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Illuminating a Risk for Breast Cancer: A Preliminary Ecological Study on the Association Between Streetlight and Breast Cancer

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Abstract

Artificial light at night (ALAN) for elongating photophase is a new source of pollution. We examined the association between measured ALAN levels and breast cancer (BC) standard morbidity ratio (SMR) at a statistical area (SA) level in an urban environment. Sample size consisted of 266 new BC cases ages 35-74. Light measurements (lux) were performed in 11 SAs. A new calculated variable of morbidity per SA size ($SMR_{35\text{-}74}/km^2$) was correlated with the light variables per road length, using Pearson correlations ($P < .05$, 1-tailed). Looking for a light threshold, we correlated percentage of light points above SA light intensity median with $SMR_{35\text{-}74}/km^2$. $SMR_{35\text{-}74}/km^2$ was significantly and positively strongly correlated with mean, median, and standard-deviation (SD) light intensity per road length ($r = .79$, $P < .01$, $R^2 = .63$; $r = .77$, $P < .01$, $R^2 = .59$; and $r = .79$, $P < .01$, $R^2 = .63$). Light threshold results demonstrate a marginally significant positive moderate correlation between percentage of points above 16.3 lux and $SMR_{35\text{-}74}/km^2$ ($r = .48$, $P < .07$; $R^2 = .23$). *In situ* results support the hypothesis that outdoor ALAN illumination is associated with a higher BC-SMR in a specific area and age group. Moreover, we suggest an outdoor light threshold of approximately 16 lux as the minimal intensity to affect melatonin levels and BC morbidity. To the best of our knowledge, our attempt is the first to use this method and show such association between streetlight intensity and BC morbidity and therefore should be further developed.

Keywords

light pollution, artificial light at night, breast cancer, urban, standard morbidity ratio, light intensity, ecological study, statistical area

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Introduction

The World Health Organization denotes on its website several known and well-documented breast cancer (BC) risk factors such as genetics, reproductive factors, and lifestyle factors including overweight, obesity, and physical inactivity.[1] However, it does not refer to one of the significant environmental changes that took place in the past 140 years—the invention of the electric light bulb, resulting in a widespread excessive use of artificial light at night (ALAN) to elongate the day for socioeconomic benefit.

Natural light/dark cycles are the main time keeper or "zeitgeber" for the entrainment of the biological clock that acts also as a calendar with daily and seasonal changes.[2] The characteristics of light such as short wavelength (SWL) light of ~440 to 520 nm, intensity and duration, function as an external signal for the mammalian biological clock. These signals conduct the synchronization of body physiology, immune and behavioral rhythmic functions, thus adjusting them to the temporal environmental changes.[2-9] Light/dark cyclic input received via the non–image-forming photoreceptors of the eye's retina, containing the photopigment melanopsin, entrains the biological clock with the environment.[8,10] Moreover, it results in an output—the neurohormone melatonin (MLT) synthesized and secreted by

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the pineal gland—during the dark phase of the 24-hour cycle. This hormone, MLT, among others, signals environmental temporal changes to cells, tissues, and organs, including the suprachiasmatic nucleus cells of the biological clock, situated in the hypothalamus region.[11,12]

In 2007, the World Health Organization, International Agency for Research on Cancer Monograph Working Group, passed a resolution recognizing "shift work that involves circadian disruption is probably carcinogenic to humans (2A)."[13] Subsequent to that, declarations and decisions of the American Medical Association (AMA) in 2012 and 2016 determined that "AMA Adopts Community Guidance to Reduce the Harmful Human and Environmental Effects of High Intensity Street Lighting."[14] The AMA resolution specifies that blue-rich light emitting diodes (LED) used for street lighting operate at a wavelength that efficiently suppresses MLT during the night.[14] ALAN containing strong emission of SWL (~440 to 520 nm), emerging from a diversity of sources, highly suppress MLT production, where blue and white LEDs are the most efficient suppressors.[6,15,16] Therefore, this artificial exposure greatly disrupts the natural light cycles, pineal MLT synthesis and secretion. Consequently it may affect humans' physiology, immune function, and health, including BC.[5,6,16-22]

A continuing increase in exposure to indoor and outdoor ALAN as a part of worldwide urbanization in developing and developed countries may be, among others, a part of the increasing rates of BC.[1,16,23,24] Urban populations are characterized by population size, density, heterogeneity, and distance from other centers.[25] In Israel, according to the Israeli Bureau of Statistics (IBS), an urban settlement is defined as having more than 2000 residents, with no reference to illumination infrastructure, social, or other characteristics.[26] Outdoor illumination in urban areas may include metal halide, mercury vapor, fluorescent, and blue-white LED illuminations, which all contain strong SWL emissions and, therefore, highly suppress MLT production. Furthermore, today's indoor lighting (TV, cellular and smart phones, as well as other electronic and electrical devices) have strong SWL emissions, which also contribute to the inhibition of pineal MLT production.[6,15,16,27] Inhibition of MLT production during the night and across numerous years may lead to an increased risk of BC.[28]

Different approaches were used to examine this hypothesis including ecological studies using ALAN data from satellites,[29-33] case-control studies using questionnaires to analyze individual lighting habits and BC risk factors,[34-36] or laboratory studies exposing healthy subjects to different light intensities to measure MLT levels.[37,38] Nevertheless, we fail to find any study that uses *in situ* outdoor light intensities in the urban environment in order to challenge this hypothesis.

Following mounting evidence on the nexus between hazardous outdoor lighting and BC together with the AMA resolution referring to outdoor lighting as harmful, we decided to study the possible association between outdoor light intensity and BC morbidity in the city of Ashkelon.

We hypothesized that if exposure to outdoor ALAN illumination is associated with a higher risk of BC development, then women who had been exposed to higher levels of outdoor light per road length were likely to exhibit, *ceteris paribus*, higher BC standard morbidity ratios (SMR) per statistical area (SA) size.

To test this hypothesis, we correlated light intensities (*de facto*) per road length of 11 SAs in Ashkelon, an Israeli city, with BC SMRs per SA size of a defined group (age 35-74) during the years 2004 to 2012.

Materials and Methods

This study refers to new BC cases in the city of Ashkelon during the years 2004 to 2012. Streetlight measurements were conducted during 2015-2016 in order to look for associations between ALAN intensities and BC incidence. Although there is no overlap between ALAN data collection time and BC diagnosis, we assumed there was no substantial change in light infrastructure over the years; therefore, light measurements represent a proxy of light intensities 10 to 15 years prior to diseases diagnosis.[39-41]

Region of Study: Statistical Areas in the City of Ashkelon

The city of Ashkelon is situated on Israel's southern coast of the Mediterranean Sea (Figure 1). The city's history began in biblical times, and since 1950 modern urbanization has accelerated. In the southern part of the city, we find a power plant station that has produced and supplied electricity since 1990. Moreover, since 2006 Ashkelon has been within the firing zone of rockets from the Gaza strip. However, data published by the Israeli Cancer Registry states that BC rates in Ashkelon region during the years 2001 to 2011 were lower than the expected in Israel by 7% to 8%[42]; therefore, we assumed that women in the city of Ashkelon are probably less exposed to different BC risk factors and thus the effect of ALAN exposure will be prominent over other affecting variables.

