

'Stronger focus on the m of conducting studies'

Following Prof Peter Sawicki (2004 to 2009) and Prof Jürgen Windeler (2010 to March 2023), Dr Thomas Kaiser has been the third Director of the Institute for Quality and Efficiency in Health Care (IQWiG) since April 2023. In the cover interview with 'Monitor Versorgungsforschung' , Kaiser, one of the founding members of the 'special-purpose organisation of the non-profit Foundation for Quality and Efficiency in Healthcare', sets out his goals for the coming years. The convinced EbM expert wants to strengthen international links and participation in EU projects and - as he says - dedicate himself to 'more scientific investment beyond the processing of our commissions'.

Im Interview: Dr. med. Thomas Kaiser, Director of IQWiG

>> The early years of IQWiG, I remember well, were characterised by Prof. Dr. Peter Sawicki, a diabetologist and previously co-editor of the pharmacocritical Drug Telegram: the term 'eminence-based' made the rounds. This was followed in September 2010 by Prof Dr Jürgen Windeler, previously head of the Evidence-Based Medicine Department of the Medical Service of the National Association of Statutory Health Insurance Funds, and with him the discussion about efficacy and effectiveness as well as the quality and benefits of registry data. What's next for you, Dr Kaiser, who has headed IQWiG since 1 April 2023, almost exactly two years ago?

I think it would be great if one day I could represent IQWiG as an 'international institution' on the one hand and as a constructive supporter of better studies on the other. The first comes about almost automatically because IQWiG has to become an international institution simply because the EU has set the appropriate framework conditions for this. Since January of this year, we have had the early benefit assessment of medicinal products at European level, or EU HTA for short, which alone will lead to greater internationalisation of the institution. Medical devices will follow.

Their authorisations are granted at European level. The BfArM is active for Germany in this context.

Correct, but only for the authorisation. At European level, a comparative benefit assessment will be introduced for medicinal products and individual medical devices - similar to the AMNOG. IQWiG will be responsible for the majority of this for Germany, and the Federal Joint Committee for a small part. To this end, co-operations with other European HTA institutions will be concluded, European committees will be appointed and, of course, everything will be conducted in English. IQWiG's tasks in the field of medicinal products will primarily be carried out by Beate Wieseler and her team, who chair the methods group at European level. We will also use this opportunity to prepare and publish international publications if they serve IQWiG's objectives.

ethods

Do you want to produce more of your own publications?

Exactly. During my term of office, I would like to further advance the Institute as a whole. One of these will be stronger international links and participation in EU projects, which has only been sporadic so far; the other will be a move towards more scientific investment beyond the processing of our commissions. Of course, our main focus will continue to be on processing the commissions we have been awarded - in particular the benefit assessments - but we will also create opportunities and scope for scientific work. Incidentally, this is not l'art pour l'art, but essential if we want to do not just good, but excellent work on the commissions that we face as a European institution. To achieve this, it is also important to continue to develop scientifically.

„Studies must be feasible. This is especially true in the area of very rare diseases, where the evidence base is relatively often not good enough.“

In which area, for example?

For example, we not only want to further develop the AMNOG procedure - as has already been done - but also work together with the evidence-based medicine community to place a stronger focus on the methods used to conduct studies. The further development of methods has so far mainly focussed on how studies can be assessed and how systematic reviews can be conducted. Now, however, we have begun to look beyond the purely procedural issues and are also focussing more on how study conduct methods can be further developed and improved. Our aim is not only to conduct more good and meaningful studies more efficiently and safely, but above all to conduct feasible studies. This is a crucial point that must never be ignored: studies must be feasible. This is especially true in the area of very rare diseases, where the evidence base is relatively often not good enough. This is certainly partly due to logistical difficulties, but is also due to the fact that either existing study designs and options for statistical data collection and analyses are not used or have not yet been conclusively researched and developed.

