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GLOBAL CO-DISTRIBUTION OF LIGHT AT NIGHT (LAN) AND CANCERS OF PROSTATE, COLON, AND LUNG IN MEN

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The incidence rates of cancers in men differ by countries of the world. We compared the incidence rates of three of the most common cancers (prostate, lung, and colon) in men residing in 164 different countries with the population-weighted light at night (LAN) exposure and with several developmental and environmental indicators, including per capita income, percent urban population, and electricity consumption. The estimate of per capita LAN exposure was a novel aspect of this study. Both ordinary least squares (OLS) and spatial error (SE) regression models were used in the analysis. We found a significant positive association between population exposure to LAN and incidence rates of prostate cancer, but no such association with lung cancer or colon cancer. The prostate cancer result is consistent with a biological theory and a limited number of previous studies of circadian disruption and risk. The LAN-prostate cancer connection is postulated to be due to suppression of melatonin and/or disruption of clock gene function. An analysis holding other variables at average values across the 164 countries yielded a risk of prostate cancer in the highest LAN-exposed countries 110% higher than in the lowest LAN exposed countries. This observed association is a necessary condition for a potentially large effect of LAN on risk of prostate cancer. However, it is not sufficient due to potential confounding by factors that increase the risk of prostate cancer and are also associated with LAN among the studied countries. (Author correspondence: portnov@nrem.haifa.ac.il)

Keywords Prostate cancer, Epidemiology, Geography, Incidence rates, LAN

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INTRODUCTION

Male cancer rates tend to vary worldwide, showing high incidence rates in some countries and relatively low ones in others. According to the World Health Organization (WHO), prostate cancer is the most common cancer in men, with some 245,000 males succumbing to it annually worldwide (American Cancer Society, 2007). In Bangladesh, its age-standardized rate (ASR) does not exceed 0.3 per 100,000, while in the United States, it reaches 124.8 per 100,000. The second most common cancer in men (and with a greater mortality) is lung cancer, which shows a similar variation of ASRs. In Fiji, lung cancer ASR does not exceed 0.5, while in Hungary, it is 94.6 cases per 100,000 (see Figure 1).

