# Digital Screen Time and the Risk of Female Breast Cancer: A Retrospective Matched Case-Control Study

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### **ABSTRACT**

Background: As the use of electronic devices such as mobile phones, tablets, and computers continues to rise globally, concerns have been raised about their potential impact on human health. Exposure to high energy visible (HEV) blue light, emitted from digital screens, particularly the so-called artificial light at night (ALAN), has been associated with adverse health effects, ranging from disruption of circadian rhythms to cancer. Breast cancer incidence rates are also increasing worldwide.

**Objective:** This study aimed at finding a correlation between breast cancer and exposure to blue light from mobile phone.

Material and Methods: In this retrospective matched case-control study, we aimed to investigate whether exposure to blue light from mobile phone screens is associated with an increased risk of female breast cancer. We interviewed 301 breast cancer patients (cases) and 294 controls using a standard questionnaire and performed multivariate analysis, chi-square, and Fisher's exact tests for data analysis.

**Results:** Although heavy users in the case group of our study had a statistically significant higher mean 10-year cumulative exposure to digital screens compared to the control group (7089±14985 vs 4052±12515 hours, respectively, *P*=0.038), our study did not find a strong relationship between exposure to HEV and development of breast cancer.

**Conclusion:** Our findings suggest that heavy exposure to HEV blue light emitted from mobile phone screens at night might constitute a risk factor for promoting the development of breast cancer, but further large-scale cohort studies are warranted.

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### Keyword

Visible Light; Blue Light; Mobile Phones; Digital Screens; Cancer; Breast Cancer; Circadian Disruption; Melatonin; Light Pollution; Screen Time; Circadian Rhythm

### Introduction

lectromagnetic radiation has existed in various forms since the beginning of the universe, with light being one of the most recognizable and essential [1]. However, the growing concern over light pollution caused by artificial light at night (ALAN) is having adverse effects on human health and the environment [2]. ALAN can <sup>1</sup>College of Medical, Veterinary & Life Sciences, University of Glascow, Glasgow, GB

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Received: 28 October 2023 Accepted: 2 November 2023 originate from both outdoor sources, such as streetlights and billboards, and indoor sources, such as electronic devices like TVs, smartphones, and laptops. Exposure to ALAN can disrupt the natural light cycle perceived by the eyes, leading to disturbances in the human circadian rhythm [3]. In a recent review, Lech et al. highlight the importance of optimizing the lighting environment and suggest that costeffective interventions can be implemented to achieve this goal [4].

Visible light with short wavelength (blue light) has been found to be disruptive for circadian rhythms and melatonin production. Circadian rhythms are biological cycles that occur over a 24-hour period and synchronize many physiological activities in the human body [5]. These rhythms are regulated by a master biological clock located in the suprachiasmatic nucleus (SCN) of the hypothalamus. Visible light stimulates the circadian photoreception cells in the human eye, which then trigger the SCN biological clock to respond to the light-dark cycle [6]. The circadian rhythms also modulate the synthesis and secretion of melatonin, a hormone that regulates the sleep-wake cycle. Exposure to light at night can disrupt melatonin production and cause circadian disruption [3]. This disruption can have significant biological consequences, including carcinogenic effects [7, 8]. Strong evidence suggests that circadian disruption can elevate the risk of breast cancer, and melatonin plays an important role in this phenomenon [3]. The exposure to ALAN, originated from outdoor sources, such as streetlights and billboards, and indoor sources, such as electronic devices like TVs, smartphones, and laptops, might there be a significant risk factor for promoting the development of breast cancer.

While exposure to blue light at night is a known disruptor, a study conducted by Harvard researchers suggests that the impact of blue light on circadian rhythms may be more complex than previously thought [9]. Numerous studies demonstrate a higher incidence

of breast cancer in female night shift workers [10-14]. The International Agency for Research on Cancer (IARC) has classified night shift work as "probably carcinogenic" due to limited epidemiological evidence suggesting a link between night shift work and an increased risk of breast cancer and other types of cancer [15]. This classification is based on the consideration of the carcinogenic mechanisms of alterations in the light/dark schedule, which can disrupt circadian rhythms and melatonin production.