At the end of 2014, the city had 126 800 inhabitants and the municipal area included approximately 46 km^2 in 32 SAs. The population density was 2754.2 inhabitants per km^2.[43] SAs (defined by the IBS) are small homogeneous units, as much as possible, allowing statistical analysis for research purposes. Out of 32 SAs, 11, which are in the residential area of the city, were selected for the present research (Figure 1). The selected SAs represent neighborhoods older than 20 years with changes limited mostly to natural population growth and minimum changes in illumination infrastructure over the years. For example, 2006 estimates of construction data show a growth of 1475 inhabitants in 461 residential units in the entire city of Ashkelon.[44] In order to

Figure 1. Research area: Ashkelon's statistical areas. The map was retrieved out of the "Compendium of Maps—Society in Israel Report No. 7, 2014" and it describes the SAs in the city of Ashkelon. Marks and names that are not relevant to this research were removed, and the writing was changed to English. SAs of the study are colored with dark gray. Actual size of each SA is described in the section, "Land Uses Description of SAs."

control maximum of the possible affecting variables, SAs with large commercial and services areas, large parks, hotels, or industrial areas were not part of the research. Six of the SAs were selected in a row from the southwest parts of the city, and 5 SAs were selected in a row from the northwest parts of the city, unless there was a massive urban development that made us deviate from the row (north).

Land Uses Description of SAs

Geographical data and estimations of SA sizes were obtained from the Internet using Google Maps (https://maps.google.com/) and *govmap* site (http://www.govmap.gov.il/). Road length in kilometers was measured using AutoCAD 2017.

SAs in the Southern Part of the City

SA-313 covers an area of about 0.52 km^2 of which 0.34 km^2 are totally separated and serve for dwelling. The rest of the area is a natural open area; therefore, we used only the dwelling area for the statistical analysis as the rest is irrelevant regarding exposure to ALAN. Road length measured in the dwelling area is 5.50 km. Moreover, out of the constructed area we estimate 80% with 4- to 5-floor buildings while 20% are public buildings like a 2-floor mall, a synagogue, schools, a swimming pool, and a local community center.

SA-314 covers an area of about 0.28 km^2 with measured road length of 4.77 km. Approximately 90% of it is a dwelling area of which 95% are 3- to 4-floor buildings and 5% are private homes. About 5% of the entire area is covered with public buildings like a synagogue and a school, community centers, and a sports hall. Moreover, 5% consists of bare open areas.

SA-322 covers an area of about 0.21 km^2 with measured road length of 3.83 km. Roughly 50% of it is a dwelling area with 4- to 5-floor buildings. Forty percent of the entire area is covered with public buildings such as a 2-floor mall, a synagogue, a community center, and schools. An estimated 10% more consists of open areas, which serve as large parking lots with hardly any overhead lights.

SA-323 covers an area of about 0.35 km^2 with measured road length of 5.12 km. Approximately 90% of it is a dwelling area of which 50% has 3- to 4-floor buildings and 50% are private homes. An estimated 5% of the entire area is covered with public buildings such as a synagogue and a school. Moreover, 5% consists of bare open areas.

SA-315 covers an area of about 0.13 km^2 with measured road length of 2.09 km. Approximately 85% of it is a dwelling area of which 100% are 3- to 4-floor buildings. An estimated 5% of the entire area is covered with public buildings like a synagogue and a community center. Moreover, 15% consists of bare open areas.

SA-316 covers an area of about 0.42 km^2 with measured road length of 6.99 km. Approximately 90% of it is a dwelling area of which about 60% are 3- to 4-floor buildings, 30% are 2-floor buildings, and 10% are 10-floor buildings. Five percent of the entire area is covered with public buildings like a synagogue, schools, a commercial center, and a community center. Moreover, 5% consists of natural open areas and sports fields.

SAs in the Northern Part of the City

SA-114 covers an area of about 0.97 km^2 with measured road length of 16.08 km. Approximately 75% of it is a dwelling area of which about 80% are private homes, 15% are 6- to 12-floor buildings, and 5% are 3-floor buildings. An estimated 10% of the entire area is covered with public buildings like a synagogue, a school, and a commercial center. Moreover, 15% consists of natural open areas.

SA-122 covers an area of about 0.60 km^2 with measured road length of 16.84 km. Approximately 75% of it is a dwelling area of which about 80% are private homes and 20% are 6- to 12-floor buildings. An estimated 10% of the entire area is covered with public buildings like a synagogue, a hotel, and a sports club. Moreover, 15% consists of natural open areas.

SA-123 covers an area of about 0.85 km^2 with measured road length of 14.17 km. Approximately 75% of it is a dwelling area of which about 90% are private homes and 10% are 9- to 12-floor buildings. An estimated 10% of the entire area is covered with public buildings like commercial centers and a school. Moreover, 15% consists of natural open areas.

SA-214 covers an area of about 0.30 km^2 with measured road length of 6.53 km. Approximately 85% of it is a dwelling area of which about 50% are private homes, 20% are 5- to 6-floor buildings, and 15% are 3- to 4-floor buildings. An estimated 5% of the entire area is covered with public buildings like synagogues. Moreover, 10% consists of natural open areas.

SA-215 covers an area of about 6.48 km^2 of which only 0.37 km^2 are totally separated and serve for dwelling. The rest of the area is bare open land; therefore, we used only the dwelling area for the statistical analysis as the rest is irrelevant regarding exposure to ALAN. Road length measured in the dwelling area is 9.90 km. Moreover, approximately 75% of the dwelling area is covered with private homes; an estimated 10% are public buildings like a school and a local community center. Moreover, 15% consists of natural open areas between the buildings.

Demographic Data

Comprehensive data of SAs in Ashkelon were extracted from the official 2008 Census[45] and from the Compendium of Maps—Society in Israel Report No. 7, 2014,[46] conducted by the IBS. The year 2008 is the midpoint of the study period, and the census data of 2008 is the best corresponding available data for this period (2004-2012). Therefore, we selected 2008 to represent the status of each SA, assuming minimum changes in population size and composition. Most of the development in Ashkelon was and is at the north and northeast parts of the city with minimum construction and external migration into old neighborhoods. Thus, we assume that most BC patients reported during the years 2004 to 2012 lived in this area 10 to 15 years prior to the disease detection and were roughly exposed to the same outdoor light intensities during the years. Demographic data describing the different SAs are presented in Table 1.

Data on Artificial Light at Night

Light intensity measurements were carried out during clear moonless nights between the last quarter and the first quarter of moon phases and began an hour after total sunset. Four SAs were measured during May 2015 and 7 SAs were measured during April and May 2016 due to logistic challenges. Number of light sampling points ranged from 25 to 90 and was selected to represent the vicinity, depending on the accessibility and size of the SA. The measurements were taken using a light meter (EZDO Lux/Fc Light Meter DL-204 s/n 121001141) that was situated in each point at

Table 1. Demographic Data of Statistical Areas in Ashkelon 2008.

