PEER-REVIEW REPORT

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

the manuscript reviewed the current records of the spatial distribution of the SUD epidemic in the U.S. across different periods, revealing the spatiotemporal patterns that had preceded the occurrence of outbreaks. By analyzing the epidemic of SUD related deaths, the authors also described the epidemic behavior in areas with high incidence of cases. Furthermore, the authors described the demographic factors to target for public health strategies and discussed future challenges in the study and control of the SUD epidemic in the U.S.. The review is very detailed and comprehensive, describing the current situation and providing reference for more accurate public health prevention and control policies in the future.

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The review by Cuadros DF, et al., discussed the recent update on spatial epidemiology of substance use disorder (SUD) in U.S.A. This can help us with understanding SUD' spatial epidemiological features, and thus is an interesting report.

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SPECIFIC COMMENTS TO AUTHORS

General comments:　The authors attempt to address an important and timely topic (the opioid crisis in the USA), and how spatial epidemiology has the potential to play a vital role in identifying hotspots and aiding mitigation efforts. However, some major revisions are needed before this paper can be published.　The review type is unclear (it should be stated in the title) – narrative/literature, scoping, or systematic (in the Discussion, the authors refer to the paper as a study). However, this paper falls short as a narrative literature review summarizing the body of literature. It mainly reports previous work/studies carried out by the authors (which is very good(!), but not the only examples). It might be possible to restructure it (perhaps as a mini-review), but the review should include more findings from other researchers, identify gaps or inconsistencies in existing literature, develop research questions or identify new research streams or patterns of usage.　It states in the paper that the challenges and future implementation of spatial epidemiology will be discussed, but where are these points? The authors state there is a shortage of geospatial analysis in tackling the SUD crisis, but is this supported by the literature? Were opportunities missed (chronological assessment

of the use of geospatial analysis in the literature)? Please show evidence based on findings from a more comprehensive literature review.   The methods are missing (databases searched, terms used, timeframe, etc.). Grey literature is included, so this should be noted. Please include the type of software used to create the figures. Clear definitions are needed - substance use disorder or opioid use disorder – it seems like the review is focused on the latter but is using the former term. In addition, the review is too broad in terms of topics (lessons from malaria and HIV are helpful but should be limited and those figures deleted), and too much is written about basic GIS / spatial epidemiology (should be shortened).   Specific comments: The English writing style is good, but some minor revisions are needed: naloxone is not a brand (please use lower case), basic instead of basal health, comorbidities (delete "adverse health" – repetitive), 22 million not 22,000,000.   Delete figure 1A 1B – relevance to a review on SUD in USA? Discussion of these cases is useful but there's too much emphasis with these figures. These could be included in supplemental material, though.   References need improvement – error message (11), incomplete citation (46) , repeat citations (32, 41), and incomplete literature search. Below are examples of potential papers identified from a PubMed search – "geospatial" AND "opioids":   Kline D, Hepler SA. Estimating the burden of the opioid epidemic for adults and adolescents in Ohio counties. Biometrics. 2021 Jun;77(2):765-775. doi: 10.1111/biom.13295. Epub 2020 Jun 2. PMID: 32413155; PMCID: PMC7666653.   Anwar T, Duever M, Jayawardhana J. Access to methadone clinics and opioid overdose deaths in Georgia: A geospatial analysis. Drug Alcohol Depend. 2022 Sep 1;238:109565. doi: 10.1016/j.drugalcdep.2022.109565. Epub 2022 Jul 7. PMID: 35839618.   Tighe P, Modave F, Horodyski M, Marsik M, Lipori G, Fillingim R, Hu H, Hagen J. Geospatial Analyses of Pain Intensity and Opioid Unit Doses Prescribed on the Day of Discharge Following Orthopedic Surgery. Pain Med. 2020 Aug 1;21(8):1644-1662. doi: 10.1093/pm/pnz311. PMID: 31800063; PMCID: PMC7530566.

Cobert J, Lantos PM, Janko MM, Williams DGA, Raghunathan K, Krishnamoorthy V, JohnBull EA, Barbeito A, Gulur P. Geospatial Variations and Neighborhood Deprivation in Drug-Related Admissions and Overdoses. J Urban Health. 2020 Dec;97(6):814-822. doi: 10.1007/s11524-020-00436-8. PMID: 32367203; PMCID: PMC7704893. Peterman NJ, Palsgaard P, Vashi A, Vashi T, Kaptur BD, Yeo E, Mccauley W. Demographic and Geospatial Analysis of Buprenorphine and Methadone Prescription Rates. Cureus. 2022 May 30;14(5):e25477. doi: 10.7759/cureus.25477. PMID: 35800815; PMCID: PMC9246456.

Dworkis DA, Weiner SG, Liao VT, Rabickow D, Goldberg SA. Geospatial Clustering of Opioid-Related Emergency Medical Services Runs for Public Deployment of Naloxone. West J Emerg Med. 2018 Jul;19(4):641-648. doi: 10.5811/westjem.2018.4.37054. Epub 2018 May 15. PMID: 30013698; PMCID: PMC6040905. Stewart K, Cao Y, Hsu MH, Artigiani E, Wish E. Geospatial Analysis of Drug Poisoning Deaths Involving Heroin in the USA, 2000-2014. J Urban Health. 2017 Aug;94(4):572-586. doi: 10.1007/s11524-017-0177-7. PMID: 28639058; PMCID: PMC5533669. Hallas D, Klar RT, Baldyga JA, Rattner I, Waingortin R, Fletcher J. Traditional and Nontraditional Collaborations to Improve Population Health Using Geospatial Information SystemMaps: Analysis of the Opioid Crisis. J Pediatr Health Care. 2019 May-Jun;33(3):309-322. doi: 10.1016/j.pedhc.2018.10.006. Epub 2019 Mar 20. PMID: 30902507. Stoicea N, Costa A, Periel L, Uribe A, Weaver T, Bergese SD. Current perspectives on the opioid crisis in the US healthcare system: A comprehensive literature review. Medicine (Baltimore). 2019 May;98(20):e15425. doi: 10.1097/MD.0000000000015425. PMID: 31096439; PMCID: PMC6531094.

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The manuscript reviewed the importance of studying spatiotemporal patters of the SUD epidemic for health prevention and control of this epidemic in the future. And this manuscript is worthy of publication.