7 Harnessing data to manage biomedical technologies

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Routine and real-world data (RWD) – data that are generated during normal health system activities – can be deployed to advance evidence for medical technologies such as drugs, medical devices, combination products and precision medicine. Health systems have typically relied on evidence generated through prospective trials to inform the biomedical technology ecosystem, including discovery, research, policy and practice. While highly rigorous, clinical trials have a number of limitations. Scientific advances and changing global health needs, together with growing volume of electronic data and the technology to analyse them, mean that evidence from prospective trials can and should be complemented by real-world evidence (RWE) generated from routine data. Using examples and survey results, the chapter discusses the opportunities, challenges and policy implications of using RWD in regulating, pricing and using biomedical technology. It provides recommendations for policy makers and other stakeholders on how to implement a new data-driven approach to manage biomedical products more effectively.

7.1. Introduction

Data generated in health care are well suited to inform the development, regulation and use of biomedical technologies (Box 7.1). Almost all activity in a modern health system generates electronic data – clinical, demographic, administrative, and financial. These data contain valuable information, including how treatments, drugs, medical devices and medical products perform in routine clinical use. This information can help improve drug discovery, research and development, regulation, health technology assessment (HTA), pricing, and clinical practice. It can lead to better technologies and therapies, and more informed decisions on their use and management by patients, providers, regulators and payers.

Traditionally biomedical science has relied on prospective research methods – most classically the randomised controlled trial (RCT) – to generate evidence and knowledge on the safety, efficacy and other measures of performance of medical products. RCTs are, and will continue to be, the gold standard of producing evidence in medicine. But they are complex and costly. Meanwhile changing disease patterns, emerging health needs and recent advances in the biological sciences are creating new challenges that are difficult to manage with prospective research methods alone.

A need has emerged for evidence from prospective research to be supported by evidence extracted from routine data. This was not feasible when routine or real-world data (RWD – Box 7.1) were stored in paper records and ledgers, scattered across many health care facilities and organisations, which was a factor for the separation of research from practice – a separation that has become embedded in the health sector.

The world has changed. Digitalisation and the development of technologies to store, manage and make sense of vast amounts of electronic data mean that these can be put to work. The resulting knowledge can complement evidence from prospective research in answering a growing range of questions about the performance of medical products and health care interventions. This model of continuous, iterative learning and improvement of products and services has been the norm in a range of other industries for some time. It is yet to be embraced systematically in the health sector.

This chapter focuses on how a new approach that harnesses RWD to complement existing knowledge can be instituted to better manage medical technologies and products in health systems. The challenges to the traditional approach are discussed, along with the opportunities presented by the emergence of digital technology. Several examples are used to illustrate how routine and RWD have been used to generate valuable knowledge regarding the performance of medical products. However, health systems are not harnessing the full potential of RWD in this regard, with the key barriers centred on capacity, governance and infrastructure. The chapter finishes with a set of actions required by policy makers and other stakeholders to overcome these challenges and usher in an approach that is better suited to 21st century needs and opportunities.

Box 7.1. Terminology used in this chapter

Biomedical technology (medical products)

A 2017 OECD report on managing new technologies in health care defined health technology as "the application of knowledge to solve practical clinical and health problems, including products, procedures and practice styles that alter the way health care is delivered" (OECD, 2017[1]). The technology discussed in this chapter – biomedical technology – is a subset of health technology that primarily comprises:

- pharmaceutical products (drugs and medicines)
- medical devices – instruments, appliances, implants or reagents for in vitro use, software, material or other similar or related article, intended for the specific medical purpose(s) of diagnosis, prevention, monitoring, treatment or alleviation of disease or injury; investigation, replacement, modification, or support of the anatomy or of a physiological process; supporting or sustaining life; control of conception, and does not achieve its primary intended action by pharmacological, immunological or metabolic means (WHO, n.d.[2]).
- products that combine two or more of the above (drug eluting cardiac stents, or therapies based on identification of genetic and other biomarkers – commonly referred to a precision medicine).[1]
- Technology can also encompass scientific discovery and improvements in the quality of care delivery more broadly. While routine data can certainly be used to advance these elements, they do not feature prominently in this chapter.

Routine health data

Routine, or routinely collected, data are data generated by clinical or administrative activities that occur in a health system. Routine data may include administrative and/or clinical data generated by health care facilities, cost data, insurance claims, medication dispensing data, and mortality.

Medical records are also a type of routine data, containing information of patient contact with a health care system including diagnoses, therapies, laboratory and imaging results, outcomes and contextual information on demographics. Electronic medical records are being increasingly implemented. These can be maintained at local level in individual medical practices or hospitals or as part of a universal electronic health record (EHR) capturing all interactions with the health care system. The repurposing of electronic medical record data across a population is much simpler if these are consolidated or can be linked.

Data collected in disease or clinical registries are considered routine if the registry is perennial (as opposed to established for a specific, time-limited study). Registry data can also be a rich source of information on specific treatments or diseases.

Routine data can contain health, financial and other information. For example:

- clinical information such as morbidity and mortality, contact with health services, or hospital admissions;
- patient-reported outcomes measured using a number of available condition-specific or generic instruments;

  economic or financial outcomes of the using of medical and non-medical resources and their associated costs.

Real-world data; real-world evidence

The terms real-world data (RWD) and real-world evidence (RWE) are coming into regular use and feature in this chapter. RWD simply describes data relevant to health and health care generated outside the research setting of. clinical studies and trials. RWD can draw on a wide range of data sources, including: routine data; genomic and other "omics" data; health surveys; observational studies; data from wearable devices; and social media.

Real-world evidence (RWE) is the insight or knowledge derived from the analysis of RWD, based on a specific research question or questions. Generating RWE requires a research plan, analysis and interpretation of RWD, which is but one of several inputs. The United States' Food and Drug Administration (FDA) simply defines RWE as 'evidence from clinical experience'.

1. Precision medicine is defined as refining the understanding of disease prediction and risk, onset and progression in patients, to inform better selection and development of evidence-based and targeted therapies and associated diagnostics. This is achieved by taking into account the patient's genomic and other biological characteristics, as well as health status, medications patients are already prescribed and environmental and lifestyle factors (OECD, 2017[1]).

7.2. Scientific progress, changing disease burden and financial pressures are challenging the conventional approach to evidence generation

Under the existing model, evidence and knowledge regarding the benefits, risks, harms and costs of biomedical technology are generated in dedicated research settings. Prospective research methods, such as the RCT, are the conventional means to assess the clinical effects of products and therapies.[1] The results of clinical trials inform and influence *inter alia* regulatory (market entry) authorisation, health technology assessment (HTA), and reimbursement decisions. Results also influence how the product is used in the clinical setting including how information for patients its benefits and risks is framed. Researchers and industry also use this evidence to refine existing products and discover new ones with good therapeutic potential.

After a product has entered routine clinical use, the information captured in medical records and other sources has traditionally not been used to re-evaluate its performance outside the prospective research setting. The separation between biomedical research and medical practice is a defining characteristic of medicine (and, as discussed later, a vestige of the pre-digital era). It can impact many aspects of health care and medical practice, affecting patient outcomes and the way in which resources are allocated (O'Mahony, 2019[2]).

In terms of the biomedical technology ecosystem, the existing paradigm of knowledge-creation is being challenged on several fronts: cost considerations, establishing effectiveness, changing health needs and rising expectations, and the statistical power to detect rare effects and advance the promise of precision medicine.

7.2.1. Clinical trials are the gold standard, but come at a high cost

RCTs are highly useful to generate robust evidence about new (hitherto unused) products. But they have some important limitations. They can be very complex and therefore costly to undertake. Prospective studies require a dedicated infrastructure including a sponsor, investigators and other staff. The planning and preparatory phase alone can take years. Institutional review can add another layer of complexity (and cost) in some jurisdictions (Silberman and Kahn, 2011[3]).

