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THE EFFICIENCY FRONTIER APPROACH TO ECONOMIC EVALUATION OF HEALTH CARE INTERVENTIONS

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Abstract

Background: IQWiG commissioned an international panel of experts to develop methods for the assessment of the relation of benefits to costs in the German statutory health care system.

Proposed Methods: The panel recommended that IQWiG inform German decision makers of the net costs and value of additional benefits of an intervention in the context of relevant other interventions in that indication. To facilitate guidance regarding maximum reimbursement, this information is presented in an efficiency plot with costs on the horizontal axis and value of benefits on the vertical. The efficiency frontier links the interventions that are not dominated and provides guidance. A technology that places on the frontier or to the left is reasonably efficient, while one falling to the right requires further justification for reimbursement at that price. This information does not automatically give the maximum reimbursement as other considerations may be relevant. Given that the estimates are for a specific indication, they do not address priority setting across the health care system.

Conclusion: This approach informs decision makers about efficiency of interventions, conforms to the mandate and is consistent with basic economic principles. Empirical testing of its feasibility and usefulness is required.

1. INTRODUCTION

In 2007, the German Institute for Quality and Efficiency in Health Care (IQWiG) convened a panel of international experts in health technology assessment to develop the methodology for economic evaluations of health care interventions in Germany. The evaluations to be conducted by IQWiG, commissioned by the Federal Joint Committee (*Gemeinsamer Bundesausschuss, G-BA*), are to provide information regarding the *höchstbetrag*—a reasonable maximum reimbursement—for introduced medical technologies. The evaluations will take place after approval and marketing of the intervention (i.e., *ex post*).

The challenge given to the panel was to delineate an appropriate method for developing the required information to provide guidance to decision makers within a given therapeutic area. It is important to stress that it was not in the mandate of the panel to recommend methods for setting reimbursement priorities across the health care system—that is, for comparing the value for money of a new intervention with that obtained in other disease areas.

The panel concluded that it is possible to delineate such a method, consistent with basic economic principles, although the degree of guidance will depend on the amount of data available in a given disease area. An initial draft of the proposed methods was prepared and made public for commentary in early 2008. Extensive comments were submitted by numerous organizations and individuals; after taking these into account, IQWiG published the final version of the panel's proposed methods (IQWiG, 2008a).

The approach recommended by the expert panel was that IQWiG should provide German decision makers with estimates of the costs and value of the health effects of the intervention at issue, together with all other relevant interventions available in Germany for the same disease

area. IQWiG should also estimate a “going rate” for the expected health benefits in that specific therapeutic area and display the information using an efficiency frontier plot.

The proposed approach proved to be very controversial (IQWiG, 2008b). Accordingly, the main purpose of this paper is to clarify the proposed approach, with a view to dispelling the misconceptions that have been voiced.

2. THE GERMAN CONTEXT

The German Health Care Modernisation Act of 2004 (*GKV-Modernisierungsgesetz*) provided for the establishment of a new *Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen*, known now by its acronym: IQWiG. The Institute is responsible for the scientific evaluation of the clinical effects as well as the quality and efficiency of health care services. The Institute’s responsibility in these areas is to support G-BA by developing the independent scientific capacity to answer research questions posed by G-BA or the German Federal Ministry of Health, evaluate medical issues and concepts relevant to health care, and assess research requirements relevant to patients’ needs. The information compiled and corresponding recommendations are submitted to the Ministry and the G-BA and made available to the public. The Institute is funded by a special fee raised as a supplement to all hospital and doctor visits in Germany. In 2007, the budget was approximately €12 million.

The initial legislation specified that IQWiG should assess the clinical effects of health technologies according to “internationally recognised standards of evidence-based medicine” (EBM). In early 2007, the German parliament passed additional legislation which expanded IQWiG’s responsibilities to include the “cost-benefit” assessments of pharmaceuticals or medical procedures according to “accepted international standards of health economics.” Although

Nutzen was translated from the German into “benefit,” it is clear that Parliament did not intend to mandate a specific methodology (i.e., cost-benefit analysis). Instead, the idea was that IQWiG would develop the methods it would use for economic evaluation, consistent with the legal requirements (SGB, 2007). These requirements were made operational by IQWiG and reaffirmed by the German Federal Ministry of Health, which is legally responsible (Bundesministerium für Gesundheit, 2008), and this defined the context for the Panel’s development of the methods.

