

The Vision for Real World Data – Harnessing the Opportunities in the UK

Demonstrating Value with Real World Data



White Paper
September 2011

Foreword

We all recognise that data about patients' use of medicines in normal clinical practice, or in settings which reflect the reality of healthcare delivery – Real World data – are likely to become increasingly important in decisions that affect patients' access to medicines.

For the past few years, the ABPI's Innovation campaign has focused on the importance of gathering Real World data and the significant role this plays in ensuring equitable access to new innovative medicines by patients. As the pharmaceutical industry seeks to demonstrate further the value of our products, we have examined the current and potential future importance of Real World data; reviewed the perceived challenges to collecting this data in the UK; and considered how we can harness the opportunity to develop the UK as a centre of excellence in this area.

In developing this Discussion Paper, we have canvassed the opinion of colleagues as to how they see the UK's potential for collecting Real World data. It has been heartening to have lively debates about the merits of the UK, and what we, as an industry, can do to harness this unique opportunity. From the quotes below, you can see that these views are shared across our key stakeholders, with Real World data taking on an increasingly important role in the delivery of healthcare.

We hope that this paper encourages further discussion and a realisation of the key role for all stakeholders in establishing the UK as a world leader in the conduct of Real World data studies to the ultimate benefit of the patient.

Dr Allison Jeynes-Ellis

Medical & Innovation Director, ABPI

“Extrapolating results from clinical trials, for which patients are often highly selected for age, co-morbidity and performance status, to clinical practice can be very challenging and restrictive. Evaluating and hopefully confirming the safety and the potential benefits of new therapeutic options in real world clinical practice bridges this important gap in our knowledge for the benefit of patients.”

Professor David Cunningham, Consultant Medical Oncologist

“The use of Real World data is vital not only to support quality improvement of the services we currently offer, but also if we are to build the services and therapies of the future on a solid foundation of evidence, and clinical outcomes. There is a great opportunity to transform the use of Real World data in the United Kingdom into meaningful information for critical decision-making, research, development and innovation internationally.”

Professor Andrew Morris, Director, Biomedical Research Institute, University of Dundee

“Real World data from registries and databases established primarily for audit purposes are increasingly demonstrating their important secondary role in research. This powerful and cost effective approach to research should be fostered where appropriate, guided by informed interpretation of the method and data.”

Dr Jonathan Potter, Clinical Director, Clinical Effectiveness and Evaluation unit (CEEu) at the Royal College of Physicians

“The UK research environment has been through a difficult period, but now with the changes being made by Government and the more positive and collaborative attitude of many academic partners I think things are starting to improve. We pioneered randomised controlled trials here, and now I firmly believe that the UK should be a leader in the development and implementation of this new equally important type of research, ‘Real World data studies’. We have the health system, and increasingly the culture of ‘research at the centre of healthcare’, which should greatly facilitate and not hinder this. I think that this report is a great step towards achieving this goal.”

Dr David Gillen, Senior Director and Head of International Medical Affairs, Gilead Sciences

“The use of Real World data is key to resolving uncertainty about the value of a medical intervention in routine clinical practice. I am delighted the ABPI is taking this initiative.”

Professor Adrian Towse, Director, Office of Health Economics

“We have a wealth of patient and system data in healthcare which can provide in many cases real time information to monitor trends and patient outcomes. The challenge is to use these data optimally to inform practice and guide future research. Good analytical systems which link data can further improve the benefits of these data and prevent a continued over-reliance on the randomised controlled trial as the only source of information.”

Professor Derek Bell, Professor of Acute Medicine, Director NIHR CLAHRC for NW London, Imperial College London

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Executive Summary

‘Real World data’ has been defined, for the purposes of this document, as: data that are collected outside the controlled constraints of conventional randomised clinical trials to evaluate what is happening in normal clinical practice.

- The conduct of Real World (RW) studies presents a unique proposition to encourage the investment, innovation and the use of skills brought by the pharmaceutical industry in the UK. The investment in studies that demonstrate the value of medicines and aid the development of new practices in the NHS yields many benefits. It maximises the use of resources, benefits patients and their compliance with taking their medicines, and facilitates collaboration between the pharmaceutical industry, academic researchers and clinicians.
- The high costs and complexity of conducting randomised clinical trials in the UK is counterbalanced by the relatively lower costs and simplicity with which RW data studies can be set up and conducted in the UK. This can maximise investment more quickly, add value to the evaluation of a new medicine, and encourage the faster access to innovative medicines by patients.
- Presentation of RW data is going to become increasingly important in decisions that affect patients’ access to medicines. Given the capability and capacity developed in the last decade, the UK has a unique opportunity to become a centre of excellence for the collection and analysis of RW data to be used by healthcare decision-makers both in the UK and worldwide.
- In the past, decisions about whether to grant access to new medicines in national markets were mainly informed by data generated from clinical trials, particularly randomised controlled trials (RCTs). Increasingly, there is a recognition of the role played by data about patients’ use of medicines in normal clinical practice or in settings better reflecting the reality of healthcare delivery.
- Recent reforms of the health system in England, including the publication of the White Paper and the Department of Health (DoH) consultation document on Value Based Pricing, highlight the Government’s intention to improve healthcare outcomes for patients. It is important for the pharmaceutical industry to demonstrate that its medicines can contribute to that improvement. The collection and use of RW data can enable all parties to achieve their objectives and, ultimately, to maximise patients’ health gains.
- The UK already has a comparative advantage in conducting RW data studies due to:
 - The marked influence of the UK on global decision-making through recognition of its world class Health Technology Assessment (HTA) processes;
 - The unique ‘cradle to grave’ healthcare system with many existing healthcare databases and disease registries;
 - The strong links already in existence between the pharmaceutical industry and academia, enabling access to the required skills for the collection, analysis and use of RW data. These include epidemiology, research methodologies, health informatics, health economics, Patient Reported Outcome Measures (PROMs), etc.
- In order to establish the UK as a world leader in the conduct of RW data studies and overcome some of the challenges of the current research environment, the UK and the pharmaceutical industry needs a strategy for change.