The considerable resource requirements limit the number of trials that can be conducted, restricting the number of research questions that can be explored for a particular product or disease. This is a considerable limitation when potential questions and possibilities are proliferating *inter alia* through the explosion of genomic data, advances in biological understanding of diseases and the growing number of competing products on the market. For instance, over 60 new therapeutic indications in haematology-oncology were approved in 2018 alone in the United States (FDA, 2019[4]).

This has concrete consequences for patients, clinicians, regulators and payers. For example:

- 'Combination therapy' is emerging as one of the more promising treatment modalities in oncology. The many drugs and therapies that can potentially be combined in various sequences and doses (as well as basing them on patient-related biomarkers) create a large number of possible therapeutic permutations. The emergence of sequencing-based genomic assays and the (potentially) hundreds of mutations in many cancer subtypes raises the combinatorial complexity to unprecedented levels (Allegretti et al., 2018[5]). It would be impossible to investigate even a small percentage of these relying on prospective research alone.
- When a new product enters a crowded market, it is not feasible to conduct head-to-head RCTs on comparative performance with all alternative treatments. This was recently illustrated following European approval of a new antidiabetic drug (canagliflozin) which has 18 relevant comparators (against few of which the new drug had been investigated in RCTs (EUnetHTA, 2014[6]). The lack of evidence of comparative performance between on-market products leaves clinicians, HTA agencies and payer organisations with significant uncertainty in their decisions.
- In some medical conditions, the benefits and risks of a treatment can be predicted by individual patients' demographic and physiological characteristics (the underlying principle of precision medicine, discussed in more detail below). But it is costly to generate the evidence necessary for developing these prospectively. The Vienna Prediction Model (VPM) used to guide clinicians in the initiation and duration of anticoagulant therapy (to manage the risk of bleeding) was developed on the back of a prospective study that took approximately 17 years, at a cost of over EUR 12 million (Eichinger et al., 2010[7]). Establishing similar algorithms in this fashion for the growing constellation of therapies and treatments is not feasible.

7.2.2. Effectiveness and rare events are difficult to establish prospectively

Clinical trials are typically based on planned and pre-authorised protocols. Suitable participants (subjects) are carefully selected and enrolled. This places natural limits on the number and the diversity of participants. In many cases, patients that do not fit specific criteria based on co-morbidities or age, for example. These individuals are screened out to increase the likelihood of isolating the effect of the intervention under investigation. This means that the enrolled patient sample may not be representative of the patients who will eventually use or receive the product. In an extreme example, a study to test dangers of mixing alcohol with a drug to treat sexual dysfunction in women was conducted using a sample of 23 men and two women (Yale School of Medicine, 2015[8])

Given the nature of medical devices (e.g. the difficulty of using placebo controls and double blinding in clinical trials as well as the incremental innovation cycles in which they are developed), the evidentiary requirements may be less rigorous than for pharmaceutical products, for which placebo-controlled trials are generally required. Nevertheless, device trials follow a similar process, with prospective design and careful patient selection (OECD, 2017[1]).

As such, clinical trials generally only provide evidence of product *efficacy* – the product's performance under ideal and controlled circumstances created by judicious selection of participants, careful administration of treatment and attentive follow-up (Singal, Higgins and Waljee, 2014[9]; Eichler et al., 2011[10]). This is distinct from the *effectiveness* of a product-- how it performs under normal clinical

conditions, accounting for external patient, provider and systemic factors that may modify the intervention's effect, but that can reasonably be expected in routine clinical use. While evidence of efficacy is needed for regulatory approval, decision-making in health care and health policy also requires evidence of effectiveness.

Moreover, prospective trials are rarely large enough to detect rare treatment effects and outcomes. Studies with a small number of participants are common. Even in a controlled trial of 2 000 patients, which is not a particularly small number of participants, 1 000 patients would be exposed to the intervention with the other 1 000 forming the control group. Say the intervention has an unknown effect that occurs in one administration per 1 000. The probability of *not* observing this effect at least once in a trial of that size is a substantial 37%.[2] Even if it were observed, an accurate statistical estimate of the underlying effect of the intervention would be impossible to make with such a small number of observations. Moreover, if there is a natural background effect occurring irrespective of patients' receiving the intervention, detecting an increase becomes even more challenging.

Of course, infrequent outcomes can be adverse or beneficial. Their detection can facilitate avoiding unnecessary harm or elucidate additional benefits for patients. For example, it took two years and 61 deaths to withdraw benoxaprofen (Opren) from the market, a drug launched in 1980 following clinical trials involving over 3 000 participants. Either way, studies of much greater size are required to accurately gauge risks and identify any associated predictive variables prospectively (Eichler et al., 2018[11]).

In addition, gene or cell therapies will increasingly form the basis of future medical interventions. These products bring unique challenges for evidence generation. Some may only require once-in-a-lifetime administration. Intended and unintended effects, their onset and duration, will in some cases only be evident after long periods, perhaps decades. These factors will challenge the traditional paradigm for reasons similar to those outlined above.

7.2.3. Changing health needs and disease profiles create further challenges

Chronic conditions are becoming the most pressing public health issue in all regions of the world. Generating evidence on the prevention, management and even cure of debilitating, but not necessarily fatal, long-term conditions is challenge.

For example, Alzheimer's disease – a debilitating form of dementia – is an emerging global health and welfare problem and a matter of major policy concern. In the absence of a cure, initiating treatment after symptoms develop may be too late to prevent or reverse decline and alter the patient outcome. Potential preventive and curative therapies – whether pharmacological, mechanical, neuro-electronic or comprising a combination of modalities – may be most successful when initiated in people with (suspected) indicative biomarkers years or even decades before the appearance of any clinical signs or symptoms (Eichler et al., 2018[11]). Other chronic and degenerative diseases including cancer, diabetes, and cardiovascular and arthritic diseases present similar research challenges.

Appraising the performance of such treatments (which may be administered in various combinations – similar to the oncological therapies discussed above) would be very challenging and costly in a dedicated research setting. Patient follow-up would need to span a very long time (potentially an entire lifetime), and require a massive sample, not only to account for attrition of study participants, but also to create sufficient statistical power that can elucidate the predictive validity of the pre-morbid characteristics and biomarkers.

7.2.4. Fulfilling the promise of precision medicine will be difficult under the existing model

The emergence of precision medicine presents another challenge that radically reorients interest in clinical studies from coherence to inter-individual variation.

In the highly structured context of a clinical trial, variance is considered noise that needs to be screened out in order to maximise internal validity and the chance of demonstrating a treatment effect. But the biological and genetic basis for the variance is now understood to be potentially predictive of the patient's response to therapy. Understanding the associations will facilitate getting the right interventions to the right patients (and avoid it being given to the wrong patients) – thus helping to advance the promise of precision medicine. This transforms inter-individual variance from an inconvenience to be minimised to the key focus of the research.

Conventional trials are underpowered for the complexity presented by numerous biomarkers that reflect this variance, and the requirement for participants to be homogeneous is irreconcilable with the genetic, molecular and therapeutic diversity central to the precision medicine approach.

This is arguably *the* area where the intelligent use of routine and RWD can add the most value. A recent systematic review of the opportunities and challenges of routine data analysis in health and biomedical science identified precision medicine as that the most frequently discussed opportunity for advancement (Galetsi, Katsaliaki and Kumar, 2019[12]).

7.2.5. Raised expectations are a further challenge to the current approach

Precision medicine currently embodies the decades-long advancement of biomedical science. This advancement has – for better or worse – raised the expectations of patients, their families and carers and the public. This presents another challenge to the traditional paradigm, perhaps ironically given the central role played by prospective research methods in this progress.