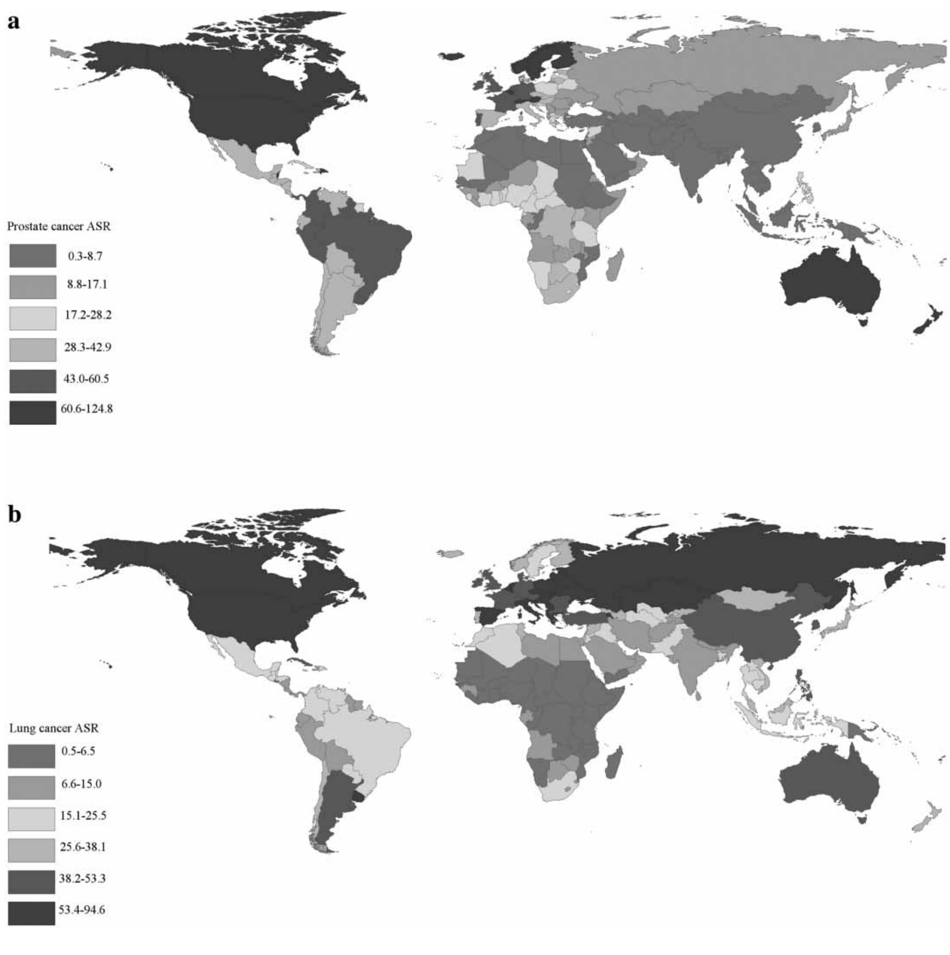

FIGURE 1 Worldwide distribution of (a) prostate and (b) lung cancers (age-standardized rates per 10,000 residents). Mapped using data from the International Agency for Research on Cancer (IARC; Parkin et al., 2005).

A comprehensive study of global differences in cancer rates has been conducted by the International Agency for Research on Cancer (IARC; see Parkin et al., 2001a, 2001b, 2005). During this ongoing research, the estimates of prevalence, mortality, and incidence of the 26 most common cancers were collected for 20 geographic regions of the world. Although the IARC study is apparently the most comprehensive analysis of global patterns of cancer morbidity and mortality carried out to date, it does not discuss in detail the possible risk factors and their association with cancer rates.

Although several population-level studies of cancer risk factors have been carried out, most of these studies were focused on specific cancers (such as breast and liver cancers) and mainly among women (Althuis et al., 2005; Bonner et al., 2005; Bray et al., 2004; Brody et al., 2007; Kloog et al., 2008). The present study attempts to investigate the relationships between light at night (LAN) and the incidence of the three most common cancers in men worldwide (i.e., prostrate, lung, and colon cancer), using age-standardized rates (ASR) of male cancers available for 164 countries. This new analysis is an extension of previous work showing a significant co-distribution of LAN and breast cancer in women in Israel (Kloog et al., 2008). Several other population-level variables that are thought to have an effect on cancer risk are also included in the analysis. Our a priori hypothesis was that LAN would be significantly associated with risk of prostate but not lung cancer in men. To the best of our knowledge, this study is a novel one and the first of its kind to link worldwide male cancer rates and various risk factors (including exposure to LAN) on a global level.

The results of population level, or ecological, studies are important in providing context for studies in subpopulations of people using case-control and cohort designs. If no association is found at the population level in a study with good statistical power, then that would be evidence against a strong effect of a putative risk factor. A positive association is a necessary precondition for there to be a wide effect in society at large, taking into account the accepted statistical tools used in epidemiology studies. We predicted an association of LAN with prostate cancer based on a biological theory (Stevens et al., 2007) and limited epidemiology (Conlon et al., 2007; Kakizaki et al., 2008; Kubo et al., 2006), but no association with lung cancer.

RESEARCH METHOD

Cancer Data

The data on cancer ASRs in men were obtained from the GLOBOCAN 2002 database, maintained by the IARC (Parkin et al., 2005). ASR is a summary measure of a rate that a world population would have if it had a standard age structure (Parkin et al., 2005) and is calculated per 100,000 residents per year. The cancer data for 2002, the most recent data available, were used in the study. Data were obtained for the three most common cancers in men—prostate, lung, and colon—which worldwide account for about 38% of all new cases of cancer in men annually (American Cancer Society, 2007). The conduct of this study conformed to the ethical standards of this journal (Portaluppi et al., 2008).

Explanatory Variables

Descriptive statistics of the research variables used in the analysis are presented in Appendix A.