Recommendations

In order to develop the UK to become a centre of excellence for RW research the following actions are recommended:

- Measure current pharmaceutical industry activity in RW data collection in the UK to define a baseline against which to benchmark any change in the RW data environment (i.e. activity, ease of implementation, acceptance, value) in the future.
- Lobby at a national level with all key stakeholders for the need for change in the approval processes, skills and capabilities, and acceptance of RW data to enable the UK to optimise return on investment in the area.
- Develop a toolkit for UK pharmaceutical companies to present the case to their global colleagues for collecting, analysing and using RW data in the UK.
- Engage at a national and European level to streamline the regulatory environment for the conduct of RW data studies. Encourage clarification or amendment of the current regulatory guidance to maximise the opportunities for RW data collection throughout the product lifecycle.
- Encourage NHS partnership with the pharmaceutical industry in the collection and interpretation of RW data and engage with the wider medical community to ensure RW data are published in the respected medical journals alongside more traditional clinical trials.
- Improve the incentives for NHS centres to engage in RW studies, including those that are industry-sponsored.
- Lobby for national investment in the development of research capabilities based on electronic health records in the UK and lever the opportunities for industry access to data collected in this way for the purposes of research.
- Adopt a consistent approach to internal pharmaceutical company procedures, including the involvement of all relevant individuals for the review and approval of RW study protocols that take into consideration the differences between RW studies and clinical trials and their relevant regulatory requirements.

This document sets out to highlight the importance of conducting RW data studies to the UK pharmaceutical industry, their uses, and the ultimate gain for patients. It details the key actions that the UK pharmaceutical industry and wider life sciences research sector need to take in order to harness the opportunity for the UK to be regarded as a centre of excellence for conducting RW data studies.

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Glossary

ABPI	Association of the British Pharmaceutical Industry
AMS	Academy of Medical Sciences
B:R	Benefit: Risk Assessment
CTIMP	Clinical Trial of an Investigational Medicinal Product
DoH	Department of Health
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicines Agency
FDA	Food and Drug Administration
GPRD	General Practice Research Database
HED	Health e-data
HES	Hospital Episode Statistics
HRSS	Health Research Support Service
HTA	Health Technology Assessment
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
MEMO	Medicines Monitoring Unit
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NIHR	National Institute for Health Research
OHE	Office of Health Economics
ONS	Office for National Statistics
PAES	Post-Authorisation Efficacy Studies
PAS	Patient Administration System
PICS	Prescribing Information and Communications System
PPRS	Pharmaceutical Price Regulation Scheme
PROM	Patient Reported Outcome Measure
PSUR	Periodic Safety Update Reports
PV	Pharmacovigilance
QALY	Quality-Adjusted Life Year
RCT	Randomised Controlled Trial
R&D	Research and Development
RMP	Risk Management Plan
RSS	Research Support Services
RW	Real World
SOP	Standard Operating Procedure
VBP	Value Based Pricing

Section 1: Purpose of this document

- There has been increasing interest in the use of Real World (RW) data to demonstrate the value of a medicine to patients and to the NHS, and also to evaluate current clinical practice and burden of disease.
- This ABPI discussion paper examines the current and potential future importance of RW data to the pharmaceutical industry and the significant role this plays in ensuring equitable access by patients to new innovative medicines.
- The document sets out a vision for the UK as global centre of excellence for the collection, analysis and use of RW data and the strategies required to achieve this.
- The document is aimed at key stakeholders within the ABPI membership, Health Technology Assessment (HTA) bodies, Department of Health (DoH), NHS, and the wider life sciences research sector.



‘Real World data’ has been defined for the purposes of this document as: data that are collected outside the controlled constraints of conventional randomised clinical trials to evaluate what is happening in normal clinical practice.

Section 2: Introduction

The healthcare environment is constantly evolving and the adoption of new medicines into the marketplace is increasingly reliant on ever-more sophisticated evidence-based criteria. For a long time, randomised controlled trials (RCTs) have been considered the gold standard for generating clinical data on efficacy and safety, to inform product registration and subsequent prescribing. However, because of their inherent limitations and the characteristics of new and innovative medicines, it is simply not possible to obtain all relevant data through an RCT methodology; more pragmatic approaches need to be employed to collect and use RW data. Analyses from these data are increasingly playing an important role in ensuring that medicines are accepted by national policy makers and are adopted into practice.

The Government set out its vision for the NHS in the White Paper *Equity and Excellence: Liberating the NHS*¹, published in July 2010. The White Paper states that:

“...in order for the Government to achieve their ambition for world-class healthcare outcomes, the NHS must move away from meeting targets and be focused on quality and outcomes.”