Patient groups increasingly expect rapid access to drugs that have the potential to improve or cure their conditions and a growing number of promising treatments are being fast tracked for marketing approval. This necessitates the close monitoring of, and continued reassessment of risks and benefits post-approval – using clinical practice to also generate evidence at the same time.

Furthermore, these technologies often come with high price tags, so assessing their outcomes in routine practice becomes necessary to confirm their cost-effectiveness. Collectively, these issues illustrate the need for a new approach to generate evidence and knowledge in health care.

7.3. Digitalisation makes a new paradigm possible

The existing approach to creating knowledge in biomedical science is characterised by a separation of evidence generation from everyday health care activity – or research from practice. In many ways, this is a legacy of the pre-digital age, when all clinical and administrative activity had to be recorded in hard copy. The resulting data were buried in paper ledgers and medical records, scattered across disparate health care provider organisations and administrative agencies. Systemic aggregation and analysis of these data were technically and logistically impractical. It is hardly surprising that little thought was given to the knowledge and learning that they could potentially generate. Reliance on the research setting, and its separation from routine activity became institutionalised. Ignoring the potential of re-purposing existing data was habituated.

7.3.1. Routine and real-world data open new possibilities for generating evidence and knowledge

As has been mentioned out a number of times already in this report, the digital era has revolutionised the nature of data, information and communication. In health care, digitalisation commenced not long after the appearance of personal computers in the mass market. Administrators implemented these information technologies in their organisations, and most non-clinical routine health care data became electronic.

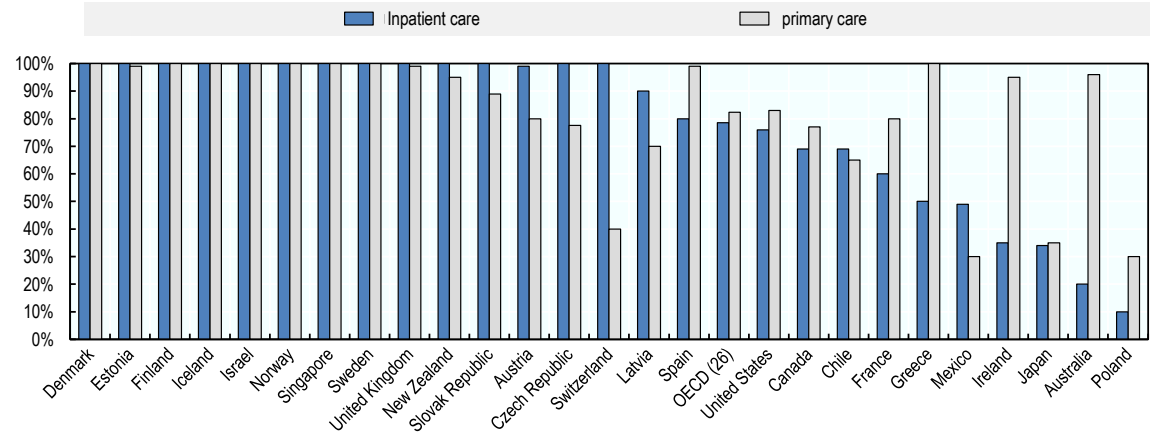
Digitalisation of clinical data (patient records) has progressed more slowly but is accelerating (Oderkirk, 2017[13]). In many OECD countries, electronic medical records have been implemented across health care sectors, including 100% of primary and inpatient care.

The diffusion of electronic medical and health records in OECD countries was, in 2016, estimated to be 81% for primary care physician practices, and 76% for inpatient care (Figure 7.1). Implementation is reported to have increased considerably since 2012 (OECD, 2013[14]). Within a few years, the vast majority of patient encounters with any part of the health care system in developed countries will be recorded digitally, and the resulting data stored electronically.

Clinical data can be very granular, especially if free text is included, and can be a source of rich information about various aspects of the care process, including the performance of medical technologies. Linking clinical data with administrative information such as costs and expenditure enables insights into the real-world economic performance of care and its constituent parts. This knowledge can not only improve decision making regarding approval, HTA and pricing but also be deployed to spur future innovation, including the repurposing of existing technology as well as development of new treatments.

Figure 7.1. The majority of clinical records is in electronic form

Percentage of primary care physician offices and acute care hospitals using electronic medical records, 2016



Note: United Kingdom: England, Scotland and Northern Ireland (excludes Wales)
Source: OECD Survey of Electronic Health Record System Development and Use, 2016; Oderkirk (2017[13]), "Readiness of electronic health record systems to contribute to national health information and research", https://dx.doi.org/10.1787/9e296bf3-en.

Electronic data are non-rivalrous. They can be shared, used and analysed *ad infinitum*, which means that they can be a source of ongoing knowledge generation and learning. The potential for useful insights and learning is magnified when they are linked, especially at the patient- level. And the potential knowledge grows even further when other forms of real-world data can be linked – ranging from administrative and registry data to environmental and social data.

7.3.2. Other industries put their data to work to drive improvement and learning

A learning system is characterised by the way it links routine practice to the accumulation of knowledge in order to spur continuous improvement and innovation. A range of industries and endeavours have brought together doing with learning to deliver better services and products, generating commercial benefits as well as considerable consumer surpluses.

Airlines and aircraft manufacturers gather real-time flight data and integrate these data with historical information to improve operational safety, efficiency and performance. A routine commercial flight will transmit over 146 000 data points that will be analysed by the airlines, and manufacturers of the aeroplane and engines for continuous improvement and identification of risks. This has contributed to advances in engineering and performance (OECD, 2017[15]). Air travel is one of the safest modes of transport available and has never been cheaper or more accessible to the public.[3]

Modern agricultural machinery is equipped with sensors and transducers (like modern medical equipment) that collect and transmit by the internet a range of data on a range of variables: performance, environmental conditions, crop quality. Various actors (manufacturers, agricultural scientists) use these data in combination with information on weather patterns, soil composition, geolocation and historical crop yields to continually raise agricultural productivity, develop better products and equipment. (OECD, 2017[15]) This 'precision agriculture' approach enabled by continuous analysis and use of data can is reducing waste and improving global crop yields, with projected increases of up to 30% (National Institutes of Health, 2019[16]; OECD, 2017[15]).

The paradigm of using everyday data to improve quality and performance of products and services is perhaps most visibly deployed by online platforms trading in tangible and intangible goods. Firms such as Google, Amazon, Apple, Microsoft and Uber all harness data from daily customer interactions to continually improve their services.[4] This data-driven innovation has generated immense consumer welfare over the past two decades (Brynjolfsson, Hu and Smith, 2003[17]; Brynjolfsson, Eggers and Gannamaneni, 2018[18]).

7.3.3. Learning from real-world and routine data is demonstrably possible in the health sector

Learning is not yet an explicit goal of RWD, and many institutional barriers exist to creating an ecosystem conducive to continuous learning, even in the context of biomedical technologies. Nevertheless, some forward-thinking agencies and systems are deploying RWD for this purpose.

Regulators are already using routine data to monitor safety

Routine data are already deployed to inform providers and policy makers, predominantly on the safety of biomedical products (OECD, 2019[19]). For example, the European Medicines Agency used registry and administrative data to quantify the risk of metformin use in patients with renal impairment, showing a much lower risk than previously estimated. This led to a modification of contraindications on the product label without the need for an expensive prospective post-marketing study (Li et al., 2016[20]).

Four large administrative claims databases in the United States were used to compare several diabetic drugs for risk of subsequent cardiovascular events and amputations.[5] Over 700 000 de-identified patient records were used in the study, which generated knowledge relevant to patients, providers, regulators and payers. For example:

- One class of drug (SGLT2i) was associated with a significantly lower risk of heart failure than the other class investigated – both overall and in a sub-population with pre-existing cardiovascular conditions;
- No difference in heart failure risk was observed between a specific drug (canagliflozin) and others in the same class;
- No difference in amputation risk was observed between the drug classes – both overall or in the sub-population with pre-existing cardiovascular disease.

