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Defining Spatial Epidemiology: A Systematic Review and Re-Orientation

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Abstract

Background.—Spatial epidemiology has emerged as an important subfield of epidemiology over the past quarter century. We trace the origins of spatial epidemiology and note that its emergence coincided with technological developments in spatial statistics and geography. We hypothesize that spatial epidemiology makes important contributions to descriptive epidemiology and analytic risk factor studies, but is not yet aligned with epidemiology's current focus on causal inference and intervention.

Methods.—We conducted a systematic review of studies indexed in PubMed that used the term "spatial epidemiolog*" in the title, abstract, or keywords. Excluded papers were not written in English, examined disease in animals, or reported biologic pathogen distribution only. We coded the included papers into five categories (review, demonstration of method, descriptive, analytic, intervention) and recorded the unit of analysis (i.e., individual vs. ecological). We additionally examined papers coded as analytic ecologic studies using scales for lexical content.

Results.—A total of 482 papers met the inclusion criteria, including 76 reviews, 117 demonstrations of methods, 122 descriptive studies, 167 analytic studies, and 0 intervention studies. Demonstration studies were most common from 2006 to 2014, and analytic studies were most common after 2015. Among the analytic ecologic studies, those published in later years used more terms relevant to spatial statistics (IRR =1.3, 95%CI: 1.1, 1.5) and causal inference (IRR =1.1, 95%CI: 1.1, 1.2).

Conclusions.—Spatial epidemiology is an important and growing subfield of epidemiology. We suggest a re-orientation to help align its practice with the goals of contemporary epidemiology.

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Introduction

Spatial epidemiology has arrived as a bona fide subfield of epidemiology.[1] Peer-reviewed research output labeled as "spatial epidemiology" has grown exponentially over the last three decades,[2] and established scientific journals,[3] conferences,[4] and textbooks[5–11] are now dedicated to its pursuit and disciplinary distinction. Spatial epidemiology now receives comparable billing alongside such mainstays as the disease-based subfields (e.g., cancer epidemiology, infectious disease epidemiology) and those organized by scales of scientific inference (e.g., molecular epidemiology, social epidemiology).[12–15] Authors of academic textbooks generally agree on what spatial epidemiology is—"the study of the geographical or spatial distribution of health outcomes"[16]; "concerned with describing, quantifying, and explaining geographical variations in disease"[10]; "the description of spatial patterns, identification of disease clusters, and explanation or prediction of disease risk".[7] In contrast, the parent discipline of epidemiology is commonly defined as having three complementary and sequential objectives—describing distributions of health and ill-health within populations, analyzing possible causes of the observed distributions, and intervening upon identified causes to improve health at a population level.[13,17–21] In this paper we argue that spatial epidemiology makes critical contributions to descriptive epidemiology (e.g., through disease mapping and cluster detection), which is essential for guiding resource allocation and hypothesis generation. However, we also propose that the subfield's historical context and current practice limit its ability to contribute to epidemiology's higher order objectives of analyzing possible causes and testing interventions to improve population health.[17,22] We suggest a re-orientation of our evolving subfield to bring it in line with contemporary epidemiology.

The Role of Space and Place in Epidemiology

Every student of epidemiology learns that the discipline's origins are spatial. Classic examples include John Graunt's 1662 observations that mortality was socially and spatially structured, with a higher rate among residents of London compared to residents of rural areas[23,24]; John Booth's 1889 "poverty maps" that characterized socioeconomic conditions for residents of London streets[25]; W.E. Burghardt Du Bois's 1899 place-based survey studies that documented structural disadvantage for residents of majority Black neighborhoods in Philadelphia[26]; and John Snow's 1854 investigation of cholera fatalities around the now infamous water pump in London's Soho district.[27,28] Snow's work is often emphasized above all others.[29] The common narrative—typically presented with some poetic license[30]—is that Snow documented fatalities by interviewing family members of those who had died[31] and that, on the evidence he produced, authorities removed the handle of a pump near the corner of Broad and Cambridge Streets. The key visual accompanying this story is, of course, a map.

The role of space in epidemiology has seen marked shifts in the last two centuries, corresponding with distinct eras for the discipline. Through the mid-to-late 19th century, prevailing theory held that disease was caused by miasma, a poisonous vapor emanating from decaying animal and vegetable matter, and it followed logically that prevention should emphasize improved sanitation.[32] The primary tool of the "miasma era" of epidemiology was population-level data, and an essential datum was a spatial reference, which enabled comparison between locations and identification of possible environmental causes upon which to intervene. Despite these strong beginnings, epidemiologic investigation of spatial structures dwindled in the early 20th century. Reflecting the new position of infectious disease as the leading cause of death across the Western world,[33] germ theory became the dominant explanation for disease in humans. Maps remained useful for understanding transmission routes and identifying affected populations[34]; for example, Wade Hampton Frost's 1910 map of a typhoid outbreak in West Virginia demonstrated how case locations varied by space and time.[35] However, disease identification and prevention became mostly a laboratory science. This "infectious disease era" of epidemiology was marked by intense focus on the individual, prevention through vaccination, and treatment through antibiotics and patient isolation.

By mid-century, spatial considerations began to creep back into the health sciences. The emerging field of medical geography documented that disease frequency differed systematically across geographic areas[36] and that environmental conditions explained some of these regional differences.[37] Medical geographers helped re-frame environmental conditions as exposures but were criticized for paying scant attention to the way social organization affected the health of individuals, and for explaining away social conditions with nebulous references to "culture".[38,39] At the same time, chronic diseases overtook infectious diseases as the leading causes of death and disability in the developed world,[33] heralding the new "chronic disease era" of epidemiology. To investigate possible causes, epidemiologists relinquished an understanding of specific biologic mechanisms of disease, focusing instead on identifying a web of potential causes.[40] Spatially structured exposures were once again incorporated into some epidemiologic studies, though researchers did not need to describe any mechanism by which an exposure might cause a disease before investigating their associations. The approach is often described as risk factor or "black-box" epidemiology, in reference to the mysterious causal processes by which exposures might affect outcomes.[41]

