VALUE IN HEALTH ▮ (2016) ▮▮▮–▮▮▮

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Balancing the Optimal and the Feasible: A Practical Guide for Setting Up Patient Registries for the Collection of Real-World Data for Health Care Decision Making Based on Dutch Experiences

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ABSTRACT

Objectives: The aim of this article was to provide practical guidance in setting up patient registries to facilitate real-world data collection for health care decision making. **Methods:** This guidance was based on our experiences and involvement in setting up patient registries in oncology in the Netherlands. All aspects were structured according to 1) mission and goals ("the Why"), 2) stakeholders and funding ("the Who"), 3) type and content ("the What"), and 4) identification and recruitment of patients, data handling, and pharmacovigilance ("the How"). **Results:** The mission of most patient registries is improving patient health by improving the quality of patient care; monitoring and evaluating patient care is often the primary goal ("the Why"). It is important to align the objectives of the registry and agree on a clear and functional governance structure with all stakeholders ("the Who"). There is often a trade off between reliability, validity, and specificity of data elements and feasibility of data collection ("the What"). Patient privacy should be carefully protected, and address (inter-)national and local regulations. Patient registries can reveal unique safety information, but it can be challenging to comply with pharmacovigilance guidelines ("the How"). **Conclusions:** It is crucial to set up an efficient patient registry that serves its aims by collecting the right data of the right patient in the right way. It can be expected that patient registries will become the new standard alongside randomized controlled trials due to their unique value.

Keywords: decision making, observational studies, real-world data, registries.

Introduction

Globally, there is an increasing trend to use real-world data to inform decision making in health care. Real-world data are often collected using a patient registry. A *patient registry* can be defined as "an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes" [1].

Regulatory authorities (United States Food and Drug Administration and European Medicines Agency [EMA]) can require real-world data collection for safety surveillance and risk assessment (e.g., Risk Evaluation and Mitigation Strategy by the Food and Drug Administration and risk management plan by the EMA) [2]. Furthermore, reimbursement agencies increasingly use real-world data in decision making. This was, for example, seen in the Netherlands where a coverage with evidence development policy was implemented in 2006 [3]. This policy aims to guarantee early access to expensive drugs that have an added therapeutic value and an expected budget impact of at least 2.5 million euros [4]. In exchange, it is required to collect data regarding appropriate drug use, effectiveness, and cost-effectiveness in real-world clinical practice. These data are intended to

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1098-3015$36.00 – see front matter

http://dx.doi.org/10.1016/j.jval.2016.02.007

complement the findings from clinical trial(s), and to evaluate a drug's real-world value after 4 years of initial reimbursement. As a consequence of the introduction of this policy, the number of patient registries has been rapidly increasing in the Netherlands.

In this article, we provide practical guidance in setting up patient registries for the collection of real-world data. Although guidance for designing patient registries exists [1], we specifically address practical issues. This article is based on our involvement in setting up patient registries in the Netherlands for various types of cancer (i.e., melanoma, lung, prostate, renal cell, hematological, colorectal, and head and neck cancer). We first discuss the mission and goals ("the Why") of patient registries and highlight issues related to stakeholders and funding ("the Who"). After that, challenges and solutions will be discussed regarding the type and content of a patient registry ("the What") and the identification and recruitment of patients, data handling, and pharmacovigilance ("the How"). Last, we discuss the main challenges in balancing the optimal and the feasible in setting up patient registries.

Mission and Goals ("the Why")

Why Use a Patient Registry and How to Guarantee Valorization of Outcomes?

The mission of most registries is improving patient health by improving the quality of patient care; monitoring and evaluating patient care is therefore often the primary goal. This goal may be operationalized in several ways. For example, patient registries are one of EMA's tools to gain insight into risks of a product in real-world clinical practice [2]. Patient registries can also provide information on appropriate use (i.e., is a product used in the right way in the right patients), effectiveness, costs, and cost-effectiveness in real-world clinical practice [5]. Furthermore, registries can include essential information on patient-reported outcome measures (PROMs) in case data are prospectively collected. Moreover, patient registries can inform public health planning (e.g., registering causes of disease to illustrate the need for a prevention program) [6]. It is important to be very specific about how the primary goal of monitoring and evaluating patient care will be operationalized and/or interpreted. Ultimately, this will ease the other steps in setting up patient registries.