The results for heart failure were consistent with those of (much smaller) clinical trials. However, the amputation risk results deviated from previous findings. For example, canagliflozin was associated with increased risk of amputation in a previous study of 10 000 patients (Neal et al., 2017[21]; Ryan et al., 2018[22]).

Shah et al. (2015) focused on the clinical safety of proton pump inhibitors (PPIs) – one of the most commonly prescribed classes of drug in the world – examining their association with adverse cardiovascular effects. These effects were previously recognised among PPI users with pre-existing cardiovascular problems. The study sought to examine the existence of the association in the general population, thus requiring a sample large enough to be representative of the population. The authors analysed two large datasets containing 2.9 million individual patient records spanning 1994-2011. The results suggested a previously unknown association between PPI use and an elevated risk of heart attack in the general population, including among younger patients (Shah et al., 2015[23]).

The pre-eminent example of harnessing routine and RWD to create evidence for policy and practice is the United States Food and Drug Administration's (FDA) Sentinel initiative (Box 7.2) – a nation-wide electronic pharmacovigilance programme that accesses personal health data of over 200 million patients. What distinguishes Sentinel from other regulatory uses of RWD is its systematic nature – it operates continuously in the background of all health system activity rather than relying on isolated, ad-hoc investigations or voluntary reporting. Sentinel has been institutionalised and the fact that ten years after its inception it still rates as one of the best examples of regulatory RWD use is perhaps an indictment of how slow health systems have been to embrace this approach offered by digital technology and electronic data.

Box 7.2. The Sentinel initiative

The Sentinel initiative of the United States FDA accesses personal health data of over 223 million United States residents to monitor adverse effects in approved pharmaceuticals and medical devices in routine clinical use. The data are scattered across a large number of health care organisations, payers, providers and agencies. The key feature of this programme is its distributed nature. Custodians (referred to as "partners") maintain full control over their data, which remain behind existing firewalls. At no stage does the Sentinel programme take possession of any data.

The distributed system is based on common standards to ensure that all data are formatted to agreed specifications. This enables Sentinel to send electronic queries about the safety of technologies in current use to which the partner returns only the results. Notably, administrative (claims) data form the backbone of the Sentinel system due to their reliability in providing complete longitudinal information on the application and outcomes of biomedical interventions. However, the infrastructure also enables links with EHR and registry data.

The Sentinel initiative has generated important knowledge not discernible from clinical trials, to enable several important regulatory decisions. Examples include identification of intussusception risks associated with rotavirus vaccines, as well as evidence suggesting no association between human papillomavirus vaccination and blood clotting (FDA, 2015[24]). The programme has thus eliminated the need for expensive post-marketing studies in a number of products, saving millions of dollars (Ball et al., 2016[25]). More recently it has been deployed to conduct pragmatic (retrospective) clinical trials using the data at its disposal. For example, an 80 000-person randomised study tested the effect of educational mailing to people with atrial fibrillation who were not receiving anti-coagulants (Platt et al., 2018[26]).

In addition to the distributed infrastructure, other key reasons for the success include trust and transparency. Data partners are actively involved in every step of the engineering and analytical processes. They have the ability of opt out of specific investigations. All evaluation protocols, including coding and specifications, as well as completed analyses, are published on the Sentinel website (http://www.fda.gov/safety/fdas-sentinel-initiative). The initiative was launched in 2008, initially as a pilot scheme called 'mini Sentinel' extended to its current scope and scale in 2016.

Evaluating effectiveness and comparative performance of medical products are also possible

Monitoring the safety of products is fundamental to regulating medical technologies across a health system. However, real-world and routine data can also be deployed to inform several other decisions in the medical technology ecosystem including marketing authorisation, HTA, pricing and appropriate clinical use. The volume of research and number of published studies that use real-world data to assess the effectiveness and cost-effectiveness of medical products is on the rise, creating promise as well as caution (Kim and Kim, 2019[27]; Farmer et al., 2017[28]). Nevertheless, real-world data studies have been used to establish evidence for cost-effectiveness and comparative effectiveness.

For example, coronary stenting is one of the interventions used to re-establish blood flow in coronary vessels. Stents used are either simple bare-metal stents (BMS) or drug-eluting stents (DES), which also slowly introduce an anti-coagulant into the blood flow. While DES have been shown to perform better, they are also more expensive. A recent study in Chinese Taipei assessed the comparative cost-effectiveness of the two products using seven years of health insurance claims data (Cheng et al., 2019[29]). While the study has some limitations, the findings suggest that DES are cost-effective over a five-year timeframe compared to BMS, partly due to a reduction in the number of subsequent medical interventions in DES recipients. Such information will be of interest to HTA agencies and payers, as well as providers and patients.

In another study focusing on PPIs, data from the Irish Health Services Executive Primary Care Reimbursement Services (HSE-PCRS) pharmacy claims database[6] were used to investigate potential cost reductions in PPI use. Several scenarios were modelled that would reduce expenditure without compromising effectiveness including switching to the cheapest medicine at initiation and after three months and substitution with another drug class (H2 antagonist). In 2007 over EUR 88 million was expended on PPI therapy for 469 708 claimants. The projected cost reductions under the five scenarios were considerable, ranging from 34% to 46% or EUR 30–EUR 40 million per annum (Cahir et al., 2012[30]). As 113 million PPIs are prescribed globally each year, the results of this and Shah et al (2015[23]) are of interest beyond Ireland.

Taipale et al (2017[31]) assessed pneumonia risk associated with use of benzodiazepine and Z-drugs (sedatives) among community-dwelling adults with Alzheimer's disease. The authors accessed the Medication Use and Alzheimer Disease (MEDALZ) cohort study that combined four datasets: prescriptions, claim reimbursements, hospital discharges and causes of death. Almost 50 000 eligible older adults diagnosed with Alzheimer disease were identified in the data. From this sample, 8 501 taking sedatives were matched 1:1 with those not taking the drugs. The results showed an association with increased risk of pneumonia among patients taking benzodiazepines, but not among those taking Z-drugs. The risk of pneumonia was greatest within the first 30 days of use. (Taipale et al., 2017[31]). This knowledge can be used for developing and updating clinical practice guidelines, and for informing patients (and their carers) of risks associated with using these medications.

Evidence from studies using routine data can identify ways to reduce health care expenditure without compromising patient outcomes. A recent retrospective study of over 14 000 older adults with type 2 diabetes assessed the effect of switching from analogue insulin to human insulin. No clinically significant difference was observed (Luo et al., 2019[32]). However, the financial impact of policy based on this evidence could be profound. The majority of adult diabetics in the United States are treated with analogue insulin, which accounts for significant growth in expenditure on diabetes medications. A vial of human insulin can be purchased for USD 25 compared to a retail price of up to USD 320 for the analogue equivalent (Lipska, 2019[33]).

Nyström et al (2017) compared insulin therapy with oral glucose-lowering drugs (specifically SGLT2 and dipeptidyl peptidase-4 (DPP4) inhibitors) for their association with mortality, cardiovascular events and

severe hypoglycemia. The investigators linked patient-level data from three national datasets to create a sample of 37 603 patients. Of these, 21 758 were matched 1:1 with patients on traditional insulin therapy (bringing the total sample size to over 59 000). The data were of sufficient size and quality to enable comparison of the two novel drugs with insulin, showing that the SGLT2 inhibitor (dapagliflozin) was associated with a lower risk of mortality and cardiovascular events while the DPP-4 inhibitor was only associated with lower risk of mortality compared to insulin treatment (Nyström et al., 2017[34]).

