

Cost-Effectiveness of an Antibacterial Envelope for CIED Infection Prevention in the US Healthcare System from the WRAP-IT Trial

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Abstract:

Background - In the WRAP-IT trial, adjunctive use of an absorbable antibacterial envelope resulted in a 40% reduction of major cardiac implantable electronic device (CIED) infection without increased risk of complication in 6,983 patients undergoing CIED revision, replacement, upgrade, or initial cardiac resynchronization therapy defibrillator (CRT-D) implant. There is limited information on the cost-effectiveness of this strategy. As a pre-specified objective, we evaluated antibacterial envelope cost-effectiveness compared to standard-of-care infection prevention strategies in the US healthcare system.

Methods - A decision tree model was used to compare costs and outcomes of antibacterial envelope (TYRX) use adjunctive to standard-of-care infection prevention vs. standard-of-care alone over a lifelong time horizon. The analysis was performed from an integrated payer-provider network perspective. Infection rates, antibacterial envelope effectiveness, infection treatment costs and patterns, infection-related mortality, and utility estimates were obtained from the WRAP-IT trial. Life expectancy and long-term costs associated with device replacement, follow-up, and healthcare utilization were sourced from the literature. Costs and quality-adjusted life years (QALYs) were discounted at 3%. An upper willingness-to-pay (WTP) threshold of \$150,000 per QALY was used to determine cost-effectiveness, in alignment with American College of Cardiology and American Heart Association (ACC/AHA) practice guidelines and as supported by the World Health Organization (WHO) and contemporary literature.

Results - The base-case incremental cost-effectiveness ratio (ICER) of the antibacterial envelope compared to standard-of-care was \$112,603/QALY. The ICER remained lower than the WTP threshold in 74% of iterations in the probabilistic sensitivity analysis and was most sensitive to the following model inputs: infection-related mortality, life expectancy, and infection cost.

Conclusions - The absorbable antibacterial envelope was associated with a cost-effectiveness ratio below contemporary benchmarks in the WRAP-IT patient population, suggesting that the envelope provides value for the US healthcare system by reducing the incidence of CIED infection.

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Key words: pacemaker; implanted cardioverter defibrillator; infection; cost-effectiveness; antibiotic; willingness to treat

Nonstandard Abbreviations and Acronyms

ACC	American College of Cardiology
AHA	American Heart Association
CIED	Cardiac Implantable Electronic Device
CRT-D	Cardiac Resynchronization Therapy Defibrillator
CRT-P	Cardiac Resynchronization Therapy Pacemaker
EHRA	European Heart Rhythm Association
FFS	Fee-For-Service
GFR	Glomerular Filtration Rate
HP	High-power (ICD/CRT-D)
ICD	Implantable Cardioverter Defibrillator
ICER	Incremental Cost-Effectiveness Ratio
LP	Low-power (pacemaker/CRT-P)
MS-DRG	Medicare Severity Diagnosis Related Groups
NNT	Number Needed to Treat
NYHA	New York Heart Association
PADIT	Prevention of Arrhythmia Device Infection Trial
QALY	Quality Adjusted Life Year
QOL	Quality of Life
TAVR	Transcatheter Aortic Valve Replacement
US	United States
WHO	World Health Organization
WRAP-IT	Worldwide Randomized Antibiotic Envelope Infection Prevention Trial
WTP	Willingness-to-Pay



Prevention of Arrhythmia and Electrophysiology

Introduction

Infection is one of the most serious complications of cardiac implantable electronic device (CIED) therapy, often times requiring prolonged hospitalization and complete device extraction.¹⁻³ In a recent report based on the global WRAP-IT trial, CIED infections were associated with a greater than three-fold increase in all-cause mortality, a reduction in quality of life (QOL) for 6 months, and a disruption in CIED therapy in 36% of patients.⁴ Costs in the US were estimated at \$55K for the hospital, and assuming Medicare fee-for-service (FFS) or Medicare Advantage: \$26K for the payer and \$2.1K for the patient, or \$57K to the payer and

\$1.5K to the patient, respectively. Given the significant clinical and financial burden on patients and the healthcare system, infection prevention is of prime importance.

The WRAP-IT trial was designed to evaluate the safety and efficacy of an antibacterial envelope (TYRX™ absorbable antibacterial envelope, Medtronic, MN, US), and reported a 40% reduction in major CIED infection with antibacterial envelope use, with no increase in procedure- or system-related complications in patients undergoing CIED revision, replacement, upgrade, or initial cardiac resynchronization therapy defibrillator (CRT-D) implant.^{5,6} The use of the antibacterial envelope was recently recommended in the 2019 European Heart Rhythm Association (EHRA) International Consensus document, which was endorsed by a number of professional societies/associations comprised of experts in cardiology.⁷ This analysis evaluates the cost-effectiveness of the antibiotic envelope in the entire WRAP-IT trial cohort and in defined clinical subsets within the US healthcare system.