Risk factor spatial epidemiology has produced important knowledge about associations between spatially structured exposures with health behaviors and health outcomes. For example, measures of social disadvantage are associated with poorer health outcomes of many kinds,[42] suggesting that intervening to reduce social disadvantage could improve health at a population level. Concepts from social epidemiology[43] and prevention science[44] add that intervening on these so-called fundamental causes could re-shape the health of entire populations; hence, scientific investigations are essential. Although many researchers have suggested theoretical mechanisms linking upstream spatially structured exposures to downstream health outcomes,[45] detecting these relationships statistically requires no understanding of the social mechanisms that produced them. This criticism echoes a debate in the broader discipline of epidemiology. Around the turn of the 21st century, many commentators argued that, rather than measuring relative associations ever more precisely (particularly for environmental exposures on which intervention is impractical), epidemiologists should collectively focus on high prevalence exposures and outcomes that were most likely to be improved by intervention.[22,46] In response, emerging approaches emphasized that population distributions of health and ill-health arise due to multiple interconnected complex systems, and that clear social or biological theories must inform reductionist empirical analyses.[47,48]

The advances of the last several decades have broadened conventional definitions of epidemiology. Miquel Porta,[13] in the *Dictionary of Epidemiology*, defines epidemiology as, “The study of the occurrence and distribution of health-related events, states, and processes in specified populations, including the study of the determinants influencing such processes, and the application of this knowledge to control relevant health problems”. This definition is consistent with other published suggestions[49] in that it contains three main parts. *Description* of the distribution of health-related states plays an important role for allocating resources and developing hypotheses. *Analysis* of statistical associations with exposures are useful to identify correlates (i.e., risk factors) and potential causes of health outcomes. *Interventions* which modify causes to improve the health of populations are an ultimate goal of epidemiology and its subfields.[18–21] This definition has valid criticisms, including that it overly reflects individualized biomedical models of disease and embodies a collective preference towards studies of individuals over studies of populations.[50,51] However, it provides a useful roadmap for locating spatial epidemiology within its parent discipline.

Reconciling Contemporary Epidemiology and Spatial Epidemiology

While space has always been an important element of epidemiology, the term “spatial epidemiology” emerged in the late 20th century,[2] pre-dating epidemiology’s broader reckoning with the shortcomings of risk factor methods, and coinciding with (or perhaps because of) notable advances in geographic methods and spatial statistics.

The advances in geographic methods are exemplified most notably in the development of Geographic Information Systems (GIS), which were first proposed in 1968 as an efficient method for storing map contents and automating their analysis.[52] In contrast to electronic mapping and cartography, which were also developing around that time, the key features of GIS were the use of a uniform coordinate system, which allowed multiple data sources to be overlaid within a common reference and geographic extent, and the linkage to underlying attribute tables, which allowed users to store information about feature “layers” and conduct map algebra.[53] The longstanding industry leader ESRI (Redlands CA) was established in 1969 and released its ArcGIS family of packages in 1999.[54]

The advances in spatial statistics also prompted the development of new computer programs. Some such programs facilitated spatial descriptive studies, such as the National Cancer Institute’s SatScan, released in 1997 to enable detection of univariable spatial clusters.[55] Others facilitated spatial associational studies, such as WinBUGS (1997) which implemented fully Bayesian spatial analysis,[56] R-spdep (2002) which created spatial weights matrices,[57] QGIS which provided an open-source alternative to the costly ESRI products (2002),[58] and GeoDA (2003) which combined a usable map interface with novel spatial statistical methods.[59] These dedicated software packages complemented GIS add-ons, such as location-allocation algorithms, which were developed as early as the 1970s to conduct intervention studies that changed places, spaces, and health systems in efforts to directly improve the health of populations.[60–64]

Perhaps reflecting the newly available spatial statistical and geographic software, spatial epidemiology began to coalesce as a subfield at the turn of the millennium.[1] People trained in the disciplines of statistics and geography led the charge, for example by convening the multidisciplinary *GeoMed* conference on “spatial statistics, spatial epidemiology, and geographical aspects of public health” (1997),[4,65] and establishing the subfield’s flagship journal *Spatio and Spatio-temporal Epidemiology* (2009).[66] Nine books have since been published with titles that include the terms “spatial” and “epidemiology”; almost all were written by people with primary affiliations outside epidemiology (Table 1).

Spatial epidemiology’s multidisciplinary roots serve the subfield well. The statistical methods available for epidemiologic investigations of spatially structured data have a robust empirical and theoretical basis, and training in these techniques is readily available. The conventions of cartography, geography, and geographic information sciences—refined over centuries—are widely encouraged and used.[67] These various influences bode well for descriptive spatial epidemiology, including disease mapping and cluster detection, and for risk-factor studies of individual-level and ecologic data. However, because statistics and geography have different objectives compared to epidemiology, the subfield may not be well-equipped to address epidemiology’s present-day criticisms of risk factor studies. Theory and causal inference are likely to receive little attention. Understanding the structural conditions that produce observed distributions may be a low priority. Testing interventions to improve population health will be exceedingly rare.

The aim of this paper is to identify incongruence between the goals of epidemiology and the current practice of spatial epidemiology, as described in peer-reviewed studies. To achieve that aim, we conducted a systematic review of published papers to summarize what authors say spatial epidemiology is, describe what authors do when they say they are doing spatial epidemiology, and compare this practice with epidemiology’s commonly stated objectives of describing distributions, analyzing associations (in service of establishing causation), and testing intervention. We focus specifically on instances when authors invoke the term “spatial epidemiology” because the presence of a common lexicon is a defining feature of a subfield,[1] and because spatial epidemiology is the most common name for this scientific area. Similar search strategies have been implemented in other areas of public health science (e.g., global mental health,[68] intersectionality[69]). Admittedly, the approach will omit papers that report research that is spatial epidemiology in essence but not in name, and those published under the auspices of adjacent fields (e.g., medical geography, environmental epidemiology, spatial statistics, geographical epidemiology[70]). However, our goal is to help advance our specific subfield. We hypothesized that spatial epidemiology—as a relatively new subfield—makes important contributions to descriptive epidemiology and analytic risk factor studies, but that it is not yet aligned with the parent discipline’s contemporary focus on causal inference and intervention. Per convention, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[71]

METHODS

Study Design

We conducted a systematic review of spatial epidemiologic studies. On January 13, 2022, we searched PubMed using the Boolean term "spatial epidemiolog*", capturing all studies that used the terms "spatial epidemiology", "spatial epidemiologic", "spatial epidemiologist", or "spatial epidemiological". Papers eligible for inclusion were those published in English that used the term "spatial epidemiolog*" in the title, abstract, or keywords. Papers that used the term "spatial epidemiolog*" only in the author affiliation were excluded. Also excluded were papers examining disease in animals, and papers reporting biological pathogen distribution only (i.e., with no quantitative assessment of health behaviors or health outcomes in humans). The search strategy and inclusion criteria were developed based on our methodological expertise conducting spatial epidemiologic studies[72–75] to balance feasibility and breadth.

