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ORIGINAL RESEARCH

Financial Incentives for Transcatheter Aortic Valve Implantation in Ontario, Canada: A Cost-Utility Analysis

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BACKGROUND: Transcatheter aortic valve implantation (TAVI) is a minimally invasive therapy for patients with severe aortic stenosis, which has become standard of care. The objective of this study was to determine the maximum cost-effective investment in TAVI care that should be made at a health system level to meet quality indicator goals.

METHODS AND RESULTS: We performed a cost-utility analysis using probabilistic patient-level simulation of TAVI care from the Ontario, Canada, Ministry of Health perspective. Costs and health utilities were accrued over a 2-year time horizon. We created 4 hypothetical strategies that represented TAVI care meeting ≥1 quality indicator targets, (1) reduced wait times, (2) reduced hospital length of stay, (3) reduced pacemaker use, and (4) combined strategy, and compared these with current TAVI care. Per-person costs, quality-adjusted life years, and clinical outcomes were estimated by the model. Using these, incremental net monetary benefits were calculated for each strategy at different cost-effectiveness thresholds between $0 and $100 000 per quality-adjusted life year. Clinical improvements over the current practice were estimated with all comparator strategies. In Ontario, achieving quality indicator benchmarks could avoid ≈26 wait-list deaths and 200 wait-list hospitalizations annually. Compared with current TAVI care, the incremental net monetary benefit for this strategy varied from $10 765 (±$8721) and $17 221 (±$8977). This would translate to an annual investment of between ≈$14 to ≈$22 million by the Ontario Ministry of Health to incentivize these performance measures being cost-effective.

CONCLUSIONS: This study has quantified the modest annual investment required and substantial clinical benefit of meeting improvement goals in TAVI care.

Key Words: aortic valve stenosis ■ cost-benefit analysis ■ health care costs ■ heart valve prosthesis implantation ■ quality improvement ■ quality indicators ■ transcatheter aortic valve replacement

Aortic stenosis is the most common valvular heart disease in adults and is an increasing worldwide health and economic burden.[1] Mortality from severe aortic stenosis approaches 50% within 2 years of symptom onset without treatment.[2] Transcatheter aortic valve implantation (TAVI) is a minimally invasive alternative to surgical valve replacement. TAVI is strongly recommended for patients with severe symptomatic aortic stenosis at high or prohibitive surgical risk and is increasingly considered for patients at intermediate to low risk of perioperative mortality.[3–5]

Access to TAVI in Canada is limited to a small number of centers that have the infrastructure, funding, and expertise to offer the procedure.[6] In Ontario, Canada, growing demand for TAVI has outpaced system capacity and affected the standard of care.[7,8] Presently, TAVI care in Ontario fails to meet the Canadian Cardiovascular

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CLINICAL PERSPECTIVE

What Is New?

- A novel application of cost-effectiveness analysis methods was used to determine the maximum cost-effective investment in transcatheter aortic valve implantation care that should be made at a health system level to meet quality performance targets.
- Between ≈$14 to ≈$22 million can be invested cost-effectively by the Ontario, Canada, Ministry of Health to meet transcatheter aortic valve implantation quality performance targets.

What Are the Clinical Implications?

- In Ontario, achieving quality indicator benchmarks could avoid ≈26 wait-list deaths and 200 wait-list hospitalizations annually.

Nonstandard Abbreviations and Acronyms

CCS	Canadian Cardiovascular Society
INMB	incremental net monetary benefit
TAVI	transcatheter aortic valve implantation

Society (CCS) TAVI quality indicator targets for elective wait times, permanent pacemaker implantation, and length of stay (LOS).[6–10] Unacceptably long wait times have been associated with worse functional capacity, lower quality of life, impaired postprocedural recovery, and higher mortality.[11–14] High incidence of permanent pacemaker implantation during the index hospitalization has been associated with worse postprocedural outcomes.[6,15] Shorter LOS has been associated with clinical benefits and lower costs.[6,9,16] Given the importance of these metrics, additional resources are required to meet CCS quality indicator targets. However, it remains unclear what financial resources can justifiably be dedicated toward meeting these benchmarks.

The question of how to determine the upper limit of acceptable, cost-effective investment in quality-improvement programs is a relatively recent application of cost-effectiveness frameworks.[17] Rather than comparative economic evaluation typical of this method, this application compares standard care with a hypothetical scenario in which the proposed quality improvements are in place.[17] We sought to use this method to determine the maximum cost-effective investment in TAVI that can be made by the Ontario Ministry of Health to meet quality indicator goals.

METHODS

We performed a cost-utility analysis using a patient-level simulation from the Ontario Ministry of Health perspective. Ontario is Canada's largest province, with a publicly funded single-payer health care system that serves a population of ≈14 million. TAVI has been approved for use in Ontario since 2012 and is currently funded across extreme-, high-, intermediate-, and low-risk populations. We adhered to the Canadian Agency for Drugs and Technologies in Health guidelines for economic evaluations and the Consolidated Health Economic Evaluation Reporting Standards statement.[18,19] As this is a simulation study, ethical approval was not required. The authors declare that all supporting data are available within the article (and its online supplementary files).

Model Structure

A probabilistic discrete-time simulation was performed with 1-week time steps (cycles). The population considered in the model was adults with severe aortic stenosis referred for TAVI in Ontario. Per-person costs, quality-adjusted life years (QALYs), and clinical outcomes were estimated over a 2-year time horizon. We used within-cycle correction to account for biases occurring with discrete time rather than continuous time. Costs and effectiveness were discounted at an annual rate of 1.5%, as per Canadian Agency for Drugs and Technologies in Health recommendations.[18] The model was developed on TreeAge Pro, version 2020.

All patients entered the model in the wait-list state, and were assigned a wait time for elective TAVI from a log-normal time-to-event distribution that resembled wait times in Ontario over the study period.[20] Patients could stay on the wait-list, proceed to elective TAVI, or be hospitalized pre-TAVI (Figure 1). Those hospitalized pre-TAVI could undergo an urgent procedure or be discharged back to the wait-list, where repeated hospitalizations were possible. At the time of TAVI, patients could receive a permanent pacemaker. LOS was assigned from a log-normal distribution resembling current practice and adjusted for TAVI urgency.[21] Intensive care unit (ICU) LOS was estimated as one third of the total LOS, consistent with available data.[22] Patients could stay well or be rehospitalized post-TAVI. At any point in the simulation, patients could die. Undergoing an urgent TAVI, receiving a permanent pacemaker, longer LOS, and prior hospitalization increased the probability of hospitalization or death.

