NDT Perspectives

Health economics and European Renal Best Practice—is it time to bring health economics into evidence-based guideline production in Europe?

Maria C. Haller¹,²,³, Raymond Vanholder⁴,⁵, Rainer Oberbauer¹,²,⁶, Carmine Zoccali⁴,⁷ and Wim Van Biesen¹,⁵

¹Center for Medical Statistics, Informatics and Intelligent Systems (CeMSIIS), Section for Clinical Biometrics, Medical University of Vienna, Vienna, Austria, ²Department of Nephrology and Transplantation, KH Elisabethinen, Linz, Austria, ³ERBP, European Renal Best Practice, Methods Support Team, Ghent University Hospital, Ghent, Belgium, ⁴ERBP, European Renal Best Practice, Ghent University Hospital, Ghent, Belgium, ⁵Nephrology Unit, Ghent University Hospital, Ghent, Belgium, ⁶Department of Nephrology, Medical University of Vienna, Vienna, Austria and ⁷CNR-IBIM, Clinical Epidemiology and Physiopathology of Renal Diseases and Hypertension of Reggio Calabria, Calabria, Italy

Correspondence and offprint requests to: Wim Van Biesen; E-mail: wim.vanbiesen@ugent.be

ABSTRACT

Medical management of patients with kidney disease is complex and resource intensive. In times of limited health care budgets, economic evaluations have become more important over the past few years in identifying interventions with a beneficial cost-effectiveness to maximize the benefits served from the available resources. However, integrating evidence from health-economic evaluations into clinical practice guidelines remains a challenge. European Renal Best Practice (ERBP), the official guideline body of the European Renal Association–European Dialysis and Transplant Association (ERA–EDTA) herewith presents some lines of thought that need consideration in the discussion on incorporating health-economic considerations into clinical guideline development.

Keywords: clinical practice guidelines

WHY THIS QUESTION?

Medical management of renal patients is complex and resource intensive, and puts substantial financial pressure on health care systems around the world [1]. This burden is further enhanced, not only by the continuously growing population of chronic kidney disease patients, but also by innovations in renal medical care, which are often cleverly marketed as ‘advances which your patient deserves’. In this era, there is also an increasing belief that ‘everything is and should be possible for everyone’, further inflating the budgets spent on health care. In this context, and in times of crisis and financial restrictions, economic considerations gain importance, and economic evaluations of health care interventions are increasingly demanded, not only to provide objective evidence for ‘value’ of money spent, but also to maximize the possible benefits of the available resources by avoiding that money is wasted on spurious interventions, while potentially beneficial therapies cannot be applied because of lack of resources.

Evidence-based clinical practice guidelines have emerged as an important tool to improve health care. Until now, most guideline bodies have focussed on ‘scientific evidence’ to support their recommendations. Important progress has been made to better define ‘relevant questions’ and ‘relevant outcomes’ and grading strength of recommendations [2, 3]. Linking health economy issues to clinical practice guidelines is a complex issue in initiatives encompassing the whole European scenario, similar to the case of European Renal Best Practice (ERBP). In Europe, the gross domestic products (GDPs) and the associated health resources vary substantially with the richest country having a per capita GDP 69 times higher than that at the opposite extreme [4]. In such a scenario, health priorities may not coincide across countries and therefore, decisions on competing health issues may vary to an important extent among countries. Only a limited number of guideline issuing bodies, e.
g. the British National Institute of Clinical Excellence, explicitly take economic considerations into account when producing guidance.

ERBP, the guidance body of the European Renal Association–European Dialysis and Transplant Association (ERA–EDTA), believes that it is time to start considering health-economic aspects when formulating recommendations, by taking into account the restrictions imposed by the need to attain a sustainable health care budget and the risk that the need to reimburse Intervention A might imply that Intervention B becomes unaffordable.

