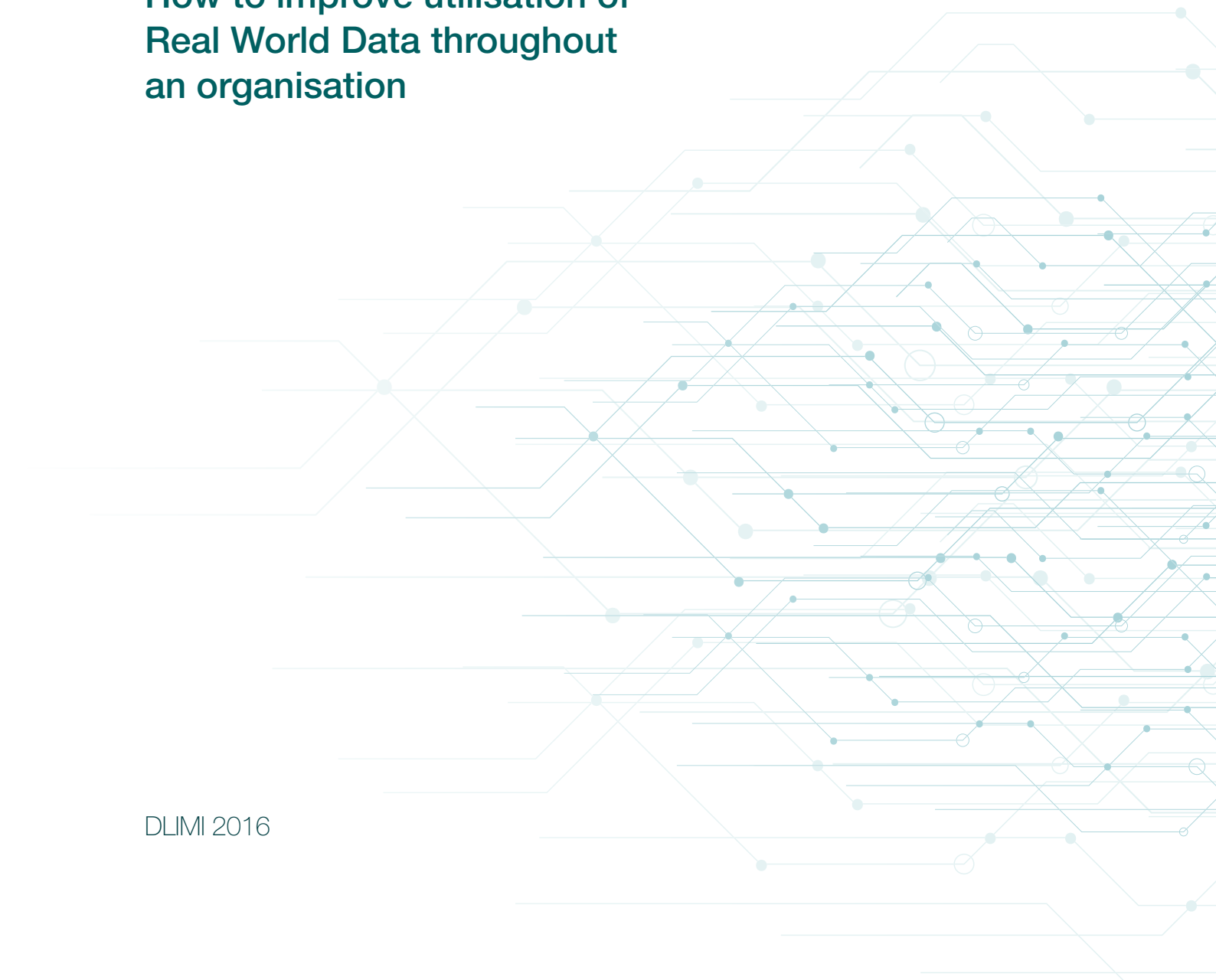
DLIMI

WHITEPAPER

BEYOND REAL WORLD EVIDENCE

How to improve utilisation of Real World Data throughout an organisation



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INTRODUCTION

Real World Evidence (RWE) has demonstrated real business value by enabling medical researchers to analyse Real World Data (RWD) with the aim of documenting drugs' health effect in natural patient populations. However, RWD also holds significant value for other business areas in pharmaceutical organisations. This white paper suggests ways of improving utilisation of RWD throughout the organisation and thereby take the next step beyond Real World Evidence.

