Reply to the Editor:

All properly conducted model-based economic evaluations should be a synthesis of best available evidence. It is important to note that economic models need to be updated once new evidence is available. The methods and assumptions used in our economic evaluation on transcatheter aortic valve implantation (TAVI) were appropriate because the evaluation was based on the best evidence available at the time of the analyses. Nevertheless, evidence on TAVI has grown rapidly in the past 2 years. We appreciate the comments raised by Osnabrugge and Kappetein and agree that a reexamination of the model with the new evidence is warranted.

Our analysis of TAVI compared with surgical aortic valve replacement (SAVR) grouped the patients undergoing transfemoral (TF) or transapical (TA) approach into 1 treatment arm. The reported clinical data from the Placement of Aortic Transcatheter Valve (PARTNER) cohort A also grouped these 2 different TAVI approaches to show the noninferiority of TAVI in terms of 1-year mortality. This was based on a sample size calculation of 650 patients at approximately 85% power.¹ The stratified clinical event rates provided in the Supplementary Appendix were not appropriate to use because of the lack of statistical power. It was estimated that 450 patients would need to undergo TF placement to show noninferiority of TAVI compared with SAVR at 85% power; however, only 244 patients were assigned to TF placement in the trial. It was therefore necessary to use utility values derived from the New York Heart Association functional classes, because this was the only relevant source that provided data for a similar patient population (ie, patients undergoing TF and TA grouped together). Now that the full details of the PARTNER cohort A quality of life study are available,² we have imputed these EQ-5D utility

values into our analysis (Table 1). TAVI was dominated by SAVR when using these EQ-5D utility values observed in both the TF and TA arms. TF compared with SAVR had an incremental cost-effectiveness ratio of \$67,934/quality-adjusted life year (QALY) when the difference in utility values at years 2 to 20 of the model was assumed to be 0.09 in favor of TF.

The evidence on the long-term survival of patients undergoing TAVI is not available. Therefore, in the model, we directly used the mortality observed in the PARTNER trial for the first year and the mortality of the general public for the subsequent years. However, this approach does not imply that the survivals predicted by the model are comparable to those of the general public as argued by Osnabrugge and Kappetein. There were other mortalities caused by stroke, myocardial infarction, and acute kidney injury considered throughout the time horizon. We believe this is a reasonable approach to predict the survivals for the patient population. Of note, this base-case analysis was also supplemented by the scenario analyses with different mortality assumptions. As suggested by Osnabrugge and Kappetein, the use of survival functions to fit patient-level data is another approach. This approach is obviously conditional on the access to patient-level data and is also subject to criticism. If there was any mortality benefit from TAVI observed at the end of the trial, the use of fitted survival functions is likely to enlarge the difference in favor of TAVI.³

Osnabrugge and Kappetein also were concerned about some resource use and cost inputs in the model. To address these concerns, we updated our 1-way sensitivity analyses (Table 1). Increasing the cost of balloon valvuloplasty improved the cost-effectiveness of TAVI, whereas changes in the length of hospital stay after SAVR had no impact. At high SAVR procedural costs or lower

TAVI valve costs, TAVI gained less QALYs at lower costs compared with SAVR. The short-term probability of acute kidney injury was incorrectly listed in Table 1 of our original article, and the correct value of .011 was used in our model.

The trial-based economic evaluation by the PARTNER investigators used patient-level data to estimate the cost-effectiveness of TAVR compared with standard therapy from a US perspective.⁴ Detailed costing was performed at an individual level using hospital-billing data. This is in contrast to the estimation of costs in our model, which were mainly based on average costs of long-term complication health states and may account for the difference in lifetime costs observed (incremental cost of \$79,837 and \$31,029, respectively). Larger values for incremental life-years (LYs) and QALYs (1.6 LYs and 1.3 QALYs compared with 0.9 LYs and 0.6 QALYs in our analysis) can be accounted for by the use of exponential models for survival extrapolation and a lower discount rate of 3% compared with 5% used in our model. Consequently, overall results were more favorable in our analysis with a reported incremental cost-effectiveness ratio of \$51,324/QALY compared with \$61,889/QALY in the trial-based analysis.

