Basic Principles of Health Economics Applied – How to Assess if Transcatheter Aortic Valve Implantation is Worth the Investment

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Abstract

This article attempts to present some highlights from the rich economic literature pertaining to interventional cardiology and transcatheter aortic valve implantation (TAVI). There are currently more questions than answers, not surprisingly given the pace of technological change in interventional cardiology. For clinicians who work in a strictly regulated environment and have limited control over their use of medical technologies, this article will hopefully shed some light on the motives for policy decisions. For clinicians who make decisions on the resources used to treat their patients, it aims to provide the means of looking for evidence that will allow for informed decisions from both clinical and economic perspectives.

Keywords

Health economics, economic evaluation, cost-effectiveness, transcatheter aortic valve implantation

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A Primer on Health Economics

The objective of this technical paper is to provide a user-friendly primer on economic evaluation applied to aortic valve replacement. We will firstly present the general concepts of economic evaluation with a specific focus on the reasons why the results of academic research may not be relevant to the physicians in charge of managing a department or to hospital directors, and secondly illustrate those concepts with the practical example of transcatheter aortic valve implantation (TAVI).

As cardiovascular diseases are a leading cause of mortality and make up around 10 % of total health expenditures in developed countries, any change in practice has an effect on medical expenditures. This explains the scrutiny to which interventional cardiology has been subjected, first on coronary interventions and later on the use of TAVI, which led in turn to questions about the effectiveness of this additional spending at the population level.

The general purpose of an economic evaluation in the field of healthcare is to relate the costs of a diagnostic or therapeutic strategy to its outcomes. The two components of the evaluation are thus a measure of effectiveness and an estimate of costs. Economic evaluation is currently both a decision tool and an evolving academic discipline.

The comparison of medical strategies that both use different resources and yield different outcomes requires a comparative approach on two criteria – the costs and the medical outcomes. Cost-effectiveness analyses compare strategies with costs expressed in monetary terms

and outcomes expressed in a single medical unit; for example, lives saved, life years, or quality-adjusted life years (QALY). The latter takes into account the value that people would assign to a period of time lived in a certain condition (e.g. with the effects of a stroke). The final result of a cost-effectiveness analysis is often expressed as a ratio of cost to life years gained or cost to lives saved (termed incremental cost-effectiveness ratio [ICER]). A positive result means that the increase in costs results in a better medical outcome. The lower the cost-effectiveness ratio, the more efficient is the strategy.

Comparing any two strategies yields one of the following four situations:

- In very simple cases, the strategy of interest scores better on both outcome and cost, i.e. yields greater effectiveness at lower cost than the other strategy, it is superior (dominant).
- If the strategy of interest yields lower effectiveness at higher cost, it is inferior (dominated).
- If it yields greater effectiveness at higher cost, we need to decide whether the incremental costs are worth paying compared to the effectiveness gained.
- If it yields lower effectiveness at lower cost we need to decide whether the achieved cost-savings are justified compared to the effectiveness lost.

In the case of the first two situations the decision is straightforward. In the last two situations a trade-off needs to be made between costs and effectiveness and strategies to be compared based on the cost-effectiveness ratio.¹

Figure 1: The Cost-effectiveness Plane Used to Propose Recommendations on the Adoption of New Technologies Based on Their Effectiveness and Their Costs Relative to the Reference Strategy

Grades of recommendation: Grade A technologies should clearly be introduced or continued, and grade E technologies should not be introduced or should be abandoned. Technologies in the upper right quadrant are more effective and more costly than their alternatives, whereas those in the lower left quadrant are less effective and less costly. Introduction of technologies in the upper right quadrant and abandonment of the technologies with the same shading in the lower left quadrant lead to similar degrees of cost-effectiveness. QALY = quality-adjusted life years. Reproduced from Laupacis, et al., 1992.¹

Table 1: Grades of Recommendation for the Adoption and Appropriate Utilisation of New Technologies

A.	Compelling evidence for adoption and appropriate utilisation The new technology is as effective as or more effective than the existing one and is less costly
B.	Strong evidence for adoption and appropriate utilisation a) The new technology is more effective than the existing one and costs less than US\$20,000/QALY gained b) The new technology is less effective than the existing one, but its introduction would save more than US\$100,000/QALY gained
C.	Moderate evidence for adoption and appropriate utilisation a) The new technology is more effective than the existing one and costs US\$20,000 to US\$100,000/QALY gained b) The new technology is less effective than the existing one, but its introduction would save US\$20,000 to US\$100,000/QALY gained
D.	Weak evidence for adoption and appropriate utilisation a) The new technology is more effective than the existing one and costs more than US\$100,000/QALY gained b) The new technology is less effective than the existing one, but its introduction would save less than US\$20,000/QALY gained
E.	Compelling evidence for rejection The new technology is less effective than or as effective as the existing one and is more costly

QALY = quality-adjusted life year. Table 1 is a companion of Figure 1 and reproduced from Laupacis, et al., 1992.¹

Figure 1, completed by the explanatory Table 1, depicts the cost-effectiveness plane with each of the four situations. This representation is commonly used to assess innovations in interventional cardiology. The cost-effectiveness plane is used to propose recommendations on the adoption of new technologies based on their effectiveness and their costs relative to the reference strategy.

