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Public Health

journal homepage: www.elsevier.com/puhe

Original Research

Study types and reliability of Real World Evidence compared with experimental evidence used in Polish reimbursement decision-making processes

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ARTICLE INFO

Article history:
Received 29 June 2016
Received in revised form
16 December 2016
Accepted 19 December 2016
Available online 20 January 2017

Keywords:
Real World Evidence
RWE
Decision making
Reimbursement

ABSTRACT

Objectives: The aim of this study was to identify the relationship and impact between Real World Evidence (RWE) and experimental evidence (EE) in Polish decision-making processes for the drugs from selected Anatomical Therapeutic Chemical (ATC) groups.
Study design: Descriptive study.
Methods: A detailed analysis was performed for 58 processes from five ATC code groups in which RWE for effectiveness, or effectiveness and safety were cited in Agency for Health Technology Assessment and Tariff System's (AOTMiT) documents published between January 2012 and September 2015: Verification Analysis of AOTMiT, Statement of the Transparency Council of AOTMiT, and Recommendation of the President of AOTMiT.
Results: In 62% of the cases, RWE supported the EE and confirmed its main conclusions. The majority of studies in the EE group showed to be RCTs (97%), and the RWE group included mainly cohort studies (89%). There were more studies without a control group within RWE compared with the EE group (10% vs 1%). Our results showed that EE are more often assessed using Jadad, NICE or NOS scale by AOTMiT compared with RWE (93% vs 48%). When the best evidence within a given decision-making process is analysed, half of RWE and two-thirds of EE are considered high quality evidence.
Conclusions: RWE plays an important role in the decision-making processes on public funding of drugs in Poland, contributing to nearly half (45%) of all the evidence considered. There exist such processes in which the proportion of RWE is dominant, with one process showing RWE as the only evidence presented.

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http://dx.doi.org/10.1016/j.puhe.2016.12.025

Introduction

Many healthcare decision-makers are developing policies that integrate evidence from different sources, showing the importance of data collected beyond clinical trials.[1] Evidence from 'real world' practice and utilization is seen as a way of bringing healthcare decision-making closer to reality and to the characteristics of individual patients, in effect making healthcare more personalized and effective.[2] The International Society for Pharmacoeconomics and Outcomes Research, in its Real-World Task Force Report, lists six of the most common sources of Real World Evidence (RWE), which include: supplements to traditional registration randomized clinical trials (RCTs), large simple trials (practical clinical trials), registries, administrative data, health surveys and electronic health records and medical chart reviews.[1] In general, RWE is used to supplement experimental evidence (EE) to gain a better understanding of a drug's benefit/risk profile, helping to create an economic model or value demonstration and generating information beneficial to market launch planning.[3]

Nonetheless, there are numerous barriers which impede the full realization of benefits from RWE, one of these being data quality. It is important to note that the majority of RWE is not collected for research purposes. Inconsistencies in data may exist due to methods that do not yet have wide acceptance for statistical validity.[2] According to the International Society for Pharmacoeconomics and Outcomes Research report,[1] in regard to evidence, it is essential to recognize variable quality of data, the research design, the quality of the information collected and how the data are used. However, as approaches in technology assessment differ, it is difficult to determine which studies provide stronger evidence.[1] RWE is based on many different types of research with different study designs and/or different data sources. Consequently, there is a lack of widely accepted methodological consensus for RWE across the scientific community and pharmaceutical industry, which can lead to interpretation problems.[4]

Specifically in Poland, reimbursement decisions are made by the Minister of Health, supported by the Agency for Health Technology Assessment and Tariff System (AOTMiT). Pharmaceutical companies must submit applications to the Ministry of Health, containing a full Health Technology Assessment (HTA) report analysing clinical effectiveness, cost-effectiveness and budget impact. The report is assessed by the AOTMiT, which issues three types of documents: Verification Analysis (VA), Statement of the Transparency Council of AOTMiT (STC), and Recommendation of the President of AOTMiT (RPA).[5] Marketing authorization holders should include both EE and RWE in their applications. As has been analysed, RWE related to effectiveness or safety and effectiveness alone was identified in 53% of VAs, 21% of STCs and 35% of RPAs.[6]

There is a growing need for RWE, which has been identified as supportive data to experimental trials by clinicians, national payers and administration in Poland. However, access and quality of existing data are perceived as limited. While sources of RWE in Poland include registers, records, lists, inventories and other medical data, they contain a narrow range of data, lack some data or the data are fragmented among healthcare providers, creating data that are not valuable. However, currently there exist several registers maintained by the Ministry of Health, medical databases created by the National Health Fund (pol. Narodowy Fundusz Zdrowia; NFZ) or sets of data collected by scientific associations which seem to contain complete and comprehensive data.[7]

The aim of this study was to identify and quantify the relation between RWE and EE in decision-making processes on public funding of drugs in Poland. We also planned to characterize the evidence assessed by AOTMiT to present detailed data, separately for both EE and RWE, on study types, number of patients in studies and assessment of quality, ultimately performing a comparison between the two types of evidence.

Methods

We performed a descriptive study on the quality and type of RWE in Polish decision-making processes, selected from 174 processes whose documents were published by AOTMiT between January 2012 and September 2015.[8] There were 88 RWE-containing processes for drugs with Anatomical Therapeutic Chemical (ATC) codes at the time of the analysis. The processes were qualified for the detailed analysis if they contained RWE related to effectiveness and safety or effectiveness alone in one of the three types of AOTMiT documents: VA, STC and RPA. The second criterion for selection was to include the ATC groups with at least five RWE-containing processes. Such an approach led to the inclusion of processes for the following ATC groups (first level): A—alimentary tract and metabolism ($n = 7$); J—General antiinfectives for systemic use ($n = 11$); L—antineoplastic and immunomodulating agents ($n = 24$); N—nervous system ($n = 10$); R—respiratory system ($n = 6$). At this stage, any duplicates were excluded. The final number of qualified processes was 58 (Fig. 1).

Essential data gathered for the analysis, for both RWE and EE, included the type and number of trials, assessment of the methodological quality of clinical trials, and number of participants. If quality data were not available in the AOTMiT documents, we attempted to assess the evidence based on available information.

Analysis of the relationship between EE and RWE

For the descriptive assessment of the evidence data on effectiveness or efficacy and their role in reimbursement processes, the following categories were created for both types of evidence (RWE and EE): 'in favour of assessed intervention', 'in disfavour of assessed intervention', 'similar to comparator', 'no data' and 'not available'. For the assessment of the relation between two types of evidence (RWE and EE), the following categories were created: 'confirmation', 'negating in favour', 'negating to disadvantage', 'neutral', 'not available.' It should be noted that we did not assess individual studies nor any relationship between them, but rather we extracted and collected the assessments made by experts from the AOTMiT. We have combined the evaluation data for the studies separately in each decision-making process and presented the relationship between conclusions from EE and RWE for the processes separately.