7.3.4. Statistical methods and techniques as well as veracity of routine data require continued development and refinement

Despite the much larger samples enabled by retrospective studies using routine data, it is clear that such research designs have inherent limitations and can be prone to risks of bias (Kim and Kim, 2019[27]). However, methodologists are devising new approaches, techniques and methods – propensity score matching being one example – to attempt to overcome these limitations (Goodman, Schneeweiss and Baiocchi, 2017[35]).

Researchers in Sweden identified 24 retrospective studies using routine (registry) data in that country alone. The majority of these studies concerned cardiovascular and psychiatric drugs and linked prescribing data with two to three other sources. However, only two of the studies contributed to new knowledge, and the majority (15) had a high risk of bias based on a checklist from the Swedish Council on HTA focusing on subject selection, treatment, assessment, exclusion, reporting and conflicts of interest. The most frequently occurring problems were biases with selection, treatment and assessment. Authors concluded that observational retrospective studies based on routinely collected data such as registries could contribute to the evidence, but must deploy techniques to counter the inherent methodological limitations and risks of confounding in retrospective studies. Pharmaco-epidemiological expertise should form a part of the design and execution of such studies (Wallerstedt and Hoffmann, 2017[36]).

Nevertheless, the field is advancing, producing some noteworthy results. Fralick and colleagues (2018) replicated the results of an RCT to compare the effectiveness and safety of two drugs used to treat hypertension. The retrospective study used insurance and claims data of 640 951 patients. Results were almost identical to those of the RCT. However, while the original trial took approximately seven years at a cost of tens of millions of dollars, the study using real-world data took 12 weeks at less than a hundredth of the cost (Fralick et al., 2018[37]).

Similarly, the Vienna Prediction Model (VPM) for anti-coagulant therapy (outlined previously) was developed based on evidence generated by using prospective studies that took 17 years to conduct at a cost of EUR 12 million. The VPM was validated retrospectively using the clinical records data of just over 900 patients, pooled from several studies of venous thromboembolism risk prediction. This took six months at a cost of under EUR 100 000 (Marcucci et al., 2015[38]).

This is not the say that the original prospective research was unnecessary or that the new approaches using routine or RWD render clinical trials obsolete. Rather, the new techniques have reached a standard where the evidence they generate can be used by policy makers, practitioners and patients – at comparatively little cost. In addition, the techniques will continue to improve with further effort and use of data for retrospective studies.

Data quality, completeness and reliability also play an important part. Deficiencies in data veracity seriously undermine the robustness of any secondary research that is conducted using routine and real-world data. As described in other chapters of this report, data quality and completeness vary considerably across OECD member countries. Moreover, the standards and semantics used to encode information are not consistent, leading to problems with interoperability and linkage of data sets within and across countries.[7]

Data reliability and provenance may also be an issue in some circumstances. Here specific technologies and innovations can assist. Blockchain technology, for example, is used to ensure the provenance of

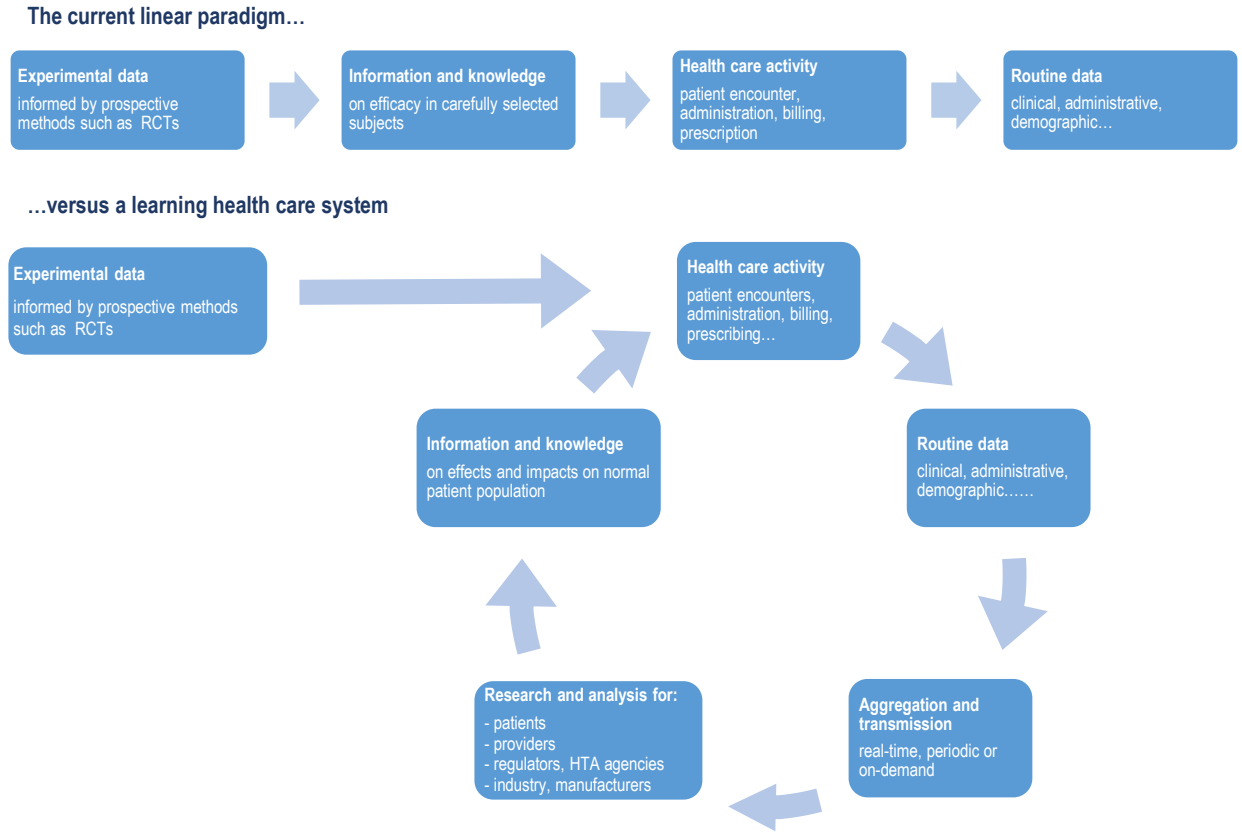
medical products and could be deployed to validate the accuracy of health data. Overall, however, addressing this issue requires governments to implement harmonised and fit-for-purpose health data governance frameworks – a key prerequisite of putting data to work that is discussed below and in other chapters of this report.

7.3.5. Real-world evidence to complement, not replace, traditional knowledge generation

The relinquishing of clinical trials in favour of studies using RWD is certainly not suggested. RCTs will continue to be the gold standard of generating information on the efficacy of new therapies and interventions. However, knowledge generated retrospectively is now well placed to complement evidence generated in the research setting given the (a) ubiquity of RWD in the digitalised environment, and (b) available methods and techniques available to create evidence from them at a fraction of the cost of prospective research. No valid reason exists to not provide researchers with opportunities to use routine data for this purpose and, at the same time, continue to advance the reliability and robustness of research design and methods.

The contrast between the current and the new approach of evidence creation is illustrated in Figure 7.2. In the 'learning health care system' paradigm, experimental data from prospective trials are still needed to generate evidence on new technologies, but this then feeds into a cycle that harnesses routine data for continuous, iterative learning and knowledge generation.

Figure 7.2. The current linear approach versus the cycles of improvement where RWD complements experimental data



Source: Adapted from OECD (2017[1]), *New Health Technologies: Managing Access, Value and Sustainability*, https://dx.doi.org/10.1787/9789264266438-en.

7.4. Patients and the public want and expect their data to be put to work

Despite their ubiquity, their non-rivalrous nature and the existence of methods to exploit them, using routine data to generate evidence about the performance of medical technologies still tends to be isolated and ad-hoc. However, to deploy them more systematically by academia as well as relevant agencies and authorities for public benefit requires some reflection on the attitudes and dispositions of the data subjects themselves – patients and the public, the latter both as potential patients as well as the basis for societal values and preferences.

