IQWiG in Dialog 2023

„How do you assess the quality of health economic evaluations?“

Abstracts

Health economic evaluations in IQWiG's methods paper 7.0 – What is different?

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IQWiG revised the requirements for conducting a health economic evaluation (HEE) in the methods paper. The focus was on an HEE in the context of the procedure based on the Act of the Reorganization of the Pharmaceutical Market (AMNOG) according to § 35b Social Code Book (SGB) V. The Federal Joint Committee (G-BA) can commission IQWiG to carry out an HEE and at the same time request the pharmaceutical company to submit a dossier for the HEE. One basis for this is decision-analytic modelling, which makes it possible to consider a longer time horizon than in the benefit assessment. The development of the models often requires information that is not covered by the content of the upstream benefit assessment and that must be obtained from other data sources (e.g. information on different types of costs or epidemiological studies). The aim of the HEE is to provide an information synthesis as a complement to the benefit assessment, in particular for price negotiations.

The initial focus of the revision was on the methods for creating a de-novo model. These methodological specifications form the basis for the submission of a dossier by the pharmaceutical company. The presentation will focus on the main changes to methods paper 7.0 and the individual elements of a HEE in the context of the AMNOG procedure.

How does the STIKO consider predictions of the health economic effects of vaccinations in Germany?

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In Germany, the Standing Committee on Vaccination (STIKO) makes recommendations on the implementation of vaccinations under the Infection Protection Act. The main tasks of the STIKO include the development of a vaccination calendar for infants, children and adults. It also determines which vaccinations should be given to the entire population or to specific groups (risk groups), at what time and at what intervals. On the basis of the STIKO's recommendations, the Federal Joint Committee (G-BA) decides whether a vaccination should be included in the vaccination directive and thus become a compulsory service of the statutory health insurance (SHI) funds. The G-BA thus decides whether the costs of this preventive measure should be borne by the SHI funds.

According to its rules of procedure, the STIKO determines its methodological approach based on the current state of scientific knowledge. When developing vaccination recommendations, it follows the systematic methodology of evidence-based medicine. Since 2011, the methodological procedure has been laid down in a Standard Operating Procedure (SOP), which is updated as required. When developing vaccination recommendations, the STIKO primarily carries out an epidemiological-medical risk-benefit assessment. In addition to the individual benefit for the vaccinated person, the benefit of vaccination for the entire population, which is achieved through direct and indirect effects, must also be taken into account. In most European countries, the consideration of health economic aspects in decisions on vaccination programmes is standard practice, whereby the health economic evaluation of vaccines poses particular challenges (herd effects, long observation periods, partial decline of vaccine protection, etc.).

As part of a project funded by the German Federal Ministry of Health, a national symposium „Consideration of health economic evidence in the introduction of new vaccines in Germany“ was held in 2015, building on the results of an international expert workshop. Based on the discussions and literature searches, the „Methods for the implementation and consideration of modelling for the prediction of epidemiological and health economic effects of vaccinations for the STIKO“ were developed, adopted by the STIKO in 2016, included in the SOP, and published. According to these methods, the STIKO can use epidemiological modelling and health economic evaluations as additional evidence when developing vaccination recommendations. However, the results of health economic modelling should not be used to recommend or reject vaccinations on the basis of defined quality-adjusted life year (QALY) thresholds, but rather to compare alternative vaccination or prevention strategies.

On the basis of medical-epidemiological analyses, the STIKO can carry out mathematical modelling and health economic evaluations to develop not only effective, but also efficient vaccination strategies and to examine their effects on the epidemiology of the disease as well as on the costs to the health care system or society. Uncertainty analyses on various aspects of a vaccination strategy are also performed. Incremental cost-effectiveness ratios (ICERs) provide information on the most efficient vaccination strategy, but the STIKO‘s decision is primarily influenced by other factors, including the number needed to vaccinate (NNV). Concrete examples are used to discuss, from the user perspective, how the STIKO has taken predictions of the health economic effects of vaccination into account in its decisions since 2016.

Health economic evaluations in the AMNOG procedure: necessary or risky?

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For over 10 years, there has not been a single application for a health economic evaluation (HEE) according to § 35b Social Code Book (SGB) V in reimbursement procedures based on the Act on the Reorganization of the Pharmaceutical Market (AMNOG), even though health economic aspects such as the monetization of added benefit, budget impact and potential savings play an important role in negotiations. There is a need for the systematic implementation of HEEs at an early stage as a complementary component of pricing. This would support rational, evidence-based pricing. The presentation will outline the challenges and opportunities of early HEEs in the AMNOG procedure.

