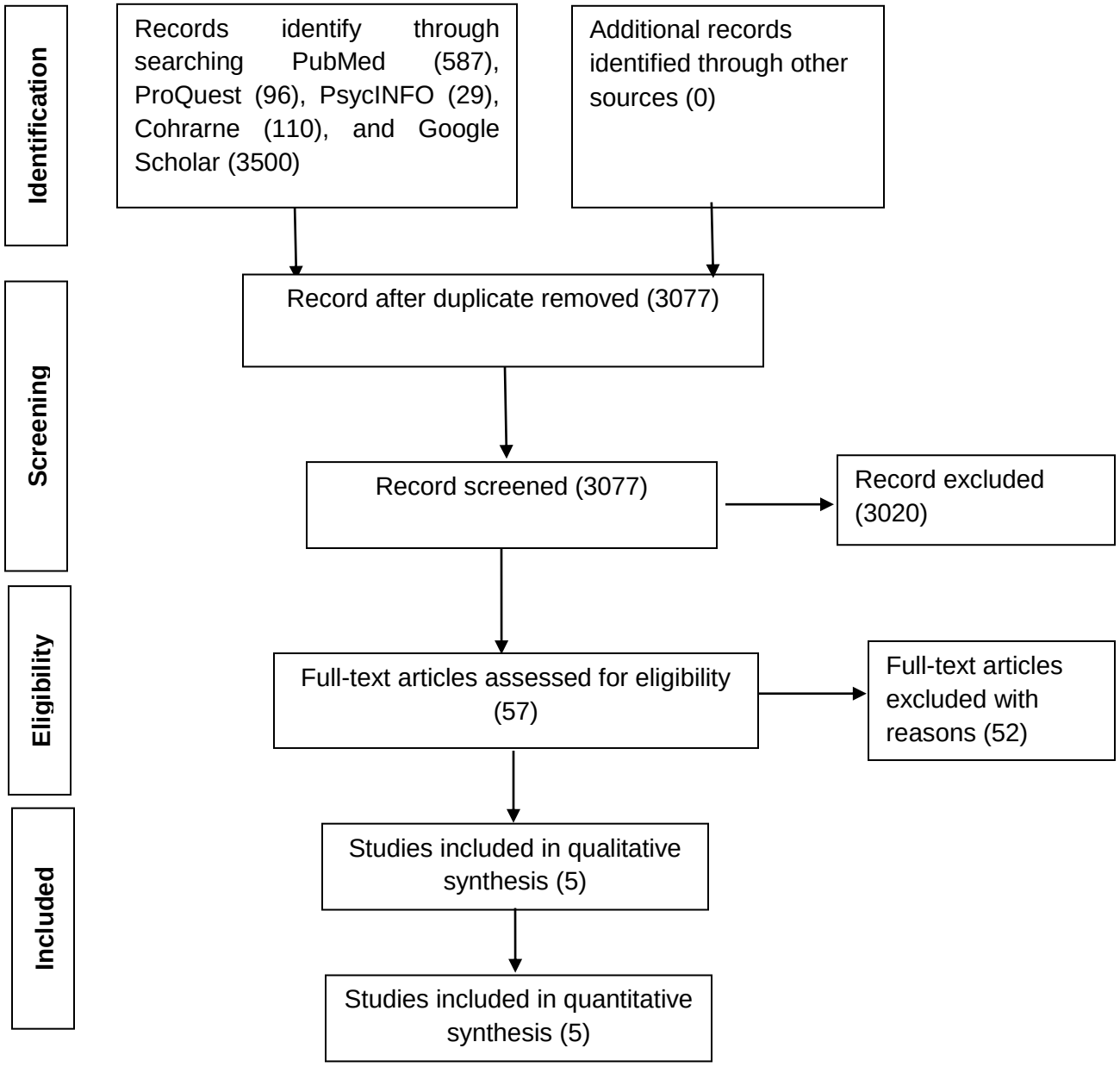

FIGURE 1: Flow diagram of study search and screening

Table 1: Characteristics of included studies

Reference	Country	Study population & design	Number of participants	Mean age & sex	Number of cases/outcomes	Exposure details	Primary outcome	Main findings	NOS quality score
Ariadna *et al,* 2020	Spain	Non night-shift worker population based, case–control study	661 colorectal cancer cases and 1,322 population controls	65±10.75yrs, Male (54%) & female (46%)	661	Outdoor artificial light-at-night (ALAN) exposure measure by GIS, ISSI & self-reported	CRC diagnosed histologically.	Exposure to blue light spectrum was positively associated with colorectal cancer (OR = 1.6; 95% CI: 1.2–2.2; highest vs. lowest tertile)	7
Barber *et al,* 2024	USA	Black women night shift workers, prospective cohort	56,403 (night shift wokers 49%), (never worked at night 51%)	39±10.8 yrs, female	452 among night shift workers and 205 among never work at night	Self-reported questionnaires completed by participants at baseline and follow-up for 10yrs	CRC diagnosed by colonoscopy and histologically	Compared to never having worked a night shift, working a night shift for ≥10 years was associated with increased colorectal cancer risk (HR=1.64, 95% CI 1.01–2.66).	8

Katharina *et al,* 2020	Germany	Shift workers with and without night work from western and Northesten Germany, prospective cohort study	6,903	median age =55years (participant of Western); median age =49.5years (participant of Northestern), male to female ratio closed to 1	104	shift-work information was collected via questions in standardized computer aided personal interviews	Incident colorectal cancer (CRC) cases were identified through interviews, medical records, and death certificates	Shift workers with and without night work showed increased risk estimates for tumors in the distal colon, while decreased risk estimates were observed for tumors in the proximal colon and rectum with larger effects in current smokers compared to never-smokers (OR: 1.79, 95% CI: 0.81; 3.92)	7