Female breast cancer is a leading cancer type diagnosed globally, accounting for 11.7% of all cancers in 2020, and is also the leading cause of cancer death in women, with incidence rates on the rise [16]. In 2017, Harvard scientists estimated the cumulative exposure to residential outdoor artificial light at night (ALAN) of 109,672 women from 1989 through 2013 using time-varying satellite data. This study showed that exposure to ALAN may contribute to invasive breast cancer risk [17]. Epidemiological evidence concerning the potential health risks associated with alterations in the light/dark schedule is growing. A systematic review conducted by Urbano et al. in 2021, which included 10 cohort and 7 case-control studies, found a positive association between exposure to artificial light at night and breast cancer risk [18]. However, results from the sister study by Sweeney et al. published in 2022, failed to show any association [19].

The use of digital devices such as mobile phones, tablets, and computers is rapidly increasing worldwide, and their visible light emissions can have adverse effects on circadian physiology, alertness, and cognitive performance levels [20]. While humans have evolved under predominantly yellow light, digital screens emit high levels of high energy visible (HEV) blue light. The photoreceptor cells in the human eye, known as rods and cones, are most sensitive to different wavelengths of light in the visible spectrum. Rhodopsin is the visual pigment contained in the rods, which

are photoreceptors that have a peak sensitivity around 500 nm wavelength and are responsive to blue-green light, while the cones are most sensitive to light at around 555 nanometers, which is in the green-yellow region of the spectrum. Long wavelength cones (L-Cones), medium (M cones), and short (S cones) are sensitive to red light (peak sensitivity at 564 nm), green light (peak at 533 nm) and blue light (peak at 437 nm), respectively [21]. This means that the human eye is more sensitive to shorter wavelengths of light, including HEV blue light, which has a wavelength of around 400-500 nanometers. This sensitivity to blue light can be potentially harmful to human health when exposure occurs at night, as it can interfere with the body's natural sleep-wake cycle. The use of smartphones, tablets, or laptops at night may affect biological rhythms and increase the risk of breast cancer by suppressing the release of melatonin induced by exposure to the blue light of these devices.

It is common practice among adolescents and young adults to use electronic devices with illuminated screens, such as laptops, tablets, and mobile phones, in bed before sleeping. However, this habit is associated with reduced nighttime sleepiness, poorer sleep quality, delayed melatonin production, increased body temperature, decreases in nocturnal melatonin production, and disorders in attention levels during the daytime [22-24], and should be avoided. Epidemiological and laboratory studies also show that dysregulated circadian rhythms can be a potential carcinogen [25, 26]. Given the widespread use of digital screens, it is important to investigate the potential association between screen time during the night and breast cancer risk in the adult female population. This retrospective casecontrol study aims to assess this association.

### Material and Methods

### Study Participants

This retrospective matched case-control

study included 301 patients diagnosed with breast cancer (all stages) and 294 controls. The case group consisted of patients referred to a breast cancer clinic in Motaharri clinic of Shiraz between 2016-2020, with their cancer diagnosis made within the past three years. All women over 18 years old living in Fars and neighboring provinces of Iran and with confirmed breast cancer diagnosis through histological studies over the past three years were included in the study after providing their informed written consent. Women who were not willing to participate were excluded.

### Control Group

The control group was selected based on the National Institute for Health and Care Excellence (NICE) guidelines [27]. Non-sick women with matched age and socioeconomic factors (education, income, employment, and residential address) were included. Contact information, including residential addresses and telephone numbers of the control group, were recorded for further review in the study registry system.

If cancer patients provided their written consent, their information was transferred to the research team for further evaluation. These individuals were then evaluated for eligibility according to NICE criteria prior to participation in the study [27]. The number of subjects in the control/case group was selected as approximately 1:1 in order to minimize the role of known confounding factors.

