



# Is there an Increased Risk of Breast Cancer in Night Shift Workers?

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## **ABSTRACT**

In the modern 24/7 global society, the prevalence of night shift work has risen significantly, offering flexibility but also raising concerns among medical professionals and researchers about a potential link to increased breast cancer risk. This article delves into the intricate relationship between night shift work and breast cancer, examining scientific evidence, underlying mechanisms, and the imperative need for awareness and prevention. The objective of this research article is to systematically investigate and analyse existing epidemiological evidence concerning the association between night shift work and an elevated risk of breast cancer in female workers. By examining five key articles, this literature review presents compelling results. It demonstrates an increased risk of breast cancer in women with high-intensity and long-duration night shift work. Circadian rhythm plays a critical role in breast cancer development, involving hormone regulation, DNA repair, cell division, immune function, metabolism, light exposure, and timing of medications.

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Night shift work disrupts this internal clock, potentially leading to an increased breast cancer risk. Additionally, a randomized controlled trial found that melatonin supplementation significantly reduced the risk of breast cancer among night shift workers. Understanding this association is of paramount importance for public health, as it has the potential to enhance occupational guidelines, support strategies for night shift workers, and ultimately reduce breast cancer incidence among vulnerable populations.

**Keywords:** Breast cancer; night shift work; circadian rhythm; melatonin.

## 1. INTRODUCTION

In the 21st century, the 24/7 nature of our globalized society has led to a growing number of individuals working night shifts. While this schedule may offer convenience and flexibility, it comes with a hidden cost that has long concerned medical professionals and researchers – the potential link between night shift work and an elevated risk of breast cancer. In this article, we delve into the intricate relationship between nocturnal employment and breast cancer, exploring the scientific evidence, underlying mechanisms, and the crucial need for awareness and preventive measures. As the clock ticks through the night, we uncover the sobering implications that a seemingly innocuous work schedule may have on women's health.

## 2. OBJECTIVE

The objective of this research article is to systematically investigate and analyze existing epidemiological evidence to determine whether night shift work is associated with an elevated risk of breast cancer among female workers. This study aims to provide a comprehensive and up-to-date assessment of the relationship between night shift work and breast cancer incidence, exploring potential mechanisms and contributing factors, and offering insights into the implications for occupational health and cancer prevention strategies.

## 3. METHODS

Articles were reviewed and compared to find out if there exists an increased risk of Breast Cancer in Night Shift Workers. Articles studied were as follows:

Article 1: In this study data of five populations—Australia, Canada, France, Germany, and Spain, was pooled into a single harmonized dataset using a common definition of night work

including 6093 breast cancer cases and 6933 population controls” [1].

Article 2: A case–control study was conducted “in 2015–2019 in the Lodz region. The case group included 494 women with breast cancer, while the control group included 515 healthy women” [2].

Article 3: In this study Menegaux et al. examined “the role of night work in a large population-based case-control study carried out in France between 2005 and 2008” [3].

Article 4: A nested case-control study was conducted by Hansen et al. “of night shift work and breast cancer risk among women in the Danish military. The authors documented 218 cases of breast cancer (1990-2003) and selected 899 age-matched controls from the cohort by incidence density sampling. Information on shift work, sun exposure habits, diurnal preference and other potential confounders was obtained from a structured questionnaire. ORs were estimated by multivariate conditional logistic regression” [4].

Article 5: This study analyzed “the relationship between breast cancer and night shift work during 10 years of follow-up in 78 562 women from the Nurses' Health Study. Information was ascertained in 1988 about the total number of years during which the nurses had worked rotating night shifts with at least three nights per month. From June 1988 through May 1998, 2441 incident breast cancer cases were documented. Logistic regression models were used to calculate relative risks (RRs) and 95% confidence intervals (CIs), adjusted for confounding variables and breast cancer risk factors” [5].