Monitoring and evaluating patient care may not immediately improve patient health but may improve the health of future patients. It is essential to frequently discuss findings with clinicians and ensure a quality-of-care feedback loop. Furthermore, outcomes can be used in the development of clinical guidelines. Table 1 provides an overview of the mission and goals of the registries in which we are involved. All registries ensure transparency to the public through presentations and publications [7–14]. However, only the melanoma registry (Dutch Melanoma Treatment Registry [DMTR]) fortnightly provides clinicians with online benchmarked feedback regarding a predefined set of quality indicators developed by the professional organization. These quality indicators will be shared at a hospital level with health care insurers, patient organizations, and the general public in the near future. Quality-of-care improvement by using a structured feedback loop to clinicians was not part of the initial aims of most of the registries. This may be explained by the fact that most of the registries in which we are involved were funded by manufacturers and mainly set up for reimbursement purposes. Besides reimbursement purposes, the melanoma registry (DMTR) was set up for monitoring quality of care, which was obligated by the professional organization.

Important lessons to feedback loops are that agreement needs to be reached on the type of indicators that will be collected, how they will be measured, and the way they will be presented. In addition, the data need to be representative for all patients within a certain hospital (e.g., starting data collection on patients with a worse prognosis will initially lead to biased feedback) and the data need to be case-mix–corrected to allow valid comparisons between hospitals (or clinicians), especially when it concerns outcomes indicators. To correct for differences between patients at baseline, the registry should contain a sufficient number of observations and sufficient data on the relevant prognostic factors. Last, a user-friendly (Web-based) application is needed to facilitate a quality-of-care feedback loop.

Stakeholders and Funding ("the Who")

Who Are Involved in the Registry?

Broad support for the registry is needed to maximize its benefits. Identifying and engaging relevant stakeholders is key to the success of a patient registry. Stakeholders include clinicians, patients, researchers, governmental parties, health care insurers, and manufacturers. Involvement from professional organizations and clinical experts (including key opinion leaders) improves the valorization of results. Involvement of patient representatives secures patient participation and may help ensure that the aims of the registry are pursued with minimal burden to patients. Participation of manufacturers may support funding of the registry. Table 2 illustrates the involvement of stakeholders in the registries in which we are involved.

Stakeholders can, however, have conflicting interests. An essential and potentially time-consuming step is aligning the aims of the registry with these interests. It is important to determine the main objectives with key stakeholders at an early stage. It is also crucial to establish a clear and functional governance structure including a description of tasks, responsibilities, and decision-making processes. In the prostate cancer registry (CAstration-resistant Prostate cancer RegIstry), clinical data and health-related quality of life data are collected in two separate projects with separate funding and study protocols; however, both projects are carried out by the same project team. The project team is the core executive body, responsible for the day-to-day management of the registry, coordination, and adherence to the planning and protocol. The project team is advised by a clinical steering committee as well as a general assembly. The clinical steering committee has decision-making power regarding the clinical and scientific aspects of the registry (e.g., data collection and publication of results) and includes balanced representatives of urologists, medical oncologists, and radiotherapists of the participating hospitals and the Dutch uro-oncology study group. The general assembly represents all relevant stakeholders (including all involved manufacturers and representatives of the Dutch prostate cancer patient organization). Scientific proposals are judged by the steering committee, and the writing team includes the involved project team members and a selection of the steering committee and the subinvestigators from the participating hospitals.

Another issue may be related to data ownership (including publishing rights), (level of) data access, and data sharing. For example, when multiple manufacturers fund the registry, they may not be willing to share product-specific data. In this case, detailed product-specific data can be shared with the product-owner, whereas aggregated data can be shared with other companies. By allowing variation in the level of data sharing [15], competing parties can participate and benefit from collaboration within the same registry.

Who Funds the Registry?

It is crucial to secure sufficient funding for all activities related to the registry to ensure viability and sustainability. Activities