Interventional procedure overview of leadless cardiac pacemaker implantation for bradyarrhythmias

Contents

Table 1 Abbreviations

Abbreviation	Definition
6MWT	6-Minute Walk Test
AF	Atrial Fibrillation

AV	Atrioventricular
AVF	Arteriovenous Fistula
CAD	Coronary Artery Disease
CHD	Congenital Heart Disease
CHF	Congestive Heart Failure
CIEDs	Cardiac Implantable Electronic Devices
COPD	Chronic Obstructive Pulmonary Disease
DC-TV	Dual-chamber Transvenous (DC-TV)
ESRD	End Stage Renal Disease
GLS	Global Longitudinal Strain
HR	Hazard Ratio
HRQoL	Health-Related Quality of Life
HTN	Hypertension
LPs	Leadless Pacemakers
LV	Left Ventricular
LVEF	Left Ventricular Ejection Fraction
MAPSE	Mitral Annular Plane Systolic Excursion
M-mode	Motion-mode
MINORS	Methodological Index for Non-Randomised Studies
NIH	National Institutes of Health
NOS	Newcastle-Ottawa Scale
NICE	National Institute for Health and Care Excellence
NT-pro-BNP	N-terminal pro B-type Natriuretic Peptide
OR	Odds Ratio
PAR	Post-Approval Registry
PACES	Pediatric and Congenital Electrophysiology Society
ROBINS-I	Risk of Bias Tool for Non-Randomised Studies
RV	Right Ventricular
TAPSE	Tricuspid Annular Plane Systolic Excursion
TLR	Transvenous lead removal
TPS	Transcatheter Pacing System
TTE	Transthoracic Echocardiography
TVPs	Transvenous Pacemakers
VP	Ventricular Pacing
SD	Standard Deviation
sdHR	Sub-distribution Hazard Ratio

The condition, current treatments, unmet need and procedure

The condition

Bradyarrhythmias are abnormal heart rhythms that can result in a slow heart rate (bradycardia), usually defined as less than 60 beats per minute. There are a range of causes including diseases such as sick sinus syndrome or atrioventricular (AV) block. The most common causes are the natural ageing process, ischaemic heart disease, heart valve disorders and heart failure. If untreated, bradycardia may lead to fatigue, fainting, palpitations, dizziness, heart failure and an increased risk of death.

Current practice

The treatment depends on the underlying cause and the symptoms. If treatment is needed, bradyarrhythmias are usually managed with pacemakers as described in NICE technology appraisal guidance on dual-chamber pacemakers for symptomatic bradycardia due to sick sinus syndrome and/or atrioventricular block and dual-chamber pacemakers for symptomatic bradycardia due to sick sinus syndrome without atrioventricular block. Dual-chamber pacing is recommended for symptomatic bradycardia caused by sick sinus syndrome, AV block, or a combination of both. Single-chamber ventricular pacemakers may be used for AV block alone or with sick sinus syndrome in people with continuous atrial fibrillation (AF), or people who have specific factors such as frailty or comorbidities that influence the balance of risks and benefits in favour of single-chamber pacing.

Unmet need

Bradyarrhythmias are usually managed with transvenous pacemakers (TVPs). However, these are associated with lead and generator-related complications, including lead failure and infection, which contribute to long-term morbidity.

Leadless pacemakers (LPs) provide an option for people who cannot have a conventional TVP. There are also some groups of people who might particularly benefit from LPs, such as those with previous device infection or endocarditis, vascular access issues, or high risk of infection.

The procedure

The aim of implanting a LP is to detect cardiac bradyarrhythmias and deliver electric pulses to help regulate the heartbeat. LPs can provide single-chamber (right ventricle pacing) or dual-chamber pacing (atrial pacing or AV pacing).

The procedure is usually done under local anaesthesia in a cardiac catheterisation laboratory. Fluoroscopic guidance is used and intracardiac echocardiography or contrast may be needed to assist or guide implantation in the desired location in the heart chamber (right ventricle or atrium). For single chamber LP implantation, the proximal end of an LP is attached to a deflectable delivery catheter system and is usually inserted percutaneously via the femoral or jugular vein using an introducer sheath. It is then advanced into the right atrium through the tricuspid valve, into the right ventricle and positioned near the apex or lower septum. Once positioned, the LP is securely implanted into the endocardial wall using a fixation mechanism. Electrical measurements are taken and, if satisfactory, the LP is released from the catheter and the catheter is removed. If the position is suboptimal, the LP can be detached from the endocardium and repositioned before the release of the delivery catheter.

The pacemaker delivers electrical impulses that pace the heart through an electrode at the distal end of the device and is adjusted using an external programming system. A catheter retrieval system is used for removal and replacement of the LP when needed.

A dual chamber LP system consists of 2 devices implanted percutaneously in a single procedure into the target chamber - 1 in the right atrium and another in the right ventricle.

Outcome measures

The efficacy outcomes included successful implantation rate, adequate pacing performance, 6-minute walk test (6MWT), cardiac function, length of hospital stay, health-related quality of life and device durability. Safety outcomes included cardiac perforation, cardiac tamponade, pericardial effusion, pulmonary oedema, AF, device failure (dislodgement, migration, embolisation, malfunction, battery issues), repeat surgery (for device retrieval and revisions), venous thromboembolism, vascular complications, bleeding, infections, mortality, pacemaker syndrome, cardiomyopathy, pericarditis, activity restrictions, overall complication rates and other device- or procedure-related adverse events. Some of the measures used which are not self-explanatory are detailed in the following paragraphs.

Adequate pacing performance

Adequate pacing performance is evaluated based on several key parameters. The pacing threshold, or capture threshold, should ideally be less than or equal to 1.5 V at 0.4 ms pulse width for ventricular pacing (VP) and less than or equal to 1.0 V at 0.4 ms pulse width for atrial pacing, with lower values preferred to reduce battery consumption and ensure effective capture. Sensing amplitude, which reflects intrinsic signal detection, should be 5 mV or more for ventricular

sensing (R-wave amplitude) and 1.5 mV or more for atrial sensing (P-wave amplitude) to ensure proper sensing and minimise the risk of under-sensing events. Pacing impedance, which helps assess lead integrity and connection, should be between 300 to 1,500 ohms. Values outside this range may indicate lead failure, insulation damage, or poor connection. The percentage of VP should ideally be less than 40% in non-dependent people to minimise unnecessary pacing but should be 100% in pacemaker-dependent individuals. AV synchrony of more than or equal to 90% is considered optimal for dual-chamber pacemakers, ensuring physiological pacing and reducing the risk of AF.

Global Longitudinal Strain (GLS)

GLS is an advanced echocardiographic parameter that measures myocardial deformation, reflecting left ventricular (LV) systolic function more sensitively than ejection fraction (EF). It quantifies the percentage of myocardial shortening during contraction, with more negative values indicating better function. The normal range for GLS is typically between -18% to -22%, with values closer to zero suggesting impaired LV function. A GLS less negative than -16% is often considered abnormal and may indicate early myocardial dysfunction.

