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VIEWPOINT

Why stating hypotheses in grant writing is usually necessary

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In this viewpoint, we explore the provocative argument by Hernán and Greenland, presented in JAMA, regarding the traditional necessity of stating hypotheses in grant applications. They propose that this convention may hinder the explorative nature of research, calling for a reevaluation that could impact global research practices and methodologies. Hypotheses provide a structured framework crucial for clarifying research questions and facilitating successful funding. However, Hernán and Greenland merge grant writing with research execution, potentially undervaluing the strategic role of hypotheses. We discuss the perspectives of philosophers Karl Popper and Thomas Kuhn, emphasizing the essential role of hypotheses in fostering scientific progress through critical scrutiny and paradigm shifts. While acknowledging the value in Hernán and Greenland's flexibility for data-driven research, we assert that hypotheses remain fundamental in guiding scientific inquiry, balancing innovation with traditional rigor. Our discussion aims to contribute to the evolution of research methodologies, ensuring they are both innovative and grounded in systematic, hypothesis-driven approaches.

In their thought-provoking commentary published in *JAMA* (1), Miguel A. Hernán and Sander Greenland propose a reevaluation of the traditional necessity to state hypotheses in grant applications, suggesting that this practice might be unnecessary and even detrimental to the essence of research to explore effects with precision and openness. Our motivation to engage with Hernán and Greenland's discourse, particularly given its publication in a prestigious platform like *JAMA*, stems from an understanding of the profound impact this debate can have on clinical practices and research methodologies. The conversation extends beyond academic discourse, affecting how research is conceptualized, funded, and executed globally. Engaging in this dialogue is essential for developing research methodologies that combine innovation with the rigor necessary for significant advancements in medical science and beyond.

The original purpose of the Hernán and Greenland article, as inferred from its title, appears to focus on the role of hypotheses in grant writing. However, the content extends beyond this to encompass the implementation of research, blurring the lines between these distinct phases. In grant writing, hypotheses are crucial as they encapsulate the research question, direction, and rationale, providing a clear and structured framework for the study (2–4). They serve as foundational elements that guide the research's conceptual and analytical trajectory, facilitating successful grant acquisition.

However, Hernán and Greenland's blend of the grant-writing process with research execution overlooks the foundational role hypotheses play in the former. While their call for flexibility and data-driven approaches in research execution is valid and valuable, it somewhat diminishes the importance of a well-articulated hypothesis in securing grant funding. This overlook can lead to underestimation of the strategic importance of hypotheses in guiding the research journey, accommodating new data, and fostering unanticipated discoveries.

Expanding upon the philosophical perspectives of Karl Popper and Thomas Kuhn provides a richer understanding of this debate. Karl Popper and Thomas Kuhn are two of the 20th century's most influential philosophers of science. Each offers distinct perspectives on the role of hypotheses in scientific progress and the dynamics of paradigm shifts. Popper, known for his theory of falsifiability (5), argues that scientific theories should be framed in such a way that they can be rigorously tested and potentially disproven. According to Popper, the growth of scientific knowledge is an evolutionary process driven by the cycle of conjectures and refutations. He proposes that scientists put forward bold hypotheses and then attempt to falsify them. In this view, hypotheses are crucial as they offer clear, testable propositions that challenge the status quo. Popper contends that the inability to falsify a hypothesis does not confirm it as accurate but merely upholds it as the best approximation of truth currently available. Thus, for Popper, the hypothesis-driven approach is central to scientific discovery, as it encourages robust testing and critical scrutiny, leading to the elimination of errors and the advancement of knowledge.

On the other hand, Kuhn introduces the concept of scientific paradigms (6,7) which he defines as universally recognized scientific achievements that, for a time, provide model problems and solutions to a community of practitioners. According to Kuhn, normal science operates within the confines of the current paradigm, focusing on solving puzzles that the paradigm delineates. However, when the paradigm encounters anomalies, it cannot be explained, this may lead to a scientific crisis and the eventual emergence of a new paradigm—a paradigm shift. For Kuhn, hypotheses are embedded within the prevailing scientific paradigms, guiding what questions scientists ask and how they interpret data. He suggests that significant scientific progress—paradigm shifts—occurs not just by accumulating facts or disproving hypotheses within the current paradigm, but by fundamentally changing the conceptual framework through which scientists view the world.

Thus, from both Popper's and Kuhn's perspectives, hypothesis-driven approaches are fundamental to the dynamics of scientific progress. They support the systematic and critical examination of our theories and practices, promoting continuous improvement and adaptation in our quest to understand the universe. These approaches encourage not only the refinement of existing knowledge within current paradigms but also the revolutionary shifts that redefine scientific understanding. In essence, by fostering a rigorous, question-driven approach to research, hypotheses play a vital role in both the evolutionary and revolutionary aspects of scientific advancement.

In contemporary scientific research, a clear distinction emerges between traditional hypothesis-driven studies and hypothesis-free investigations typical of 'big data' approaches, such as genome-wide association studies (GWAS) (8). Traditional methods, deeply rooted in specific, testable hypotheses, remain essential for targeted scientific inquiries. Conversely, GWAS and similar big data methodologies analyze extensive datasets to identify potential correlations without initial hypotheses. These explorations, while not immediately grounded in hypothesis testing, often generate findings that necessitate subsequent hypothesis-driven research. Such sequential approaches ensure that statistically significant results from large-scale data analysis are rigorously tested for

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their biological significance, thereby bridging the gap between statistical discovery and biomedical insight. This iterative cycle of discovery and validation embodies the dynamism and adaptability of modern scientific practice.

While Hernán and Greenland raise significant points that warrant serious consideration, it is essential to reflect on the broader implications of their arguments, particularly in the context of their publication in a high-impact journal like *JAMA*. The discourse surrounding the role of hypotheses in scientific research is vital, as it shapes the future of how we approach, understand, and solve the complex problems facing the medical and scientific communities. It is our hope that by adding our voice to this conversation, we can contribute to the ongoing evolution of research methodologies that are both innovative and grounded in the robust traditions of scientific inquiry.

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