

## ORIGINAL ARTICLE

# Cost-effectiveness of Micra™ VR leadless pacemaker in patients with bradycardia and atrial fibrillation in Australia

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**Abstract**

**Background:** Micra™ VR Transcatheter Pacing System (Micra VR) is a single-chamber transcatheter leadless pacemaker. Absence of leads and subcutaneous pocket reduces or completely eliminates the risk of complications associated with the conventional transvenous pacemakers (TVPM). When compared with TVPM, the leadless technology provides a quicker postimplantation recovery and causes less cosmetic concerns/discomfort providing better patient experiences in the long run. We performed a modeled cost-utility analysis of Micra VR versus TVPM for the management of patients with bradycardia.

**Methods:** We developed a Markov model comparing Micra VR to TVPM over the device battery life of 17 years. Key data inputs were drawn from the MICRA Coverage with Evidence Development (CED) study. Costs were obtained from Australian sources. The analysis is from the perspective of the Australian healthcare system.

**Results:** The risks of complications, including device-related events, in real-world clinical practice were relatively low for TVPM. The magnitude of cost savings arising from risk reductions provided by Micra VR was however sizable, offsetting roughly a quarter of its additional device cost. Over the 17-year model period, Micra VR was associated with an estimated incremental cost of A\$4277 and an incremental quality-adjusted life years (QALYs) of 0.09 when compared with TVPM, yielding an incremental cost-effectiveness ratio of A\$47 379 per QALY gain.

**Conclusions:** Micra VR is likely to offer a cost-effective alternative to the conventional TVPM technology for the management of patients with bradycardia.

**KEYWORDS**

atrial fibrillation, bradycardia, cost-effectiveness, leadless pacemaker, pacemaker

## 1 | INTRODUCTION

Bradycardia, or cardiac bradyarrhythmia, is an abnormally slow heart rhythm as a result of the disturbance of the generation or

conduction of cardiac electrical activity. Pacemakers have gained a well-established clinical place in the management of bradycardia. Nearly 20 000 new pacemakers were implanted in Australia in 2021, translating to 755 implants per million.<sup>1</sup> Single-chamber ventricular

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pacemakers are typically used for patients with chronic atrial fibrillation (AF) with atrioventricular (AV) block and persistent bradycardia or patients with sinus node dysfunction (SND) with bradycardia. Conventional single-chamber transvenous pacemakers (TVPM) have a long history of use and have essentially remained unchanged over time with reliance on a pulse generator which sits in a subcutaneous pocket and a connecting transvenous lead system. TVPM's reliance on the subcutaneous pocket and leads represent the key source of device-related complication risks. Complications such as infections and lead dislodgements are relatively infrequent, however, can cause significant patient burden with high economic consequences. The patient population primarily consists of elderly patients with a high co-morbidity rate, in whom infections and lead complications could be catastrophic. Infection, in particular, is problematic with a reported 12-month mortality rate of 36% and a cost per case of ~A\$100 000 with high cardiac care unit (CCU)/intensive care unit (ICU) dependency.<sup>2-4</sup>

Micra™ VR Transcatheter Pacing System (Micra VR) is a single-chamber implantable transcatheter leadless pacemaker (LPM) placed directly into the right ventricular myocardium via the femoral vein. Whilst offering the same pacing capability as TVPMs, LPMs do not require a subcutaneous pocket or leads, reducing the aforementioned complication risks. The device insertion is conducted percutaneously, providing a faster and more satisfactory postprocedural recovery than TVPM implantation.<sup>5</sup> Additionally, the absence of the subcutaneous pocket eliminates the visible lump on the chest that occurs with a TV system, resulting in less cosmetic concerns/discomfort and the absence of leads anchored into the myocardium eliminates long-term restriction in upper body movement caused by leads.<sup>6</sup>