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Increasing demand for documentation of drugs' effectiveness in the real world.

THE INCREASING DEMAND FOR DATA AND EVIDENCE FROM THE REAL WORLD

In recent years, existing procedures for introducing new drugs, and for reaffirming the market relevance of existing drugs, have begun to be challenged. Increasingly, purchasers, medical authorities and Health Care Providers (HCPs) all demand documentation of the effectiveness of drugs in a real world setting.

Traditionally, the medical and market values of a drug were measured by randomised controlled trials (RCTs) showing the drugs' clinical efficacy and safety profile. Although RCT evidence is still a qualifying factor in the assessment of drugs, evidence from 'the real world' is increasingly used to supplement RCT results with the aim of improving market position. There are a number of reasons for this:

- National health budgets are under pressure, with ageing populations and growing demand for treatments. As a result, pharmaceutical spending needs to be prioritised.

- Politicians increasingly demand data on drugs' health effectiveness and benefits in 'the real world', and this demand, in turn, is translated into one of the criteria by which drugs are assessed by healthcare authorities.

- Health authorities are especially keen to access 'real world understanding' when evidence from RCT is not seen as strong, as for example when an RCT is based on a selected group of trial participants not representative of the patient population using the drug.

> *"In a Danish context, there is a dilemma in terms of getting fast access to new medicines, which is a political priority, and at the same time being able to deliver real effectiveness data since this delays the introduction of the medication. Conditional introduction along with protocolled studies may be an option. Likewise, results from Real World Evidence studies may be used when updating the treatment guidelines".*
>
> *Jørgen Clausen, Chief Economist/Lif Denmark 2016* [1]

It is also a known fact that some drugs have a markedly different health effect and safety profile than had been shown in the RCT. This naturally encourages HCPs to request data on drugs' effects in the patient population in the 'real world'. Medical research teams based in hospitals are responding to this request by conducting controlled studies among actual patient populations in order to provide real world evidence about health effect. Hospitals and regional governments now have dedicated research teams conducting effectiveness studies on selected treatments in order to optimise budgets.

Alert to these developments, the pharmaceutical industry is beginning to focus on delivering 'real world' data and scientific evidence on the use and benefits of drugs. In the healthcare and pharmaceutical sector, Real World Data and Real World Evidence are now very much on the agenda!

> *"Our RWE capability is generating valuable insights that we are using to inform business decisions we make every day in discovery, business development and commercial development of launch to late-stage products".*
>
> *Brian Sweet, Executive Director of Health Alliances, AstraZeneca, Oct. 2, 2012* [2]

Two approaches dominate the field of RWE:
A traditional medical approach and a Big Data approach.

Traditional medical approach versus Big Data approach

In the search for documentation of medical treatments' health effect in 'the real world' two approaches seem to be dominant:

1. A traditional medical approach favoured in the medical and safety units of pharmaceutical companies and among scientific researchers
2. A novel Big Data approach mainly taken by data scientists and non-medical communities within the pharmaceutical industry

The traditional medical approach focuses on Real World Evidence. It does not see this kind of evidence as something new. Instead, it treats Real World Evidence studies as equivalent to familiar studies such as observational studies, non-intervention studies, epidemiology studies, and register-research studies.

These studies draw on well-defined and structured data sources. This approach assumes that genuine evidence fits into the well-known medical hierarchy in which RCT head-to-head studies and meta-RCT studies set the highest evidential standard. As a result, this approach often seeks to emulate RCTs in its thinking and methodology which prioritises internal of study designs, use of study protocol and a meticulous focus on confounding factors.