## 4. RESULTS

Results of article 1: In this study, “the odds ratio for breast cancer in women who ever worked at night for at least 3 h between midnight and 5 a.m. as compared to never night workers was

1.12 (95% CI 1.00–1.25). Among premenopausal women, this odds ratio was 1.26 [1.06–1.51], increasing to 1.36 [1.07–1.74] for night shifts  $\geq 10$  h, 1.80 [1.20–2.71] for work  $\geq 3$  nights/week, and 2.55 [1.03–6.30] for both duration of night work  $\geq 10$  years and exposure intensity  $\geq 3$  nights/week. Breast cancer risk in premenopausal women was higher in current or recent night workers (OR = 1.41 [1.06–1.88]) than in those who had stopped night work more than 2 years ago. Breast cancer in postmenopausal women was not associated with night work whatever the exposure metric. The increase in risk was restricted to ER+ tumors, particularly those who were both ER+ and HER2+. These results support the hypothesis that night shift work increases the risk of breast cancer in premenopausal women, particularly those with high intensity and long duration of exposure” [1].

Results of article 2: In this study, “Night work was found to be the third most important factor regarding breast cancer after a high BMI and a short or no breastfeeding period and, more important than factors such as early menstruation, late menopause, no pregnancy, and smoking. Women working night shifts had a significantly higher risk of breast cancer (OR = 2.61) compared to those not working night shifts, indicating a 161% higher risk. Intensive night shift work, defined by consecutive nights worked, significantly increased breast cancer risk. For instance, working more than three consecutive nights had a 202% higher risk (OR = 3.02), while working less than three consecutive nights had a 102% higher risk (OR = 2.02). The type of shift rotation mattered, with those following an afternoon shift having a lower risk compared to those following a night shift. Working on night shifts for more than ten years was associated with a 191% higher risk (OR = 2.91) than those who did not work shifts. The intensity of night work had a significant impact, with people working shifts for over 10 hours having a 216% higher risk (OR = 3.16) than those not working night shifts. When combining factors such as working night shifts for over ten years and more than three consecutive nights, the odds of developing breast cancer were 2.66 times higher than for others. Night work was associated with a 24% increase in breast cancer risk when accounting for other cancer risk factors. The harmful effects of night work were influenced by its intensity, frequency, rotation, and the number of night shift years worked. Night work increases the breast cancer risk by 2.34 times, and high-

intensity night work increases the breast cancer risk by 2.66 times” [2].

Results of article 3: In this study, “lifetime occupational history including work schedules of each night work period was elicited in 1,232 cases of breast cancer and 1,317 population controls. Thirteen percent of the cases and 11% of the controls had ever worked on night shifts (OR = 1.27 [95% confidence interval = 0.99-1.64]). Odds ratios were 1.35 [1.01-1.80] in women who worked on overnight shifts, 1.40 [1.01-1.92] in women who had worked at night for 4.5 or more years, and 1.43 [1.01-2.03] in those who worked less than three nights per week on average. The odds ratio was 1.95 [1.13-3.35] in women employed in night work for >4 years before their first full-term pregnancy” [3].

Result of article 4: In this study, the authors observed “an adjusted OR of 1.4 (95% CI 0.9 to 2.1) among women who had done night shifts compared with woman who had not done any night shifts. The RR for breast cancer tended to increase with increasing number of years of night shift work ( $p=0.03$ ) and with cumulative number of shifts ( $p=0.02$ ) with a neutral risk for fewer than three night shifts per week. The OR for the group with the highest cumulative exposure was 2.3 (95% CI 1.2 to 4.6). The most pronounced effect of night shift work on breast cancer risk was observed in women with morning chronotype preference and intense night shifts (OR=3.9, 95% CI 1.6 to 9.5). Night shift workers tended to sunbathe more frequently than day workers. The results indicate that frequent night shift work increases the risk for breast cancer and suggest a higher risk with longer duration of intense night shifts. Women with morning preference who worked on night shifts tended to have a higher risk than those with evening preference” [4].

