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The role of patient-reported outcomes in the regulatory approval of medical devices

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To the editor – A medical device is an instrument, appliance, or material manufactured for the purpose of diagnosing, monitoring or treating patients' conditions.[1] Integrating the patient's voice throughout the medical device development lifecycle may provide valuable information to inform the evaluation and surveillance of medical devices.[2]

One way to systematically collect information on the impact of a medical device from a patient perspective is through the use of patient-reported outcomes (PROs). PROs are any report of a patient's health including symptoms, physical functioning, psychological impact and wellbeing, without the interpretation of the patient's response by a clinician or others.[2] Measuring the potential risks and benefits of a medical device at an early stage is essential to avoid negative patient outcomes, as highlighted in the Independent Medicines and Medical Devices Safety Review – First Do No Harm.[3]

The inclusion of PROs in clinical trials can provide evidence regarding the safety and effectiveness of a health intervention, which have the potential to inform patients, clinicians, and policymakers about the impact of the intervention and its effects on patients' health.[2] In 2020, the US Food and Drug Administration (FDA) published a draft guidance regarding the use of PROs in medical device evaluation.[4]

As of February 2021, there were 2997 phase 3 medical device clinical trials registered on ClinicalTrials.gov under the headings "medical device", "in vitro device", "in vitro diagnostic" and "IVD". Of these 2997 trials, 580 (19%) reported using at least one validated PRO measure. Of the 580 trials using a PRO measure, 149 (26%) used at least one PRO in the evaluation of a primary outcome and 526 (90%) of a secondary outcome. Interventions relating to respiratory, musculoskeletal, circulatory, and oncology conditions were more commonly evaluated among PRO medical device trials. The most common disease-specific PRO measures used were the St George's Respiratory Questionnaire and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30), while the most common non-disease-specific measures included the 36-Item Short Form Health Survey (SF-36) and the EuroQoL 5-Dimension (EQ-5D). The SF-36 and EQ-5D are generic instruments focused on general aspects of health-related quality of life, irrespective of the disease or condition of the patient.

Furthermore, the inclusion of PROs in medical devices trials has significantly increased since the introduction of the FDA PRO Guidance in 2009, from 20% in 2009 to 29% as at January 2021. Between 2009 and 2015 the FDA Centre for Devices and Radiological Health (CDRH) observed an increase of over 500% in the number of pre-market submissions that include PRO measures.[5]

Examples of FDA-approved medical devices incorporating PROs include ReActiv8 Implantable Neurostimulation System, an implantable pulse generator used to activate the key muscles in the lower back and; the Osseo-anchored Prostheses for the Rehabilitation of Amputees (OPRA)™ Implant System. OPRA™ is intended for use in adults who have above-the-knee amputations and who have or are anticipated to have rehabilitation problems with conventional socket leg prothesis or cannot use one. The medical devices' PRO data in combination with clinical outcomes demonstrated improved quality of life based on EQ-5D and SF-36, respectively, and informed labelling claims. Further information can be found in the FDA summary of safety and effectiveness data (SSED) and labelling data.[6]

To maximise the impact of PRO trial data to inform regulatory decision-making and health policy, optimal design, analysis and interpretation of PRO data is crucial. Unfortunately, the quality of PRO trial design, analysis and reporting in clinical trials is often suboptimal.[7] The new FDA draft guidance regarding the use of PROs in medical device evaluation,[2] and references contained within the guidance, is a welcome first step to guide device developers in the use of PROs.

A number of other key guidance documents aim to promote high quality PRO trial design, analysis, reporting, and to minimise research waste[8], with tools and resources freely available from the PROTEUS consortium at www.theProteusConsortium.org. These resources include: the SPIRIT PRO Extension, which provides guidance to improve the completeness of trial protocols including PROs;[7] International Society for Quality of Life Research minimum standards for PRO measures in patient-centred outcomes and comparative effectiveness research;[9] ongoing work from the SISAQOL-IMI (Setting International Standards of Patient-Reported Outcomes and Quality of Life – Innovative Medicines Initiative) initiative focussed on standardising the analysis and interpretation of PRO and quality of life from oncology trials; the CONSORT PRO Extension,[10] which provides recommendations aimed at facilitating optimal reporting guidance of trials including PROs and; tools to graphically display and interpret PRO data.

Adherence to existing PRO guidance has the potential to promote the collection of robust PRO data, which can inform medical device approval. Although the resources discussed provide key guidance to stakeholders, these do not provide device-specific recommendations with examples mainly derived from drug development. There is a need to provide further tools, training and support to facilitate optimal integration of PROs in medical device development.

The number of clinical trials incorporating PROs has increased over time. The integration of PRO data throughout the lifecycle of the medical device has the potential to provide information around the safety and effectiveness of medical devices from initial development through to longer term surveillance. In addition, integrating PROs in medical device development can also facilitate the collection of adverse event data whilst engaging and protecting patients.[3]

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Author contributions

SCR, APD and MJC conceived the idea; SCR. developed the first draft; and all authors made substantial revisions and approved the final manuscript.

Competing interests

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