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Tools and Techniques - Statistics: Comments on a cost-effectiveness study of TAVI for patients with inoperable aortic stenosis

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Introduction

A cost-effectiveness analysis (CEA) of a medicine or medical device is one of the bridges between clinical decision making and policy making. This paper highlights important aspects of a CEA by considering how Reynolds et al estimated the cost-effectiveness of transcatheter aortic valve implantation (TAVI) versus standard non-surgical therapy for patients with inoperable aortic stenosis (AS)[1].

PICO

The PICO (population, intervention, comparator, outcome) concept used in assessing the quality of effectiveness studies can also be applied in CEAs. The first three elements are clear from the study design: Reynolds et al used the PARTNER study, a randomised controlled trial (RCT) of TAVI in two populations, one of which was "inoperable" patients, who underwent TAVI or standard non-surgical therapy[2-4]. Finally, this CEA has multiple outcomes (costs, life expectancy and quality of life) although cost-effectiveness is the primary one.

Costs

Costs are calculated by combining resource use (e.g., number of hospital days) and unit costs (e.g., cost per day). Reynolds reported these elements separately, which helps when judging the quality and generalisability of a CEA; poorer CEAs generally have limited documentation. The cost difference in the first year was approximately $50,000, slightly more than the costs of TAVI.

Quality of life and QALYs

Quality of life (QOL) in the PARTNER trial was measured using the EQ-5D (range: –0.109, 1). Mean QOL ("utility") scores were 0.59 (TAVI) versus 0.57 (standard therapy). QOL scores are combined with survival to form quality-adjusted life-years (QALYs). With assumptions, TAVI patients had 0.70 QALYs in the first year and patients with standard therapy had 0.61 QALYs (difference: 0.09 QALYs).

Extrapolation beyond the first year

Differences in survival and QOL after the first year, plus the fact that many patients were still alive at the end of follow-up, were compelling reasons to extrapolate into the future. However, this presents an important dilemma. Should a CEA only focus on what was observed during the study or should it include what might happen beyond follow-up? A CEA based only on observed results is attractive but probably underestimates the cost-effectiveness of TAVI. However, an

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analysis using extrapolated results requires various assumptions which may not be valid. The authors Reynolds et al used statistical measures to decide which extrapolation approach best fitted the observed data and estimated the total life expectancy following TAVI to be 3.1 years versus 1.2 years for standard therapy.

Discounting

Discounting refers to the conversion of future costs and effects (i.e., health) into their net present value. Reynolds used the most common discount rate of 3% for both costs and effectiveness. In many cases, discounting does not influence the results, but it all depends on the timing of costs and health.

Cost-effectiveness

Reynolds found that TAVI increases both costs ($79,837, discounted) and life expectancy (1.6 years) versus standard therapy. By dividing costs by life expectancy, we conclude that TAVI use is associated with an additional $50,212 per life-year gained: this is referred to as the incremental cost-effectiveness ratio (ICER). The extra cost to gain one QALY is $61,889.

Uncertainty

All estimates of effectiveness and cost-effectiveness are just that: estimates. So how much uncertainty is there surrounding these estimates? Sensitivity analysis is a common way to answer this and Reynolds et al used two types. First, they performed one-way sensitivity analyses, varying input parameters one by one to see how they affected the results. The biggest effect was seen when effectiveness was measured in QALYs versus life expectancy. This is understandable since improvement in QOL is much smaller than a life-death distinction. The costs of "non-cardiovascular events" also affected the ICER; excluding them reduced the ICER to $33,860 per life-year gained. One likely explanation: TAVI increases life expectancy and a longer life is associated with greater healthcare costs.

Reynolds et al also performed a probabilistic sensitivity analysis. They created 5,000 populations to derive 5,000 estimates of the differences in costs and life expectancy and found a range in incremental life expectancy of approximately 1.1 to 2.3 years, a range in incremental costs of $60,000 to $100,000 and a range in ICER of approximately $40,000 to $60,000.

Conclusions

Reynolds et al estimated the ICER for TAVI versus standard therapy at about $50,000 per life-year gained ($62,000 per QALY gained). They concluded that TAVI is cost-effective, arguing that thresholds are often far above $50,000 and that widely used cardiovascular technologies such as ICD have similar ICERs. However, no cut-and-dried answer is available here. Cost-effectiveness is just one of the factors considered in reimbursement decisions.

Quality and transferability

One needs to consider both quality and transferability/relevance of a CEA. The quality of the study by Reynolds appears good, but it is clear that the study may have limited relevance to other settings. For example, Reynolds et al used the perspective of the US healthcare system. This perspective means that all costs incurred within the healthcare sector are included and that these costs should reflect actual costs. Use of a payer perspective means costs should be based on tariffs (which may differ from actual costs). This study may therefore be of limited relevance for American third party payers. More importantly, this study may be even less relevant for decision makers in other countries because of important differences between countries (e.g., costs, quality of care). Ultimately, each CEA is unique and even CEAs using the same RCT may differ; the same PARTNER trial was applied in various CEAs that yielded different estimates of the cost-effectiveness of TAVI **(Table 1)**. Possible reasons include different study designs, different cost calculation methods, different QOL/QALY calculation methods, and different extrapolation methods.

Conclusion

Insight into the strengths and weaknesses of CEAs is best gained by studying CEAs of a familiar treatment and slowly learning the different elements. Space limitations preclude a detailed discussion of relevant issues. More details can be found in the online document; various articles and books provide good general

Table 1. Comparison of cost-effectiveness studies examining TAVI for inoperable aortic stenosis patients.

		Effectiveness (quality-adjusted life-years, QALYs)			Effectiveness (life-years)			Costs			Incremental cost-effectiveness ratio
		TAVI	Standard therapy	Difference	TAVI	Standard therapy	Difference	TAVI	Standard therapy	Difference	
USA	Reynolds[1]	2.03	0.73	1.30	2.78	1.20	1.58	$149,740	$69,903	$79,837	$61,413
USA	Simons[9]	1.93	1.19	0.74	2.93	2.08	0.85	$169,100	$83,600	$85,500	$115,541
Belgium	Neyt[10]	not reported	not reported	0.74	not reported	not reported	0.88	not reported	not reported	€33,243	€44,923
Canada	Sehatzadeh[11]	1.80	1.16	0.64	2.71	1.72	0.99	$79,755	$48,552	$31,203	$48,908
UK	Murphy[12]	1.63	1.19	0.44	2.54	2.24	0.30	£28,016	£12,176	£15,885	£36,102
UK	Watt[13]	2.36	0.80	1.56	not reported	not reported	not reported	£30,200	£5,000	£25,200	£16,154

information about CEAs[5,6]. An understanding of CEAs is one step toward the ability to judge the quality and relevance of CEAs. Checklists like those by Drummond help the reader conduct a critical appraisal of a CEA, while transferability checklists help to judge their transferability[7,8].

Conflict of interest statement

The author has no conflicts of interest to declare.

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