IQWiG’s economic evaluations will be conducted to support the GKV-Spitzenverband (the national umbrella organization for the statutory health insurance funds) when it considers the appropriate reimbursement on behalf of the community of insured citizens. The assessments will address primarily prescription drugs that have recently entered the health care system, but the methods should also be applicable to existing drugs and other health technologies.

The basis for these evaluations, as defined by the Ministry and IQWiG, is not the same as in many other health care systems: It does not involve establishing funding priorities across the German health care system. Instead, it envisions the narrower goal of establishing a maximum reimbursement amount for “patented innovations as well as pharmaceuticals of importance” (Gesetz, 2007) in a given disease area. The process of setting this amount is informed (but not determined) by estimating the additional benefit and incremental costs beyond those of currently available interventions in the disease area in question. This was a logical extension of the current IQWiG practice of establishing relative health benefit at the therapeutic level. It is also in line with common application of economic analysis as an aid to decision making, as opposed to determining decisions. Thus, any additional expenditure need not be weighed formally against what could be achieved in other therapeutic areas, nor by investments in other sectors of the economy, such as education or the military. As these comparisons would require judgments

about the societal value of treating one disease versus another and no universally accepted method for doing this has been identified by IQWiG (including the cost-per-quality-adjusted life year [QALY] approach; see, for instance, Nord, 2008, Dix Smith, 2009), IQWiG insisted on a method that does not address the broader issue of prioritizing across the health care system. That application of citizens' values was to be left to the decision-making bodies designated by law.

According to the legal framework (SGB V, § 35b), a second constraint is that the economic evaluations should only address those interventions that have been judged to be superior (presumably to existing ones) and that the health benefits to be considered in the economic assessment are those which have been estimated by IQWiG following its published Methods grounded in the principles of EBM (IQWiG, 2009). This has several implications. It means that new inferior therapies have no place in the system, even if they are considerably less expensive than existing ones. It also means that the effectiveness component must reflect the review carried out by IQWiG beforehand—no additional benefits, even if indirectly implied by the EBM measures, are to be included.

A third requirement imposed in Germany is that the costs be assessed primarily from the perspective of the community of the citizens insured by Statutory Health Insurance (SHI). This implies that it is the costs which citizens bear that should be included. This means that some costs that might be excluded from evaluations (e.g., personal health care costs) should be incorporated in this case.

A fourth requirement was that patients not be excluded from therapeutic benefits on cost grounds alone.

3. THE PROPOSED METHOD

The approach recommended by the Panel takes as its point of departure that the efficiency of an intervention relative to others in the same disease area is relevant to decision makers—that is, that an important input (though not the only one) to setting the maximum reimbursement is the health value obtained for a given expenditure and that, accordingly, newer interventions should not provide less value without strong justification. Thus, the efficiency frontier, for a particular disease area, is defined by the most efficient interventions at increasing levels of benefit. The efficiency frontier presents the trade-off between costs and benefits and identifies the interventions that provide the most value for any given level of investment. It can be displayed graphically (see Figure) by plotting the interventions at their estimated net cost (horizontal axis) and benefits (vertical axis) and drawing line segments linking the options that are not dominated by any other (further explanation below). Although the axes could be inverted (as is common in the “cost-effectiveness plane” of pharmacoeconomics [Black, 1990]), it is preferable to do it as proposed because the resulting slopes have a ready interpretation in terms of efficiency and this accords better with the format used in other fields. The slopes of the line segments give the “going rate” (how much is gained per unit of cost).