Right Ventricular Free Wall Strain (RVFWS)

Right Ventricular Free Wall Strain (RVFWS) is an echocardiographic measure of the deformation of the RV free wall during contraction. The normal range for RV free wall strain is typically more negative than -20%, with values less negative than -17% suggesting impaired RV function.

Tricuspid Annular Plane Systolic Excursion (TAPSE)

TAPSE is a measure of right ventricular (RV) function that evaluates RV longitudinal systolic performance. TAPSE is measured using TTE and the systolic displacement of the annulus is recorded in millimetres. A lower TAPSE

value, typically less than 17 mm, suggests impaired RV function and is often seen in conditions such as pulmonary hypertension (HTN) and heart failure.

Mitral Annular Plane Systolic Excursion (MAPSE)

MAPSE assesses the longitudinal contraction of the LV myocardium, to evaluate LV function. Like TAPSE, MAPSE is measured using TTE, recording the displacement of the mitral annulus during systole. Normal values usually exceed 10 mm. A reduced MAPSE value indicates impaired LV function, which is commonly seen in people with heart failure or cardiomyopathy.

N-terminal pro B-type Natriuretic Peptide (NT-pro-BNP)

NT-pro-BNP is a biomarker that reflects cardiac stress and heart failure. It is released by the heart in response to increased ventricular wall tension due to volume overload or myocardial dysfunction. Elevated NT-pro-BNP levels are associated with worsening heart failure, with values above 125 pg/mL in non-acute settings or 300 pg/mL in acute settings indicating a significant risk of heart dysfunction.

Health-related Quality of Life

The SF-36 is a widely used questionnaire that measures health-related quality of life (HRQoL) across eight domains, including physical and mental health. Each domain is scored from 0 to 100, with higher scores indicating better health. Scores are summarised into physical and mental component scores, standardised to a mean of 50 (SD 10). Normal values in the general population typically range from 70 to 95, and a change of 5–10 points is considered clinically meaningful. It is commonly used to assess the impact of illness or treatment on peoples' overall well-being.

The 6-Minute Walk Test (6MWT)

6MWT is a functional exercise test used to evaluate a person's cardiovascular endurance and overall functional capacity. During the test, the person is instructed to walk as far as possible within 6 minutes on a flat, measured surface. The total distance covered in metres is recorded and compared over time to assess disease progression or response to treatment. A normal 6MWT distance varies by age, sex, and comorbidities, but in healthy adults, it typically ranges from 400 to 700 metres. Distances below 300 metres often indicate significant impairment in cardiovascular or pulmonary function.

Evidence summary

Population and studies description

This overview of interventional procedures is based on data from 1,098,766 people across multiple studies, including a randomised controlled trial (RCT) (Garweg 2023), 4 systematic reviews with meta-analyses (Inoue 2024, Wu 2023, Mhasseb 2025, Oliveira 2024), 5 registry studies (El-Chami 2024, El-Chami 2024, Shah 2023, Panico 2024 and Ueyama 2024), 4 prospective studies (Tjong 2018, Amrani 2020, Molitor 2024 and Knops 2023) and 2 retrospective studies (Cabanas-Grandio 2020 and Strik 2023). Among these, 70,394 people had LP implantation. There was considerable overlap in studies between the systematic reviews. Most studies were conducted in the US and Europe. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 16 studies as the key evidence in table 2 and table 3, and lists other relevant 126 studies in appendix B, table 5.

The RCT (Garweg 2023) compared the outcomes of LP with conventional TVP using single-chamber VP. The study cohort included 51 people with a mean age of 82.5 years, and 61% were male. The study employed standardised echocardiographic assessments conducted at baseline, 6 months, and 12 months, along with NT-proBNP measurements at baseline and 12 months.

The systematic review and meta-analysis by Inoue (2025) synthesised evidence on the safety and optimal timing of LP implantation following the removal of cardiac implantable electronic devices (CIEDs) because of infection. Data from 16 observational studies (n=653) published between 2015 and 2024 were included. The mean age was 77 years, 69% were male, with a mean left ventricular ejection fraction (LVEF) of 56%. The average follow-up was 14 months, ranging from 6 to 47 months across studies. Results were grouped based on LP implantation timing—either during CIED removal, or after a set interval.

The meta-analysis by Mhasseb (2025) compared the safety profile of TVPs and LPs. The study included data from 19 observational studies, comprising 12 retrospective cohort studies and 7 prospective cohort studies, conducted across various regions, including the US, Italy, France, Spain, and Japan. The total sample size was 972,479 people, with 57,974 having LPs. The mean age ranged from 70 to 90 years, and the proportion of males ranged from 52% to 70%. The prevalence of comorbidities varied, with AF (89%), HTN (90%), diabetes mellitus (46%), and coronary artery disease (CAD) (56%). Follow-up durations ranged from 30 days to over 5 years.

The systematic review and meta-analysis by Oliveira (2025) included 21 observational studies, with 47,229 people, of whom 12,199 had LP implantation. The study population had a mean age of 80 years and 56% were male. Among the included studies, 8 were prospective and 13 were retrospective, with no RCTs identified. The mean follow-up periods ranged from 6 to 24 months.

The meta-analysis by Wu (2023) included data from 8 observational studies with a total of 464 people with complete or high-grade AV block and sinus node dysfunction with or without AF. There were 3 multicentre prospective studies, 3 single-centre prospective studies, and 2 single-centre retrospective studies. The study population had a mean age of 76.3 years and 44% were female. The

follow-up duration across studies ranged from immediate post-procedure outcomes to a maximum of 12 months, with most studies reporting follow-up durations of less than 3 months.

El-Chami (2024) conducted a multinational, non-randomised, prospective registry study (the Micra VR Post-Approval Registry, PAR) to evaluate the long-term performance of the LP in real-world clinical settings. The study enrolled 1,809 people across 179 centres in 23 countries between July 2015 and March 2018, with a median follow-up duration of 51.1 months and a leading-edge follow-up of 86.7 months. The mean age of the study population was 75.6 years, with a median age of 79 years (IQR 71.0 to 84.0), and 39% were female (701 out of 1,808). There was a high prevalence of comorbidities, including atrial tachyarrhythmias (76%), congestive heart failure (CHF) (15%), chronic obstructive pulmonary disease (COPD) (10%), CAD (22%), HTN (65%), diabetes (27%), renal dysfunction (22%), and dialysis dependency (8%).

A comparative effectiveness analysis conducted by El-Chami (2024) evaluated the long-term outcomes (over a follow-up period of 2 years) of a LP in comparison to a traditional dual-chamber TVP in a large cohort of US Medicare population. A total of 118,110 people were included, of whom 7,552 had a LP and 110,558 had a TVP. The mean age was 79.0 years (range 21 to 105) in the LP group and 78.7 years (range 23 to 106) in the TVP group. The proportion of females was 48% in the LP group and 47% in the TVP group. People in the LP group had a higher burden of comorbidities compared to those in the TVP group.

