EDITORIAL

Overcoming hurdles: measurement of health-related outcomes associated with national level medicines usage in Ireland

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Abstract

Public discourse on medicine provision predominantly focuses on overall expenditure. However, current literature suggests measurement of alternative indicators can provide a method to benchmark or ameliorate medicine provision. Previous research has investigated the viability of using health-related outcome metrics, such as the number of patients treated, quality-adjusted life-year gain and life-year gain, to provide macro-level estimates on medicines' societal contributions. This editorial provides an overview of the evolving healthcare landscape surrounding medicine usage estimation and valuation in Ireland and offers recommendations on how improved methods of measuring health-related outcomes may help ameliorate efficiencies and the sustainability of a healthcare system.

Keywords: drug utilisation, health economics, life years gained, number of patients treated, pharmacoeconomics, quality-adjusted life years

Introduction

Consideration of the provision of medicines at a national level or health systems level predominantly focuses on one major factor, expenditure. This focus is understandable as healthcare payers have a finite level of resources at their disposal. Indeed, pharmaceutical expenditure is an area that will always be of interest to a healthcare payer or government, as pharmaceuticals are a crucial element of health service provision.[1] In 2016, total expenditure on pharmaceuticals in Ireland amounted to €2 billion, or 15% of overall health spend.[2] Changing demographics, improved treatment of multiple chronic conditions, and the development of specialist medicines means that future budgets will come under increased pressure.

Expenditure of this magnitude needs to be evaluated carefully to ensure that the anticipated outcomes are delivered.[3] Ireland is no different to any other country when it comes to this challenge.[4,5] However, focusing exclusively on expenditure and cost-containment measures may not be the most appropriate mechanism of providing an improved and sustainable healthcare system.[6]

There have been a number of valuable government and academic reports published[2] that provide an analysis of the current and projected medicines expenditure. These are beneficial documents for planning a sustainable healthcare system. However, additional metrics addressing health-related outcomes associated with such investments have not been part of the remit of these reports. At this moment in time, the number of patients nationally being treated with medicines, for how long and what outcomes said patients achieve are poorly quantified.

A more holistic, value-based healthcare system approach is required, with a focus on real-life outcomes on the wider healthcare system and society. This is not a new concept and has been previously discussed.[7] Potential benefits of a focus on outcomes would include:

- validated and improved patient outcomes
- reduced healthcare resource utilisation cost
- continuous improvement of the healthcare system
- a more informed understanding of the benefits that investment in medicines bring to a healthcare system and society.

Current Irish healthcare landscape

In terms of capacity for monitoring population health outcomes, the Irish healthcare system is actively increasing its efforts in this field. Certain disease areas have a rich set of data and outcomes measures. One of the most high-profile and long-standing registries is the National Cancer Registry of Ireland (NCRI).[8] Over time, reports and analyses conducted by the registry have provided worthwhile insights into whether we are improving our delivery of cancer care and offer a benchmark of performance in comparison to other jurisdictions. The outcomes data provided by bodies such as the NCRI are an important driver in our efforts to improve healthcare delivery and the impact of healthcare policy changes.

However, for a country of Ireland's size, it is impractical to rely on multiple registries and specialised monitoring platforms to measure healthcare outcomes across diverse therapeutic areas and the severity of the disease. A coordinated national approach drawing on the skills and expertise of multiple stakeholders may be a more resource-efficient option.

In May 2017, an Irish cross-party parliamentary committee published the 'Houses of the Oireachtas Committee on the Future of Healthcare "Sláintecare" report'.[9] Sláintecare details reform proposals that, if delivered, will establish a universal, single-tier health service where patients are treated solely on the basis of health need. It also proffers the reorientation of the health system 'towards integrated primary and community care, consistent with the highest quality of patient safety in as short a time-frame as possible'.[10] The creation of an eHealth Ireland programme within the Irish Health Service Executive (HSE) has indicated a willingness to move towards a strategy that supports a more efficient healthcare system in line with the goals of Sláintecare. Central to Ireland's eHealth strategy is the development of a national Electronic Health Record (EHR), which has been identified by HSE national directors and clinical leaders as a key capability requirement for the future delivery of effective and efficient care.[11]

The Open Data portal is also a step change within the HSE culture in terms of transparency and empowerment of citizens, clinicians, care providers, and researchers to make better decisions, spur innovation, and identify efficiencies whilst ensuring that personal data remain confidential.[12] Although welcome, all these initiatives are currently a work in progress and require significant support and sustained investment to function as desired.