In an interview with 'Ersatzkasse Magazin' (1), you stated that you would like IQWiG to become involved at an even earlier stage in the future and to contribute its expertise to a greater extent when studies are being set up, i.e. when the necessary evidence is being generated. How will this be done beyond the advisory services already offered?

In principle, we have already had various points of contact for some time, for example through data collection accompanying the application. Here we are involved in the consultations of the Federal Joint Committee, drawing up very specific study concepts and reviews of study protocols and statistical analysis plans on its behalf. We also have experience in outlining and discussing trial studies in the area of method evaluation.

However, it is not (yet) the Institute's mandate to conduct studies itself.

Nor do we assume that we will receive such a mandate, nor is this IQWiG's aim. However, our aim is to contribute our expertise in evidence generation to an even greater extent in the regulatory context of the G-BA. Ultimately, everyone benefits from this: patients, doctors and those responsible for studies.

Where exactly do you want to make greater use of your expertise?

These are questions such as: How can we conduct better studies?

What are good recruitment strategies? What options are there for working with certain endpoints? How can missing values be avoided or dealt with? How can patient-reported outcomes be included on a regular basis? These are all important topics where we want to be scientifically active on a general level and thus provide assistance. This also benefits us and the G-BA: the better the studies and their results are, the easier and more valuable our work will be in future.

We are well aware that there are many groups that already have very good experience of conducting studies.

That's true. But we have a different perspective when we analyse studies. We have a great deal of expertise and experience to be able to say quite precisely why the results presented to us are not as good as they could be if perhaps just a few small details had been done differently in advance. You can learn very well ex post what you could have done better at the beginning. And we should make use of this, instead of always complaining that a study didn't go well.

The pharmaceutical industry will certainly be grateful. I know of no manager in the pharmaceutical industry who wants to waste money and set up studies whose results are not or only partially recognised afterwards, for example because the endpoints were not chosen correctly. But wouldn't that rather be the task of clinical research or health services research?

Certainly, although the latter may not yet be so aware of the problems we face. However, this may also be a question of the general research culture, which always - and this is perfectly understandable - wants to research new things instead of bringing about a cycle of improvement through accompanying research. This is precisely what drives us.

IQWiG is currently involved in the EU project RealiseD (2) with the aim of developing clinical studies for good evidence on very rare diseases in order to arrive at effective therapies more quickly.

The EU RealiseD project is explicitly aimed at researching how to conduct better comparative studies on very rare diseases.

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From which we can certainly also learn for other indications.

Certainly. Derivations will be possible, although we are primarily concerned with very rare diseases. This is specifically about questions of data collection and specific statistical methods that can be used to create new findings without losing too much certainty.

Where do you see your role here as an HTA institution?

We no longer just want to evaluate after the fact, but to help answer the question of whether a new drug for a very rare disease offers an advantage over existing treatment options from the outset. This requires suitable instruments, some of which still need to be developed in order to be able to answer the questions that arise in the course of the final benefit assessment with the best possible studies rather than just any studies. I therefore think it is great that we have succeeded in becoming part of this important project, in which many scientific organisations and the pharmaceutical industry are participating alongside a number of European regulatory authorities.

IQWiG in a project together with pharmaceutical companies would probably not have existed in this form under Sawicki and Windeler.

I don't want to judge whether this would not have been possible under the leadership of my two predecessors. It was a very different situation back then than it is today.

You were there when the institute was founded.

Exactly. Let's briefly go back to 2004, when the Institute for Quality and Efficiency in Healthcare was founded as part of the implementation of the SHI Modernisation Act in order to improve the quality and efficiency of patient care in Germany. Until then, the pharmaceutical industry, for example, could charge high prices for new drugs without having to prove that they were better than the previous standard of care. When this changed with the IQWiG, it came as a shock to some. Also because some perhaps assumed that we were working against the pharmaceutical industry. But this is not true, because in my opinion the aim was - and still is - always to make the best possible decisions for the benefit of patients based on the best possible data.