In the Big Data approach, studies based on clear hypotheses, deductive reasoning, and well-defined structured data sources are not seen as mandatory. Nor is it believed to be necessary to follow a strict protocol, for that matter. Instead, the Big Data approach explores vast amounts of data looking for statistically meaningful patterns in the use, and sometimes the effects, of medical treatment in a real world setting. In the best of cases, this approach would view their approach as having high external validity. A favoured example is Google's Flu Trend, which predicted influenza epidemics via Internet searches in the first generation of this approach, and in some cases these studies secured real benefits for public health authorities in the US[3]. Recent innovations within Big Data and healthcare, such as IBM's Watson, have demonstrated how artificial intelligence can support medical decisions and drug development[4]. These studies are sometimes called 'Real World Evidence studies'. Regrettably, however, this may lead to confusion between the traditional medical approach and the Big Data approach[5].

A mutual quest for Real World Knowledge

The differences between these two approaches may seem unimportant, and perhaps even academic, but they are important because they pinpoint the potential for wider utilisation of data in pharmaceutical companies. At DLIMI we acknowledge that the term 'Real World Evidence' is often understood in pharmaceutical companies in accordance with the traditional medical approach and Real World Evidence in this context is seen as an important supplement to RCT. However, there is a great potential across all business areas for a wider use of data and we see Real World Evidence, in a broader context, as a result of what we refer to as Real World Data (RWD). At DLIMI we consider RWD one of the four main data-driven knowledge domains in the pharmaceutical industry:

1. Research & Development (R&D)
2. Randomised Clinical Trials, (RCT)
3. Real World Data (RWD)
4. Big Data (BD)

Real World Evidence is a result of Real World Data, which in turn is one out of four critical data-driven knowledge domains.