	Statistical Area										
Demographic Data	313 S	314 S	322 S	323 S	315 S	316 S	114 N	122 N	123 N	214 N	215 N
Total population size	4300	5600	4000	5000	2200	4300	4700	3900	4200	3000	3300
Number of women (35-74 years)	1145	1342	889	1176	561	1035	1040	938	948	667	705
Women's age (median)	49	38	34	37	46	43	32	38	37	34	31
Mean number of children per woman	2	2.1	1.9	2	2.2	2	2.2	2.3	1.9	1.7	1.6
Per capita income (NIS/month)	2416	2765	2888	3259	2397	2904	5146	6186	6350	3832	4929
National poverty ranking[a] by income	5	5	5	4	5	5	3	3	2	3	2

Abbreviations: S, south; N, north.
[a]National poverty ranking: 1 = low poverty; 5 = high poverty.

Table 2. Breast Cancer Data of Statistical Areas in Ashkelon.

	Statistical Area										
	313 S	314 S	322 S	323 S	315 S	316 S	114 N	122 N	123 N	214 N	215 N
Number of BC cases, N = 266 (women aged 35-74 years), 2004 to 2012	41	31	18	19	12	20	33	25	29	19	19

Abbreviations: S, south; N, north; BC, breast cancer.

140 cm height and not under direct streetlights or trees. All measurements were performed twice and a mean value was calculated.

Breast Cancer Data

Data of new BC cases between the years 2004 and 2012 were provided by the Cancer Registry of the Israeli Ministry of Health. The sample size consisted of 266 new BC cases between the ages of 35 and 74 years (Table 2). This age group represents women with 10 to 15 years of exposure to ALAN as matured women with probable minimum background diseases as confounders. Matching BC cases to SA was made by zip code. In case of a conflict as a result of zip code passing through 2 SAs a decision was made by matching the woman's age to the median age of the SA provided by the IBS. Sixty-three women in the aforementioned ages were missing zip codes; therefore, they were removed from the study.

Standardized morbidity ratios with 95% confidence intervals (CIs) of BC were calculated for each SA (Table 4). SMR is the ratio of the total number of the observed BC cases (2004-2012) to the expected number of BC cases for a particular/standard population, taking the age of patients into account. Since the population of the study is only women, gender was not a variable.

Preparation of Variables for Statistical Analysis

For preparing the variables and analyzing BC and ALAN data, we used SPSS19 and Excel 2010.

Light variables that are represented by light intensity per road length in each SA in Ashkelon include mean_lux/km, median_lux/km, and standard deviation (SD)_lux/km. In the urban environment there are residences along roads and transportation routes with streetlights. Therefore, we assume that the longer the illuminated roads are in the SA the greater the exposure to outdoor lighting. Using standard deviation as a variable helps us detect the range of light intensity in each SA; therefore, it is important for understanding the spatial distribution and variability of light in those areas. Furthermore, we used the median of each SA to calculate the percentage of light points above it in the additional SAs, aiming to help us look for a threshold. The percentage of points above the median of SA 315 in the additional SAs produced a significant result in the tested correlation with $SMR_{35\text{-}74}/km^2$.

BC variables include SMR with 95% CI for women aged 35 to 74 and $SMR_{35\text{-}74}/km^2$ of each SA in order to control age as well as density of BC cases of the SA. Since we examined only 11 SAs we had to focus on a small number of variables, which may be influencing BC apart from ALAN; therefore, we added the variables per capita income and number of births.

Statistical Analysis

In this study, we examined 11 SAs; for that reason the statistical analysis includes Pearson correlations with significance of $P < .05$ (1-tailed) and Mann-Whitney test in order to compare SAs.

Table 3. Light Intensities of Statistical Areas in Ashkelon.

Statistical Area	Light Intensity (Mean_lux)	SD	Light Intensity (Median_lux)
313 S	**12.87**	10.75	**10.65**
314 S	9.37	11.62	4.40
322 S	10.46	11.79	6.70
323 S	**13.18**	11.43	9.60
315 S	**15.99**	10.28	**16.30**
316 S	10.83	9.38	7.34
114 N	**14.91**	**11.89**	**11.70**
122 N	**12.70**	7.01	**12.45**
123 N	9.30	**6.87**	9.75
214 N	9.95	8.35	7.85
215 N	10.91	9.24	8.95

Table 4. Breast Cancer SMR_{35-74} of Statistical Areas in Ashkelon.

Statistical Area	SMR_{35-74}	95% CI
313 S	**1.36**	**0.97-1.84**
314 S	0.91	0.62-1.29
322 S	0.84	0.49-1.33
323 S	0.67	0.41-1.06
315 S	0.82	0.42-1.44
316 S	0.77	0.47-1.18
114 N	**1.31**	**0.90-1.85**
122 N	**1.05**	**0.68-1.56**
123 N	**1.20**	**0.80-1.73**
214 N	**1.27**	**0.76-1.98**
215 N	**1.34**	**0.80-2.09**

Abbreviations: SMR, standard morbidity ratio; CI, confidence interval.
Notes. The bolded values represent higher SMR_{35-74} levels of the expected.

Best correlations results were of road length (km) versus SMR and light intensity mean_lux/km, median_lux/km, and SD_lux/km versus SMR_{35-74}/km^2. Moreover, looking for positive strong correlations, we tested the correlations between SMR_{35-74}/km^2 versus percentages of points above median (light threshold) of each SA. Following this we tested the association between SMR_{35-74}/km^2 and number of births as well as per capita income. Furthermore, looking for disparities, we compared the SAs in the southern part of the city with the SAs of northern part of the city using the Mann-Whitney test.

Results

Mean and median light intensities (lux) of the 11 SAs are presented in Table 3. Mean light intensities of SAs 313, 323, 315, 114, and 122 are higher than 12 lux. However, median light intensities (lux) of SAs 313, 315, 114, and 122 are higher than 10 lux and SD varies between 6.87 lux in SA 123 and 11.89 lux in SA 114.

Table 5. Breast Cancer SMR_{35-74}/km^2 of Statistical Areas in Ashkelon.

Statistical Area	BC Density	SMR_{35-74}/km^2
313 S	**166.47**	**4.03**
314 S	**134.90**	**3.23**
322 S	**120.71**	**4.06**
323 S	71.69	1.94
315 S	**133.02**	**6.44**
316 S	69.30	1.83
114 N	50.27	1.35
122 N	51.99	1.77
123 N	27.19	1.42
214 N	73.48	**4.23**
215 N	64.55	**3.61**

Abbreviations: SMR, standard morbidity ratio; BC, breast cancer; N, north; S, south.

Calculated SMR_{35-74} with 95% CI for each SA in Ashkelon is presented in Table 4. SAs 313, 114, 122, 123, 214, and 215 have higher BC rates than expected while SAs 314, 322, 323, 315, and 316 have lower BC rates than expected.

Likewise, BC density (total number of BC cases 2004-2012 per km^2) is higher than 120 BC cases per km^2 in SAs 313, 314, 322, and 315, while BC density in SAs 323, 316, 114, 122, 123, 214, and 215 is lower than 72 BC cases per km^2. Furthermore, calculated SMR_{35-74}/km^2 shows higher rates than 3.0 in SAs 313, 314, 322, 315, 214, and 215 (data presented in Table 5).