In order to demonstrate quality and outcomes, it will be important to evaluate normal clinical practice, embracing a variety of RW data methodologies. The White Paper makes extensive reference to the importance of the conduct of research² and the use of research evidence, as key elements of the NHS. It recognises that:

“Research is vital in providing the new knowledge needed to improve health outcomes and reduce inequalities.”

In the past, analyses based on RW data have been criticised for lacking the robust scientific methodology of RCTs. However, with the shift in NHS priorities described above, the focus of clinical development needs to reflect these revised priorities to ensure a well-rounded development and market access plan that includes not only RCTs but also more pragmatic research in real clinical practice. In his Harveian Oration in 2008³, Professor Sir Michael Rawlins, Chairman of the National Institute for Health and Clinical Excellence (NICE), reasoned that we need a new approach to analysing clinical evidence. He said that:

“Randomised controlled trials (RCTs), long regarded as the ‘gold standard’ of evidence, have been put on an undeserved pedestal...Observational studies are also useful and, with care in the interpretation of the results, can provide an important source of evidence about both the benefits and harms of therapeutic interventions.”

These changes are well recognised by the pharmaceutical industry and the need for a change in focus towards demonstrating the value of a new medicine is echoed by the ABPI. In response to the DoH guidance on Value Based Pricing (VBP) discussed later in this document, Richard Barker, Director General of the ABPI, said⁴:

“Our industry must demonstrate the full value of its medicines, it is for Government to put in place processes which assess that full value, and then secure access to that value for NHS patients.”

In developing this document it has been important to consider how, as an industry, we are currently using RW data; how we would ideally like to use it in the future; what needs to change; and specifically the risks of failing to develop the expertise in the UK. It is essential to consider

this in the context of the requirements of decision-makers in the evolving NHS to ensure that any action plan is aligned with these requirements. We have presented a strategy to:

- Ensure that the UK maintains and develops its world class expertise in the collection and use of RW data for both local and global decision-makers;
- Support changes in the UK environment to encourage the implementation of RW data studies throughout the product lifecycle;
- Equip UK affiliate companies with the tools to be able to present the rationale for performing RW research in the UK to their global colleagues.

Section 3: Real World data and their importance for the pharmaceutical industry

In the context of the wider UK research environment

The past decade has seen the UK's share of global commercial clinical trial activity decline significantly. Whilst still attracting between 8 and 10% of global commercial trials, the UK only completes between 2 and 3% of global patient activity, a reduction from 6% in 2000⁵. The industry has identified some of the reasons behind this, including: slow start-up times; low patient recruitment to time and target; high and variable costs. One strategy to help counteract this shift is to look at other types of research that can be carried out in the UK in a timely and cost efficient way. A growth in research using RW data is one way to ensure continued growth of the UK in the research arena.

The term 'RW data' or 'RW research' covers a wide range of research methodologies and very different data sources, including:

- Patient registries;
- Existing electronic health records;
- Routinely collected administrative data;
- Primary patient level data collection (prospective or retrospective);
- Population health surveys.

If companies are able to translate non-UK clinical trial evidence into meaningful quality arguments and demonstrate the true value to, and impact on, the NHS, the need for data in addition to RCT data is becoming more widely accepted. This need is evident in both the pre- and post-approval settings for new medicines. Pre-approval, RW data may be used to evaluate unmet clinical need, describe pathways of care, and collect resource use, for example in preparing for a health technology assessment as part of the reimbursement process. During the post-marketing phase for a medicine, RW data are used to demonstrate the value and safety of a medicine in the marketplace in a way that is aligned with NHS priorities, patient needs and national agendas. In some instances, RW data collection may be essential to satisfy regulators' requirements where interim conditional approval has been granted to a new medicine.

As the NHS goes through its most radical changes yet – with the empowerment of healthcare professionals and providers, greater choice and control for patients, and the shifting focus away from targets towards outcomes and quality – its requirements for RW data to inform change will become more demanding. NHS decisions will be based on evidence of value in the commissioning of care, payment for services and, importantly, payment for future new medicines. Even more challenging, these changes are happening against the backdrop of a financial crisis and recent recession, with tight financial management required over the coming years and the likelihood of no real increases in health funding.

It is likely that the NHS will be collecting and using more RW data with which to make local decisions about healthcare delivery in the future. It is crucially important therefore for the

pharmaceutical industry and NHS to work together to demonstrate the value of new medicines, to ensure these data are used appropriately to facilitate access to innovative medicines for patients, and not to slow down this process.

In the context of the UK pricing and reimbursement model

The current system of pricing for prescription medicines falls under the Pharmaceutical Price Regulation Scheme (PPRS). Within the current system, the National Institute for Health and Clinical Excellence (NICE) carries out an HTA of specific medicines and provides a recommendation to the NHS on the circumstances in which the medicine is both clinically and cost effective. This is done on the basis of the application of a cost-effectiveness threshold expressed as a cost per Quality-Adjusted Life Year (QALY).

Initiatives like the Patient Access Scheme (PAS) allow flexibility in the cost-effectiveness thresholds for the assessment of medicines for some conditions. The introduction of the Cancer Drugs Fund, to assist with patient access to beneficial innovative cancer drugs, has helped to provide patient access to drugs that may not otherwise have had a favourable NICE recommendation. However, these were not intended as long-term solutions.