Clinical utility of Micra VR has been supported by a range of clinical studies.<sup>7-10</sup> For example, the Micra Investigational Device Exemption (IDE) study reported a 12-month freedom from major complication rate of 96%.<sup>7,8</sup> The study also demonstrated that, relative to a predefined historical control group of TVPM patients, the leadless technology reduced the risk of major complications at 12 months (hazard ratio [HR]: 0.52 [95% CI]: 0.35, 0.77;  $p = .001$ ). Observational studies conducted in real-world settings have provided further support to these clinical trials. Recently, a comparative assessment of Micra VR versus TVPM was conducted in a large patient record review in the US—the Micra Coverage with Evidence Development (CED) study.<sup>11,12</sup> Based on US Medicare data, when compared with TVPM, Micra VR was associated with significantly fewer reinterventions (adjusted hazard ratio (HR) 0.62,  $p = .003$ ) and chronic complications (adjusted HR 0.69,  $p < .0001$ ). The CED study was presented as the primary source of clinical data for Micra VR to support its reimbursement coverage on the Medicare Benefits Scheme (MBS) and on the Prescribed List of Medical Devices and Human Tissue Products in Australia.

The current study presents a modeled cost-utility analysis of Micra VR versus single-chamber TVPM for the management of patients with bradycardia from the Australian healthcare providers' perspective.

## 2 | METHODS

### 2.1 | Model structure

This economic model is to evaluate differential risks of device-related reinterventions and complications between Micra VR and TVPM and quantify associated implications in terms of health-care costs and quality-adjusted life years (QALYs) over time. The model is hence built on the principle of a Markov cohort analysis (Figure 1). At baseline, a cohort of patients receive the implantation procedure under the allocated treatment strategy (i.e., Micra VR or TVPM) and enter the "Alive with pacemaker" state. The only events that trigger a transition to "Dead" (= absorbing state) are an infection resulting in death and an other-cause death. Other clinical events (including nonfatal infection) are assumed to be transient, thus their QoL and cost implications are to be completely absorbed within one model cycle. To avoid potential double-counting, only a selection of device-related reinterventions and complications are included for consideration by the model. One model cycle consists of 12 months.

The cohort's baseline age is set at 77 years with 41.8% being female to reflect the Australian patient population.<sup>13</sup> Age and sex are the only demographic variables that may impact to the cost-effectiveness results of the current model as they determine the rate of other-cause mortality. Other patient demographics and disease characteristics are as per the Micra CED study population and hence implicit within the clinical inputs from the trial.<sup>11</sup> Half-cycle corrections are applied in all cost and QALY calculations except for the initial implantation costs as these costs are entirely incurred at or immediately after baseline for all patients. The model horizon is set at 17 years to match the typical battery life of the current generation Micra VR device. All cost and QALY outputs are discounted at 5% per annum according to the current guidance by the Australian decision maker.

### 2.2 | Model inputs

#### 2.2.1 | Clinical event rates

The Micra CED study is the primary source of clinical inputs. This study was an observational, continuously enrolling cohort study of Micra in the US Medicare population. The study utilized Medicare administrative claims that were linked to device registration data, allowing reliable identification and follow-up of patients and clinical events relating to device-related reinterventions and complications. This study hence provides real-world evidence for the analysis of event risks among patients living with Micra VR or single-chamber TVPM. This study design also afforded a large sample size, including a total of 16 431 patients (Micra VR:  $n = 6219$ ; TVPM:  $n = 10212$ ). In the Micra VR cohort, the mean age was  $79.5 \pm 9.5$  years and 44.1% were female. In the single-chamber TVPM cohort, the mean age was  $82.0 \pm 8.1$  and 43.2% were female. To account for differences in baseline characteristics between the study cohorts, propensity