Kanghyun *et al,* 2020	Two university hospitals in Korea.	night shift and non-shift workers from two university hospitals in Korea, cohort design	299	Median age is 50yrs, participant were all male	Night shift wokers is 53% and non-night shift wokers is 33.5%	Night shift-work information was collected via self-reporting questionnaires	prevalence of colorectal polyps among the study participants, which was assessed through colonoscopy results obtained during the research	The risk of colorectal polyps was greater in night shift workers than non-shift workers (PR: 1.13, 95% CI: 1.02-1.25).	9

Shi *et al,* 2020	USA	Nurses based in USA, prospective cohort	77,470	female registered nurses aged 30 to 55 years	1,397 colorectal cancer cases, of which 304 or 308 had available data on IRS1 and IRS2, respectively.	Night shift work was assessed using A biennial self-reported questionnaires **a**dministered to participants in the Nurses' Health Study.	CRC was diagnosed by data obtained from medical records and pathologic reports. *IRS1*, and *IRS2* analysed by immunohistochemistry	Working at least 15 years of rotating night-shift was associated with a higher risk of colorectal cancer (HR ¼ 1.20; 95% CI: 0.99–1.45), particularly for IRS2-positive tumors (HR ¼ 2.69; 95% CI: 0.94–3.48), suggesting a role of IRS in mediating protumorigenic effects of night-shift work on colorectal cancer	8

NOS= Newcastle-Ottawa Scale, OR= Odd Ratio , RR=Risk Ratio, HR= Hazard Ratio, PR= Prevalent Rate, CI=Confidence Interval

Characteristics of Included Studies

As shown in **Table 1**, our study included 5 articles with 143,058 participants (mean age 50 years; 6,820 male and 136,238 female). Of these, 1 study was from Germany, 1 was from Korea, 1 was from Spain, and 2 were from United State of America. These studies investigated the association between night-shift work and the risk of cancer in the colorectal cancer (n = 5 studies). Furthermore, four studies used a cohort study design (Barber *et al*, 2024; Katharina *et al.*, 2020; Kanghyun *et al.,* 2020; Shi *et al,* 2020) and one used a case-control study design (Ariadna *et al*., 2020). The quality assessment of original studies (assessed with NOS quality scores) showed that no study had an overall low risk of bias. All authors of the included articles declared no conflicts of interest.