Methods

We adapted a published decision tree model⁸ to compare costs and outcomes of antibacterial envelope use (TYRX™ absorbable antibacterial envelope, Medtronic, MN, US) adjunctive to standard-of-care infection prevention strategies vs. standard-of-care alone over a lifelong time horizon. The WRAP-IT trial protocol was approved by the ethics committee at each participating institution and associated national and local regulatory agencies. All patients provided written informed consent. Due to the proprietary nature of the data collected for this trial, data will not be made publicly available.

All analyses were performed from the perspective of an integrated payer-provider entity (e.g. provider-owned health plan), which provides the most comprehensive overview of financial

impact to the hospital and healthcare system. The analysis was performed over the full patient lifetime and used a willingness-to-pay (WTP) threshold of \$150K per quality adjusted life year (QALY) in alignment with American College of Cardiology (ACC)/American Heart Association (AHA) practice guidelines⁹ on cost/value methodology and supported by the World Health Organization (WHO)¹⁰ and contemporary literature.^{11, 12}

Model Structure

The decision tree model (Figure 1) was developed in Microsoft Excel (Microsoft Corporation, Redmond, WA) to assess the cost-effectiveness of the antibacterial envelope vs. standard-of-care infection prevention alone. Each event following the initial procedure was characterized by a node that occurred with a given probability, and each branch represents a mutually exclusive pathway. Total costs and pay-offs were calculated by summing the product of the pathway probabilities and the corresponding costs and outcomes. The decision tree models events over the 12 months; however, the overall model was extended to a lifetime perspective by assigning lumped cost/benefit estimates at each 12-month endpoint. The structure of the model remains the same for all analyses, only model inputs change.

Model Inputs

Clinical inputs to the model including the standard-of-care infection rate, antibacterial envelope effectiveness, infection treatment costs and patterns, mortality at 12 months, and quality of life (QOL) were based on WRAP-IT trial results.^{4, 6} Long-term life expectancy and utilities (single cardinal values between 0 and 1 reflecting the health-related QOL of an individual at a point in time)¹³ were derived from prior cost-effectiveness modeling.¹⁴ Hospital costs were used as a surrogate for integrated payer-provider entity costs. Expected lifetime costs for device follow-up, replacement, and healthcare utilization were derived from prior estimates.¹⁴⁻¹⁶ Model input

values for the base case (the primary analysis) and standard errors are included in Table 1, and more detail behind the model inputs are included in the supplemental material (Supplement Tables S1-4).

Analysis

Total lifetime costs and QALYs were simulated to calculate the incremental cost-effectiveness ratio (ICER) for the base case. We conducted one-way sensitivity analyses and a probabilistic sensitivity analysis to assess the impact of model inputs and parameter uncertainty. Cost-effectiveness for sub-groups defined based on known CIED infection risk factors (number of prior procedures, age, depressed renal function, immunocompromised, procedure type)²⁰ were also calculated by adjusting the standard-of-care infection rate of each sub-group with all other model inputs unchanged. Lifetime costs and QALYs were discounted at a discount rate of 3% for all analyses. All currency reflects 2017 US dollars.

Results

Base case analysis

Table 2 shows the results of the base case analysis. The antibacterial envelope resulted in 8.117 life-years (6.925 QALYs) saved at a cost of \$37,598, while standard-of-care alone resulted in 8.111 life-years (6.919 QALYs) saved at a cost of \$36,929. The ICER of the antibacterial envelope compared to standard-of-care alone was \$112,603/QALY; the antibacterial envelope is cost-effective at a WTP of \$150K.

Sensitivity analyses

Results of the one-way sensitivity analyses show that the ICER was most sensitive to infection-related mortality, life expectancy, and infection cost (Figure 2). Additional parameter values

were considered during the one-way sensitivity analysis (Supplement Table S5); however, the model was not overly sensitive to these values (Supplement Table S6). Figure 3 shows the results of the probabilistic sensitivity analysis, where each dot corresponds to the resulting cost per QALY of a model iteration, and the continuous line shows the WTP threshold of \$150K per QALY. The probabilistic sensitivity analysis found that the ICER remained lower than the WTP threshold in the majority (74%) of iterations.

Sub-group analyses

The following cut-points for levels of cost-effectiveness are calculated from the model by varying the standard-of-care infection rate (while holding all other model inputs constant): the therapy is cost-effective (ICER below the \$150K WTP threshold) when the standard-of-care infection rate is $\geq 1.0\%$, is highly cost-effective (ICER below \$50K) when the standard-of-care infection rate is $\geq 2.0\%$, and is cost saving when the standard-of-care infection rate is $\geq 4.0\%$. The therapy is less economically attractive at standard-of-care infection rates below 1%. See Table 3 for the cost-effectiveness of sub-groups based on known CIED infection risk factors.