A multicentre retrospective registry study by Shah (2023) was conducted across 13 centres in the US, 1 in the UK, and 1 in Italy, using data from the Pediatric and Congenital Electrophysiology Society (PACES) registry. A total of 63 people were enrolled, with a mean age of 15 years; standard deviation (SD) 4.1 years and 59% were male. Of the 63 children and young people, 32% had congenital heart disease (CHD), 29% had previous cardiac surgery and 22% had a prior

pacemaker implantation. The mean follow-up was 9.5 months, ranging from 2 to 32 months.

The multicentre, retrospective, observational study by Strik (2023) was based in France and included 35 young adult people aged between 18 and 40 years, with 21 males (60%). The cohort had a mean LVEF of 57%. Indications for LP implantation included congenital AV block (n=3), postoperative AV block (n=7), post-heart transplantation (n=2), muscular dystrophy syndrome (n=5), symptomatic paroxysmal AV block (n=8) and symptomatic sinus node dysfunction (n=10). The mean follow-up period was 26 months; SD 15 months.

Amrani (2020) conducted a prospective observational study in Spain on 129 people over 70 years old who had LPs for single-chamber pacing. The outcomes were stratified into 2 groups based on age: 41 people aged 90 years or older and 88 people younger than 90 years. Sex distribution differed between the groups, with 18 males (44%) and 23 females (56%) in the 90 years and older cohort, compared to 32 males (36%) and 56 females (64%) in the younger cohort. Both groups had a high prevalence of comorbidities, and AV block was the main pacing indication. Follow-ups were done at 7 days, and at 1-, 3-, 6-, and 12-months post-implant, then annually.

A retrospective cohort study (Panico 2024) in France compared outcomes of LPs versus single-chamber TVPs implantation in 384 people on haemodialysis. After 1:1 propensity score matching, 178 people were included (89 in each group), with a mean age of 77.9 years and 30% female. Comorbidities were common: chronic heart failure (63%), AF or flutter (67%), ischaemic heart disease (55%), and diabetes (74%). Median follow-up was 24 months (range 7 to 37).

Molitor (2024) conducted a prospective study in Switzerland and the Netherlands comparing internal jugular versus femoral vein approaches for LP implantation in 200 people (mean age 81.2 years, 60% male). In the jugular group, primary

indications included AV block (39 people), AF-related conditions (32), and sick sinus syndrome or pauses (29). AF was more common in the femoral group, though detailed indications were not provided. Comorbidities were prevalent, with 73% having AF, 36% CAD, 43% valvular disease, 37% chronic kidney disease, and others including COPD, diabetes, cancer, and prior stroke. Follow-ups were on days 1 and 14 with clinical reviews and device checks.

Knops (2023) conducted a prospective multicentre study across 55 sites in the US, Canada, and Europe to assess the safety and performance of a dual-chamber LP in 300 people (mean age 69.2 years, 62% male). Main pacing indications were sinus node dysfunction (63%) and AV block (33%). The primary safety outcome was freedom from serious device- or procedure-related events within 90 days. Performance was evaluated at 3 months by atrial capture and sensing, and by AV synchrony while seated, targeting at least 70%.

The prospective multi-centre clinical trial study (Tjong 2018) involved 726 people undergoing Micra transcatheter pacing system (TPS) implantation across 56 centres in 19 countries between December 2013 and May 2015. The cohort had a mean age of 76 years, with 59% being male. The primary outcomes measured included health-related quality of life, patient satisfaction, and activity restrictions post-implantation.

The comparative retrospective study (Cabanas-Grandío 2020) examined 106 people (64 with TVPs and 42 with LPs) undergoing single-chamber pacemaker implantation from December 2016 to March 2018 across four tertiary hospitals in Spain. The participants had an average age of 79.8 years, with significant differences in age and diabetes prevalence between the groups. Quality of life was assessed using the SF-36 questionnaire at baseline and 6 months post-implantation.

The retrospective cohort study by Ueyama (2024) analysed data from 10,338 Medicare fee-for-service beneficiaries aged 65 or above who had transcatheter aortic valve replacement (TAVR) followed by permanent pacemaker implantation between January 2017 and December 2020 in the USA. Among them, 730 people (7%) had LPs and 9,608 (93%) had TVPs. People were identified using procedure codes from national Medicare claims databases. The study aimed to compare short- and midterm outcomes between the 2 pacemaker types using propensity score overlap weighting to adjust for confounding. The primary outcome measures included in-hospital complications, and midterm outcomes up to 2 years, including all-cause mortality, heart failure hospitalisation, infective endocarditis, and device-related complications.

Table 2 presents study details.