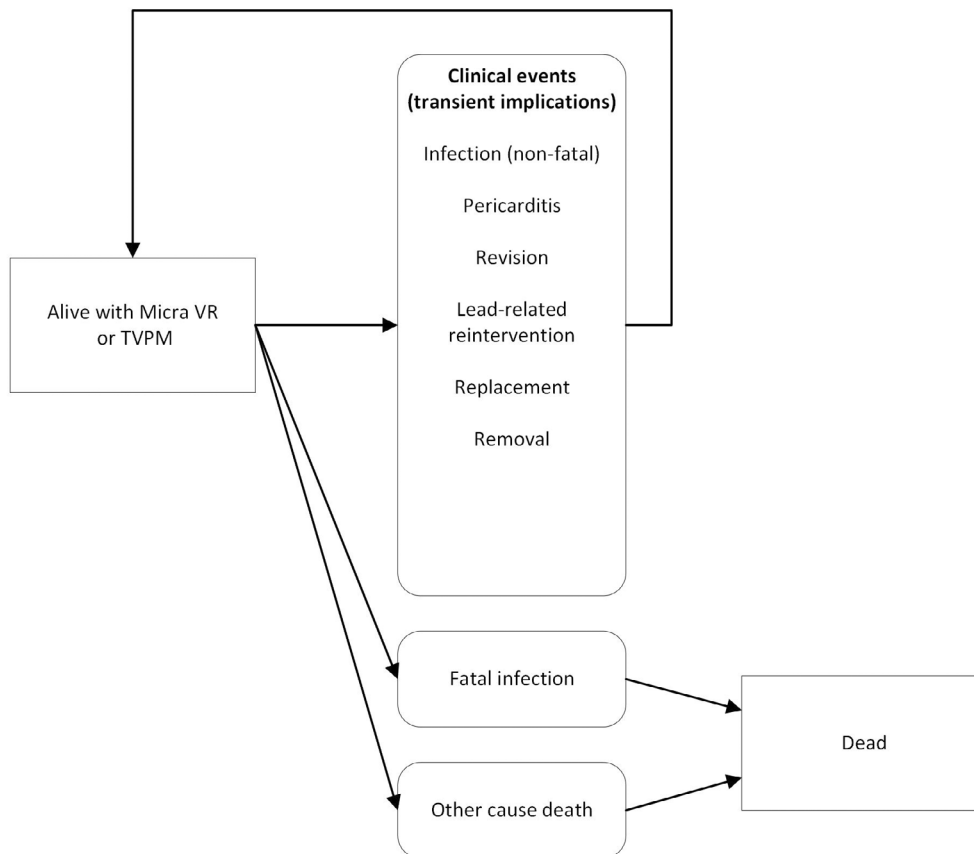


FIGURE 1 Schematic of the modeled cost-utility analysis of Micra VR versus single-chamber TVPM. TVPM, transvenous pacemaker.

TABLE 1 Annualised probabilities of device-related reintervention/complication in the 1st year and +2nd years post implantation based on the MICRA CED study.

| Event                        | Micra VR             |                       | TVPM                 |                       |
|------------------------------|----------------------|-----------------------|----------------------|-----------------------|
|                              | 1st year postimplant | +2nd year postimplant | 1st year postimplant | +2nd year postimplant |
| Infection <sup>a</sup>       | 0.03%                | 0.01%                 | 0.53%                | 0.10%                 |
| Pericarditis                 | 1.35%                | 0.26%                 | 0.66%                | 0.13%                 |
| Revisions                    | 0.09%                | 0.03%                 | 0.45%                | 0.15%                 |
| Lead-related reinterventions | 0.00%                | 0.00%                 | 0.53%                | 0.16%                 |
| Replacement                  | 0.95%                | 0.11%                 | 0.38%                | 0.04%                 |
| Removal                      | 0.03%                | 0.01%                 | 0.60%                | 0.24%                 |

Abbreviation: TVPM, transvenous pacemaker.

<sup>a</sup>36% resulting in fatality.<sup>14</sup>

score overlap weighting was performed. At the time of the development of the current model, 2 years of follow-up data were available with a mean follow-up time of 477 days for Micra VR and 518 days for TVPM, respectively. Further details of the Micra CED study can be found in another publication.<sup>11</sup>

Model inputs for reintervention/complication risks are summarized in Table 1. Mortality associated with the reintervention or complication events was not assessed in the Micra CED study. A 12-month mortality rate of 36% is applied to those experiencing infection based on a large US retrospective patient record review.<sup>14</sup> The elevated mortality risk is completely absorbed within 12 months

with no ongoing implications beyond this period. Other modeled events are assumed to cause no additional mortality. The model captures other-cause mortality each cycle and the associated risk is assumed to be as per the age-/sex-specific rates expected in the general Australian population.<sup>15</sup>

### 2.2.2 | Utilities

Utility inputs are summarized in Table 2. No QoL data were collected in the MICRA CED study, and hence additional QOL studies are

utilized. The utility value for patients experiencing an infection is informed by a randomized controlled trial (RCT) of infection management following the implantation of cardiac implantable electronic devices (CIEDs).<sup>16</sup> A mean utility decrement of up to 0.10 was demonstrated following infection onset ( $p = .001$ ) and the QoL impact lasted up to 6 months in this study. After applying a pragmatic half cycle correction, the duration of this utility decrement is assumed to be 3 months in the current model, translating to a disutility of  $-0.025$  per event.