A questionnaire was developed based on all known (or suspected) risk factors of breast cancer [28, 29] to measure environmental and occupational exposure to ionizing and nonionizing radiation, including exposure to blue light from digital displays, and radiofrequency radiation from cell phones, Wi-Fi routers, mobile base stations, and cordless phones, as well as diet and lifestyle. The questionnaire also examined extensively demographic factors, physiological parameters, lifestyle, diet, occupational exposure to other detrimental factors (factors other than ionizing and non-ionizing

radiation), and drugs. To reduce recall bias about the level of mobile phone use (either call time or using mobile phones for surfing the Internet or accessing social media), information regarding surfing time was limited to recent years. All interviews were conducted face-to-face by a female interviewer from the research team who had received necessary training for a relaxed interview, and the results were carefully reviewed and monitored by all project managers. Participants' weight and height were measured using standard tools before each interview. After the interviews, a number of samples were randomly selected to verify the information.

### Interviews

All individuals were interviewed at the Motahari Breast Cancer Clinic of Shiraz University of Medical Sciences, located in the Motahari Clinic. A female interviewer conducted all the interviews in simple Persian language to reduce interviewees' stress and minimize the effect of inter-reviewer variations in terms of social communication skills and body language. Interviewees were also asked about potential confounders such as the frequency and type of oral contraceptive pills (OCP) they used. Regarding screen time, the main focus was on screen time during the night time (dim light condition). The data collected by the interviewer were reviewed by the project lead members. It took approximately 30-40 minutes to complete the interview questionnaire for each participant.

### Statistical Analysis

For statistical analysis, the frequency distribution of categorized variables was compared using the Chi-square test ( $\chi$ 2) or Fisher's exact test. The independent t-test was used to compare the mean values of continuous variables between the case and control groups. The unconditional logistic regression model was also used to determine the odds ratios (OR) and 95% confidence interval (CI) to determine

the possible association between non-ionizing radiation exposure and breast cancer. All statistical tests were performed on a 2-tailed level with a significance level of 0.05. All analyses were performed using SPSS 19 software.

### Results

The exposure to light at night that originated from outdoor sources, such as streetlights and billboards, and indoor sources, such as electronic devices like TVs, smartphones, and laptops, as illustrated in Figure 1, might be a significant risk factor for promoting the development of breast cancer. It is known that of alterations in the light/dark schedule can disrupt circadian rhythms and melatonin production, as schematically illustrated in Figure 2. This might be a mechanism behind HEV induced cancer. Figure 3 illustrates a possible mechanism for how too much screen time could, through dysregulation of the biological rhythms, increase the risk of breast cancer.

Table 1 presents demographic information and other important parameters of the participants in the control and case groups. To minimize the effects of confounding factors, the case and control groups were matched. Family history of breast cancer was also considered and attempts were made to eliminate its effect as much as possible. Table 1 also compares the marital status of participants, history of breast cancer in first-degree relatives, family history of other cancers, family economic status, history of exposure to ionizing radiation, and exposure type in the control and case groups.

Table 2 shows the frequency of participants in the control and case groups with respect to the number of hours of digital display use in three groups: low exposure, medium exposure, and high exposure. The difference observed in weekly hours of digital screen use between the breast cancer and control groups was not statistically significant (P=0.214). Table 2 also shows the frequency of participants in the control and case groups with respect to the



**Figure 1:** Illustration of exposure to artificial light at night (ALAN), originated from outdoor sources, such as streetlights and billboards, and indoor sources, such as electronic devices like TVs, smartphones, and laptops.