As always, this is a question of communication according to the old German proverb: 'As you shout into the forest, so it echoes back. There were certainly some wrong moves on both sides at the time.

I don't want to rule that out either. There are only human beings working on both sides. HTA organisations and the pharmaceutical industry play different roles on the same playing field, and this cannot and should not be ignored. But we are not opponents. The pharmaceutical industry plays an important role in drug development and without the drugs researched in this way, people would be much worse off than they are today. We are well aware that it is not only the pharmaceutical industry that is responsible for drug research. There are many good examples of how the development of medicines has improved people's lives and how studies have been carried out for their authorisation that have delivered really good and meaningful results. On the other hand, there are also examples of studies that have not provided sufficient answers to the questions of patient care. And this is another reason why we have quite a few medicines in the healthcare system whose significance for healthcare we can hardly categorise due to a lack of data. Our task is to point out this gap. Now, however, we also want to help consider how studies and thus the evidence base can be improved. This is the path into the future that I would like to take with the Institute. I realise that this will not be an easy path. After all, it is always easier to criticise than to improve.

Doesn't this also include a broader understanding of endpoints?

If there is good evidence that other endpoints indicate what

you actually want to see in order to clearly describe the benefit, then these are suitable endpoints. It goes without saying that these must be validated. As IQWiG, we are therefore very interested in creating the best possible data and research infrastructures in order to be able to answer precisely such questions. This is not just about making individual studies better, but also, for example, about defining and validating good intermediate endpoints that can be used in the future to be able to say even earlier whether a drug or therapy is beneficial or not.

You just mentioned a research infrastructure: doesn't that also mean closer integration of the institute with university institutions?

If it helps to improve the current situation, then definitely. First and foremost, we will work on ensuring better mutual understanding in general. This also includes better understanding what each other does and what limitations there are in the actions of institutes like us and on the part of the universities. I also see this as a task for me personally: to establish as many contacts as possible with important institutions, universities and their chairs.

In what specific ways has healthcare improved in these more than 20 years at IQWiG? Or should the whole thing be seen more as a step-by-step innovation?

If I had to give an evidence-based answer, I would find it very difficult because it would require a controlled comparison. You would have to define a kind of zero point in order to be able to determine what has happened in the past two decades with and without IQWiG in terms of evidence-based evidence. Of course, it can be said that there has been very significant progress during this time, for example in the treatment of cancer. However, this is not our achievement, but that of drug research. Our merit is certainly that we are helping to ensure that these active substances are used precisely where there is actually particular progress - and are not used, or at least used more cautiously, where this is not the case. In addition, the Institute has been responsible for the development and provision of generally understandable information from the outset. This enables all those directly involved in treatment to make evidence-based decisions about healthcare services.



Dr. med. Thomas Kaiser

has been Director of IQWiG since 1 April 2023. 1990 degree in systems development; 1999 degree in human medicine; 2002 co-founder of DIeM - Institute for Evidence-Based Medicine, Cologne; 2002 to 2004 appointed expert in working groups for disease management programmes in the Coordination Committee and the Federal Joint Committee; 2005 doctorate in medicine; 2008 winner of the Bill Bill Bill Award. med.; 2008 winner of the Bill Silverman Prize of the Cochrane Collaboration (together with three other IQWiG employees); 2011 winner of the David Sackett Prize of the German Network for Evidence-Based Medicine 2011 (awarded to IQWiG's Drug Evaluation Department). From the foundation of the Institute for Quality and Efficiency in Health Care (IQWiG) in 2004 until 2023, Head of the Drug Evaluation Department.

Keyword transparency: IQWiG has the legal mandate to provide health information for patients. Where do you stand on this? And are you succeeding in reaching people?

On our website www.gesundheitsinformation.de, we provide information on the diagnosis and treatment of the 300 most common diseases in Germany.

Do patients use this service?