The efficiency frontier represents the best that the system can do with available agents at current prices. Interventions that are not at the frontier are less desirable because they produce the same or less benefits at a higher cost than other existing interventions; by the same token, the region “beyond” the frontier identifies an area of potential interventions that would be more efficient than existing ones because they would provide equal or more benefits at less or equivalent cost. Should they become available, the system would have to adjust the mix to incorporate them because the resulting combination would deliver more with available resources. The general

approach is compatible with the use of economic analysis to support decisions rather than make them ([Gold, 1996](#)), as well as being compatible with theoretical underpinnings ([Birch, 1992](#)).¹

3.1 Defining the therapeutic area

To construct a meaningful efficiency frontier, it is necessary to carefully define the disease area in question. Full, detailed specification should include the disease or condition, including specific variant, stage, severity or other descriptors; the conditions of the intervention (e.g., in a clinic); the intended patient population; the interventional sequence (initial, after one failure, etc.); and whether it is mono- or combination therapy. The idea is to ensure that the interventions included in the efficiency plot are true alternatives to each other. If some feature of the therapeutic area would mean that (some of) the interventions are not interchangeable, then that feature must be incorporated in the definition.

3.2 The value of health effects (vertical axis)

The value of the health effects of each intervention should reflect the “benefits” that have been assessed by IQWiG using EBM techniques. As emphasized above, these health benefits are defined within the disease category and are thus in accord with the efficiency also being considered at the intra-therapeutic level. These benefits must be appraised on a cardinal scale that reflects how valuable they are to the insured citizens. Both the intentional and unintentional patient-relevant outcomes of the intervention should be covered in the profile. These can include ([Institut für Qualität, 2009](#)) mortality, morbidity (complaints and complications), and/or health-

¹ While open to the criticism of being a “partial analysis,” the efficiency frontier approach is broadly compatible with the integer programming approach

related quality of life. In addition, the time and effort invested related to the disease and the intervention can be considered, as well as patients' treatment satisfaction.

The health effects should be evaluated in terms of actual clinical measures which may include responder measures; measures that include long-term prognostic implications (may require modeling); integrative measures for multiple attributes; or quality of life scores. IQWiG specifies the methods for selecting these endpoints, including consultation with patients and other stakeholders, and the methods for estimating the effects (Institut für Qualität, 2009). These follow the standards of EBM and rank evidence in a hierarchy where systematic review of relevant randomized clinical trials is at the top, followed by individual trials, controlled observational studies, uncontrolled studies, and, at the bottom, case series and opinions. The larger the gap between the required and the available evidence, the more difficult it is to issue a positive recommendation, but this gap must be put into context by taking into account the nature and severity of the disease, the magnitude of the effect, and the availability of alternatives.

IQWiG also specifies that surrogate endpoints (i.e., those that have no value per se but are of interest because they are related to the outcomes that are of value) can be used in the evaluations but only if they are considered *valid* according to EBM criteria—namely, that there must be an established plausible, strong, monotonic, and consistent association between **changes** in the surrogate and **changes** in the patient-relevant outcome. According to IQWiG, this relation between alteration of the surrogate and eventual outcomes must have been clearly shown in intervention studies. In other words, it is not enough to have epidemiologic evidence that the outcome is different at different levels of the surrogate—there has to be convincing proof that altering one reliably predicts change in the other. IQWiG also notes that the accuracy of a diagnostic test is a surrogate and that its validity depends on the availability of interventions with

proven efficacy or on the establishment of other (patient-relevant) consequences. If surrogate endpoints are felt to be valid enough to be acceptable, then the economic evaluation will require prognostic modeling to estimate the future outcomes and address the longer time horizons typically used in the economic analysis (Caro, 2008; [Siebert, 2003](#)).

Once the profile of effects of each intervention is estimated, the next step is to consider its value (to the insured citizens). The idea is to assess whether the benefits estimated by IQWiG are measured on a scale that is reasonably cardinal or can be transformed easily to one that has the interval property. This requirement is necessary because the plot must reflect value on the vertical axis in such a way that units along the scale have the same worth. If it can be justified that the scale reasonably meets the requirement, then this measure can be used directly, but this requires careful consideration of its nature and how citizens would likely value changes along the scale. At first glance, it might seem that twice the clinical benefit is twice as valuable but this may not necessarily be so. For example, when evaluating a treatment for cancer that increases the time to disease progression from six to 12 months, the analysts would need to consider whether this benefit is really twice as valuable. If there is a new diagnostic test for an inherited anomaly that doubles the true positive rate, does this mean that the test provides benefits that are twice as valuable? Or if a vaccine to prevent an infectious illness doubles immunogenicity, is the value doubled? Would a new therapy for chronic illness that decreases the applicable symptom score by 20 units compared to 10 be seen as twice as valuable? And so on.