Instruments

We uploaded a full list of papers found in the PubMed search into Covidence (Veritas Health Innovation, Melbourne, Australia),[76] an online tool for screening and extracting data for systematic reviews. We also uploaded a data collection instrument to facilitate coding of eligible papers. The instrument comprised two main items that extracted definitions of spatial epidemiology and then categorized studies into 5 types: "reviews" were papers that synthesized spatial epidemiologic theory or methods; "demonstrations" presented geographic or statistical methods using synthesized or observed health data; "descriptive" studies reported measures of disease frequency for outcomes only; "analytic" studies reported measures of association for outcomes and at least one exposure; and "interventions" reported measures of association for experimental studies where individuals or groups were assigned to an exposure status.

Papers that were coded as descriptive, analytic, or intervention studies were eligible for 6 additional items. These quantitative papers were categorized according to the units of analysis (individual-level vs. ecological); the study design (cross sectional, time series, case-comparison, cohort/panel, quasi-experiment, or experimental); the outcome type (chronic disease, injury, infectious disease with human-human transmission, zoonotic disease with animal-human transmission, or environmental condition where the outcome was a feature that was theorized to affect health outcomes that were not directly assessed [e.g., exposure to air pollution]); the spatial unit (state, county, city, ZIP code, census tract, census block group, school district, or other); the temporal unit (multi-year, year, month, week, day, or other); and the extent (country, state, county, city, or other).

Screening and Data Extraction

A team of six data collectors (ANG, BRB, CAM, CNM, SF, SU) screened the papers found in the PubMed search to identify eligible papers, then extracted data from eligible papers using the instrument described above. To maximize inter-rater reliability, we completed the screening and data extraction in stages.

To complete the screening, first, we randomly selected ten papers based on title and abstract for English language (inclusion criterion) and animal studies (exclusion criterion). We discussed discrepancies then repeated the procedure three times until all team members agreed about definitions. We then screened the remainder of the papers. The abstracts and titles were all screened by two of the six members of the data collection team and discrepancies were discussed during a weekly meeting. Second, one team member conducted a full-text review to ensure that the Boolean term "spatial epidemiolog*" was found in the title, abstract, keywords, or main text. Screening and data collection took precisely one year and was completed on January 13, 2023.

Lexical Assessment

A final group of analyses characterized the use of terms in a subset of spatial epidemiology papers over time. Papers included in the subset were those we categorized as "analytic" studies and where the unit of analysis was "ecological". These inclusion criteria ensured that the papers had roughly comparable methods, in that they related aggregated outcomes to at least one area-level exposure across multiple polygons (e.g., ZIP Codes or Census Tracts). The lexical assessment involved three steps. First, we compiled lists of commonly used terms and identified their use in the included papers. Second, we developed scales of lexical content. Third, we assessed changes in lexical content over time.

We began by developing lists of 10 to 20 commonly used terms from epidemiology, geography, and statistics. Because the ultimate goals of contemporary epidemiology are inferring causation and testing interventions, we also generated additional lists of terms germane to causal inference and intervention. We developed these five lists in discussion among the authorship group, based on our collective expertise in this area of scientific inquiry. We then collapsed the terms into regular expressions within each list. For example, the list for causal inference included the term "mediat*", to capture mediation, mediator, mediating, and mediate. We used the PyMuPDF library in Python to perform full-text searches of PDF files, then calculated dichotomous variables indicating the presence or absence of the terms in each included paper. We combined measures for terms that refer to the same construct and are unlikely to be used together in the same paper (e.g., authors might use the term "ecological fallacy" or "ecological bias" but are unlikely to use both).

Principal components analyses identified scales of terms from each list among the included papers. We used a backwards stepwise procedure in which all 10 to 20 terms were included in a first analysis, then we removed the term with the eigenvector closest to zero and performed repeated analyses until all remaining terms had eigenvectors ≥ 0.4. The sum of the binary values for these remaining terms yielded a lexical scale for each field. We generated a second lexical scale for each field by removing the terms that were included in the first scale and repeating the full backwards stepwise procedure.

Finally, we assessed changes in the use of terms in the included papers over time using Poisson regression. The units of analysis were the included papers, the dependent measures were the lexical scales, and the independent measure was the year in which the paper was published. Incidence rate ratios can be interpreted as the relative change in the use of terms from each lexical scale per year.

RESULTS

Screening

The PubMed search found 962 papers, including one duplicate. Figure 1 shows the PRISMA flow chart to report the results of the screening procedure. The title and abstract review excluded 263 papers that were either not in English or reported studies of disease in animals. The full text review excluded 216 papers where "spatial epidemiolog*" was stated only in the author affiliations (n=204) or could not be found (n=12). This procedure yielded a final census of 482 papers (Supplementary Table S1).

Defining Spatial Epidemiology

We extracted 39 published definitions of spatial epidemiology (Table 2) extracted from papers published from 2005 to 2021. Definitions published in earlier years tended to emphasize descriptive epidemiologic methods. For example, Osfeld, 2005,[77] wrote that, "Spatial epidemiology is the study of spatial variation in disease risk or incidence." Definitions published in later years also tended to include reference to analytic spatial epidemiology. El-Ghitany, 2019,[78] wrote that, "Spatial epidemiological methods provide a basis for disease investigation through which hotspots and disease determinants can be identified." All definitions that included analytic spatial epidemiology also included descriptive spatial epidemiology. Only four papers—published in 2015,[79] 2017,[80] 2021,[81] and 2021[82]—had definitions that referred to interventions in spatial epidemiology. The most concise definition that included all three aspects of epidemiologic inquiry was written by Kirby, 2017:[80] "Spatial epidemiology encompasses research that incorporates the spatial perspective into the design and analysis of the distribution, determinants, and outcomes of all aspects of health and well-being across the continuum from prevention to treatment".