Of course they do. IQWiG's subsidiary website www.gesundheitsinformation.de had 3.7 million visitors in January 2025 who were looking for information on topics such as shared decision making, but also on various diseases and active substances.

What about those population groups that are less likely to request health information?

Unfortunately, the website only reaches the group that actively searches for health information on the Internet. We need to do much better in the future in order to reach those target groups that are more frequently affected by health problems but belong to population groups that are generally labelled as educationally disadvantaged. We have already carried out projects to find out how such groups can better access health information that is important to them and are currently taking the next step by working with intermediaries - organisations, clubs, associations, etc. - to do this. However, we are also in the process of developing health information specifically for people who find it somewhat more difficult to access written information. This could be videos, short podcasts or direct discussions with peer groups, for example, for which we then provide evidence-based information in various languages.

So far, this information is only available in German and English.

This will, and must, change. The use of artificial intelligence will certainly also be a great support for us, although a cultural context must always be taken into account, which requires people who are familiar with different cultures.

You studied systems development (1990) and are also a medical doctor (1999) with a doctorate (2005). You co-founded the Institute for Evidence-Based Medicine in 2002, won the Bill Silverman Prize of the Cochrane

Collaboration in 2008 and the David Sackett Prize of the German Network for Evidence-Based Medicine in 2011. Which of the skills and experience you have acquired are most useful in your day-to-day work?

All of them, actually. When we talk about research and data infrastructures, for example, it helps to have an understanding of data sets and structures. I also have a strong affinity for AI thanks to my profession as a system developer. Incidentally, I also do this privately: at home, where I make art with AI and set up the necessary servers myself. Shortly after I took up my post, we set up an internal AI working group at the institute. Its basic aim is to familiarise all employees with the topic of AI in general and to work out which AI applications can generally help us in our day-to-day work - such as translations, improving and automating work processes with AI or literature screening, selecting studies and extracting data, etc. But the topics also include AI in research. However, AI is also used in the diagnosis of X-ray images, in assessments based on medical histories or in triages.

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The areas of application for AI are extremely diverse.

So countless and diverse that we have even set up an AI playground. Here we give our employees the opportunity to learn and see what AI can and cannot do. AI will definitely change the way we work and evaluate. That is foreseeable.

To what extent?

We will see. But we need to stay on the ball in order to recognise as quickly as possible when it is best to use which of the ever faster developing AI innovations to become even better and more efficient.

In response to another question from 'Ersatzkasse Magazin' as to whether you see any developments in the studies that are presented to you, you replied: 'In some cases, we can definitely observe positive developments, for example in the endpoints reported by the patients themselves. Quality of life and symptoms are now investigated more frequently than was the case at the beginning of the AMNOG.' What is the general situation regarding the inclusion of PROMs and PREMs in the AMNOG?

PREM, i.e. whether someone was more or less satisfied with something, has not proved to be a viable approach in the SGB-V context. It is different with symptoms reported by patients, because the aim is always to establish how people are really feeling.

These are then questions such as: What symptoms and side effects do they have? How are these individually assessed and weighted?

Precisely. If, for example, you neglect the impact of diarrhoea as a side effect of drug therapy on quality of life, you ignore an important consequence for patients. However, this side effect must be weighted in comparison to the desired change, for example whether a large tumour has become slightly smaller. The decisive factor is not just whether the tumour has become smaller, but how the patient is doing. If I don't collect PROMs, I always have a blind spot when it comes to the patient's experience.

Are PROMs collected in a sufficiently consistent and structured way?

PROMs traditionally play a subordinate role in the context of drug authorisation and assessment, as they do not have to be collected for authorisation. There are of course exceptions, such as in pain therapy, where the reduction of pain, recorded as a PROM, is the primary target criterion. Nevertheless, we are seeing a trend among some pharmaceutical companies to increasingly collect PROMs. However, this is not because they need the data collected in this way for marketing authorisation purposes, but because it is relevant to care issues.