Discussion

This analysis is the first to leverage randomized controlled trial data to quantify the lifetime impact of using the absorbable antibacterial envelope adjunctive to standard-of-care infection prevention, on healthcare resource use, costs, and patient-centric outcomes in the US healthcare system. We found that when used in patients with an increased risk of CIED infection, the antibacterial envelope has an ICER of \$112,603/QALY compared with standard-of-care alone, which is below the WTP level of \$150K/QALY. This finding is robust to the sensitivity analyses, showing ICERs lower than the WTP with most reasonable variations in model inputs.

An estimated 1.5 million patients worldwide receive a CIED each year.²¹ Infections are one of the most feared complications leading to substantial morbidity and three-fold risk of mortality.⁴ In spite of best practice, 1-4% of CIED procedures are associated with infection within 12 months,^{6, 22-25} and risk accumulates over the lifetime of the patient.²⁶ The impact of a CIED infection to the healthcare system is substantial, with each event costing \$48,000 to \$55,000 to treat.^{1, 25, 27-29} To date, only the TYRXTM absorbable antibacterial envelope has been shown to significantly reduce the risk of CIED infection with the addition of pre-operative antibiotics.⁶ In addition to the prior finding that the antibacterial envelope is clinically effective, this analysis suggests that the envelope is also cost-effective in the US healthcare system.

When considering the most appropriate perspective for a cost-effectiveness analysis in the US healthcare system, competing incentives between stakeholders (third-party payers, hospitals, clinicians) serve to distort economic analyses from traditional perspectives. For example, from a strict third-party payer perspective there is no reimbursement for the antibacterial envelope, so the use of the antibacterial envelope would result in no cost. From a strict hospital perspective, reimbursement from the payer for the treatment of an infection limits the impact of true costs. Further complicating matters, prior reports have shown significant discrepancies between hospital costs and reimbursement.⁴ Such discrepancies are plausible given the mechanism of reimbursement under Medicare Severity Diagnosis Related Groups (MS-DRG). Patients with a CIED infection typically are treated by a hospital admission involving removal of the infected device, a prolonged hospital stay (2-4 weeks) on intravenous antibiotics and temporary device therapy to clear the infection, then a replacement CIED implant. Because of the MS-DRG payment mechanism, the hospitals receive only one payment for the entire inpatient stay. This payment is usually driven by the most expensive procedure performed during

the inpatient stay, which is usually the implant of a new CIED. This means that while the hospital has spent significant resources stabilizing the patient, removing the infected system, and having the patient occupy a bed for several weeks, the hospital is not paid for these costly activities – instead the hospital is paid the same as if the patient had arrived for a *de novo* CIED implant. In order to fairly and comprehensively account for all costs and benefits experienced by the health care ecosystem, this analysis was performed from the perspective of an integrated payer-provider entity, such as a provider-owned health plan.

We believe the integrated entity described above represents the concept of value in healthcare as described by the Porter Model for value in health.³⁰ It collects all costs and outcomes of the full cycle of care into a single perspective, minimizing conflicting goals; and the ICER is the inverse of the Porter Model definition of value (patient-centric health outcomes achieved per dollar spent). Although not fully aligned with payers and providers that are not part of an integrated system, our findings are aimed to inform the decision-making process at the time of a CIED procedure by accounting for the patient, provider, and payer perspectives.

The tacit WTP for the US healthcare system has been \$50K per QALY. While the origin of this threshold is unclear, it is sometimes attributed to cost-effectiveness analyses of hemodialysis that has its origin approximately 50 years ago.³¹ Assuming acceptance of this threshold as a fair benchmark for value at the time, it is reasonable to consider updating it over time at the standard rate of inflation.³² A simple inflation adjustment of \$50k from 1980 would yield a WTP in 2017 dollars of \$169K per QALY.³³ More recent estimates of the cost-effectiveness of standard, hospital-based hemodialysis for end-stage renal disease are consistent with this rough gauge and range from \$125K-\$150K per QALY.

The above considerations are consistent with those discussed in the 2014 ACC/AHA practice guidelines,⁹ US based healthcare value assessment organization statements,¹¹ and perspectives published in peer-reviewed journals,¹² which generally recommend consideration of \$150K per QALY as a reasonable WTP. Given this understanding, we believe it is reasonable to use a contemporary benchmark of \$150K per QALY, and to further characterize sub-groups that have an ICER below \$50K per QALY as high value, those with an ICER between \$50K-\$150K as intermediate value, and those with an ICER above \$150K as less economically attractive.

The ICER for the antibacterial envelope reported here lies within the range of cost-effectiveness results seen for other cardiovascular therapies. Based on a four-year time horizon, CRT-D therapy had an ICER of \$58K as compared to ICD therapy alone in patients with standard CRT-D indications.³⁴ The CardioMems™ device was found to have an ICER of \$71K in NYHA Class III patients.³⁵ The cost-effectiveness of Sacubitril vs. Valsartan in patients with systolic heart failure ranged from \$45 to \$144K in separate estimates.^{36, 37} Transcatheter aortic valve replacement (TAVR) had ICER estimates that ranged from \$39,964-\$116,500 when compared to medical management; however, it was considered a disruptive therapy for a population with no other treatment options.³⁸ TAVR ICER estimates also ranged from \$32,000-\$252,400 when compared to surgical valve replacement in patients with high risk of surgical mortality. At a base case ICER of \$112,603 and the range of ICERs reported for higher risk sub-groups, the antibacterial envelope therapy is commensurate with these other therapies.