No disutility estimates specifically relevant to device-related reintervention events (revision, lead-related reintervention, replacement and removal) were identified in the literature. A comparative health-related QoL study of Micra and TVPM evaluated SF-36 scores during the first 6-months postimplantation, demonstrating patients receiving Micra had significantly higher scores in most domains over the follow-up period.<sup>5</sup> It is possible to map these SF-36 scores to EQ-5D utility values based on a published equation, as demonstrated in Figure 2.<sup>18</sup> During the periods immediately following the implementation procedure, the utility value for the TVPM cohort exhibited a drop ( $-0.073$  at week 1 and  $-0.025$  at month 3; both vs. baseline) that did not completely disappear after 6 months. No such utility decrement was evident with Micra. The initial utility decrement (i.e.,  $-0.073$ ) observed with TVPM is taken as the QoL loss experienced by patients undergoing a device-related reintervention and the

duration of this QoL loss is assumed to be 1.5 months. This approach is justified because these reinterventions would require a procedure not dissimilar to the initial implantation. Conservatively, the same estimate is also assumed for the Micra arm of the model.

The model additionally accounts for QoL implications of quicker postimplantation recovery offered by Micra VR over TVPM.<sup>5</sup> As depicted in Figure 2, the absolute difference between the two arms in changes from baseline at 6 months is 0.061 (0.033 vs.  $-0.028$ ) favoring the Micra cohort. Based on this, the model applies a one-off disutility of 0.031 to TVPM in the first cycle. Furthermore, when compared with TVPM, Micra VR causes less cosmetic concerns/discomfort and less activity restriction (e.g., upper body movement especially the arm ipsilateral to the device pocket).<sup>6</sup> To capture this, patients living with TVPM are assumed to experience a QoL loss equivalent to the aforementioned utility loss of 0.061 for 1 month or approximately 30 days each year (equating to the mean utility decrement of 0.005 each year). For simplicity, QoL implications due to the effectiveness of pacing in preventing symptoms of bradycardia, such as syncope, dyspnoea and palpitations, are omitted.

### 2.2.3 | Cost inputs

Cost inputs are summarized in Table 3. All costs are expressed in Australian dollars. Many of the resource items are costed by using the current pricing approved by the Australian payers. For the treatment of infection, an Australian costing study is referenced, adjusted to the 2023 values.<sup>4</sup> For the treatment of pericarditis, patients are assumed to receive colchicine 0.5 mg twice daily for 3 months plus two specialist consultations.<sup>19</sup>

TABLE 2 Utility inputs for the modeled cost-utility analysis of Micra VR versus TVPM.

| Health state/event  | Input    | Source/notes  |
|---|----------|---|
| Baseline/no complication                                    | 0.70     | Based on the 6-month EQ-5D value for Micra VR [5]   |
| Disutility caused by reintervention/complication, per event |          |   |
| Infection   | $-0.025$ | Utility loss of 0.10 lasting 3 months [16]  |
| Pericarditis  | $-0.003$ | Utility loss of 0.039 (reported for "nonspecific chest pain") lasting 1 month [17]  |
| Revisions   | $-0.009$ | Utility loss of 0.073 lasting 1.5 month (conservatively assuming the QoL loss to disappear after 3 months with half cycle correction) [5] |
| Lead-related reinterventions                                |          |   |
| Replacement   |          |   |
| Removal   |          |   |
| Other QoL implications                                      |          |   |
| Postimplantation QoL loss                                   | $-0.031$ | Disutility of 0.061 lasting 6 months (half cycle correction performed), applied to TVPM only [5]  |
| On-going QoL loss due to TVPM                               | $-0.005$ | Disutility of 0.061 lasting 1 month (or approximately 30 days of the year) each year, applied to TVPM only [5]                            |

Abbreviation: TVPM, transvenous pacemaker.