GDP per Capita

GDP per capita ($US) is a commonly used measure of population welfare that reflects differences in the diet and lifestyles of different socio-economic strata (Hulshof et al., 1991, 2003). As several previous studies indicated, cancer rates tend to be higher among high income than across low income strata and are significantly higher in developed than in developing countries (American Cancer Society, 2006; Bray et al., 2004).

LAN Emission

According to several recent studies, excessive exposure to LAN may be a risk factor for developing certain cancers (Anisimov 2006; Haus, 2007; Kloog et al., 2008; Stevens, 2005; Verkasalo et al., 1999) hypothesized to be affected by circadian disruption. A variety of mechanisms have been proposed, including suppression of melatonin (MLT) secretion by the pineal gland leading to increased tumor growth (Blask et al., 2005), depression of immune and thermoregulatory functions (Haim et al., 2005; Nelson, 2004), and/or direct disruption of clock gene function in the suprachaismatic nuclei leading to alterations in cell-cycle regulation (Stevens & Rea, 2001). The LAN variable was thus used to explore whether country-specific cancer rates tend to increase with exposure to LAN. Using simple average country LAN exposure estimates may result in a bias, caused by a country's differences in geography and population structure. For instance, if simple country-wide LAN averages are calculated, large and unevenly populated countries, such as Canada and Australia, are likely to exhibit very low average levels of LAN. To minimize this bias, we used a novel method of calculating LAN exposure, which took into account both a country's geographic distribution of population and its local LAN intensities (see the subsection on GIS analysis for more detail).

Percent Urban Population

Living in cities is often associated with a considerable amount of physiological stress as a consequence of high residential densities, traffic congestion, and air pollution, which may increase cancer risk (Han & Naeher, 2006). In addition, residents of urban areas are exposed to more environmental, second-hand smoking due to high residential densities, which is another cause of cancer (Volzke et al., 2006). Dietary differences and reduced physical activity associated with urban living may also play a role in the development of cancer.

Electricity Consumption (kWh per Capita)

Electricity consumption may be an indicator of socio-economic development and industrial emission of gaseous substances associated with electricity production (Gram-Hansenn & Petersen, 2004; Jumbe, 2004). Per capita electricity consumption may also serve as a proxy for electromagnetic field exposure (EMF) exposure, which, although controversial as a causal agent, could be a possible risk factor for the development of cancer (Davis et al., 2006; Demers et al., 1991; Roosli et al., 2007).

Regional Indicators

Our preliminary examination of cancer distribution maps (see Figure 1) revealed clusters of countries with quite similar cancer rates (e.g., East Asia is a clear example of such clustering). In order to take this ASR clustering into account, several dichotomous variables (termed "regional indicators") were included in the analysis as additional predictors: Middle East, Africa, East Europe, Asia, South America, and Middle Asia. Each indicator takes on value 1 if a country is located in a particular geographic region and zero otherwise (such as in North America, Australia, and Western Europe).

Data Sources

Data for the present analysis were obtained from the two main sources. Country-level data on per capita GDP, percent urban population, and per capita electricity consumption for 1998–1999 were obtained from the ESRI ArcGIS ™ database and the CIA World Fact Book (Central Intelligence Agency, 2006; ESRI, 2007). Data on nighttime illumination (LAN) were obtained from the U.S. Defense Meteorological Satellite Program

(DMSP, 2004). The DMSP satellite provides continuous reading of the entire Earth surface during the nighttime as it cycles around the globe. The satellite image for 1996/97, used in the analysis, was constructed by the DMSP by averaging daily readings of the satellite sensors and removing cloud cover.

GIS Analysis

In recent years, Geographic Information Systems (GIS) have become an important research tool for cancer-related studies (Banerjee et al., 2003; Kloog et al., 2008; Krieger et al., 2002; Maheswaran et al., 2002; O'Leary et al., 2004; Scott et al., 2002). In these studies, GIS is used to calculate the distance between residences and hazardous waste sites, as well as to account for the spatial clustering and variation of cancer cases and to capture spatio-temporal heterogeneity in survival patterns. In the present study, GIS technology was used for matching country-specific cancer rates with the LAN levels obtained from satellite images. The task was performed using the "spatial join" tool in the ArcGIS 9™ software, which joins data from two geographic layers by appending attributes from one layer to another, based on the relative location of features in the layers (Minami & ESRI, 2000).