Figure 1 Flow chart of study selection

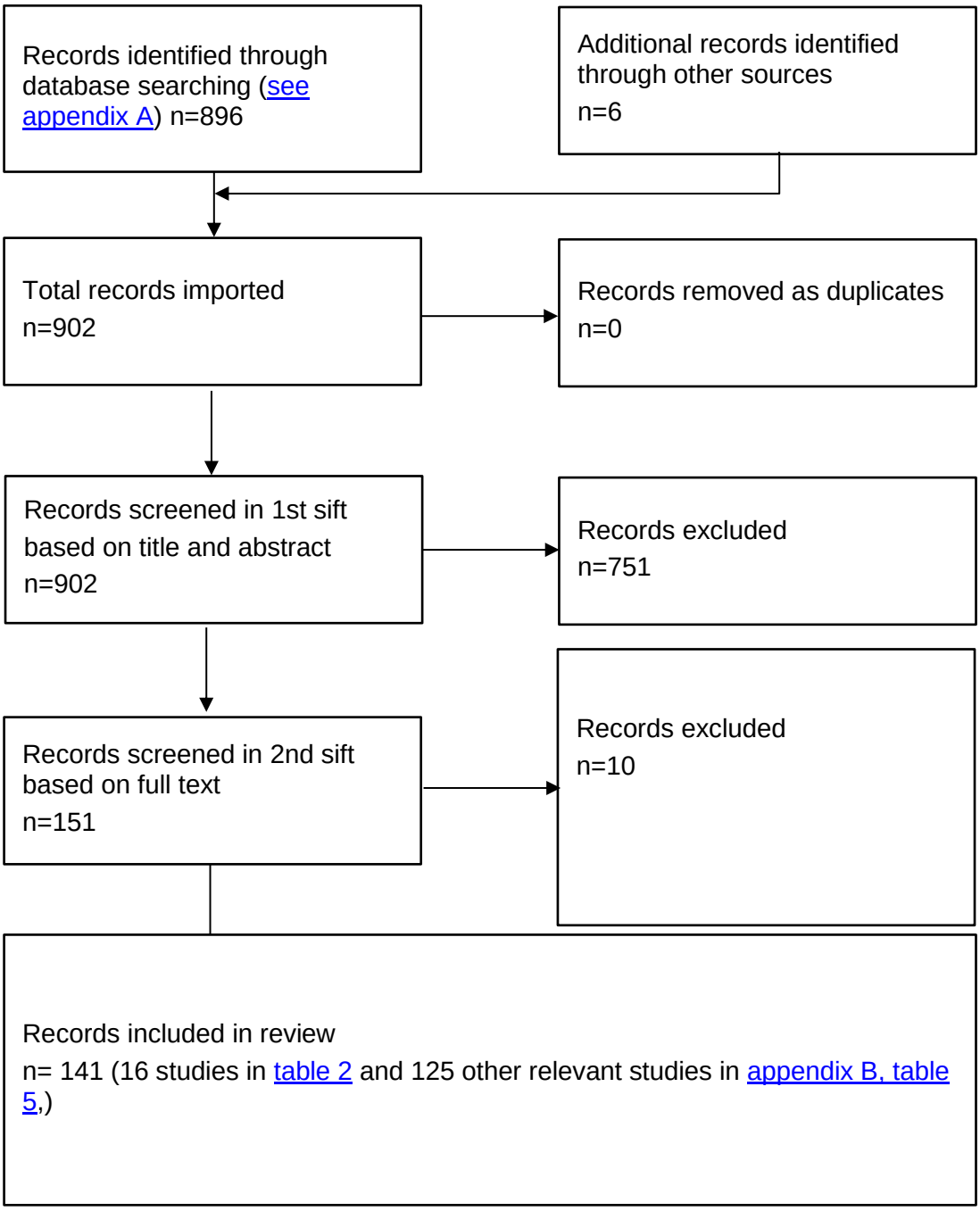

Table 2 Study details

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
1	Garweg C, 2023, Belgium	n=51 Mean age: 82.5 years (SD 4.6) Male: 61% Indications: • severe bradycardia • sinus node dysfunction • high-degree AV block Comorbidities: • arterial HTN (78%) • diabetes mellitus (21%) • previous AF (61%) • CAD (27%) • COPD (8%)	Prospective, randomised, non-inferiority, single-centre study.	18 years or older; Class I or II indication for single-chamber VVI pacemaker; LVEF greater than 40%; adequate baseline echocardiographic image quality; no previously implanted cardiac devices or mechanical valves; no pre-existing conditions challenging or precluding conventional pacemaker implantation; capable and willing to provide informed consent.	Intervention group (n=27): LPs (Micra LP) implanted via femoral approach targeting RV mid-septum or basal outflow tract; Control group (n=24): TVP (single-chamber VVI pacemaker, Medtronic Advisa ADSR03) implanted transvenous with RV pacing lead, also targeting mid-septum or basal RV	12 months; echocardiography at baseline, 6 and 12 months; NT-pro-BNP measured at baseline and 12 months; clinical assessments at day 10, 1, 6, and 12 months.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		renal impairment (mean eGFR ~60 mL/min) Median CHA2DS2-VASc score around 4.			outflow tract initially, apical positioning considered secondary if necessary.	
2	Inoue N, 2024, Japan	n=653 Mean age: 76.9 years Male: 69%; Mean LVEF: 56% (95% CI: 52% to 59%). Common comorbidities: • HTN (62%) • diabetes mellitus (32%) • chronic kidney disease (26%) • COPD (14%) • sinus node dysfunction (17%) • AV block (40%) • AF with bradycardia (30%)	Systematic review and meta-analysis of 16 studies: 1 prospective 7 retrospectives 4 case series 4 unclear designs	Included clinical studies and case series reporting 2 or more cases of CIED removal because of infection followed by LP implantation. Outcomes assessed: all-cause mortality or reinfection after LP implantation. Excluded were reviews, single-case reports, abstracts, indications other than infection, unclear follow-up durations, additional cardiac devices other than LPs, animal studies, and	LP implantation done either simultaneously (immediate strategy: median interval of 0 days) or staged after extraction of infected CIEDs (delayed strategy: median interval of 8 days).	Mean=14 months (SD 9.3); outcomes monitored included mortality rates (all-cause mortality) and occurrences of reinfection.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
				non-English literature.		
3	Mhasseb C, 2025, Lebanon	n=972,479 People with cardiovascular diseases needing permanent pacemaker implantation. Sample size: ranged from 62 to 580,925, mean age ranged from 70 to 90 years. Common comorbidities included: • AF (43 to 96%) • HTN (59 to 90%) • CAD (17 to 56%) • diabetes mellitus (18 to 45%) • hyperlipidemia • peripheral vascular disease	Meta-analysis including 19 observational studies (no RCTs): 7 prospective observational cohort 12 retrospective observational cohort studies or database analyses. High methodological heterogeneity (I^2 varied from 3% to 99%).	Studies comparing TVP and LP, published between 2018 and 2023, in English, with safety-related outcomes: major complications, reintervention, mortality, device malfunction, thromboembolic events, infections, pneumothorax, and haemothorax.	LP, specifically Micra (Medtronic, Minnesota – 17 studies), versus conventional TVP.	Varied widely among studies: from immediate post-procedure (in-hospital outcomes) up to long-term follow-ups ranging from 6 months to approximately 3.5 years (median follow-up durations ranged from 180 days to 39 months across studies).
4	Oliveira VMR, 2025, Brazil	n=47,229 (12,199 LP)	Meta-analysis of 21 observational studies:	Studies published up to September 2023 comparing LP with	LP: primarily Micra (Medtronic,	Varied widely among studies: from immediate

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		Mean age: 80 years (SD 10); 26,646 (56%) males.	8 prospective 13 retrospectives No RCTs included.	TVP, reporting on effectiveness or safety endpoints; adults needing VP.	Minnesota) – 15 studies; Nanostim – 2 studies; both Micra and Nanostim – 3 studies; unspecified – 1 study. LP compared to conventional TVP.	post-procedure (in-hospital outcomes) up to 24 months. Mean follow-up ranged between 6 months to 24 months across studies.
5	Wu S, 2023, China	n=464 Mean age: 76.3 years (SD 4.2); Females: 44%. Indications for pacing included: • complete or high-grade AV block • sinus node dysfunction (with or without AF) VP burden varied (from about 10% in sinus node dysfunction to about	Systematic review and meta-analysis, including 8 observational studies: 3 prospective multicentre 3 prospective single centres 2 retrospective single centre All studies published between 2018 and 2022.	Studies evaluating LP with AV-synchrony algorithm. Reported AV synchrony outcomes post-implantation. Excluded case reports, reviews, non-human studies, duplicated cohorts, studies with combined interventions (ablation or defibrillation) and studies not reporting AV synchrony.	LP, specifically Micra AV (Medtronic, Minneapolis, Minnesota, USA) in 100% of included studies. Accelerometer-based AV synchrony algorithm in VDD pacing mode versus conventional VVI pacing mode.	Immediate post-procedure (in-hospital outcomes) up to a maximum of 12 months follow-up (most studies reported follow-up durations less than 3 months).