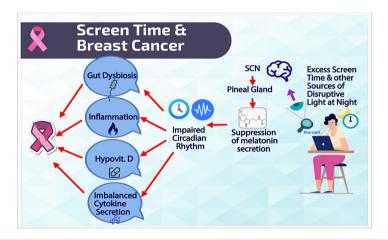
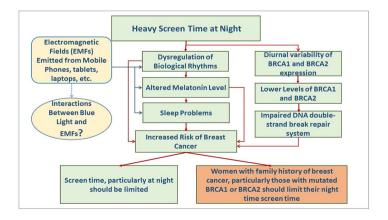


Figure 2: Illustration of how exposure artificial light at night (ALAN), might increase the risk for breast cancer through mechanisms such as suppression of melatonin secretion and dysregulation of biological rhythms. (SCN: Suprachiasmatic Nuclei)



**Figure 3:** A possible mechanism for how too much screen time could, through dysregulation of the biological rhythms, increase the risk of breast cancer.

**Table 1:** Frequency and relative frequency of participants in the control and case groups, demographic information, and some other important parameters.

| 04                                       | lation                    | Controls        | Controls |                 |      |  |
|--|---------------------------|-----------------|----------|-----------------|------|--|
| Study popu                               | iation                    | No. of subjects | %        | No. of subjects | %    |  |
|  | Under 20                  | 2               | 0.7      | 0               | 0    |  |
|  | 20-30                     | 27 9.2          |          | 18              | 6    |  |
| Age at recruitment, years                | 31-40                     | 107 36.4        |          | 63              | 20.9 |  |
|  | 41-50                     | 94              | 32       | 98              | 32.6 |  |
|  | 51–60                     | 50              | 17       | 75              | 24.9 |  |
|  | Over 60                   | 14              | 4.8      | 47              | 15.6 |  |
|  | Total                     | 294             | 100      | 301             | 100  |  |
|  | Under High School Diploma | 151 51.4 173    |          | 173             | 57.5 |  |
|  | High School Diploma       | 78              | 26.5     | 70              | 23.3 |  |
| Education                                | Associate Degree          | 21              | 7.1      | 16              | 5.3  |  |
|  | Bachelor's Degree         | 43              | 14.6     | 40              | 13.3 |  |
|  | Master's Degree or Higher | 1               | 0.3      | 1               | 0.3  |  |
| Margarian .                              | Single                    |                 | 7        |                 | 8.4  |  |
| Marital status                           | Married                   |                 | 93       |                 | 91.6 |  |
| F " !! ! ! ! ( D                         | Negative                  |                 | 89       |                 | 94   |  |
| Family Histort of Breast Cancer          | Positive                  |                 | 11       |                 |      |  |
| F  | Negative                  |                 |          | 84.3            |      |  |
| Family Histort of Other Cancers          | Positive                  |                 | 21       |                 | 15.7 |  |
| History of Exposure to Ionizing          | Negative                  |                 | 18       |                 | 46.3 |  |
| Radiation                                | Positive                  |                 | 82       |                 | 53.7 |  |
| Total Number of Functions to             | Less than 3 Times         | 30.6            |          |                 | 46.4 |  |
| Total Number of Exposure to              | 3-5 Times                 |                 | 52.7     |                 | 36.6 |  |
| Ionizing Radiation                       | Over 5 Times              |                 | 16.7     |                 | 17   |  |
| Course of Europeurs to Innimine          | Radiography               |                 | 34.7     |                 | 68.3 |  |
| Source of Exposure to Ionizing Radiation | Radiography+CT Scan       |                 | 65.3     |                 | 29.3 |  |
| Raulation                                | Radioscopy                |                 | 0        |                 | 2.4  |  |
|  | Low                       |                 | 85       |                 | 74.7 |  |
| Family Income                            | Medium                    |                 | 15       |                 | 25.3 |  |
|  | High                      |                 | 0        |                 | 0    |  |
| Smoking status                           | Smoker                    | 39              | 13.3     | 41              | 13.9 |  |
| Smoking status                           | Nonsmoker                 | 254             | 86.7     | 253             | 86.1 |  |
| Alcohol consumption                      | Never regular             | 287             | 100      | 243             | 100  |  |
| Alcohol consumption                      | Current drinker           | 0               | 0        | 0               | 0    |  |
| Contracentive Pills                      | Yes                       | 117             | 45.5     | 126             | 48.6 |  |
| Contraceptive Pills                      | No                        | 140             |          |                 | 51.4 |  |
| Physical Exercise                        | Yes                       | 64              |          |                 | 45.5 |  |
| r nysical exercise                       | No                        | 229             | 78.2     | 163             | 54.5 |  |