The "spatial join" was performed in two steps. In the first step, a worldwide radiance-calibrated satellite image of nighttime illumination, which reports average nightlight intensity in 1996/97 measured in light radiance units (i.e., nanowatts/cm^2/sr), was imported to the ArcGIS 9™ software. The image reflects a fraction of light escaped into the space and detected by the satellite's sensors. Although these satellite measurements are a magnitude lower than actual LAN levels detected on the ground, they represent accurately the relative levels of nightlight intensity observed in the localities (DMSP, 2004). The original image size was 43,200 by 21,600 pixels, with an average pixel size of about 350 × 350 meters. The geostatistical tools available in GIS for working with raster (pixel) images are rather limited. Therefore, for the consequent analysis, the original nighttime illumination image was converted into a vector map using the ArcGIS 9™ "raster-to-feature" conversion tool. The conversion resulted in a polygon layer (i.e., map) containing approximately 3,800,000 polygons characterized by various LAN intensities, with a minimum LAN value of 0 (no illumination) and a maximum value of 255 nanowatts/cm^2/sr (maximum illumination).

The polygon layer thereby obtained was overlapped with a map showing the location of all major populated places (>1,000 residents) of the world obtained from the Geonames database (Geonames, 2008). In the next step, average LAN values were calculated for each populated place i by obtaining LAN values from the LAN intensity polygon into which the populated place i fell. The locality-specific LAN values (LAN_i) obtained were then multiplied by the population size of localities (POP_i) and summed for each country j under study. Next, these summary values were divided by the total population size of the country's populated places (ΣPOP_{ij}) to obtain the average LAN exposure estimate per person ($\overline{LAN_j}$) in each country (j) under study (see Appendix 2):

$$\overline{LAN}_j = \sum_{i=0}^{n} LAN_{ij} \times POP_{ij} / \sum_{i=0}^{n} POP_{ij}$$

where n is the total number of populated places in country j.

Statistical Analysis

To identify and measure the significance of factors affecting the selected cancer rates, several statistical techniques were used. First, we started with an ordinary least squares (OLS) model. During the analysis, multicollinearity and normality were tested, and their results were found satisfactory (tolerance > 0.4). (The tolerance statistic estimates the degree of inter-collinearity between independent variables; its values vary between 0 and 1, with values approaching zero indicating that a strong multicollinearity may be present. In econometric studies, tolerance values greater than 0.1 are considered to be satisfactory [Kinnear & Gray, 2007]. The tolerance value of 0.4 is considerably higher than 0.1, thus indicating that the multicollinearity between the explanatory variables is well within acceptable limits.) The analysis was performed separately for all cancer types using the following linear model:

$$\begin{aligned}\text{Cancer incidence rate} = {} & \text{B0(constant)} + \text{B1}^*\text{(electricity consumption)} \\ & + \text{B2}^*\text{(GDP per capita)} + \text{B3}^*\text{(LAN)} \\ & + \text{B4}^*\text{(percent of urban population)} \\ & + \text{B5}^*\text{(Middle East)} \\ & + \text{B6}^*\text{(Africa)} + \text{B7}^*\text{(East Europe)} \\ & + \text{B8}^*\text{(Asia)} + \text{B9}^*\text{(South America)} \\ & + 10^*\text{(Middle Asia) and} + \varepsilon\,\text{(random error term)}\end{aligned}$$

where B0, . . . , B10 are regression coefficients. During the analysis, several other functional forms of the model (e.g., log-linear and double-log forms) were tested, and only the results of the best performing (linear) model are reported in the following discussion.