What is the correct amount of money that a society should pay to prolong the life expectancy of one person by one year? Some countries have set an explicit threshold, others not. In 2003 the World Health Organization suggested that this threshold should be based on the per capita country gross domestic product (GDP). An intervention that prolongs life by one year at a cost <1 times per capita GDP is 'cheap' and a strategy that prolongs life by one year at a cost >3–5 times per capita GDP is 'expensive or even too expensive'. In the UK the threshold usually mentioned is £30,000 or US\$50,000 as shown in Figure 1.²

Other countries, such as the US, do not use such thresholds on the grounds that they result in discrimination between populations. However, there is a general consensus that cost information is important to inform comparative effectiveness research for policy decisions.³

This cost-effectiveness plane is widely used to study innovations in interventional cardiology, as shown in the next part of this chapter. The discussion on threshold for the adoption of technologies has been made more scientific by efforts to quantify uncertainty. Uncertainty concerns both the medical result (e.g. reduction of mortality or major adverse cardiac events) as well as the resources used (and possibly their costs). It is now common for economic evaluations of coronary intervention to use more sophisticated representations of uncertainty. Bootstrap replications, for example, show 1,000 possible ICERs, each obtained by taking a random effectiveness result and dividing it by a random cost result both chosen within a specified range.

Figure 2 shows the cost-effectiveness plane on which the difference in QALY and costs of TAVI versus surgical valve or standard treatment in high-risk patients has been materialised by 1,000 dots, each one representing a possible result, given the uncertainty in the Placement of AoRTic TraNscatheter Valves (PARTNER) trial results. On this graph, drawn from the trial results, TAVI appears to provide better outcomes at higher cost. The QALY benefit in favour of TAVI is shown by the fact that most simulations are on the right-hand side of the plane.⁴

It is possible to translate the uncertainty scatter plot into a more readable decision tool, known as the acceptability curve. To build the acceptability curve, the software counts how many dots are below a given cost-effectiveness threshold and produces a probability. An example of an acceptability curve is shown in the left part of Figure 2. In this case, there is a 70 % chance that TAVI is more cost-effective than standard treatment if the decision-maker (e.g. the government or Ministry of Health) accepts to pay over €60,000 to save one additional year of life in good health. If the decision-maker agrees to spend only approximately €40,000 to save one additional year of life in good health, both treatments are equivalent.⁴

An article on health economics would be incomplete if it left the reader with the impression that policy decisions result from the calculations described above. The framework for the analysis of how policy-makers use the information provided by health professionals or health economists is provided by Goddard et al. in their article on 'priority setting in health'.⁵ The world of healthcare delivery is not limited to clinicians and economists; it includes other stakeholders such as politicians, payers, interest groups and the industry. Public and professional institutions seek to maximise their power and influence in the healthcare sector, and policy-makers seek to maximise their political support. Consumers (patients) are utility-maximising and

Figure 2: Cost-effectiveness Plane (Left) and Cost-effectiveness Acceptability Curve (Right) for Transcatheter Aortic Valve Implantation in Inoperable Patients

A practical illustration of the cost-effectiveness plane: the costs and survival of patients randomised to TAVI or surgery/standard care are compared using a simulation model. The uncertainty in the difference between the cost and the gain in life years is represented by dots, which result from replications. Below is the acceptability curve of the use of TAVI instead of surgery or standard care. The X axis is the estimated cost-effectiveness ratio (in euros, to gain one additional year in good health) and the Y axis the probability that the real ratio is above the estimated value. QALY = quality-adjusted life years; TAVI = transcatheter aortic valve implantation. Graph reproduced from Neyt, et al., 2012.⁴

healthcare providers (in the private sector) are profit-maximising. With this in mind, the processes of organisation and delivery of health services and technologies appear more complex than the application of the results of economic evaluations would predict.

Politicians select programmes that maximise votes or that minimise their personal or corporate risk of liability. They prioritise implementation of technologies that benefit a large share of the population (or the population whose support is most important for politicians). Patient interest groups will support the technologies that benefit their members and increase their legitimacy as patient advocates. This latter point implies that interest groups will also seek to expand the use of technologies to the largest possible population rather than to a selected group; often with the support of the industry, which thus increases its market share. Interest groups will also make use of the policy-makers' concern for political support and render politically dangerous the denial of services. This is possible when the population concerned is very large, such as patients at risk for heart disease.