Health-related outcome measurements

On the topic of measuring health-related outcomes, there have been commendable approaches to address this problem described in other jurisdictions.[13] Soini and colleagues have devised a method, which utilised data from prescription databases, to provide an estimate of the health-related impact associated with medicines usage.[14] Unfortunately, EHRs and prescription databases are currently inaccessible for research purposes in Ireland.[15] Therefore, alternative approaches need to be considered.

When it comes to measuring value or health-related outcomes, there is no universal measure that can be utilised to provide guidance on whether an appropriate level or improvement of care is provided.[16] A recent research collaboration between University College Cork (UCC) and Pfizer Healthcare Ireland has attempted to examine three potential health-related outcome measures and whether they could be used in an Irish context to evaluate national level health outcomes associated with medicine utilisation. These include:

1. number of patients treated
2. quality-adjusted life years (QALYs)
3. life years gained (LYG).

These metrics were chosen as they can facilitate comparison across disease areas and healthcare settings. They are also well-established measures and widely recognised by multiple stakeholders in many fields. These outcome measures play a major part in initial medicine evaluation and reimbursement decisions in the Irish healthcare system. A summary of the methodology and results is provided subsequently.

Summary of methodology

A pilot feasibility analysis was undertaken to focus on medicines in the Pfizer product portfolio supplied in Ireland in 2017.[17] The database of medicines supplied for the year 2017 was obtained from IQVIA (formerly IMS Health). It provided an indication of usage across state medicine schemes and out-of-pocket private payments by patients. This dataset provided a full breakdown of medicines provided to pharmacies in Ireland. The quantities of Pfizer medicines supplied for the year 2017 were translated into patient number estimates, based on the licensed indication and posology of the medicine. The number of patients treated was then applied to the LYG and QALYs associated with the treatment of primary indication of each medicine. Published studies, grey literature, and internal Pfizer economic models provided the required QALY and LYG data.

To provide an estimate of medication usage in Ireland, three factors needed to be considered, namely, medicine posology, patient adherence and duration of treatment. Medicines may be licensed for multiple indications. Data sources used in this project do not provide patient-level or indication-specific analysis. Summary of Product Characteristics (SmPCs), the World Health Organisation's (WHO) anatomical therapeutic chemical/defined daily dose (ATC/DDD) system,[18] published studies, clinical trial information[19] and expert opinion directed researchers to the primary (by volume) indication, and it was assumed that all patients used medicines as directed for treatment of the primary indication. Adherence was assumed to be 100% for the estimated dose and duration of all therapies.[20] Where SmPCs indicated a

stopping date or limited duration of therapy, this was chosen as a duration in which patients derived benefit from the medicine. In the case of chronic treatments or those with an undefined duration, targeted literature searches were conducted to identify the duration of therapy from clinical trials or real-world usage.

Other than the data outlined in the medication usage section, no further requirements were necessary to estimate the number of patients who received treatment with medicine in 2017. It was possible to provide an estimate of patients treated from the following equation:

$$\text{Patients treated in 2017} = \frac{\text{Total unit volumes provided}}{\text{Drug usage per day} \times \text{Duration of therapy}}$$

LYG and QALY estimates were identified through targeted searches of PubMed, the National Centre for Pharmacoeconomics (NCPE) website in Ireland, the National Institute for Health and Care Excellence (NICE) website and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) scientific database. In the event that a suitable published source was unavailable, internal Pfizer cost-effectiveness models were reviewed for quantifiable LYG and QALY benefits.

The benefit of the chosen treatment was compared to the standard of care identified in the relevant publication or economic model. The incremental benefit was combined with the estimated number of patients treated in 2017, to derive an estimate of the LYG or QALY gains associated with a medicine.

Results

It proved feasible to estimate the impact of a portfolio of medicines across multiple disease areas and reimbursement schemes, particularly using patients treated and QALY gains as a health-related outcome metric. A representative selection of 29 Pfizer medicines fully or partially funded by the state was estimated to provide a health benefit of 21,538 additional QALYs to >508,242 citizens.[21] An estimate of the number of patients treated and of QALY gains were available for all 29 medicines examined. LYG outcomes were non-quantifiable for 17 of these medicines.[17] In general, medicines that had been developed in more recent times were easier to generate QALY estimates for due to published economic assessments being available. In terms of medicine classes, anti-infective medicines were the most difficult to provide a valid estimate. This was mainly due to the historic nature of many anti-infectives and the lack of utility data from legacy clinical trials.