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		100% in complete AV block).				
6	El-Chami MF, 2024, Multinational (23 countries)	n=1,809 LP (2,667 historical controls) Mean age: 75.6 years (SD 13.4) Median age: 79 years (IQR: 71 to 84) Female: 39% (701/1808) Comorbidities: • Atrial tachyarrhythmias: 76% (1,373/1,808) • CHF: 15% (279/1808) • COPD: 10% (177/1808) • CAD: 22% (398/1808) • HTN: 65% (1173/1808) • Diabetes: 27% (479/1808)	Micra VR PAR, non-randomised, prospective registry study Multinational: 179 centres, 23 countries Data collection: Implant to 9 years post-implant Comparator group: Historical control (2,667 people with TVPs, studies 2000 to 2012) Outcomes adjudicated by Clinical Events Committee Statistical analysis: Fine–Gray competing risk models, propensity score overlaps weights	People having Micra VR LP implantation Class I or II indications for pacing No comorbidity restrictions Enrolment July 2015 to March 2018 Exclusion: previous enrolment in pre-market trials	Micra VR LP Implantation Device model: MC1VR01, Medtronic, Inc., Minnesota, USA	Median follow-up: 51.1 months (IQR: 21.6 to 64.2)

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		• Renal dysfunction: 22% (389/1808) • Dialysis: 8% (143/1808) Pacing Indication: • Bradyarrhythmia with AF: 63% • AV block: 12% • Sinus node dysfunction: 10% • Syncope: 14%				
7	El-Chami MF, 2024, USA	n=118,110 (n=7,552 LP, n=110,558 TVP) Mean age: LP AV: 79.0 years (SD 10.2); (range: 21 to 105) TVP: 78.7 years (SD 8); (range: 23 to 106) Female: • LP AV: 48% • TVP: 47% Key Comorbidities (LP AV versus TVP):	Comparative effectiveness analysis using Medicare administrative claims linked to device registry data. People identified via device implantation registry and Medicare claims. Adjusted using propensity score overlap-weighted	US Medicare Fee-for-Service (FFS) population undergoing first-time pacemaker implantation (LP AV or TVP) between February 2020 and December 2021.	LP (Micra AV, Medtronic) versus TVP	2 years post-implantation.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		• End stage renal disease (ESRD): 15% versus 2% • Renal dysfunction: 48% versus 34% • Diabetes: 46% versus 38% • CHF: 41% versus 31% • COPD: 25% versus 21% • AF: 40% versus 45% • AV block indication: 74% versus 48% Charlson Comorbidity Index: • LP AV: 5; SD 3.4 • TVP: 3.9; SD 3.0	analysis to control for population characteristics.			
8	Shah MJ, 2023, USA, UK, and Italy	n=63 Mean Age: 15 years (SD 4.1) Weight: 55 kg (SD 19)	Retrospective registry study, multicentre Study Setting: 15 centres, including	Inclusion criteria: People aged 21 years or younger	Micra Transcatheter LP (Medtronic), implanted via	Mean follow-up duration of 9.5 months (SD 5.3); range: 2 to 32 months, median:

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		Sex: 58% male CHD: 32% Prior cardiac surgery: 28% Indications for LP: • Sinus bradycardia or sinus pauses=33% (21/63) • Atrial standstill= 1/63 • AV node dysfunction or AV block=63% (40/63) • Other conduction abnormalities=1/63 24 (38%) had symptomatic bradycardia. Prior pacemaker: 14 (22%) had a prior pacemaker (transvenous: 5, epicardial: 9).	the US, UK, and Italy.	LP implantation (Medtronic) Complete LP procedure documentation Clinical follow-up of 1 week or more Exclusion criteria: People older than 21 years Incomplete procedural data Follow-up less than 1 week	femoral (87%) or internal jugular (13%) venous access. Micra VR was used in 97% of people, and Micra AV in 4.8%.	10 months. Follow-up data categorised in 4-month intervals: 1 to 4 months, 5 to 8 months, and 9 to 12 months.
9	Strik M, 2023, France	n=35 young adult people, with 21 males (60%) and average	Multicentre (4), retrospective, observational	People aged between 18 and 40 years who had	Implantation of the Micra VR LP (Medtronic)	The mean follow-up was 26 months

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		age of 34 years (SD 8). People had the following characteristics: height: 165 cm (SD 29) weight: 66 kg (SD 19) LVEF of 57% (SD 14%) Indications: • congenital AV block (3 people, 9%) • postoperative AV block (7 people, 20%) • post-heart transplantation (2 people, 6%) • muscular dystrophy syndrome (5 people, 14%) • symptomatic paroxysmal AV	study conducted between 2015 and 2021.	implantation of a LP for any indication. The protocol was approved by the ethics committee at each of the 4 participating centres, and all the people provided written and informed consent.		(SD 15); range: 6 to 60 months.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		block (8 people, 23%) • symptomatic sinus node dysfunction (10 people, 29%)				
10	Amrani AE, 2020, Spain	n=129 Age: 41 people aged 90 years or above (mean age 92.9 years; SD 2.4) 88 people aged less than 90 years (mean age 83.9 years; SD 4.1). Gender Distribution: ≥90 Years: 18 males (44%) and 23 females (56%) <90 Years: 32 males (36%), 56 females (64%) Comorbidities: HTN: 36 (86%) in ≥90 years, 73 (83%) in <90 years.	Prospective observational study: People were divided into 2 groups based on age: 90 and above and younger than 90 years.	People older than 70 years with indications for single-chamber pacing. Specific indications for LP implantation included previous TVP infection, absence of upper vascular access, and clinical need assessed by the treating physician.	Micra LPs implanted via transcatheter approach. The procedure was performed under conscious sedation and local anaesthesia.	At 7 days, and 1, 3, 6, and 12 months after implantation, with subsequent annual follow-ups. Electrical parameters and clinical outcomes were monitored throughout the follow-up period.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		Diabetes mellitus: 9 (22%) in ≥90 years, 23 (33%) in <90 years. Chronic kidney disease: 24 (59%) in ≥90 years, 31 (35%) in <90 years Structural heart disease: 14 (34%) in ≥90 years, 49 (56%) in <90 years AF: 9 (22%) in ≥90 years, 10 (11%) in <90 years CHF: 4 (10%) in ≥90 years, 36 (41%) in <90 years. Indications for Pacing: AV block: 29 (71%) in ≥90 years, 61 (69%) in <90 years AF with slow ventricular response: 8 (20%) in ≥90 years, 11 (13%) in <90 years Sinus node dysfunction: 4 (10%)				