The Practice of Spatial Epidemiology

Among the 482 eligible papers, 76 were reviews, 117 were demonstrations, 122 were descriptive, 167 were analytic, and 0 were interventions (Figure 2). The first eligible paper that used the term "spatial epidemiolog*" was a review published in 1981. Demonstrations tended to be the most common paper type from 2006 to 2014, then from 2015 to 2020 analytic studies became more common and have continued an increasing trend; descriptive studies have also become more common in recent years. For example, of 72 eligible papers published in 2021, 32 were analytic and 21 were descriptive.

Table 3 reports the key study design features of the 167 papers that we classified as "analytic epidemiology". There were 75 papers that used individuals as the units of analysis and 92 that were ecological studies with spatial polygons as the units of analysis. Study designs mostly consisted of cross-sectional studies (n = 121). There were also 14 time series, 16 case-comparison, and 15 cohort or panel studies.

Lexical Assessment

A total of 92 papers met our criteria as analytic ecologic studies; we therefore included these in our lexical assessment. We developed two scales within each category (epidemiology, geography, statistics, causal inference, intervention) composed of two to four terms. Table 4 reports the eigenvectors for the included terms, the eigenvalues for the extracted principal components, and the proportion of variance explained by each component. For example, the first scale extracted for epidemiology included the terms “bias”, “confound”, and “ecological fallacy” (or “ecological bias”). The Eigenvalue was 1.6 and the first principal component explained 52% of pooled variance for these terms, indicating that the scale had moderate internal consistency.

Results for the Poisson models are shown in Table 5. A 1-year increase in the publication year was associated with a 29% increase in the use of terms for the first principal component for statistics (IRR = 1.3; 95%CI: 1.1, 1.5), which comprised the terms “spatial weight”, “spatial error”, and “spatial lag”. A 1-year increase in the publication year was associated with a 15% increase in the use of terms for the second lexical scale extracted for causal inference, which comprised the terms “causa”, “conceptual”, and “mechanis” (IRR = 1.2; 95%CI: 1.1, 1.3). Scales for epidemiology, geography, and interventions were not associated with the year of publication. Table e2 reports the distribution for counts of terms for each extracted scale, demonstrating little overdispersion.

DISCUSSION

Spatial epidemiology is a relatively new subfield of epidemiology that has emerged over the past quarter century. This systematic review found that definitions of spatial epidemiology have become more expansive over time, and that analytic studies have overtaken descriptions of methods and disease distributions as the predominant focus. We found that descriptive spatial epidemiology has an essential role for guiding resource allocation and generating hypotheses, and that—reflecting its forebears’ disciplinary backgrounds in geography and statistics—the subfield has contributed meaningfully to the development of geographic and statistical methods for examining health data. Moreover, more recently published studies tend to use terms from spatial statistics and those consistent with contemporary epidemiology’s focus on causal inference. However, opportunities for further growth remain. Foundational epidemiologic constructs (e.g., bias, confounding) are rarely invoked. Intervention studies labelled as “spatial epidemiology” are exceedingly rare. Thus, while the current trajectory of spatial epidemiology is promising, further evolution is necessary if the subfield is to contribute more fully to epidemiology’s ultimate goal as “a tool to change the world, not merely to study the world.”[20,21]

Substructures—or in our case, subfields—are an inexorable part of growth in human organizations. As the pool of people present within an organization increases, individual members’ ability to monitor the whole organization decreases, specialized terminology and expertise develop, and new levels of organization emerge. In the sciences, growth is a product of available funding, employment opportunities, and graduation rates, and is a sign of the overall health of a discipline. Epidemiology has grown considerably by many measures over the last several decades[83,84]; and consistent with expectation, many subfields have emerged. For example, in 1982, Perera and Weinstein coined the phrase "molecular epidemiology" and described the subfield as an off shoot of environmental epidemiology, to suggest a renewed rigor in evaluating chemical exposures using objective laboratory-based analyses of biomarkers in biological specimens.[85] Two decades later, Wild defined "exposomics" to bring attention back to the essential role of environmental exposures to a field that had become heavily focused on measuring DNA, RNA, metabolites, and protein fragments in biologic samples.[86] Similar to molecular epidemiology and exposomics, spatial epidemiology has emerged as subfield with the critical mass of like-minded scientists and in response to newly available technologies and data. The benefits are considerable. Labelling a subgroup of scientists as belonging to a newly defined group confers legitimacy that helps attain funding and can assist with publications—the hallmarks of academic success.[87,88] It encourages interdisciplinarity, which is associated with greater impact.[89] It helps concentrate skills, which helps to develop a common lexicon and produce scientific advances. It gives a unified sense of purpose. Spatial epidemiology achieves such benefits for its members. Although loosely organized, it is a domain-spanning scholarly field with the capacity to connect disciplines[90] and its appeal and capacity for further growth is immense. However, there are also important costs. As scholarly products increase and new sub-fields emerge, opportunities for miscommunication and scholarly silos are great. Our findings are of value here. The subset of papers for which we conducted the lexical assessment (i.e., the analytic ecologic studies) rarely used foundational terms from epidemiology, and we identified no change in their use over time. Locating spatial epidemiology as a subfield of epidemiology —with important influences from geography and spatial statistics—will provide a well-established base, will continue to improve rigor, and will minimize confusion.