The 2010 Department of Health consultation on Value Based Pricing (VBP)⁶ proposes a new system for innovative medicines placed on the market from January 2014. It recommends a system whereby NICE continues to be the world leader in the pharmaco-economic evaluation of drugs through the HTA process. However, rather than applying a standard cost-effectiveness threshold to all medicines, the Government would apply weightings to the benefits provided by new medicines reflecting a range of price thresholds. These thresholds would be explicitly adjusted to reflect a broader range of relevant factors to calculate the full value of a new product.

Therefore, it will be essential for the pharmaceutical industry to focus its research efforts to demonstrate the additional benefits of its new medicines above and beyond the efficacy and safety demonstrated in randomised clinical trials and reduce the uncertainty surrounding the value of a medicine at the time of launch. Data on unmet medical need, current burden of disease and wider societal benefits of a medicine, which are reported to be important factors in influencing the cost threshold for pricing and reimbursement, will be best demonstrated through the collection of RW data.

The international perspective

The need for RW data is universal, and there is a growing body of evidence about this from many countries⁷. Consideration therefore needs to be given to the types of RW data required to support the market access of a new medicine and the transferability of these data between different markets (see Table 1).

This opens up two opportunities for the UK:

- The opportunity to ensure that any UK-specific data are collected in a timely manner for new medicines to facilitate faster NHS uptake and access for patients to new innovative medicines.
- The opportunity for the UK to position itself as a centre of excellence for RW data collection, to support its own and other countries' requirements for RW data that is generalisable across a number of healthcare systems.

Table 1: A summary of different types of RW data and the potential for transferability between countries

Data type	UK data applicable to other countries
Clinical outcomes (e.g. measures of morbidity and mortality)	√
Patient-reported outcomes	√ (in some cases)
Safety data	√
Natural history of disease progression	√
Prescribing patterns	? may depend on local policy and funding decisions
Utility data for economic modelling	?
Epidemiology	? will depend on country and disease
Treatment pathways	x
Resource use	x
Service delivery	x
Patient experience of service	x

As Table 1 demonstrates, it is much easier to generalise health-related data than resource use or costs data. Data that can be affected by local health policy or local healthcare models will more usually require sourcing on a country-specific basis.

A shift to continuous benefit: risk assessment in Europe

Furthermore, new pharmacovigilance (PV) legislation was approved in Europe in December 2010 that contains a new obligation for companies to perform post-authorisation efficacy studies (PAES) in certain circumstances⁸.

This legislation will come into force in July 2012 and its implementing guidance is currently being drafted. This will include guidance as to when PAES can be requested by an EU Competent Authority. The European Federation of Pharmaceutical Industries and Associations (EFPIA) has submitted a paper to the European Medicines Agency (EMA) and the European Commission stating when they think PAES should and should not be requested⁹.

In parallel, the benefit: risk assessment (B:R) section of periodic safety update reports (PSUR) and risk management plans (RMPs) in the EU is also being re-examined and a more in-depth assessment of medicinal product B:R is anticipated as a result of the revision of the PV legislation. PSURs and RMPs will in effect become B:R periodic reports and the EMA is seeking to have this position adopted globally via ICH¹⁰.

These developments in tandem will result in a clear shift towards continuous assessment of benefit as well as risk after a product is on the market in Europe. Sources of good quality RW data will be essential for companies to meet regulatory authority expectations going forward, and the UK is in a strong position to be a centre of excellence for RW data collection, as explained in Section 5.

The patient perspective

“We will put patients at the heart of the NHS, through an information revolution and greater choice and control.” (White Paper)

It has become more widely accepted that patients’ assessment of healthcare interventions are an essential component in defining value. Reflecting this, 2009 saw the introduction of the routine collection of Patient Reported Outcome Measures (PROMs) into the NHS. The document *Getting the most out of PROMs: putting health outcomes at the heart of decision making*¹¹ describes the importance of PROMs and their relevance to patients, commissioners, providers and clinicians within the changing NHS environment.

PROMs are reflected as indicators throughout the NHS Outcomes Framework for 2011/12¹², along with patient experience of the healthcare they receive, as one of the five key domains at the core of the framework. It will be essential for the pharmaceutical industry to reflect these outcomes in demonstrating the value of its medicines and the services that support them.

Section 4: The perceived challenges for Real World data in the UK

There are many different types of research that fit under the banner of RW data studies and these rely on different study designs and different data sources. There is no widely accepted scope for RW data across the pharmaceutical industry, and this can lead to inconsistencies in communication and interpretation.

A survey was undertaken by the Office of Health Economics (OHE)¹³ in 2009 to examine industry’s views on the relevance of RW data, the investment the industry currently makes in the collection of these data, and the perceptions of the benefits and barriers of conducting these studies in the UK, rather than elsewhere. The survey focused specifically on RW data for the HTA process.

Responses were received from 29 British pharmaceutical companies: 41% of those contacted. Around three quarters reported they were engaged in collecting Real World data of some kind in the UK. Data collection efforts were more common for health service costs, resource use and treatment pathway, clinical outcomes, burden of disease and patient outcomes data. The collection of data on patients’ ability to work, patient costs and impacts on patients’ caregivers/family was much less common.

