Qeios

Peer Review

Review of: "The Unregulated Majority: Who Ensures Quality in Non-Submission Real-World Studies?"

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1. Independent researcher

The commentary from Mr. Sagkriotis is well-written and questions the rigor of industry-sponsored RWD and RWE used in non-regulatory studies. It raises the valid and important concern that without rigorous standards and reviews, the results from these studies can be misleading for clinicians.

That said, despite the recent revision, the commentary remains too generalized. Additionally, the commentary does not provide clarification on the types of RWD/RWE it is addressing except for disease registry data. Please note that not all RWD are created equal and that if the commentary is primarily addressing the gaps behind registry data, then clarifying language is needed, down to the title.

Detailed Feedback:

Introduction

1. Third paragraph - The authors assert that the majority of RWE produced in the pharmaceutical sector is not designed for submission to regulatory or health technology assessment (HTA) authorities. Couldn't this be said of non-pharmaceutical sector RWE studies as well? If so, are the non-pharmaceutical RWE studies also plagued with the same issues being raised in the commentary and should be subject to the same oversight? Would address if this is believed to be true.
2. Fourth paragraph - Agree with the statements leading up to the last sentence that support the use of RWE in clinical trial augmentation. However, the relevance of the last sentence in this paragraph is unclear. Please explain how to extend these clinical trial models to a purely RWD/RWE study. If the RWD/RWE study design is that of a disease registry, please add this clarifier.
3. Fifth paragraph - Please clarify how patients are contributing data.

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The Blind Spot

1. In bullet one, remove the '.' after 'protocols' in the phrase "full protocols. without proper adjustment"
2. Registries are repeatedly mentioned in bullets 3) and 6). Again, are the cited issues primarily with registries? If so, would add clarification language where appropriate. If not, would add non-registry examples.
3. First paragraph after the numeric list cites issues with RWE studies in oncology as using enrollment criteria similar to that of clinical trials. Are these RWE studies serving to replicate results of clinical trials? If so, shouldn't they include similar I/E criteria as the clinical trial? Please clarify what the purpose of these cited oncology RWE studies is.

Proposed Framework

The proposed framework is logical and would certainly subject RWE studies to more rigorous oversight. However, is this framework applicable to all RWE studies or to a subset (e.g., pharmaceutical vs. non-pharmaceutical, registry vs. non-registry, etc.)? If to a subset, please clarify the subset. That said, if the framework is applicable to all RWE studies, it may be too cumbersome for many to comply.

Declarations

Potential competing interests: No potential competing interests to declare.