7.4.1. Patients support secondary use of their data for scientific advancement

Those with most to gain from the new approach to managing medical technology – patients – are mostly in favour of their health data being used to generate new knowledge and facilitate access to better treatments. The European Patients' Forum (EPF), and EU-wide coalition of patient representative groups, have actively lobbied EU institutions to lower impediments to the use of personal health data for secondary purposes during debates on the EU data protection regulation (which came in to force in 2018 as the GDPR). In what was referred to as the 'datasaveslives' campaign, patient groups argued that privacy protection could be reconciled with use of personal health data for health care, public health and research purposes. While informed consent to such uses of data is an obligation and should be the default arrangement, EPF argued for exemptions in cases where it was not feasible to obtain consent or re-consent from data subjects (EPF, 2019[39]).

In the United States, patient advocacy groups support the Institute of Medicine's recommendations to enhance the productivity of health research with RWD, while maintaining or strengthening the privacy protections of personally identifiable health information (National Academies, 2009[40]). For example, the Friends of Cancer Research organisation actively supports the use of routine data in drug discovery, development and regulation (Friends of Cancer Research, 2016[41]).

Protecting privacy is a central component of efforts to harness routine data for research and other purposes. Arguably, the most vulnerable group in this regard are people with rare diseases, who – by definition – are at greater risk of identification during studies especially if these involve data linkage. Nevertheless, evidence suggests that patients suffering from rare diseases – while concerned about data security and misuse – support their data (e.g. biosamples and genetic information) being shared internationally for research purposes (McCormack et al., 2016[42]).

7.4.2. The public is also in favour if the necessary protections are in place

That patients are positively disposed to their personal data being deployed to improve care and outcomes is perhaps no great surprise. While privacy concerns are important for patients, they do not necessarily trump the use of data for purposes that can benefit others.

What about citizens and the public more broadly, who may not be as personally invested in the availability of, and access to, better medical interventions for specific diseases? Evidence suggests that the public generally expresses a similar disposition to patients, provided that they are confident that data remain secure and are used for the common good rather than commercial purposes. In a 2017 public consultation of EU residents, 83% of respondents either agreed (30%) or strongly agreed (53%) with the statement "Sharing of health data could be beneficial to improve treatment, diagnosis and prevention of diseases across the EU". Moreover, 73% of respondents said that they would be willing to share their health and personal wellbeing data with others through a secure infrastructure. The majority of respondents identified improved possibilities for medical research as a reason for supporting cross border transfer of medical data, a higher proportion than for the purpose of their own treatment (European Commission, 2018[43])

However, people are not supportive of *all* types of secondary use of their data. Other surveys suggest that support is generally conditional on the belief that data will be used to further the common good and people are less in favour of re-use of data by commercial organisations (Skovgaard, Wadmann and Hoeyer, 2019[44]). The backlash to the sharing of 1.6 million NHS patients personal data with DeepMind, a subsidiary of Google's parent company Alphabet, is an example of this prevailing sentiment (Loughran, 2016[45]). Meanwhile, Google and the University of Chicago Medical Center are facing a class-action because patient records shared in order to with the technology giant without stripping information, which, if combined with other personal data already in Google's possession (such as geolocation, social media and web browsing), could potentially identify individuals (New York Times, 2019[46]). The latter not only illustrates attitudes towards personal health data being in the possession of for-profit corporations, but also the regulatory complexities of 'Big Data' and the potential privacy risks posed by data linkage.

It is clearly difficult to generalise about preferences regarding the secondary use of personal health data. This suggests a need for more nuanced ways to exert control over them. Given the potentially limitless use and re-use of electronic data, appropriate consent mechanisms need to be developed as well as ways to track who accesses personal health data. The foundation is a strong data governance frameworks and regulations. Technologies such as blockchain can also be deployed to enable better authorisation, control and transparency regarding what happens with data. For example, blockchain is beginning to be used (in Estonia, for example) to verify consent, and monitor access to personal health data.

7.5. Most countries are not using data to their full potential

Despite the willingness and desire of patients *and* citizens, and the availability of analytical and statistical methods, countries have been slow to deploy the potential of routine health data.

7.5.1. Countries vary in their capacity to deploy clinical data for knowledge generation

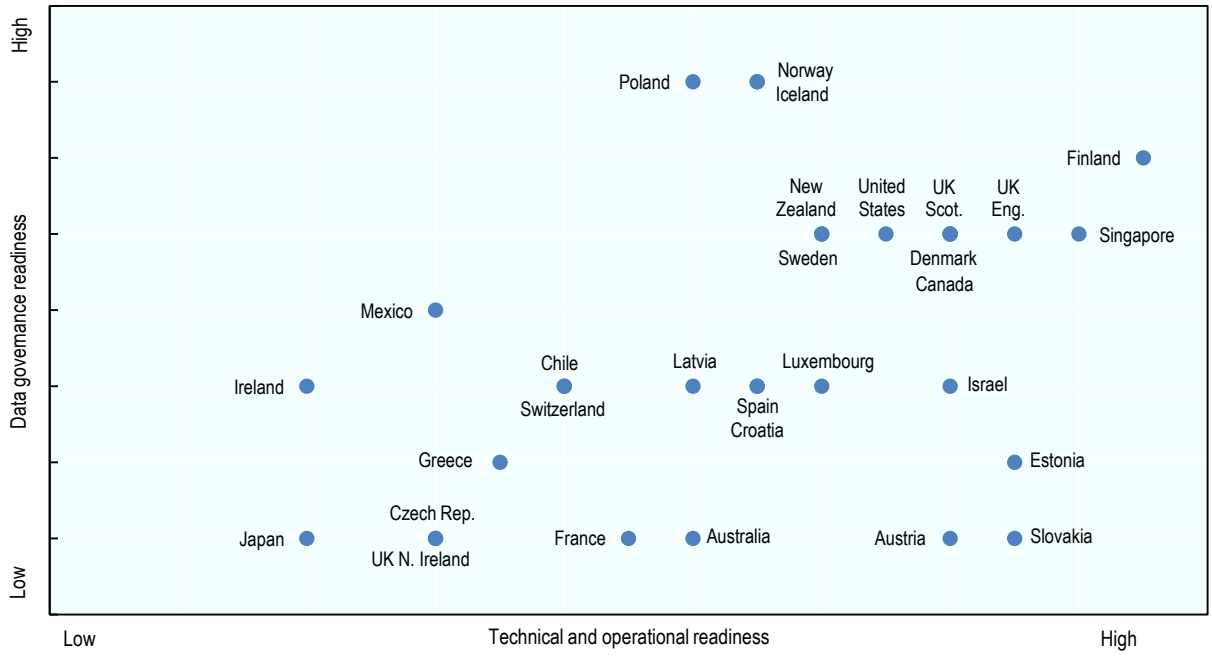
Clinical data collected in electronic health records (EHRs) present a potentially rich source of information and knowledge on the performance of medical products. EHRs are being adopted quickly in OECD countries (Figure 7.1). However, the technical and governance capacity of countries to harness these data for secondary purposes, including knowledge-generation on the performance of medical products, varies (Figure 7.3).

7.5.2. Countries report using routine data to inform policy in a limited way

A 2018 survey of 26 countries (including 23 OECD member countries) revealed that the majority collect routine data that contain information on the performance of medical products.[8] Surveyed countries reported that their routine health data are principally used to extract information on pharmaceutical consumption and aggregate spending (22 countries). Eighteen 18 countries reported using these data to monitor provider compliance, and 15 used them to track quality of prescribing. Meanwhile, 14 countries reported using routine data for pharmacovigilance (the safety of medicines) and 11 to evaluate their effectiveness (Figure 7.4). Routine data were less frequently deployed for the assessment of comparative effectiveness and cost-effectiveness, or to inform HTA and pricing decisions (OECD, 2019[19]).

