Neighborhood factors and the risk of cutaneous T-cell lymphoma: A systematic review

To the Editor: Cutaneous T-cell lymphomas (CTCLs) are a rare group of non-Hodgkin's lymphomas. While their exact pathogenesis is unknown, environmental factors have been postulated to influence their incidence and severity. This is supported by the evidence of geographic disparity in incidence rates on a country/regional level as well as case clustering within non-consanguineous married couples or residents of small boroughs.[1] We conducted a systematic review to elucidate the influence of neighborhood factors (the space in which people live and engage in everyday activities) on CTCL incidence, prevalence, and severity.

Two independent investigators (J. T./L. K.) searched MEDLINE, Web of Science, EMBASE, and CINAHL on July 28, 2023, for studies exploring the association between the neighborhood factors and the incidence, prevalence, and severity of CTCL. Preferred Reporting Items for Systemic Reviews and Meta-Analyses guidelines were followed.[2] The

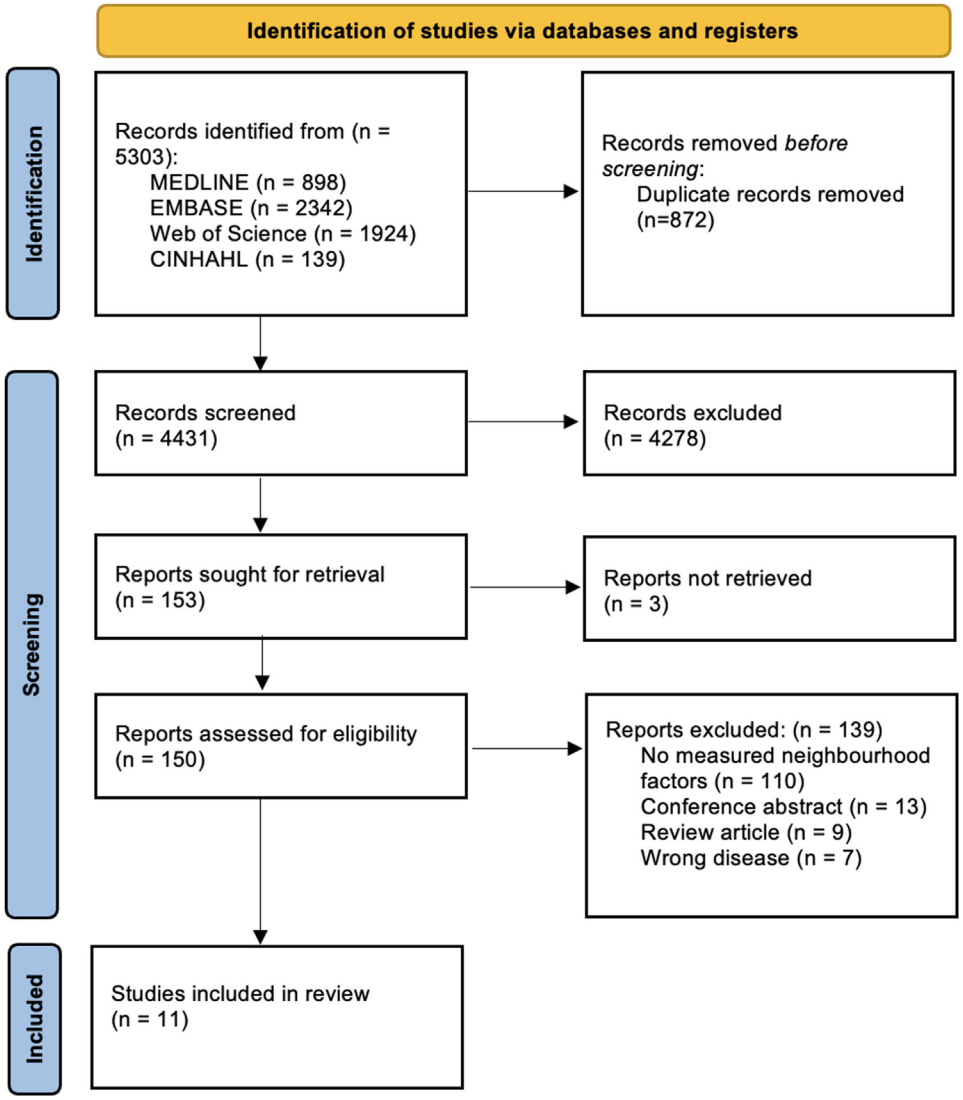

Fig 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

Table I. Characteristics and results of included studies

Author	Location	Sample size	Neighborhood factor	Outcome	Result
Clough	Georgia, USA	1239	Benzene and TCE concentration	SIR	Benzene: $\beta = 0.34$, $P < .001$, TCE: $\beta = 2.1$, $P = .0078$
Kayishunge	Arkansas, USA	143	Benzene and TCE concentration	SIR	Benzene: $\beta = 0.29$ ($P < .001$) TCE: $\beta = 0.005$ ($P < .001$)
Maghfour	Louisiana, USA	774	Benzene and TCE exposure	SIR	Benzene: 0.24 $\mu g/m^3$, $P = .12$ TCE: 0.010 $\mu g/m^3$, $P = .98$
Leeuwen	Australia	322	Latitude (°S)	IRR	<29 °S: 1.0 (Ref) 29-36 °S: 1.98 (95% CI: 1.43-2.73) >37 °S: 1.72 (95% CI: 1.20-2.46); $P < .018$
Destefano	USA	1598	UV exposure	Age adjusted incidence	0.542 (high UV) versus 0.705 (low UV) per 100,000 persons hazard ratio: 1.3; (95% CI: 1.20-1.41); $P < .001$
Henry	New Jersey, USA	5787	Geographic neighborhood clustering	SIR	Cluster of CTCL detected in 1992 in Bergen County (SIR 1.84), $P = .0011$
Moreau	Pittsburgh, USA	274	Geographic neighborhood clustering	Case density per 100,000	Observed/expected ratio: 3/1, $P < .001$
Litvinov	Texas, USA	3037	Geographic neighborhood clustering	IR	Geographic clustering of patients in 3 communities (Katy, spring, and Houston memorial area) where CTCL IR were 5-20 times higher than the expected population rate in Texas.
Wiese	New Jersey, USA	1163	Geographic neighborhood clustering	SIR	No statistically significant areas of elevated CTCL risk in New Jersey compared to the statewide average.
Cai	USA	14,942	Metropolitan vs nonmetropolitan	IR and APC	Metropolitan: IR: 8.96; APC: 0.68% [CI: 0.16-1.20] Nonmetropolitan: IR: 4.85; APC: 0.66% [CI: 2.03-0.73].
Ghazawi	Canada	6685	Industrial exposure	IR	Visual clustering of high IR was observed in highly industrial cities whereas some cities with low industrial presence were spared

APC, Annual percent change; *CI*, confidence interval; *CTCL*, cutaneous T-cell lymphoma; *IR*, incidence rate; *IRR*, incidence rate ratio; *RR*, relative risk; *SIR*, standard incidence rate; *TCE*, trichloroethylene.