Fig 1. The four data-driven knowledge domains in the pharma-industry

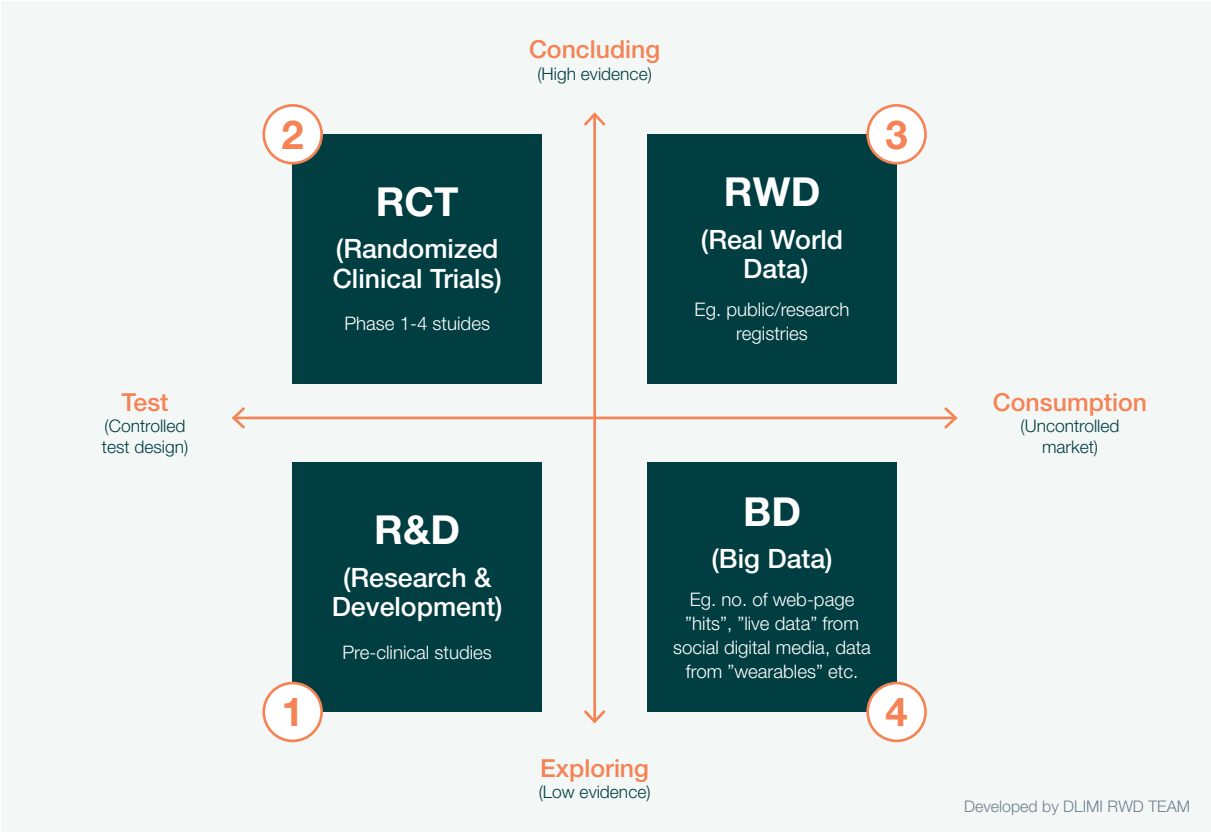

Figure 1 shows how the central data-driven knowledge domains of the pharma industry are suspended between two axes: A knowledge axis (i.e. explorative knowledge production versus conclusive evidence production) and an environment axis (i.e. the controlled test setting versus the open market).

Research & Development has been highly data-driven for a number of years. As a supplement to traditional laboratory R&D, Computer-aided drug design has enabled more rapid development of medical compounds[6]. Exploratory analysis of genome data is another example of data driven research aiming to improve drug development[7]. Although Research & Development is conducted in a controlled environment in a scientific and structured manner, it often has an explorative nature. This can be seen, for example, when the potential of compounds for medical purposes is investigated and identified.

Likewise, RCT needs to collect and utilise data when a drug is tested with the aim of providing documentation and evidence on efficacy and safety, or the relative effectiveness of the drug. These studies are controlled, conclusive, and based on a selective patient population.

On the other side of the axis we find data on the actual *consumption* of medicine, produced in an uncontrolled environment, i.e. the market. In this context Big Data can be understood as something that involves less structured, user-generated data from the Internet, wearables, and so on, and which reflects perceptions and user-behaviour connected with medical treatments. Understood in this way, Big Data is becoming an increasingly important source of new knowledge for the pharmaceutical industry.

Finally, Real World Data can be seen as typically structured sets of data on the consumption of medicines in the market and healthcare system, which can – with the propper methods – be used to produce evidence about drugs' effects outside the controlled clinical trial setting. Beside their association with non-intervention studies, which use actual patients as primary sources of information, Real World Data are most often found in medical databases, clinical registries and similar repositories overseen by public authorities, insurance companies and medical societies. They can also be found in sales data and traditional market research data.

> *"The ongoing quality improvements to clinical databases have made it possible to conduct analyses of treatment effects and safety – right down to the level of the drug. They cannot replace randomised studies, but once evidence from the controlled studies is ready, registers and databases can be used to explore how this resonates with real world patients and the treatments they're given".*
>
> *Anders Green, Professor of Clinical Epidemiology at the University of Southern Denmark*[8]

Real World Data is a prerequisite of Real World Evidence, and affiliated to both RCT and Big Data, depending on the level of the evidence, data sources and field of interest.

Real World Data is affiliated to both RCT and Big Data, and the exact nature of the affiliation depends on the evidence (high evidence vs. highly explorative), on data sources (highly structured vs. less structured) and on the field of interest (test vs. consumption). Accordingly, at DLIMI we see Real World Data as a tool for tackling the differing needs of different recipients. We see Real World Evidence as one methodological paradigm, among medical communities within the larger domain of Real World Data, which produces evidence that is suited to the needs of such recipients. To stress this point, we see Real World Data as a prerequisite of Real World Evidence.

At DLIMI, we have conducted numerous studies based on Real World Data from medical registries identifying prescribers' treatment patterns, patients switching between medications or identifying patients' social profiles. These studies, however, include *all* patients and prescribers and not just a sample. Depending on the method employed, Real World Data studies can identify unmet needs among patients and new avenues of drug development. It can also document health benefits in the broader patient population, taking drug testing beyond the clinical trial, and it can help to shape a stronger position among payers, key opinion leaders, and others, because it offers an improved documentation of effect.