**WHAT DO HEALTH ECONOMICS IN FACT IMPLY?**

In general, health-economic analyses are designed as ‘cost-consequence’ studies to determine the cost-effectiveness of medical interventions by relating costs of health care on one side to the effectiveness of health care on the other. Depending on which measure of effect is used, different approaches exist, such as the cost-effectiveness, cost–utility and cost–benefit analyses.

‘Cost-effectiveness analyses’ use the ‘natural’ unit of the particular health effect of interest (for example, years free of dialysis, graft years saved, fistulas created, infections prevented, cancers detected) as yardstick to measure effects. While these natural units are simple to interpret, the obvious disadvantage is a lack of comparability across studies using different end points, making it complicated to compare different interventions that cannot be gauged by the same yardstick: it is impossible to evaluate whether Intervention A with a certain amount of money spent per year free of dialysis is more or less cost-effective than Intervention B with a certain amount of money spent per fistula created.

‘Cost–utility analyses’ provide more comparable results by using ‘standardised’ units, but this comes at the expense of cumbersome measures of effectiveness that by definition are artificial. ‘Cost–utility analysis’ uses a combination of quantity and quality of life (QoL) as effectiveness measures: quality-adjusted life years (QALYs). QALYs weigh each additional year of life gained by the particular medical intervention under investigation by the QoL during that year. However, there is no general definition of ‘quality of life’ and thus various assessment tools can be used, which again might hamper comparability, even leading to conflicting results. Moreover, the QoL depends on numerous patient-related factors, such as the underlying disease and its stage, as well as age and socioeconomic factors, which might seriously hamper generalizability of the obtained results outside that of the actual study situation. In addition, the use of a standard measure such as QALY inherently leads to utilitarian ethics, with all its related pitfalls: it is difficult to decide whether it is better to do an Intervention A leading for 10 patients to 0.1 QALY or an Intervention B leading for 1 patient to 1 QALY.

‘Cost–benefit analyses’ translate effectiveness measures into financial values and are therefore prone to ethical dilemmas, because a certain amount of money is proposed as being justified to maintain health, indirectly making a judgement of how much money a life is worth.

It is essential to point out that, in general lines, the discussion on the importance of accurately, objectively and transparently selecting outcomes in health-economic analysis is comparable with that in the production of guidelines in general. It is thus vital to assure that the chosen outcome is valid, and that results are not reported simply as ‘cost-effective’, but that it is made explicitly clear how this validity was assessed, and what exactly is understood by the term ‘cost effective’ by explaining all factors taken into the equation.

**HOW SHOULD WE USE HEALTH-ECONOMIC ANALYSES IN GUIDELINE PRODUCTION?**

The basic principle of producing evidence-based guidelines is pooling the best available evidence according to a predefined methodology to formulate recommendations based on the strength of the identified evidence. The same principles can be applied to health-economic analyses. Assessment of cost-effectiveness can be incorporated at different stages within the guideline development process.

A first option is to include health-economic considerations as early as at the stage of topic selection. Interventions in renal medicine that are financially most pressing could be given priority for upcoming guideline topics, to evaluate whether their therapeutic use should be recommended or not, or to recommend the most cost-effective mode (if different effective options are available).

A second possibility is to include health economics at the very beginning of the development process of a particular guideline, when proper PICO (Patient-Intervention-Comparator-Outcome) questions are formulated [5]. Health-economic data could be framed as important outcome parameters in the comparison of different potential interventions. Questions in this regard can be formulated directly to address issues of cost-effectiveness, e.g. is advocating ‘fistula first’ in predialysis patients after one unsuccessful attempt associated with an increased cost-effectiveness ratio compared with initiating dialysis via a central vein catheter?

