The Imperative for Health Economics Assessment in Acute Kidney Injury

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The increasing cost of health and medical care services mandates the need for rigorous assessment of the full costs and benefits of all new therapies, programs, devices, diagnostics, and other interventions, in order to ensure that the limited resources are devoted to those endeavours that are expected to achieve that maximal outcome. Health economics (HE) is the discipline that employs economic concepts and tools to help decision makers determine how to best allocate scarce resources to improve health and health care \cite{1}. Comprehensive economic evaluation does not merely tabulate the financial costs associated with a program but rather assesses all of the economic and clinical consequences, in terms of costs and benefits, of using new or established therapies or implementing a new health care program, as compared to available alternatives.

Containing the cost of health care has become a core concern for all health care systems, especially in view of rising health care costs and shrinking health care budgets. From a conceptual standpoint, this is easy to comprehend if we think of resource allocation as a process that encompasses investments to the health care system within the whole economy as well as to different and competing activities within the health care system itself. Avoiding waste and inefficient use of resources allows the possibility of investing in other worthwhile projects that could not otherwise be undertaken. Moreover, a detailed approach to cost assessment and budgeting ensures the financial sustainability of any program over the long term.

The evaluation of economic impacts in health care is part of a more comprehensive decision-making process, in which the contributions of different disciplines should be collectively integrated. This means that any effort should be made to find a common language and to use a standardized terminology among different yet complementary sciences. The task of bringing physicians, engineers, biologists, technicians, economists, and others together to understand one other and arrive at a consensus on issues concerning investments and choices of new health care services is not simple. This approach, however, represents a necessary step to undertake the common pathway towards improvement of health care services and ultimately health outcomes. Since comparative economic analysis provides better quantitative insight about strategies and techniques that are superior with respect to the available alternatives, HE should be considered a precious and powerful tool serving the scope of an efficient health care plan and effective patient care.

Several techniques exist for HE evaluation and are briefly shown in table 1. All techniques use similar approaches to estimate costs, but they differ in the methods employed to measure the health-related consequences of all alternatives and choices under investigation.
In order to compare alternative projects on the basis of both costs and benefits, the incremental cost-effectiveness ratio (ICER) is usually computed. It is the key tool of every cost-effectiveness analysis and is obtained as the ratio between the difference in cost and the difference in effect of 2 alternative interventions A and B:

$$ICER = \frac{C_B - C_A}{E_B - E_A}.$$ 

The ICER represents the extra investment required for an additional health benefit and can be employed as a decision tool by means of defining a willingness-to-pay threshold. If the incremental cost per unit of health benefit is below such threshold, then the (more costly) intervention should be adopted [1].

In addition, all HE analyses have several common attributes that require specification (table 2).

Health expenditure is driven by several factors. The demographic structure of a population, the income growth and the structure of health funding (the mix of public and private spending) play crucial roles, but technological progress is currently perceived and considered the most important supply factor affecting the entire process of development, production, delivery and financing of health care [4].
### Table 2. Key steps in HE evaluation