| Chudu manulatian |                  | Controls        |      | Cases           |      |
|------------------|------------------|-----------------|------|-----------------|------|
|                  | Study population | No. of subjects | %    | No. of subjects | %    |
| UDT history      | Yes              | 45              | 17.4 | 24              | 88.8 |
| HRT history      | No               | 214             | 82.6 | 190             | 11.2 |
| Menopause        | Pre Menopause    | 178             | 69   | 83              | 29   |
|                  | Post Menopause   | 79              | 31   | 201             | 71   |
| BMI              | Under 19         | 16              | 5.5  | 6               | 2    |
|                  | 19-27            | 165             | 56.3 | 123             | 41   |
|                  | Over 27          | 112             | 38.2 | 171             | 57   |

HRT: Hormone Replacement Therapy, BMI: Body Mass Index

**Table 2:** Exposure of control and case participants to the High Energy Visible (HEV) blue light generated by digital display screens.

| Vorichio                                    |           | Numb    | Dualua              |         |
|---|-----------|---------|---------------------|---------|
| Variable                                    |           | Control | Breast cancer group | P value |
|   | <7        | 112     | 85                  |         |
| Digital Screen Use (hours/week)             | 7-14      | 42      | 42                  | 0.214   |
|   | >14       | 23      | 29                  |         |
|   | <0.25     | 33      | 22                  |         |
| Digital Screen Use in Dim Light (hours/day) | 0.25-0.50 | 44      | 31                  | 0.885   |
|   | >0.50     | 42      | 25                  |         |
|   | <7        | 79      | 94                  |         |
| Size of Mobile Phone/Tablet Screen (inches) | 7–15      | 126     | 90                  | 0.03    |
|   | >15       | 86      | 91                  |         |

number of hours of use of digital display screens in low light conditions, in the three groups of low exposure, medium exposure, and high exposure. No statistically significant difference was found between the breast cancer and control groups in terms of daily hours of digital screen use in dim light (P=0.885). However, the size of the digital display screens used showed a statistically significant difference between the breast cancer and control groups (P=0.03).

### Heavy Users

Table 3 presents the frequency of "Heavy User" participants in the control and case study groups regarding digital screen time. It also shows the frequency of "Heavy User" participants in the control and case study of the use of digital display screens in low light conditions (late night hours). The cumulative case study of the use of digital display screens in low light conditions (late night hours) is also presented in the Table 3.

# Findings of Logistic regression model

In the logistic regression model, univariate logistic regression was used to select important variables, and then multivariate logistic regression was performed with variables of age, average working time with digital screens, screen size of these devices, history of use of

screens (years), cell phone use for calls (talk mode), standby time (cell phone use when it is switched on but there are no calls, internet use, etc.), cellular internet use, cordless phone use, and sleep disorders. The history of screen use (years of use) was statistically significant, with an odds ratio (OR) of 0.725, 95% confidence interval (CI) of 0.595-0.883, and *P* value of 0.001, indicating that the risk of breast cancer decreased by 0.725 with a one-year increase in screen use. The variable of mobile phone daily standby time was also statistically significant, with an OR of 0.380, 95% CI of 0.244-0.592, and *P* value less than 0.001, indicating

decreased odds of occurrence by 0.380 with an hour increase in daily mobile phone use in standby mode (non-talk mode, only switched on). Table 4 summarizes the results of the logistic regression model.