The 2-year time horizon was intentional, as it best approximates the time from referral to 1-year post-TAVI, a time period that has direct health policy relevance.[20,23] In fiscal year 2018/2019, the Ontario Ministry of Health began exploring an alternative funding model in which reimbursement is bundled for the management of patients

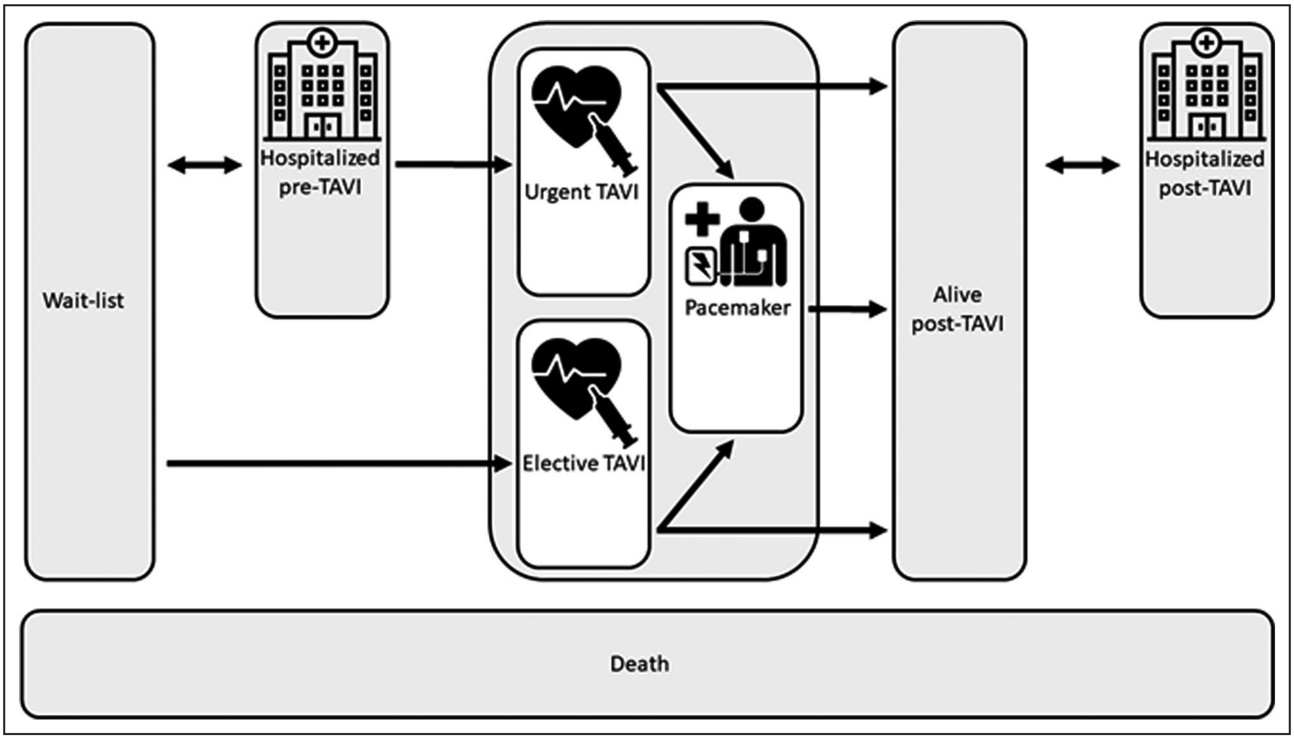

Figure 1. Model schematic.
Patients enter the simulation in the wait-list state, and are assigned a wait time for elective transcatheter aortic valve implantation (TAVI) from a log-normal time-to-event distribution. Patients could stay on the wait-list, proceed to elective TAVI, or be hospitalized pre-TAVI. Those hospitalized pre-TAVI could proceed to urgent TAVI or be discharged back to the wait-list, where repeated hospitalizations were possible. At the time of TAVI, patients could receive a permanent pacemaker. Patients could stay well or be rehospitalized post-TAVI. At any point in the simulation, patients could die.

with aortic stenosis from referral for valve replacement to 1-year postprocedure.[24,25] By modeling the costs and consequences of improved TAVI care within this funding period, the resultant savings represent the maximum cost-effective investment toward quality improvement that can be added to this proposed reimbursement model.

Our probabilistic analysis consisted of a 2-dimensional simulation, in which 1000 first-order (inner loop) Monte Carlo simulations represented individual patient variability and 1000 second-order (outer loop) Monte Carlo simulations accounted for parameter uncertainty. In 2-dimensional simulation, sets of input parameters are drawn from their respective probability distributions as the outer loop, and then inner loop trials of individual simulated patients with unique characteristics are performed using each set of parameters.[26] The process is iterated to produce outcomes with increased precision while allowing for both representation of individual heterogeneity and uncertainty in parameter inputs.[26]

Strategies

We created 4 hypothetical strategies that represented TAVI care meeting ≥1 of the quality indicator targets and compared these with current TAVI care: (1) reduced wait times, (2) decreased hospital LOS, (3) decreased pacemaker use, and (4) a combined strategy. The reference case (standard care) was defined as follows: mean wait time of 19 weeks, mean hospital LOS for TAVI of 2 ICU and 4 ward days, and a 14.7% probability of permanent pacemaker insertion.[15,20,22] These values were drawn from reports of current TAVI care, with values no earlier than from 2017. In the wait-time reduction strategy, in agreement with published benchmarks, mean wait time for elective TAVI was reduced to 10 weeks, with a maximum wait time of 12 weeks, and patients hospitalized on the wait-list underwent TAVI within 2 weeks of discharge if not earlier.[5] Because consensus about targets for TAVI LOS and pacemaker implantation does not yet exist, goals for these performance indicators were estimated, and checked for reasonableness against available literature.[27–29] In the LOS reduction strategy, mean TAVI LOS was one third of the reference case. In the pacemaker reduction strategy, the rate of permanent pacemaker implantation was reduced to 5%. The fourth strategy was a combination of these 3 comparator strategies (Table 1).[24]

Data Sources

Input model parameters were derived from a targeted literature search. Wherever possible, data were derived

Table 1. Details of Reference Case and Comparator Strategies

Strategy	Parameter	Value	Source
Reference case	Median wait times (wk)	19.14	CCS, 2019[6]
	Median LOS after elective TAVI (d)	6	Sud, 2017[21]
	Pacemaker insertion (%)	14.7	Aljabbary, 2018[15]
Reduced wait times	Median wait times (wk)	10	Asgar, 2019[5]
Reduced length of stay	Mean total LOS (d)	2	Expert consultation
Reduced pacemaker use	Pacemaker insertion (%)	5	Expert consultation
All performance measures	Median wait times (wk)	10	Asgar, 2019[5]
	Mean total LOS (d)	2	Expert consultation
	Pacemaker insertion (%)	5	Expert consultation

CCS indicates Canadian Cardiovascular Society; LOS, length of stay; and TAVI, transcatheter aortic valve implantation.

from studies of TAVI in Ontario. Costs, counts, and utilities were sampled from γ, Poisson, and β distributions, respectively. Wait times were modeled as log-normal distributions. Postprocedural hospitalization and mortality were modeled as exponential distributions. Hazard ratios (HRs), count ratios, and risk ratios were sampled from γ distributions. Table 2 summarizes all the parameters used in the model. All costs were adjusted to 2019 Canadian dollars.

Most costs came from a study that identified predictors of health care costs in patients undergoing TAVI in Ontario across 3 phases of care: from referral to the procedure; an early postprocedural phase (days 0–60 postprocedural); and a late postprocedural phase (>60 days postprocedural).[30] Weekly costs for outpatient care were calculated as the difference between total and inpatient health care costs for each of the phases in this study, divided by the number of weeks in the phase, yielding weekly costs of $457 (SD, $186) on the wait-list, $1121 (SD, $1805) in the first 8 weeks after the procedure, and $205 (SD, $546) from thereafter.[30] Costs for preprocedural hospitalization and postprocedural readmission were similarly derived from this study: $7270 (SD, $13 643) in the preprocedural phase and $9223 (SD, $6918) postprocedure.