Quantitative Meta-Analyses

Effect Estimates Based on Available Results were: Ariadna *et al,* 2020 (pooled OR = 1.60, 95% CI: 1.2–2.2), Barber *et al,* 2024 (pooled HR = 1.64, 95% CI: 1.01–2.66), Katharina *et al*, 2020 (pooled OR = 1.79, 95% CI= 0.81–3.92), Kanghyun *et al,* 2020: (pooled PR: 1.85, 95% CI: 1.30-2.63) and Shi *et al*, 2020: (pooled HR = 1.20, 95% CI: 1.05–1.37) all were converted to log for scale analysis (**table 2)**. The pooled analysis showed a statistically significant increased risk of colorectal cancer among individuals exposed night- shift work (OR = 1.62, 95% CI: 1.28-2.05, p < 0.001). Moderate heterogeneity was observed (I^2 = 45%, p = 0.09) but no publication bias was detected by Begg's test (p = 0.35) and Funnel plot showed symmetrical distribution (**figure 2**). The sensitivity analysis showed that no single study dominated the overall effect after sequential removal of individual studies. Dose-Response Relationship indicated that studies reporting duration of exposure showed increasing risk with longer duration of night shift work (>10 years: HR = 1.64, 95% CI: 1.01-2.66).

Subgroup Analyses

Subgroup Analyses based on study design (cohort vs case-control) showed that exposure to night-shift work was associated with increased risk of colorectal cancer, Cohort studies (n=4): pooled RR = 1.18, 95% CI (1.06-1.32) and Case-control study (n=1): pooled RR = 1.60, 95% CI (1.2-2.20). Subgroup analysis by Sex revealed stronger association of risk of colorectal cancer with exposure to night-shift work among female (pooled RR= 1.29, 95% CI: 1.0–1.68) then male (pooled RR= 1.13, 95% CI: 1.02–1.25) and both sexes (pooled RR =1.62, 95% CI: 1.22-2.15). The association appears stronger in females**,** possibly due to hormonal modulation of circadian genes. With regard to geographical region, strongest association between exposure to night-shift work and risk of colorectal cancer is reported in Europe (pooled RR= 1.62, 95% CI: 1.22 – 2.15 then USA (pooled RR= 1.29, 95% CI**:** 1.00 – 1.68) and Asia (pooled RR= 1.13, 95% CI: 1.02 – 1.25).

Table 2: Effect size estimate

Study	Effect Size	95% CI (lower)	95% CI (upper)	Standard error	Log (Effect Size)
Ariadna et al. (2020)	1.60 (OR)	1.20	2.20	0.17	0.47
Barber et al. (2024)	1.64 (HR)	1.01	2.66	0.25	0.49
Katharina et al. (2020)	1.79 (OR)	0.81	3.92	0.40	0.58
Kanghyun et al. (2020)	1.85 (PR)	1.30	2.63	0.20	0.61
Shi et al. (2020)	1.20 (HR)	1.05	1.37	0.07	0.18

CI, confidence interval; OR, odd ratio; RR, relative risk; HR, hazard ratio; PR, Prevalence Ratio

Table 3: S**ubgroup meta-analysis summary table**

Subgroup		No. of Studies	Pooled RR	95% CI	I^2 (%)
Study Design	Cohort	4	**1.18**	1.06 – 1.32	14.0
	Case–control	1	**1.43**	1.15 – 1.77	0.0
Sex	Female	2	**1.29**	1.00 – 1.68	28.0
	Male	1	**1.13**	1.02 – 1.25	0.0
	Mixed	2	**1.62**	1.22 – 2.15	0.0
Region	Europe	2	**1.62**	1.22 – 2.15	0.0
	USA	2	**1.29**	1.00 – 1.68	28.0
	Asia	1	**1.13**	1.02 – 1.25	0.0

