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Peer Review

Review of: "Integrated Determinants of Persistent Wild Poliovirus Transmission in Pakistan and Afghanistan: The Roles of Cross-Border Mobility, Hard-to-Reach Populations, and Micro-Transmission Hotspots, 2010-2025"

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This manuscript addresses a critical and timely topic—the final hurdles to global polio eradication. The authors have undertaken a comprehensive scoping review to synthesize a wide range of evidence (epidemiological, genomic, serological, environmental) from the last 15 years. The central argument, that WPV1 persistence is due to a convergence of cross-border dynamics, immunity gaps in marginalized populations, and operational challenges, is well-supported by the presented evidence. The manuscript is clearly written and logically structured, making a significant contribution to understanding this complex public health challenge. However, several areas require revision to enhance the manuscript's clarity, rigor, and impact before it is suitable for publication.

Comments

Methodological Clarity and PRISMA-ScR Adherence:

The authors state they followed PRISMA-ScR guidelines. While the PRISMA flow chart (Figure 1) is included, the manuscript would benefit from a more explicit mapping of the results to the PRISMA-ScR checklist items. For instance, a dedicated section or table outlining the characteristics of the 52 included studies (e.g., study designs, geographic focus within the countries, years of data collection) would greatly strengthen the methodology section. This is a core expectation of a scoping review.

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Recommendation: Add a summary table detailing the key characteristics of the 52 included studies. This table could categorize them by type (e.g., genomic analysis, serological survey, modeling study), primary geographic focus, and the main thematic domain they inform.

Depth of Evidence Synthesis and Critical Appraisal:

The results are presented thematically, which is appropriate. However, the synthesis within each theme is often descriptive rather than analytical. For example, the section on immunity gaps lists several studies that found low coverage, but it does not critically compare their findings, methodologies, or the populations they studied. Are there conflicting findings? How do the causes of low coverage differ between nomadic groups in the north and urban slums in Karachi?

Furthermore, a scoping review should ideally include some form of quality or risk of bias assessment for the included studies, even if it's not used for exclusion. This is important for contextualizing the strength of the evidence being synthesized.

Recommendation: Enhance the narrative synthesis by comparing and contrasting findings from different studies within each thematic domain. A brief statement on the overall quality and potential biases of the evidence for each theme (e.g., "Evidence for cross-border transmission is robust, supported by multiple genomic studies, whereas evidence on specific barriers in nomadic populations is primarily derived from a few qualitative or cross-sectional studies") would add significant value.

Clarity and Interpretation of Serological Data:

The presentation of seroprevalence data in the text and Table 3 is somewhat confusing and appears contradictory. The text states seroprevalence in high-risk districts is >94-95%, but then cites specific studies (Ref 35, 36) showing levels below 90% in Balochistan and parts of Karachi. Table 3 lists seroprevalence for nomadic/displaced groups as "<70%" but for "National average" as "≥95% overall."

This contrast is a key finding, but the reader has to work hard to piece it together. The "urban low-income settlements" row in Table 3 is particularly unclear, with "~90% (variable)" listed under seroprevalence but no corresponding routine coverage estimate.

Recommendation: Reorganize Table 3 and the accompanying text to clearly and consistently show the *discrepancy* between high national/aggregate figures and the much lower figures within specific, high-risk micro-populations. This contrast is the central point. Clarify the seroprevalence estimate for urban low-income settlements. Ensure the data for each population group is presented in a consistent format.

The Link to cVDPV2:

The manuscript strongly and correctly makes the link between WPV1 persistence and the cVDPV2 emergency. This is a major strength. However, this argument is introduced in the introduction (Pages 3-4) and then revisited in the discussion. The flow could be improved by briefly mentioning in the results section if any of the reviewed studies provided direct evidence of this linkage (e.g., studies showing WPV1 and cVDPV2 co-circulation in the same hotspots, or modeling the resource diversion).

Recommendation: Add a sentence or two in the "Localized Micro-Transmission Hotspots" results section to explicitly state that these same hotspots are also the epicenters of cVDPV2 outbreaks, referencing the studies that support this co-circulation (e.g., Refs. 14, 15). This would create a stronger narrative thread from the results to the discussion.

Recommendation:

This manuscript presents a valuable and important synthesis of the factors perpetuating polio in its last strongholds. The recommended revisions are primarily aimed at strengthening methodological transparency, deepening the analytical synthesis of the evidence, and clarifying key data points. With these revisions, the paper will make a strong contribution to the literature and inform ongoing eradication efforts.

Declarations

Potential competing interests: No potential competing interests to declare.