The cost of TAVI included the cost of the procedure plus the cost for inpatient care in ICU and on the ward. Costs for the TAVI procedure were collected from a cost-utility study of elective TAVI for patients at intermediate surgical risk in Ontario, estimated as $31 540 (SD, $10 513).[22] Costs per day in the ICU and on the ward for the TAVI hospitalization were derived from a cost-utility analysis of TAVI for intermediate surgical risk patients in Canada as $3345 (SD, $1357) and $1000 (SD, $215), respectively.[22] Permanent pacemaker insertion added a cost increment of $11 839 (SD, $3946).[31]

Health-related quality-of-life utility values for the preprocedural and postprocedural health states were collected from a clinical trial of patients who underwent TAVI and were estimated as 0.73 (SD, 0.022) and 0.783 (SD, 0.036), respectively.[32] The utility for any inpatient hospitalization (0.56 [SD, 0.23]) was derived from a study of patients hospitalized for heart failure.[33]

A population-based study of patients with aortic stenosis in Ontario informed the annual probability of wait-list hospitalization (38.8%), the proportion of patients undergoing urgent TAVI (19.8%), and the monthly probability of post-TAVI hospitalization in patients who underwent elective (14.5%) and urgent (20.3%) TAVI.[20] The annual probability of wait-list mortality was derived from another population-based study of patients with aortic stenosis in Ontario.[10] A cohort study in patients with aortic stenosis who were hospitalized provided the probability of death during a preprocedural hospitalization (8.5%).[34] The probabilities of in-hospital mortality during the TAVI procedure (3% for elective and 6.1% for urgent TAVI) and the annual probability of mortality after urgent TAVI (29.1%) were derived from a US cohort study of the Society for Thoracic Surgery/American College of Cardiology TVT (Transcatheter Valve Therapy) registry.[35] The annual probability of mortality after elective TAVI (8.6%) was derived from a cohort study of TAVI outcomes in Ontario.[22]

The HR of a preprocedural hospitalization (1.62) on mortality was collected from a population-based study with patients referred for TAVI.[11] Another study with patients hospitalized for heart failure provided the risk ratio of a hospitalization on readmission while on the wait-list (1.47).[34] HRs for pacemaker insertion on postprocedural mortality (1.40) and hospitalization (1.28) were derived from Aljabbary et al.[15] An HR of urgent TAVI versus elective on postprocedural mortality (1.80) was derived from a population-based study of 2170 patients undergoing TAVI in Ontario.[20]

Assumptions

We assumed that elective and urgent TAVI have the same procedure cost but may differ with respect to complication rates and hospital LOS. The distribution of elective TAVI wait times was restricted by a minimum and maximum wait time (ie, in the reference case, no

Table 2. Input Parameters

Parameter	Value (95% CI)	Source
Probabilities		
Annual hospitalization (wait-list)	0.389 (0.19–0.59)*	Elbaz-Greener, 2019[20]
Annual mortality (wait-list)	0.052 (0.02–0.29)	Albassam, 2020[10]
Mortality (preprocedural hospitalization)	0.085 (0.057–0.113)	Braga, 2018[34]
Urgent TAVI	0.198 (0.09–0.39)	Elbaz-Greener, 2019[20]
Perioperative mortality (elective TAVI)	0.03 (0.01–0.05)	Kolte, 2018[35]
Perioperative mortality (urgent TAVI)	0.061 (0.03–0.09)	Kolte, 2018[35]
Monthly hospitalization (post-TAVI)	0.156 (10.4–20.8)*	Elbaz-Greener, 2019[20]
Annual mortality (post-TAVI)	0.086 (0.057–0.115)*	Tam, 2018[22]
Costs (2019 CAD)		
Weekly wait-list care	457 (277–648)	Tam, 2020[30]
Wait-list hospitalization	7270 (3636–14 540)	Tam, 2020[30]
TAVI procedure	31 540 (21 027–42 053)	Tam, 2018[22]
Pacemaker insertion	11 839 (7893–15 785)	Tam, 2020[31]
ICU care (per day)	3345 (1988–4702)	Tam, 2018[22]
Ward care (per day)	1000 (785–1215)	Tam, 2018[22]
Weekly postprocedural care (early phase)	1119 (749–1488)	Tam, 2020[30]
Weekly postprocedural care (late phase)	200 (100–400)	Tam, 2020[30]
Postprocedural hospitalization	9223 (4611–18 447)	Tam, 2020[30]
Utility weights		
Wait-list care	0.73 (0.708–0.752)	Arnold, 2015[32]
Hospitalization	0.56 (0.33–0.79)	Ambrosy, 2016[33]
Postprocedural care	0.783 (0.745–0.817)	Arnold, 2015[32]
Ratios		
Cost ratio of pacemaker on early postprocedural care	1.43 (1.36 –1.50)	Tam, 2020b[30]
HR of hospitalization on wait-list mortality	1.62 (1.15–2.28)	Elbaz-Greener, 2018[11]
HR of pacemaker insertion on mortality	1.40 (1.01–1.94)	Aljabbary, 2018[15]
HR of pacemaker implantation on hospital readmission	1.29 (1.15–1.46)	Aljabbary, 2018[15]
Risk ratio of hospitalization on preprocedural readmission	1.47 (1.37–1.58)	Braga, 2018[34]
HR of urgent procedure on mortality	1.80 (1.24– 2.62)	Elbaz-Greener, 2019[20]
HR of urgent procedure on readmission	1.35 (1.04–1.75)	Elbaz-Greener, 2019[20]
HR of TAVI LOS per day on readmission	1.03 (1.01–1.05)	Sud, 2017[21]
LOS for urgent vs elective TAVI	1.56 (1.11–2.17)	Arbel, 2017[16]

CAD indicates Canadian dollars; HR, hazard ratio; ICU, intensive care unit; LOS, length of stay; and TAVI, transcatheter aortic valve implantation.
*Variables indicated by the asterisk were calibrated in the model to match these parameters.

patient could wait <5 weeks or >51 weeks for elective TAVI). This assumption was made to overcome the potential for mathematically possible but not clinically realistic waits. Parameter inputs without measures of uncertainty were assumed to have an SD of one third the effect estimate, as previously described.[22,36]

Statistical Analysis

Our primary outcome was the incremental net monetary benefit (INMB) of each comparator strategy versus the reference case, calculated using the formula: $INMB = (\Delta QALY \times \lambda) - \Delta costs$, for 5 cost-effectiveness thresholds (λ). We varied λ from $0 to $100 000 per QALY. At a cost-effectiveness threshold of $0 per QALY, the INMB is affected only by costs. An INMB <$0 is not cost-effective for the given threshold λ, whereas a value >$0 is cost-effective. We used the difference between the resultant INMB and $0 to indicate the maximum cost-effective investment that could be made per patient to achieve the performance indicators of the strategy.

Secondary outcomes of this study were clinical performance indicators outlined by the CCS: wait-list mortality; 30-day post-TAVI hospitalization; 30-day post-TAVI mortality; 1-year post-TAVI hospitalization;

and 1-year post-TAVI mortality.[6] We selected these clinical outcomes for 3 reasons. First, although we anticipate that these clinical outcomes will improve when TAVI performance targets are met, it is unknown how much improvement could be expected. Evaluating these clinical outcomes in our hypothetical strategies may give insight into how the TAVI performance targets will affect clinical outcomes. Second, we may identify TAVI performance targets that should take funding priority by comparing the clinical improvements expected across strategies: the performance target associated with greatest clinical improvement may be a more desirable quality-improvement focus. Third, our reference case scenario should estimate clinical outcomes that match those that have been described for current practice. We can therefore use these secondary outcomes to calibrate and validate our model.

