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Observational Study

Artificial night light and thyroid cancer

Artificial light and thyroid cancer

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Abstract

BACKGROUND

The occurrence of thyroid cancer (TC) has increased in recent decades. Exposure to Outdoor Artificial Light at Night (ALN) is associated with an increased risk of cancer.

AIM

In this study, we investigated the impact of ALN, as a significant environmental pollutant, on TC incidence worldwide.

METHODS

The assessment involved analyzing satellite ALN data in conjunction with TC incidence data (Adjusted Standardized Rate, ASR), while considering the quality of cancer registries (QCR), Gross Domestic Product per person (GDP), and health expenditure per person (HEP) for each country.

RESULTS

Results indicated a correlation between higher ASR and ALN exposure percentages, particularly in countries with higher GDP or HEP quartiles (all $p < 0.05$). Significant differences in ASR were observed across QCR levels, both high and low quality (all $p < 0.05$), but not in countries without registry activity. However, when evaluating ASR against ALN exposure percentages while considering GDP/HEP quartiles or QCR levels, no significant associations were found (all $p > 0.10$).

CONCLUSION

The findings suggest a potential link between higher GDP and adverse health conditions, serving as possible risk factors for TC, rather than a direct association with ALN. **Limitations include the use of cross-sectional data, temporal misalignment, and reliance on ALN as a socioeconomic proxy.** It is proposed that light pollution might be connected to a lifestyle conducive to carcinogenesis. Additionally, the presence of higher GDP/HEP could enhance access to diagnostic resources, potentially facilitating TC diagnosis and inclusion in cancer registries.

Key Words: Lighting; Human; Epidemiology; Thyroid; Cancer

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Core Tip: We explored the impact of Outdoor Artificial Light at Night (ALN) on thyroid cancer (TC) worldwide. While a correlation was found between higher TC rates and ALN exposure in countries with greater economic indicators (GDP and HEP), the association disappeared when accounting for registry quality. The findings suggest that high GDP may be more closely linked to health conditions and TC risk factors than ALN, possibly indicating a lifestyle connection to carcinogenesis. While correlations between ALN and economic factors are observed, a direct link of ALN to TC remains

unconfirmed. Additionally, higher GDP/HEP could contribute to better diagnostic access, aiding TC diagnosis and registry inclusion.

INTRODUCTION

The occurrence of thyroid cancer (TC) has increased in recent decades, in contrast to the incidence of most solid tumors in developed countries, which either remains stable or decreases. The reasons for this increase are still unclear; this epidemiological discrepancy compared to other neoplasias merits further research. Outdoor Artificial Light at Night (ALN) is ubiquitous in the modern world and exposure to it is one of the major environmental pollutants ^[1]. Light pollution has increased to such an extent that it no longer affects not only residents of large cities, but also those living in more remote areas. Exposure to ALN is associated with an increased risk of cancer ^[2]. The association of ALN with carcinogenesis is relatively novel. It has been suggested that exposure to ALN reduces nocturnal production of melatonin, which acts as a tumor suppressor ^[3]. However, little data focused on TC in relation to light pollution have been presented in the literature so far [3]. In this study we aimed to assess, worldwide, the potential impact of ALN on TC, using available satellite ALN data and reported TC epidemiological data.