## 3 | RESULTS

### 3.1 | Base case analysis

Table 4 summarises the base-case results from the cost-utility model. The cost per intervention is represented by the total implantation cost because the cost of intervention is entirely absorbed at baseline; reflecting the higher prosthesis cost of Micra VR driving a higher cost of intervention (A\$12 158 vs. A\$6503). The additional cost associated with the Micra VR device was partly offset by cost savings in terms of complication management and device-related reinterventions, providing an estimated cost savings of A\$1378 per device life. This resulted in an overall incremental cost of A\$4277 with Micra VR. Micra VR was shown to provide 0.090 additional QALYs over TVPM overall. Disaggregation of this QALY difference is provided in Table 5. QALY implications of the complication avoidance are relatively minor in the overall QALY benefits for Micra VR with the infection-related mortality and nonfatal events providing 0.019 and 0.0006 additional QALYs, respectively. The Micra VR was associated with an incremental cost-effectiveness ratio (ICER) of A\$47 379 per QALY gain.

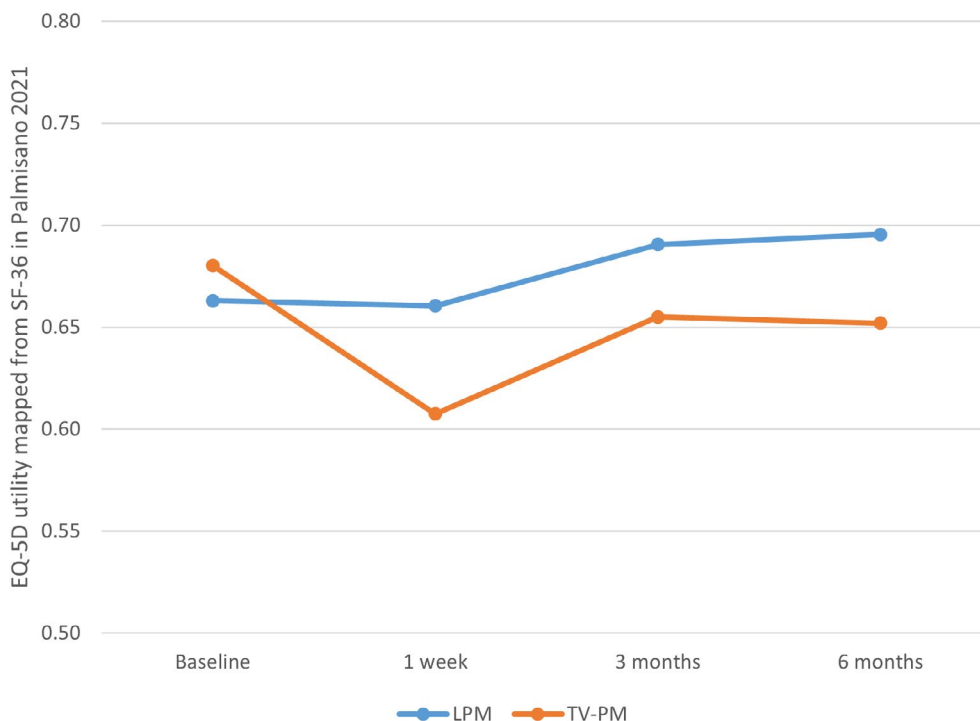


FIGURE 2 EQ-5D utility scores converted from SF-36 reported in Palmisano<sup>5</sup>—changes over 6 months following the index implantation. TVPM, transvenous pacemaker.

TABLE 3 Cost inputs for the modeled cost-utility analysis of Micra VR versus TVPM.

| Healthcare resource use                            | Input                                   | Source/notes   |
|--|---|--|
| Initial implantation, Micra VR                     | A\$12 158                               | Current prosthesis/MBS benefits, hospital stay                                   |
| Initial implantation, TVPM                         | A\$6503                                 | Current prosthesis/MBS benefits, hospital stay                                   |
| Treatment of infection                             | A\$118 839                              | [4]  |
| Revision, removal and lead-related re-intervention | A\$2075                                 | Current MBS benefits, hospital stay  |
| Device replacement                                 | A\$12 158 for Micra VR/A\$6503 for TVPM | As per the initial implant   |
| Treatment of pericarditis                          | A\$146                                  | Specialist consults and medication (cost using current MBS benefit and PBS cost) |

Note: All costs are reported in 2023 Australian dollars.