The maximum cost-effective budgets that can be made available by the Ontario Ministry of Health to meet TAVI quality indicator goals at our center and across the entire province were estimated as the per-person costs and benefits produced by our model multiplied by the number of annual TAVIs performed. The expected total clinical improvements at our center and across the province were similarly calculated. For these calculations, we assume an annual completion of 300 TAVIs at an example hospital (Sunnybrook Health Sciences Centre), and 1300 in Ontario.

Our primary analysis was probabilistic, with outer-loop iterations accounting for parameter uncertainty. In addition, we performed a series of deterministic 1- and 2-way sensitivity analyses to evaluate the consequences of our modeling assumptions, and to determine how the results may change if quality-improvement initiatives fall short of achieving the published performance goals. All sensitivity analyses were performed with 20 000 microsimulation trials and a cost-effectiveness threshold of $50 000 per QALY.

To determine the optimal number of iterations for the inner and outer loops, empiric "sample size" determination was performed by repeating analysis with different numbers of outer and inner loops, and identifying the "sample size" at which average cost for the reference case stabilized. The lowest number of outer and inner loops that resulted in stable average values was determined to be 1000 and 1000, respectively, a total of 1 000 000 simulations (Figure S1).

Calibration and Validation

Key clinical measures (probability of wait-list hospitalization, probability of 1-year postprocedural mortality, and probability of 30-day postprocedural hospitalization) were calibrated in the reference strategy (ie, the current status quo) using the Nelder-Mead algorithm for 1000 iterations of 20 000 microsimulation trials. Goodness of fit was assessed using simple sum of square differences, with a best goodness of fit of 2.319×10^{-3}. Time to TAVI and wait-list mortality in Ontario were used for external validation. All model outputs were within the 95% CI of the published data, indicating good model fit (Figure 2). These calibration and validation variables were selected as they are important for our results and are clinically meaningful. The congruence of probability distributions to real-world data was assessed visually by plotting both on the same axes (Figure S2).

RESULTS

Wait-time reduction was the single performance indicator associated with greatest improvement in clinical outcomes, but cumulative improvements over the reference case were observed in the combined strategy (Table 3). Wait-time reduction corresponded to decreased wait-list mortality (from 4.6±0.7% to 2.7±0.5%), fewer wait-list hospitalizations (from 36±2% to 21±1%), and a lower rate of the higher-risk urgent TAVI (from 18±1% to 10±1%). Isolated reductions in pacemaker use or hospital LOS did not yield marked postprocedural improvements.

Incremental costs and effectiveness were calculated for each iteration (Figure S3). The INMB for each strategy versus the reference case was calculated at 4 common cost-effectiveness thresholds (Table 4). All INMB estimates were >$0 at all cost-effectiveness thresholds. Because INMB values >$0 are cost-effective at the selected cost-effectiveness threshold, positive INMB estimates represent the maximum cost-effective investment that can be made per patient. Our results demonstrate that between $10 765 (±$8721) and $17 221 (±$8977) per person can be justifiably invested to achieve all TAVI performance targets considered, depending on the cost-effectiveness threshold adopted. Smaller budgets could be justified for quality improvement initiatives that accomplish fewer TAVI performance targets. For initiatives focused only on wait-time improvement, a budget from $1083±$5720 to $7342±$5992 per person can be justifiable, depending on the cost-effectiveness threshold adopted. If one only focused on pacemaker rate reduction, investment of only between $1112±$421 to $1248±$497 per person could be justified.

At Sunnybrook Health Sciences Centre, 1 of the 11 TAVI centers across Ontario, around 300 TAVIs are performed annually. Depending on the cost-effectiveness threshold adopted, an annual budget between $3 229 632 and $5 164 632 could be dedicated toward meeting all performance indicator goals (ie, creating the combination strategy). Across the province of Ontario, with around 1300 TAVIs per year, this annual budget is estimated between $13 995 072 and

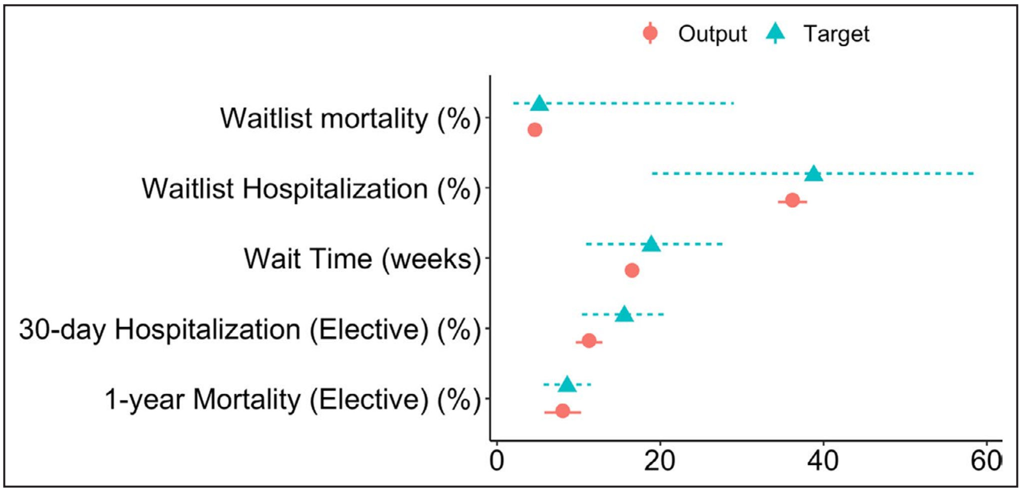

Figure 2. Calibration and external validation.
We compared model-predicted outputs with the real-world data used in model parameterization to ensure that the model was functioning as expected: overlap of model predictions with observed real-world data would indicate good model performance and ensure the external validity of our results. For each variable considered, the simulation output observed and its corresponding 95% credible interval (orange circle) was plotted against a target from the literature with its corresponding 95% CI (blue triangle). The units for each comparison are shown in parentheses. We found that all model outputs for clinically meaningful variables were within the 95% CIs for their respective real-world data, indicating good model fit. For example, the model predicted wait time of 16.6 weeks was sufficiently similar to the target (18.9 [95% CI, 10.3–27.6] days), as was the model predicted proportion of patients experiencing wait-list mortality (4.6%) vs its respective target (5.2% [95% CI, 2%–29%]).

$22 380 072. If all performance targets were achieved, this should correspond to 26 fewer wait-list deaths annually, 200 fewer wait-list hospitalizations across the province per year, and 45 fewer postprocedural deaths at 1 year.

In deterministic 1-way sensitivity analysis, no change in any variable resulted in a negative INMB (using a cost-effectiveness threshold of $50 000 per QALY) (Figure 3). The 3 variables with greatest influence on the results were the magnitude of LOS reduction, the cost of ICU care, and the cost estimate for post-TAVI care in the late phase. The lowest INMB observed ($5322) was with no reduction in LOS in the combined strategy (but reduced wait time and reduced pacemaker insertion). The highest INMB ($16 721) was observed when daily ICU care costs increased to $4702. Two-way sensitivity analyses confirmed the demonstrated positive INMB for combinations of pacemaker insertion rates, LOS reduction, and wait time, including combinations in which the hypothetical strategy fell short of the quality indicator target (Figure S4).