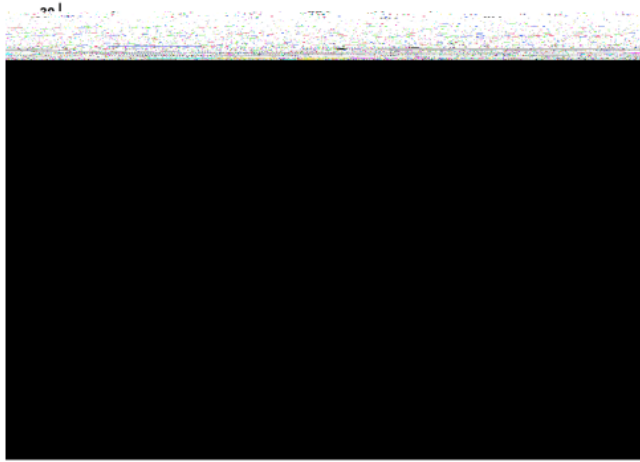
MATERIALS AND METHODS

To study the potential impact of ALN on TC, published satellite data on light pollution worldwide in 173 countries were used ^[1] (for a global image of ALN circa 2016 please see https://www.nasa.gov/specials/blackmarble/2016/globalmaps/BlackMarble_2016_3km.jpg). In particular, exposure levels - per % population and per % surface area of each country - to ALN > 87 $\mu\text{cd}/\text{m}^2$ & ALN > 688 $\mu\text{cd}/\text{m}^2$ (levels at which the ability to view the natural night sky is lost and where the Milky Way is no longer visible, respectively) were used. These thresholds were chosen because the 87 $\mu\text{cd}/\text{m}^2$ level corresponds to 50% more night luminance compared to normal, whereas the 688 $\mu\text{cd}/\text{m}^2$ level denotes

the total loss of the natural appearance of the night sky ^[1]. Light pollution data were estimated with reference to the corresponding - per country - TC incidence data as provided by the World Health Organization and the Global Initiative for Cancer Registry Development (<https://gco.iarc.fr/>). In particular, we used the standardized - per age and per 100.000 population of each country - TC incidence (Adjusted Standardized Rate, ASR). The normality of the data distribution was assessed by the Kolmogorov-Smirnoff test To assess financial influences (as an indirect measure of living conditions and lifestyle) data were collected for Gross Domestic Product per person (GDP) for each country (<https://data.worldbank.org/indicator/NY.GDP.PCAP.CD>) and health expenditure per person (HEP) for each country (<https://data.worldbank.org/indicator/SH.XPD.CHEX.PC.CD>) from the World Bank. The quality of cancer registries (QCR, classified in three groups as either high quality registries, registries of lower quality or no registry activity, per the Global Initiative for Cancer Registry Development; <https://gco.iarc.fr/>) was also noted. Comparisons of ASR and ALN exposure percentages were done according to GDP/HEP quartiles or QCR levels with the Kruskal Wallis test (KW, with statistical significance set at $p < 0.05$). The ASR was evaluated against ALN exposure percentages, conditioned for GDP/HEP quartiles and QCR levels, with Kendall's Tau test (KT, due to non-normal data distribution, with statistical significance set at $p < 0.05$). Statistical analyses were done with Minitab v.17.1 (Minitab Inc, State College, PA, United States, 2010) and JASP v0.15 (JASP Team, University of Amsterdam, NL, 2021).

RESULTS

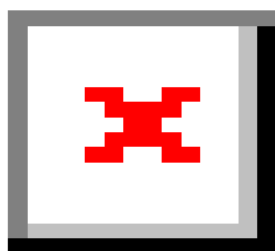
The median value worldwide, per % population or per % area, of ALN > 87 $\mu\text{cd}/\text{m}^2$, was 67.3% and 7.5%, while ALN > 688 $\mu\text{cd}/\text{m}^2$ was 34.6% and 0.7%, respectively. The median ASR was 4.2/100,000 population. There were significant differences of ASR and ALN exposure percentages by GDP quartiles or HEP quartiles (Figures 1 and 2).



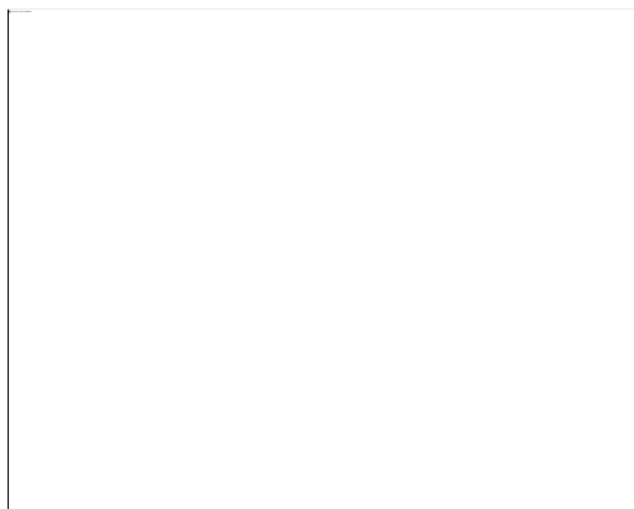
1a

1b

[Figure 1]. Plots of ASR by GDP [1a] or HEP [1b] quartile, taking into account QCR level; horizontal lines are the 25th, 75th percentile, with the median in between