Contrary to early findings, when only the data of "Heavy Users" groups were analyzed, the pattern of results was entirely different for some parameters. This analysis showed that exposure to digital screens at night was particularly higher in breast cancer patients compared to the control group. Cumulative use of digital display screens in low light conditions was also higher in the breast cancer group

Table 3: Use of digital screens in control and case groups in top 25% Heavy Users.

|   |          | Sample<br>Size | Mean    | SD     | Significance          |
|---|----------|----------------|---------|--------|-----------------------|
| Screen Time Per Week (hours/week) Screen Time ≥14 h/week  |          | 63             | 18.7    | 8.8    | NS ( <i>P</i> =0.561) |
|   |          | 68             | 19.3    | 9.4    |                       |
| Screen Time in Dim Light (hours/day) Screen Time ≥1 h/day |          | 39             | 1.95    | 1.14   | NC (D-0.073)          |
|   |          | 21             | 1.55    | 1.02   | NS ( <i>P</i> =0.073) |
| Cumulative Screen Time in Dim Light (hours) Screen        | Controls | 54             | 12141.7 | 4922.9 | NO (D-0.00)           |
| Time ≥8,400 h   | Cases    | 31             | 13827.4 | 6713.6 | NS ( <i>P</i> =0.08)  |

NS: Non-significant, SD: Standard Deviation

**Table 4:** Univariate logistic regression model is firstly used to select important variables and then multivariate logistic regression model with variables of age, average working time with digital screens, screen size of these devices, history of use of screens (years), cell phone use for calls (talk mode), stand-by time (cell phone use when it is switched on but there are no calls, internet use, etc.), cellular internet use, cordless phone use, sleep disorders is done.

|             | Predictor                                       | Odds Ratio<br>(OR) | CI (95%)         | Significance       |
|-------------|---|--------------------|------------------|--------------------|
| All Users   | The history (years) of screen use               | 0.725              | 0.595-0.883      | <i>P</i> =0.001    |
| All Users   | The daily use of mobile phone in standby mode   | 0.380              | 0.244-0.592      | <i>P</i> <0.001    |
|             | Using digital screens >30 min/day in dim light  |                    |                  |                    |
| Heavy Users | before sleep in breast cancer patients compared | 1.156              | 0.6307 to 2.1202 | NS <i>P</i> =0.630 |
|             | to controls                                     |                    |                  |                    |

CI: Confidence Interval, NS: Non-significant

than in the control group. The extent to which these findings are consistent with a non-linear J-shaped dose-response model is discussed in the "Discussion" section of this paper.

### Discussion

Recent research suggests that women with a family history of breast cancer, particularly those who carry mutated *BRCA1* or *BRCA2*, should limit their screen time at night [30]. Using sunglasses with amber lenses or night mode settings, which decrease susceptible women's exposure to smartphones' HEV blue light before sleep, can mitigate the dysregulation of circadian rhythm and decrease the risk of breast cancer. A study performed in Spain also reports a link between exposure to blue artificial light at night and an increased risk of breast and prostate cancers [31].

From a broader perspective, natural light and its daily cycles are essential for all living organisms [32]. However, exposure to light at night, particularly short-wavelength visible light emitted from digital screens of mobile phones, tablets, laptops, and even TVs, can represent a risk to human health and increase the risk of female breast cancer, possibly through changes in biological rhythms. At first glance, this study found no statistically significant difference in the exposure to light emitted from digital screens between the breast cancer group and the control group. However, this may be due to factors such as the control group's higher level of screen time in low light conditions (night hours) compared to the cancer group.

It is noteworthy that substantial evidence links only exposure to light at night with an increased risk of cancer. However, when assessing the 10-year cumulative exposure to digital screens in heavy users of both the breast cancer and control groups, the mean exposure was higher in the breast cancer group than in the control group, although not statistically significant. This finding highlights the need for further attention to cumulative exposures.

Using a logistic regression model, the number of years of screen use time and the average daily standby time were statistically significant. However, when only heavy user individuals were included in the analysis, the pattern of results was quite different. The time factors, such as exposure to digital screens, especially at night hours (low light condition), cumulative digital screen use in low-light conditions, were higher in the cancer group compared to those of the control group. For example, the likelihood of using digital screens for more than 30 min/day in dim light conditions was higher in breast cancer patients, indicating that cancer patients had a higher chance of being a heavy digital screen user. However, whether these findings show a J-Shaped dose-response model requires further investigation.