Abbreviations: MBS, Medicare Benefits Schedule; PBS, Pharmaceutical Benefits Scheme; TVPM, transvenous pacemaker.

### 3.2 | Sensitivity analysis

Sensitivity analyses supported the robustness of the base case results, as summarized in Table 6. Many of these are based on scenario-based

sensitivity analyses exploring extreme values (see Discussion). Utility inputs employed to capture the QoL benefits arising from the leadless design are key drivers of the cost-effectiveness of Micra VR versus TVPM. Halving or doubling the duration of QOL loss due to infection

| Treatment strategy                              | Micra VR  | TVPM    | Difference                 |
|---|-----------|---------|----------------------------|
| <b>Costs</b>                                    |           |         |                            |
| Implantation                                    | A\$12 158 | A\$6503 | A\$5655                    |
| Management of complications/<br>reinterventions | A\$302    | A\$1679 | -A\$1378                   |
| Total   | A\$12,460 | A\$8182 | A\$4277                    |
| QALYs   | 5.966     | 5.876   | 0.090                      |
| Incremental cost-effectiveness ratio            |           |         | A\$47 379 per<br>QALY gain |

**TABLE 4** Incremental cost-effectiveness ratio for Micra VR vs TVPM—17-year analysis, discounted at 5% per annum.

Abbreviations: TVPM, transvenous pacemaker; QALYs, quality-adjusted life years.

**TABLE 5** Disaggregation of QALY for Micra VR versus TVPM—17-year analysis, discounted at 5% per annum.

| Treatment strategy   | Micra VR | TVPM    | Difference |
|--|----------|---------|------------|
| Life years   | 8.523    | 8.496   | 0.027      |
| QALYs at the baseline utility of 0.70 with no other disutilities | 5.966    | 5.948   | 0.019      |
| QoL loss due to complications                                    | -0.0003  | -0.0010 | 0.0006     |
| QoL loss due to postrecovery (6 months) <sup>a</sup>             | 0.000    | -0.041  | 0.041      |
| Long-term QoL implications due to lead/pocket <sup>a</sup>       | 0.000    | -0.030  | 0.030      |
| QALYs, total (= base case)                                       | 5.966    | 5.876   | 0.090      |

Note: Presented figures may be affected by rounding.

Abbreviations: TVPM, transvenous pacemaker; QALYs, quality-adjusted life years.

<sup>a</sup>No disutilities captured for Micra VR because the incremental differences between the two strategies were applied (as disutilities being applied to TVPM).

or other complications resulted in only a small change in the ICER. Halving or doubling the duration of TVPM postimplant QOL loss resulted in an ICER of A\$55 921 and A\$36 292 respectively. Making similar adjustments to the on-going QOL impact due to TVPM similarly changed the ICER to A\$61 160 or A\$32 660 respectively. Varying the risk of infection by plus or minus 20% also had notable impacts (A\$52 776 and A\$42 421 respectively), but this was primarily via the associated cost implications, not the QoL implications. Reducing the baseline age or discount rate had a substantial effect on the ICER. Similarly, reducing the model duration to 12 and 15 years changed the ICER to \$53 952 and \$49 191 respectively. Complication risk or cost of complication were not significant drivers of the model.

## 4 | DISCUSSION

The LPM technology, reflecting its integrated design and implantation site, offers a solution to device-related complications

traditionally experienced with the leaded technology. Infection is a serious complication, associated with significant mortality and morbidity.<sup>16</sup> Pocket complications such as pocket erosion could also suggest low grade, indolent infection.<sup>2</sup> The treatment of infection involves device and lead removal, antibiotic treatment, and subsequent device and lead re-implantation if indicated and is typically associated with a lengthy hospital stay with CCU/ICU dependency.<sup>2,3,20</sup> The cost of illness studies on CIED infection in Australia and internationally confirm high treatment costs.<sup>3,4,21,22</sup> Other long-term device-related complications/malfunctions such as generator or lead breakdowns and dislodgement would require an immediate re-intervention and if necessary extraction/replacement of the implantable devices, causing high patient burden if they occur. Nonetheless, the risk reductions offered by Micra VR were not a significant driver of cost-effectiveness for Micra VR versus TVPM overall. It should be nonetheless noted that previous device-related complications and reinterventions are known as a significant risk factor for future infections,<sup>23</sup> and these secondary implications were omitted from the model, thus providing a conservative view on the cost/QALY implications of a safety advantage offered by Micra VR over TVPM. The integrated design and the transfemoral implantation route offer additional QoL benefits for Micra VR in the short-term as well as in the long-term, which represented an important determinant of the cost-effectiveness of Micra VR in the current model.