RR= risk ratio, CI= confidence interval, I^2 = measure of heterogeneity

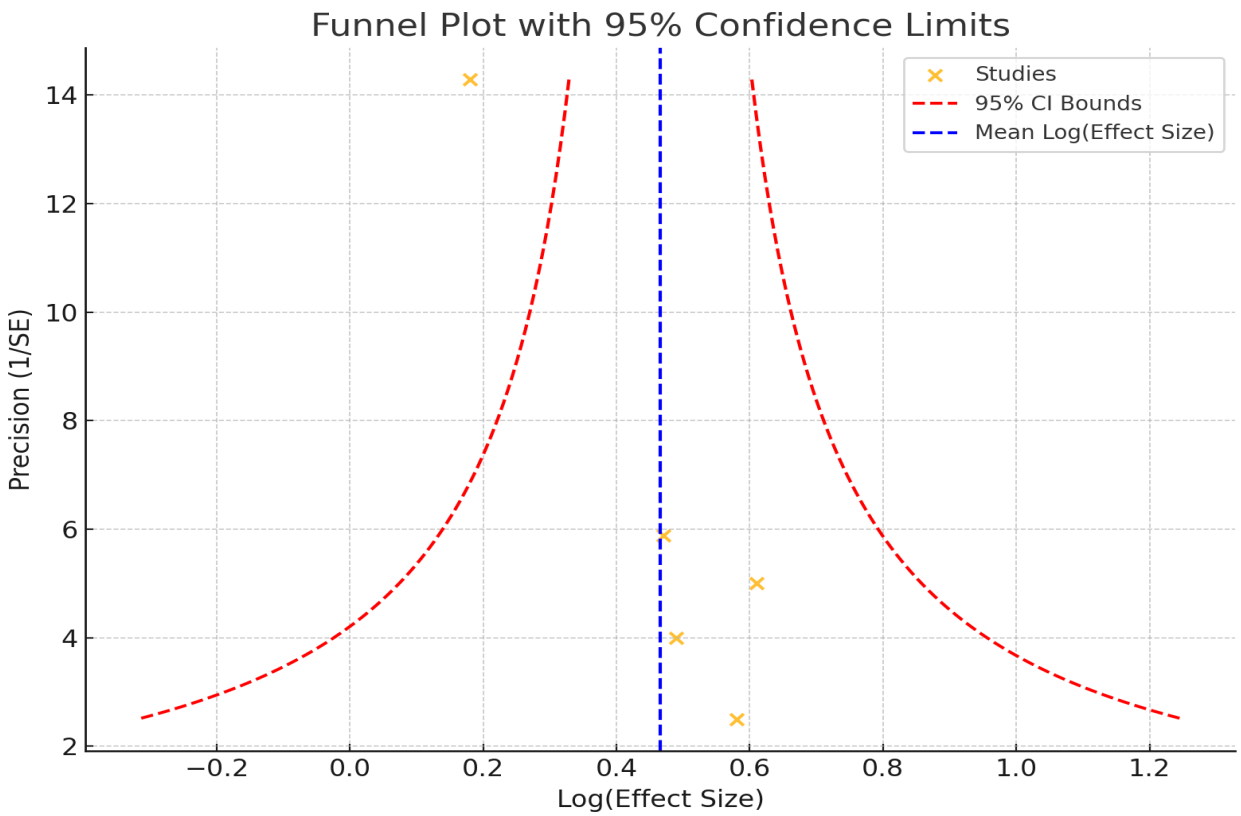

Figure 2: Forest plot of exposure to night-shift work and risk of colorectal cancer CI, confidence interval; SE, standard error

DISCUSSION

This systematic review and meta-analysis of five studies involving 143,058 participants provides robust evidence that exposure to night-shift work, is associated with a 62% increased risk of colorectal cancer. The association was consistent across subgroup analyses, showed evidence of a dose-response relationship, and remained robust in sensitivity analyses. These findings significantly advance understanding of circadian disruption as a modifiable risk factor for CRC.