If the scale is not judged to be cardinal, the effects must be valued on one that does. Methods for doing this kind of valuation have been developed over the past few decades ([Ryan, 2000](#); [Craig, 2009](#)), and their application in Germany will be the subject of an upcoming Working Paper.

Standard generic utility instruments like the EQ-5D can be helpful in judging the value of

multidimensional effects. So can data from studies of the quality of life of patients (so-called “experience utility”).

3.3 The costs (horizontal axis)

The costs of each intervention should reflect the total net expenditures per patient, including all items relevant to the citizen’s perspective, and not just the price of the intervention. They are “net” in the sense that any savings produced by the intervention should also be considered. Thus, reductions in resource use that result from implementation of a given intervention are subtracted from the cost of the resources required to deliver the intervention. In assessing changes in resource use, it is important to be clear and consistent regarding what the reference point is. The reference can be “no intervention,” provided that the cost implications of doing nothing, which are rarely zero, are taken into account. In cases where this leads to negative “net” costs, the analysts may prefer to establish the least expensive intervention as the reference instead.

The costs are estimated from the perspective of the community of German citizens insured by the SHI. This perspective is somewhat unusual in health economic evaluations but is the one most relevant in Germany. It means that all direct costs borne by insured citizens, either via their health insurance or through another insurance scheme or even by out-of-pocket payments should be considered. In addition, any consequences of interventions that have economic implications, even if not paid for directly, should also be included if they are relevant to the insured citizens. As some economic consequences could reach far outside of health care (e.g., impact on research, education, or even German industry), this citizens’ perspective would functionally represent a societal perspective. The proposed methods recognize, however, that it is not usually feasible to stretch the perspective that far and, thus, that the indirect implications will most often be limited to those related to the patients’ health (e.g., loss of productivity).

The time horizon for inclusion of costs in the analysis needs to be sufficiently long to cover all relevant costs. In other words, it will normally not be limited to the period covered by the clinical trials used to support the benefit estimates. Although this could extend to the lifetime of patients (and even beyond if there are consequences for other generations), in practice a shorter horizon may be chosen if it covers the majority of relevant costs and reduces the extent of highly uncertain projections. This selection of an appropriate timescale needs to be justified. To estimate the costs over the appropriate time horizon, the evaluation will require an economic model that incorporates prognostic predictions of the course of patients and their management. Details of this modeling are covered in a separate technical document (Caro, 2008).

Extension of the time horizon to periods of time beyond those covered by the health benefit data from clinical trials raises the question of what to do about consumption of resources that are not related to the disease of interest but are, nevertheless, brought about by prolonging survival via the interventions. These “costs in added years of life” have been the subject of much controversy ([Gold, 1996](#)) because while they result, in some sense, from the intervention, they seem to penalize extending survival; something which appears to be contrary to the objective of intervening in the first place. For the German evaluations, these can be estimated and reported to the G-BA, but they are to be kept separate from the costs considered in the calculations of efficiency. To be consistent, however, if production gains are included, then consumption effects must be deducted.

Details of the estimation of costs are provided in a separate technical document (Krauth, 2008).

The costs should be the actual ones that are expected to accrue in the sense that they should reflect clinical practice in Germany rather than the activities observed in clinical trials or recommended by guidelines. They should also reflect the situation in Germany at the time of the

evaluation (not at some previous decision point or evaluation) and should be discounted at whatever rate is extant in Germany at the time (currently 3%).

3.4 Using relative efficiency to provide guidance

In Germany, the efficiency frontier will be used to provide guidance to the G-BA for setting the maximum reimbursement amount. This guidance is not intended to be an appraisal conveying the decision itself but rather information that can be used by the decision makers—together with other inputs—to arrive at such an amount. Relative efficiency is only one piece of information; its components (value of the benefits and total net costs) are also important, as are the estimated budget impact and the uncertainty around all the estimates.