DISCUSSION

This study applies a novel application of cost-effectiveness analysis to determine the maximum

Table 3. Clinical Outcome Estimates for Each Strategy Versus the Reference Case

Variable	Reference case	Wait-time reduction	LOS reduction	Pacemaker reduction	All performance measures
Wait-list mortality, %	4.64±0.67	2.66±0.5	4.64±0.67	4.64±0.67	2.66±0.5
Wait-list hospitalizations, %	36.2±1.78	20.83±1.25	36.2±1.78	36.2±1.78	20.83±1.25
Wait-list duration (time to TAVI), wk	16.54±0.34	10.01±0.12	16.54±0.34	16.54±0.34	10.01±0.12
Urgent TAVI, %	18.2±1.22	10.46±0.96	18.2±1.22	18.2±1.22	10.46±0.96
Pacemaker use, %	14.01±1.05	14.3±1.1	14.01±1.05	4.75±0.66	4.84±0.68
Length of stay for TAVI admission, d	6.95±4.91	6.76±4.81	1.99±1.65	6.95±4.91	1.92±1.62
30-d Post-TAVI mortality, %	0.86±0.43	0.5±0.28	0.87±0.43	0.86±0.43	0.5±0.28
30-d Post-TAVI hospitalizations, %	11.28±1.63	11.21±1.56	10.11±1.17	11.29±1.65	10.11±1.09
1-y Post-TAVI mortality, %	8.05±2.25	4.62±1.38	8.05±2.25	8.06±2.27	4.62±1.39
1-y Post-TAVI hospitalizations, %	26.57±4.29	26.57±4.05	23.32±2.18	26.59±4.3	23.52±2.03

LOS indicates length of stay; and TAVI, transcatheter aortic valve implantation.

Table 4. INMBs for Each Strategy Versus Reference Case

Cost-effectiveness threshold, $/QALY	INMB vs reference case, $			
	Wait-time reduction	LOS reduction	Pacemaker reduction	All performance measures
0	1083.26±5720.59	8565.7±6260	1111.97±420.99	10 765.45±8721.01
25 000	2648.15±5742.65	8570.04±6262.54	1146.22±418.03	12 379.23±8754.47
50 000	4213.05±5795.92	8574.38±6265.47	1180.47±430.78	13 993±8808.49
75 000	5777.94±5879.55	8578.72±6268.81	1214.71±457.93	15 606.78±8882.7
100 000	7342.84±5992.28	8583.06±6272.55	1248.96±497.13	17 220.56±8976.6

INMB indicates incremental net monetary benefit; LOS, length of stay; and QALY, quality-adjusted life year.

investment in TAVI that can be justifiably made by the Ontario Ministry of Health: up to $13 993 (±$8808) per person can be invested to meet quality indicator targets, assuming a cost-effectiveness threshold of $50 000 per QALY. Our results demonstrate that incentives of up to ≈$22 million for TAVI quality improvement in Ontario may be economically justifiable. The 2021 Ontario provincial budget has committed $300 million toward reduced procedural wait times and ≈$780 million toward investment in services for which demand is increasing, including cardiac services specifically.[37] Our estimates for TAVI quality-improvement funding would represent a fraction of these committed funds and should therefore be a feasible spending target.[17]

Our results, and the methods to produce them, are of relevance to Canada as well as health care systems internationally. Rapidly increasing demand for TAVI is a worldwide phenomenon with major impact on health care resource planning.[38] Further increases in annual referrals up to 177 000 and 90 000 in Europe and North America, respectively, well above current rates, may be expected if results from ongoing trials, such as the EARLY TAVR (Evaluation of TAVR Compared to Surveillance for Patients With Asymptomatic Severe Aortic Stenosis) trial, favor TAVI in low-risk and asymptomatic patients (EARLY TAVR, clinicaltrials.gov: NCT03042104).[38] However, economic constraints have restricted capacity building, and TAVI programs currently able to offer a high standard of care may become overwhelmed as referrals increase.[38] Financial investment in TAVI might be a solution in health care systems already experiencing this strain or help

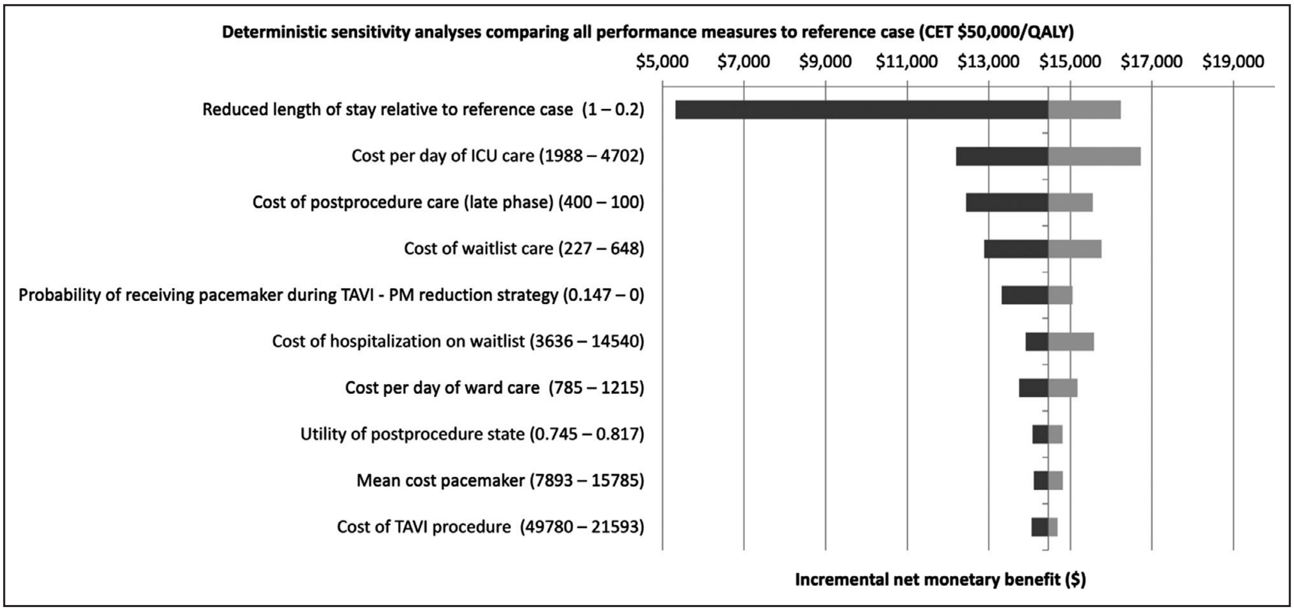

Figure 3. Tornado diagram of all performance measures vs base case (cost-effectiveness threshold [CET] $50 000/quality-adjusted life year [QALY]).

Deterministic 1-way sensitivity analyses compared the sensitivity of our model results with changes in single parameter values. The reference base was compared with the strategy with all performance targets met, with a CET of $50 000 per QALY. No variable change resulted in an incremental net monetary benefit <$0. The greatest sensitivity was observed with changing length of stay (LOS) relative to the reference case: if no decrease in LOS is accomplished, cost-effective investment cannot exceed $5322 per person. ICU indicates intensive care unit; PM, pacemaker; and TAVI, transcatheter aortic valve implantation.

minimize deterioration in the standard of care in other programs. However, because financial incentives toward TAVI would add costs to the health care system, the ideal investment would not exceed the value of the health gains produced.[39,40] Cost-effectiveness analysis uses a formal method to combine economic and clinical outcomes into a single measure of value.[17] Pandya et al (2020) recently developed a quantitative approach to determine the upper bound for financial incentives using cost-effectiveness analysis, and we have adapted their approach for TAVI.[17] Our article demonstrates how health economic modeling may reveal the magnitude of resources from the perspective of the health care payer that can be dedicated toward incentivizing program change.