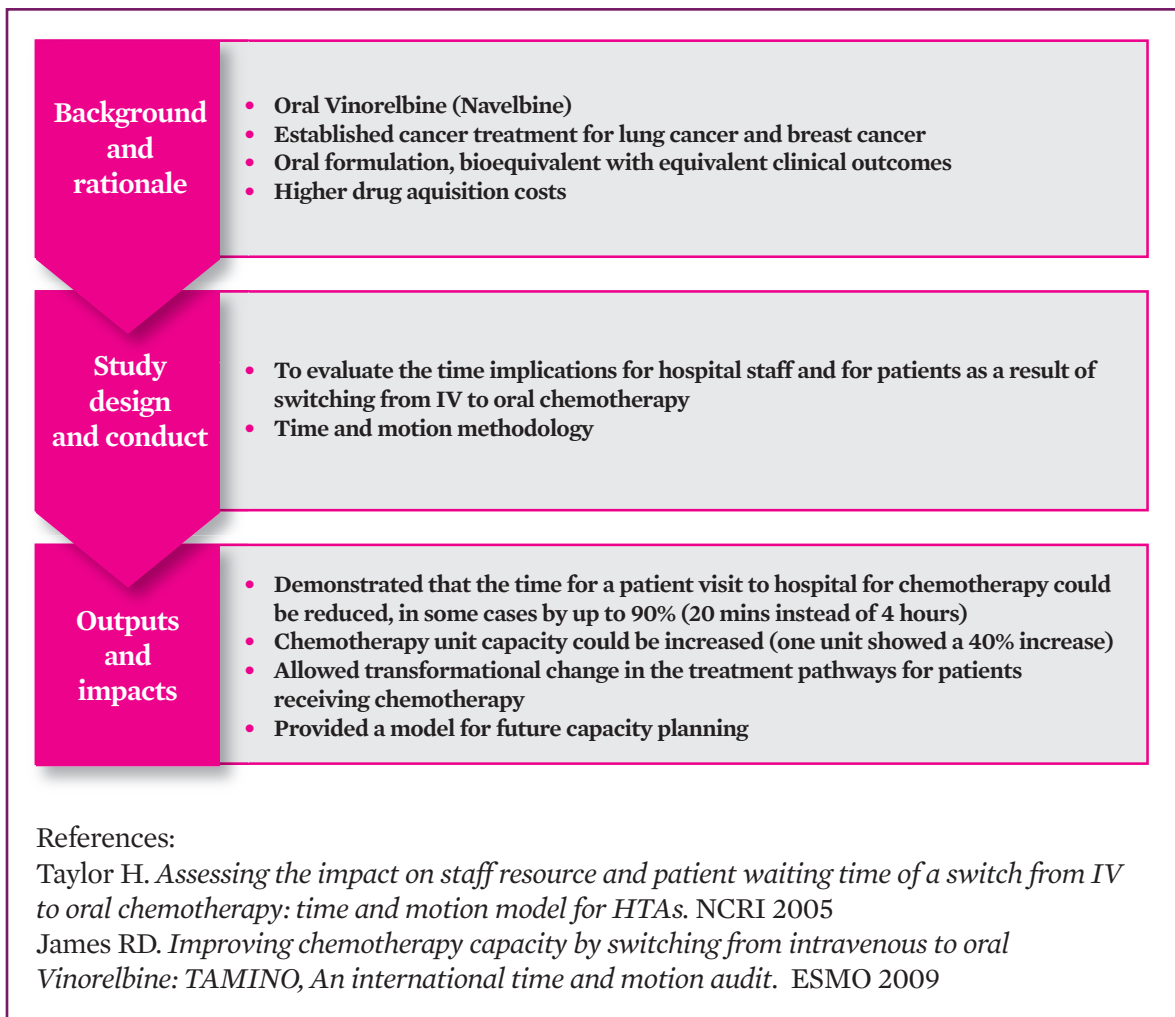
The availability of local expertise on HTA was a leading factor in choosing to undertake such studies in the UK; other factors cited as important were the perceived importance of local data to NICE and the perceived influence of NICE on HTA decisions in other markets, particularly elsewhere in Europe.

The main barrier to conducting these studies in the UK was stated as cost and the difficulty in obtaining ethical and NHS approvals. Views on whether evidence collected alongside use had a positive effect on NICE decisions were somewhat equivocal: most felt that in cases where they had submitted such data, they were only somewhat important to NICE decision-making.

Devlin N, Peperell K, Gillen D, Radway-Bright E. *The collection and use of real world data: Results from a 2009 survey of British pharmaceutical companies.* Presented at ISPOR, Prague, November 2010

The Pharmanet survey on observational research has been carried out for the past four years, with over 1000 respondents from over 25 global pharmaceutical companies¹⁴. This reflects a similar picture in terms of the increased use of observational study designs, the type of studies being performed and the reason for the studies. It also suggests that although there has been some progress made in terms of the wider understanding of the collection, analysis and subsequent use of RW data within the pharmaceutical industry, there was still considerable variation in both the knowledge base and also experiences of using RW data.

There is a growing body of examples where RW data has been essential for the market access of a product (see example below), despite the perception that these data are not always given sufficient importance by bodies such as NICE. It is essential that successes are shared within the industry so that confidence increases across the sector and there is a forum for sharing knowledge and experiences.



