Clinical trials data and patient databases

Transparency, value and access

A new open access to clinical trials data, coupled with enhanced real world patient records bring the potential for new metrics of value, a better understanding of comparators and the opportunity for new modes of pricing.

In April 2014, the European Union voted overwhelmingly to accept new clinical trials regulations that pave the way for far greater transparency and access to data. Simultaneously, improvements in patient record keeping in most EU countries – moving towards and beyond the Scandinavian model - make real world assessments of product or therapeutic class performance a reality for the first time.

The pharmaceutical industry needs to step up to make the most of the opportunities that these advances bring or face increasing payer pressure and criticism.

Clinical trial transparency and new data availability – the opportunities:

The registration of all clinical trials has been common place in the industry for some time via clinicaltrials.gov. Access to trial design and a simple one-stop reference for ongoing and completed research has proved a useful tool for payers and the industry in understanding the competitive landscape and planning for effective clinical trial design.

The new regulations in Europe promise to go a step further – ensuring that summary results are quickly made public (within 1 year of the end of the trial) and requiring complete study reports to be made public. It should be noted that these measures are brought in line with the existing clinical trials directive. This means that “clinical trials” has a very broad meaning and will cover non-interventional studies and surveys to which the clinical trials directive applies.

Although only applicable to new trials this represents a treasure trove of information for payers and for the industry alike. As an example, a quick search of ongoing trials in melanoma (https://www.clinicaltrialsregister.eu/) – a disease in which several new agents promise to transform the lives of patients and in which payers have a keen interest in the future development of the market – shows that there are 331 trials including large scale registrational trials as well as smaller observational studies. Detailed information on trial objectives and design are already available via this valuable resource.

Coupling this resource with enhanced and more joined up patient records, for example the Danish electronic single patient record, allows the real world perspective on care, patient outcomes and therapeutic use to be applied to the evidence base with real and positive consequences for the payer, the pharmaceutical industry and the patient.

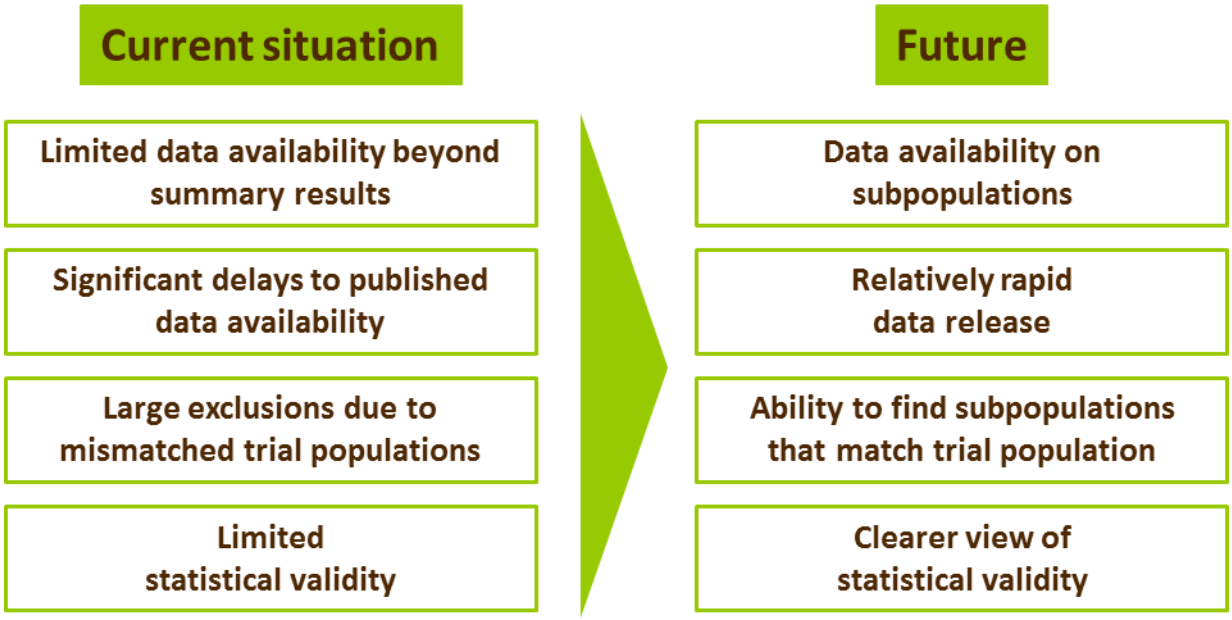
The future use of data: defining the standard of care

One of the vexed questions of both clinical trial design and health technology assessment is the definition of a standard of care with which comparisons should be drawn. Triangulating real world therapeutic use, which may lag behind the evidence base, with comparators used in recent clinical trials can bring a useful perspective beyond the current paradigm.