To date, there has been little evidence directly addressing the economic implications of using an antibacterial envelope. A report on cost-effectiveness in the United Kingdom healthcare system⁸ used a pooled estimate of effectiveness from trials published prior to WRAP-IT. This report found the antibacterial envelope to be cost saving for patients with an ICD or CRT-D

device and cost-effective when baseline probabilities of infection exceeded 1.38-1.95% depending on clinical subset. Given the paucity of such evidence, there have been attempts to use surrogate measures of efficiency, such as number needed to treat (NNT). The NNT that can be calculated directly from the WRAP-IT study is approximately 200, however the NNT cannot be interpreted in isolation from a full consideration of the, benefits, risks, and costs of the therapy, which we take up in the current report. Out of context, the NNT may appear to be a large value, however, the WRAP-IT trial established that there was benefit without increased risk of complications, and this report suggests that the costs are commensurate with the benefits of the envelope.

Different patients present for CIED therapy distinctly, for bradycardia, ventricular arrhythmias and systolic dysfunction. In addition, the pre-procedural comorbidities and the intensity of the CIED procedure distinguish these patients clinically and has an impact on the estimates of cost-effectiveness (Table 3). For example, envelope use in patients who have experienced a prior CIED infection could reasonably be considered high value, while patients with pacemakers and one or fewer prior procedures and no other risk factors could be considered less economically attractive. Recent evidence from the PADIT trial^{20, 39} provides a tool to estimate infection risk based on patient-specific factors, which may further inform use of the antibacterial envelope. While the primary finding of this analysis is that the antibacterial envelope is cost-effective in the WRAP-IT trial population, the sub-analyses accounting for patient-specific factors provides some insight into how to assess the use of the antibacterial envelope in these clinical subsets of patients.

It is important to keep this economic analysis in perspective as helpful in broad, policy level decision-making, without applying it as a sole decision criterion in the context of an

individual patient. In particular, there may be patient-level heterogeneity that was not modeled in this analysis. For example, a patient receiving a pacemaker without other risk factors may not appear to warrant envelope use from an economic perspective alone. However, if that patient also had a prosthetic valve, the consequence of a CIED infection may lead to consequences related to the valve as well. Other examples include a patient with a simple generator change with older leads leading to multiple post-infection procedures including lead extractions, a patient with no venous access on the opposite side leading to the need for either a trans-iliac or epicardial system, or a CRT patient where the ability to access the same coronary venous branch after extraction and replacement would be compromised.⁴⁰ There is no substitute for clinical judgement in cases that are complicated by factors that are hard to measure, inclusive of potential consequences of infection should it occur.

Our analysis has several limitations that should be acknowledged. Some model inputs were derived from sources outside of the WRAP-IT trial (Table 1); however, data were selected from WRAP-IT whenever available and most inputs did represent an in-trial analysis. Costs and benefits were modeled beyond the directly observed results from the WRAP-IT trial, however the results were robust to the sensitivity analyses. The model did not explicitly account for age-related impacts to utility or healthcare costs; however, the impact of these factors is attenuated by the compound discounting of costs and outcomes over time. The model was particularly sensitive to post-infection mortality with the ICER above the WTP range toward the limit of the sensitivity analysis, however mortality risk after infection has been demonstrated in other analyses.^{41, 42} The utilities for patients with and without CIED therapy were modeled independently and may have led to an overestimation of variability of the probabilistic sensitivity analysis, but this is a conservative assumption. Patients from the WRAP-IT trial were not all

from the US, but the clinical application and outcomes of CIED therapy are relatively standardized around the world, and costs were estimated from the US subset of patients. Sub-group analyses were not powered in the original trial and represent hypothesis level evidence only. Infection risk factors used in the sub-group analyses represent clinical factors known prior to the procedure as these are reasonably well established in prior literature, other less well understood risk factors, such as those related to the procedure, could also impact baseline infection risk resulting in directional changes in cost-effectiveness. Patients on chronic oral immunosuppressive agents or on hemodialysis were excluded from the WRAP-IT trial, however, history of immunosuppressive therapy and history of renal dysfunction (GFR <60 ml/min/1.73m²) were used as surrogates for the sub-group analysis. The results of this analysis are applicable only to the patient populations that were defined by the WRAP-IT trial inclusion criteria and may not be generalizable to the full CIED procedure population.

Conclusion

The absorbable antibacterial envelope was associated with a cost-effectiveness ratio below contemporary benchmarks in the WRAP-IT patient population, suggesting that the envelope provides value for the US healthcare system by reducing the incidence of CIED infection.