Understanding of the RW data environment

The success of a RW data study relies partly on RW data being the most suitable choice to meet the required objective. Non-interventional RW data cannot replace the safety and efficacy data generated by RCTs but can help support those data by allowing actual versus expected efficacy and safety to be evaluated in the context of a real clinical setting. Hence, RW data can reduce the uncertainty exhibited by new medicines at the time of launch by improving the information on the benefits and risks and developing evidence on real-life effectiveness. The regulatory frameworks in place for research in the UK currently limit the opportunities for this type of work prior to a new medicine being licensed.

It is important not to forget the value of RW data in understanding unmet medical need, burden of illness, NHS resource use, patient pathways, service delivery and prescribing patterns, which are all crucial elements of demonstrating the wider value of a new medicine.

Timing is important to ensure that RW data studies are not categorised as a Clinical Trial of an Investigational Medicinal Product (CTIMP) under the current UK regulatory frameworks. Table 2 below identifies typical objectives/purposes for RW studies and at what stage these types of studies can be carried out outside of the clinical trial setting within the current regulatory environment.

Table 2: Types of RW data projects feasible in the pre- and post-licence period for a medicine within the current regulatory frameworks

Purposes of RW data collection	Pre-Licence	Post-Licence
1) Describing current treatment patterns for a patient group for baseline information	✓	✓
2) Measuring healthcare related resource use and burden of illness	✓ (if disease related)	✓ (if related to new intervention)
3) Evaluating prescribing patterns of the new medicine		✓
4) Evaluating clinical outcomes associated with the new medicine		✓ (comparative or non-comparative)
5) Collecting quality of life data for economic modelling	✓ (if disease state based)	✓
6) Patient experience or patient-reported outcomes in real clinical practice	✓ (baseline information on current management)	✓ (if related to new intervention)
7) Evaluating service delivery and the impact of service improvement activities	✓	✓
8) Collecting patient safety data on the use of the new medicine		✓ (or conditional approval)
9) Understanding patient profiles in the disease area	✓	✓

Regulatory and governance frameworks: the impact on the speed of RW studies

Current research regulatory and governance frameworks apply to all forms of healthcare research – both RCTs and RW data studies designed for the purpose of research. However, there are clauses within the current regulations that appear unnecessarily restrictive when compared to the risks and benefits of RW data studies, and which prove inhibitory to their conduct.

In addition, there is currently wide variation in the time taken, and indeed the decisions made across the UK, whilst implementing these frameworks at a local level, for all types of research including RW data studies. Currently this can inhibit the initiation and conduct of RW data studies or be a cause of failure for these studies.

Inconsistency with the interpretation of the definition of ‘research’ by different committees creates a hurdle with ethical review for non-interventional research. In order to receive an ethical review, an experienced researcher may first need to justify that a non-interventional study is in fact a piece of research. However, the process itself is streamlined and timely.

The majority of the challenges facing UK researchers sit within the Research and Development (R&D) approval system rather than the ethical approval process. The National Institute for Health Research (NIHR) co-ordinated system for gaining NHS Permission (CSP) and the NIHR Research Support Services (RSS) are intended to streamline activities for researchers carrying out a multi-centre study. However, there are limitations on the type of studies eligible for review through this process. Commercial studies are not generally included unless they are ‘adopted’ onto the NIHR portfolio; and many observational research studies do not meet the criteria for this, as they are frequently descriptive rather than hypothesis-driven in nature.

The requirements for the assessment of a submission, for studies that fall into research, service evaluation or audit categories, lack consistency between NHS Trust R&D offices in the UK. This is further hindered because there are currently no standardised templates specifically designed for non-interventional research – i.e. legal agreements and contracts for commercial researchers or costing templates – which leads to the need for much longer negotiations.

Unlike the ethical review process, there are currently no fixed timelines for the R&D approval process. In addition, the variability in the knowledge of the requirements for non-interventional research, coupled with the variability in processes, and the decisions made, results in a very lengthy and often unnecessarily costly process for researchers.

It is essential that the pharmaceutical industry has sufficient knowledge and training or access to expertise on the regulatory and governance frameworks currently in place to operate efficiently and successfully within them.

RW data studies: defining standards

Although there are internationally-agreed standards that cover some elements of the conduct of RW data studies, as yet no UK-specific standards exist that cover the full breadth of research that may be defined as RW data studies, either for the methodological approaches adopted or the requirements during implementation or analysis. It is essential that the pharmaceutical industry works within a framework that ensures transparency and integrity around the collection, analysis and use of RW data to ensure consistency across the sector. This is reflected in the ABPI Code of Practice for the Pharmaceutical Industry 2011 with the inclusion of a new clause relating to non-interventional studies of marketed medicines, which states:

“Companies must publish the summary details and results of non-interventional studies of marketed medicines in a manner consistent with their parallel obligations with respect to clinical trials.”¹⁵

The skill mix required

Research skills specific to RW data, such as methodological expertise, health informatics and epidemiological skills, are not in such abundant supply within the pharmaceutical industry as those required for the design and implementation of more traditional RCTs. There is a need to ensure the appropriate internal skills and capabilities are available to underpin the strategic development and practical implementation of RW data studies. Furthermore, educational strategies need to be developed for the maintenance and continued development of these skills in the future.