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		in ≥90 years, 36 (41%) in <90 years.				
11	Panico A, 2024, France	n=384 adult people with ongoing haemodialysis implanted with a first-time single-chamber pacemaker between 2017 to 2020. Indications: cardiac conduction disorders Demographics: Age: Mean 77.9 years (SD 8.6), Median: 80 years (IQR 74 to 84). Female: 30% (n=27). Comorbidities: • chronic heart failure: 63% (n=56) • AF or flutter: 67% (n=60) • ischemic heart disease: 55% (n=49) • Diabetes: 74% (n=66).	Retrospective cohort study using propensity score matching (1:1) to balance baseline characteristics. Data was sourced from the French REIN registry and linked to the SNDS national health database.	Inclusion Criteria: Adult (≥18 years) haemodialysis population First-time implantation of a single-chamber TVP or LP between January 2017 - December 2020 Matched from the REIN registry and SNDS database Exclusion Criteria: History of any previous pacemaker or defibrillator implantation	LP group (n=89): Majority implanted with Medtronic Micra LP. TVP group (n=89): Conventional single-chamber TVPs.	Median 24 months (range 7 to 37 months).

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		Vascular Access for Dialysis: • Arteriovenous fistula: 75% (n=67) • Catheter: 21% (n=19) Baseline Health Conditions: • high risk for pacemaker-related infections • venous stenosis due to frequent vascular access use.				
12	Molitor N, 2024, Switzerland and Netherlands	n=200. 100 jugular approaches (University Hospital Zurich: n=50, Haga Teaching Hospital: n=50) + 100 femoral approach (comparison group, Zurich only) Mean Age: 81.2 years (SD 8.29)	Prospective study comparing jugular vein approach versus femoral vein approach for LP implantation in 2 tertiary centres.	People with indication for LP implantation No contraindications for standard femoral implantation No severe valvular disease preventing pacemaker implantation	Micra LP implantation via the internal jugular vein. Right internal jugular vein punctured under ultrasound guidance. Standard 9Fr sheath	At day 1 and day 14 post-implantation Monitoring through clinical records, hospital visits, and pacemaker interrogation

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		Gender: 60% male Primary Indications (for the jugular approach group only, n=100): • AV block: 39 (39%) • Tachy-brady syndrome or planned AV node ablation in AF: 32 (32%) • Sick sinus syndrome or pre-automatic pauses: 29 (29%) Comorbidities: • AF (73%) • CAD (36%) • valvular disease (43%) • chronic kidney disease (37%) • COPD (13%)		No history of superior vena cava obstruction No active infection at the time of implantation	followed by 27Fr introducer. Pacemaker delivered via guidewire-assisted catheter technique. Device positioned at inferior (25%), mid (50%), or high (25%) ventricular septum. Compared to standard femoral implantation group	

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		• peripheral artery disease (18%) • diabetes mellitus (24%) • cancer (14%) • previous stroke (20%)				
13	Knops RE, 2023, USA, Canada, Europe (55 centers)	n=300 Male: 62%, Female: 38% Age: 69.2 years (SD 13.5) BMI: 28.1 (SD 5.6) • Sinus-node dysfunction: 63% • AV block: 33% • Previous ablation: 20% • Tricuspid valve disease: 24% • Arrhythmia history: 45% (nonventricular), 4% (ventricular)	Prospective, international, multicentre, single-group study, evaluated safety & performance of dual-chamber LPs.	Inclusion: standard indication for dual-chamber pacing, age 18 or above Exclusion: • mechanical tricuspid-valve prosthesis • inferior vena cava filter • preexisting pacing or defibrillation leads • electrically active implantable medical devices	Dual-chamber LP (Aveir DR i2i, Abbott Medical) implanted percutaneously via the femoral vein, with 2 separate LPs (1 in the right atrium and 1 in the right ventricle), using an active fixation helix for endocardial attachment and beat-to-beat wireless communication	Primary follow-up period was 90 days

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		• Previous lead extraction: 8%			to maintain AV synchrony.	
14	Tjong FVY, 2018, Multiple countries (56 centers across 19 countries), with notable involvement from the Netherlands (Amsterdam UMC, University of Amsterdam).	n=720 implanted with a LP. Mean age: 76; SD 11 years. Gender: 59% male. Clinical indications aligned with class I or II guidelines for VVIR pacing.	Prospective multicenter clinical trial	People suitable for VVIR pacing as per clinical guidelines.	Implantation of a Micra LPs.	At baseline, and then at 3 and 12 months post-implantation.
15	Cabanas-Grandío, 2020, Spain	n=106 (64 TVPs and 42 LPs); average age 79.8 years; baseline characteristics included demographic factors such as sex distribution and prevalence of diabetes.	Comparative retrospective study between LPs and TVPs with follow-up assessments.	Age 18 or more, indication for single-chamber pacemaker implantation, absence of cognitive impairment, ability to complete the SF-36 questionnaire, and ability to provide informed consent.	Single-chamber pacemaker implantation (the research did not specify the brand names of the LPs or TVPs)	6 months post-implantation, with additional assessments at 1 month for some people.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
16	Ueyama HA, 2024, USA	n=10,338 (LP=730, TVP=9,608), median age 82 years, male: 434 (60%) in LP group and 5,398 (56%) in TVP group. Conditions (LP versus TVP): • AF (55% versus 33%) • end-stage renal disease (14% versus 4%) • congestive heart failure (85% versus 81%) • anaemia (70% versus 63%) • prior stroke or TIA (14% versus 10%) • complete heart block (59% versus 78%)	Retrospective cohort study using Medicare claims data	People aged 65 or above who had TAVR between January 2017 to December 2020 with permanent pacemaker (LP or TVP) implanted during same admission.	Micra VR and Micra AV LPs (Medtronic USA), compared to TVPs.	Median duration of 17.3 months (IQR: 7.4 to 29.5), until the occurrence of an outcome event, death, disenrollment from Medicare Part A and B, or up to 2 years post-procedure, whichever came first.