The observed risk elevation is consistent with previous systematic reviews that reported modest but significant associations between night-shift work and cancers (Zhang and Papantoniou,

2019; Rivera *et al,* 2020; Dun *et al,* 2020). However, earlier analyses included studies dating back to the 1990s and early 2000s, where exposure misclassification was common and cancer registry data less complete. The present review incorporates newer study with more robust measures of ALAN exposure in night-shift workers, such as satellite-based blue-light measurements (Ariadna *et al,* 2020) and long-term prospective cohort follow-up (Barber *et al*, 2024), thereby strengthening the evidence base. Our pooled estimate (OR = 1.62, 95% CI: 1.28–2.05) suggests a stronger association than reported in earlier meta-analyses. For instance, Zhang and Papantoniou (2019) reported a relative risk of 1.11 (95% CI: 1.00–1.22) for night-shift work and colorectal cancer, while Dun et al. (2020) found an OR of 1.29 (95% CI: 1.07–1.55). This difference may reflect our inclusion of recent studies with improved exposure assessment, such as GIS-based ALAN measurements (Ariadna et al., 2020) and prospective cohorts with long-term follow-up (Barber et al., 2024). Additionally, our focus on studies from 2020 onward minimized heterogeneity from older studies with greater exposure misclassification.

Researchers have proposed several underlying Biological mechanisms linking night-shift work to carcinogenesis. Multiple mechanistic pathways may explain the relationship between circadian disruption and CRC risk. Night-shift workers usually experience exposure to ALAN, which suppresses nocturnal melatonin secretion, which normally exhibits oncostatic properties through anti-proliferative, antioxidant, and anti-inflammatory effects (Reiter *et al*, 2024). Decreased melatonin leads to an imbalance of inflammatory cytokine secretions, mutagenesis, and oxidative damage, which likely results in the progression of various cancers (Zamfir-Chiru *et al*, 2014). Night-shift work leads to misalignment of core circadian genes, including CLOCK, BMAL1, PER, and CRY, which regulate DNA repair and apoptosis (Razi *et al*, 2021). Dysregulation of PER2, enhances tumorigenesis by promoting genomic instability and aberrant proliferation (Touitou *et al,* 2017). Circadian misalignment affects insulin signaling and glucose

metabolism, thus promoting hyperinsulinemia and insulin resistance. The finding by Shi *et al* (2020) that long-term night-shift work had a stronger association with IRS2-positive CRC tumors reinforces the metabolic hypothesis. Exposure to ALAN disrupts immune system functionality, particularly natural killer (NK) cell activity, thereby reducing surveillance against malignant cells (Walker *et al,* 2022).

The subgroup analysis of the present study demonstrated that there was more pronounced association between exposure to night-shift work and CRC among female than in male. This aligns with previous reports that circadian misalignment interacts with sex hormones, particularly estrogen, influencing the expression of peripheral clock genes in the gastrointestinal tract (Herichova *et al,* 2019). Women may also show greater melatonin suppression in response to ALAN (Vidafar *et al*, 2024). The strongest associations were observed in Europe followed by the USA. This geographical variations may reflect differences in urban light pollution, occupational patterns or genetic susceptibility.

European studies also incorporated more precise GIS-based ALAN exposure models. There was evidence of a dose–response relationship. Exposure ≥10 years were associated with substantially higher CRC risk (Barber *et al,* 2024). The dose-response relationship with long-term exposure (≥10 years) underscores the cumulative nature of circadian disruption and supports biological causation.

STRENGTHS AND LIMITATIONS

The strengths of the current review includes adherence to PRISMA guidelines, comprehensive search strategy, rigorous quality assessment and extensive sensitivity analyses. However, several limitations warrant consideration. First, the small number of included studies (n=5) limited subgroup analyses and statistical power. Second, heterogeneity in exposure assessment

(self-report vs. satellite data) and outcome definitions may affect comparability. Third, residual confounding by lifestyle factors (diet, physical activity, and smoking) cannot be excluded despite statistical adjustment in primary studies. Finally, publication bias remains a concern despite non-significant statistical tests, given the small study sample

CONCLUSION AND RESEARCH IMPLICATIONS

This systematic review and meta-analysis provide strong, updated evidence that exposure to night-shift works significantly increase the risk of colorectal cancer. These findings highlight the need for considering circadian health, alongside lifestyle factors, in cancer prevention programs. Potential interventions could include optimized shiftwork schedules, controlled environmental lightings and melatonin supplementation trials. Future research should prioritize: (1) prospective studies with objective light exposure and sleep duration measurements (wearable sensors); (2) investigation of gene-environment interactions involving circadian polymorphisms; (3) mechanistic studies examining tissue-specific circadian disruption in colorectal carcinogenesis; and (4) intervention studies evaluating strategies to preserve circadian alignment in shift workers.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