The residuals of the OLS model were tested for the presence of spatial autocorrelation using the Moran's I test statistic. The test showed significant clustering of residuals (Z-Moran's I = 0.535–4.372, $p < 0.001$), which necessitated the use of spatial dependency (SD) models to take the spatial dependency of residuals into account and improve the robustness of regression estimates (Anselin, 1999). The spatial error regression tests were performed using the GeoDa^{TM} spatial analysis software. In addition to standard statistical tools, GeoDa^{TM} includes a range of spatial autocorrelation tools, which take into account the degree of spatial dependency between neighboring observations (Anselin et al., 2005).

In recent years, spatial auto-correlation (SAC) and spatial auto-regression (SAR) analysis has gained momentum in ecological and epidemiology studies (Clayton et al., 1993; Portnov et al., 2007; Rezaeian et al., 2006). SAC/SAR techniques help to examine the relationship between a value of a variable at one location and nearby values of the same variable, making it possible to accommodate spatial dependency effects in conventional linear statistical models (Griffith, 2003).

RESULTS

Table 1 shows the risk factors affecting leading male cancer rates. All models in Table 1 are OLS models, estimated separately for the following three cancer types: prostate, lung, and colon. The models appear to provide a very good fit ($R^2 = 0.762–0.785$) and have a high degree of generality ($F = 38.240–55.940$, $p < 0.001$).

As expected, per capita GDP (ln) is positively associated with ASRs across all models (see Table 1). Only lung cancer appears to exhibit a significantly positive association between ASR and percent country's urban population.

Among the three cancers analyzed, only prostate cancer exhibited a significant positive correlation with LAN exposure (b = 0.150, t = 2.916, $p < 0.01$) and per capita electricity consumption (b = 0.012, t = 3.683; $p < 0.01$).

Notably, in most models, regional indicators emerged as highly significant ($p < 0.01$), thus indicating that cancer rates do appear to cluster regionally. Thus, for example, in the case of prostate cancer, regional indicators for Africa, Middle East, Eastern Europe, Central Europe, and Asia exhibited a negative sign, implying that in these regions prostate cancer ASRs appear to be significantly lower than in Western Europe and North America. In contrast, lung cancer rates in Eastern Europe appear to be higher than elsewhere, as indicated by significant positive signs of their regional indicators ($p < 0.01$). This may be due to a having large share of traditional industries and widespread tobacco smoking. Because most models exhibited significant Z-Moran's I values (0.535–4.746, $p < 0.001$; see Table 1), thus showing a spatial dependency of regression residuals, spatial error (SE) regression was conducted. The

TABLE 1 Factors affecting male cancer rates (method: OLS regression)

Variable	Prostate		Lung		Colon	
	B*	t†	B*	t†	B*	t†
(Constant)	3.934	0.269	−11.809	−0.882**	−20.724	−2.424#
Electricity consumption per capita (kWh)	0.012	3.683**	0.006	1.836	0.003	1.499
GDP per capita (ln), $US	5.425	3.258**	4.364	2.858**	5.769	5.920**
Light at night (nanowatts/cm^2/sr)	0.150	2.916**	−0.076	−1.608	−0.040	−1.327
Urban population (%)	−0.032	−0.502	0.192	3.304**	0.020	0.537
Middle East	−40.834	−9.651**	−18.649	−4.808**	−19.868	−8.024**
Africa	−24.035	−4.871**	−21.594	−4.774**	−16.243	−5.626**
East Europe	−25.771	−5.819**	25.102	6.183**	5.019	1.936
Central Asia	−38.657	−7.351**	−3.680	−0.763	−17.948	−5.832**
Eastern Asia	−40.553	−8.798**	−7.102	−1.681	−12.900	−4.782**
South America	−2.908	−0.695	−16.553	−4.313**	−15.136	−6.177**
Number of observations‡	164		164		164	
R^2	0.762		0.763		0.785	
R^2 adjusted	0.747		0.748		0.771	
F§	49.106**		49.365**		55.940**	
Z-Moran's‖	0.535		2.720**		4.746**	

