MSD Health Forum 2023 ‚RWE - Fit-for-Purpose' workshop

Supply-related data and agile project management - what do they have to do with each other?

Cochrane postulates that ‚the best available evidence' (www.cochrane.org) must be the basis for medical decisions and that the quality of the study design is therefore crucial. From this it can be concluded that, in addition to randomised controlled trials (RCTs), healthcare-related data can also be used. Questions relating to particularly rare diseases, which increasingly include ever smaller subgroups of common diseases (individualised therapies, e.g. based on certain genetic characteristics), as well as increasingly important endpoints such as Patient-Reported Outcome Measures (PROMs) and Patient-Reported Experience Measures (PREMs) cannot be clarified in an RCT. Instead of a specific study design, the focus should be on the quality of studies. It is therefore by no means a question of weakening requirements, but rather of consistently increasing the quality of studies in which new data sources can also be included. The following text is a reflection on the workshop ‚RWE - Fit-for-purpose' at the MSD Health Forum 2023, on the one hand, and some thoughts on the undogmatic handling of data sources based on ideas from management theory, on the other.

>> Some basic ideas from general management theory could be interesting for the consideration of healthcare-related data in healthcare research.

To this end, it is necessary to consider why the topic of agile project management has become so important in general management theory.

Very simply, the basic idea of agile project management is that you should proceed step by step, constantly evaluate interim results and then define new goals. Complex issues cannot be predicted over a long period of time because far too many influencing factors become relevant and corresponding adjustments are necessary. The aim is not to reduce the overall costs, but to insert intermediate steps and make new decisions again and again - a sensible approach, especially for complex interventions.

The following diagram illustrates the relationship:

In this comparison, the logic of RCT is more like the classic waterfall approach: extensive preliminary work is done, then the study starts, changes are avoided and at some point the answer emerges. Other influencing factors are avoided as far as possible. Classic studies therefore often systematically exclude patient groups (e.g. those with various comorbidities, pregnant women, the very elderly, etc., to name just three). The importance of this approach should not be called into question - but one should ask oneself critically whether this approach is the best for all care issues.

Different questions lead to different study designs

The starting point for the best possible study design should always be the research question and the framework conditions. This means that the components of time, costs, quality and measurability must be considered together and simultaneously. The time component results from how quickly results should or must be available (e.g. for vaccines against rapidly mutating viruses). The cost component is determined by the available budget (e.g. often in the case of DiGA).

The discussion about traditional studies and RCTs versus healthcare-related data is largely dominated by the AMNOG and, more recently, the DiGA procedure. However, the AMNOG procedure is only one of many different fields of application in which decisions have to be made about suitable data sources. What may be the right study design for a new drug launch is by no means necessarily right for many other healthcare-related issues. Healthcare-related data offer new options when either very quick decisions have to be made (e.g. for vaccines, but also for rapidly developing digital offerings), the implementation or continuation of RCTs is not ethically required, e.g. due to a recognisable survival benefit, or very long-term relationships are to be observed in healthcare-related settings.

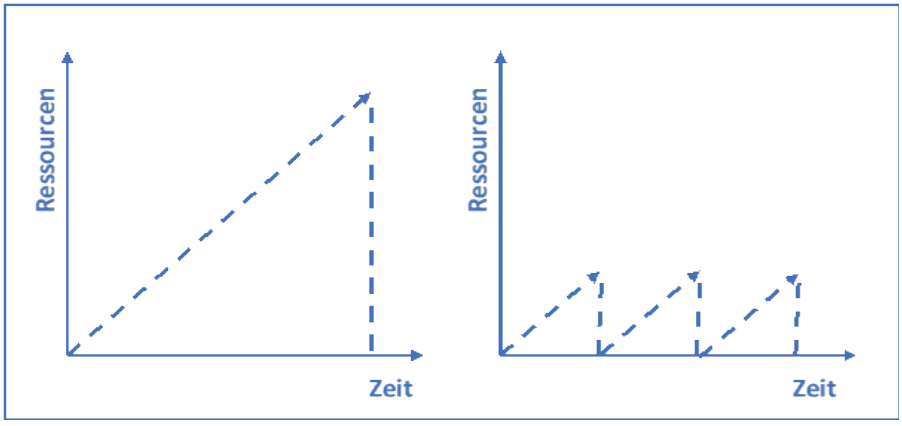


Fig. 1: Waterfall project management versus agile project management (own illustration).