A comparison of the results from our cohort A analysis and that presented by Reynolds⁵ at the TransCatheter Therapeutic conference is limited by the fact that the analysis by Reynolds was a trial-based approach using only 12 months follow-up and thus may not have captured all of the long-term costs and benefits of TAVR and SAVR. It will be important for Reynolds to model the lifetime effects of these 2 comparators to obtain more reliable estimates of cost-effectiveness.

Despite extensive review by an expert advisory panel and subsequent approval by the Food and Drug Administration, the appropriate use

TABLE 1. One-way sensitivity analysis of various model parameters

	TAVI vs SAVR	TAVI vs SM
PARTNER EQ-5D values		
Base case (NYHA converted to EQ-5D utilities)	Dominated	\$51,324/QALY
EQ-5D utilities from the TF arm	Dominated*	\$46,701/QALY†
EQ-5D utilities from the TF arm (assume 0.03 difference at ≥ 2 y)	\$13,031,292/QALY	NA
EQ-5D utilities from the TF arm (assume 0.06 difference at ≥ 2 y)	\$135,163/QALY	NA
EQ-5D utilities from the TF arm (assume 0.09 difference at ≥ 2 y)	\$67,934/QALY	NA
EQ-5D utilities from the TA arm	Dominated	NA
Cost of balloon valvuloplasty		
Base case (\$29,600)	NA	\$51,324/QALY
\$15,000	NA	\$75,473/QALY
\$20,000	NA	\$67,203/QALY
\$25,000	NA	\$58,933/QALY
\$30,000	NA	\$50,662/QALY
\$35,000	NA	\$42,392/QALY
\$40,000	NA	\$34,121/QALY
Length of stay after SAVR		
Base case (36 d)	Dominated	NA
10 d	Dominated	NA
15 d	Dominated	NA
20 d	Dominated	NA
25 d	Dominated	NA
30 d	Dominated	NA
35 d	Dominated	NA
40 d	Dominated	NA
Procedural cost of SAVR		
Base case (\$32,784)	Dominated	NA
\$25,000	Dominated	NA
\$30,000	Dominated	NA
\$35,000	Dominated	NA
\$40,000	Dominated	NA
\$45,000	TAVI costs \$1063 less at 0.102 less QALYs	NA
\$50,000	TAVI costs \$6063 less at 0.102 less QALYs	NA
Cost of TAVR valve		
Base case (\$39,796)	Dominated	\$51,324/QALY
\$15,000	TAVI costs \$13,642 less at 0.102 less QALYs	\$10,310/QALY
\$20,000	TAVI costs \$8642 less at 0.102 less QALYs	\$18,580/QALY
\$25,000	TAVI costs \$3642 less at 0.102 less QALYs	\$26,851/QALY
\$30,000	Dominated	\$35,121/QALY
\$35,000	Dominated	\$43,391/QALY
\$40,000	Dominated	\$51,662/QALY
\$45,000	Dominated	\$59,932/QALY

NA, Not available; NYHA, New York Heart Association; PARTNER, Placement of Aortic Transcatheter Valve; QALY, quality-adjusted life year; SAVR, surgical aortic valve replacement; SM, standard management; TA, transapical; TAVI, transcatheter aortic valve implantation; TF, transfemoral. *Difference in EQ-5D utility score at 1 year was equal to 0.01 as reported by Reynolds et al.² †Utilities values for TF placement in inoperable patients obtained from Neyt and Van Brabandt.³

of the SAPIEN (Edwards Lifesciences, Irvine, Calif) heart valve for high-risk operable patients remains uncertain. Unfortunately, uncertainty surrounding the benefits and risks of TAVI largely affects estimates of the incremental cost-effectiveness. Although recently available evidence has shed some light, uncertainty still remains significant.

Brett Doble, MSc^a

Feng Xie, PhD^{b,c}

^aCentre for Health Economics
Faculty of Business and Economics
Monash University

Clayton, Victoria, Australia

^bDepartment of Clinical
Epidemiology and Biostatistics
McMaster University

Hamilton, Ontario, Canada

^cPrograms for Assessment of
Technology In Health Research
Institute

St Joseph's Healthcare Hamilton
Hamilton, Ontario, Canada

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