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Table 1. Detailed Model Inputs

Model Parameter	Base Case Value	Standard Error	Source
Baseline Infection Rate	1.2%	0.18%	WRAP-IT
TYRX Effectiveness	0.6	0.15	WRAP-IT
TYRX Cost	\$953	N/A	Medtronic
Infection Treatment Cost <ul style="list-style-type: none"> No extraction Full extraction no replacement Extraction with replacement 	\$16,592 \$45,694 \$67,586	\$5,050 \$10,085 \$9,739	WRAP-IT
Infection-Related Utility (QOL)	-0.09	0.03	WRAP-IT
Mortality at 12 Months <ul style="list-style-type: none"> No infection Infection, no extraction Infection, partial extraction Infection, complete extraction 	5.2% 23.8% 23.8% 14.6%	0.3% 2.4% 2.4% 5.1%	WRAP-IT
Life Expectancy (discounted years) <ul style="list-style-type: none"> No CIED Pacemaker ICD CRT-P CRT-D 	5.5 7.4 7.8 4.2 7.8	0.55 0.74 0.78 0.42 0.78	 Mealing et al. (2016) ¹⁴
Long-term Utility with CIED (QOL) <ul style="list-style-type: none"> Pacemaker ICD CRT-P CRT-D 	0.841 0.870 0.842 0.850	0.0044 0.0048 0.0102 0.0033	WRAP-IT
Long-term Utility without CIED (QOL) <ul style="list-style-type: none"> Pacemaker (not replaced) ICD (not replaced) CRT-P (not replaced) CRT-D (not replaced) 	0.771 0.870 0.661 0.662	0.08 0.09 0.07 0.07	Feldman et al. (2005) ¹⁷ Udo et al. (2013) ¹⁸ Bundgaard et al. (2019) ¹⁹
Lifetime Costs (discounted) <ul style="list-style-type: none"> No CIED Pacemaker ICD CRT-P CRT-D 	\$22,015 \$26,485 \$35,159 \$26,183 \$45,662	\$4,403 \$5,297 \$7,032 \$5,237 \$9,132	Mealing et al. (2016) ¹⁴ Kilgore et al. (2017) ¹⁵ Munawar et al. (2018) ¹⁶

CIED, cardiac implantable electronic device; CRT-P/D, cardiac resynchronization therapy pacemaker/defibrillator; ICD, implantable cardioverter defibrillator; QOL, quality of life

Table 2. Base Case Analysis Results

	Standard-of-Care Alone	Antibacterial Envelope
Costs through 12 Months	\$842	\$1,479
Costs after 12 months	\$36,087	\$36,119
Total Lifetime Costs	\$36,929	\$37,598
Cost difference (US \$)	\$669	
Life-years saved	8.111	8.117
Life-years difference	0.006	
QALY saved	6.919	6.925
QALY difference	0.006	
ICER	\$112,603	

ICER, Incremental Cost Effectiveness Ratio; QALY, quality-adjusted life years

**Table 3.** Cost-Effectiveness of Sub-groups

Sub-group	WRAP-IT Standard-of-Care Infection Rate	ICER (per QALY)	Level of Value
Prior CIED Infection	5.8%	Dominant	Cost Saving
Hx Immunocompromised	4.0%	\$312	High Value
HP: ≥2 Prior Procedures	2.4%	\$32,396	High Value
LP: Revision/Upgrade	2.4%	\$32,396	High Value
Hx Renal Dysfunction	1.7%	\$65,422	Intermediate Value
HP: Revision/Upgrade	1.5%	\$80,520	Intermediate Value
LP: ≥2 Prior Procedures	1.1%	\$127,186	Intermediate Value
HP: =1 Prior Procedure	1.0%	\$144,686	Intermediate Value
LP: =1 Prior Procedure	0.9%	\$166,074	Less Economically Attractive
CRT-D: <i>de novo</i> Implant	0.5%	\$337,184	Less Economically Attractive

Cost Saving = antibacterial envelope results in lower cost compared to standard-of-care alone. Renal dysfunction is defined as GFR <60 ml/min/1.73m². Prior procedures is inclusive of all procedures including *de novo* implant.

CIED, cardiac implantable electronic device; CRT-D, cardiac resynchronization therapy defibrillator; HP, high-power device (ICD or CRT-D); Hx, history; ICD, implantable cardiac defibrillator; LP, low-power device (pacemaker or CRT-P)

Figure Legends:

Figure 1. Decision Tree Analysis. The decision tree model was developed in Microsoft Excel (Microsoft Corporation, Redmond, WA, US). Each event following the initial procedure was characterized by a node that occurred with a given probability, and each branch represents a mutually exclusive pathway. The total costs and pay-offs associated with either treatment option was calculated by multiplying the pathway probabilities by the corresponding costs and outcomes and summing the expected costs and pay-offs. The decision tree time horizon is 12 months and the model is extended to a lifetime perspective by assigning lumped cost/benefit estimates at endpoints A-H. CIED = cardiac implantable electronic device.