2a



2b

[Figure 2]. Plots of ALN exposure percentages by GDP [2a] or HEP [2b] quartile; boxplots indicate the 25th, 75th percentile, with the median in between

Higher ASR and ALN exposure percentages were noted with higher GDP quartiles or HEP quartiles (all $p < 0.05$, KW). Differences in ASR were significant for QCR of high quality and lower quality (all $p < 0.05$, KW), but not for data with countries with no registry activity. Evaluation of ASR against ALN exposure percentages, taking into account GDP/ HEP quartiles or QCR levels did not yield significant results (KT ranged from -0.145 to +0.272, all $p > 0.10$)(Figure 3 and Supplemental Figure 1).



[Figure 3] Scatterplots of ASR by ALN exposure percentages with Locally Weighted Scatterplot Smoothing trendlines

DISCUSSION

The global scale of the ALN problem is illustrated by the fact that, according to available data, 83% of the world's population lives under conditions of severe light pollution ^[1]. In our study we aimed to clarify the nature of the relationship between ALN and TC, taking into account GDP or HEP and level of QCR. We noted differences in ASR by GDP quartiles and HEP quartiles worldwide; however ASR was not associated with exposure to ALN. Moreover, the higher the QCR was the higher ASR

was noted. Thus, financial indicators were associated with the incidence of TC, whereas ALN was not associated with its incidence.

Currently, the annual rate of thyroid cancer's new cases worldwide is increasing, estimated at about 20 % from 1990 to 2013. The rise recorded is similar in Europe, the United States of America, Canada and Australia, although changes in increased incidence are greater in low income countries compared to high income countries [4, 5]. The causes of this "epidemic" remain largely unclear [6]. It may represent a true increase or simply an increase in diagnoses of subclinical tumors that would otherwise have caused no symptoms, had they gone undetected [7]. Possibly, the ease of diagnosing very small tumors, due to advances in medical technology and screening programs, may play a role [8-10]. Perhaps, however, some factors related to lifestyle are also to blame.

Research has already identified some factors that affect the likelihood of developing thyroid cancer. Genetics, exposure to ionizing radiation and iodine intake have been found to increase the risk [4]. There are also studies that have associated air pollution, obesity, smoking and alcohol intake to thyroid cancer [11, 12]. Recently, a study published also inculcated light pollution [3]. The researchers reported that city lights at night suppress melatonin (which may regulate estrogen activity, has antineoplastic properties and assists in the adaptability of humans to their environment) and disrupts circadian rhythms, which is also a risk factor for carcinogenesis [13].

Regarding the data that we used, the satellite night illumination data used in this work were from 2016; these were obtained with VIIRS (Visible Infrared Imaging Radiometer Suite), and are considered to be very accurate [1]. The VIIRS ALN data are also considered to be a proxy of socioeconomic conditions. Data for the latter, which we used, were from 2019 and 2020, mostly before or at the beginning of the Covid-19 pandemic. The thyroid cancer incidence data which were used were also from 2019-2020. Experts argue that the latency period from the beginning of the neoplastic process to diagnosis of thyroid cancer is approximately 2.5 years [14]. Thus, for ALN *vs* thyroid cancer incidence, this study takes into consideration this lag time. However, the

temporal misalignment of cross-sectional data from different years (2016 for ALN, 2019-2020 for TC incidence, and 2019-2020 for economic data) may have affected the accuracy of the associations studied, especially considering the latency period for TC. Another limitation of the study is that the accuracy of epidemiological data for cancer incidence may not be satisfactory in countries with low quality cancer registries or without cancer registries. This introduces potential bias, as the accuracy of TC data may vary widely between countries. The VIIRS ALN data may be a proxy of socioeconomic conditions [15, 16], but to a different degree depending on the country [17, 18]; the relationship may be more accurate in richer vis-à-vis poorer ones [19]. Thus, the relationship between ALN data and socioeconomic conditions may not be uniform across all countries; while we recognize this, we have to accept a consequent degree of uncertainty in the interpretation of results. According to our results, light pollution might be associated with a lifestyle leading to carcinogenesis, but we were not able to delve deeply into specific lifestyle factors. Another caveat, regarding the analysis performed for this study is that all the data which were used were cross-sectional; while the use of such data is commonly implemented, particularly in the social sciences, experts argue that there are limits to the representability of such an approach.