Hospital managers may not see the greater benefit of a new technology when it falls outside the perimeter of their hospital. For example, the cost computations described above use the academic guidelines, which mandate the estimation of costs from the viewpoint of the producer (e.g. the healthcare systems as a whole).⁶ This method of computation is not what managers have in mind because it aggregates resources within and outside the hospital and ignores financial incentives such as tariffs, fees and reimbursement. If the cost of TAVI is included in a diagnosis-related group (DRG), a high-volume hospital may negotiate discounts and therefore make a profit if ultimately the DRG reimbursement is higher than the cost of purchasing and implanting the TAVI. However, if the TAVI is reimbursed on top of a DRG at a national price including the discount, the incentive to perform TAVI may become negative. In a similar manner, the use of drug-eluting stents that reduce the risk of repeat stenosis may ultimately reduce healthcare costs for the system but not for the hospital, which is accountable for the revenues and expenditures related to each intervention.

Cost-effectiveness of Transcatheter Aortic Valve Implantation – What is the Evidence?

In order to apply the concepts presented above to TAVI, it is useful to distinguish four different types of data sources available to guide medical and economic decision-making:

- clinical data;
- cost data;
- cost-effectiveness analysis with primary patient data; and
- health economic modelling.

We will briefly review the evidence for TAVI in these categories using a selection of the current literature and then discuss some related caveats.

Clinical Data

Most of the clinical evidence currently available on TAVI is drawn from national or trans-national registries such as French Aortic National CoreValve and Edwards (FRANCE), PARTNER EU or Edwards SAPIEN Aortic Bioprosthesis European Outcome (SOURCE), which suggest that TAVI is a safe and clinically effective intervention.⁷⁻⁹ To date, a single randomised controlled trial (RCT) has demonstrated that TAVI is a clinically effective intervention – the PARTNER trial, led in the US.¹⁰ One-year mortality outcomes in the PARTNER trial showed that TAVI was non-inferior to surgical aortic valve replacement (SAVR) in patients who were eligible for SAVR (cohort A), and superior to the standard treatment in patients who were ineligible for SAVR (cohort B). The findings of the two-year follow-up with respect to mortality and adverse events were consistent with those of the one-year follow-up.^{11,12} TAVI was also associated with improvement in quality of life, although results varied by cohort.¹³

Cost Data

Alongside some of the above-mentioned studies, data on cost have been collected and analysed. Costing studies are generally descriptive and aim at informing about the exact cost that an innovation incurs for a specific type of payer. The latter can be a hospital, health insurance or the patient, and the results of a costing study can vary greatly depending on the perspective taken. In France, for instance, the mean initial hospital

Table 2: A Selection of the Literature Reporting Cost-effectiveness Data for Transcatheter Aortic Valve Implantation in Inoperable Patients

Year of Publication	Type of Analysis	Payer Perspective	Interventions Studied	ICER Reported	ICER in US\$ (2010)*	Source
2012	Cost-effectiveness analysis with primary patient data	US healthcare system	TAVI versus standard care	US\$50,200/LYG US\$61,900/QALY	US\$50,200/LYG US\$61,900/QALY	¹⁵
2012	Health economic modelling	US healthcare system	TAVI versus standard care TAVI versus SAVR	US\$40,000/QALY US\$53,000/QALY	US\$39,200/QALY US\$51,900/QALY	¹⁷
2012	Health economic modelling	Belgian public healthcare payer and patient payments	TAVI versus standard care TAVI versus SAVR	€42,600/LYG €45,000/QALY €750,000/QALY	US\$49,300/LYG US\$52,100/QALY US\$868,100/QALY	⁴
2012	Health economic modelling	UK national health service (NHS)	TAVI versus standard care	£16,000/QALY	US\$24,000/QALY	¹⁸
2013	Health economic modelling	Canadian health care system	TAVI versus standard care TAVI versus SAVR	US\$36,000/LYG US\$51,000/QALY US\$870,000/LYG and TAVI dominated for QALY	US\$29,500/LYG US\$41,800/QALY US\$713,600/LYG and TAVI dominated for QALY	¹⁹
2013	Health economic modelling	UK NHS	TAVI versus SAVR	TAVI dominates for LYG and QALY	TAVI dominates for LYG and QALY	¹⁶

ICER = incremental cost-effectiveness ratio; LYG = life year gained; QALY = quality-adjusted life year; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation.
* Conversion of costs by currency and year performed using <http://epi.ioe.ac.uk/costconversion/default.aspx>.

stay cost related to TAVI was €35,164 (US\$40,619) to the hospital, based on the materials, human resources and overhead costs incurred by 287 patients of a national registry in 2009.¹⁴ Using a similar approach, patients in the PARTNER B cohort were reported to incur a cost of US\$78,542 to the hospital in 2010.¹⁵ The authors of the French study further reported that since August 2012 (taking into account a decrease in hospital cost over time), the mean tariff for a TAVI hospital stay is €3,000 (US\$3,500) below the cost to the hospital, which means that there is a gap between the cost incurred by the hospital and the reimbursement obtained.