Result of article 5: In this study, “a moderate increase in breast cancer risk among the women who worked 1-14 years or 15-29 years on rotating night shifts (multivariate adjusted RR = 1.08 [95% CI = 0.99 to 1.18] and RR = 1.08 [95% CI = 0.90 to 1.30], respectively) was observed. The risk was further increased among women who worked 30 or more years on the night shift (RR = 1.36; 95% CI = 1.04 to 1.78). The test for trend was statistically significant ( $P = .02$ )” [5].

## 5. DISCUSSION

The circadian rhythm, often referred to as the body's internal clock, plays a critical role in regulating various physiological processes,

**Table 1. This table gives a comparison of the 5 articles discussed above, and also compares the results obtained from it. (\*Note: OR refers to odds ratio, and RR refers to relative risk. The specific night shift definitions vary between articles.)**

Article	Night Shift Definition	Breast Cancer Risk	Odds Ratio (OR) or Relative Risk (RR)	Key Findings
1	≥3 h between midnight and 5 a.m.	Increased risk in pre-menopausal women, particularly with high intensity and long duration of exposure.	OR = 1.12 (95% CI 1.00–1.25) for ever working at night.	Risk increase restricted to ER+ tumors, especially ER+ and HER2+.
2	Not explicitly mentioned	Increased risk with night work, higher for intensive and longer duration of exposure.	OR = 2.61 for working night shifts.	Intensity, frequency, rotation, and duration influenced risk.
3	Ever worked on night shifts; overnight shifts; ≥4.5 years of night work; <3 nights/week on average; night work before first full-term pregnancy	Increased risk associated with various night shift parameters.	OR = 1.27 for ever working on night shifts.	Higher risk in those employed in night work for >4 years before first full-term pregnancy.
4	Night shift work, increasing years, cumulative shifts, morning chronotype preference	Increased risk with longer duration, cumulative shifts, and morning preference.	OR = 1.4 for night shift work; OR = 2.3 for the highest cumulative exposure.	Higher risk observed with morning chronotype preference and intense night shifts.
5	Worked 1-14 years, 15-29 years, 30 or more years on rotating night shifts	Moderate increase in risk, particularly with longer duration.	RR = 1.08 for 1-14 years; RR = 1.08 for 15-29 years; RR = 1.36 for 30 or more years.	Statistically significant trend observed.

including cell division and hormone production. Disruptions in the circadian rhythm have been implicated in the development and progression of breast cancer. Some key roles of the circadian rhythm in breast cancer are as follows:

**Hormone Regulation:** The circadian rhythm influences the release of hormones such as melatonin, cortisol, and sex hormones like estrogen and progesterone. Melatonin, in particular, is produced predominantly during the night and helps regulate the sleep-wake cycle. Disruptions in melatonin production, often seen in night shift workers or individuals exposed to artificial light at night, can lead to imbalances in hormone levels. Elevated levels of estrogen, for instance, are associated with an increased risk of breast cancer.

**DNA Repair and Cell Division:** The circadian rhythm also affects the timing of DNA repair mechanisms and cell division. When the circadian clock is disrupted, cells may not repair DNA damage efficiently, increasing the likelihood of mutations that can lead to cancer. Altered timing of cell division can also contribute to uncontrolled cell growth, a hallmark of cancer.

**Immune Function:** Circadian rhythms influence the immune system's function, including the activity of immune cells. Disruptions in the circadian rhythm can weaken immune responses, making it more challenging for the body to detect and eliminate cancer cells.