Heavy users of digital screens, such as mobile phones, tablets, and laptops, may be at a higher risk of developing cancer or other adverse health effects due to several factors including higher exposure to blue light, more sedentary behavior and less physical activity [33]. Although heavy users in the case group of our study had a statistically significant higher mean 10-year cumulative exposure to digital screens compared to the control group (7089±14985 vs 4052±12515 hours, respectively, P=0.038), generally our study did not find a strong relationship. Therefore, it would be premature to draw firm conclusions about the effects of blue light emitted from digital screens on breast cancer risk in women. It is possible that different factors contributed to these negative findings.

Firstly, the cases in our study were individuals referred to the recruiting clinic between 2016-2020 with breast cancer diagnosed no later than 3 years earlier, during the incidence period of 2013-2020. Blue-light emitting screens were not in widespread use for many years before the first (and even the most recent) diagnoses. It is possible that users were not yet fully at risk of developing cancer from exposure to such screens.

In addition, the possible effect of other blue light emitting devices should be considered. Blue light emitting devices now may include TVs, computer screens, mobile phones, and indoor/outdoor lighting. A limitation of our study was this point that not all of these sources were included in our exposure assessment.

Moreover, people who spend a lot of time on watching TV, may spend less time on mobile phone screens. Additionally, exposure to the melanopic band of light (wavelength of ~480 nm) may not be increased in the same way by all types of LED lights/screens. Some LEDs may not have higher emissions in such a band than non-LED sources of indoor/out-door lighting. Finally, at least to some extent, there were differences in age, education and BMI between cases and controls. These characteristics may be associated with differences in digital screen time.

Further studies, similar to the one conducted by Harvard in 2017, would be advantageous based on our research findings. The Harvard study estimated cumulative LAN exposures of 109,672 women from 1989 through 2013 using time-varying satellite data [17]. The Harvard study showed that exposure to residential outdoor LAN may contribute to invasive breast cancer risks [17]. However, the Harvard study has limitations, including that it was conducted on nurses and cannot be extrapolated to the entire female population, personal exposure to HEV blue light emitted from digital screens was not accurately measured, and the key role of exposure to short-wavelength visible light, especially the blue light from digital screens, was ignored.

Based on our research findings, conducting further studies similar to the one carried out in Spain would be advantageous. This study showed a correlation between exposure to LAN, particularly short-wavelength blue light, and an increased risk of breast and prostate cancers [31]. However, the study conducted in Spain had major shortcomings, including inadequate data collection and lack of accurate

measurements of personal exposure to blue light emitted from digital screens.

Some of our findings partially support reports indicating no correlation between exposure to LAN and an increased risk of breast cancer. For example, a study by Johns et al. collected data on the level of bedroom light and sleeping patterns of 105,866 participants without a history of breast cancer and showed no evidence that LAN exposure increased the risk of subsequent breast cancer [34]. However, this study had major shortcomings, including ignoring the key role of exposure to blue light emitted from widely used digital screens on melatonin suppression and poor study design [35].

On a broader perspective, our findings may support those of a recent study that found the expression profile of BRCA1 and BRCA2 genes in lymphocytes regularly changes over a 24-hour period. The study suggests a relation of the DNA double-strand break repair system with the biological clock, and lower levels of BRCA1 and BRCA2 found in shift workers may be one of the potential factors related to the higher risk of breast cancer [36]. Based on our findings, it can be hypothesized that heavy screen time, through mechanisms such as suppression of melatonin secretion and dysregulation of biological rhythms, might increase the risk of breast cancer, as illustrated in Figure 2.