Internal pharmaceutical industry processes

The lack of consistency in the interpretation of the scope of RW data, and also the current regulatory and governance frameworks and their applicability to RW data studies, has led to similar inconsistencies in the internal Standard Operating Procedures within pharmaceutical companies. Again this proves a further hurdle to the successful initiation of RW data studies. It is crucially important that these inconsistencies are addressed and aligned during the implementation of the Academy of Medical Sciences's (AMS) regulatory and governance recommendations.

With the increasing reliance on RW data, companies need to consider the appropriateness of any internal procedures for these types of data collection studies. It is essential that the right individuals are involved in the internal process, the proper risk assessments are carried out, and the appropriate justification given for the study to global departments.

The NHS environment

To date, commercial RW data studies have not been associated with the same investment or incentives for NHS involvement as clinical trials. Whilst incentives do not have to be solely financial, there is a need to consider the appropriate financial frameworks to encourage wider involvement in these studies, such as investment in research departments' infrastructure and resources.

The NIHR's costing template for commercial research for use by local NHS Trust R&D departments in the the UK has been modelled on classic clinical trial processes. However, they are widely used for assessing the conduct of RW data studies, in the absence of anything more specific to RW data collection. In many cases, this can cause misalignment between the lower budgets available from the pharmaceutical industry and the costs being requested by local NHS Trusts for these types of studies. Whilst the drive from NHS investigators to collaborate with the pharmaceutical industry on RW data studies can help overcome these barriers, the need for protracted local negotiations can be detrimental to their timely approval.

There is a wealth of existing healthcare data stored in the UK in existing databases and disease-based registries, and whilst these provide an enormous opportunity for the extraction of RW data, they are not without challenges if used for the purposes of research. There is an understandable inconsistency in the way patients' data has been entered into these systems, as the primary use for some of these has been administrative functions not healthcare research. To maximise the potential for these data, the appropriate skills should be in place both for the capture and entry of the information and for the data management and analysis applied to it. Similarly, there is a need to explore the potential frameworks for the industry to work in partnership with the NHS and be able to access information from these existing datasets for agreed purposes.

Section 5: The UK as a centre of excellence for Real World data collection

UK influence on global decision-making in medicine development

It is recognised that the majority of the pharmaceutical companies work in a global market and the UK is only one of the important healthcare sectors. In fact, the UK may represent only a small share of the global revenue for a medicine, but it has a significant influence on access to medicines in other countries. From an HTA perspective, recommendations on the most cost effective use of medicines developed by UK bodies such as NICE are formally or informally used to make coverage decisions in other countries, including emerging markets. In addition, the influence of NICE has been increasing since the establishment of NICE Scientific Advice and NICE International, which are NICE divisions providing assistance to, respectively, companies and healthcare systems/governments across the world.

With this in mind it is important to consider the attributes we have in the UK to promote ourselves as a centre of excellence for RW data studies.

As discussed earlier, the UK has one of the most well-developed HTA processes in the world through NICE and this is widely considered a model of best practice.

“NICE has some influence on the pharmaceutical industry, but the extent of any global impact isn’t easy to assess. Having said that however, it is very clear that NICE certainly has had a considerable impact over the last 10 years on healthcare systems across the world. Our expertise in health technology assessments is viewed as world class, and increasingly, that knowledge has been sought by a variety of countries.”¹⁶

Similarly there is already a wave of support for the UK to be a centre of excellence for these types of studies. In a recent survey of UK pharmaceutical companies:

“86% of participants said that they considered there were some particular strengths or advantages of using the UK as a base for these (RW data to support HTA submissions) studies, compared to other countries.”¹⁷

The advantages for keeping this work in the UK were quoted as including:

“Availability of UK expertise in the HTA evidence collection, the fact that local data is important to NICE, and crucially that NICE decisions influence HTAs in other important non-UK markets.”

Attractive NHS environment

The UK has a unique ‘cradle to grave’ healthcare system, with the General Practitioner being a gatekeeper to most of the health and social care requirements of an individual throughout his or her life. This offers the opportunity to collect several years’ worth of follow-up data for any individual within the healthcare setting. The UK already has a wealth of electronic databases developed over the past 20 years containing patient information with provisions in place to maintain patient confidentiality. In addition there are several disease-specific databases, e.g. cancer registries and national audit databases; and health-related administrative systems, e.g. Hospital Episode Statistics (HES), which hold valuable information relating to healthcare provision in the UK. These are often an often untapped resource, as currently many of these systems are unable to ‘talk’ to each other and hence link primary care patient data to information on secondary care services or other elements of care that the patient may have need to access.

Progress is being made towards linked datasets in the UK. This can become a unique selling point for the UK – not just for RW outcome data, as described in this document, but also for the optimisation and recruitment for clinical trials and also for ongoing pharmacovigilance capabilities¹⁸. Ongoing investment and support for this initiative is required to maximise the enormous research potential it affords the UK in the area of RW data.

Some examples of local and national initiatives that demonstrate the UK's growing expertise in this area and the value of these types of systems include:

- Birmingham NHS Foundation Trust has developed two systems: (a) the Prescribing Information and Communications System (PICS), a decision support tool incorporating medicine prescribing and administration data which it has been using for many years; and (b) HED (health e-data) – incorporating HES data from England, linked to death data from the Office for National Statistics (ONS). This enables extraction of outcome data for anywhere in England, as well as facilitating feasibility of studies. Data from North America is also held and available for use.
- There is an established network of regional NHS Quality Observatories that already hold valuable datasets relating to patient care.
- The General Practice Research Database (GPRD) is the world's largest computerised database of anonymised longitudinal medical records from primary care. It is frequently used by EMA and FDA and more than 900 publications have been published in top tier peer-reviewed journals from these data.
- In Scotland there are established record linkage systems, e.g. the Medicines Monitoring Unit (MEMO), providing the ability to track patients across primary and secondary care.