Numerous data sources for Real World Data studies

If the potential of Real World Data is to be fully realised, a clear understanding of the data sources and medical databases on which it draws will be required. This will include an understanding of how to access relevant data through collaboration with public authorities regulating the use of Real World Data. At this time, more than 50 medical registries and databases in Denmark alone are viable for Real World Data studies.

It can be seen, then, that Real World Data may have a bearing on a number of disciplinary fields and business areas within an organisation, each of which comes to the table with its own question to be answered. This underlines one of the key benefits in building Real World Data capabilities across organisations: Real World Data studies involve, among other things, finding, accessing, compiling and analysing the 'correct' data. Broader utilisation of Real World Data across business areas helps to pave the way for a common vocabulary and understanding of 'correct' data across business area in the organisation.

Fig 2. Business areas and Real World Data sources

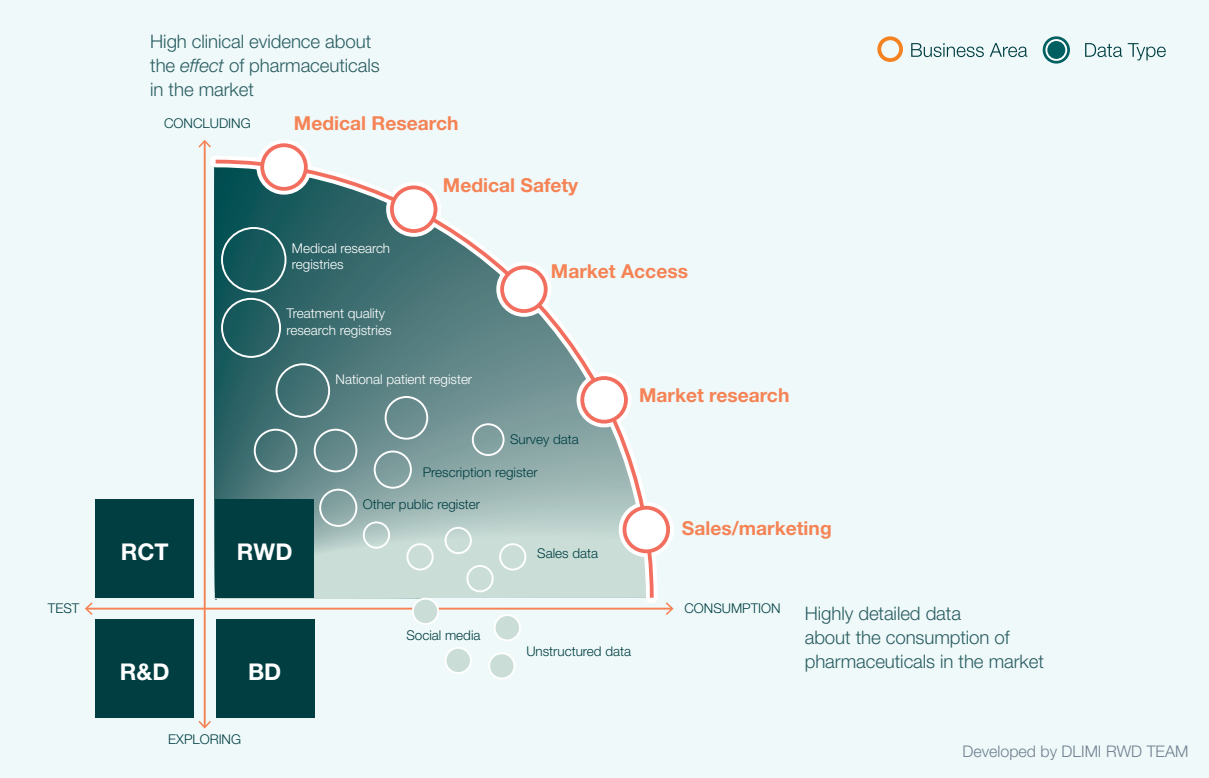

Figure 2 zooms in on the Real World Data domain and pinpoints how separate business areas in an organisation typically use a variety of data sources in accordance with their unique fields of interest and business purpose.