BC morbidity of women aged 35 to 74 years was correlated with road length of each SA. We assumed it may be a proxy to light exposures (intensity, duration, and wavelength) as city roads are normally lit with streetlights. Results demonstrate a marginally significant positive moderate association ($r = .50$, $P < .06$; $R^2 = .25$; Figure 2).

BC morbidity of women aged 35 to 74 per km^2 (SMR_{35-74}/km^2) was significantly, positively strongly, correlated with mean light intensity per road length (lux/km), and 63% of the variation in Ashkelon's SAs morbidity can be explained by the variation in mean light intensity ($r = .79$, $P < .01$; $R^2 = .63$; Figure 3).

Moreover, SMR_{35-74}/km^2 was also significantly ($r = .77$, $P < .01$; $R^2 = .59$) correlated with the median light intensity (lux) per road length (Figure 4) and with the standard deviation (lux) per road length ($r = .79$, $P < .01$; $R^2 = .63$; Figure 5). Fifty-nine percent and 63% of the variation in Ashkelon's SAs morbidity in the specified age group can be explained by the variations in median light intensity per road length and standard deviation per road length, respectively (positive, strong correlations).

Median light intensities (lux) of the 11 SAs (Table 3) were used to calculate the percentage of light points above

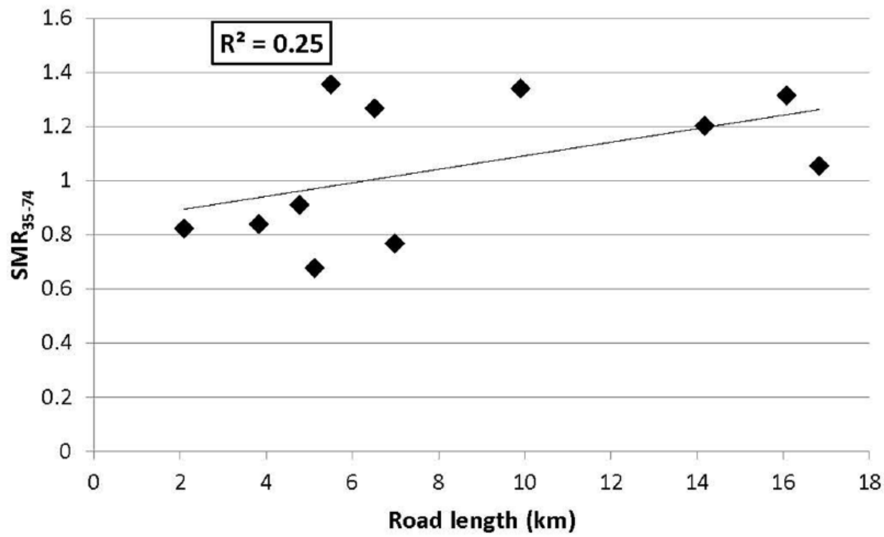

Figure 2. Road length versus $SMR_{35\text{-}74}$.

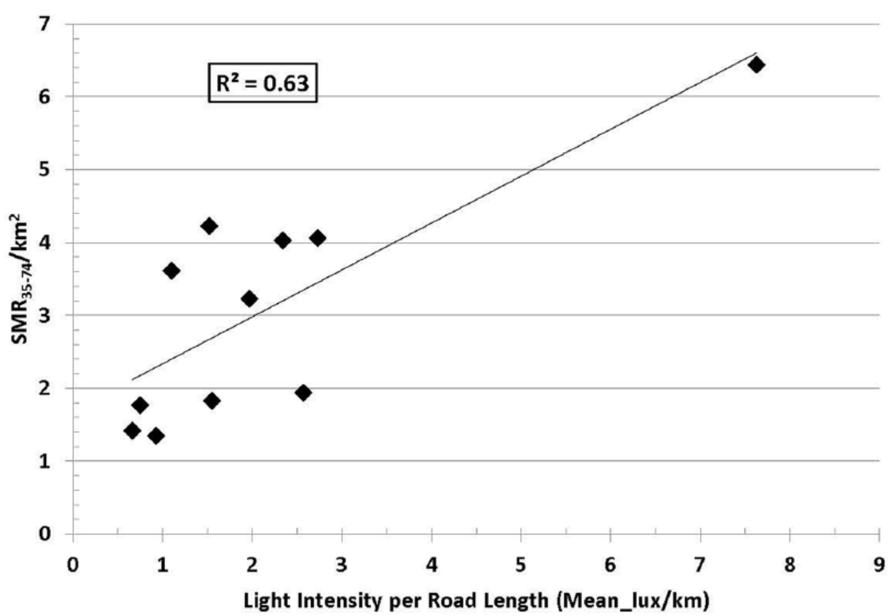

Figure 3. The effect of mean light intensity per unit of road length on SMR per SA size.

each median in every SA, looking for a light threshold. This light threshold (a selected median of 1 SA) will be a threshold above which we find significant positive correlations. SA 315 demonstrated the highest median light intensity, and therefore, we assumed, it was also applicable as a threshold. In Figure 6, we present the correlation between $SMR_{35\text{-}74}/km^2$ versus percentage of points above the median of SA 315 (16.3 lux). Results demonstrate a marginally significant positive moderate correlation between percentage of points above 16.3 lux (light intensity above threshold) and $SMR_{35\text{-}74}/km^2$ ($r = .48$, $P < .07$; $R^2 = .23$).

Other risk factors tested like birth rates showed no significant correlation to $SMR_{35\text{-}74}/km^2$ ($r = -.16$, *ns*), while per capita income - presented a negative significant correlation with $SMR_{35\text{-}74}/km^2$ ($r = -.61$, $P < .05$). Moreover, applying Mann-Whitney test in order to compare the southern part of

