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Recommendations for primary studies evaluating therapeutic medical devices were identified and systematically reported through reviewing existing guidance

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Abstract

Objectives: The aim of the study was to review existing recommendations on study design, conduct, analysis, and reporting for primary studies of therapeutic medical devices (TMDs) and the closely related field of interventional procedures.

Study Design and Setting: We performed a targeted literature review of publications with recommendations for study design, conduct, analysis, and reporting for primary studies of TMDs and related technologies. We combined an electronic database search with a systematic screening of tables of content of selected journals and scanning the reference lists of relevant articles.

Results: We identified 40 publications authored or commissioned primarily by regulators, health technology assessment agencies, and expert groups. We identified study designs of randomized clinical trials that specifically address the quick, incremental development of TMDs and provider and patient preferences. The importance of contextual factors for TMD interventions should be considered during the selection of patients, providers, and centers, as well as in data collection and analysis. We also identified guidance for the analysis and quantification of learning curves as well as for the design and analysis of large registries of high quality.

Conclusion: The methodology to conduct primary research for TMDs should be disseminated to support improvement of the evidence base for health technology assessments.

Keywords: Medical devices; Implants; Comparative effectiveness; Health technology assessment; Study design; Recommendations

1. Introduction

An essential precondition for performing a systematic review of comparative effectiveness (CE) of therapeutic medical devices (TMD) as part of health technology assessments (HTA) is the understanding of the design, conduct, analysis, and reporting of primary studies for the evaluation of TMDs. TMD evaluation in primary research faces several challenges including the incremental development of TMDs with short life cycles that may lead to device modifications in trials and may not be easy to track in observational studies (OSs). In addition, the physical mechanism of action may prevent blinding of treatment arms, provider and patient preferences may hinder equal recruitment and proficiency in study arms, and many TMDs, especially implants, are imbedded in more complex interventions or systems of care [1–4]. Finally, highly invasive procedures for implants not only include the risk of TMD failures but also the risk of complications from surgery. These factors pose challenges for linking outcomes to specific elements and properties of the intervention. Contextual factors, such as individual and institutional learning, should also be considered to properly quantify the effect and ensure an adequate implementation of findings [1–4]. OS designs for the evaluation of long-term effectiveness and safety (e.g., registry-based studies) play a more important role and therefore more sophisticated methods of analysis are required to adjust the data for potential biases.

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What is new?

Key findings

- Primary studies for the evaluation of clinical effectiveness and safety of high-risk therapeutic medical devices for market access and long-term follow-up face several challenges: The physical mode of action, rapid incremental development, patient and provider preferences, and the user and context dependency of the intervention make study design, conduct, and analysis more demanding. We reviewed recommendations from the literature on this topic to provide health technology assessments producers with the necessary knowledge on methods for primary research for therapeutic medical devices.

What this adds to what was known?

- We identified and compiled recommendations for designing, conducting, and analyzing experimental and observational primary studies for therapeutic medical devices. There are various methodological approaches to deal with technology-specific challenges HTA producers should be familiar with.

What is the implication and what should change now?

- The lack of high-quality primary research is one of the main obstacles in the evaluation of therapeutic medical devices. HTA should further take a proactive view and engage with manufacturers in early dialogs to improve the quality of primary studies. At the same time, we should pay attention to the need for incentives that take into account regulatory requirements and market conditions.

To support the work of HTA producers and to provide the necessary knowledge for evaluating primary studies in the field of TMDs, we performed a literature review of recommendations on study design, conduct, analysis, and reporting for primary studies of TMDs and the closely connected field of surgery. We also compiled systematic overviews of study designs for TMDs. Our study should provide a starting point for HTA producers to become familiar with the recent status of TMD evaluation in primary research and to provide recommendations for more in-depth reading. This article complements our recommendations for conducting a systematic review of CE of TMDs in this issue [5].

2. Methods

Our work includes the following steps: (1) a targeted literature search on methods for evaluating TMDs and related technologies in primary studies; (2) the extraction of existing recommendations for the design, conduct, and analysis of primary studies for TMDs and related technologies; (3) the extraction of general recommendations from reporting guidelines of primary studies with attributes important for TMDs; and (4) the narrative synthesis of recommendations from the literature.

2.1. Search strategy

A detailed description of our search strategy is given in part I of this article series [5]. Briefly, we combined multiple search approaches, including a targeted literature search that combined electronic database search, table of content screening, and using the advanced search function in selected journals (see Appendix A Figure). We searched the home page of the US Food and Drug Administration (FDA), the HTA database of the Center for Reviews and Dissemination, the International Society for Pharmacoeconomics and Outcomes Research good practices publications for methodological guidance of special interest for TMDs, and the Enhancing the QUAlity and Transparency Of health Research Network home page. References of retrieved key articles were screened, in addition, we asked three experts in the field to complement our search. The search was initially conducted in July 2013 and updated in April 2014. We also considered results from a systematic literature search for European [6] and non-European [7] HTA agency guidelines for medical devices (MDs) from two European Union projects on MDs, after personal communication with our colleagues. Meanwhile, the results are published [6,7] (See Appendix A Table 1).

2.2. Inclusion and exclusion criteria and literature selection

We included methodological publications addressing the design, conduct, analysis, and reporting of experimental and observational primary studies for the evaluation of clinical effectiveness of TMDs or surgical procedures. We also included reporting guidelines for nonpharmaceutical interventions and reporting guidelines that focused on important attributes for TMDs, such as the description of the intervention. Publications were excluded from the review if they did not meet one of the previously listed requirements or the studies evaluated telemedicine. All publications that were included by one reviewer after the title/abstract screening were retrieved and screened in full text. Subsequently, at least two reviewers (A.C.-F., T.H., M.A., and P.S.-I.) read the publications and jointly decided about the inclusion or exclusion according to the listed criteria (see Appendix A Table 2).

2.3. Extraction of documents

For each of the included texts, we extracted the following relevant items into tabular form: first author and year of publication, affiliation of the authors and funding, conflict of interest, country of affiliations/institutions, a short description of relevant topics and methods, and type