Real World Data and Real World Evidence in Singapore: Are We Ready?

An International Society of Pharmacoeconomics and Outcomes Research Singapore Regional Chapter (ISPOR-S) Meeting

On 5th November 2018, the ISPOR-S held its very first members-only event under the newly inaugurated Executive Committee – a 1.5-hour panel discussion on the topic of real world data (RWD) and real world evidence (RWE) in Singapore. Over 20 representatives from the pharmaceutical and medical technology industry, public hospital institutions and academia engaged in a lively exchange of knowledge and insights on the challenges and potential of RWE generation and utilisation.

The discussion was moderated by Assistant Professor Hwee-Lin Wee (President, ISPOR-S 2018/2019), and opened with an overview of the issue by Mr Hansoo Kim (President of the ISPOR Australia Regional Chapter), with Dr Ken Lee (Chief Medical Officer of Asia-Pacific, IQVIA), and Mr Ng Kwong Hoe (Principal Head of Evaluation, Agency for Care-Effectiveness, Ministry of Health, Singapore) presenting the industry and payer perspectives, respectively.

What is ‘real world data’ or ‘real world evidence’?

The panel discussion addressed both RWD, defined in a recent publication from the ISPOR-International Society for Pharmacoepidemiology task force as data obtained outside the context of randomised controlled trials (RCTs) generated during routine clinical practice, as well as RWE, referring to the clinical evidence on the usage, advantages and risks of a medical intervention generated from the analysis of RWD.

Where are the sources of real world data?

The feasibility of generating RWE relies heavily on the availability of RWD, which can be obtained through observational studies, electronic health records (EHR), claims and billing databases, registries, and personal devices or applications.

Sources of RWD differ between countries and accessibility to those RWD sources can pose an additional challenge. Mr Kim shared that, in Australia, a single-payer system and reimbursement of medications through the Pharmaceutical Benefits Scheme allow collection of prescription data at a national level. However, 90% of these data cannot be accessed, except for treatments in exceptional indications (such as renal cancer, for which all prescription data are available). Registries are another platform for RWD collection in Australia, and include the Victorian Lung Cancer Registry, the Australia & Asia Pacific Clinical Oncology Research Development (ACCORD) database and state-based epidemiology registries. Finally, manufacturers may collect RWD as part of early access programmes, although such data are not often published.
Dr Lee presented several RWD initiatives in Singapore, including a collaboration to develop the largest liver cancer registry in the region. This project involves hospitals, academia, industry, and other partners across 9 Asia-Pacific countries, including the National Cancer Centre and the Singapore Clinical Research Institute. Mr Ng mentioned that RWD in Singapore includes registries and electronic medical records. The more important question is whether these data are fit for purpose.

What are real world data and evidence used for?

From a regulatory perspective, RWD are historically collected for post-marketing safety monitoring and surveillance. Since recent changes in U.S. FDA legislation – the 21st Century Cures Act passed in 2016 – aimed at expediting approval for new medicines, attention has turned to the role of RWE for new drug approvals and label extensions. Mr Ng and Mr Kim felt that this has its pros and cons. Nonetheless, Mr Ng mentioned that the evidence requirements to gain positive reimbursement recommendations are much higher than for regulatory approval given HTA needs to address questions on comparative evidence as well as cost-effectiveness of the newer health technology. RWE usually complements clinical trial data and strengthens the evidence base for a medical technology.

RWE is particularly important in conditional reimbursement schemes, where a positive decision may be given initially on the condition that future RWD will be collected. This is practised in Australia – Mr Kim presented 3 examples where RWD were collected after the initial decision and were used to confirm the drug’s effectiveness (nivolumab), to support pricing negotiations (pembrolizumab) and to decide on continued coverage (crizotinib).

Mr Kim added that RWD on epidemiology, clinical treatment pathways, prescribing patterns, and healthcare resource utilisation can provide useful information for understanding the burden of disease, treatment landscape, and the potential impact of a medical technology on clinical practice or healthcare delivery. These allow decision-makers to consider the future costs and implications on healthcare systems following a reimbursement decision.