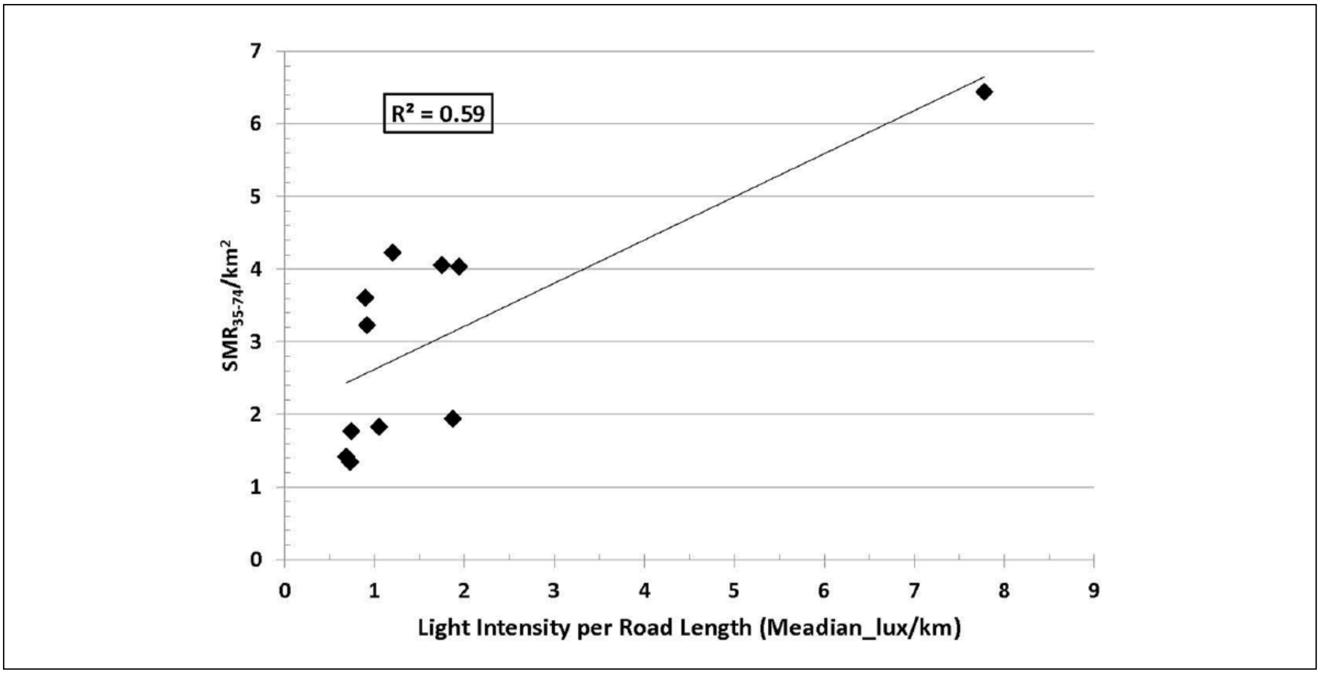

Figure 4. The effect of median light intensity per unit of road length on SMR per SA size.

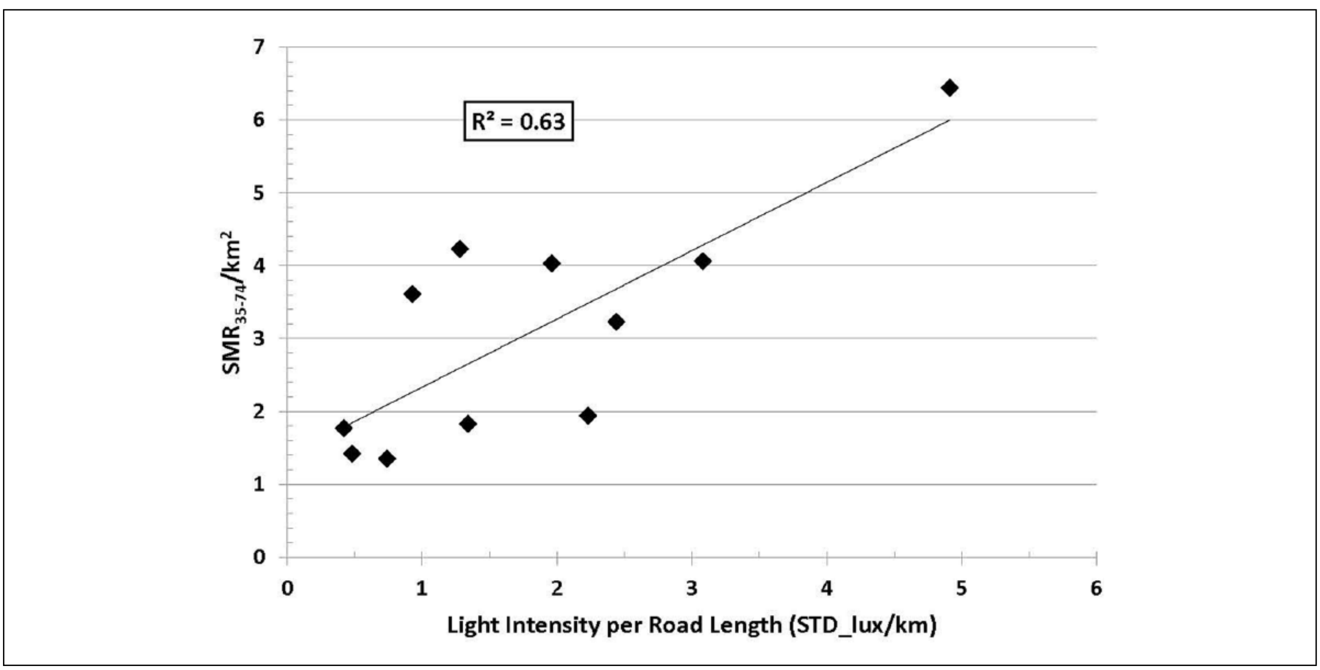

Figure 5. The effect of SD light intensity per unit of road length on SMR per SA size.

the city with the northern part resulted in a significant difference between the 2 parts regarding ALAN levels per road length (mean lux/km $Z = 2.74$, $P < .01$; median lux/km $Z = 2.37$, $P < .05$; SD lux/km $Z = 2.74$, $P < .01$) whereas the southern part of the city displays higher ALAN levels per road length in all ALAN variables. Furthermore, a marginal significant difference was noted between the southern part of the city and the northern part of the city regarding traditional $SMR_{35\text{-}74}$ with higher rates than expected in the northern part of the city ($Z = 1.83$, $P < .1$). Nevertheless,

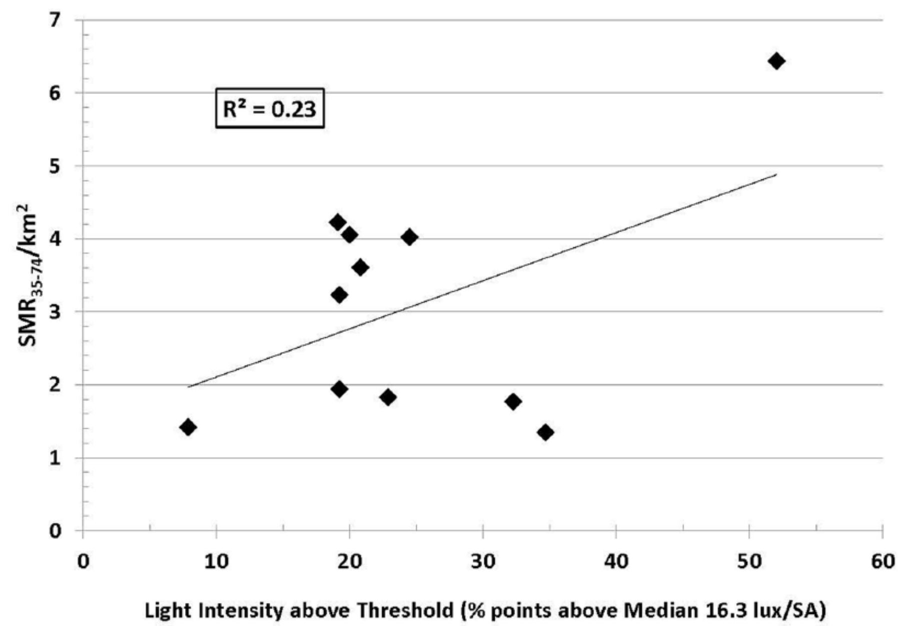

Figure 6. The effect of light threshold on SMR per SA size.

significant higher rates of BC density ($Z = 2.37$, $P < .05$) were revealed in the southern part of the city. No significant difference was revealed between the 2 parts of the city in the new calculated variable SMR_{35-74}/km^2 ($Z = 1.28$, *ns*). Applying the new suggested calculation method controls not only the age, as in traditional SMR, and not only the size of the area as in BC density, but also combines both of them into one variable, SMR_{35-74}/km^2. Controlling all the affecting variables, that is, light intensity per road length, SA size and age of BC-patients will yield, we estimate, a more accurate result. Likewise, we present a significant difference ($Z = 2.73$, $P < .01$) between the southern part of the city and the northern part regarding income level per capita with higher per capita income in the north. Furthermore, there was no significant difference between the 2 areas concerning birth rates ($Z = 0.56$, *ns*).