A shared approach to Real World Data in organisations

A lack of shared approach between different business areas, or between disciplinary understandings, are likely to limit the integration and use of Real World Data as a tool for evidence-based decision-making in your organisation. Internal alignment, by which we mean a shared approach to, and clarity about, purpose, is critical for the successful employment of Real World Data across an organisation. It enables the full benefits of Real World Data to be harvested.

Real World Data is a prerequisite of Real World Evidence, and affiliated to both RCT and Big Data, depending on the level of the evidence, data sources and field of interest.

Fig 3. Real World Data focus between business areas

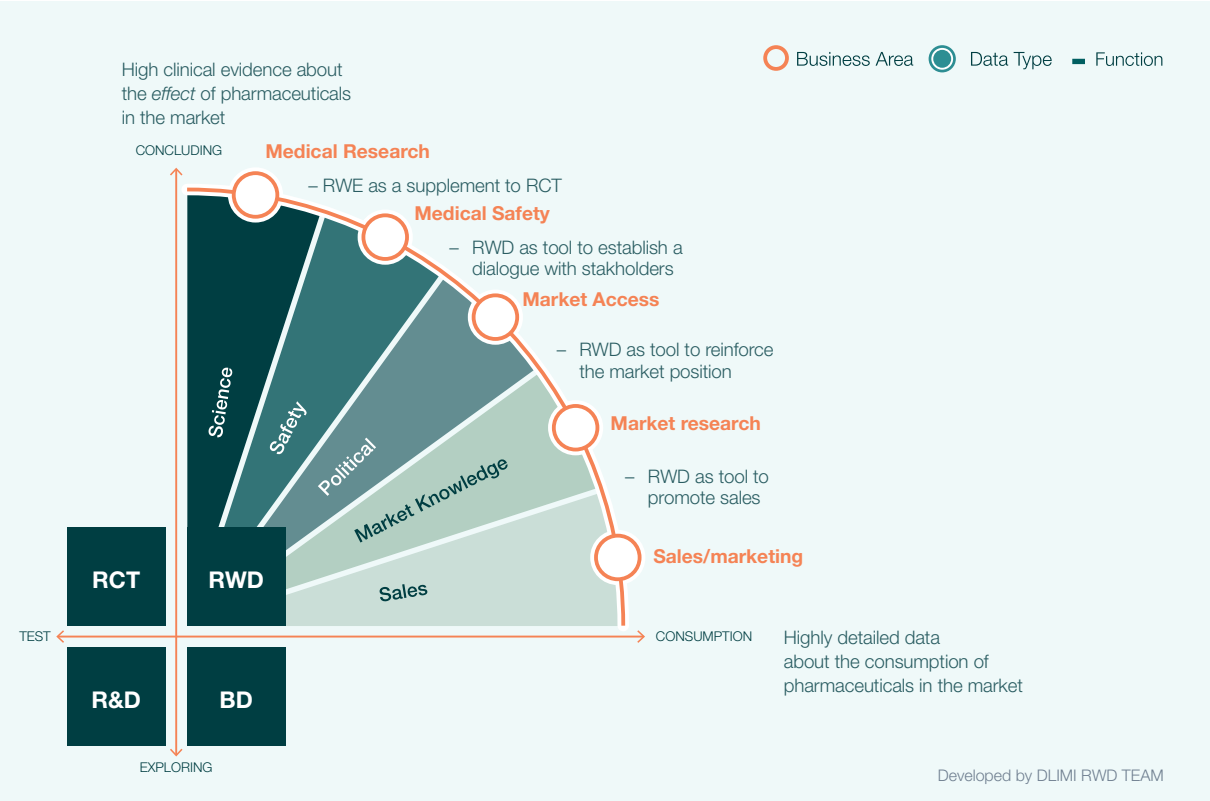

Figure 3 pictures the diverse agendas of different divisions in a typical pharmaceutical company. Real World Data studies are driven by various purposes, and as a result their function and focus vary from one business area to another.

Each business area tends to have its own focal point, legitimate disciplinary core and business processes. The point is, however, that broader utilisation of Real World Data across these separate areas will help to facilitate collaboration across areas and thus add value to the organisation as such.