*regression coefficient
†*t*-statistic
‡number of valid observations list-wise
§standard error of the estimate
‖Spatial dependency of regression residuals index
#indicates a 0.05 significance level
**indicates a 0.01 significance level

TABLE 2 Factors affecting male cancer rates (method: spatial error model)

	Prostate		Lung		Colon	
Variable	B*	t†	B*	t†	B*	t†
(Constant)	3.951	0.281	−15.010	−1.132	−14.310	−1.694
Electricity consumption per capita (kWh)	0.012	3.728**	0.003	1.935	0.003	2.483#
GDP per capita (ln), $US	5.417	3.389**	3.831	2.649**	4.917	5.309**
Light at night (nanowatts/cm^2/sr)	0.154	3.156**	0.024	0.450	−0.027	−0.814
Urban population (%)	−0.032	−0.530	0.119	2.349#	0.005	0.183
Middle East	−40.863	−10.207**	−6.094	−0.944	−20.115	−5.103**
Africa	−23.961	−5.098**	−10.349	−1.611	−14.053	−3.548**
East Europe	−25.809	−6.143**	11.960	2.021#	11.341	3.109**
Central Asia	−38.751	−7.765**	−7.049	−1.011	−13.524	−3.174**
Eastern Asia	−40.557	−9.240**	1.923	0.385	−9.496	−3.018**
South America	−3.036	−0.766	−1.052	−0.193	−8.011	−2.345#
λ (lambda)‖	−0.043	−0.399	0.971	118.618**	0.876	31.135**
Number of observations‡	164		164		164	
R^2	0.762		0.807		0. 825	
SEE§	11.566		9.567		6.282	
Log likelihood	−634.193		−607.954		−537.928	

*regression coefficient
†z-value
‡number of valid observations list-wise
§standard error of the estimate
‖spatial autoregressive coefficient
#indicates a 0.05 significance level
** indicates a 0.001 significance

results are reported in Table 2. Although the SE models provide better fits than the OLS ones ($R^2 = 0.762–0.785$, see Table 1; vs. $R^2 = 0.762–0.825$; see Table 2), they indicate the same trends as the OLS models, that is, a positive association of most ASR with GDP per capita and the same relationships with LAN and electricity consumption as in the OLS model.

Although throughout the analysis, the multicollinearity of research variables was tested and found within tolerable limits (tolerance > 0.4), even this relatively low level of multi-collinearity may bias regression estimates. Therefore, we used the stepwise multiple regression (SMR) method to include only statistically significant variables in the resulting model. (The SMR method is not used in spatial auto-correlation analysis, and the stepwise selection of predictors was not performed for constructing spatial dependency models.) The results are reported in Table 3. Similar to the previously reported model, LAN, electricity consumption, and per capita GDP emerged as the key factors affecting prostate cancer rates ($p < 0.01$); per capita GDP and percent urban population were the key factors in the lung cancer model ($p < 0.01$); and per capita GDP is a key determinants of colon cancer rates ($p < 0.01$). All regional indicator variables exhibited a negative association with all cancer types, apart from those of East Europe, for which regional indicators exhibited a significant positive association with both lung and colon cancers.

To estimate the relative contribution of LAN to prostate cancer ASRs, we split all the countries in our sample into three groups: countries with minimal LAN exposure (less than 15 nanowatts/cm^2/sr), countries with average LAN exposure (15–57 nanowatts/cm^2/sr), and countries with the highest LAN exposure (greater than 57 nanowatts/cm^2/sr). The Jenks "natural breaks" method of the ArcGIS9™ software was used to classify countries into the groups. This method determines the best arrangement of values into classes by comparing the sum of squared differences of values from the means of their classes, and thus identifies "break points" in the data values by picking the class breaks that best group similar values and maximize the differences between classes (Minami & ESRI, 2000). Next, the values of all other variables (apart from LAN) were set constant to the average values observed in each group, and a sensitivity test of prostate cancer ASRs to changes in LAN values was run, using the "prostate cancer" model reported in Table 1. The results of the sensitivity test are reported in Table 4. As Table 4 shows, with the values of all other variables fixed, the increase of LAN from 8.60 nanowatts/cm^2/sr (the average LAN value in the group of countries with minimal LAN exposure) to 28.95 nanowatts/cm^2/sr (countries with average LAN exposure) corresponds to an increase of 30.5% in prostate cancer ASR. A further increase in LAN value to 99.21 (the maximum LAN exposure) corresponds to an increase of 80.2% in prostate cancer ASR.