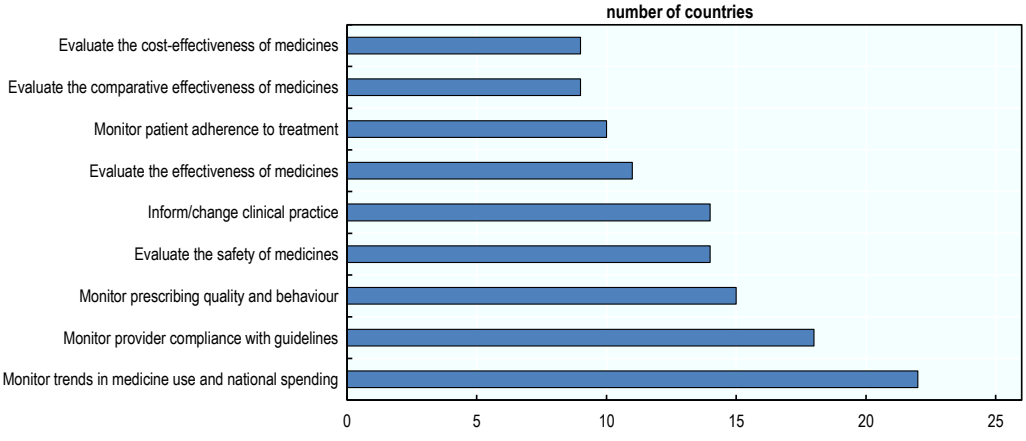
Figure 7.3. Countries vary in their preparedness to put EHR data to work

Data governance and technical/operational readiness to develop nation-wide information from EHRs, 2016



Note: Technical and operational readiness is the cumulative score of nine indicators each valued at one point: EMR coverage, information sharing among physicians and hospitals, defined minimum dataset, use of structured data, unique record identification, national standardisation of terminology and electronic messaging, legal requirements for adoption, software vendor certification and incentives for adoption. Data governance readiness is the cumulative score of four indicators: national plan or priority for secondary data use, dataset creation, and contribution of EHR data to monitoring and research which are each valued at one point; and legal issues impeding dataset creation which subtracts one point.
Source: OECD Survey of Electronic Health Record System Development and Use, 2016; Oderkirk (2017[13]) "Readiness of electronic health record systems to contribute to national health information and research", https://dx.doi.org/10.1787/9e296bf3-en.

Figure 7.4. Routine data are mostly used for monitoring medicine use, expenditure and compliance



Note: In most cases, the routine data described only cover medicines dispensed in the community setting and not medicines dispensed in hospitals.
Source: OECD (2019[19]), "OECD survey on use of routine data in pharmaceutical policies", https://www.oecd.org/health/health-systems/Using-Routinely-Collected-Data-to-Inform-Pharmaceutical-Policies-Analytical-Report-2019.pdf.

Importantly, the *extent* to which information derived from routine data is used to inform regulatory and other policy decisions was not assessed. While a growing number of retrospective studies using routine data are being published (with some examples outlined in Section 7.5.1), the extent to which this evidence is used to change policy and practice remains largely unknown.

Some national agencies tasked with regulating and assessing biomedical products are beginning to use the evidence generated by such studies in their decisions. For example, the Transparency Commission (CT) of the French High Authority for Health (HAS), which evaluates the therapeutic benefit of products, has in the past considered studies that used routine data to assess treatments for bladder cancer, exposure to acne medication during pregnancy and investigate the misuse of benzodiazepines. The latter resulted in a decision to reduce the drugs' reimbursement rate from 65% to 15%. In other countries, such as Germany, for example, responsible agencies are more reluctant to accept evidence that was not generated in prospective clinical trials (OECD, 2019[19]).

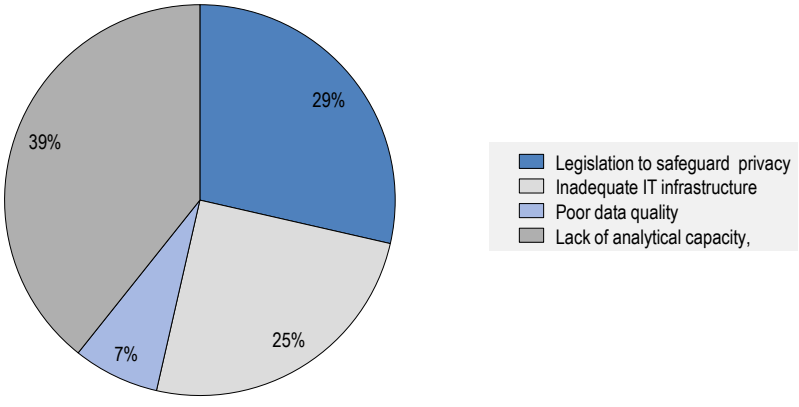
However, most surveyed countries (19/26) reported that routine data were *not used to their full potential* which suggests that there is still some way to go (OECD, 2019[19]).

7.5.3. The key barriers concern capacity, infrastructure and governance

Although some progress is evident, a range of challenges continue to inhibit the use of routine data for informing decisions in health systems. These challenges appear to be related to capacity, infrastructure and governance. Countries responding to the 2018 survey on use of routine data in pharmaceutical policy listed the following as the main barriers to harnessing these data: lack of analytical capability including human resources (39%); restrictions imposed by legislation to protect patient privacy (29%); inadequate information infrastructure (25%) and poor data quality (7%) (Figure 7.5).[9]

Reports of a lack of analytical capacity are noteworthy. The survey concerned only claims, administrative and prescribing/dispensing data, which are typically well structured and standardised. It did not include EHR data, which are more heterogeneous and unstructured. If there is insufficient capacity for the analysis of relatively straightforward datasets, then it can be assumed that this will be even more problematic for more complex data sources. It underscores the need to invest in capacity and human capital to put data to work in a productive and fruitful way.

Figure 7.5. Key barriers to using routine data for pharmaceutical policies concern analytical capacity, infrastructure and governance



Source: OECD (2019[19]), "OECD survey on use of routine data in pharmaceutical policies", https://www.oecd.org/health/health-systems/Using-Routinely-Collected-Data-to-Inform-Pharmaceutical-Policies-Analytical-Report-2019.pdf.

Similar barriers are reported for clinical data. For example, not all countries have, or are in the process of establishing, a comprehensive EHR system ("one patient one record") or an infrastructure that enables the sharing of information across various electronic platforms used by health care organisations and providers. The use of consistent minimum data sets and international data standards is increasing but deficiencies persist (e.g. data elements for surgical procedures or patient-reported outcomes) (Oderkirk, 2017[13]).

Some countries remain without unique patient identifiers, the absence of which make it very difficult to track care processes and outcomes longitudinally across cycles of care, providers and organisations. Lack of data quality and completeness is also common, problematic if they are to be used to complement high-quality evidence from RCTs (Oderkirk, 2017[13]).

Many counties also report legal constraints that limit their ability to use routine data for secondary purposes. For examples, health care provider organisations and authorities in many countries are only authorised to share EHR data for purposes directly related to care for the patient whose data are being shared. This makes secondary use to generate general knowledge from them impossible. Legal frameworks to protect privacy often also restrict the use of routine data to for research purposes (see also Chapter 8).

Another common challenge is a lack of procedural and institutional gatekeeping. This leaves stakeholders with insufficient clarity on who may lawfully access data, under what circumstances and for what purpose (Oderkirk, 2017[13]). Well-intended laws and policies, many of which predate digitalisation, can impede innovative uses of electronic data. With such problems precluding effective secondary use at national levels, creating a global ecosystem for the use of RWD will be extremely challenging.