Cost-Effectiveness Analysis with Primary Patient Data

The only study designed to compare clinical and economic data between patients receiving TAVI, surgical replacement or standard medical care to date is the PARTNER trial, and cost-effectiveness results are only published on the cohort B, comparing TAVI with standard care in inoperable patients. Projecting costs and gains over a patient's lifetime, the authors reported an incremental cost-effectiveness ratio for TAVI of US\$50,200 per year of life gained or US\$61,889 per QALY gained.¹⁵

Health Economic Modelling

When no primary, comparative patient data are collected, modelling provides a way by which cost-effectiveness can be estimated for a given context (e.g. age groups or health systems). This is generally done by simulating the events (adverse events, death) occurring in a virtual cohort of patients, drawing on data from the literature (e.g. on survival probabilities, changes in quality of life after adverse events, etc.). The available studies using modelling techniques seem to converge at the conclusion that TAVI is favourable in inoperable patients when compared with standard medical care. However, when comparing TAVI and SAVR, results differ largely, for instance between a study in the National Health Service (NHS) context reporting TAVI to be dominant¹⁶ and a Belgian study finding an ICER of €750,000 (US\$868,100) per QALY⁴ (see Table 2).

What Caveats Should be Kept in Mind?

The particularity of the current evidence on TAVI stems from the fact that almost every economic evaluation bases at least a part of its analyses on the sample of 358 patients in the PARTNER cohort B, of

whom only 65 % consented to the collection of hospital billing data and all of whom (in the intervention group) received a valve from a single manufacturer.¹⁵ This seems to be a slim basis for drawing final conclusions on the cost-effectiveness of TAVI. In the following section, we will briefly review some further implications in terms of:

- the patient population;
- the health system context; and
- methodological choices, all of which are closely interrelated.

Firstly, most studies report on TAVI in a selective population of severely ill patients, either in the scope of the PARTNER trial or of registries. Yet, a main question for clinicians and payers is whether it may be worthwhile to extend the application of TAVI to less severe patients. Partly addressing this question, a recent study by Canadian colleagues reported an ICER of CA\$51,000 (US\$41,800) per QALY gained for inoperable patients (TAVI versus standard care) while TAVI (versus SAVR) was found to be dominated for operable patients.¹⁹ This implies that TAVI may be less cost-effective in patients in less severe condition. However, since no patient-based evaluation was explicitly designed to answer the question, the currently available evidence can only provide indications about the cost-effectiveness in a wider patient population.

Secondly, differences in health system and population characteristics are often considerable and may for instance concern unit costs or the baseline prevalence and incidence of cardiovascular diseases. An illustration is the difference in TAVI procedure cost, which was reported to be US\$1,530/hour in the PARTNER trial and only £524/hour (US\$785) in a UK analysis.^{15,18} Such variation may in part explain the differences in the reported ICER and are most likely rooted in distinct payment and organisational arrangements, besides potential differences in the calculation method. Therefore, the country in which a study has been conducted must always be considered when judging and comparing cost-effectiveness results.

Finally, the variation in results of the presented studies may in part be due to assumptions and methodological choices made in the process of health economic modelling. For instance, the study of Neyt and colleagues

simulated the outcomes of their patient cohort (TAVI versus SAVR) over the period of only one year (based on the rationale that there was no significant survival difference in the PARTNER trial for these patients), leading to an ICER of €750,000/QALY (US\$868,100).⁴ Conversely, Gada and colleagues modelled the outcomes in their analysis over the lifetime of the patients and found an ICER of US\$53,000/QALY.¹⁷ Other choices to be made for such types of modelling analyses include what events will be considered in the follow-up (e.g. stroke, re-hospitalisations) and how quality of life will be taken into account. It is important to be aware that such assumptions always have to be made in modelling analyses, which is why it is worthwhile to carefully read the methods section of a publication before interpreting the results.

Conclusion

This article has attempted to present some highlights from the rich economic literature pertaining to interventional cardiology and TAVI. There are currently more questions than answers, not surprisingly given the pace of technological change in interventional cardiology. For clinicians who work in a strictly regulated environment and have limited control over their use of medical technologies, this article will hopefully shed some light on the motives for policy decisions. For clinicians who make decisions on the resources used to treat their patients, we have aimed to provide the means of looking for evidence that will allow for informed decisions from both clinical and economic perspectives. ■

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