What about quality of life? One could assume that the inclusion of the quality of life dimension will increase as the EU HTA begins, as other countries are already much further ahead than we are.

In fact, some countries are not much further ahead than we are in this respect because we are quite a pioneer. This has been an important issue since IQWiG was founded, and we continue to attach great importance to patient-reported outcomes.

Finally, let's look at an AMNOG detail: the benefit assessment of the active substance pembrolizumab (3): How is it that IQWiG sees a lower benefit in an assessment, while the ESMO (4), a European specialist organisation, sees the highest possible assessment? One might assume: Evidence is evidence. Or does it depend on how you look at it?

It is quite obvious where the difference lies. In the ESMO assessment, only the observed benefit in terms of recurrence plays a role. IQWiG also described the advantage of the active substance for recurrences, but weighted it differently from the ESMO. This is because the recurrences achieved are offset by a high proportion of severe and very severe side effects. In addition, the study presented showed that there was no improvement in quality of life, although recurrences were reduced.

So the fact that severe side effects are caused did not play a role in the ESMO assessment?

Exactly. This is exactly what we consider to be inadequate, to put it mildly. That explains the difference between the two assessments. In this respect, you are right on the one hand: evidence is evidence. On the other hand, it makes sense to not only look at 30 per cent of the evidence, but to always consider 100 per cent of the evidence, if it is available. Unfortunately, a consideration of the advantages and disadvantages is not visible in the ESMO assessment, although life-threatening side effects or even side effects associated with hospitalisation occurred in some cases.

We will ask the ESMO why this is the case. Finally: If you had a wish now and there was a new federal minister sometime in March or

April: What would you wish for IQWiG?

That he or she would do as much as possible to promote research in Germany. This includes recognising the general value of research, supporting existing research infrastructures and establishing new ones, but also asking important research questions themselves.

For example?

Let's take the discussion about the treatment of people with long Covid. So far, there are no authorised drugs for the treatment of the various symptoms, only off-label therapies. Of course, it is possible to enable off-label use just like that. However, it would make more sense to combine this with evidence generation with reliable results, as the NHS has done in the UK, in order to learn for future patients and continue to improve treatment options.

When did the British do this?

At the beginning of the coronavirus pandemic. Even back then, the UK decided to pragmatically launch a randomised care-related and interventional study in hospitals - a first-class example of health-care research, by the way. I would like to see something like this, or at least something similar, from the future health minister: Not to want to know everything possible with the help of research approaches that are not so broadly based, but to focus on a very central research question that is central to the respective field of application, but then to investigate this with certainty of results and not just with a kind of 'accompanying evaluation'.

Does this work with the different research culture that we have here in Germany as opposed to Anglo-Saxon countries?

The research culture is of course a crucial point. That's why I'm talking about setting up a research infrastructure, not a data infrastructure, for which you also need a modern research culture in order to be able to conduct research not only quickly but also pragmatically when in doubt.

What do you mean by quickly?

Well, it only took the British nine days from the initial idea of conducting such a study to the recruitment and enrolment of the first patient. But you can only do that if you are focussed and if you can make use of an existing and proven research infrastructure.

A truly lofty goal.

We still have a lot to do, don't we? I didn't come here as head of the institute to sit back and relax. I'm here to make the world a little bit better. No more and no less.

With a sense of mission.

And with a sense of mission: above all, I want to make good use of my life and working hours.

Dr Kaiser, thank you for talking to us. <<

The interview was conducted by MVF editor-in-chief Peter Stegmaier.

Literature/Links:

1: https://www.vdek.com/magazin/ausgaben/2023-05/thomas-kaiser-interview-iqwig.html
2: https://www.iqwig.de/presse/pressemitteilungen/pressemitteilungen-detailseite_138372.html
3: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1026/
4: https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-for-solid-tumours/esmo-mcbs-scorecards/scorecard-373-1

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