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Time to address the spatiotemporal uncertainties in COVID-19 research: Concerns and challenges

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The rapid spread of COVID-19 across the globe has led scholars to speculate about the environment's role in the incidence and prevalence of this disease (Shakil et al., 2020). It makes intuitive sense that some environmental settings may facilitate transmission. An increasing number of studies has examined possible physical and social environmental determinants of COVID-19. Frequently applied are ecological study designs using grouped COVID-19 and (open) environmental data (e.g., Worldpop, Google Earth Engine) corresponding to an areal unit (Wakefield, 2008). In some cases, socio-demographics (Sannigrahi et al., 2020) and measures of exposure such as air pollution (Fattorini and Regoli, 2020), humidity (Ma et al., 2020), and temperature (Sarmadi et al., 2020) were found to be associated with infection rates. However, at least two methodological caveats - resonating wellestablished sources of bias in geospatial data analyses - are shared amongst many of these studies. To assist COVID-19 research to make more fruitful progress in the future, we highlight potential concerns and challenges with two aims: 1) emphasizing the critical role of acknowledging geographical principles related to the spatial and temporal unit of analysis; and 2) arguing for exposure assessments centering on people rather than areas when assessing COVID-19 transmission.

First, many (if not all) of ecological COVID-19 studies to date have utilized imprecise and spatially and temporally unaligned data on an ad hoc basis. We posit that data decisions are driven by what COVID-19 datasets were publically available and the paucity of readily available exposure data. Such datasets are often limited to the municipality, county, or even country level for privacy reasons, and utilizing secondary data provides rapid empirically-based recommendations for health policy. However, spatially aggregated data across space and over time susceptible to the modifiable areal unit problem (MAUP) (Openshaw, 1981) and the modifiable temporal unit problem (MTUP) (Cheng and Adepeju, 2014). The former emphasizes that analytical differences may occur depending on the size of the areal units used (the scale effect) and the way the study area is divided (e.g., municipalities vs. districts) (the zoning effect). The latter stresses that results also depend on the way data are temporally aggregated (e.g., weeks vs. months) and which temporal segmentation schemes are applied (e.g., first day per week/month vs. middle of the week/months) (Cressie, 1998). While some attempts have been made to assess daily COVID-19 patterns and reduce the risk of the MTUP (e.g., Badr et al., 2020), it is likely that COVID-19-associations remain dependent on the state of the

epidemic. Different data periods considered in an ecological analysis (e.g., the first month vs. the first three months since the outbreak) likely manifest in different spatiotemporal COVID-19 incidence patterns and thus altered correlations.

Both the MAUP and MTUP represent fundamental methodological problems shown to bias statistical inference and result in spurious models (de long and de Bruin, 2012; Wang and Di, 2020), Limited space-time granularity can result not only in underpowered studies but also in conclusions based on geographic scales that are too large to uncover meaningful COVID-19-environment associations and effectively inform policy. Of similar importance, the possibility of confounding from using ecological inference is substantial due to the neglect of person-level factors (e.g., age) (Greenland et al., 1994). Thanks to considerable efforts undertaken to quickly understand COVID-19 risk factors, recent ecological analyses are more comprehensively adjusted for potentially important confounders including the epidemic stage, measures for containment, socio-demographic and meteorological conditions, etc. (Klompmaker et al., 2020). These efforts have considerably reduced residual confounding, but regardless of the strength of an observed (well-adjusted) ecological association, neither can conclusions on the cause-and-effect relationships be made nor can the associations be transferred to the individual-level (ecological fallacy) (Robinson, 2009; Wakefield, 2008). We, therefore, urge for conceptually-stronger observational research designs including retrospective case-control studies based on register linkage data enriched with high-resolution environmental determinants derived on a residential address level by means of geographic information systems. Prospective cohort studies may not be practical in light of ethical issues regarding the exposure of people to a health-threatening risk in which specific population groups (e.g., those with pre-existing illness) appear to be disproportionately affected.

Second, when studying highly contagious infectious diseases such as COVID-19 where viral transmission occurs through largely face-to-face interaction (Wiersinga et al., 2020), assessing transmission risk based solely on people's residential neighborhoods seems questionable. Despite partial lockdowns, people can be exposed to different environments at nonhome locations (e.g., home improvement stores, grocery stores) and en-route along their mobility path when traveling between their day-to-day activity places. Disregarding the timing and duration that people are exposed to environments beyond their home gives rise to another methodological concern, the uncertain geographic context problem (UGCoP) (Kwan, 2012). This concern describes misspecification of the geospatial context that manifests in the over- and underestimation of the "true" exposure to environments, and ultimately results in inferential errors. Relatedly, epidemiological and environmental data should be temporally aligned as closely as possible to reduce temporal context uncertainties; a temporal misalignment can obscure or distort COVID-19exposure associations and falsely render environmental factors as correlates or not (Helbich, 2019). To address context uncertainties from people's day-to-day mobility behavior, we call for individual rather than area-centered approaches using location-tracking technologies.

With strict privacy regulations and data security in place and without the need for primary data collection, researchers should take advantage of mobile phone data. Movement patterns and activity locations can be inferred based on the specific cellular towers and the handovers from one tower to another assigned to phones (Oliver et al., 2020). Since such data can play a critical role in retrieving fine-grained information on space-time mobility and social interaction on a population-level, we urge for alliances between research labs and telecommunications operators for mobility-based exposure assessments.

Taken together, while a methodological and epistemological pluralism is inevitable in spatial analyses on COVID-19, we caution against an uncritical application of area-aggregated data and reiterate the importance of inherent scale-time dependencies and contextual uncertainties arising through human mobility.

Declaration of competing interest

The authors have no conflict of interest to declare.

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