Progress with streamlining the regulatory and governance frameworks

The Academy of Medical Sciences (AMS) has recently recommended drawing together existing systems for research governance and ethics approval to streamline this process in the UK. This is a move that has already been welcomed by the ABPI membership and the wider life sciences community. These frameworks, however, cover all types of healthcare research (including RCT and RW data studies) and it is essential that RW data studies are considered specifically as progress is made towards addressing this important recommendation. This offers an opportunity for the UK to be a more attractive environment for the conduct of RW data studies.

Skills and education

The strong links that the UK pharmaceutical industry has with the academic community are crucial in ensuring that the appropriate skills are identified and developed to support this growing area of RW research. As this report has demonstrated, RW data can encompass a vast array of data sources producing data for a wide variety of purposes and posing a number of methodological challenges. The pharmaceutical industry has a responsibility to ensure that the personnel involved in RW data locally have the appropriate knowledge level, or secure the necessary support for the design, collection, analysis and subsequent use of these data.

Section 6: Harnessing the opportunity: a strategy for change

This document highlights a number of key actions for the pharmaceutical industry and wider life science research sector that are essential in order to harness the opportunity for the UK to become a centre of excellence for RW data studies. These are summarised below:

Strengthen the case for the UK to develop its capabilities for the conduct and use of RW data studies

- Measure current pharmaceutical industry activity in RW data collection in the UK to define a baseline against which to benchmark any change in the RW data environment (i.e. activity, ease of implementation, acceptance, value) in the future.

- Lobby at a national level with all key stakeholders for the need for change in the approval processes, skills and capabilities, and acceptance of RW data to enable the UK to optimise return on investment in the area.
- Develop a toolkit for UK pharmaceutical companies to present the case to their global colleagues for collecting, analysing and using RW data in the UK.

Encourage initiatives to overcome the challenges facing RW research in the UK

- Engage at a national and European level to streamline the regulatory environment for the conduct of RW data studies. Encourage clarification or amendment of the current regulatory guidance to maximise the opportunities for RW data collection throughout the product lifecycle.
- Encourage NHS partnership with the pharmaceutical industry in the collection and interpretation of RW data and engage with the wider medical community to ensure RW data are published in the respected medical journals alongside more traditional clinical trials.
- Consider the incentives and financial frameworks for the NHS to engage in RW studies including those that are industry-sponsored.
- Lobby for national investment in the development of research capabilities based on electronic health records in the UK and lever the opportunities for industry access to data collected in this way for the purposes of research.
- Adopt a consistent approach to internal pharmaceutical company procedures, including the involvement of all relevant individuals for the review and approval of RW study protocols that take into due consideration the differences between RW studies and clinical trials and their relevant regulatory requirements.

Conclusions

In an environment that is moving to encourage faster access for patients to new innovative medicines, RW data allows more informed decision-making to help drive towards this goal. The investment in studies that demonstrate the value of medicines and aid the development of new practices in the NHS yields many benefits. It maximises the use of resources, benefits patients and their compliance with taking their medicines, and facilitates collaboration between the pharmaceutical industry, academic researchers and clinicians. Furthermore, the high costs and complexity of conducting RCTs in the UK is counterbalanced by the relatively lower costs and simplicity with which RW data studies can be set up and conducted in the UK, allowing much faster generation of data with which to demonstrate value to patients.

The UK has a comparative advantage in conducting RW data studies. The establishment and consolidation of HTA bodies such as NICE have led to the development of a highly-specialised labour force in the field of HTA, which is viewed as world class. The influence of these bodies reaches internationally and as such wider UK acceptance of RW data to measure value is also likely to be reflected globally.

This report describes a UK pharmaceutical industry already well placed to adapt to the growing demand for RW data to demonstrate the value of its medicines to healthcare decision-makers around the world. In order to capitalise on this position it will be necessary to develop, maintain and share RW data capabilities across the pharmaceutical industry to ensure the appropriate internal skills, processes, resources and standards are available to underpin the strategic development and practical implementation of RW data programmes. Work is already underway by the ABPI through the development of a comprehensive practical guide to collecting RW data, which seeks to provide clarity around the definitions, use and practical issues which arise when undertaking RW data studies.

There is a pressing need to lobby for clarity or change in the current regulatory and governance framework relating to the collection of RW data, to ensure that this is streamlined such that it does not inhibit the successful collection and use of RW data. Furthermore, there is a need to secure continued investment in the development of UK research capabilities based on electronic health records if the potential for the UK to become a centre of excellence for the conduct of RW data studies is to be optimised. Crucially important is the need to consider the financial frameworks that can be developed to support partnership working between the pharmaceutical industry and the NHS on the collection and use of RW data in the future.

This document presents a unique proposition to encourage investment and innovation by the pharmaceutical industry in the UK, whilst providing essential information to healthcare decision-makers worldwide and, ultimately, better care for patients. A consultative process will be encouraged with key stakeholders in the UK to gain support for, and commitment to, driving change through the initiatives detailed.

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