Our findings also prompt us to continue conducting studies on female shift workers. While some recent reports have suggested that LAN may not always affect melatonin production [37], a recent study on female nurses showed hypomethylation of *TP53* and *BRCA1* in current and former night shift (NS) workers with less than 12 years of night shift work. The study also revealed a correlation between telomere length (TL) and the number of years worked on NS, suggesting that markers associated with night shift work may contribute to cellular aging, genomic instability, and cancer development [38]. Shift workers have also

been found to have lower levels of *BRCA1* and *BRCA2*, which are genes involved in DNA double-strand break repair. This may be a potential factor associated with the higher breast cancer risk observed in night shift workers [39].

A pooled analysis of population-based case-control studies that included complete work history on the potential link between night shift work and breast cancer showed a higher risk in pre-menopausal current or recent night shift workers (OR=1.41, |1.06-1.88|) compared to women who had stopped night shift work more than 2 years earlier. The authors concluded that night shift work increases the risk of breast cancer in pre-menopausal women [40].

A Norwegian cohort study on the effects of shift work on TL and its association with breast cancer risk demonstrated that intensive night work schedules, such as working six consecutive nights for more than 5 years, were associated with decreased telomere lengths (-3.18, 95% CI: -6.46 to -0.58, *P*=0.016). Moreover, in workers with long periods of consecutive night shift schedules, telomere shortening was associated with an increased risk of breast cancer. These findings suggest that telomere shortening may be linked to the duration and intensity of night work [41].

In breast cancer patients, moderate exposure to night work was linked to DNA methylation in core circadian genes (*CLOCK*, *BMAL1*, *CRY1*, and *PER1* genes) in nurses working night shifts compared with controls. Therefore, it can be suggested that epigenetic regulation of *CLOCK*, *BMAL1*, *CRY1*, and *PER1* may be involved in the increased breast cancer risk observed in shift workers [42].

We acknowledge that our study, as with any retrospective study, has certain limitations, such as potential difficulties in accurately estimating past exposures. Nevertheless, we made efforts to utilize appropriate study design, statistical methods, and meticulous consideration of potential biases in order to mitigate these

inherent limitations.

### Conclusion

Natural light and its daily cycles play a crucial role in regulating the biological rhythms of living organisms. However, LAN, especially the HEV blue light emitted from digital screens, may pose a risk to human health and increase the incidence of breast cancer by disrupting these rhythms. Our study highlights the need for further investigation into the potential link between heavy screen time and an increased risk of breast cancer associated with cumulative exposure to HEV blue light emitted from mobile phone screens at night. Moreover, our findings suggest that the cumulative exposure to short-wavelength blue light emitted from digital screens of mobile phones at night is a more crucial factor than the quality and quantity of short-term exposures. These findings prompt us to fully review all of the previous studies demonstrating a higher incidence of breast cancer in female night shift workers. However, it is premature to draw firm conclusions, as we still do not fully understand the extent to which blue light emitted from digital screens may affect the risk of breast cancer in women. Large-scale cohort studies should be conducted to increase our understanding of the possible correlation between heavy use of digital displays at night and breast cancer.

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### **Authors' Contribution**

S. Tahmasebi, SAR. Mortazavi, SMJ. Mortazavi and A. Taleie designed the study.

L. Sihver, JC. Lech and JS. Welsh served as senior consultants throughout all stages of the project. S. Nematollahi performed the statistical analyses. A. Rezaianzadeh, A. Zamani supervised the statistical analyses. At. Zamani was the EMF consultant for the project. K. Mega prepared the reports. L. Sihver edited, revised and submitted the manuscript. All authors have read and approved the manuscript.

## **Ethical Approval**

This study was approved by the Institutional Review Board (IRB) of Shiraz University of Medical Sciences (SUMS). All protocols used in the study were approved by the SUMS Ethics Committee (permit No. IR.SUMS. MED.REC.1398.057).

### **Informed Consent**

All women diagnosed with breast cancer provided informed written consent to participate in the study. Women who were unwilling to participate were excluded.

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### Conflict of Interest

SMJ. Mortazavi, as the Editorial Board Member, was not involved in the peer-review and decision-making processes for this manuscript.

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