Discussion

The growth of human population and the expansion of urbanized areas are accompanied by ALAN increases globally.[6,47] Numerous different and varied means of illumination contribute to ALAN and increase nocturnal light pollution. Street lighting, billboards, architecture, indoor light sources, and different kinds of transportation all compose the lit urban night environment. Of these, street lighting is the most continuous, permanent, and intense source of lighting in the urban environment.[48] This continuous increase of nocturnal urban light pollution and exposure to ALAN with different spectral composition, duration, intensity, and spatial pattern affects the natural environment including human health and BC.[6,16,35]

The results of this study indicate a positive strong association between exposure to outdoor ALAN per road length and SMR_{35-74} per SA size (km^2). Since it is an ecological study lacking individual data and limited in data on potential confounders, it cannot provide a cause for BC morbidity; rather, it points to the aforementioned association between an exposure and an outcome. In this study, we point for the first time, to the best of our knowledge, to the importance of the geographical scenery together with the urban light performance (*de facto*) in relation to BC morbidity using a new 3-"dimensional" (3D) calculation method. This new suggested method integrates and controls 3 potentially affecting variables (light intensity per road length, SA size, and age) into a single correlation in order to obtain more accurate and significant results in a specific area. These results will help us lighten areas at risk and look for tailor-made solutions in order to reduce the hazard in those areas.

The first indication was achieved by correlating road length (as a proxy for light exposure) with BC SMRs. Results (moderate positive with marginal significance) indicated a probability to integrate road length into a new variable in order to enhance the expression of the spatial distribution of light. Dispersion of *in situ* outdoor light intensities along a specific road length of every SA enabled us to identify disparities that eventually displayed a significant positive strong association with BC-morbidity.

Using the measures of central tendency helped us represent light intensity in the study area. The following results of mean lux/km and median lux/km correlated significantly with BC SMR_{35-74}/km^2. Furthermore, both measures were significantly higher in the southern part of the city. In addition, the SD measure provided us with the range of light intensity in each SA. Measuring light intensity in the city of Ashkelon presented us a significant difference between the northern part and the southern part. In the northern part of the city, we find better maintained light infrastructure with relatively small SD intensity affected by a continuum of functioning street illumination. However, in the southern part of the city SD was greater and it represents a large range of light intensities from strong lightened areas to very dark areas. In Ashkelon, like in most of the developed world, much of the lighting infrastructure has aged. Monitoring streetlights is a manual task that relies on inspection and incident reports. Furthermore, the means to monitor how much light reaches the street or penetrates human's indoor habitat are limited and therefore we find a large range of light intensities in the city of Ashkelon, as in other places.[49] However, typical light intensity in most homes range from 100 to 300 lux, main road street lighting (average street-level illuminance) is approximately 15 lux, lighted parking lot present about 10 lux, and residential side street (average street-level illuminance) is approximately 5 lux.[50]

Results of a study conducted by Burgess and Molina in 2014 show that subjects who were exposed to light of approximately 65 lux in their homes delayed their MLT onset by an average of 1:03 hours.[51] A phase delay of about 1 hour has been shown to negatively affect alertness[52] and performance.[53,54] Moreover, exposure to typical indoor low light intensity of ~100 lux during the early biological night can also suppress MLT levels.[37,55] Nevertheless, most people are exposed to both indoor and outdoor ALAN, even in relatively low intensities, as we presented in our study. Therefore, a probable additive effect of the exposure to light emerging from both environments may cause a significant inhibition of MLT production.[50] Low MLT levels are associated with numerous diseases including BC,[18,31,56,57] presumably through epigenetic changes such as global DNA methylation.[58,59] The intensity and duration of ALAN required to disorder circadian rhythms and MLT production under field conditions is unknown,[50] but numerous studies suggest impacts on species, including humans, affected by prevalent low-intensity light such as urban sky glow or vehicle lights.[50,60] Following this information, light thresholds are crucial in order to have the opportunity to avoid light health consequences. In this study, we tried to expose a possible lighting threshold from the data collected in the field. The percentage of light points (in every SA) above the median light intensity of SA 315 (16.3 lux) in the southern part of the city presented a positive marginally significant association with SMR_{35-74}/km^2. This median light intensity, which is also the highest median result obtained in all SAs, was prominent over other medians, with a marginal significant positive result. Therefore, we suggest this may be a threshold that can influence BC morbidly. SA 315 is the smallest of all the SAs measured, with no apparent difference in land uses. It is surrounded with relatively main roads as in other SAs. However, possibly because it is the smallest, light reflects and influences much of the area and therefore light intensity measured is greater. Additional results from this study support this supposition; mean light intensity in SA 315 is the highest (15.99 lux), BC density in this SA is of the highest calculated in the research (133.02 total BC cases per SA size), and calculated SMR_{35-74}/km^2 in SA 315 is the highest (6.44). However, traditional SMR calculation for this SA shows a lower BC SMR than expected (SMR 0.82, CI 0.42-1.44) and is in contradiction with this idea. Traditional SMR represents only one dimension, age, and does not refer to the other affecting variables. Therefore, this probably can explain the difference in the results. Nevertheless, further field and laboratory study with a greater sample size is needed in order to establish this preliminary supposition of the suggested threshold.

Advanced study of the disparities between the northern part of the city and the southern part of the city shows that the southern part displays significantly higher ALAN levels per road length in all ALAN variables and significantly higher rates of BC density. However, marginal significantly higher rates of traditional SMR_{35-74} were revealed in the north of the city and no significant difference between the 2 parts regarding the new calculated SMR_{35-74}/km^2. These diverse results may be due to the sample size, classification method of BC cases per SA, or not taking into consideration all affecting variables. We should consider examining the association between light intensity and BC SMR along highly illuminated transportation routes (mainly SWL illuminated) and, separately, residential areas with low typical light intensity. This way we would use light homogenous geographical areas rather than using heterogenic light distribution in a defined SA. Other risk factors tested like birth rates do not support the trends we revealed in our study. We find no correlation between SMR_{35-74}/km^2 and birth rates. Higher birth rates are associated with lower BC risk,[61] with no reference to SA size. However, 2 varied results regarding per capita income were obtained. Higher per capita income is correlated with higher BC risk[62] as the traditional SMR presents in the northern part of the city but higher SMR_{35-74}/km^2 are significantly correlated with low income, as was revealed in our study.

