Editorial

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Journal of **Comparative Effectiveness Research**

Journal of Comparative Effectiveness Research welcoming the submission of study design protocols to foster transparency and trust in real-world evidence

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"Publishing RWE study protocols in a peer-reviewed journal adds another level of scrutiny (and ultimately trust in the study design), where the protocol can be analyzed and evaluated through the journal's peer-review process."

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Well-designed and executed randomized controlled trials (RCTs) are widely considered the gold standard for studies that form the basis of drug approvals. The reliability of RCTs in informing evidence-based medicine is based on the accurate reporting of the design, conduct and analysis of RCTs, allowing the limitation of bias. Several efforts have been made to provide guidance to authors on the reporting of RCTs through the development of guidelines, such as Consolidated Standards of Reporting Trials (CONSORT) and Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT), both of which are in the process of being updated [1].

Noninterventional studies that form the basis of real-world evidence (RWE) are now a common part of the drug development process to fill the evidence gaps that RCTs leave. For instance, natural history studies, which chart the progression of a disease, are now being utilized in rare disease drug development to provide rich data about a disease that can even be used as a historical control arm for a single-arm clinical trial [2,3]. However, guidance on reporting the design of RWE studies is less clear. The multidisciplinary, multidatabase and collaborative nature of RWE [4] makes these studies complex and to be considered credible and transparent, it is recommended they follow a prespecified analytic protocol [5]. Steps are being made to enable researchers to develop clear and reproducible RWE study protocols, for instance through the recently published HARmonized Protocol Template to Enhance Reproducibility (HARPER), which builds on other templates such as the Structured Template and Reporting Tool for Real World Evidence (STaRT-RWE) [6,7]. Industry are also keen to build trusted partnerships with healthcare providers regarding real-world data [8].

Why are publicly accessible study protocols needed in RWE?

With increased focus on RWE to aid drug development as well as regulatory and health technology assessment decisions, it is important there is no ambiguity in the communication about the design and conduct of RWE studies. Creating, registering and publishing protocols for RWE studies fosters transparency and builds trust in the quality of the research being carried out. Several stakeholders have called for study protocols to be made publicly available; in 2022, the Real-World Evidence Transparency Initiative, a partnership between ISPOR, the International Society for Pharmacoepidemiology, the Duke-Margolis Center for Health Policy and the National Pharmaceutical Council, published a report describing a plan for making registration of RWE studies routine [9]. In their latest guidance

published in June 2022, the National Institute for Health and Clinical Excellence RWE framework called for registering the study protocol before implementing the study to help improve trust in RWE studies.

How can journals help?

Like RCTs, an increasing number of RWE study protocols are being registered on publicly accessible platforms. In fact, the Real-World Evidence Transparency Initiative have released their own site, the Real-World Evidence Registry [10], which they say is "a fit-for-purpose platform to register their study designs before they begin work to facilitate the transparency needed to elevate the trust in the study results".

In addition to registering a protocol, researchers are also encouraged to publish their study design, either through presentation at a conference or publication in a journal; articles that are being welcomed by many journals. Publishing RWE study protocols in a peer-reviewed journal adds another level of scrutiny (and ultimately trust in the study design), where the protocol can be analyzed and evaluated through the journal's peer-review process. A journal publication also provides a citable and measurable reference for the study protocol.

The *Journal of Comparative Effectiveness Research* (JCER) is committed to improving the standards of RWE research by publishing RWE study protocols. From 2023, JCER is moving to a fully open access publishing model, where all articles will be published under a CC BY-NC-ND license. Authors who publish their study protocol in JCER are also encouraged to later publish the study results in the journal, where the articles will be linked, and the authors will receive discounts on the associated open access fees.

There are many benefits to publishing a RWE study protocol in JCER. The journal is indexed on Medline, enabling the researcher community to read, learn about and possibly collaborate on the ongoing study. The journal publishes digital features such as videos and infographics alongside articles, providing authors with a platform to visually explain a more complex aspect of the protocol such as the methodology or statistical analysis. Furthermore, JCER encourages authors to include a plain language summary in their article, providing an overview of their work written in nontechnical language that can enable a wider audience to learn more about the study.

As always, feedback from our readers is welcome and we are happy to receive any presubmission enquiries if you are interested in submitting a study protocol to us.

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