

Peer Review

Review of: "The Contentious Origins of SARS-CoV-2: A Comprehensive Review of Current Knowledge"

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This review provides a timely and comprehensive synthesis of the peer-reviewed scientific literature concerning the origin of SARS-CoV-2, focusing primarily on publications between December 2023 and January 2025. Given the persistent global impact of the COVID-19 pandemic and the ongoing debate surrounding the virus's emergence, a critical examination of the latest evidence is highly valuable. The authors' stated goal is to analyze the evolving body of evidence, which is a crucial step in moving towards a more definitive understanding of this complex issue. A significant strength of this review is its systematic approach to synthesizing a large volume of recent scientific literature. The authors clearly outline their search strategy, inclusion and exclusion criteria, and the databases used (PubMed and Scopus). This transparency in methodology enhances the credibility of the review and allows readers to understand how the included studies were selected. The focus on peer-reviewed empirical data is also a strong point, ensuring that the review is grounded in scientific evidence rather than speculation. The review effectively presents the two primary hypotheses regarding the origin of SARS-CoV-2: natural zoonotic spillover and a laboratory-related event. It clearly articulates the "dominant narrative" of a zoonotic origin, detailing the converging lines of evidence that support this theory. These include phylogenetic analyses demonstrating genomic similarities with bat coronaviruses, the epidemiological link to the Huanan seafood market, and the historical precedent of other zoonotic coronavirus outbreaks. The explanation of "strong phylogenetic evidence" is particularly well-detailed, providing a clear understanding of the metrics and reasoning behind this support. Furthermore, the review thoughtfully addresses the complexities within the zoonotic narrative, such as the discovery of related Sarbecoviruses in bats and the ongoing search for a definitive intermediate host. The discussion of reverse zoonosis is also a valuable addition, highlighting the increasing concern about human-to-animal transmission and

the potential for establishing animal reservoirs. These sections demonstrate a nuanced understanding of the multifaceted nature of viral transmission and evolution. While the review robustly presents the evidence supporting a zoonotic origin, it also critically examines the laboratory leak hypothesis. A key strength here is the clear statement that this hypothesis "lacks direct scientific support" and is primarily based on circumstantial evidence and speculation. The review highlights the absence of direct evidence, the consistency of genetic analysis with natural evolution, and the limitations of risk assessment tools that rely on subjective criteria. This balanced approach, while clearly favoring the zoonotic hypothesis based on current evidence, maintains scientific openness by acknowledging that a lab leak cannot be categorically excluded. The review also excels in its discussion of the broader context surrounding the origin debate, emphasizing the critical importance of scientific inquiry, transparency, and international collaboration. The authors rightly point out how the politicization of the debate and the spread of misinformation undermine public trust in science and impede effective pandemic response. This humanized aspect of the review, acknowledging the real-world challenges in communicating scientific findings, adds a valuable dimension beyond the purely technical. Opportunities for improvement exist in several areas to further strengthen the review's impact and clarity. While the review synthesizes recent findings, a more explicit discussion of how these new data specifically address or refine the uncertainties highlighted in previous reviews by the same authors could provide a clearer trajectory of the evolving evidence. Connecting the current findings back to the specific gaps identified in earlier analyses would offer a more cohesive narrative of progress in the field. One area that could benefit from further elaboration is the discussion of the risk assessment tools, such as the modified Grunow-Finke assessment tool (mGFT). While the review correctly notes that these tools rely on subjective criteria and expert opinion, a brief explanation of *how* these tools are structured and the types of subjective criteria they incorporate would provide readers with a better understanding of their limitations and why their suggestions of an unnatural origin are considered less scientifically robust than empirical data. Furthermore, while the review provides a comprehensive summary of key recent findings in Table 2, integrating a more detailed discussion of the most compelling *specific* pieces of new empirical evidence within the main text could enhance the persuasive power of the review. For example, a deeper dive into a particularly strong new phylogenetic analysis or a significant new finding from environmental sampling at the Huanan market could more effectively illustrate the weight of evidence accumulating in favor of the zoonotic origin. Finally, the recommendations provided in the conclusion are highly relevant and forward-looking, emphasizing the need for strengthened surveillance, transparency, a One Health approach, refined risk assessment tools, improved communication, and international collaboration. To

make these recommendations even more impactful, a brief discussion of the practical challenges in implementing these strategies, particularly in the face of geopolitical barriers and resource constraints, could add a layer of realism and provide a more complete picture of the path forward. In conclusion, this review makes a valuable contribution by providing a current and critical synthesis of the scientific evidence surrounding the origin of SARS-CoV-2. Its strengths lie in its systematic methodology, clear presentation of the dominant zoonotic narrative and critical examination of the lab leak hypothesis, and its emphasis on the importance of scientific inquiry and transparency. By considering opportunities to further connect new findings to previous uncertainties, elaborate on the limitations of specific tools, highlight key empirical evidence, and discuss the practicalities of implementing recommendations, the review can enhance its clarity, impact, and provide even more comprehensive guidance for navigating this complex and crucial scientific debate.

Declarations

Potential competing interests: No potential competing interests to declare.