Assessment of the quality of health economic models from industry's perspective

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In a number of countries, reimbursement decisions for innovative medicines are made on the basis of health economic evaluations. For this purpose, decision-analytic models are created that summarize existing knowledge and provide information on the cost-effectiveness of the drug in question. There are many guidelines and recommendations on how to build such decision-analytic models. However, there is some leeway in the construction of decision-analytic models. Benchmarks for assessing the quality of health economic models influence how this leeway is used. The aim of this presentation is to describe the assessment of the quality of health economic models from an industry perspective.

Health economic models are used for decision making and summarize existing knowledge in a single mathematical model. There are always gaps in knowledge that need to be filled with plausible assumptions. In particular, there are ethical and practical constraints on the design of clinical trials that prevent the generation of evidence of the highest level. In contrast to clinical trials, which aim to find out whether a drug is effective (qualitative decision-making), health economic evaluations aim to estimate the consequences of treatment as accurately as possible. To avoid systematic underestimation of the value of innovative products, surrogate parameters, mathematical assumptions and expert opinions play an important role.

Overall, a pinpoint estimate of the value of innovative products is hardly possible with structurally conservative methods. It is important that economic models include relevant and known evidence. It is also important that economic models make clinically plausible assumptions. This is because structurally conservative assumptions systematically underestimate the value of the innovative product.

Conclusion: In order to ensure access to innovations for all patients, health economic models should not systematically underestimate the value of innovative products. This must be taken into account when assessing the quality of health economic models.

GRADE approach to the certainty of conclusions of modelled evidence

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The aim of the presentation is to introduce the conceptual approach of GRADE for assessing the trustworthiness of information gained from modelling studies (GRADE Guideline 30, Brozek et al., Journal of Clinical Epidemiology 2021). It explains how the approach was developed and how it can be applied. GRADE Guideline 30 is the result of a detailed literature search and international multidisciplinary expert consultations and describes how to assess the certainty of evidence from models in the context of systematic reviews, health technology assessments and health care decisions.

In principle, the domains that determine the certainty of evidence from models are the same as those already considered in the GRADE approach (risk of bias, indirectness, inconsistency, imprecision, publication bias, effect size, dose-response relationship and direction of residual confounding). The assessment depends on the nature of the model inputs and the model itself, and whether evidence from a single model or from multiple models is being assessed. GRADE suggests the following considerations for selecting the best available evidence from models

1. De novo development of a model specific to the situation of interest.
2. Identification of an existing model whose results provide the highest level of certainty for the situation of interest, either „off the shelf“ or after adaptation.
3. Use of information from several models.

GRADE has also provided a summary of relevant interdisciplinary terminology to facilitate communication between disciplines.

In summary, the GRADE conceptual approach provides a framework for using evidence from models in health care decision-making and for assessing the certainty of evidence by means of one or more models.

Decision-analytic modelling from a modeller's perspective

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Health technology assessment (HTA) is the assessment of existing or new health technologies from various perspectives. In this context, the „key principles" of HTA must be taken into account. The areas to be assessed („domains") include benefits, harms, costs, and ethical, social, patient-related and legal aspects. Evidence on these domains comes from randomized controlled clinical trials, observational studies, cost catalogues, descriptive databases, and other sources. These evidence components should be brought together in a systematic and transparent way over a time horizon long enough to cover the relevant events and health states. Decision-analytic models are typically used for this purpose.

In Germany, decision-analytic models are used for health economic evaluations in the context of reimbursement procedures based on the Act on the Reorganization of the Pharmaceutical Market (AMNOG). In the assessment of cost-effectiveness, 4 domains in particular play a role as model or outcome parameters: The trade-off between benefits and harms can either be represented by incremental harm-benefit ratios or, for health economic evaluations, integrated with the help of utility values (e.g. quality-adjusted life years, QALYs). The trade-off between incremental benefits and costs (efficiency) is made using incremental cost-effectiveness ratios. Recent modelling also highlights the quantitative and explicit trade-off between efficiency and (in)equality (net benefit distribution).

The presentation will briefly describe the individual steps of decision-analytic modelling (e.g. depiction of the PICO question, definition of perspective and analytical time horizon, selection of model type and outcomes, simulation technique, calibration/validation, causality, uncertainty analysis) from a modeller's perspective with the corresponding standards, recommendations and quality criteria for the methodology (e.g. ISPOR-SMDM Joint Modelling Task Force) and the reporting of results (e.g. Consolidated Health Economic Evaluation Reporting Standards, CHEERS). In addition, open questions in the context of the German procedure with reference to the methods paper 7.0 will be discussed.