Patient age was an important driver for the cost-effectiveness. This is reflective of the background mortality and the timing of cost versus health benefit accrual. The cost of Micra VR is entirely incurred close to the baseline whilst its benefits are delivered over time. The high background mortality of the modeled cohort hence becomes a challenge from the perspective of cost-effectiveness because many die before gaining the full benefits of Micra VR (e.g., >40% of the cohort die after 10 years in the current model). This is a challenge commonly experienced in the cost-effectiveness analysis of a medical device or any technology where the treatment cost occurs once and upfront (e.g., gene therapies). Use of a lower discount rate could be justified and necessary should the cost-effectiveness of these innovative technologies be fairly evaluated. The model duration of 17 years is based on the simulated battery longevity of the current Micra VR model.<sup>24</sup> Any impacts of device failure/replacement have been incorporated in the model. When the model duration is reduced to 12 years to reflect the battery life of the first

TABLE 6 Sensitivity analysis.

| Tested variable                           | Input       | Incremental cost | Incremental QALY | ICER      |
|---|-------------|------------------|------------------|-----------|
| Base-case analysis                        | -           | A\$4277          | 0.090            | A\$47 379 |
| Clinical inputs                           |             |                  |                  |           |
| Infection risk                            | Up by 20%   | A\$4564          | 0.086            | A\$52 776 |
|   | Down by 20% | A\$3991          | 0.094            | A\$42 421 |
| Other complications risks                 | Up by 20%   | A\$4289          | 0.090            | A\$47 476 |
|   | Down by 20% | A\$4265          | 0.090            | A\$47 282 |
| Cost inputs                               |             |                  |                  |           |
| Costs of infection                        | Up by 20%   | A\$3990          | 0.090            | A\$44 195 |
|   | Down by 20% | A\$4565          | 0.090            | A\$50 563 |
| Costs of other complications              | Up by 20%   | A\$4265          | 0.090            | A\$47 247 |
|   | Down by 20% | A\$4289          | 0.090            | A\$47 510 |
| Utility inputs                            |             |                  |                  |           |
| Duration of QoL loss, infection           | Halved      | A\$4277          | 0.090            | A\$47 458 |
|   | Doubled     | A\$4277          | 0.091            | A\$47 221 |
| Duration of QoL loss, other complications | Halved      | A\$4277          | 0.091            | A\$47 206 |
|   | Doubled     | A\$4277          | 0.090            | A\$47 466 |
| Duration of TVPM postimplant QoL loss     | Halved      | A\$4277          | 0.076            | A\$55 921 |
|   | Doubled     | A\$4277          | 0.118            | A\$36 292 |
| On-going QoL impact due to TVPM           | Halved      | A\$4277          | 0.070            | A\$61 160 |
|   | Doubled     | A\$4277          | 0.131            | A\$32 660 |
| Other inputs                              |             |                  |                  |           |
| Baseline age                              | 50 years    | A\$3986          | 0.118            | A\$33 693 |
|   | 60 years    | A\$4022          | 0.115            | A\$35 070 |
| Discount rate                             | 3.5%        | A\$4187          | 0.096            | A\$43 613 |
|   | Taken out   | A\$3919          | 0.113            | A\$34 564 |

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; QoL, quality of life; TVPM, transvenous pacemaker.

generation Micra VR device the ICER increased to \$53952. The battery life of LPM devices in general has achieved a significant improvement with the second generation device. As discussed above, many patients do not outlive their device and therefore device replacement due to battery depletion is often not an issue.

