Patient Registries as Instruments for HTA Outcomes Research: A European Perspective

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Introduction
Health Technology Assessment (HTA) analysis of drugs and devices is increasingly in need of real-world data to address aspects of clinical effectiveness and economic evaluation in a health-policy relevant manner, as in the case of Access with Evidence Generation (AEG) or conditional reimbursement models [1,2]. The focus being on proving the benefit of interventions in the usual circumstances of health care practice rather than the ideally controlled environments where intervention efficacy is usually tested in accordance to the definitions adopted by the High Level Pharmaceutical Forum of the European Commission and published in their report on the core principles of relative effectiveness (2008). Repositories holding such valuable real-world data collections are health care provider databases, clinical study databases, and patient registries. The latter are of particular interest for their large size, extended period of follow up, and existing procedures for long-term data curation and maintenance. The introduction of electronic tools for data collection, analysis, and dissemination opens a new host of opportunities for improving both the quality and the utilization of patient registry data alongside other data sources.

KEY POINTS . . .
Registry data can offer more realistic information on the effectiveness of treatments and supply the major model parameter inputs for epidemiology data in health technology assessment economic modelling, provided that the registries are complete, easily available, and regularly updated.

Currently, there is lack of harmonisation and standardisation in registry data collection and analysis methods, a shortage of methodological guidance, and a number of obstacles concerning data access, privacy and confidentiality, and policies for study approval.

Inclusion of cost and resource use data to patient registries would enable the formation of a representative European population data set, permitting longer follow-up on issues of effectiveness and safety.

A common problem for researchers is locating potentially relevant data collections and subsequently assessing their suitability for answering the questions at hand.

The PAitant REgistries INTiatives (PARENT) Joint Action is a collaborative project of the European Commission and selected EU Member States to advance the cross-border use of patient registries in Europe (www.patientregistries.eu). The Action is a response to the Directive 2011/24 requirement of developing guidance on effective methods for utilizing medical information for the purposes of public health and research. PARENT has grounded its work on the definition of patient registries provided by the US Agency for Healthcare Research and Quality [3], so we understand registries as data collections created through observational study methods, which can be used to evaluate the outcomes of a population that has either had the same disease, condition, or exposure to certain factors. The Joint Action started in the context of the Second Programme of Community Action in the Field of Health—the main EU Health Strategy implementation instrument [4]—which placed emphasis on the use of cross-border e-Health instruments. For PARENT, the e-Health instrument in question is ICT-enabled patient registries. In other words, registries that base and execute their full lifecycle of operations on the use (and with the assistance) of state-of-the-art health information technology (HIT) solutions. Across EU countries, a sustained effort has been ongoing for more than a decade to develop regional and national health information infrastructures based on the use of information systems and electronic health records (EHRs)[5]. PARENT aspires to utilize this effort in order to streamline the process of electronic collection, processing, and use of data not only for health care services provision, which has largely been placed emphasis on the use of cross-border e-Health instruments. For PARENT, the e-Health instrument in question is ICT-enabled patient registries. In other words, registries that base and execute their full lifecycle of operations on the use (and with the assistance) of state-of-the-art health information technology (HIT) solutions. Across EU countries, a sustained effort has been ongoing for more than a decade to develop regional and national health information infrastructures based on the use of information systems and electronic health records (EHRs)[5]. PARENT aspires to utilize this effort in order to streamline the process of electronic collection, processing, and use of data not only for health care services provision, which has largely been...
Use of Patient Registries in European HTA

Due to resource constraints, all new interventions that are effective cannot be introduced into the health care system. A useful tool to illustrate the costs and health outcomes associated with different treatment options and facilitate the necessary prioritization between new interventions are health economic evaluations. In HTA economic modelling analyses, registry data are used as major model parameter inputs for epidemiology data. Overall, registry data may serve as a source of more realistic information on the 'effectiveness' of treatments. The prerequisites for such use are registries that are complete, easily available, and regularly updated.

In the context of collaboration between EUHTA Joint Action 2, the European Society for Cardiology (ESC) and PARENT Joint Action, the Norwegian Knowledge Center (NOKC) undertook a validation of the ESC's atrial fibrillation registry case report form by utilising NOKC's HTA report on new oral anticoagulants for atrial fibrillation. The PICO (Patient–Intervention–Comparator–Outcome) parameters for this comparison were defined as follows: P: atrial fibrillation patients; I: dabigatran, rivaroxaban, apixaban; C: warfarin, dabigatran, rivaroxaban, apixaban; O: survival, morbidity, safety. The data sets were compared along the following axes: population and risk factors, risk assessment, interventions and comparisons, outcomes, costs, and resource use. Based on the findings, the registry of the ESC can be used to give input for relative effectiveness assessment (real world use) and economic evaluations, as well as for monitoring patient treatment, compliance, and follow-up in Europe. Its present data content, however, does not cover costs and resource use data which are necessary for economic evaluations. Such data categories could be foreseen for future inclusion in registries, thus enabling the formation of a data set from a European population which is representative of the different countries and would permit longer follow-up on issues of effectiveness and safety.