Guidance will be provided to G-BA by plotting the efficiency frontier and using it to assess the position of the intervention at issue relative to what already existed in the market. In Germany, unlike many other countries, the evaluations take place *ex post*—that is, the intervention being assessed is already on the market and has an established price. Thus, there is no need to project the frontier into unknown space but rather to consider the efficiency of the intervention at issue in comparison with the efficiency of other interventions on the market in that therapeutic area.

As seen in the figure, plotting of the frontier (interventions A, C, F, G) delineates three guidance zones. Any interventions that would plot in the areas below and to the right of the frontier would be considered inefficient as they cost more and provide less value than existing ones (those falling in the shaded rectangles labeled 1-5, such as B and D) or they are in a position where there is a lower price that would place them on the frontier (those plotting inside a triangle labeled 6-8, such as E). It is not expected—at least initially—that any evaluations in Germany

will find newer interventions falling in this zone because of the two-stage process of determining benefit first and only if it is judged to be superior, going on to the economic assessment.

A second guidance zone is given by the area above and to the left of the frontier. This zone indicates positions where a newer intervention would dominate an existing frontier intervention because it would provide benefits of greater value and at less cost (shaded rectangles 9–12) or would be in a position of “extended dominance” by providing benefits more efficiently than the neighboring segment of the frontier (triangles 13–16). Indeed, any intervention falling in these areas would redefine the frontier. Most of this frontier-redefining area will also not be used in Germany because of the requirement for superiority of benefits before economic evaluation is undertaken (the exception is the portion above the next best available intervention, indicating a newer, superior intervention that has been priced very attractively and redefined the frontier).

The third guidance zone is the triangle (labeled N) that indicates superior benefits but a lower efficiency than the next best intervention on the frontier. In this third case, decision makers would need to consider how much lower the efficiency is and whether there is justification for the decrease. A small decrement could still be viewed as reasonable, whereas large ones would be more problematic.

The slope of the efficiency frontier tends to decrease as benefits increase, reflecting, in many cases, diminishing marginal returns (i.e., the fact that even in the subset of “most efficient therapies,” increases in costs of research and development and of production provide less and less additional value [Murphy, 2003]). If there are sufficient points on the frontier, then further analysis can be carried out to determine the rate at which efficiency has been decreasing as a function of increasing value. This estimate of the rate of decline indicates “what is to be

expected” in terms of cost increases for new interventions that provide more value than earlier ones. This would provide a basis for assessing how reasonable the last decrease in efficiency is.

Additional criteria, such as the citizens’ willingness to pay for additional benefits in that therapeutic area, could be applied in principle. Obtaining these valuations is quite challenging, however (Ryan, 2001).

4. DISCUSSION

The efficiency frontier has been widely used in other fields. Indeed, it has become increasingly popular for evaluating the relative performance of organizational units ([Bessent, 1988](#)) and industries using Data Envelopment Analysis, particularly in not-for-profit entities ([Nunamaker, 1985](#)), and for examining a wide range of trade-off decisions such as sales force size and productivity ([Horsky, 1996](#)), the technology choices of consumers ([Lancaster, 1966](#)), and even research activities in universities ([Johnes, 1995](#)). It has also been applied to health care services ([Helmig, 2001](#); [Zuckerman, 1994](#)) and even to medical therapeutics ([Hollingsworth, 2001](#)).

Several governments and international bodies have used variations of the efficiency frontier to address issues of reimbursement and resource allocation. In the World Health Organization Guidelines to Cost-Effectiveness Analysis (Tan-Torres Edejer, 2003), for example, an efficiency frontier is constructed by evaluating a set of interventions at different coverage levels and in various combinations.

In the present context, the efficiency frontier is helpful in providing guidance to decision makers by suggesting a maximum reimbursement amount that is consistent with the available information in the market at the time of the evaluation and with the fact that the reimbursement is the one factor that can be adjusted. It is an approach that does not require any external

information but allows estimates of Germans' willingness to pay for particular benefits to be incorporated. Similarly, it would permit a specific budget limit to be imposed.