7.6. Making better use of data requires concerted and coordinated policy action

Advancing the use of routine and RWD to improve the biomedical technology ecosystem requires action on a number of fronts and from multiple stakeholders: political leaders and policy makers, health care providers, researchers, industry, and patient groups and civil society. In the end, all stand to gain from the resulting approach to generating more advanced knowledge on medical technologies.

7.6.1. Countries must implement a governance framework the enables data use while maintaining privacy and security

The *OECD Council Recommendation on Health Data Governance* (the Recommendation), aims to help countries establish governance frameworks and infrastructure to enable learning through use of existing data. It lays out the fundamental elements for national frameworks and infrastructure (in technical as well as legal and policy terms) that enable the harnessing of real-world data for public benefit (OECD, 2019[47]).

The Recommendation asks governments to implement the technical requirements, not only harmonised data elements and formats and interoperability standards, but also state-of-the art cybersecurity methods. It also requires policies that minimise barriers to sharing data for various purposes – including research, regulation and other aspects of the biomedical technology ecosystem – in a way that maximises privacy, obtains informed consent where appropriate, and ensures compliance with other policy instruments such as the EU General Data Protection Regulation (GDPR).

The Recommendation also places considerable emphasis on transparency, public communication and stakeholder engagement – in an explicit acknowledgement of the central role of trust in establishing a new way of looking at and using personal health data (OECD, 2019[47]). In this regard, leadership is required to:

- Promote the benefits that can flow from putting real-world data to work, and thus shifting the discourse from using personal health data as a risk, to failing to use these data as the risk – in terms of the foregone benefits to individual patients and societies.

- Dispel the idea of a trade-off between data protection and secondary use of these data. It is not a zero sum game. In fact, a risk management approach and careful implementation of best practices and other mechanisms as described in the Recommendation can enable the achievement of both objectives.

7.6.2. Building and investing in capacity and infrastructure is key

A lack of analytical capacity and the necessary infrastructure are among the key barriers to realising the potential of routine and RWD in managing medical technologies. Countries must invest in the requisite capacity and expertise within the workforce to be able to manage and use these data in a secure way (a key aspect of governance), and apply the analytical techniques to extract valuable knowledge from them. Continued improvement to statistical and analytical techniques that manage bias and other inherent limitations of observational research methods also requires investment, in partnership with the research community.

Data need to be of sufficient quality and depth to enable good research to produce valuable evidence and knowledge. A key advantage of observational studies is their statistical power created by a large samples. This means that different types of data need to be linked and aggregated across jurisdictions, settings, agencies and organisations. In the case of rare diseases or precision therapies, data need to be shared between countries (see Chapter on cross-border data sharing). This requires investment in infrastructure that enables technical linkage, meaning that various data are encoded in a way that permits amalgamation and analysis. Developing common data and interoperability standards, as well as harmonising legal and governance frameworks, within and across countries is key.

Finally, generating complementary evidence from routine and RWD on how medical products perform is only the first step. Policy makers and other actors need to able apply this knowledge efficiently and meaningfully in regulation, HTA, pricing, and in clinical practice. This should also be a catalyst for further research. Relevant agencies must be empowered to apply the evidence in their decision making. Without policy to enable this, much of the effort will be wasted.

7.6.3. Other stakeholders also play an important role

Patient groups, as outlined above, have been vocal in their support for enabling secondary use of real-world data, and in this way have ensured that regulatory mechanisms such as the GDPR contain the necessary provisions that enable using personal health data for the public benefit.

Other stakeholders can play an important role. Civil society must be an active participant in this discussion, pushing for needed transparency in how data are used, how they are protected and what is then done with the resulting knowledge from their use.

The scientific community can reinforce the idea that using RWD is one way to address growing global health challenges by harnessing technological opportunities. Certainly one role for the research community is to make more apparent the risks of *not* using RWD to complement the clinical trial paradigm in addressing emerging concerns, ranging from the rise of chronic diseases as main public health issue to the inability of prospective research methods to detect rare events and deal with combination therapy. At the same time, methods and techniques used to extract knowledge from RWD must continue to be developed and refined to ensure that the evidence is of sufficient quality.

Payers, provider organisations and clinicians must play a part by recognising the secondary utility of the data produced during their daily processes. For example, for EHR data to become a valuable resource for research and policy, clinicians must embrace the electronic records not only as a key component of clinical practice but also of health system infrastructure. In turn, ensuring that all real-world data are of sufficient quality and can be pooled with those of other systems or platforms (this includes lowering the burden of entering EHR data) is a shared responsibility of industry and developers, provider organisations, payers and governments.

7.6.4. All stakeholders stand to gain

A health system that uses RWD to generate complementary knowledge benefits the entire biotechnology ecosystem. Patients are the principal beneficiaries from access to more beneficial, targeted therapies and information on their optimal use. Health professionals and providers will have better information to guide their decisions, and to discuss relative risks and benefits of treatment with their patients. The decisions of regulators, HTA bodies and payers will be informed by more robust, cumulative evidence of safety, effectiveness and cost-effectiveness, potentially avoiding high-publicity safety scandals or controversies regarding the pricing of treatments. The improved efficiency of policy and pricing decisions based on real-world evidence will be of benefit to society, with a view to getting the most value for its investment in health care.

Finally, the research-based industry will also gain through better identification of target populations and demonstration of value, as well as richer information to guide upstream R&D through, for example, more accurate evidence of unmet needs and identification of biomarkers.

7.7. Conclusion

The traditional model of separating research from practice, relying almost exclusively on prospective trials to create evidence on the performance of medical products is under strain. It limits the ability to translate scientific progress into new and better treatments for patients. It will also not enable policy makers to make increasingly complex decisions on regulation, financing and pricing, or patient care.

A new approach is needed, in which evidence from prospective research – which will remain the gold standard for generating evidence on safety and efficacy of new products and therapies – is complemented by knowledge created from routine and RWD. Such a model of continuous and iterative learning is now within reach given the rapid digitalisation of health systems and the development of attendant technologies and techniques to manage and makes sense of the growing volume of available data. The approach has been applied in other industries but some noteworthy examples in the health and biomedical research sector are emerging.

Yet overall progress has been slow. Systematising this new approach will require concerted action from policy makers and other stakeholders. The requisite capacity, data governance and infrastructure must be created to allow routine data to be put to work for this purpose, and for the resulting evidence to be effectively deployed in all parts of the technology ecosystem – from research and development, to regulation and pricing, to clinical care. This requires investment and partnering with other stakeholders.

Patient groups, civil society, the research community and industry must also play their part. A coordinated effort and international cooperation is required to ensure resources are available, uncertainty and associated concerns about the adoption of new research techniques and methods are addressed, and data and information can be shared within and across countries. This will increase the speed of implementation of an approach to managing medical technology that is more suited to current challenges, from which everybody stands to benefit.

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Notes

[1] This follows extensive laboratory and pre-clinical R&D.

[2] Probability of no events observed in 1 000 consecutive cases = $(1 – 0.001)^{1000} = 0.999^{1000} = 0.37$

[3] It must be acknowledged that regulation, global cooperation as well as economic levers such as competition have been important factors in these advances.

[4] Privacy issues are examined in a following section.

[5] Canagliflozin, which belongs to a class of drugs called sodium glucose co-transporter 2 inhibitors (SGLT2i), other SGLT2i drugs, and non-SGLT2i drugs.

[6] The database covers roughly 30% of the population of the Republic of Ireland, accounting for 74% of state expenditure on medication.

[7] See chapter on cross-border data sharing for more detail.

[8] The study focused on pharmaceutical products. The scope excluded electronic medical records.

[9] More than one response was permitted.