Limitations

This systematic review has some key limitations. Perhaps most importantly, our search strategy and inclusion criteria are likely to have excluded epidemiologic studies that use spatial analytic methods but do not explicitly use the term "spatial epidemiolog*". These restrictive steps were necessary for the study to be feasible and to achieve our goal of advancing the subfield that bears that name, but we may have overlooked important papers that contribute to this overall area of science. For example, our own experimental studies of place-based interventions were not included.[91,92] Sociologic studies of neighborhood conditions[93] and many papers from environmental epidemiology[94] are likely to meet our definition of "analytic" studies—in that they use spatially structured data to examine potential causes of health behaviors or health outcomes—but were excluded because they did not meet our strict criteria. These studies are often concerned more with causal inference and intervention than the spatial statistical methods that dominate spatial epidemiology books (Table 1), so our assessment of the overall state of the science may be biased. These limitations underscore an opportunity. They suggest that the theoretical basis and empirical methods for updating spatial epidemiology already exist, and that there is already an appetite within the scientific community to move beyond descriptive spatial epidemiology and risk factor studies. The question is not how, but when.

This Are Spatial Epidemiology

Subfield development has critical implications for academic professionalism, including the content of curriculums we use to teach students, the creation of specialty journals, criteria for faculty hiring and promotion and setting expectations for academic activity and productivity (e.g., discipline specific expectations for bibliographic statistic benchmarks). As such it is of concern to those who profess to practice spatial epidemiology, to those whose work is spatial epidemiology under another guise, and to those whose work is adjacent to spatial epidemiology, as to how this field is defined.

We find Kirby et al's, 2017 definition of spatial epidemiology to be most compelling because it combines the three main goals of epidemiology—description, analysis, and intervention—as applied to spatially structured data. However, the definition omits reference to theory and causal inference, which are critical to selecting and justifying operational decisions about the handling of spatial structures and to informing intervention.[48] Thus, we propose a new definition, that *spatial epidemiology is the application of theory and methods from epidemiology, geography, and statistics to describe spatial distributions of health outcomes and to analyze associations with possible causes to inform intervention and improve health*. This updated definition is consistent with our *a priori* hypotheses and the findings of this review, that spatial epidemiology's disciplinary origins position the subfield to contribute greatly to descriptive studies, which are essential for understanding distributions of health within populations. Consistent with the direction of contemporary epidemiology, it also encourages analytical studies that examine putative causes of disease, and intervention studies that leverage the identified causes to improve health. Achieving these higher order objectives will require more input from epidemiology methodologists and a stronger emphasis on theory and methodologic rigor than has been evident in the subfield to date. However, maintaining the foundational ties to statistics and geography is essential. The recent development of "spatial causal inference"—and the increasing trend we detected for using terms related to this endeavor in spatial epidemiology papers—showcases the great promise of this multidisciplinary partnership.[95,96]

An essential question now is, as the subfield of spatial epidemiology evolves to require greater attention on theory and more rigorous methods, how does it bridge perspectives and generate a common language and understanding of methods? We propose that a modest starting point, based on the findings of this review, is a commitment for spatial epidemiology to adhere to the conventions of contemporary epidemiology. This includes better incorporation of theory and causal inference while maintaining a focus on epidemiology's ultimate goal to actually improve the health of populations. Descriptive studies must be well-justified and reserved for resource allocation and hypothesis generation. Analytic studies should invoke causal theories to guide operational decisions (such as the choice and scale of spatial units used in analyses). And spatial statistical and geographic methods can provide essential tools to help achieve the common goals of epidemiology (to describe, analyze, and intervene) rather than serving as ends unto themselves.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability:

Included articles were extracted from PubMed. The full list of included articles can be accessed in eTable 1.

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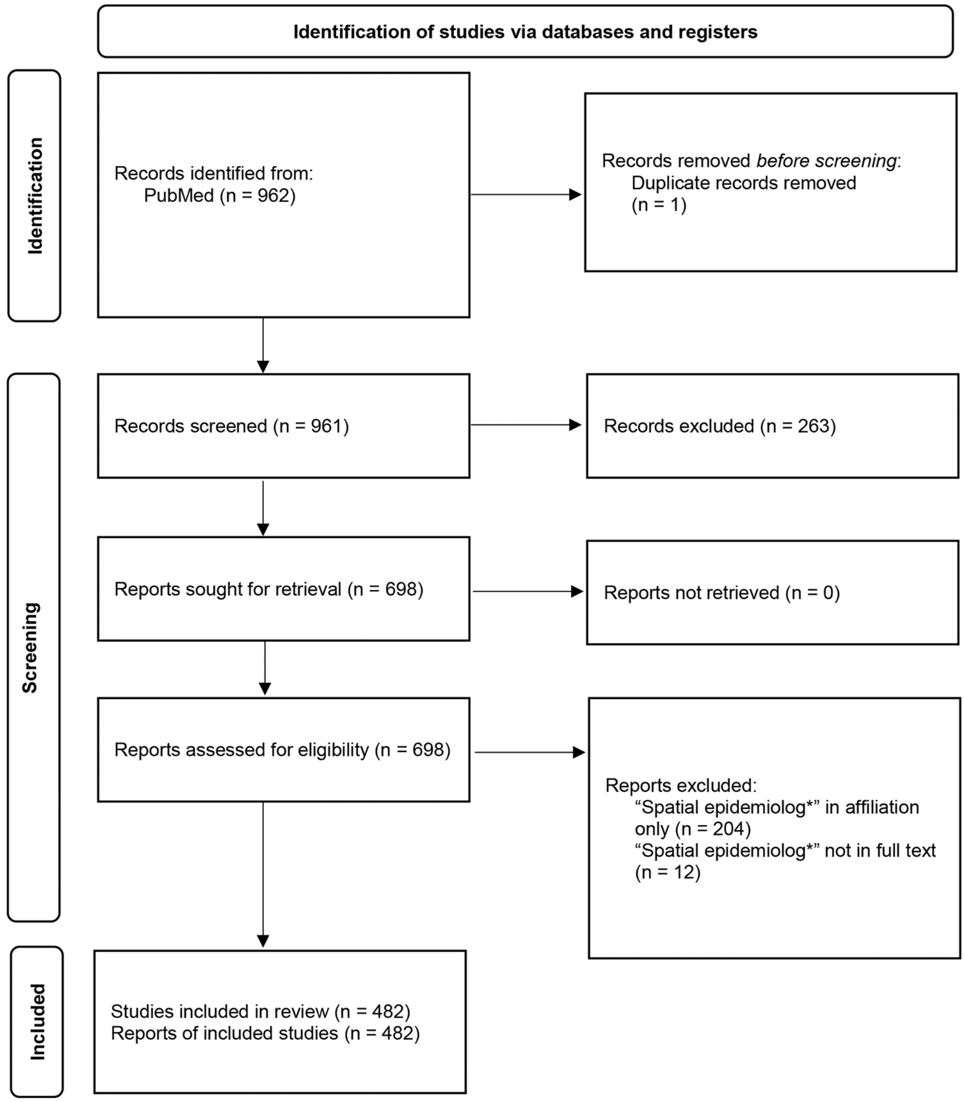

Figure 1.
PRISMA flow diagram.