A third option is to include health-economic considerations when framing the strength of the statements. ERBP believes that the possibility to have divergence between the level of evidence and the strength of recommendation is an important feature of the GRADE system: an intervention for which there is strong evidence of health benefit can still be accompanied by a recommendation with weak strength or can even not be recommended, when the achieved benefit is only documented on surrogate outcomes. Likewise, it should also be possible to downgrade strength if advantages are too limited to outweigh cost. This allows to protect physicians from having to prescribe expensive treatments, or from personal ethical conflicts if they cannot provide a certain treatment to their individual patient.

A final alternative is to involve health economics at a later stage of the guideline production, after recommendations have
been developed, by investigating the cost-effectiveness of a particular recommendation.

Independent, however, from the stage when cost-effectiveness assessment is incorporated into the guideline development process, data synthesis is the critical methodological aspect to provide evidence-based decision guidance. In the last decade, comparative effectiveness research (CER) has gained widespread interest in many areas of medicine. The primary goal of CER is to improve the delivery of health care, and this at the most cost-effective way. Different treatments are compared directly head to head for specific conditions. This allows cost-effectiveness comparison for issues of major public-health impact like weight loss interventions in obese people.[6] CER compares interventions only head to head in one specific setting, thus evaluations between different treatments of different diseases, such as with the cost per QUALY approach, can be avoided. As the system creates clarity on what the cost (and thus the reimbursement) for a current treatment of a specific disease is, new interventions can only be introduced when they are either more effective or cheaper for the same effectiveness. This requires availability, comparability and generalizability of the literature supporting the guideline. In health-economic assessment, several difficulties arise from this requirement. First, the availability of health-economic evaluations in certain areas of medicine is limited. Second, comparability of studies is explicitly challenging, not only because of the abovementioned potential differences in effectiveness parameters, but also because the comparators used to detect a more cost-effective alternative vary across models and estimation of the ‘absolute’ cost-effectiveness of a certain medical intervention might not be straightforward. In addition, a particular medical intervention might not be considered cost-effective in the same way by different stakeholders such as hospitals, insurers, governments, patients or society in general.

Third, it might turn out to be difficult or even impossible to generalize results from cost-effectiveness assessments across borders due to discrepancies between health care and reimbursement systems. This specifically is true for results of randomized controlled trials, which mostly have fixed inclusion and exclusion criteria, making the results not generalizable to other patient cohorts or conditions. In addition, it is well known that ‘the fact of being studied’ has a beneficial impact on the outcome, even in the control group. As a consequence, CER tries to focus on the evaluation of interventions in ‘real life conditions’. In practice, this often means that they rely on observational data from registries or even administrative databases, resulting in the inherent biases related to this type of analyses.

Besides calculating the cost in terms of money, health-economic techniques can also help us to calculate another type of ‘cost’: the losses or gains a patient encounters after a certain choice, in terms of life expectancy, QoL, disruption of normal life pattern, etc. As different outcomes can be valued differently by different patients, guideline bodies should use Bayes theory or multilayer Markow modelling to calculate and represent the effect of different treatment options in a way tailored to the patient. Based on this information, patients can take the decisions that result in the outcomes they value the most, allowing real shared decision-making. This is an approach that might substantially differ from the actual ‘one size fits all’ approach. It is likely that it also will improve the patient adherence to treatment, as they can themselves compare the different options and select the most preferred one according to their preference. An important caveat of this approach is, however, the lack of available evidence to feed the models, and the validation of this type of approach. Further research in this area is certainly needed.