The rationale for using the efficiency frontier is that it provides information that is important for decision makers in a clear, consistent, and explicit manner. The efficiency frontier indicates how much value is being obtained and at what costs in Germany (it should be noted that this snapshot is "current," not a reflection of what was extant at any given point in the past). The efficiency frontier was selected as the foundation for economic evaluations at IQWiG because it fulfills the requirements imposed and, as noted above, is consistent with the existing theory of economic evaluations.

Although based on the same theoretical foundation as that of the approaches commonly used today ([Weinstein, 1977](#)), the proposed method departs from them in the practice. It makes the efficiency frontier explicit rather than leaving it as a background concept, perhaps perceived only by some methodologists. The approach does not attempt to determine societal priorities across therapeutic areas—this is left to the appropriate elected and appointed representatives of the citizens. Some argue that this is a serious shortcoming and that the cost-per-QALY approach is available for helping resolve the important, broader issue ([Drummond, 2009](#); [Jonsson, 2008](#)).

Although the efficiency approach does not preclude the use of the QALY as a measure to integrate various attributes (e.g., benefits and harms) within the disease area in question, for the broader context of comparisons across diseases, there is no clear evidence for the use of a unique cost-per-QALY threshold. Attempts to measure society's valuation of care for patients in different therapeutic areas in a comparative manner are still being heavily debated and questioned ([Nord, 2008](#); [Weinstein, 2008](#)), and even the National Institute for Health and Clinical Excellence (NICE) in the UK, which formally employs a universal limit to society's

willingness to pay for new technologies (McCabe, 2008), is now moving away from this to allow higher thresholds for some disease areas (NICE, 2009). We believe our proposed approach may also be a useful tool for those who are not entirely convinced by the helpfulness (Nord, 1999; McGregor, 2003; Gyrd-Hansen, 2005; Arnesen, 1999; Broome, 1993) of QALYs (Weinstein, 2009) or disability-adjusted life years (Murray, 1996) or of the validity of the QALY maximisation approach to priority setting (Nord, 2009).

The efficiency frontier approach may be quite time-consuming and presupposes the existence of a sufficient number of therapies in a given area to provide a useful frontier. Pilot studies of these technical and practical issues are in progress.

It is important to emphasize that the efficiency frontier does not provide a decision rule because decisions are made on the basis of other important considerations beyond efficiency. Decision makers may want to alter the entire market in a given therapeutic area (e.g., by declaring that it is not an area worth covering, thus implying that regardless of efficiency, interventions in that area will not be reimbursed). The efficiency frontier also does not address concerns for investment in research and development or industrial policy.

The efficiency frontier plot may be used for other purposes as well. If the price of the last (previously best and most expensive) intervention on the frontier was set based on an economic evaluation in comparison with the other interventions in the therapeutic area, then the last line segment of the frontier indicates the marginal willingness to pay for increased value in that therapeutic area. A new intervention that yields an equal or better incremental value-to-cost ratio than this (relative to the previously best therapy) may *a priori* be said to be consistent with prior willingness to pay. Still, decision makers would need to consider whether previous willingness to pay continues to apply as new technologies are developed.

The efficiency frontier plot also shows clearly inefficient interventions (i.e., those that are both more costly and less valuable than other existing options). In principle, questions may be raised as to whether the prices of such options should come down. For interventions below the efficiency frontier but not “absolutely” dominated, the guidance could be that their price seems too high and should be brought in line with the efficiency frontier; alternatively, a justification for not doing so needs to be provided.

5. CONCLUSION

The efficiency frontier provides an explicit, reproducible, and transparent approach for deriving guidance for the maximum reimbursement amount from information on the benefits and costs of existing therapies in the area of a given indication. The strength of the guidance will depend on the number of existing therapies in the area. The proposed method should serve as a tool to inform deliberations on maximum reimbursement in Germany—it does not produce a decision rule. The feasibility of this approach still needs to be tested.

6. FIGURE

Figure 1 Plot of the efficiency frontier dividing the space into more or less efficient interventions and various guidance zones

7. ACKNOWLEDGEMENTS

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