TABLE 3 Factors affecting male cancer rates (method: SMR analysis)

Variable	Prostate		Lung		Colon	
	B*	t†	B*	t†	B*	t†
(Constant)	−0.266	−0.023	20.000	−2.144[‖]	−21.617	−2.598[#]
Electricity consumption per capita (kWh)	0.013	3.758[#]	—	—	—	—
GDP per capita (ln),$US	5.468	4.132[#]	4.821	3.804[#]	5.957	7.167[#]
Light at night (nanowatts/cm^2/sr)	0.160	3.224[#]	—	—	—	—
Urban population (%)	—	—	0.207	3.566[#]	—	—
Middle East	−39.599	−11.820[#]	−16.899	−5.313[#]	−19.800	−8.274[#]
Africa	−21.327	−6.318[#]	−17.218	−6.476[#]	−15.946	−5.604[#]
East Europe	−24.069	−7.062[#]	28.552	9.210[#]	5.685	2.270[‖]
Central Asia	−36.100	−8.985[#]	—	—	−17.522	−5.776[#]
Eastern Asia	−38.180	−10.889[#]	—	—	−12.251	−4.707[#]
Latin America	—	—	−13.092	−4.839[#]	−14.633	−6.224[#]
Number of observations‡	164		164		164	
R^2	0.761		0.752		0.779	
R^2 adjusted	0.749		0.742		0.770	
F§	61.777[#]		19.303[#]		78.778[#]	

*regression coefficient
†z-value
‡number of valid observations list-wise
§standard error of the estimate
‖indicates a 0.05 significance level
#indicates a 0.001 significance

TABLE 4 Sensitivity test of prostate cancer ASR to plausible changes in the ground LAN intensity

LAN level	Average LAN value (nanowatts/cm^2/sr)	Estimated ACR (per 100,000 residents)	Percent change
Low	8.60	66.77	—
Medium	28.95	87.11	30.5%
High	99.21	157.01	80.2%

The values of the fixed variables were fixed as follows: GDP per capita = $US 9,000 (the average value for the "high resource" countries under study), urban population = 65.3%, and electricity consumption per capita = 131.870 kWh. In addition, all regional indicators were set to 0 (that is, ASRs are estimated for the "high resource" [i.e., developed] countries).

DISCUSSION

There are considerable regional differences in cancer ASRs in men. While countries in Asia, the Middle East, Africa, and Eastern Europe (considered "low resource" areas) exhibit relatively low cancer rates, most developed countries exhibit very high rates of cancer in men. These differences may be due to a variety of factors, including differences in genetic background, economic status, diet, amount of physical activities, obesity, exposure to environmental pollutants, and medical care, among others. As our analysis indicates, the relative risk of contracting cancer is positively associated with average income of local residents (American Cancer Society, 2006; Bray et al., 2004). Part, but not all, of this excess is probably due to better access to medical and diagnostic procedures in the "high resource" societies (Bradley et al., 2002; Madison et al., 2004; Wells & Horm, 1992). In addition, there appears to be a positive association between income, urban population, and ASRs of lung cancer. This association may be attributed to the fact that people living in urban areas are more exposed to air pollution emanating from industries and motor vehicles, as well as to environmental (second-hand) smoking, due to high residential densities.

We found a significant positive association between exposure to LAN, electricity consumption, and prostate cancer. A similar association between LAN exposure and breast cancer in women was reported in previous studies (Anisimov, 2006; Kloog et al., 2008; Stevens, 2005; Stevens & Rea, 2001; Stevens et al., 2007; Verkasalo et al., 1999). There is, of course, the potential for confounding by known and unknown factors for which we could not adjust. However, for this to have occurred, the relative risk associated with the confounder would have to be very high, and the confounder would also have to be tightly correlated with LAN exposure in the localities studied (Blair et al., 2007).