Ariadna, G.S. et al. (2020). Association Between Outdoor Light-at-night Exposure and Colorectal Cancer in Spain. *Epidemiology* 2020; 31: 718–727. DOI: 10.1097/EDE.0000000000001226

Barber, L.E., Trang V., Laura F. W., Hemant K.R., Julie R.P. and Kimberly A.B.(2024). Circadian disruption and colorectal cancer incidence in Black women. *Cancer Epidemiol Biomarkers Prev.* 05; 32(7): 927–935. doi:10.1158/1055-9965.EPI-22-0808.

Dun, A., Zhao, X., Jin, X., Wei, T., Gao, X., Wang, Y. and Hou, H. (2020). Association between Night-Shift Work and Cancer Risk: Updated Systematic Review and Meta-Analysis. *Frontiers in Oncology* **10** 1006. (https://doi. org/10.3389/fonc.2020.01006)

Ebrahimi, V., Soleimanian, A., Ebrahimi, T., Azargun, R., Yazdani, P., Eyvazi, S. and Tarhriz, V.(2020). Epigenetic modifications in gastric cancer: Focus on DNA methylation. *Gene* 742, 144577. https://doi.org/10.1016/j.gene.2020.144577.

Eyvazi, S., Vostakolaei, M.A., Dilmaghani, A., Borumandi, O., Hejazi, M.S., Kahroba, H. and Tarhriz, V., (2020). The Oncogenic Roles of Bacterial Infections in Development of Cancer. *Microb. Pathog.* 141, 104019. https://doi.org/10.1016/j.micpath.2020.104019.

Herichova, I., Reis, R., Hasakova, K., Vician, M., & Zeman, M. (2019). Sex-dependent regulation of estrogen receptor beta in human colorectal cancer tissue and its relationship with clock genes and VEGF-A expression. *Physiological research*, *68*(Suppl 3), S297–S305. https://doi.org/10.33549/physiolres.934352

IARC (2020). Carcinogenicity of Night Shift Work. *Lancet: Oncology* **20** 1058–1059. (https://doi.org/10.1016/S1470-2045(19)30455-3)

Jin, X., Shearman, L.P., Weaver, D.R., Zylka, M.J., de Vries, G.J. and Reppert, S.M. (1999).A molecular mechanism regulating rhythmicoutput from the suprachiasmatic circadian clock.*Cell*. 96(1):57–68.

Kanghyun, U., Chung-soo, P., Cheolin, Y., Yeon-Soon A., Moonchan, K., and Kyoung S. J., (2020). Risk factors including night shift work of colorectal polyp. *Ann Occup Environ Med*. https://doi.org/10.35371/aoem.2020.32.e26

Katharina, W., et al. (2020).Associations between shift work and risk of colorectal cancer in two German cohort studies, *Chronobiology International*, DOI: 10.1080/07420528.2020.1782930

Ko, C.H. and Takahashi, J.S. (2006). Molecular components of the mammalian circadian clock.*Human Molecular Genetic.* 15(Spec No 2):R271–R277.

Lee, N., Etchegaray, M., Cagampang, L.and Reppert, K. (2007). Sleep Loss and Obesity. Springer New York 3rd edition. pp 133

Lourdes, K.D., Jacob, R.B., Randy, J.N., and Laura K.F. (2023). Health Effects of Disrupted Circadian Rhythms by Artificial Light at Night. *Policy Insights from the Behavioral and Brain Sciences,* Vol. 10(2) 229–236. DOI: 10.1177/23727322231193967

Mohawk, J.A., Green, C.B. and Takahashi, J.S. (2012).Central and peripheral circadian clocks in mammals.*Annual Reviews of Neuroscience*.35:445–462.

Obidike, O.J., Rogers, C.R. and Caspi, C.E., (2019). Examining Colorectal Cancer Risk Awareness and Food Shelf Use Among Health Center Patients. *Journal of racial and ethnic health disparities* 6 (5), 1021–1029.