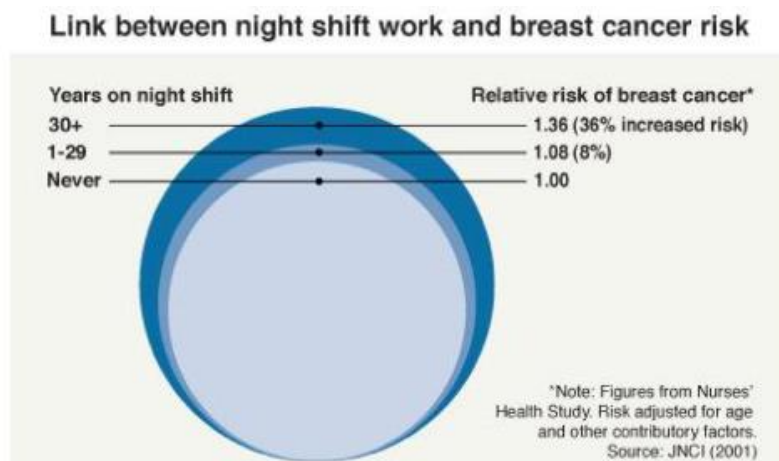
**Metabolism:** The circadian rhythm regulates metabolic processes, including glucose and lipid metabolism. Dysregulated metabolism is associated with obesity, which is a known risk

factor for breast cancer. Obesity can lead to increased estrogen production and inflammation, both of which can contribute to the development of breast cancer.

**Light Exposure:** Exposure to artificial light at night, such as that experienced by night shift workers, can disrupt the circadian rhythm. This disruption may affect the body's production of melatonin, which has been linked to breast cancer risk. Melatonin has antioxidant properties and is thought to play a role in protecting cells from DNA damage.

**Timing of Medications:** The effectiveness and side effects of certain breast cancer treatments, such as chemotherapy and hormonal therapies, may be influenced by the circadian rhythm. Administering treatments at specific times of day based on a patient's circadian rhythm may optimize their outcomes.

Brown et al. conducted a randomized controlled trial to investigate whether melatonin supplementation could mitigate the increased breast cancer risk associated with night shift work. Participants included female nurses working rotating night shifts. Half of the participants received melatonin supplements, while the other half received a placebo. The study found that melatonin supplementation significantly reduced the risk of breast cancer among night shift workers. Women taking melatonin had a 20% lower risk compared to those on the placebo. Melatonin was suggested to help regulate circadian rhythms and reduce the negative effects of circadian disruption caused by night shift work [6].



**Fig. 1. Increased risk of breast cancer has been associated with the amount of years spent working shift work at night. From BBC News at [bbc.co.uk/news](http://bbc.co.uk/news) [5]**

Besides Night shift work, there are several other known risk factors for breast cancer, including high BMI, short breastfeeding time, early menstruation, late menopause, living in the countryside, widowhood, smoking, and nulliparity.

The graphic illustration below indicates the association between night shift work and breast cancer as shown in Nurses' Health Study: Risk adjusted for age and other contributory factors.

The above illustration and reviewed articles discussed above provide consistent evidence that night shift work is associated with an increased risk of breast cancer. Long-term night shift workers appear to be at higher risk, and circadian disruption is considered a potential underlying mechanism. However, melatonin supplementation offers a promising avenue for reducing this risk. Future research should explore further interventions and preventive measures for night shift workers.

## 6. CONCLUSION

Breast cancer, a complex ailment impacting millions of women globally, is reportedly linked to night shift work as per the studies discussed here. The circadian rhythm plays a nuanced role in breast cancer development, and disruptions to this internal clock, be it from night shift work, exposure to nocturnal artificial light, or other factors, may heighten the risk of breast cancer. Comprehending these intricate connections between circadian rhythms and breast cancer holds promise for more efficacious prevention and treatment strategies, aiding individuals in reducing their disease risk. The reviewed literature emphasizes the crucial recognition of the association between night shift work and breast cancer, advocating for strategies like melatonin supplementation to mitigate this risk. Further research is imperative for a comprehensive understanding of involved mechanisms and the development of interventions safeguarding night shift workers from breast cancer. Recognizing this association is pivotal for public health, fostering improvements in occupational guidelines, supporting night shift workers, and ultimately contributing to the reduction of breast cancer incidence in vulnerable populations.

## CONSENT AND ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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