CONCLUSION

Our findings imply that intense ALN is indeed associated to financial measures such as GDP but it is the latter, and not ALN, which may create conditions that are detrimental to health and a potential risk factor for TC. It is possible that light pollution is associated with a lifestyle that leads to carcinogenesis. Furthermore, higher GDP and HEP implies better access to diagnostic means, possible facilitation of TC diagnosis and better inclusion in cancer registries. Exploring the underlying mechanisms linking light pollution, socioeconomic status, and lifestyle factors to TC risk is crucial for a more comprehensive understanding of these associations. Physicians should be aware of the potential impact of lifestyle, including exposure to ALN, on cancer risk. Further research seems imperative to elucidate the intricate relationship between ALN, lifestyle

factors, and TC. Future investigations should delve into specific aspects of lifestyle, such as sleep hygiene and circadian rhythm disruptions, to identify modifiable risk factors. The broader implications for public health should not be overlooked: public health initiatives aimed at reducing light pollution, promoting healthy sleep habits, and raising awareness about the potential impacts of ALN on health may contribute to overall cancer prevention strategies.

ARTICLE HIGHLIGHTS

Research background

Background:

The increasing incidence of thyroid cancer (TC) globally has sparked interest in identifying potential environmental factors contributing to this rise. While prior research has explored various risk factors, the association between Artificial Light at Night (ALN) and TC remains an underexplored area. ALN, a prevalent environmental pollutant, has been linked to heightened cancer risk, potentially through the reduction of melatonin, a known tumor suppressor. The study seeks to bridge this knowledge gap and provide insights into the relationship between ALN and TC on a global scale.

Present

Status:

Current global trends indicate a notable increase in TC cases, with a rise estimated at about 20% from 1990 to 2013. This upward trajectory is observed not only in high-income countries but also in low-income nations, suggesting a complex interplay of contributing factors. The study utilizes satellite data from 2016 to assess the exposure to ALN worldwide and combines it with recent TC incidence data from 2019-2020. The research aims to discern patterns and associations between ALN exposure, socioeconomic factors, and TC incidence, contributing to our present understanding of potential risk factors for this cancer type.

Significance

of

the

Study:

The significance of this study lies in its exploration of the relationship between ALN, socioeconomic conditions, and TC incidence on a global scale. With 83% of the world's

population living under conditions of severe light pollution, the study addresses a pressing concern with broad public health implications. By uncovering that financial indicators, specifically higher GDP and health expenditure, are correlated with increased TC incidence, the study highlights the importance of socioeconomic status in understanding cancer risk. Furthermore, the research calls attention to the potential lifestyle impacts of light pollution, urging physicians to consider environmental factors, including ALN exposure, when evaluating cancer risk. The study's findings propose avenues for future research, emphasizing the need for a more comprehensive understanding of the intricate relationship between ALN, socioeconomic factors, lifestyle, and thyroid cancer risk. Overall, the study contributes valuable insights to the ongoing discourse on cancer prevention and underscores the importance of addressing light pollution in public health initiatives.

Research motivation

Research

Motivation:

The motivation for this research stems from the observed global increase in thyroid cancer (TC) cases and the limited understanding of the environmental factors contributing to this rise. While various risk factors have been explored, the potential link between Artificial Light at Night (ALN) and TC remains underexplored. The study is motivated by the need to comprehensively investigate the impact of ALN on TC at a global scale, recognizing the ubiquitous nature of light pollution in the modern world.

Main Topics and Key Problems:

ALN Exposure and TC: The primary focus is on evaluating the relationship between ALN exposure and TC incidence worldwide. The study delves into the prevalence of ALN using satellite data and examines whether there is a significant association with rates of TC.

Socioeconomic Factors and Cancer Incidence: The research investigates the role of socioeconomic conditions, as indicated by GDP and health expenditure per person, in

contributing to TC incidence. Understanding how financial indicators may influence cancer rates provides a nuanced perspective on the multifaceted nature of cancer risk.