The largest QALY increment was sourced from etanercept (Enbrel®), a biological therapy primarily used for the treatment of rheumatoid arthritis. The contribution of preventative medicines was also important to the overall QALY gain. Only one vaccine was evaluated. However, it contributed to 13% of the overall QALY benefits identified. This supports a growing body of evidence that identifies vaccination as one of the most cost-effective investments that can be made within a national healthcare system.

Areas for improvement

Recent research described earlier has demonstrated that there is potential to measure health outcomes associated with medicines usage at a national level, even with limited resources. However, to improve the accuracy and relevance to an Irish healthcare system, a number of input factors could be improved upon:

1. **Adherence:** Calculations assumed 100% medication adherence rates. Unfortunately, this is unlikely to be the case.
2. **Duration of therapy:** Assumptions were made based on SmPC and trial publications rather than estimates from real-world sources.
3. **Indication:** For medicines with multiple indications, the prescribed indication is unknown.
4. **Polypharmacy:** Evaluations do not account for use of multiple medications or multiple comorbidities.
5. **Quality of life:** Quality-of-life measures are generally from trials rather than real-world data and may not have included Irish patients.

It will be difficult to overcome all these barriers immediately. Perhaps there would be merit in rolling out further pilots for high-burden disease areas or disease areas where multiple new therapies may be available in the coming years. A single organisation is unlikely to hold all the relevant data or have capacity to provide the expertise required to deliver complete solutions. Therefore, it may be beneficial to consider greater sharing of data and insights between healthcare providers, academia and industry. If a suitable method or registry was identified during an initial pilot or prioritised disease area, it could be then used as a template for future projects or further expansions.

Sustainability of healthcare systems

The collection and use of health outcomes data to inform budgetary expenditure and drive quality improvement requires strong health information systems that enable data linkage. Digital transformation in the form of a functioning patient-specific EHR is the pivotal step that will ensure these developments in outcomes measurement can occur and thus improve health systems functioning. Collaborative outcomes projects using an ATC/DDD system[18] and identified diagnosis-related groups (DRGs)[22] could be piloted to explore feasibility before more large-scale execution.

Managed entry agreements together with agreed therapeutic protocols and outcomes-based agreements have the potential to become a more regular feature of the reimbursement landscape

for novel, innovative medicines.[23] Establishment of simple mechanisms to more accurately track the utilisation and impact of pharmaceutical interventions will provide an opportunity for the Irish healthcare system to evaluate investment over time and provide timely access to new medicines in patient cohorts that derive the greatest clinical benefit. Measurement of healthcare outcomes for medicines could be facilitated for novel medicine classes or disease areas including rare diseases that account for significant expenditure.[24]

Summary

The Irish healthcare system and wider society has benefitted and continues to benefit from investment in medicines.[25] Evaluation of the medicines budget with an exclusive focus on financial expenditure may limit the performance of the overall healthcare system. Improved methods of measuring healthcare outcomes may help ameliorate efficiencies and the sustainability of our healthcare system. Using the methods described in the feasibility analysis, estimates on the number of patients treated with medicines from a wide range of pharmaceuticals available could be calculated. However, these are estimates based on assumptions derived from published

data rather than being particular to the Irish healthcare system. Continued development of initiatives such as the EHR would provide a means of improving the accuracy and understanding of performance specific to the Irish context.

There is no perfect metric for evaluating the health impact of medicines. The metrics discussed in this editorial are a useful benchmark and indicator to understand the impact over time of our medicines usage and the indicative health-related outcomes delivered for a given investment. They should not be used in isolation to determine whether we are managing the national healthcare budget appropriately; however, they have the potential to help inform this discussion.

An exciting new wave of medical innovation will play a key role in addressing the challenges faced by patients and healthcare systems. The development of gene therapies, immuno-oncology combination regimens, chimeric antigen receptor (CAR) T-cell therapies and other advanced medicinal therapeutic products represent a new frontier of medicines.[26] Thus, these new developments require even closer collaboration amongst industry, academia, healthcare providers and governments to ensure patients can continue to have access to these life-changing treatments within a sustainable framework.

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