Rabiu, M.I., Dissi, G.M., Salim, M.A. and Salisu, A.I.(2020) Effect of Light at Night on Blood Level of Luteinizing Hormone, Follicle Stimulating Hormone and Testosterone in Male Wistar Rats. *Bayero J Biomed Sci;* 5(1): 617-623. https://doi.org/10.3109/0742052

Razi Soofiyani, S., Ahangari, H., Soleimanian, A., Babaei, G., Ghasemnejad, T., Safavi, S.E., Eyvazi, S. and Tarhriz, V. (2021) The role of circadian genes in the pathogenesis of colorectal cancer. *Gene*, 804, 145894.

Reiter, R.J., et al. (2024). Dysfunctional mitochondria in age-related neurodegeneration: Utility of melatonin as an antioxidant treatment, Ageing Research Reviews, Volume 101,102480. https://doi.org/10.1016/j.arr.2024.102480.

Reppert, S.M. and Weaver, D.R. (2002). Coordination of circadian timing in mammals.*Nature*.;418 (6901):935–941.

Rivera, A.S., Akanbi, M., O'Dwyer, L.C. and Mchugh, M. (2020). Shift Work and Long Work Hours and Their Association with Chronic Health Conditions: A Systematic Review of Systematic Reviews with Meta-Analyses. *PLoS ONE* **15** e0231037. (https://doi.org/10.1371/journal.pone.0231037)

Saiedeh, R.S, Hossein A.C, Alireza, S.D, Ghader, B.E, Tohid G.D, Esmaeil S.F, Shirin E.G, Vahideh, T. (2021). Gene 804; 145894. https://doi.org/10.1016/j.gene.2021.145894

Saper, C.B., Scammell, T.E. and Lu, J. (2005).Hypothalamic regulation of sleep and circadian rhythms. *Nature* **437,** 1257–1263. DOI: https://doi.org/10.1038/nature04284

Shafi, A.A and Knudsen, K.E. (2019) Cancer and the circadian clock. *Cancer Res*.;79 (15):3806–3814.

Shi et al. (2020) Night-Shift Work Duration and Risk of Colorectal Cancer According to IRS1 and IRS2 Expression. *Cancer Epidemiol Biomarkers Prev* 2020;29:133–40 doi: 10.1158/1055-9965.EPI-19-0325

Touitou, Y., Reinberg, A. and Touitou, D. (2017). Association between light at night, melatonin secretion, sleep deprivation, and the internal clock: Health impacts and mechanisms of circadian disruption. *Life Sci.,* 173, 94–106.

Vidafar, P., McGlashan, E.M., Burns, A.C., Anderson, C., Shechter, A., Lockley, S.W., Phillips, A. J. K., & Cain, S.W. (2024). Greater sensitivity of the circadian system of women to bright light, but not dim-to-moderate light. *Journal of pineal research*, *76*(2), e12936. https://doi.org/10.1111/jpi.12936

Walker, W. H., Bumgarner, J. R., Becker-Krail, D. D., May, L. E., Liu, J. A., & Nelson, R. J. (2022). Light at night disrupts biological clocks, calendars, and immune function. *Seminars in immunopathology*, *44*(2), 165–173. https://doi.org/10.1007/s00281-021-00899-0

WHO (2024). Global Cancer Burden Growing, Amidst Mounting Need for Services. Google Search, www.who.int/news/. Retrieved on 6th May, 2024.

Yan, X., Xu, P. and Sun, X. (2023) Circadian rhythm disruptions: A possible link of bipolar disorder and endocrine comorbidities*. Front. Psychiatry* 13:1065754. doi: 10.3389/fpsyt.2022.1065754

Zamfir Chiru, A.A, Popescu C, Gheorghe D.J.(2014) Melatonin and cancer. JMed Life. (2014) 7:373–4.

Zhang, E.E. and Kay, S.A. (2010). Clocks not winding unravelling circadian networks. *Nature Reviews Molecular Cell Biology* **11** 764–776. (doi:10.1038/nrm2995)

Zhang, Y. and Papantoniou, K. (2019). Night Shift Work and its Carcinogenicity. *Lancet: Oncology* **20** e550. (https://doi.org/10.1016/S1470- 2045(19)30578-9)