The age at baseline was 77 years based on an Australian study by Ranasinghe 2019.<sup>13</sup> Some may question whether the incremental cost of the LPM is reasonable to maintain QOL in an elderly patient population. Two studies report QOL in the form of SF-36 with Micra VR versus TVPM.<sup>5,25</sup> Both studies reported statistically significant differences in favour of LPM over TVPM at 6 months on the following domains: physical functioning, role physical, mental health and physical component summary scores. Additionally, Palmisano<sup>5</sup> reported statistically significant differences in favour of LPM with respect to the domains general health, vitality, social function, role emotional and the mental component summary scores.<sup>5</sup> These studies were both conducted in patients of a similar age (~77 years), and therefore the QOL benefit is expected to be applicable to this elderly patient population. Indeed, a younger patient population is likely to have an even greater QOL benefit than presented in the model because the benefits offered by

Micra VR in terms of less cosmetic concerns/discomfort and less activity restriction may be more meaningful for younger patients.

The Micra CED study served as the primary source of clinical evidence for this model. More recently, a 3-year update has become available, providing further support to the 2-year data referenced in the current model.<sup>12</sup> This study included more than 16 000 patients and was assessed to be at low risk of bias in the context of the study design (with adequate adjustment for potential confounding via propensity score overall weights), thus representing the best available evidence to date to inform the comparison of Micra VR and TVPM. Importantly, performing an RCT comparing Micra VR (or LPM in general) with TVPM to support a superiority claim in terms of infrequent, but highly clinically relevant, complications necessitates a large sample size, challenging its feasibility. The lack of a sufficiently powered RCT could mean that the values of innovative technologies that reduce clinically important adverse events of relative infrequency are inadequately reflected in payer decision-making. A well-designed and methodologically robust observational study, such as the Micra CED study, can play a decisive role in supporting an HTA for reimbursement decisions.

No probabilistic sensitivity analysis (PSA) was explored as we believed it would add limited value. All but one clinical input, (infection-related mortality) are based on a large observational study with a sample size exceeding 16000 patients (i.e., Micra CED). Many of the cost inputs were based on the current resource pricing approved by the Australian government and thus not flexible. Some variations would of course occur in practice depending on the care needs of individual patients but establishing reliable distributions around the base case values is difficult and would result in additional uncertainty. The utility inputs can be deemed as less robust than other inputs and the presented sensitivity analyses identified them as high impact variables. Establishing reliable distributions around the base case values is again difficult and we hence considered that PSA would not add any value beyond the deterministic sensitivity analyses presented here. Several limitations are acknowledged. The CED study data were generated among the US Medicare patients and may not be as applicable to Australian patients and clinical practice. Although the pacemaker technology is well established and does not differ internationally and treatment practice and patient selection would be well harmonized between two countries, potential confounding should be noted in interpreting the model results. There is limited research in the literature that attempted to quantify QoL benefits of LPM compared to TVPM. The utility values employed by the model were EQ-5D utility scores mapped from SF-36, thus having an added layer of potential uncertainty. To reflect this, we attempted to take a conservative approach in selecting the relevant utility inputs but this is acknowledged as an important area of future research.

It should be noted that this cost-effectiveness value is a conservative estimate for the broad patient population of anyone indicated for a single chamber TVPM. Micra VR is likely to have a greater cost-benefit in patients at high risk of infection.

## 5 | CONCLUSION

Micra VR is likely to offer a cost-effective alternative to conventional single-chamber TVPM for the management of Australian patients with bradycardia and AF. As infection is a serious complication, associated with significant mortality and morbidity, a leadless cost-effective option may be advantageous, particularly for patients at high risk of infection or who will have an improved quality of life due to lack of lead restrictions and/or not having a visible reminder of a pacemaker. This cost-effectiveness analysis does not take into account any potential clinical benefit of conduction system pacing that can be achieved with a transvenous system.

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## CONFLICT OF INTEREST STATEMENT

One of the authors (Michelle Hill) is an employee of Medtronic, the manufacturer of Micra VR. The other authors are employed by THEMA Consulting Pty Ltd and received funding from Medtronic for conducting health economics research and consultancy.

## DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article.

## PRECIS

The Micra™ VR leadless pacemaker is a cost-effectiveness alternative to conventional transvenous pacemakers for the management of patients with bradycardia.

## APPROVAL OF THE RESEARCH PROTOCOL

No human participant was involved in this study.

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