Figure 2. One-way Sensitivity Analysis. Tornado chart of the range of ICER across high and low parameter input values (input values are available in Table ST5 of the supplement). Each input was varied with all others held constant. ICER values remained below the \$150K WTP benchmark for the majority of input variations. ICER = incremental cost-effectiveness ratio; WTP = willingness-to-pay.

Figure 3. Probabilistic Sensitivity Analysis. The scatterplot depicts the range of ICER given probabilistic variation in model inputs. Blue dots represent individual ICER data points, while the red dot represents the mean ICER from the probabilistic datapoints. The dashed line represents the WTP benchmark. The ICER remained lower than the WTP in the majority (74%) of iterations. ICER = incremental cost-effectiveness ratio; WTP = willingness-to-pay; QALY = quality adjusted life year.

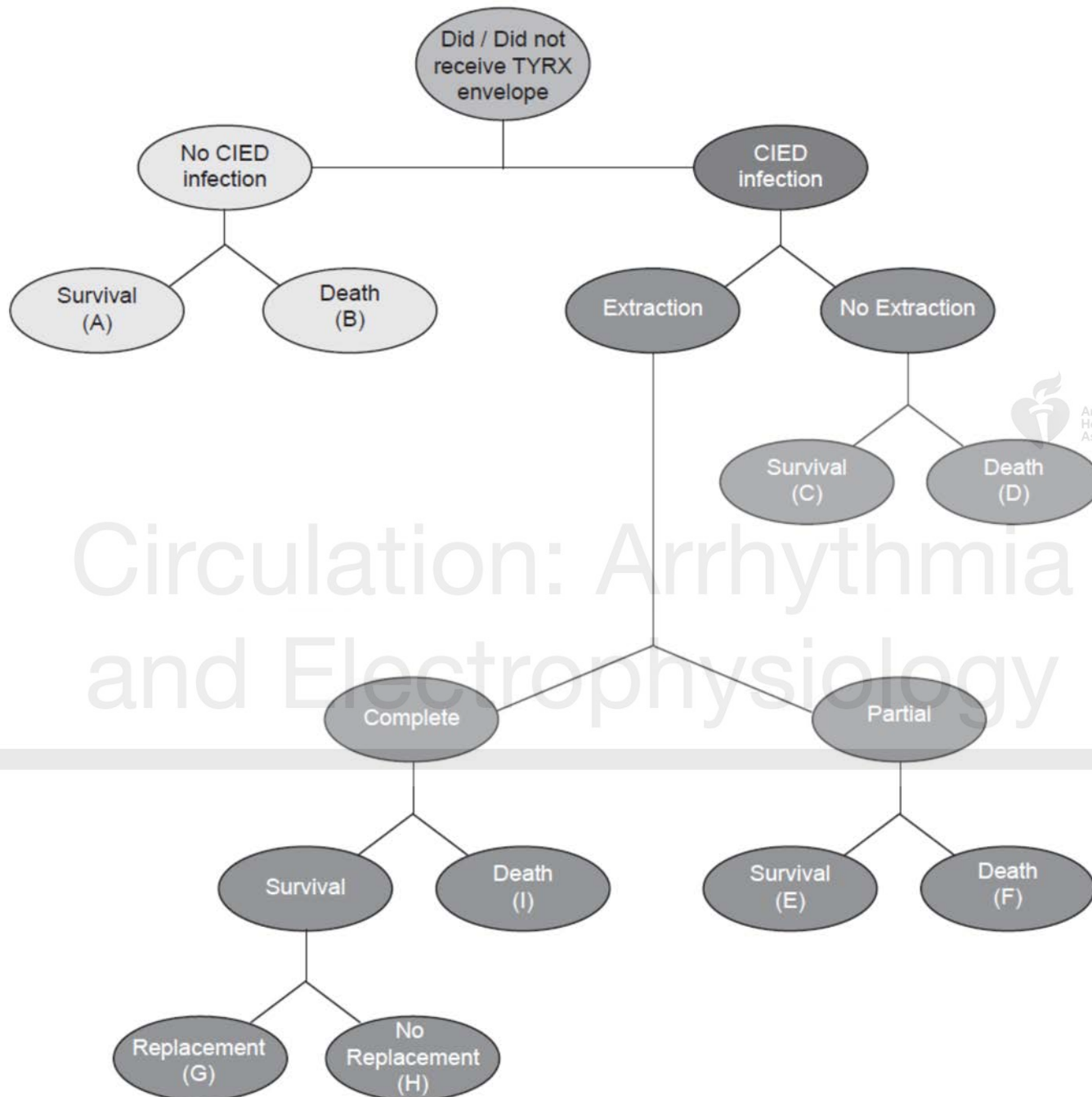
What Is Known?