Creating reliable framework conditions

It is therefore not a question of either/or, but of both/and and essentially of appropriateness. This pragmatic, agile approach requires two fundamental changes: Firstly, the dogmatic approach must give way in favour of greater openness and acceptance for different data sources and study types. And secondly, a clear and reliable framework must be defined for this. Reliability is particularly important, as the lead time can be considerable. In the current DiGA approval procedure, we repeatedly hear complaints that, on the one hand, no RCTs are required in the

guidelines, but that these are then de facto necessary in the procedure - while other study designs are only accepted with great difficulty. This creates the risk that the discussion of methods becomes an end in itself and that the full potential for demonstrating patient-relevant outcomes is not realised.

And this is where agile project management comes full circle. Healthcare-related data makes it possible, to a completely different extent, to set up ‚small sprints', generate interim results, use them as a basis for the next sprint and thus continuously generate new knowledge. For traditional project managers, it was also a huge leap to move away from traditional thought patterns and the familiar toolbox and be open to newer, more flexible approaches.

In his introduction to the topic, Prof. Dr Wolfgang Hoffmann (University Medicine Greifswald) emphasised that Germany should also look to other countries where the use of healthcare-related data is taken much more for granted - without compromising the quality of healthcare decisions. Accordingly, it was an important milestone that IQWiG explicitly emphasised in its Rapid Report A19-23 in 2020 that healthcare-related data can be used for benefit assessments.

According to Hoffmann, the current legislation also points in the right direction. The very name ‚Health Data Utilisation Act (GDNG)' is programmatic and points the way forward. In addition to the unquestionably important issue of data protection, it must also be about being able to use health data to improve patient care. Where data protection in the healthcare sector hinders or makes meaningful research impossible, harm can be caused to patients - the risks of data utilisation must therefore always be carefully weighed against the risks of non-utilisation. To this end, the methodology must also be further developed accordingly. The aim should be to utilise existing evidence as a basis for the further development of healthcare. Instead of ultimate certainties, a learning healthcare system will be more orientated towards iterative processes of evidence generation while strictly safeguarding patient safety. Ultimately, medical progress can only be achieved through the consistent utilisation of data. A regulation that both defines sensible data protection standards and guarantees access to data for research purposes is therefore crucial.

The examples presented at the workshop show the wide range of topics and approaches for generating healthcare-related data and using it to generate knowledge.

BARMER's scientific data warehouse

Utilisation of existing data for both internal management and external parties

Routine data from health insurance companies is among the most important healthcare-related data. The fact that routine data is used internally by the health insurance funds for analyses and forecasts has been common practice for years. What is new about the Science Data Warehouse is that a ‚treasure trove of data' is being processed here and made available for healthcare research. This is particularly remarkable because the data preparation required for this is complex and demanding. The BARMER Science Data Warehouse is thereforean excellent starting point for strengthening healthcare research and making routine data more available.

An important architectural decision was that the routine data should not leave BARMER. This restriction is intended to help ensure the highest possible standard of data protection.

But of course, routine data from health insurance companies can only represent one - albeit important - piece of the mosaic in the assessment of care situations, which usually has to be combined with other data sources. As Hoffmann formulated at the beginning of the workshop, it is also important to define reliable standards for this data linkage.

Healthcare-related data in oncology

The emergence of network structures and the use of digital health

Three of the presentations addressed different topics from the field of oncology. While Prof. Dr Monika Klinkhammer-Schalke (Arbeitsgemeinschaft Deutscher Tumorzentren e. V. and Head of the Centre for Quality Assurance and Health Services Research at the University of Regensburg) primarily highlighted the Germany-wide network structures of the cancer registries of the federal states with the oncological centres of excellence, Dr Oliver Schmalz and Privatdozent Dr Thomas Elter addressed specific implementations and projects.

Professor Klinkhammer-Schalke impressively demonstrated how the use of care-related data in particularcan generate added value for patients in terms of survival through the new networks and specialisations.The pooling of cancer registry data for the nationwide quality conference of the Association of German Tumour Centres together with the cancer registries of the federal states at the German Cancer Congress also clearly shows that, on the one hand, the potential is enormous, but on the other, that considerable resources are required and standards need to be defined. By demonstrating the possibilities of healthcare-related data for healthcare research and direct care, specific questions from guideline commissions and clinical treatment are increasingly being asked of this data and can be answered.

