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COMMENTARY

# Let's end "real-world evidence" terminology usage: A study should be identified by its design

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## 1. Commentary

"Real-world evidence" is a term that has been extensively presented in the medical literature in contemporary times [1]. Its meaning is elusive, but this term is usually used to refer to evidence collected outside controlled experimental studies, such as randomized controlled trials (RCTs) [2]. A broader definition of "real-world evidence" is "data collected during the routine delivery of health care" [3]. Variations of this term include "real-world data" or "real-world study."

"Real-world evidence" is important, as controlled experimental studies have inherent limitations, and/or are not ethically possible or feasible to be conducted [4]. However, the fact that term "real world" has such an elusive meaning increases the abusive usage of this "label." This led to some researchers arguing that "real-world evidence" terminology is being highjacked to push the approval of medicines based on low-quality observational data, under the compelling, and passionate argument that RCTs provide evidence with limited external validity.

Although we see truth in the arguments of both enthusiasts and critics of "real-world evidence," we will address in this commentary the fact that the abusive use of such terminology undermines research transparency, and is not aligned with major reporting guidelines.

In fact, reporting guidelines such as CONSORT [5], PRISMA [6], STROBE [7], CARE [8], STARD [9], and TRIPOD [10] require that the study identifies its design throughout the title. *Table 1* outlines the recommendation of these major guidelines regarding study design identification on the title of the report.

### *1.1. Anecdotal evidence on inconsistency usage of "real-world evidence" terminology in manuscript titles*

To assess the study design underlying the term "real-word" evidence in manuscript titles, we performed a non-structured search, selection and appraisal process at Medical Literature Analysis and Retrieval System Online (MEDLINE) for references that labelled the study with any "real-world" term variation. We used the following search strategy on September 1, 2021: "real-world"(Title) OR "real world"(Title).

We included illustrative examples of primary reports of data analysis and classified the study design by the type of analysis that was conducted in the reference. Our results are presented in *Table 2*.

The results of the anecdotal analysis presented in *Table 2* shows how inconsistent the use of "real-world" terminology was across different title reports. We highlight that, for most cases, it was almost impossible to identify the study design from the title alone, and none of the included studies was adherent to their particular reporting guideline.

There is no real gain in labelling a study as "real-world." The generic use of this terminology, especially to label studies in the title, will only lead to difficulties in triage, selection, and appraisal of the literature. Although we recognize that non-adherence of reporting guidelines is widespread and not limited to studies labelled as "real world," this confusing, and unspecific terminology is certainly not helping to increase research reporting transparency.

Our analysis was restricted to titles and did not assess the use of this terminology on the manuscript itself. We believe that the abusive labelling of "real world" studies is much worse when used in titles, especially when it excludes the identification of the study design, because of the implications to the indexation of references in biomedical literature databases.

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**Table 1.** Major reporting guidelines recommendations on study design identification along the title of the report

| Reporting guideline | Recommendations |
|---|---|
| CARE [8] | Item 1. The diagnosis or intervention of primary focus followed by the words "case report" |
| CONSORT [5] | Item 1a. Identification as a randomized trial in the title |
| PRISMA [6] | Item 1. Identify the report as a systematic review. |
| STARD [9] | Item 1. Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC) |
| STROBE [7] | Item 1a. Indicate the study's design with a commonly used term in the title or the abstract |
| TRIPOD [10] | Item 1. Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted. |

AUC, Area under the curve; CARE, for CAse Reports; CONSORT, CONnsolidated Standards Of Reporting Trials; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; STARD, STAndards for the Reporting of Diagnostic accuracy STROBE, STrengthening the Reporting of OBservational Studies in Epidemiology; TRIPOD, Transparent reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis.

**Table 2.** Examples of usage of "real-world" terminology on indexed reports at MEDLINE

| Title | Study design |
|---|---|
| Clinical Performance of the Standard Q COVID-19 Rapid Antigen Test and Simulation of its Real-World Application in Korea [11] | Diagnostic accuracy study (cross-sectional) |
| "Real-world" first-episode psychosis care in Massachusetts: lessons learned from a pilot implementation of harmonized data collection [12] | Case series |
| Real-World Satisfaction with Secukinumab in Clearing the Skin of Patients with Plaque Psoriasis through 24 Months of Follow-Up: results from US Dermatology Electronic Medical Records [13] | Cohort study (retrospective analysis of satisfaction with intervention usage) |
| Osteoporotic fractures and subsequent fractures: imminent fracture risk from an analysis of German real-world claims data [14] | Cohort study (retrospective analysis of risk factors) |
| Trends of pulmonary fungal infections from 2013 to 2019: an AI-based real-world observational study in Guangzhou, China [15] | Cross-sectional (populational database) |
| Analysis of the influencing factors related to liver and cardiac iron overload in MDS patients detected by MRI in the real world [16] | Cross-sectional (patients sampling) |
| Impact of personalized text messages from pharmacists on medication adherence in type 2 diabetes in France: A real-world, randomized, comparative study [17] | Randomized clinical trial |
| Ipilimumab in a real-world population: A prospective phase IV trial with long-term follow-up [18] | Randomized clinical trial (phase IV) |
| Real-World Experience With the SAPIEN 3 Ultra Transcatheter Heart Valve: A Propensity-Matched Analysis From the United States [19] | Propensity-matched cohort study analyzing effects of an intervention |
| The prognostic values of serum markers in hepatocellular carcinoma after invasive therapies based on real-world data [20] | Prognostic modelling study |
| Non-vitamin K antagonist oral anticoagulants in Asian patients with atrial fibrillation: evidences from the real-world data [21] | Systematic review of intervention |
| Genetics in the real world: resources for pediatric nurses using monogenic diabetes as an exemplar [22] | Single case report plus narrative review |

Further research efforts are necessary to better understand how prevalent the use of "real-world" terminology is through a systematic appraisal of published studies and to broaden the discussion outside study titles.

## 2. Conclusion

We provide anecdotal evidence that the expression "real-world evidence" does not clarify nor add any information about the study design in studies titles. This expression is being used in several study designs. We, therefore, conclude its use is diminishing transparency, and increasing the risk of misinterpretation of health research. Authors and editors of scientific journals should adhere to reporting guidelines and identify a study by its design.

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