- Infection is one of the most serious complications of cardiac implantable electronic device (CIED) therapy, often requiring prolonged hospitalization and complete device extraction until the infection is resolved.
- Impacts of CIED infection include increased risk of mortality, reduced quality of life (QOL), disruptions in CIED therapy, and significant costs to payers, hospitals, and patients.
- In the WRAP-IT trial, adjunctive use of an absorbable antibacterial envelope (TYRX™) resulted in a 40% reduction of major CIED infection without increased risk of complication in 6,983 patients undergoing CIED revision, replacement, upgrade, or initial CRT-D implant.



What the Study Adds?

- This analysis is the first to leverage randomized controlled trial data to quantify the lifetime impact of using the absorbable antibacterial envelope adjunctive to standard-of-care infection prevention, on healthcare resource use, costs, and patient-centric outcomes in the US healthcare system.
- The absorbable antibacterial envelope was associated with a cost-effectiveness ratio below contemporary benchmarks in the WRAP-IT patient population, from the perspective of an integrated payer-provider network.



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One-Way Sensitivity Analysis

■ High Input ■ Low Input

Post-Infection Mortality

Life Expectancy

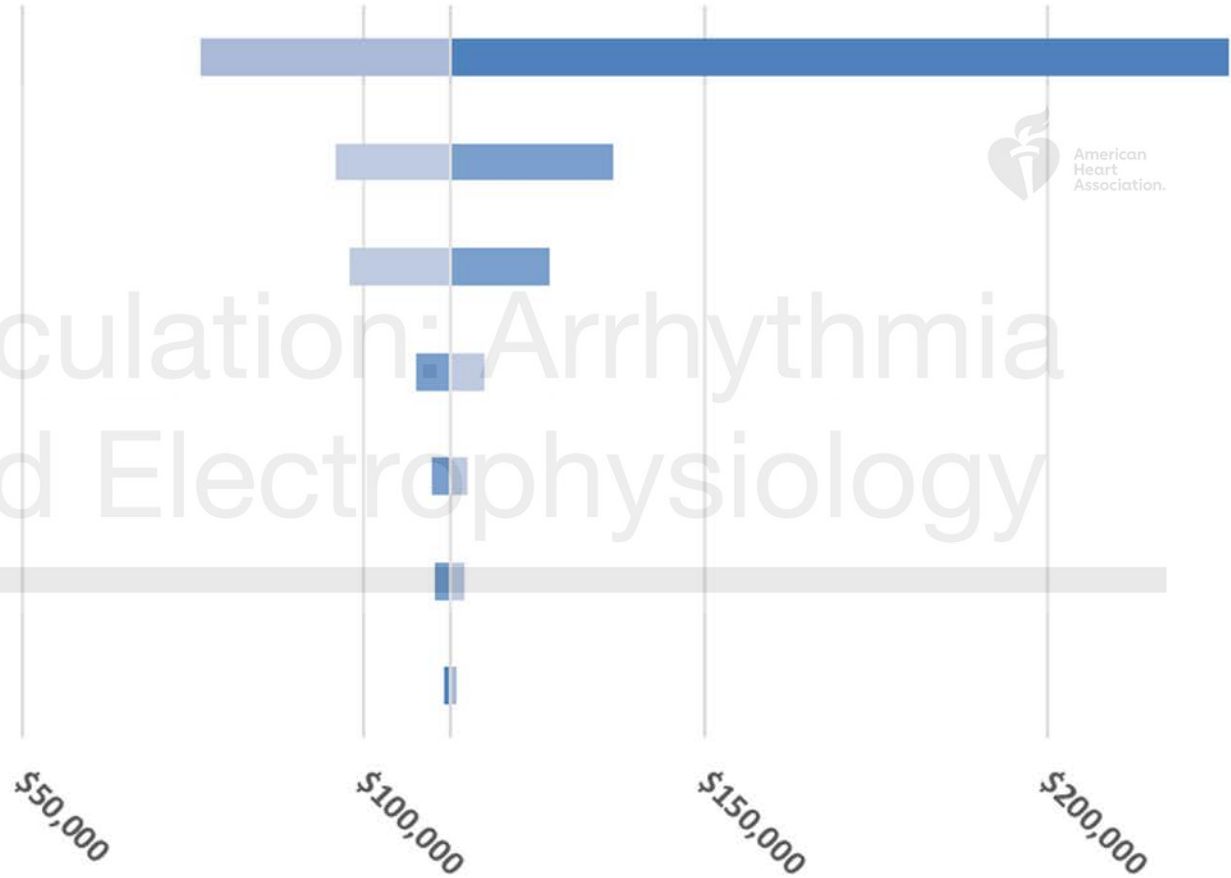
Infection Cost

Discount Rate

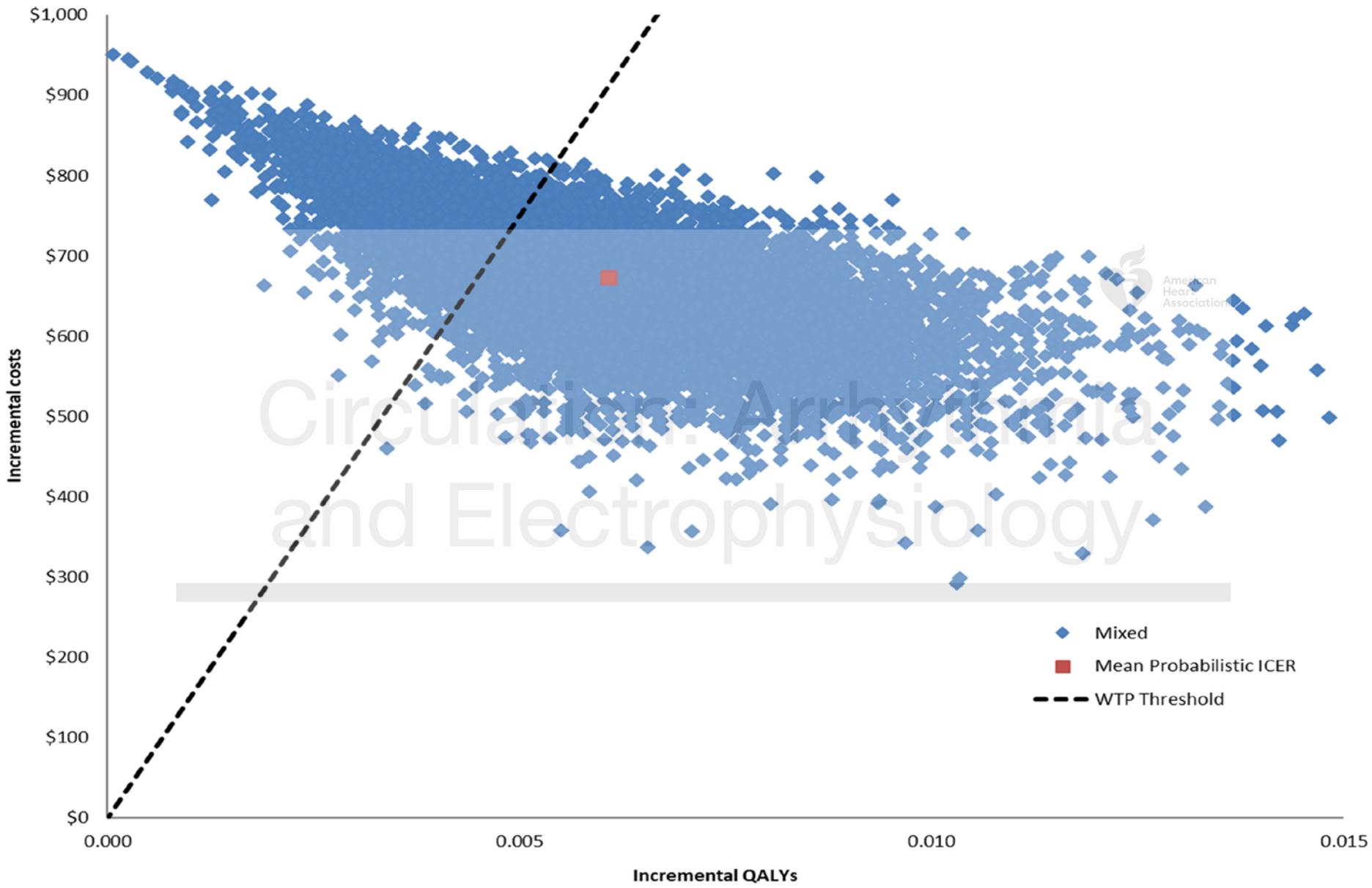
Infection Disutility

Lifetime Costs

Extraction Probability



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COST-EFFECTIVENESS OF AN ANTIBACTERIAL ENVELOPE

A PRE-SPECIFIED ANALYSIS OF THE WRAP-IT TRIAL



CIED INFECTIONS

Outcomes, Costs Per Infection

- >3X mortality risk at 1 year
- Suppressed quality of life for 6 months
- \$55,000 avg hospital cost to treat

Envelope Effectiveness

- 40% reduction of major CIED infections with TYRX



ANALYSIS METHODS

Model

- Value defined as dollars spent to achieve health outcome
- Integrated payer-provider perspective
- Decision tree based on costs and outcomes from the WRAP-IT Trial



ECONOMIC RESULTS



Cost-Effectiveness Ratio

- \$112,000 per quality adjusted life-year

Willingness-to-pay Threshold

- \$150,000 per QALY, aligned with ACC/AHA practice guideline recommendations



CONCLUSION

The TYRX absorbable antibacterial envelope was associated with a cost-effectiveness ratio below contemporary benchmarks in the WRAP-IT patient population, suggesting that the envelope provides value for the US healthcare system.