Prof. Dr Klinkhammer-Schalke particularly highlighted the ‚WiZen' innovation fund project, in which routine data from statutory health insurance and cancer registry data

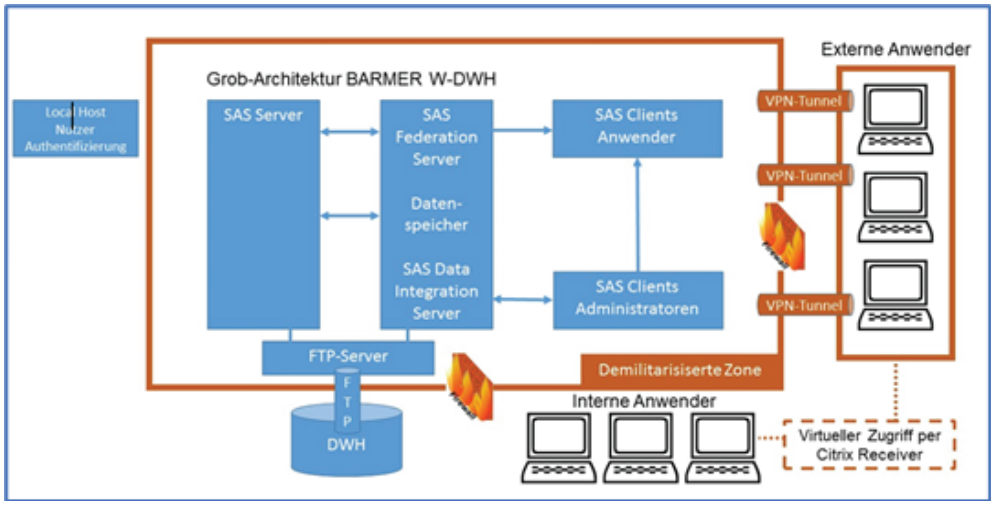


Fig. 2: Source: U. Marschall / BARMER; W-DWH is currently undergoing further development.

were used - and significant survival benefits for cancer patients through initial treatment in oncology centres certified by the German Cancer Society (DKG) were demonstrated. Accordingly, this project received a clear recommendation from the Innovation Committee for transfer to standard care.

The Onqo app by PD Dr Thomas Elter and the digital patient monitoring used by Dr Schmalz show that innovative and exciting digital health solutions and DiGAs are created when established clinicians develop digital solutions based on their clinical experience. The starting point is therefore not a possible business case, but rather the experience gained from many years of clinical work and the realisation that digital solutions can offer significant support for patients.

While Dr Oliver Schmalz from the Helios Clinic in Wuppertal is primarily concerned with side effect management, Elter, who comes from one of the most important German Comprehensive Cancer Centres (CCC), focuses on ensuring guideline-based care. This is to be achieved on the one hand through support in decision-making in tumour board conferences and on the other through a DiGA for lung cancer patients (‚onqo'), which is intended to enable users to independently recognise deviations from the optimal care pathway. An example is used here to illustrate that current DiGA requirements de facto prevent the full potential of digital companions: ‚onqo' is intended to direct patients ‚in the field' to certified centres and second opinions in the event of detected deviations from prescribed treatment standards.

However, the data collected in reality, which in this case could prove the increased referral to certified centres, may not be used to prove the benefits of the DiGA, according to Elter.

The required proof of effect through an RCT study design would also not be possible here, as proof of increased referral to centres cannot be provided by a study, which for many reasons can only be carried out in centres.

Since 75% of all lung cancer patients in Germany are still not treated in DKG-certified centres, the relevance of this problem becomes clear. Worldwide, the demand for the recognition of innovative statistical methods that enable evidence generation through digitally collected real-world data is growing louder (see EORTC position).

It won't get any easier, but patient benefit can be increased

Anyone hoping that healthcare-related data will provide an easy way to completely avoid time-consuming and costly RCTs will be disappointed. It is not about simpler, faster and cheaper, but about generating ‚the best possible evidence' for the respective question to be answered. The presentation by patient representative Nadja Will in particular made it very clear that it is not just about conducting the best possible studies, but above all about ensuring that new knowledge is shared quickly. And this issue is completely detached from the data sources, but is solely determined by the communication of the results.

Today, healthcare-related data has expanded the range of data sources and, above all, offers the potential to merge data sources and successively gain new insights in the sense of incremental innovations. This provides a great opportunity for new and important partnerships to emerge between health insurance companies, science and healthcare providers.

The basic ideas of agile project management come from software development and are primarily characterised by the fact that progress towards a major goal is achieved through many small steps. Of course, this cannot be transferred 1:1 to the healthcare sector, but it is worth thinking about how we should rethink and further develop our evidence generation - not with the aim of making everything easier, but better. And there is a lot to do!

The coronavirus pandemic has clearly shown that we have a massive deficit in available data (e.g. number of available beds in intensive care units, regional breakdown of vaccination incidence) and need to bring together all existing data sources in order to be able to react as quickly and effectively as possible. Political decisions must be based on valid data from suitable sources - and clear regulations must be created to ensure that the largely blind flight that Germany had to make during the coronavirus pandemic is not repeated.

We should be guided by the idea that data is only ever a means to an end - and that the aim is to provide patients with the best possible evidence-based care. <<

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