Quality of Cancer Registries: The study incorporates the quality of cancer registries as a variable, recognizing the potential impact of data accuracy on the observed relationships. This consideration aims to address the challenges associated with cross-country variations in the reliability of cancer incidence data.

Temporal Misalignment and Latency Period: The research grapples with the challenges posed by the temporal misalignment of data from different years, acknowledging the latency period for TC diagnosis. This highlights the complexity of studying diseases with a prolonged progression from initiation to clinical detection.

Significance for Future Research:

Holistic Understanding of Thyroid Cancer Risk: By exploring the interplay between ALN exposure, socioeconomic factors, and TC, this study lays the groundwork for a more holistic understanding of the risk factors associated with TC. Future research can build upon these findings to unravel the complex dynamics influencing cancer incidence.

Environmental Determinants of Cancer: The study contributes to the broader field of environmental determinants of cancer, emphasizing the need for researchers to consider light pollution as a potential lifestyle-related factor impacting cancer risk. This opens avenues for further investigations into the broader environmental influences on various cancer types.

Public Health Initiatives: The research highlights the potential implications for public health initiatives. Understanding the connection between ALN, lifestyle, and cancer risk suggests that interventions targeting light pollution and promoting healthy sleep habits may have broader implications for cancer prevention strategies.

Specific Lifestyle Factors: Acknowledging the limitations in exploring specific lifestyle factors in this study, future research can delve deeper into understanding the precise elements of lifestyle, such as sleep hygiene and circadian rhythm disruptions, that may

contribute to TC risk. This could lead to more targeted and modifiable risk factors for preventive interventions.

Research objectives

Research Objectives:

The research objectives of this study were multifaceted, encompassing a comprehensive investigation into the relationship between Artificial Light at Night (ALN), socioeconomic factors, and thyroid cancer (TC) incidence on a global scale. These objectives were designed to address gaps in current understanding and shed light on potential environmental contributors to the rising incidence of TC.

Main Objectives:

Assessment of ALN Exposure Worldwide:
Objective: Quantify and assess the prevalence of ALN exposure globally using satellite data.

Realized: Achieved through the analysis of ALN levels exceeding specific thresholds, offering insights into the extent of light pollution worldwide.

Examination of TC Incidence:
Objective: Analyze TC cancer incidence data from 173 countries, investigating ASR per age and per 100,000 population.

Realized: Successfully explored the distribution of TC cases, identifying patterns and variations on a global scale.

Exploration of Associations with Socioeconomic Factors:
Objective: Investigate the relationship between ALN exposure and socioeconomic conditions, specifically GDP and HEP.

Realized: Demonstrated correlations between different GDP and HEP quartiles with both ALN exposure and TC incidence, providing insights into potential socioeconomic influences.

Consideration of Cancer Registry Quality:
Objective: Integrate the quality of cancer registries (QCR) as a variable to account for

potential variations in data accuracy.

Realized: Recognized the influence of QCR on observed TC incidence rates, highlighting the importance of data quality in epidemiological studies.

Statistical

Analyses:

Objective: Employ statistical tests to analyze relationships and differences in the data.

Realized: Utilized statistical tests such as Kolmogorov-Smirnoff, Kruskal Wallis, and Kendall's Tau to assess the significance of associations.

Significance

of

Realizing

Objectives:

Holistic Understanding of Thyroid Cancer Risk: Realizing these objectives contributes to a holistic understanding of the factors influencing TC risk globally, including the novel exploration of ALN as a potential environmental contributor.

Environmental Determinants of Cancer: The study's findings underscore the broader significance of environmental determinants, emphasizing the need to consider light pollution as a lifestyle-related factor impacting cancer risk. This sets the stage for future research into other environmental influences on various cancer types.

Public Health Implications: Realizing objectives contributes to the identification of potential public health implications, with insights suggesting interventions targeting light pollution and promoting healthy sleep habits may have broader impacts on cancer prevention strategies.

Future Research: Significance: The study sets the stage for future research by highlighting the intricate relationship between ALN, socioeconomic factors, lifestyle, and TC risk. Future investigations can build upon these insights, delving deeper into specific lifestyle factors and refining preventive interventions.