EUnetHTA Joint Action 2 pilots on rapid Relative Effectiveness Assessment (REA) studies have also included real-world data (including registries). For example, one study assesses the use of zostavax for the prevention of herpes zoster and post-herpetic neuralgia and another study evaluates the use of canagliflozin for the treatment of type 2 diabetes mellitus. Through these studies, as well as through the work undertaken in the framework of the IMI GetReal project, HTA researchers have made some crucial observations. There is lack of harmonisation and standardisation in terms of the data collection and analysis methods employed with real-world data and a shortage of guidance with regard to methodological issues. Additionally, different needs for evidence and differences in standards of care across jurisdictions may affect the possibilities to collect real-world data in a standardized way. A number of obstacles have been identified that could be handled through policy actions. In terms of data controllers’ processes, these barriers relate to access to real-world data, matters of data privacy and confidentiality, and policies for study approval. The role of the EU regulatory and legal framework is a largely determining factor with respect to some of the aforementioned topics, both in a positive and in a negative sense.

The EU Legal, Regulatory, and Policy Framework Surrounding the Use of Real-World Data

An extensive amount of policy documentation addresses eHealth, health data, and cross-border provision of health care services. In the context of collaboration between EUnetHTA Joint Action 2 pilots on rapid Relative Effectiveness Assessment (REA) studies, the ESC registry of the European Society for Cardiology (ESC) has been used to give input for relative effectiveness assessment (real world use) and economic evaluations. The ESC registry is a largely determining factor with respect to some of the aforementioned topics, both in a positive and in a negative sense.

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Any use of health data in the EU takes place within a specific framework of data protection. EU Member States are currently still operating on the basis of the Data Protection Directive of 1995 (95/46/EC). A long and arduous process, however, has been ongoing for more than two years, to modify and bring that framework up to date. Currently, we are at the stage of triilogue negotiations between the Council of Ministers, European Parliament, and European Commission. The end result will be decisive; since, from the point of view of health data, the situation remains rather unclear. On the positive side, however, the proposed regulation sets up a consistency mechanism at the EU level combining an advisory role for the European Data Protection Board and a role...
for the Commission to ensure coherent application of the rules for cases with an EU-wide impact. Thus, it attempts to address the long-known problem of variation across national implementations and interpretations of the Data Protection Directive. The proposed regulation strengthens Data Protection Authorities by making sure they act in concert.

Moreover, we are also specifically targeting issues of sustainability and horizontal coordination between scientific disciplines and related policy action areas, so that the tools and collaborative environments developed by PARENT will continue to exist and develop further in the future. There are clear barriers in the way that the patient registry community currently operates versus the needs of HTA practices, (i.e., in terms of transparency, operational processes and accessibility of data). Even if we manage to improve the quality of the data that resides in registries, health technologies evolve fast, new elements appear, and the speed of input and modification of registry data is too slow to keep up with this process. A means of giving early warning to registry holders on the type of data soon to be needed, indicating corresponding updates in registry data content which may become necessary, can increase the likelihood that relevant data will be available when HTA researchers start investigating new or emerging technologies. Moreover, at present there is no fast and agile way to ensure prompt access to relevant patient registry data at the timelines imposed by rapid HTA assessment or alerting mechanisms, even when the existence of a data collection is known. One way of solving the problem could be the development of a dedicated and preferential process to support such registry data use purposes.

PARENT has identified a number of complementary areas with other real-world data initiatives (such as the IMI GetReal project and others), and we are seeking ways to align our activities to the fullest extent possible. The significance of the Guidelines and PARENT work in general, as well as its relevance specifically for HTA, has been underlined in the latest Work Plan of the 3rd Health Community Programme [13], where piloting of PARENT deliverables in the forthcoming EUnetHTA Joint Action 3 has been indicated. Before the end of the Joint Action in November 2015, we also achieved the express support of two important EU bodies established through the directive: the e-Health Network and the Health Technology Assessment Network. The aim is to improve visibility and dissemination of the tools and services available to EU registry holders who would like to bring their registries forward to the level of quality and operations demanded by modern research and health care policy making.

References