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<th>Step</th>
<th>Description</th>
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<tr>
<td><strong>Alternative options</strong></td>
<td>Identification and selection of alternative projects is important, as HE appraisal is comparative and considers different courses of action. Alternative projects may address the same issue or deliver a similar benefit through different approaches, may differ in the way and timing a healthcare service is delivered, or may be competing on the basis of the inputs used.</td>
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<td><strong>Perspective</strong></td>
<td>The adopted viewpoint determines which costs and benefits need to be included in the analysis (e.g. society, patient, payer). From a global standpoint, the usual ‘reference point’ is the societal perspective and this is usually the most comprehensive of all approaches, as all relevant costs are accounted for over the specified time horizon, regardless of who incurs them. Other perspectives may be vital as they inform key decision makers and stakeholders about the impact of health interventions from their vantage point.</td>
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<tr>
<td><strong>Time horizon</strong></td>
<td>The time period considered in the study and the time span of interest must be clearly specified. This ensures that all the relevant costs and outcomes attributable to the study’s perspective and scope are accounted for and assigned.</td>
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<td><strong>Identification and measurement of costs (inputs)</strong></td>
<td>All resources used or lost must be included. These comprise direct and indirect costs. In the first category, we can find medical (costs to the health care system for the service provision) and non-medical costs (costs of social services and incurred by the patient or relatives). Indirect costs are productivity losses due to the disease and/or its treatment. Also ‘downstream’ costs of resources consumed in the future that are still attributable to the intervention (depending on the viewpoint) must be accounted for.</td>
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<tr>
<td><strong>Identification and measurement of benefits (outcomes)</strong></td>
<td>Evidence of the effectiveness of the considered alternatives is a basic requirement of every economic analysis. It is derived from studies designed to assess if the intervention work in the real clinical setting. Economic evaluations then uses the best available estimates of effectiveness to compute the health benefits that can be expressed in different ways: disease measures (e.g. events avoided, successful treatments) or survival measures (life-years gained); QALYs; monetary values (i.e. WTP for the improvement).</td>
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<td><strong>Discounting</strong></td>
<td>Determination of the present value of future costs and benefits, to adjust for the different timing of resource use and benefits accrual. Choice of appropriate discount rate is crucial and although no consensus on the most appropriate discount rate exists, there are 2 main possibilities. The former is the real interest rate, which is the foregone return rate on alternative investments for the society. The latter is the rate that reflects social temporal preferences.</td>
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<td><strong>Uncertainty and sensitivity analysis</strong></td>
<td>Uncertainty is an inherent component of economic analyses. It is due to several factors, including lack of precision in variables estimates (e.g. discount rate, precise costs, mortality and morbidity rates, etc.), the absence of data and the reliance upon lower levels of scientific evidence, and also to inherent technical and technological limits of applied levels of scientific evidence. To attenuate uncertainty, HE analyses employ comprehensive and sophisticated sensitivity analysis to illustrate how changes in key underlying variables used in studies and models influence changes in cost, outcomes and cost effectiveness.</td>
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<tr>
<td><strong>Decision analytic models</strong></td>
<td>Decision tree and Markov models consider the consequences of clinical actions under uncertainty. These modelling techniques represent the possible evolution of events accounting for timing and probability that a subsequent health state occurs and a final outcome is obtained. Decision analytic models are particularly important in settings where the risk of disease and disease progression may continuously change over time as a result of the previous choices and events.</td>
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QALYs = Quality-adjusted life years; WTP = willingness-to-pay.
The expression 'health technology' refers to a wide range of health care services, including pharmaceuticals, devices, diagnostics, procedures and other clinical, public health and organizational interventions. Health technology assessment (HTA) is a multidisciplinary process that informs on the short- and long-term impact arising from the adoption of health technologies and considers all the following aspects: safety, efficacy, effectiveness, cost-effectiveness, organizational impact, social and ethical issues [1].

The steps that lead to the application and diffusion of a new technology can be described through the so-called technology adoption curve – a common representation in marketing that perfectly applies even to the health technology framework (fig. 1).

The early adopters play a crucial role. They can be considered the joining link between the pioneers and the majority (early or late). The pioneers often approach a new technology for the sake of innovation or because they strongly believe in its superiority; the majority need some evidence to be persuaded to invest money, change the methodology or revise the system they have been stuck to so far. Early adopters often provide them the evidence they need (thus filling the ‘adoption gap’). This category is willing to test new innovations to move beyond the current frontiers and it contributes crucially to the diffusion of the knowledge acquired by means of testing new technologies and transmitting findings about their performance.

HE models and techniques may enlarge their scope of application in the field of nephrology and acute kidney injury (AKI). AKI is indeed associated with adverse clinical outcomes and increased morbidity and mortality, longer hospital stay, additional treatments needed, increased risk of developing CKD, and reduced quality of life and has a profound economic impact. In the United Kingdom, for example, the annual cost of AKI-related inpatient care in England is estimated at £1.02 billion [5].

Owing to the negative health outcomes and economic drawbacks related to AKI and its treatment, HE evaluation of current and emerging treatment and diagnostic methods is vital, for all the previously aforementioned reasons. Taking into account the latest available clinical evidence and assessing the economic impact of alternatives would allow to make rigorous decision on resource allocation and to fill the adoption gap in a highly resource-consuming scenario.