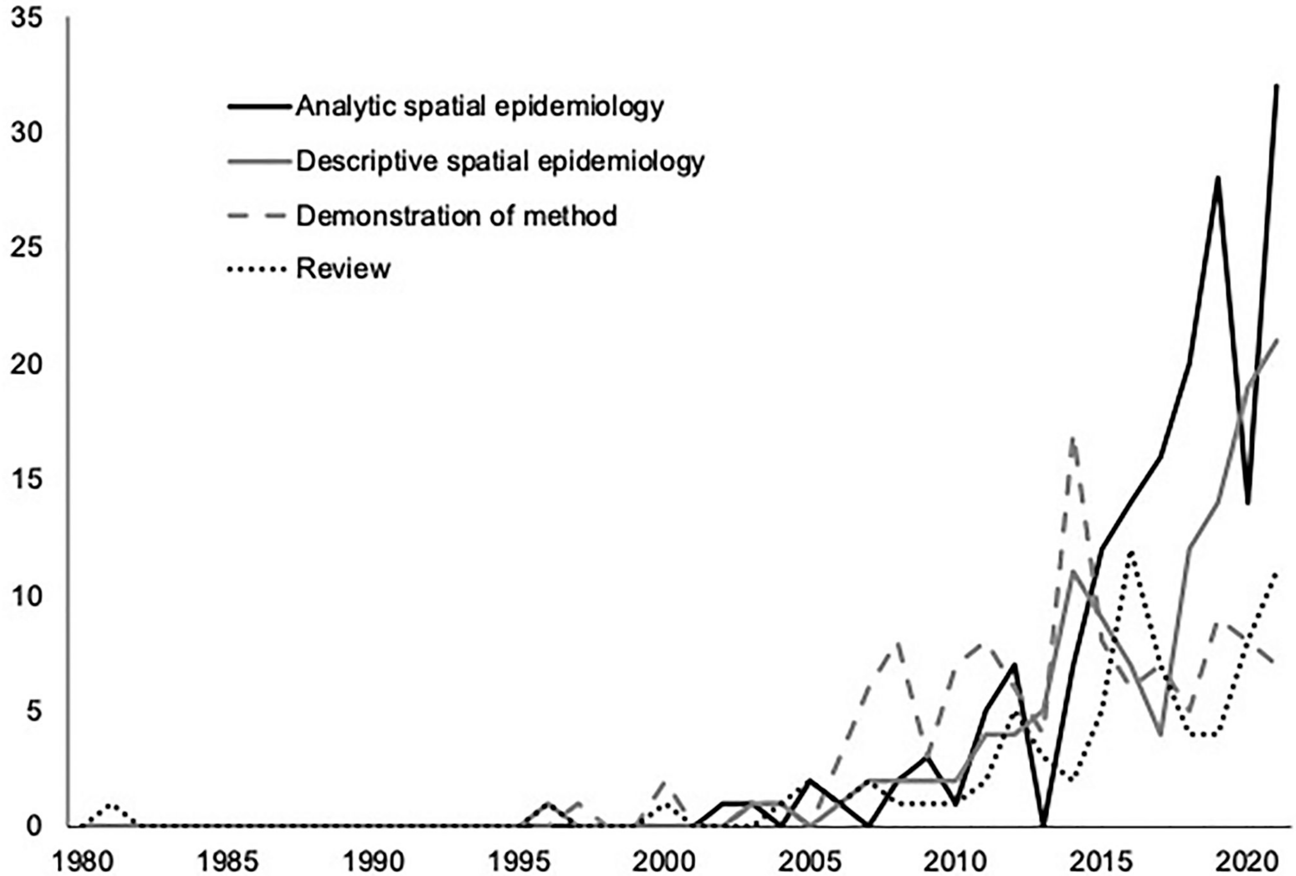

Figure 2.
Count of spatial epidemiology papers published per year by type.

Table 1.

Published books that include the terms “spatial” and “epidemiology” in the titles, according to author departmental affiliation.

First Author	Year[a]	Title	Authors	Edited Volume	Author Departmental Affiliation[*] Statistics, Biostatistics, Mathematics	Geography, GIS	Epidemiology	Other
Elliot[10]	2000	*Spatial Epidemiology: Methods and Applications*	38	Yes	15	0	11	14
Lawson[11]	2001	*Statistical Methods in Spatial Epidemiology*	1	No	1	0	0	0
Lawson[9]	2008	*Bayesian Disease Mapping: Hierarchical Modelling in Spatial Epidemiology*	1	No	1	0	0	0
Malchow[8]	2007	*Spatiotemporal Patterns in Ecology and Epidemiology: Theory, Models, and Simulation*	3	No	2	0	0	1
Pfeiffer[7]	2008	*Spatial Analysis in Epidemiology*	6	No	0	0	4	2
Lai[6]	2008	*Spatial Epidemiological Approaches in Disease Mapping and Analysis*	3	No	0	3	0	0
Shaddick[5]	2015	*Spatio-Temporal Methods in Environmental Epidemiology*	2	No	2	0	0	0
Lawson[16]	2016	*Handbook of Spatial Epidemiology*	51	Yes	31	5	8	11
Souris[97]	2019	*Epidemiology and Geography: Principles, Methods and Tools of Spatial Analysis*	1	No	0	0	0	1

[*] Some authors have multiple affiliations

Table 2.