Limitations of the Study

1. A small sample size was collected (11 SAs); nevertheless, results are significant and support the hypothesis.

2. Light intensity measure (mean, median, and SD) of SA 315 was suspected as an outlier. Discarding this point from the statistical analysis still produced significant results. Therefore, we assumed it is part of the city's diversity in light intensity and therefore we included it in the final analysis, supporting positive strong correlations.
3. BC cases were divided into SAs using zip codes with no accurate address, which could affect the calculated SMR.
4. The spectral composition and duration of light were not measured.
5. Since this is an ecological study (lacking individual data), we cannot point to causation but only an association between ALAN and BC SMR that should be further examined.
6. In this study, we focused on limited risk factors. We did not study the influence of lifestyle including physical activity and dietary habits, ethnic differences (although most of the population is Jewish and thus diversity is reduced to a minimum) and environmental pollutants, such as from the power plant. Regarding air pollution, the literature points it as a risk factor for lung cancer but not BC.[63] Nevertheless, any documented risk factors that we did not study should be included in a future study.
7. We did not refer to the differences in land use between the SAs. However, concerning this study, those differences are reflected in the measured light intensities.
8. The city of Ashkelon is situated near a conflict area and its inhabitants are suffering from continuous stress. This may be a risk factor that should be tested in a different study.

Conclusion

There is growing evidence of the nexus between ALAN, circadian disruption, MLT, and BC etiology at the population level. Different strategies are used to study this nexus including using satellite ALAN data to detect highly polluted areas. Nevertheless, in this study we present for the first time, to the best of our knowledge, a different strategy to assess light pollution and its influence on BC morbidity ratios. *In situ* light measurements per road length were used to correlate with SMR per SA size. Results support our hypothesis that outdoor ALAN illumination is associated with a higher BC SMR in a specific age group. Therefore, women who had been living in areas with higher levels of outdoor light per road length presented higher BC SMRs per SA size. Moreover, we suggested an outdoor light threshold of approximately 16 lux at 140 cm height as the minimal intensity to affect pineal MLT levels and BC morbidity. Nevertheless, one must bear in mind that we did not refer to timing, duration, and spectrum of exposures. These preliminary suppositions should be tested in future studies together and distinctly to indoor lighting. Therefore, we suggest a new measure to examine ALAN influence on BC SMR while using the specific geographical scenery of the study area. This measure will help monitor areas at risk and help better understand the spatial distribution of light with regard to BC morbidity.

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Declaration of Conflicting Interests

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References

1. World Health Organization. Breast cancer: prevention and control. http://www.who.int/cancer/detection/breastcancer/en/index2.html. Accessed September 2, 2016.
2. Pevet P, Challet E. Melatonin: both master clock output and internal time-giver in the circadian clocks network. *J Physiol Paris*. 2011;105:170-182.
3. Gaston KJ, Duffy JP, Gaston S, Bennie J, Davies TW. Human alteration of natural light cycles: causes and ecological consequences. *Oecologia*. 2014;176:917-931.
4. Arendt J. Melatonin and the pineal gland: influence on mammalian seasonal and circadian physiology. *Rev Reprod*. 1998;3:13-22.
5. Holker F, Wolter C, Perkin EK, Tockner K. Light pollution as a biodiversity threat. *Trends Ecol Evol*. 2010;25:681-682.
6. Falchi F, Cinzano P, Elvidge CD, Keith DM, Haim A. Limiting the impact of light pollution on human health, environment and stellar visibility. *J Environ Manage*. 2011;92:2714-2722.
7. Stevens RG, Blask DE, Brainard GC, et al. Meeting report: the role of environmental lighting and circadian disruption in cancer and other diseases. *Environ Health Perspect*. 2007;115:1357-1362.
8. Thapan K, Arendt J, Skene DJ. An action spectrum for melatonin suppression: evidence for a novel non-rod, non-cone photoreceptor system in humans. *J Physiol*. 2001;535:261-267.
9. Gooley JJ, Rajaratnam SM, Brainard GC, Kronauer RE, Czeisler CA, Lockley SW. Spectral responses of the human circadian system depend on the irradiance and duration of exposure to light. *Sci Transl Med*. 2010;2(31):31ra33.