Our results suggest that wait-time reduction may be a suitable priority for TAVI quality improvement in Ontario. When considering just the strategies with a single performance indicator target met (ie, not the combined strategy), wait-time reduction was associated with cost savings as well as improved wait-list and post-TAVI clinical outcomes. Sensitivity analysis demonstrated that wait-time reductions that fall short of the target may still be a cost-effective investment. The amount that can be invested cost-effectively may vary depending on what improvements materialize, but our results demonstrate that any improvement in wait times warrants some level of financial investment. Our identification of wait-time reduction as an investment priority is aligned with the extensive literature emphasizing the importance of TAVI wait times.[4,10,11,14,20,41] A strong association between TAVI capacity and wait times has led experts to call for improved TAVI capacity in Ontario, although it remains yet to be determined what increase is required or how that increase can be accomplished.[42] These questions are the focus of future work by our group.

Of note, although our study demonstrated both a decrease in post-TAVI 30-day mortality and a reduction in the proportion of patients requiring urgent TAVI, the article by Elbaz-Greener et al (2019) identified a relationship between wait time and post-TAVI mortality in unadjusted analysis, but no such association after accounting for procedure urgency.[20] These results suggest that the TAVI urgency may be a mediator for 30-day post-TAVI mortality: a reduction in the proportion of patients undergoing urgent TAVI resulting from reduced wait times may decrease postprocedural mortality.[20]

Reducing hospital LOS does not require the same capacity building and may therefore be an attractive alternative quality-improvement target. Our results indicate that the INMB for LOS reduction does not vary across cost-effectiveness thresholds, and that the clinical outcomes from this strategy resemble those from the reference case. These findings suggest that LOS reduction is primarily a cost savings from the shorter inpatient stay for TAVI, with only minimal postprocedural clinical benefits. Arbel et al (2017) identified modifiable and nonmodifiable predictors of shorter LOS following TAVI, including the use of conscious sedation instead of general anesthetic.[16] Wijeysundera et al (2016) similarly identified that a nontransfemoral approach and prolonged ICU LOS were associated with increased costs.[43] Quality-improvement programs may build on this work by incentivizing TAVI providers to adopt those modifiable practices that are associated with shorter LOS and lower costs, such as conscious sedation. Early (≤72 hours) and next-day discharge have been shown to be feasible and safe in some jurisdictions, suggesting that LOS reduction may already be the focus of existing quality-improvement programs.[4,27,28]

Although all indicators may serve as useful benchmarks for TAVI quality standards in Canada, some may be more actionable targets than others. For instance, the need for pacemaker insertion post-TAVI is primarily determined by TAVI procedural technique, the type of valve implanted, and patient factors. Our finding that only a relatively small investment can be justifiably dedicated to reducing pacemaker insertion should provide guidance to programs as they prioritize investments. We chose to include this indicator in our study, in part, to illustrate the importance of selecting a high-priority investment target; outcome indicators, such as pacemaker insertion, may be readily measured but inefficient targets for quality improvement. It is worth noting that associations between pacemaker implantation and LOS have been observed, highlighting how initiatives to reduce pacemaker insertion rates may indirectly improve TAVI care.[27]

Our study has identified the amount of additional health care funding that could be dedicated toward TAVI program improvement, and has identified wait-time and hospital LOS reductions as attractive investment priorities. The question of how best to use those resources to achieve targets may be answered by the quality-improvement literature. Pay-for-performance incentives paid directly to cardiovascular and critical care providers, although promising in theory, have tended to yield unsustainable results if not aligned with institutional objectives and existing quality-improvement initiatives.[24,44–49] Thus, financial investment in TAVI in Ontario may be most effective when paid to hospitals as incentives for restructured care delivery in alignment with the CCS TAVI Quality Project.[6]

Limitations

Although our short study time horizon was justified, Canadian Agency for Drugs and Technologies in Health recommends that a lifetime horizon be considered whenever possible. Thus, our use of a short time horizon may represent a limitation. The use of a longer time horizon in future work may address a related question of the long-term effects of TAVI performance improvements.

Another limitation is that we did not simulate patients with different risk profiles. Because few studies have identified patient characteristics as predictors of cost-effectiveness or outcomes, our choice to exclude these individual characteristics was made to minimize additional uncertainty in our estimates. As lower-risk patients become a greater part of the population served by TAVI, consideration of individual risk profiles will become more important.

That we did not model resource constraint may be considered a limitation, but this was done intentionally: we chose to model hypothetical scenarios in which targets were achieved. Resource capacity should be incorporated in future work, as improvements in quality indicators, especially wait times, will require capacity building.

An important limitation of our study is that model inputs were derived from previously published values, which may reflect recent historical rather than current practice. TAVI has been the focus of ongoing quality improvement, and CCS performance indicators have gradually approached their respective targets since the inception of the CCS TAVI Quality Project.[50] For instance, LOS has been the focus of improvement initiatives, with some jurisdictions already reporting shorter duration hospitalization than the estimate of 6 days we modeled. These ongoing quality improvements should be considered when making investment decisions.

A notable limitation is that we used expert opinion to inform our hypothetical LOS and pacemaker-reduced comparator strategies because the CCS TAVI Quality Project had not specified target values. Sensitivity analysis was especially important for evaluation of these hypothetical strategies, as it allowed us to evaluate how variation in the expert opinion provided would affect our results. Despite the lack of consensus targets for these quality indicators, our expert-provided estimates are derived from the literature. A systematic review by van Rosendael et al (2018) reported the incidence of pacemaker insertion after the use of a new-generation TAVI prosthesis ranged between 2.3% and 36.1%, with the lowest rates accomplished using the SAPIEN-3 device.[29] Our hypothetical 5% rate of pacemaker insertion is thus realistic and has already been achieved in some jurisdictions.[29] Post-TAVI LOS similarly has been extensively evaluated, with evidence that LOS <72 hours is feasible and safe.[27,28] A 2-day LOS was among the most frequently observed in the "early discharge" patients, and demonstrates the reasonableness of our hypothetical LOS strategy.

Last, our analysis considers investment using a cost-effectiveness framework, but health care payers may additionally consider budget impact in pay-for-performance policy creation. Budget impact analysis typically does not incorporate health benefits or discounting; disregarding these components in our analysis would result in different, likely lower, maximum justifiable investments. We mitigate this by reporting the INMB at a cost-effectiveness threshold of $0 per QALY (ie, Δcost).

However, despite these limitations, our study is the first to evaluate the costs and clinical benefits of meeting the CCS quality indicator goals for TAVI. This study produces evidence that may guide investment in TAVI quality improvement, such as which of the quality indicators have the potential to yield greatest benefits and thus should be prioritized.[6,51] Furthermore, we believe our results accurately reflect the experience in Ontario because most data came from studies conducted in the province. Future research would benefit from incorporating individual-level risk factors, resource constraint, and a longer time horizon. Future work may also consider a dynamic cohort in which new referrals are considered over the time horizon.