search strategy is shown in Supplementary Tables I-III, available via Mendeley at https://data.mendeley.com/datasets/d7cv8p6tsb/1. The Quality appraisal was conducted using the Quality Assessment Tool for Quantitative Studies.[3]

Of 5303 publications identified, 11 met the inclusion and exclusion criteria (Fig 1, Table I). In 2 US studies, ambient benzene (β 0.29-0.34, $P < .001$) and trichlorethylene (0.005-2.1, $P < .0078$) exposures were associated with higher standardized incidence of CTCL. Two manuscripts studied environmental ultraviolet radiation (UVR). A national US-based study reported lower age adjusted CTCL incidence in states with higher ambient UVR which was statistically significant only in early disease stages and individuals of White racial background. The Australian study supported this positive association. Other manuscripts focused on geographic clustering and association with urban living and industrial density. Three US-based studies focusing on case clustering and regional incidence rates were limited to a single state or metropolitan region (ie, Pittsburg metropolitan area and the states of Texas and New Jersey). These studies identified statistically significant clustering in Bergen County (New Jersey), Pittsburgh densely populated neighborhoods, Spring (Texas), and Houston Memorial Areas (Texas). In Spring and Houston (Texas), higher rates and case clustering of CTCL were noted along the same street/highway/stream, although no formal statistical analysis was conducted. In a populational Canadian study, several cities were identified with statistically significantly higher or lower incidence rates compared with the rest of country. Analysis of postal codes revealed that high incidence areas were grouped together and located in industrialized regions, while areas of low incidence tended to be in cities with minimal industrial presence.

Our review supports a positive relationship between air pollution, low environmental UVR and CTCL incidence. Phototherapy is a standard treatment modality for CTCL, thereby the protective effect of ambient UVR on incidence or severity (where milder cases are underdiagnosed) is plausible.[4] Benzene and chlorinated organic solvents are known carcinogens.[1] However, data are limited by small number of included studies and low to moderate risk of bias (Supplementary Table IV, available via Mendeley at https://data.mendeley.com/datasets/d7cv8p6tsb/1). While several articles reported colocalization of CTCL cases/high incidence areas with industrial presence and urban living, their descriptive nature and regional rather than populational approach precludes from further conclusions. Further research exploring the effect of living environment (eg, neighborhood, pollution, vegetation, climate metrics) on CTCL incidence, prevalence and severity is needed to better understand disease pathogenesis and enable preventive strategies.

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Funding sources: None.

Patient consent: Not applicable.

IRB approval status: Not applicable.

Key words: air pollution; cutaneous T-cell lymphoma; environmental factors; environmental ultraviolet radiation; industrialization; neighborhood factors; oncology.

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Conflicts of interest

None disclosed.

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https://doi.org/10.1016/j.jdin.2024.09.014