Research methods

Research Methods Used:

The study utilized satellite data to quantify and assess global levels of Artificial Light at Night (ALN). Novelty: Leveraged ALN data to explore its potential association with

thyroid cancer (TC), introducing a novel environmental factor to the study of cancer risk.

Integrated ALN exposure data with socioeconomic indicators such as Gross Domestic Product (GDP) and health expenditure per person (HEP). Novelty: Explored the intricate relationship between ALN, socioeconomic factors, and TC incidence, providing a nuanced perspective on potential contributing elements.

Considered the quality of cancer registries (QCR) as a variable to address potential variations in data accuracy. Novelty: Recognized and integrated QCR as an essential component, acknowledging the impact of data quality on the interpretation of cancer incidence rates.

Characteristics and Novelty of Research Methods:

The study adopted an interdisciplinary approach by combining environmental science (satellite data), epidemiology (cancer incidence data), and socioeconomic analysis. Novelty: The integration of diverse disciplines allowed for a more holistic exploration of the potential factors influencing TC, offering a novel perspective on the complex interplay between environmental and socioeconomic elements.

The research encompassed a global scale analysis, considering ALN exposure and TC incidence across 173 countries. Novelty: The global scope of the study provided a comprehensive understanding of potential patterns and variations in TC incidence, transcending regional or national boundaries.

The study integrated socioeconomic indicators such as GDP and HEP to explore their association with ALN exposure and TC incidence. Novelty: The inclusion of socioeconomic factors expanded the research beyond environmental considerations, offering a nuanced understanding of how financial indicators may contribute to cancer risk.

Statistical

Analyses:

The study applied a range of statistical tests to rigorously analyze data, including non-parametric tests (Kolmogorov-Smirnoff, Kruskal Wallis) and correlation analysis (Kendall's Tau).

Research results

ALN Exposure and TC Incidence: The global prevalence of ALN exposure was quantified, with 67.3% of the world's population experiencing ALN levels exceeding 87 $\mu\text{cd}/\text{m}^2$, and 34.6% experiencing levels surpassing 688 $\mu\text{cd}/\text{m}^2$. TC incidence, measured by the Adjusted Standardized Rate (ASR), was found to be 4.2 per 100,000 population globally. Significant differences in ASR and ALN exposure percentages were observed across Gross Domestic Product (GDP) and health expenditure per person (HEP) quartiles. Higher ASR and ALN exposure percentages correlated with higher GDP and HEP quartiles. Differences in ASR were significant concerning the quality of cancer registries (QCR). Higher ASR was noted with high-quality registries compared to lower quality ones. However, no significant association was observed with countries lacking registry activity. ASR by GDP and HEP quartiles showed higher ASR with higher economic indicators. ALN exposure percentages also increased with higher economic quartiles. ASR by ALN exposure percentages did not yield significant results, suggesting that while ALN and economic indicators are associated with TC, their direct association is less apparent.

While ALN exposure was widespread globally, the study did not find a direct association between ALN exposure and TC incidence. This challenges previous suggestions of a direct link between light pollution and cancer risk. The findings highlight a significant correlation between higher GDP and HEP quartiles with increased TC incidence. This suggests that socioeconomic conditions may play a pivotal role in the rising rates of TC. The study reveals that the quality of cancer registries influences observed TC incidence rates. The association is significant with high-quality registries but less so with lower quality or absent registries. The lack of a significant association between ALN exposure percentages and ASR suggests that, while ALN and economic indicators are associated with TC, the nature of

their relationship remains complex and may be influenced by other factors. The study contributes to a nuanced understanding of the relationship between ALN and TC by providing a global perspective. The absence of a direct correlation challenges oversimplified assumptions and underscores the complexity of environmental factors in cancer risk.

Highlighting the correlation between higher GDP and HEP quartiles with increased TC incidence, the research emphasizes the significance of socioeconomic conditions in cancer epidemiology. This expands the current understanding beyond environmental factors. The inclusion of cancer registry quality as a variable adds depth to the interpretation of TC incidence rates. Recognizing the impact of data accuracy on study outcomes enhances the credibility and applicability of the research.