In this framework, decision analytic and other modelling techniques are useful because the choices concerning

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<td>De Smedt et al. [6], 2012</td>
<td>Treatment modalities in AKI: CRRT vs. IRRT and CONS</td>
<td>CEA (QALYs)</td>
<td>Payer</td>
<td>Yes</td>
<td>CRRT not cost-effective as compared to IRRT. CRRT and IRRT not cost-effective with respect to CONS</td>
</tr>
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<td>Shaw et al. [7], 2011</td>
<td>uNGAL for AKI diagnosis after CS</td>
<td>CEA (QALYs) Decision analysis model</td>
<td>Society</td>
<td>Yes</td>
<td>uNGAL dominates current diagnostic procedures (monitoring of creatinine, blood urea nitrogen, urine output)</td>
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<td>Petrovic et al. [8], 2015</td>
<td>Biomarkers for AKI in pediatric CS</td>
<td>CEA (QALYs) Markov model</td>
<td>Third-party payer</td>
<td>Yes</td>
<td>uNGAL and sCys C dominated strategies compared to uL-FABP. uL-FABP dominating with respect to monitoring SCr</td>
</tr>
<tr>
<td>Mazairac et al. [9], 2013</td>
<td>HDF vs. HD</td>
<td>CUA (QALYs) Markov model</td>
<td>Society</td>
<td>Yes</td>
<td>HDF not cost-effective for patients with end-stage renal disease</td>
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<td>Iannazzo et al. [10], 2014</td>
<td>Intravenous iodinated CM</td>
<td>CEA (LYs) Markov model</td>
<td>Third-party payer</td>
<td>Yes</td>
<td>Iodixanol CM compared with LOCM is associated with better clinical outcomes and average cost savings</td>
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</table>

CRRT = Continuous renal replacement therapy; IRRT = intermittent renal replacement therapy; CONS = conservative treatment; CEA = cost-utility analysis; QALY = quality-adjusted life years; uNGAL = urinary neutrophil gelatinase-associated lipocalin; CS = cardiac surgery; sCys = serum cystatin C; SCr = serum creatinine; HDF = haemodiafiltration; HD = haemodialysis; ICU = intensive care unit; CM = contrast media; LYs = life years; LOCM = low-osmolar CM.
diagnostic methods, surgical procedures, monitoring of patient’s conditions, management and timing of therapies, and alternative approaches including the current diagnostic and treatment standards may have a profound impact on the subsequent evolution of patient’s outcome. Crucial choices that may have downstream consequences are those concerning, for example, contrast media procedures and the choice of the dye, the most appropriate timing of undertaking nephro-protective measures, the application of new diagnostic methods and the employment of novel biomarkers, the use of continuous versus intermittent renal replacement therapies [11–14].

Table 3 reports some of the economic studies conducted in this setting and summarizes they key features and findings.

In the diagnostic realm, new biomarkers that assess the risk for AKI, economic evaluation and HTA are likely to provide vital information to key decision makers and stakeholders, since initial investments and costs are more than likely to be offset by downstream savings due to improved health outcomes and reduced need for expensive medical services [15–21]. In general, new technologies are perceived to be expensive and, when resources of the healthcare system are scarce, there exists the risk of forgoing new investments. This has been the case for several new technologies in nephrology and intensive care in the past [22]. However, this perception is often skewed towards the present, when the initial outlays must be made and against the future, when the savings and the benefits are usually realized. In addition, when one considers cost effectiveness and the inherent assessment of overall ‘value’, improved health benefits may further justify the additional costs. Furthermore, it is entirely likely that new therapeutic and diagnostic interventions are economically ‘dominant’, in that improved benefits are procured with lower resource outlays [12–14, 23–28].

In conclusion, HE seems to be a powerful tool to help in the decision-making process, as it provides a quantitative metric regarding economic evidence on the economic in conjunction with clinical outcomes.

References

3. Heyland DK, Gafni A, Kerner P, Keenan AKI The Imperative for HE Assessment in AKI.