Published definitions of spatial epidemiology and areas of emphasis

First Author	Year	Definition	Descriptive	Analytic	Intervention
Ostfeld[77]	2005	"Spatial epidemiology is the study of spatial variation in disease risk or incidence."	✓		
Brooker[98]	2006	"Spatial epidemiology aims to investigate spatial distributions of disease to identify geographic risk factors and populations at risk, which facilitates the rational implementation of control."	✓	✓	✓
Beale[99]	2008	"…assess the geographic distribution of potential health risks and their association with environmental risk factors."	✓	✓	
Elliott[100]	2008	"Small-area studies are part of the tradition of spatial epidemiology, which is concerned with the analysis of geographic patterns of disease with respect to environmental, demographic, socioeconomic, and other factors."	✓	✓	
Wieland[101]	2008	"…a collection of methods to analyze health characteristics and location have coalesced to comprise the field of spatial epidemiology. Disease mapping, assessing the tendency of patients to cluster in space, detecting localized clusters of dis-eases, and testing for clustering around a putative environmental point source are all distinct activities within the field."	✓	✓	
Clements[102]	2009	"Spatial epidemiology is the study of the spatial distribution of disease and associated factors."	✓	✓	
Hossain[103]	2009	"…spatial epidemiology… incorporates the geographical location of events of interest which helps reduce the model variance and leads to a correct inferential procedure."	✓	✓	
Bliss[104]	2010	"In geographic spatial epidemiology, researchers use spatial data to determine whether an observed pattern of disease has arisen by chance."	✓		
Newton[105]	2011	"Spatial epidemiology combines the geographic mapping of disease distributions with pattern analysis, spatial statistics and disease modelling."	✓		
Torabi[106]	2011	"Cluster detection is an important part of spatial epidemiology because it may help suggest potential factors associated with disease and thus, guide further investigation of the nature of diseases."	✓		
Gilbert[107]	2012	"These studies that fall under the general definition of spatial epidemiology have analysed disease distribution data with the aim to characterize their spatial or temporal pattern (e.g. clustering of cases), to identify spatial predictors associated with disease presence, and in some instances to map disease risk overlarge geographical areas."	✓	✓	
Robertson[108]	2012	"Spatial epidemiology is the study of the geographical variation of disease."	✓		
Sarfraz[109]	2012	"Spatial epidemiology is the study of spatial variation in disease risk or incidence."	✓		
Fritz[110]	2013	"Spatial epidemiology is a large tent that encompasses many disciplines (e.g. disease surveillance, public health, veterinary epidemiology and disease mapping), each of which has been separately pursuing research in cluster analysis."	✓		
Kohno[111]	2014	"…spatial clustering, and its modern applications have been developed as spatial epidemiology, directed toward analyzing risk assessment for infectious diseases and various other diseases."	✓		
Torabi[112]	2014	"An important part of spatial epidemiology is cluster detection as it has the potential to identify possible risk factors associated with disease, which in turn may lead to further investigations into the nature of diseases."	✓		
Um[113]	2014	"Spatial epidemiology emerges as a key tool to identify the spread and possible causes of DED [dry eye disease] outbreaks since standard map display techniques enable the visualization of DED uncertainty and ensure more meaningful inferences from the spatial data."	✓	✓	
Hamm[79]	2015	"Spatial-epidemiological analyses of NTD distributions proceed by estimating empirical relationships between epidemiological indicators of disease occurrence (e.g., prevalence and intensity of infection) and environmental and/or	✓	✓	✓

First Author	Year	Definition	Descriptive	Analytic	Intervention
		socioeconomic variables that are usually modelled as covariates. The purpose of such models is either to provide insight into the factors that influence the spatial distribution of disease or to use the observed empirical relationships between disease and the environment for spatial prediction. Maps based on spatial predictions can serve an important practical purpose, because they can be used to target interventions (e.g., drug treatments) geographically."			
Aregay[114]	2016	"One of the main goals in spatial epidemiology is to study the geographical pattern of disease risks."	✓		
Makanga[115]	2016	"Spatial epidemiology is defined as the study of spatial variation in disease risk or incidence."	✓		
Plaza-Rodríguez[116]	2016	"Spatial epidemiology becomes then a fundamental tool as it can describe, quantify and explain the geographical variations of diseases or contaminated items."	✓		
Deilami[117]	2017	"This concept explains that disease vectors, hosts and pathogens are generally tied to the landscape with ecological determinants influencing their distribution and abundance in the environment from the perspective of potential public health risk."	✓		
Kirby[80]	2017	"…spatial epidemiology encompasses research that incorporates the spatial perspective into the design and analysis of the distribution, determinants, and outcomes of all aspects of health and well-being across the continuum from prevention to treatment."	✓	✓	✓
Roquette[118]	2017	"[Spatial epidemiology] can promote the understanding of spatial and temporal distribution patterns, helping to better identify the risk factors that influence them."	✓	✓	
El-Ghitany[78]	2019	"Geographic Information Systems (GIS) and spatial epidemiological methods may provide a basis for disease investigation through which hotspots and disease determinants can be identified."	✓	✓	
Hernández[119]	2019	"…spatial epidemiology, which leverages multiple sources of demographic and environmental factors,…"	✓		
Escobar[120]	2020	"Spatial epidemiology is the branch of epidemiology that aims to understand the geographic distribution of diseases (including their causative agents, hosts, and related factors)."	✓	✓	
Garrett-Mayer[121]	2020	"Spatial epidemiology methods are specifically suited to the estimation of spatial clustering and the identification of geographic disease clusters."	✓		
Shrestha[122]	2020	"Spatial epidemiology, as previously described, pertains to the study of geographic variations in health conditions with respect to the surrounding risk factors."	✓	✓	
Cuadros[81]	2021b	"Spatial epidemiology has emerged as a novel approach for the understanding and control of current epidemics… Place in spatial epidemiology involves exploring beyond individual characteristics to consider the social and environmental contexts experienced by individuals and how these interactions affect their health"	✓	✓	✓
Eberth[123]	2021	"…spatial epidemiology, a subfield of epidemiology concerned with describing and analyzing spatial patterns of health and well-being."	✓	✓	
Fatima[124]	2021	"Study of disease distribution and diffusion over time and space is a core theme of both health geography and spatial epidemiology."	✓		
Nayak[125]	2021	"This new discipline, 'Spatial Epidemiology,' can be described as being 'concerned with describing, quantifying, and explaining geographical variations in disease, especially with respect to variations in environmental exposures at the small-area scale.' It helps in answering some seemingly simple geographical questions like: What is the distribution of a condition in a certain geographical area? Are there any patterns found and trends in disease incidence that could help predict incidence in the future? What is the accessibility of a certain area to the nearest health center?"	✓	✓	
Ramírez-Aldana[126]	2021	"Spatial analyses allow us to understand how mortality risks are distributed through a territory, detect spatial clusters, and measure how the effects of variables associated with this risk vary within any given territory."	✓	✓	