Real World Data studies can be instrumental in engaging external stakeholders and a powerful tool for optimizing sales, marketing, and market access.

Maximising the benefits of Real World Data studies

Effective use of Real World Data in pharmaceutical organisations come about by acknowledging, discussing and clearly defining up front what the exact purpose of the Real World Data study is. Parties to this discussion need build a shared conception of what counts as 'correct' data for them, and of how the organisation stands to benefit. The real value of Real World Data studies is gained when used in a broad perspective and applied so that they also support sales, marketing, market research, market access, and so on. This may mean that an organisation's internal guidelines on matters such as market research, medical research, and pharmacovigilance need to be reviewed. Ideally, guidelines will allow Real World Data to cross between, and enrich, different business areas within the organisation.

As an illustration of the value of a broader approach, DLIMI have conducted Real World Data studies which were instrumental in engaging external stakeholders by providing relevant documentation on patient populations and treatment. In other words, Real World Data studies are capable of serving external as well as internal aims. They can be a powerful tool for optimising sales, marketing and market access efforts, and they can help to provide a platform on which fruitful dialogue with relevant stakeholders, based on strong data, is established.

> *I have benefited much from using Real World Data studies in my dialogue with decision makers. I find that Real World Data often helps in qualifying the dialogue and creates a common platform for further cooperation".*
>
> *Klavs Hundebøll, Senior Market Access Manager, Abbvie.*

Fig 4. Real World Data: Business areas, functions and stakeholders in relation to market activities