The estimate of per capita LAN exposure was a novel aspect of this study. This estimate was calculated as the average LAN exposure per person in each country under study. If there were no considerable misbalance between proportional shares of male and female populations in localities, the index in question provides a fairly unbiased LAN exposure estimate for both men and women.

Although there have been some animal experiments (Anisimov et al., 1997) and epidemiological research (Schernhammer et al., 2003) suggesting there might be an association between LAN exposure, circadian disruptions, and low MLT levels and colon cancer, the number of such studies is small and do not seem to be sufficient for drawing general conclusion on an association between LAN and colon cancer. The lack of any association between LAN and colon cancer in men in this study may add evidence that LAN is probably not a major risk factor at the population level.

Due to limitations on data availability, other risk factors, including occupation, alcohol consumption, smoking, and additional factors could not be addressed by the analysis, though the per capita income variable may capture some of their effects. In addition, it should be noted that dynamics of population movement as well as behavioral patterns that limit exposure to LAN were also not covered by the study due to unavailable data. Such information can be obtained by studies carried out on a smaller scale, such as localities within an urban space, but not on a global level. Another potential limitation is in the completeness of cancer detection and registration in developing counties where LAN exposure is low. Parkin et al. (2001c) conducted a detailed analysis of cancer registration in Kampala, Uganda, over a period of 1994 to 1996, and concluded that "it gives reassurance that published incidence rates are reasonably accurate."

In many cases, environmental health problems are better addressed by large-scale population level studies than by individual-level investigations, due to the occurrence of a large number of low-level exposures (Pekkanen & Pearce, 2001). However, a substantial drawback of population-level studies is that those associations that occur at an aggregated level may be subject to ecological confounding or fallacy (Robinson, 1958; Selvin, 1958). Several techniques were used to reduce the possibility of ecological confounding, including grouping by geographic areas and adjusting for some potential confounders, such as income levels (GDP per capita) and percent urban population, which among other things reflects population density (Elliot, 1996; Morgenstern & Thomas, 1993).

Because the results of the present study are specific for cancer in men, future studies should include a comparison of the results to a similar study done with female cancer rates. Other risk factors, such as diet, smoking habits, alcohol consumption, and family and work history, which were missing from our analysis due to lack of available data, should also be considered and added to the analysis in future studies. Information on these factors might enable a more precise estimate of the association of nocturnal light level and risk of cancer. In addition, as noted above, if any of these factors is very strongly related to risk and also with light level, then estimates of the association of light level and risk might change. To the best of our knowledge, the present analysis is the first to identify the relationship between LAN and the incidence of the most common cancers in men on a worldwide basis.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

APPENDIX A

TABLE A1 Descriptive statistics of the research variables*

Variable	Measurement unit	Minimum	Maximum	Mean	Standard deviation
Dependent variables					
Colorectal cancer	ASR per 100,000†	1.00	58.50	16.08	14.65
Lung cancer	ASR per 100,000†	0.05	94.60	25.47	21.86
Prostate cancer	ASR per 100,000†	0.30	124.80	26.47	23.80
Explanatory variables					
Electricity consumption per capita	kWh per capita	0.01	3367.42	75.66	295.29
GDP per capita	US$	463	32021	6545.73	7315.17
Light at night	Nanowatts/cm^2/sr	0.00	143.34	8.23	22.43
Urban population	% of residents living in urban areas	6.16	100.00	55.16	23.31

*Total number of cases = 164
†Age-standardized rates per 100,000 residents per year

APPENDIX B

TABLE A2 Average LAN exposure in selected countries

Country	Average LAN exposure per person (nanowatts/cm^2/sr)
Nepal	0.002
Laos	0.038
India	0.059
Guatemala	0.451
Egypt	2.028
Argentina	4.501
Israel	10.707
United States	57.540

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