In particular, improved real world data can help refine the comparator technologies to be appropriate for the patient subpopulations of greatest interest – going beyond a "one size fits all" approach to a patient by patient comparison with the best standard of care.

The future use of data: indirect treatment comparison

One of the severe limitations faced by manufacturers in therapy areas with fast paced development is to be able to compare appropriately to the evolving standard of care. Various statistical techniques have been used to conduct indirect comparisons and mixed treatment comparisons. Although occasionally accepted, these approaches have been broadly criticised by payers as lacking certainty, validity and applicability. The major limitation to the development of indirect comparison has been access to the core data (such as that found in complete study reports) allowing more precise indirect comparisons of the kind conducted on occasion by the Cochrane Collaboration.



With access to complete study reports, the industry and those interested in health economics have new opportunities to drive better and more transparent comparisons using existing techniques as well as to develop new methodologies. Simultaneously, improvements in registry and patient level data, allow interested stakeholders to analyse the real world outcomes for different therapies – validating indirect comparisons and bringing the real world perspective to comparisons.

The future use of data: subpopulation identification and patient segmentation

One of the vexed questions facing many payers is how and when to use an array of different products to get the best from the choices available. Until now, pharmaceutical companies have been limited to summary information coupled with internal data to help answer these questions. Access to complete study reports for all newer therapies in a therapeutic area can bring a new analytical power to what has historically been an art – the identification of patient subgroups and segments.

Furthermore, greater access to enhanced real world data allows patient subgroups to be subjectively defined by applying clustering approaches or to be tested in a real world setting – either approach bringing greater validity of sub-groups in the real world.

With greater visibility of data and improved patient segmentation, payers and the pharmaceutical industry can review the landscape at a greater level of detail – understanding for each therapy where the greatest benefits are seen and how previous therapies and therapeutic modalities may affect the outcomes with a given therapy.

From an industry point of view this offers several new opportunities ranging from the more precise definition of stratification, sub-population definition for pre-planned analyses and inclusion/exclusion criteria during trial design to the post-trial patient segmentation to differentiate the value arguments and economic assessment of a new therapy.

The future use of data: defining the product value proposition

Current approaches to understanding value are largely internally (product) focused. With the wider availability of data for comparators as well as enhanced real world data, new approaches based on patient benefit rather than clinical trial endpoints offer themselves up.

The qualitative description of patient experience based on detailed analysis of clinical trials coupled with real world data will bring greater understanding of the role and value of products: going beyond clinical trial endpoints to look at composite outcomes, patient quality of life and impact on the wider healthcare system.

Clinical trial transparency and new data availability – the challenges:

The wider availability of data does, of course, carry some risks and challenges for both the industry and payers in addition to the benefits.

The future use of data: handling conflicting and unexplained data

Greater data availability, in particular from real world data settings, will undoubtedly bring into the open forms of data that, for unknown reasons are conflicting or apparently at odds with common understanding. Handling these conflicts and understanding how and when to ignore data in a rational way will be critical to the informed decision making of the future.

Several tools may be used to handle conflicting data – including meta-analyses, source validation and data dependence assessment – ensuring that these techniques are robustly applied will avoid accusations of "cherry picking" of data and allow informed debate and decision making.

The future use of data: misinterpretation and misunderstanding

With availability of complete study reports in the public domain there is a risk of misinterpretation or over-interpretation of the trial data. Investigators and sponsors will need to go further both in accurately representing the data and background within the study report but also in communicating more thoroughly so that various stakeholders – payers, patient advocacy groups, media – can access and understand the data.

The future use of data: new endpoints

Assessing real world data from patient records requires new endpoints that can be appropriately interpreted. Where disease progression (in the example of serious chronic disease) is not recorded in the patient record, time to second and subsequent therapy may prove viable real world metrics.

Of course, these approaches can be criticised as being imprecise in both definition of progression and in timings, but they can yield useful data if appropriately handled. Mirroring these endpoints in and beyond clinical trials (for example in extension trials) will help build a link between real world data and clinical trials.

Clinical trial transparency and new data availability – summary:

Greater clinical trial transparency brings new opportunities but requires a structured approach from the industry and from payers. In particular, the industry needs to grasp the new opportunities that this offers through high quality statistical and qualitative analysis of comparator data, patient subpopulations and product data.

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