During the Q&A, several challenges associated with generating real world data and evidence were raised. These highlighted the importance of understanding the intent of, approaches to, and application of real world data and evidence and are outlined below.

What are some challenges in generating or using real world data or evidence?

**Interpretation**

A key feature of data from real world studies is that they reflect actual clinical practice, unlike the clinical trial setting, which is designed to minimise confounders and biases with strict monitoring and adherence to a study protocol. While the ‘real world’ element may improve generalisability, uncertainty around treatment effects derived from RWE for a medical technology may limit its usefulness, posing a challenge for determining the acceptable trade-offs between these depending on the context of its use.

**Quality**

As RWD are collected over the course of routine clinical care, lack of quality control during data collection means that substantial efforts are required for data cleaning (e.g. missing data, inconsistent data entries). RWE may be pooled from various RWD sources, each with known limitations (e.g. absence of clinical endpoints in claims data or resource data in EHRs, limited follow-up durations in registries), necessitating data aggregation and integration for a more complete understanding of the clinical picture. If database linkage will not be possible, programmes such as the Observational Health Data Sciences and Informatics Programme are available that may address standardisation of data across disparate databases.
Technical capabilities
Performing analysis on large amounts of data requires software and data models, and skilled personnel with deep expertise in data analytics and management. Dr Lee stated that including in Singapore, there is currently a shortage of technical capabilities for supporting RWE generation.

Privacy and protection
Governance around how data should be made available and used is needed to ensure patient privacy protection, while allowing accessibility to clinically meaningful data.

Costs
Extensive resource is needed to develop the healthcare or legal infrastructures and the technical capabilities that would allow collection of high-quality RWD for robust RWE generation. This contributes to high costs, and Dr Lee highlighted a need for cost-efficient methods of research and analysis.

What are some principles to consider when generating or using real world data or evidence?
Given the current challenges with RWD/RWE, the intent of collecting RWD or generating RWE should be carefully considered to inform the research approach. This could involve defining a research question that the RWD/RWE will address as a first step.

For manufacturers who are planning RWD collection or RWE generation to inform future HTA submissions, evidence gaps should be proactively identified and RWD collection or RWE generation methods tailored to fill these gaps. For this, Mr Ng would encourage manufacturers to consider the key data gaps and prioritise efforts in generating evidence to address these gaps. In Australia, consultations with the HTA body – the Pharmaceutical Benefits Advisory Committee – on RWD/RWE approaches may be arranged. Finally, Mr Kim added that capitalising on existing RWD sources may be more cost-efficient than developing large registries, for example.

In the U.S., consultations and development of a draft guidance on the appropriate use of RWD in regulatory decision-making are underway and will be published by 2021. Mr Ng posited that the Agency for Care Effectiveness currently does not intend to prescribe specific guidelines for the generation of RWD and utilisation of RWE in HTA. In general, principles of good research methodology should apply; for example, careful study design is needed, and an analysis plan should be created prior to retrieving and analysing real world data. Mr Ng also emphasised that RWE should be relevant, credible and timely.

Existing multi-stakeholder initiatives highlighted by Dr Lee demonstrate the need for cooperation and coordination at various national or regional levels; given the large scale of RWD/RWE, collaboration would play a key role in the success of these endeavours.

Attendees of the first ISPOR-S members-only event 5th November 2018.
Dr Wee - 3rd from left in front row; Mr Kim - 2nd from right in back row;
Dr Lee - not in photo; Mr Ng - 4th from left in front row.
Looking forward

Realising the value of RWD/RWE in healthcare decision-making will require a better understanding of how it should be generated and used. Accordingly, Dr Wee shared that RWD/RWE will be a key focus of the ISPOR-S 2018/2019 workplan. ISPOR-S will explore a joint initiative with HTAsiaLink, the Saw Swee Hock School of Public Health, and industry to develop regional guidelines for collecting RWD and generating RWE. A working group comprising of key stakeholders and an international advisory committee will be formed and the goal is to hold the first working group meeting at HTAsiaLink in April 2020.

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References