**HOW AND TO WHAT EXTENT SHOULD ERBP INCORPORATE HEALTH ECONOMICS IN ITS GUIDELINE DEVELOPMENT PROCESS?**

Producing clinical practice guidelines brings with it significant responsibilities and incorporating health economics into the guideline development process needs careful consideration of possible consequences. Above all, according to its mission, ERBP produces guidelines to improve the outcome of patients with kidney disease in a sustainable way through enhancing the accessibility of knowledge on patient care, in a format that stimulates its use in clinical practice. As financial pressure grows, guidelines are a powerful tool to protect individual patients who deserve the most optimal treatment independent of costs. The recommendation by ERBP of treatments that have proven to be effective, especially when they are cost-effective, can help to convince health care payers to reimburse the treatment, of course taking into account the economic situation of the country or region. Likewise guidelines have, in our view, a responsibility to foster a reasonable, cost-effective resource utilization to promote sustainable and affordable delivery of renal health care to all who are in need of medical attention. Providing cost-effectiveness data within a guideline would support and also protect physicians to not prescribe an expensive intervention that has no proven superior cost-effective benefit compared with its alternatives. This is, however, a delicate balance, especially for expensive, new interventions, which however are often presented as having seemingly substantial effects. Mostly, these interventions are strongly supported by industry, resulting in randomized controlled trials and thus evidence, whereas cheaper, and potentially similarly effective treatments, are less well investigated. Finally, discouraging expensive interventions by formulating guideline recommendations against them only because of cost could compromise funding of research in a particular area, which might hamper progress and potentially deprive patients from future developments of more effective alternatives.

The ultimate challenge of incorporating health-economic aspects into guideline production is to determine a threshold to consider a medical intervention cost-effective. Benchmarks for the cost of one QALY that the society is willing to pay in most areas of cost-effectiveness analysis were derived when dialysis was initiated, and most health economists agree that the amount should depend upon the GDP of the country involved. However, the magnitude of this amount is probably also influenced by the type of intervention (e.g. a life-saving intervention such as dialysis versus an intervention that ‘only'...
improves QoL). A major ethical drawback of the cost per QALY is that it implicitly accepts that patients with lower QoL can be deprived of treatment. The situation becomes more problematic when one has to decide to which one of several medical interventions one is willing to give priority: allocating resources to a medical Intervention A will withdraw these resources at the same time from another possible medical Intervention B and the possible incremental benefit of Intervention B will be lost. Ultimately, the answers will differ across societies, countries and individuals. Especially for ERBP, an organization intended to represent whole Europe, this is challenging, as health care systems, economic situation and political organization are quite different between countries and even regions. Therefore, guideline developing bodies should enhance accessibility to the best available evidence of cost-effectiveness, so that everybody involved can come to his/her own different solution to solve a certain health care question, adapted to the local needs and possibilities.

In conclusion, whereas many physicians have a natural aversion of the idea of incorporating macro-economic considerations in their decision-making process, the increasing emergence of expensive treatments forces the medical community to take financial issues into account. To protect the individual physician from having to take macro-economic considerations when confronted with individual patients, a policy on the societal level is indispensable. This policy should be evidence-based, and should ascertain a fair and just distribution of health care resources.

ERBP, therefore, believes that it is time to start considering the role of health economics in guideline development. We feel that it is even more important to have strong evidence to support a particular recommendation when economic considerations are taken into account. As a consequence, there is an urgent need for well-structured health-economic studies in a broad array of nephrology topics. Even if a society would spend its whole GDP for health care, not all statistically effective interventions could be financed. Therefore, both evidence and economic evaluations should be used in combination as part of a holistic decision-making process in which therapeutic options should be privileged. ERBP intends to compile evidence on whether a treatment results in the improvement of a meaningful outcome as a first step; if the answer is yes, evidence on the cost-effectiveness can be provided as a second step, and this in a way that each region can incorporate the data in its own, region-specific financial context and philosophy on health care organization. In this way, everyone involved in health care should be enabled to make decisions to improve outcomes of our patients.

ACKNOWLEDGEMENTS


CONFLICT OF INTEREST STATEMENT

The declaration of interest forms of M.C.H., R.V., C.Z. and W. V.B. is found on the webpage of ERBP: www.european-renal-best-practice.org. The declaration of interest form of Rainer Oberbauer is found on www.ERA-EDTA.org/Descartes. The authors declare that the results presented in this paper have not been published previously in whole or part.

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Received for publication: 8.3.2013; Accepted in revised form: 24.7.2013