10. Brainard GC, Hanifin JP, Greeson JM, et al. Action spectrum for melatonin regulation in humans: evidence for a novel circadian photoreceptor. *J Neurosci*. 2001;21:6405-6412.
11. Czeisler CA, Duffy JF, Shanahan TL, et al. Stability, precision, and near-24-hour period of the human circadian pacemaker. *Science*. 1999;284:2177-2181.
12. Ralph MR, Foster RG, Davis FC, Menaker M. Transplanted suprachiasmatic nucleus determines circadian period. *Science*. 1990;247:975-978.
13. Straif K, Baan R, Grosse Y, et al. Carcinogenicity of shift-work, painting, and fire-fighting. *Lancet Oncol*. 2007;8:1065-1066.
14. American Medical Association. AMA adopts community guidance to reduce the harmful human and environmental effects of high intensity street lighting. http://www.ama-assn.org/ama/pub/news/news/2016/2016-06-14-community-guidance-street-lighting.page. Published June 14, 2016. Accessed September 2, 2016.
15. Cajochen C, Münch M, Kobialka S, et al. High sensitivity of human melatonin, alertness, thermoregulation, and heart rate to short wavelength light. *J Clin Endocrinol Metab*. 2005;90:1311-1316.
16. Haim A, Portnov BA. *Light Pollution as a New Risk Factor for Human Breast and Prostate Cancers*. Berlin, Germany: Springer; 2013.
17. Hill SM, Belancio VP, Dauchy RT, et al. Melatonin: an inhibitor of breast cancer. *Endocr Relat Cancer*. 2015;22:R183-R204.
18. Blask DE. Melatonin, sleep disturbance and cancer risk. *Sleep Med Rev*. 2009;13:257-264.
19. Gaston KJ, Visser ME, Holker F. The biological impacts of artificial light at night: the research challenge. *Philos Trans R Soc Lond B Biol Sci*. 2015;370(1667). doi:10.1098/rstb.2014.0133.
20. Carrillo-Vico A, Guerrero JM, Lardone PJ, Reiter RJ. A review of the multiple actions of melatonin on the immune system. *Endocrine*. 2005;27:189-200.
21. Folkard S. Do permanent night workers show circadian adjustment? A review based on the endogenous melatonin rhythm. *Chronobiol Int*. 2008;25:215-224.
22. Emet M, Ozcan H, Ozel L, Yayla M, Halici Z, Hacimuftuoglu A. A review of melatonin, its receptors and drugs. *Eurasian J Med*. 2016;48:135.
23. Seto KC, Guneralp B, Hutyra LR. Global forecasts of urban expansion to 2030 and direct impacts on biodiversity and carbon pools. *Proc Natl Acad Sci U S A*. 2012;109:16083-16088.
24. Ferlay J, Shin H, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*. 2010;127:2893-2917.
25. Vlahov D, Galea S. Urbanization, urbanicity, and health. *J Urban Health*. 2002;79(1):S1-S12.
26. Israel Central Bureau of Statistics. http://www.cbs.gov.il/ishuvim/ishuv2013/info2013.pdf [in Hebrew]. Accessed November 1, 2016.
27. Kerenyi NA, Pandula E, Feuer G. Why the incidence of cancer is increasing: the role of "light pollution". *Med Hypotheses*. 1990;33(2):75-78.
28. Haus EL, Smolensky MH. Shift work and cancer risk: potential mechanistic roles of circadian disruption, light at night, and sleep deprivation. *Sleep Med Rev*. 2013;17:273-284.
29. Kloog I, Haim A, Stevens R, Barchana M, Portnov B, Haifa I. Light at night co-distributes with incident breast but not lung cancer in the female population of Israel. *Chronobiol Int*. 2008;25:65-82.
30. Kloog I, Stevens RG, Haim A, Portnov BA. Nighttime light level co-distributes with breast cancer incidence worldwide. *Cancer Causes Control*. 2010;21:2059-2068.
31. Hurley S, Goldberg D, Nelson D, et al. Light at night and breast cancer risk among California teachers. *Epidemiology*. 2014;25:697-706.
32. Bauer SE, Wagner SE, Burch J, Bayakly R, Vena JE. A case-referent study: light at night and breast cancer risk in Georgia. *Int J Health Geogr*. 2013;12:23.
33. Kim YJ, Lee E, Lee HS, Kim M, Park MS. High prevalence of breast cancer in light polluted areas in urban and rural regions of South Korea: an ecologic study on the treatment prevalence of female cancers based on National Health Insurance data. *Chronobiol Int*. 2015;32:657-667.
34. Keshet-Sitton A, Or-Chen K, Yitzhak S, Tzabary I, Haim A. Can avoiding light at night reduce the risk of breast cancer? *Integr Cancer Ther*. 2015;5:145-152.
35. Keshet-Sitton A, Or-Chen K, Yitzhak S, Tzabary I, Haim A. Light and the city: breast cancer risk factors differ between urban and rural women in Israel [published online July 20, 2016]. *Integr Cancer Ther*. doi:10.1177/1534735416660194.
36. Kloog I, Portnov BA, Rennert HS, Haim A. Does the modern urbanized sleeping habitat pose a breast cancer risk? *Chronobiol Int*. 2011;28:76-80.
37. Cajochen C, Zeitzer JM, Czeisler CA, Dijk D. Dose-response relationship for light intensity and ocular and electroencephalographic correlates of human alertness. *Behav Brain Res*. 2000;115:75-83.
38. Owen J, Arendt J. Melatonin suppression in human subjects by bright and dim light in Antarctica: time and season-dependent effects. *Neurosci Lett*. 1992;137:181-184.
39. McPherson K, Coope PA, Vessey MP. Early oral contraceptive use and breast cancer: theoretical effects of latency. *J Epidemiol Community Health*. 1986;40:289-294.
40. MacMahon B, Cole P, Brown J. Etiology of human breast cancer: a review. *J Natl Cancer Inst*. 1973;50:21-42.
41. Armenian HK. Incubation periods of cancer: old and new. *J Chronic Dis*. 1987;40(suppl 2):9S-15S.
42. Israeli Ministry of Health. Israel cancer incidence by districts 2001-2011 [in Hebrew]. http://www.health.gov.il/PublicationsFiles/ICR_20102014.pdf. Accessed September 3, 2016.
43. Israeli Central Bureau of Statistics. Population and density per sq.km. in localities numbering 5000 residents and more on 31.12.2014. http://cbs.gov.il/shnaton66/st02_24.pdf. Accessed September 3, 2016.
44. Degani R. Characteristics of the residential market in Ashkelon and marketing policy recommendations of land [in Hebrew]. http://www.moch.gov.il/SiteCollectionDocuments/research/r0016.pdf. Accessed September 7, 2016.
45. Israeli Central Bureau of Statistics. 2008 Census data [in Hebrew]. http://www.cbs.gov.il/census/census/pnimi_sub2_

profiles.html?MIval=%2Fcensus%2Fpnimi_sub2_profiles.html&id_topic=11&id_subtopic=1&id_subtopic2=1&Shem_Yishuv=%E0%F9%F7%EC%E5%EF. Accessed September 7, 2016.
46. Israeli Central Bureau of Statistics. Compendium of maps—Society in Israel Report No. 7, 2014 [in Hebrew]. http://www.cbs.gov.il/publications14/rep_07/pdf/maps_h.pdf. Accessed September 7, 2016.
47. Grimm NB, Faeth SH, Golubiewski NE, et al. Global change and the ecology of cities. *Science*. 2008;319:756-760.
48. Gaston KJ, Davies TW, Bennie J, Hopkins J. Review: reducing the ecological consequences of night-time light pollution: options and developments. *J Appl Ecol*. 2012;49:1256-1266.
49. Kumar S, Deshpande A, Ho SS, Ku JS, Sarma SE. Urban street lighting infrastructure monitoring using a mobile sensor platform. *IEEE Sens J*. 2016;16:4981-4994.
50. Gaston KJ, Bennie J, Davies TW, Hopkins J. The ecological impacts of nighttime light pollution: a mechanistic appraisal. *Biol Rev Camb Philos Soc*. 2013;88:912-927.
51. Burgess HJ, Molina TA. Home lighting before usual bedtime impacts circadian timing: a field study. *Photochem Photobiol*. 2014;90:723-726.
52. Taylor A, Wright HR, Lack LC. Sleeping-in on the weekend delays circadian phase and increases sleepiness the following week. *Sleep Biol Rhythms*. 2008;6:172-179.
53. Burgess HJ, Legasto CS, Fogg LF, Smith MR. Can small shifts in circadian phase affect performance? *Appl Ergon*. 2013;44:109-111.
54. Yang C, Spielman AJ. The effect of a delayed weekend sleep pattern on sleep and morning functioning. *Psychol Health*. 2001;16:715-725.
55. Zeitzer JM, Dijk D, Kronauer RE, Brown EN, Czeisler CA. Sensitivity of the human circadian pacemaker to nocturnal light: melatonin phase resetting and suppression. *J Physiol*. 2000;526:695-702.
56. Hardeland R. Melatonin in aging and disease—multiple consequences of reduced secretion, options and limits of treatment. *Aging Dis*. 2014;3:194-225.
57. Hrenak J, Paulis L, Repova K, et al. Melatonin and renal protection: novel perspectives from animal experiments and human studies. *Curr Pharm Des*. 2015;21:936-949.
58. Schwimmer H, Metzer A, Pilosof Y, et al. Light at night and melatonin have opposite effects on breast cancer tumors in mice assessed by growth rates and global DNA methylation. *Chronobiol Int*. 2014;31:144-150.
59. Haim A, Zubidat AE. Artificial light at night: melatonin as a mediator between the environment and epigenome. *Philos Trans R Soc Lond B Biol Sci*. 2015;370(1667). doi:10.1098/rstb.2014.0121.
60. Lyytimäki J, Tapio P, Assmuth T. Unawareness in environmental protection: the case of light pollution from traffic. *Land Use Policy*. 2012;29:598-604.
61. Bernstein L. Epidemiology of endocrine-related risk factors for breast cancer. *J Mammary Gland Biol Neoplasia*. 2002;7:3-15.
62. Lehrer S, Green S, Rosenzweig KE. Affluence and breast cancer. *Breast J*. 2016;22:564-567.
63. Danaei G, Vander Hoorn S, Lopez AD, Murray CJ, Ezzati M; Comparative Risk Assessment Collaborating Group (Cancers). Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. *Lancet*. 2005;366:1784-1793.