First Author	Year	Definition	Descriptive	Analytic	Intervention
Todd[82]	2021	"Spatial epidemiology is aimed at identifying patterns in the geographical distribution of health data. Analysis of the geographical distribution of disease and other health outcomes is increasingly used in epidemiology, and conducting spatial analyses allows the utilisation of local information for planning and health policy, whilst ensuring that interventions remain evidence-based.	✓		✓
Wang[127]	2021	"…spatial epidemiology improves the understanding of disease from qualitative level to quantitative level, by analyzing geographically indexed health data related to demography, environment, behavior, socio-economy, genetics, etc. Supported by geographic information science (GIS) and spatial analysis technol-ogy, spatial epidemiology describes and analyzes the spatial distribution characteristics and development pattern of epidemiological health events."	✓		
Yang[128]	2021	"Spatial epidemiological approaches in a Geographic Information Systems (GIS) environment, such as spatial clustering analysis, have previously been used to examine geographic distribution patterns of cases of disease; this has enabled efficient and cost-effective use of healthcare re-sources."	✓		

Table 3.

Study design by unit of analysis (ecological vs. individual) among analytic spatial epidemiologic studies (n = 167).

	Ecological	Individual-level	Total
Case–comparison (e.g., case–control, case–crossover)	2	14	16
Cohort or panel	3	12	15
Cross sectional	75	46	120
Experimental	0	0	1
Natural or quasi-experimental (e.g., diff-in-diff, regression discontinuity)	1	0	1
Time series	11	3	14
Total	**92**	**75**	**167**

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Table 4.

Principal components analysis eigenvectors for scales of lexical content of included papers categorized as “analytic” and “ecological” (n=92)

			Epidemiology[a]		**Geography**[b]		**Statistics**[c]		**Causal Inference**[d]		**Intervention**[e]	
Regular Expression			**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**	**1**	**2**
bias	56	(61)	0.55									
confound	28	(30)	0.61									
ecological fallacy	24	(26)	0.57									
ecologic	73	(79)		0.61								
reliab	32	(35)		0.59								
valid	47	(51)		0.53								
latitude	18	(20)			0.71							
longitude	17	(18)			0.71							
boundar	43	(47)				0.51						
point	64	(70)				0.48						
polygon	16	(17)				0.46						
small area	21	(23)				0.55						
spatial weight	16	(17)					0.52					
spatial error	9	(10)					0.60					
spatial lag	10	(11)					0.61					
autoregressi	30	(33)						0.51				
multi-level	25	(27)						0.50				
nest	22	(24)						0.46				
random effect	28	(30)						0.54				
hypothesi	57	(62)							0.45			
assum	60	(65)							0.61			
interact	61	(66)							0.66			
mechanis	30	(33)								0.65		
causa	28	(30)								0.58		
conceptual	32	(35)								0.49		
blind	2	(2)									0.48	
efficacy	11	(12)									0.54	
effectiveness	17	(18)									0.53	
implementation	28	(30)									0.44	
interven	53	(58)										0.55
stratif	17	(18)										0.53
baseline	17	(18)										0.49
prevent	80	(87)										0.42
Eigenvalue			*1.55*	*1.42*	*1.82*	*1.61*	*2.29*	*2.32*	*1.34*	*1.43*	*2.00*	*1.59*
Proportion			*0.52*	*0.47*	*0.91*	*0.40*	*0.76*	*0.58*	*0.45*	*0.48*	*0.50*	*0.40*

[a)] bias, confound, ecological fallacy (OR ecological bias), misclassification, longitudinal, cohort, case–control (OR case control), difference-in-difference (OR difference in difference), ecologic (NOT ecological fallacy OR ecological bias), reliab, valid, sensitiv, specifici

[b] modifiable areal unit problem, distance decay, small area, denominat, geographic information system, GIS, vector, raster, container (OR containment), proximity, cluster, scale, scale effect, boundar (OR edge), polygon, point, line, coordinate, latitude, longitude

[c] auto-correlat (OR autocorrelat), auto-regressi (OR autoregressi), spatial lag, spatial error, spatial weight, adjacen, nest, multi-level (OR multilevel), random effect, dependenc

[d] theor, mechanis, hypothesi, assum, causa, conceptual, directed acyclic graph, mediat, interact (OR modif OR moderat), spillover (OR interference OR SUTVA)

[e] experiment, interven, randomiz, trial, blind, control, consort, balanc, follow-up (OR follow up), stratif (OR stratum OR strata), baseline, efficacy, effectiveness, prevent, rct, implementation, natural experiment, quasi experiment

Table 5.

Poisson models for scales of lexical content per one unit increase in year of publication for included papers categorized as “analytic” and “ecological” (n=92)

	Scale	IRR	(95%	CI)	p-value
Epidemiology	1	0.98	0.93	1.04	0.542
	2	0.99	0.95	1.04	0.779
Geography	1	0.92	0.85	1.00	0.062
	2	1.01	0.96	1.06	0.774
Statistics	**1**	**1.29**	**1.09**	**1.52**	**0.002**
	2	0.98	0.92	1.04	0.459
Causal Inference	1	0.99	0.95	1.04	0.657
	2	**1.15**	**1.05**	**1.25**	**0.002**
Intervention	1	1.07	0.97	1.17	0.164
	2	1.02	0.97	1.07	0.427