CONCLUSIONS

This study has quantified the modest annual investment required and substantial clinical benefit of meeting improvement goals in TAVI care in Ontario. TAVI quality improvement goals, if met, result in overall cost savings, and can reduce overall patient mortality and health service use.

ARTICLE INFORMATION

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Disclosures

Dr Mamas is an Associate Editor of *Circulation Cardiovascular Interventions* and a board member of the European Association of Percutaneous Cardiovascular Interventions, European Society of Cardiology. Mr Woodward is Senior Vice President at CorHealth Ontario. The remaining authors have no disclosures to report.

Supplemental Material

Figures S1–S4

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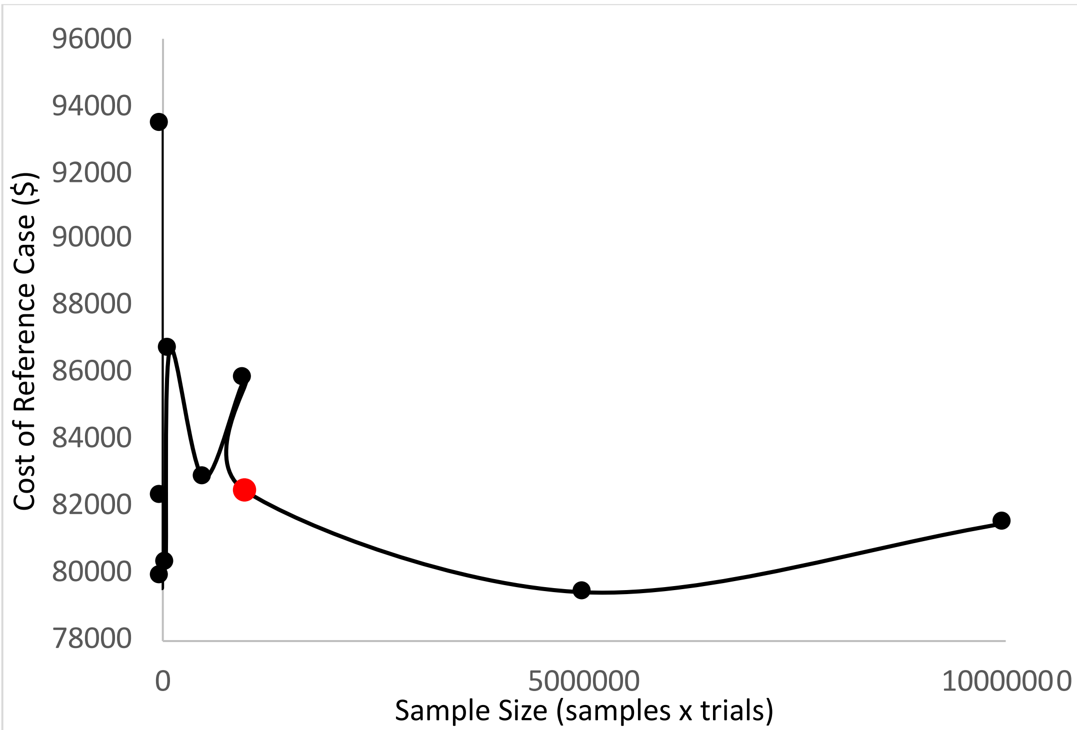
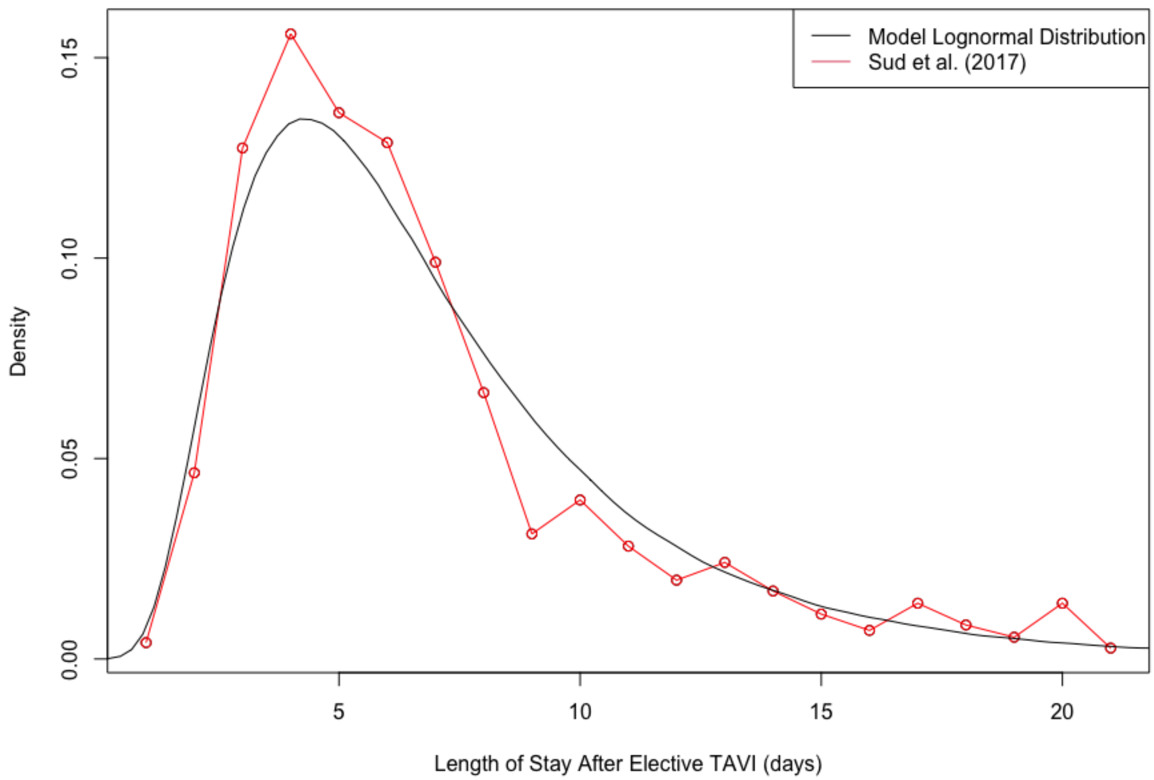
SUPPLEMENTAL MATERIAL

Figure S1. Sample size estimation.