Problems that Remain to be Solved:

While the study did not find a direct association between ALN and TC, the nature of their relationship remains unclear. Further research is needed to unravel the intricate factors influencing this link, potentially involving more specific analyses of light exposure patterns. The study highlights a correlation between higher GDP and TC incidence, but the specific socioeconomic contributors to cancer risk within these indicators remain to be elucidated. Future research should delve into the specific aspects of economic conditions influencing cancer rates. While the study considered the quality of cancer registries, further refinement in assessing and addressing data accuracy issues is essential. Future research could explore strategies to enhance the reliability of cancer incidence data, especially in regions with lower-quality registries. The research primarily focused on ALN, and while this contributes to the understanding of environmental determinants, further exploration of additional environmental factors influencing thyroid cancer risk is warranted. This could involve investigating air quality, pollutant exposure, or other relevant environmental variables. While the study identified a correlation between socioeconomic conditions and TC, the underlying mechanisms driving this association require further investigation. Future

research could explore how economic factors influence lifestyle choices, healthcare access, or other determinants impacting cancer incidence.

Research conclusions

New Theories Proposed: While this study primarily focused on empirical investigations rather than proposing new theoretical frameworks, it introduced a nuanced perspective on the relationship between Artificial Light at Night (ALN), socioeconomic factors, and thyroid cancer (TC). The absence of a direct correlation challenges existing theories that oversimplify the link between light pollution and cancer risk. The findings encourage a more complex understanding of environmental and socioeconomic influences on cancer incidence, prompting future theoretical developments in this field.

New Methods Proposed: The study did not explicitly propose new research methods but demonstrated an innovative approach through the integration of diverse methodologies. Notably, the interdisciplinary analysis, global scale examination, consideration of temporal misalignment, and incorporation of socioeconomic indicators represent methodological advancements. The study's emphasis on the quality of cancer registries as a variable and its rigorous statistical analyses contribute to methodological robustness. Future studies may adopt similar approaches to enhance the comprehensiveness and reliability of research in the intersection of environmental, socioeconomic, and cancer research.

Research perspectives

Future research should delve deeper into understanding the complex dynamics between Artificial Light at Night (ALN) exposure and cancer risk. Investigating specific patterns of light exposure, considering variations in intensity, duration, and timing, may provide a more nuanced understanding of how ALN influences cancer incidence. Further exploration is needed to identify and understand specific socioeconomic contributors to thyroid cancer (TC) risk. Future research could investigate the role of economic factors in shaping lifestyle choices, healthcare access, and environmental

exposures, refining our understanding of the socioeconomic mechanisms influencing cancer incidence. Research focusing on the improvement of cancer registry quality assessment methods is crucial. Developing strategies to enhance data accuracy, especially in regions with lower-quality registries, will contribute to more reliable and comparable cancer incidence data. This could involve collaborations to standardize data collection practices globally. Expanding the scope to include other environmental factors influencing TC risk is essential. Future studies could explore the impact of air quality, pollutant exposure, and other relevant environmental variables. This broader perspective will contribute to a more comprehensive understanding of the environmental determinants of TC. Future research should aim to refine existing theoretical frameworks related to environmental and socioeconomic influences on cancer risk. This may involve the development of more nuanced models that consider the interplay of multiple factors, including lifestyle, genetics, and environmental exposures, to better explain the observed variations in TC incidence. Investigating specific lifestyle factors, such as sleep hygiene and circadian rhythm disruptions, could provide valuable insights into modifiable risk factors associated with TC. Future research should conduct in-depth analyses to identify lifestyle elements contributing to cancer risk and explore potential interventions. Conducting longitudinal studies with extended follow-up periods could help establish causality between ALN exposure, socioeconomic conditions, and TC. Long-term observations would allow researchers to better understand the temporal sequence of events leading to cancer development and refine causal relationships. Research focusing on the development and evaluation of public health interventions is crucial. Assessing the effectiveness of initiatives aimed at reducing light pollution, promoting healthy sleep habits, and raising awareness about the potential impacts of ALN on health will contribute to overall cancer prevention strategies. In summary, the future research agenda should aim to deepen our understanding of the nuanced relationships identified in this study, refine theoretical frameworks, enhance methodological approaches, and explore additional factors contributing to TC risk. Addressing these perspectives will contribute to a more

comprehensive and actionable knowledge base in the field of environmental and socioeconomic influences on cancer incidence.¹

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