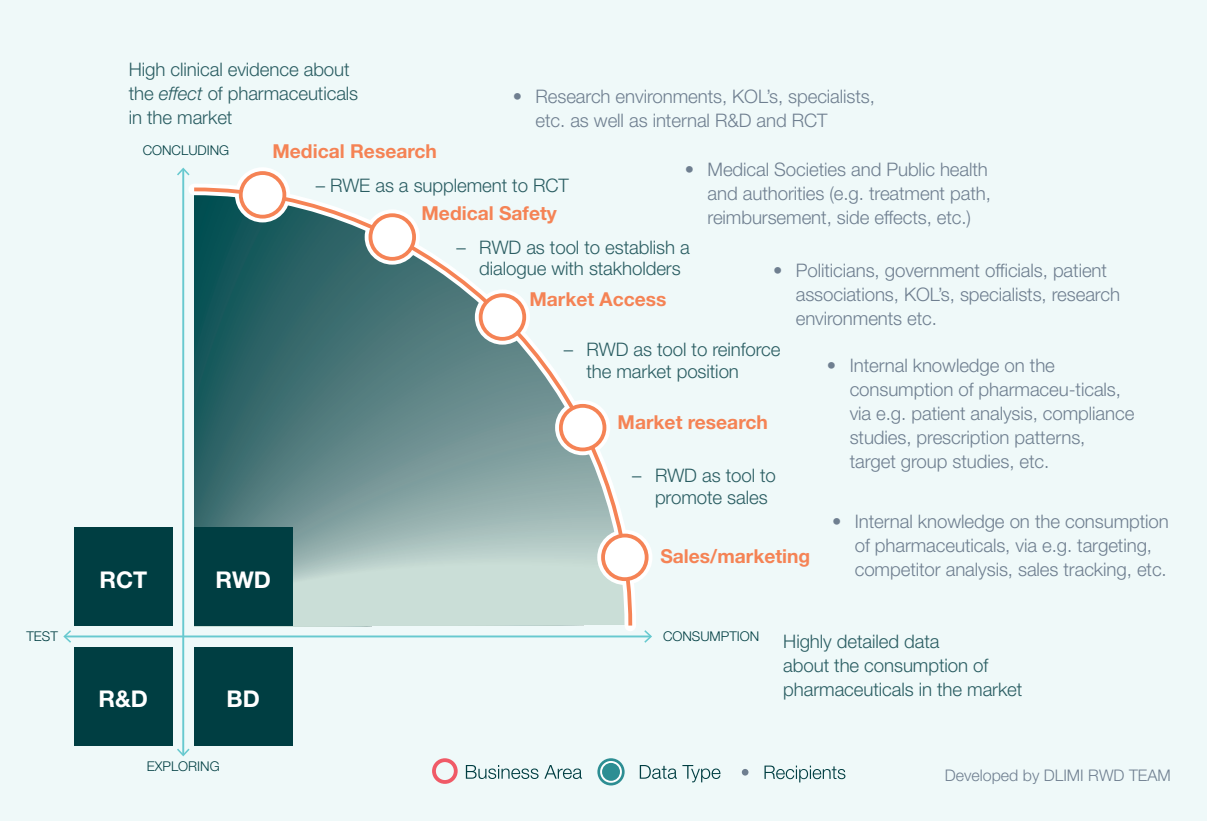

Figure 4 shows how functions and recipients vary across an organisation. This adds further complexity to the aim of internal alignment.

With the proper organisational approach, separate approaches and agendas can be translated into fruitful dialogue across the organisation. If this is to happen, the next generation of Real World Data studies will require more than the ability to design, manage and execute complex studies in dialogue with healthcare authorities and other Real World Data source owners. Organisations will also need to facilitate, align and focus separate internal business areas – each with their own mind-set, fields of interest and business purpose – in the initial phases of designing Real World Data studies.

The next generation of Real World Data studies will require the ability to design, manage and execute complex studies as well as facilitate, align and focus separate internal business areas.

Your use of Real World Data

To support your organisation and its business decisions with Real World Data studies you will need to plan, from the outset, for the integration of Real World Data in daily business activities across your organisation. Ideally, each of the relevant business areas should take part in the tailoring of the Real World Data project, so that insights, data sources, and even basic definitions of fundamental variables are aligned. In a smaller Real World Data study, this can easily be achieved with a few meetings. Larger Real World Data projects may involve more business units and internal stakeholders – none of which needs to take you outside basic project management skills.

This white paper has taken a close look at the different approaches to Real World Data and Real World Evidence. It has stressed the importance of broader use of Real World Data and its potential across the organisation, and identified the need for cross-organisational collaboration in the early stages of designing Real World Data studies. We hope that the paper will assist you in maximising your use of Real World Data across your organisation. We believe that this will be a prerequisite if internal as well as external stakeholders are to benefit fully from your Real World Data studies.

REFERENCES

1. Personal communication, 2016, Denmark

2. https://azhealthconnections.com/category/astrazeneca-news/real-world-evidence/

3. http://www.cdc.gov/flu/weekly/

4. http://www.ibm.com/smarterplanet/us/en/ibmwatson/discovery-advisor.html

5. https://www.research.ibm.com/haifa/dept/vst/mldm_rwe.shtml

6. E.g. Kore et. al. (2012) Computer-Aided Drug Design: An Innovative Tool for Modeling. Open Journal of Medicinal Chemistry, 2012, 2, 139-148 http://dx.doi.org/10.4236/ojmc.2012.24017 Published Online December 2012 (http://www.SciRP.org/journal/ojmc)

7. On the potential value of Real World Data. Perspektiv og debat, nr. 19, januar 2015, this author's translation. See e.g. http://discover.nci.nih.gov/index.jsp

8. http://www.roche.dk/content/dam/roche_denmark/da_DK/Docs/P&D%20No.%2019%20-%202015.%20Webudgave.pdf

ABOUT DLIMI

DLI Market Intelligence (DLIMI) is a leading provider of business intelligence and Real-World insight to pharmaceutical and health-related companies operating in the Nordic region. We offer pharmaceutical sales statistics on a variety of platforms as well as market research, market access support, real world studies, and consultancy services covering Denmark, Sweden, Norway and Finland.

Reference

Micheelsen, Arun (2016): Beyond Real World Evidence - How to improve utilisation of Real World Data throughout an organisation. DLIMI, Denmark

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Chief Market Researcher Arun Micheelsen is part of DLIMI's Real World Insight team. At DLIMI, Arun has conducted numerous RWD studies for the large pharmaceutical companies operating in the Nordic region. Arun holds a PhD in sociology and has extensive expertise in Real World Insight studies.