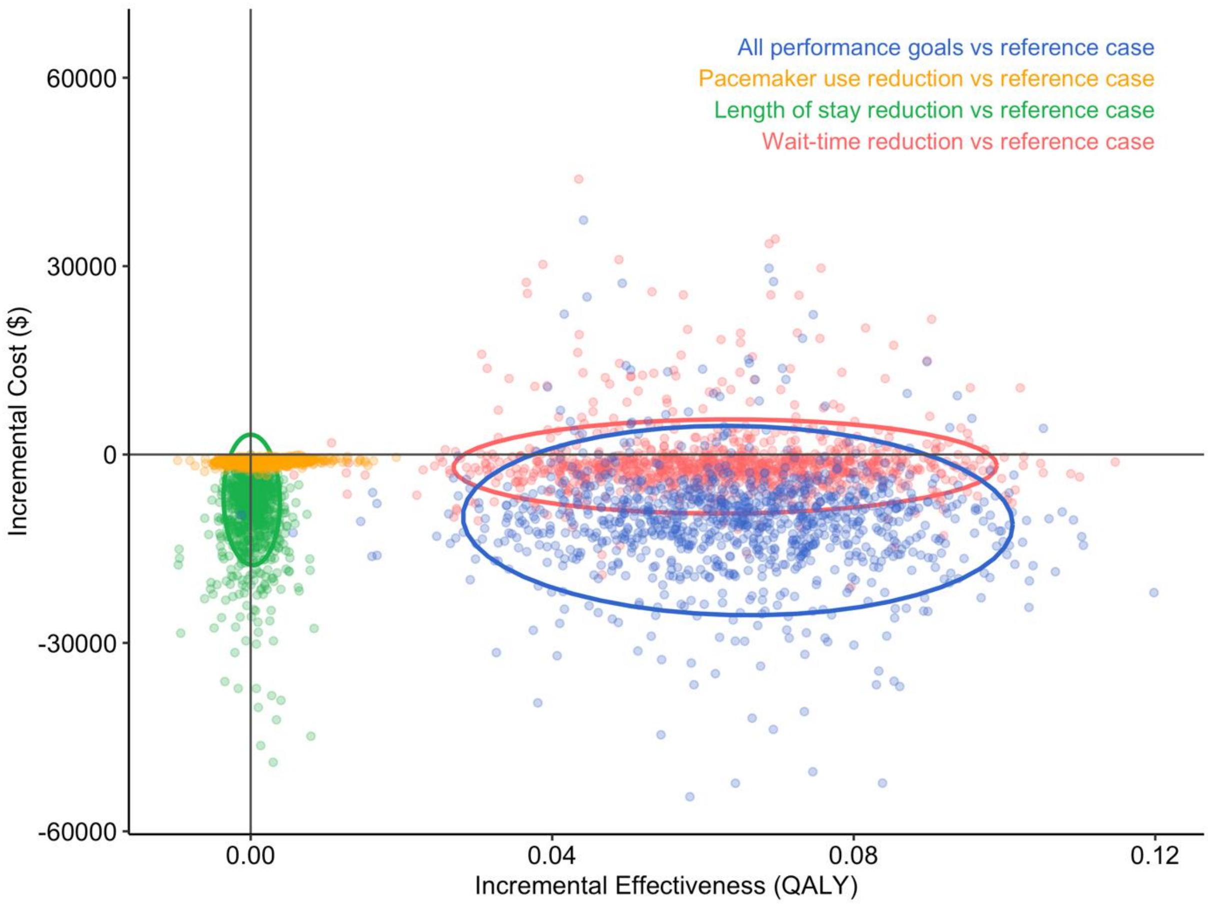
Empiric sample size determination was performed by repeating analysis with different sample sizes for outer and inner loops and identifying the sample size at which average cost for the reference case stabilized. The lowest number of outer and inner loops that resulted in stable average values was determined to be 1,000 and 1,000 respectively, a total of 1,000,000 simulations, indicated in red.

Figure S2. Comparison of Length of stay lognormal distribution to real-world data.



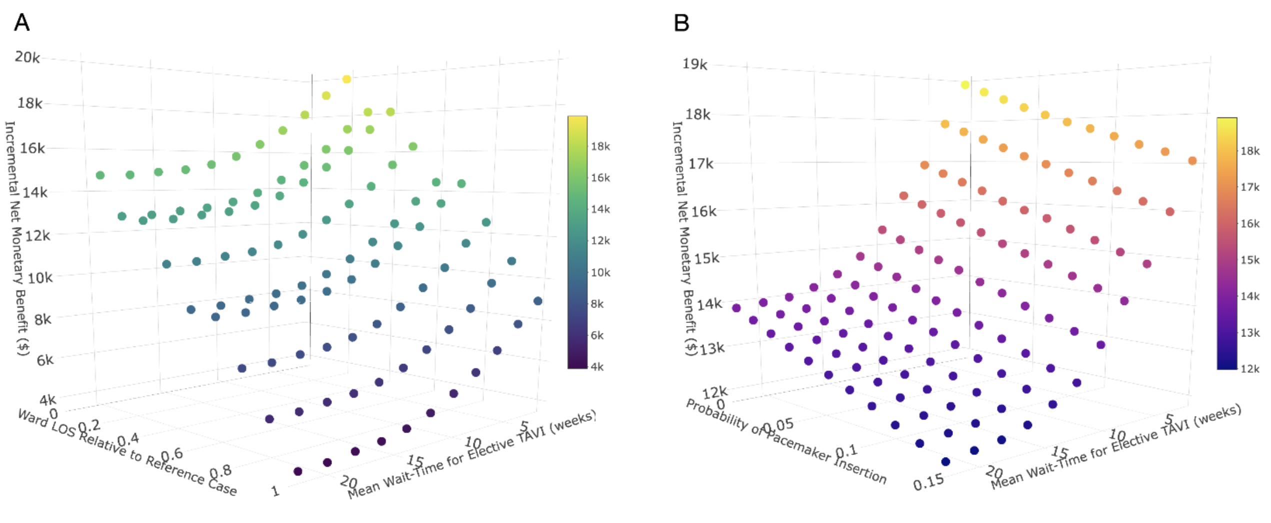
The congruence of probability distributions to real-world data was assessed visually by plotting both on the same axes. Length of stay (LOS) after elective TAVI for our model was derived from the paper by Sud et al. (2017), who reported a median LOS of 6 days, and a mean of 7.1 days. These parameters informed a lognormal distribution (black line) from which LOS was sampled for each inner loop simulation. The red points indicate the real-world data from the Sud et al. (2017) paper.[21] Overlap indicates good model fit. The resultant overall LOS for our cohort, including elective and urgent procedures, (6.8 days) is consistent with the provincial and national reporting of LOS by the Canadian Cardiovascular Society TAVI Quality Project.[16] (LOS = length of stay; TAVI = transcatheter aortic valve implantation)

Figure S3. Incremental Cost-Effectiveness Plane.



Incremental costs and effectiveness were calculated for each comparator strategy versus the reference case. Individual points represent one inner loop simulation, while the ellipses represent the 95% credible ellipses. Most simulations exist in the south-east quadrant, indicating improved effectiveness and lower costs for the comparator strategy over the reference case. The strategy with greatest effectiveness and lowest costs was the combined strategy (blue). Wait-time reduction (red) was associated with a similar improvement in incremental effectiveness, identifying wait-time reduction as a desirable quality-improvement target. Length of stay reduction (green) was predominantly associated with cost-savings over the reference case. (QALY = quality-adjusted life years)

Figure S4. Two-Way Sensitivity Analysis.



We performed two-way sensitivity analyses with combinations of comparing either length of stay reduction (A) or pacemaker insertion rate (B) and wait-time to estimate the INMB of the combined strategy versus the reference case at a cost-effectiveness threshold of $50,000 per quality-adjusted life-year (QALY). Each point plotted represents the INMB estimated from 20,000 Monte Carlo simulations using the parameters on the x and z-axes for the comparator strategy (with the reference case parameters unchanged). In both analyses, the INMB increased in a non-linear exponential fashion as wait-time in the combined strategy was decreased, indicating both that wait-time reduction falling short of the target is still cost-effective and that additional reductions in wait-time beyond the published target could justifiably receive additional investment. Linear relationships were observed between INMB and LOS (A) and pacemaker insertion (B). An interactive version of these plots is available as a supplemental file. (INMB = incremental net monetary benefit; LOS = length of stay; QALY = quality-adjusted life years)