Study no.	First author, date country	Characteristics of people in the study (as reported by the study)	Study design	Inclusion criteria	Intervention	Follow up
		• unknown indications (27% versus 7%)				

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes

Garweg, 2023	**LV Ejection Fraction (LVEF)**
	• Baseline:
	  ○ LP=58% (SD 6%),
	  ○ TVP=59% (SD 6%), p=0.637
	• 6 months:
	  ○ LP=50% (SD 8%),
	  ○ TVP=52% (SD 8), p=0.370
	• 12 months:
	  ○ LP=48% (SD 7%),
	  ○ TVP=46% (SD 9%), p=0.328
	
	Global Longitudinal Strain (GLS)
	• Baseline:
	  ○ LP=-18% (SD 4%),
	  ○ TVP=-19% (SD 3%), p=0.537
	• 6 months:
	  ○ LP=-14% (SD 4%),
	  ○ TVP=-14% (SD 3%), p=0.994
		NT-pro-BNP (pg/dL)
		• Baseline:
		  ○ LP=1,176,
		  ○ TVP=907, p=0.355
		• 12 months:
		  ○ LP=970,
		  ○ TVP=1,394, p=0.041
		
		Tricuspid Valve Regurgitation
		• Baseline:
		  ○ LP (Grade I=59%, Grade II=22%, Grade III=15%, Grade IV=4%),
		  ○ TVP (Grade I=58%, Grade II=38%, Grade III=4%, Grade IV=0%)
		• 12 months: Statistically significant; less worsening in LP versus TVP p=0.009

First author, date	Efficacy outcomes	Safety outcomes

	• 12 months:
	  ○ LP=-13% (SD 2%)
	  ○ TVP=-13% (SD 6%), p=0.878
	
	RV Free Wall Strain
	• Baseline:
	  ○ LP=-21% (SD 5%),
	  ○ TVP=-22% (SD 5%), p=0.812
	• 6 months:
	  ○ LP=-19% (SD 5%),
	  ○ Conventional=-19% (SD 5%), p=0.887
	• 12 months:
	  ○ LP=-19% (SD 5%),
	  ○ Conventional=-18% (SD 5%), p=0.794
	
	TAPSE (cm)
	• Baseline:
	  ○ LP=2.2 (SD 0.7),
	  ○ Conventional=2.1 (SD 0.5), p=0.460
	• 6 months:
	  ○ LP=1.9 (SD 0.6),
	  ○ Conventional=1.7 (SD 0.5), p=0.439
	• 12 months:
	  ○ LP=1.7 (SD SD0.4),
	  ○ Conventional=1.7 (SD 0.3), p=0.729
	
	MAPSE (cm)
	• Baseline:
		Mitral Valve Regurgitation
		• Baseline:
		  ○ LP (Grade I=67%, Grade II=30%, Grade III=4%),
		  ○ TVP (Grade I=75.0%, Grade II=21%, Grade III=4%)
		• 12 months:
		  ○ Stable in LP; worsened in TVP, p=0.304
		Procedural Complications
		• LP group: None
		• Conventional group: 1 minor complication (pocket haematoma) – resolved with further interventions (details not mentioned).
		
		NOTE: The study provided baseline, and 12-month follow-up results only for these specific safety outcomes.

First author, date	Efficacy outcomes	Safety outcomes
	○ LP=1.5 (SD 0.4), ○ Conventional=1.5 (SD 0.4), p=0.723 • 6 months: ○ LP=1.3 (SD 0.3), ○ Conventional=1.2 (SD 0.3), p=0.336 • 12 months: ○ LP=1.3 (SD 0.3), ○ Conventional=1 (SD 0.6), p=0.053 **LV End-Diastolic Volume (mL)** • Baseline: ○ LP=78.4 (SD 24.5), ○ Conventional=68.7 (SD 21.9), p=0.143 • 6 months: ○ LP=76.9 (SD 20.4), ○ Conventional=70.1 (SD 16.8), p=0.221 • 12 months: ○ LP=74.5 (SD 19.2), ○ Conventional=65.2 (SD 21.5), p=0.122 **LV End-Systolic Volume (mL)** • Baseline: ○ LP=33.5 (SD 12.8), ○ Conventional=27.2 (SD 8.5), p=0.043 • 6 months: ○ LP=38.9 (SD 13.0),	

First author, date	Efficacy outcomes	Safety outcomes
	○ Conventional=34.3 (SD 13.4), p=0.224 • 12 months: ○ LP=39.0 (SD 12.0), ○ Conventional=34.4 (SD 14.2), p=0.226 **6-Minute Walk Distance (m)** • Day 10: ○ LP=390, ○ Conventional=318, p=0.215 • 12 months: ○ LP=392.5, ○ Conventional=322, p=0.088	
Inoue, 2024		**Primary Safety Outcome:** Incidence of combined all-cause mortality and reinfection following LP implantation: • **Simultaneous implantation and extraction:** 19% (95% CI: 13 to 28%; I^2=0%) • **Post-extraction implantation:** 8% (95% CI: 4 to 14%; I^2=4%) • **Comparison:** Statistically significant increase in adverse outcomes with simultaneous approach (p=0.009). **Reinfection outcomes:**

First author, date	Efficacy outcomes	Safety outcomes
		• Reinfection specifically defined as recurrence of initial pathogen post-discharge after LP implantation. • **Findings:** No reinfections reported in any included study
Mhasseb, 2025		**All-cause Mortality:** • TVP slightly higher risk than LP (Cohen's d: -0.1; 95% CI: -0.2 to 0.01; I^2=99%). • Comparison: Difference not statistically significant (p=0.07). • **Subgroup Analysis:** Varied by follow-up (1-month, 6-month, 1-year, ≥3 years). Mortality trend slightly favoured LP, not statistically significant across subgroups (p=0.27 between subgroups). **Reintervention (device revision or extraction)** • TVP increased the risk of reintervention compared to LP (LogOR=−0.7, 95% CI −1.2 to −0.3, I^2=77%; p=0.01; 7 studies) **Major Complications:** • Composite outcomes including perforation, generator malfunction, haematoma, infection, dislodgement, pneumothorax or

First author, date	Efficacy outcomes	Safety outcomes
		haemothorax, erosion, thromboembolic events. • TVP higher risk (LogOR: -0.3; 95% CI: -0.6 to 0.1; I^2=79%). • Comparison: Difference not statistically significant (p=0.14) **Cardiac Perforation and Tamponade:** • LP: statistically significant higher risk than TVP (LogOR: 1; 95% CI: 0.6 to 1.5; p<0.001, I^2=81%; 10 papers). **Thromboembolic Events:** • LP higher risk, not statistically significant (LogOR: 0.5; 95% CI: -0.3 to 1.2; p=0.19; I^2=97%, 6 papers). **Infection Rates:** • TVP higher risk, not statistically significant (LogOR: -0.6; 95% CI: -1.7 to 0.6; I^2=98%). • Comparison: Difference not statistically significant (p=0.27) **Pneumothorax and Hemothorax:** • TVP: higher risk (LogOR: -1.1; 95% CI: -2.2 to -0.1; I^2=93%) • Comparison: TVP higher risk (p=0.04), statistically significant. **Generator Malfunction:**

First author, date	Efficacy outcomes	Safety outcomes
		• The overall effect estimate showed that TVP increased the risk of generator malfunction compared to LP, but this was not statistically significant (LogOR = − 0.5, 95% CI −1.1 to 0.2, p=0.1, I^2=97%; 11 papers) **Device or Lead Dislodgement:** • TVP has a higher dislodgement risk (LogOR: -1.1; 95% CI: -1.6 to -0.6; I^2=3%), while LP shows a lower risk. LP reduces dislodgements compared to TVP (p<0.001), which was statistically significant.
Oliveira, 2025	**Pacing Capture Threshold:** lower in LP compared to TVP: statistically significant • Mean difference: -0.2 V • 95% CI: -0.2 to -0.2 V • p<0.01 **Impedance:** No statistically significant difference LP versus TVP: • Mean difference: 32.6 ohms • 95% CI: -22.5 to 87.8 ohms • p=0.25 *(No I^2 or SD explicitly reported.)*	**Primary Safety Outcome (All-cause mortality):** • No statistically significant difference for LP compared to TVPOR: 1.4 • 95% CI: 0.7 to 3.2 • p=0.35 **Overall complications:** Statistically significant and lower with LP: • OR: 0.6 • 95% CI: 0.5 to 0.8 • p<0.01 **Lead dislodgement:** Statistically significant lower with LP:

First author, date	Efficacy outcomes	Safety outcomes
		• OR: 0.3 • 95% CI: 0.2 to 0.6 • p<0.01 **Post-procedure pneumothorax:** Statistically significant lower with LP: • OR: 0.3 • 95% CI: 0.2 to 0.5 • p<0.01 **Pericardial effusion:** Statistically significant higher with LP: • OR: 2.5 • 95% CI: 1.4 to 4.4 • p<0.01 **Cardiac tamponade:** Statistically significant higher with LP: • OR: 3.8 • 95% CI: 2.4 to 5.8 • p<0.01 **Infection:** No significant difference LP versus TVP: • OR: 0.5 • 95% CI: 0.2 to 1.4 • p=0.18

First author, date	Efficacy outcomes	Safety outcomes
		Myocardial perforation: No significant difference LP versus TVP: • OR: 1.8 • 95% CI: 0.5 to 6.5 • p=0.39 **Hematoma:** • No significant difference LP versus TVP: • OR: 1.02 • 95% CI: 0.6 to 1.9 • p=0.96 **Tricuspid regurgitation:** • No significant difference LP versus TVP: • OR: 1.2 • 95% CI: 0.6 to 2.3 • p=0.69 **Pericarditis:** Listed as prespecified but no explicit statistical results reported. **Subgroup analysis (All-cause mortality):** • Overall Risk of Bias (ROBINS-I) ○ Statistically significant subgroup interaction (p=0.02)

First author, date	Efficacy outcomes	Safety outcomes

		• **LP device used (Micra versus Nanostim):**
		  ○ No significant subgroup interaction (p=0.81)
		Meta-regression analysis (All-cause mortality):
		• Overall Risk of Bias:
		  ○ Statistically significant correlation (p=0.01)
		• Mean age: No significant correlation (p=0.52)
		• Proportion of females: No significant correlation (p=0.17)
		• Follow-up duration: No significant correlation (p=0.42)
		
		Note: I^2 statistics were not reported.

Wu, 2023	**Primary Efficacy Outcome (AV Synchrony):** • Pooled mean AV synchrony: 79% (95% CI: 72% to 86%) • High heterogeneity across studies (I^2=90%, p<0.01) • No significant predictors identified in meta-regression (age: p=0.23, gender: p=0.86, pacing indication: p=0.59, study quality: p=0.27, post-TAVI population: p=0.51)	**Overall Safety Outcomes (all studies):** • Overall complication incidence: 6.3% (22/351) **Complications Related to AV Algorithm:** • Extremely low (0.6%), 2 cases of atrial undersensing (post-TAVI subgroup) **Device/Procedure-related complications:** • Pericardial effusion: 1.1% (n=4) • Cardiac rhythm disorders: 2.3% (n=8)

First author, date	Efficacy outcomes	Safety outcomes
	Subgroup Analysis (Programmed Optimisation): • Statistically significant increase in AV synchrony post-optimisation: Mean difference 11% (95% CI: 7% to 16%, p<0.01) • Low heterogeneity (I^2=13%, p=0.33) **Secondary Efficacy Outcome (Cardiac Output, LVOT-VTI):** • Mean LVOT-VTI increased in VDD mode versus VVI mode: Mean difference: 1.9 cm (95% CI: 1.2 to 2.6, p<0.01) • No heterogeneity (I^2=0%, p=0.85)	• Device dislodgement: n=1 • Elevated pacing threshold: n=1 • Death (unrelated to device/algorithm): n=1 • Other minor complications: 1.4% (n=5) **Follow-up duration:** Immediate post-procedure (in-hospital) up to maximum 12 months • No significant heterogeneity or statistical comparisons reported explicitly for safety outcomes.
El-Chami, 2024	**Primary Efficacy Outcomes:** • Successful Implantation: 1792/1809 (99%) **Electrical Performance (at 60 months):** • Pacing threshold: 0.7; SD 0.4 V • Pacing impedance: 533 ohms; SD 101 ohms • R-wave amplitude: 13.1 mV; SD 5.7 mV • Battery longevity: Median 6.8 years remaining after 5 years; ≥5-year longevity remaining: 83.8%	**System/procedure-related major complications:** • At 30 days: 45 (2%) • At 12 months: 61 (3%) • At 36 months: 72 (4%) • At 60 months: 77 (5%, 95% CI: 4% to 6%) **System Revision Rate (60 months):** • 5% (95% CI: 4% to 6%), n=82 • Device upgrades: 41% of revisions • Elevated thresholds: 31%

First author, date	Efficacy outcomes	Safety outcomes
		• Normal battery depletion: 14% (n=12) • Explantations: 11 total (9 percutaneous, 1 surgical, 1 transplant) • **CRT upgrade rate**: 2% at 5 years (95% CI: 1% to 3%) **All-cause Mortality (60 months):** • Total deaths: 676 (40%) • Procedure-related: 5 • Sudden cardiac: 35 • Non-sudden cardiac: 113 • Non-cardiac: 345 (including 15 COVID-19) • Unknown cause: 178 **Major Complication Types (at 60 months)**: • Thrombosis: 2 (less than 1%) • Groin puncture events: 12 (less than 1%) • Cardiac effusion/perforation: 8 (less than 1%) • Pacing-related issues: 28 (2%) • Infection-related: 5 (less than 1%). • No infection-related device removals needed **Comparative Safety Outcomes (LP versus TVP at 36 months):**

First author, date	Efficacy outcomes	Safety outcomes
		• Major complications: HR 0.5 (95% CI: 0.5 to 0.6, p<0.001) • System revisions: HR 0.5 (95% CI: 0.3 to 0.7, p<0.001)
El-Chami, 2024	**No efficacy outcomes measured**	**Chronic complications (2-year):** • LP: 5% (95% CI: 5% to 6%) • TVP: 10% (95% CI: 9% to 10%) • HR: 0.5 (95% CI: 0.5 to 0.6; p<0.0001) **Device-related re-interventions (2-year):** • LP: 4% (95% CI: 3% to 4%) • TVP: 6% (95% CI: 5% to 6%) • HR: 0.62 (95% CI: 0.54 to 0.72; p<0.0001) **Specific Complications:** • **Device-related complications:** LP 3% versus TVP 7%; HR: 0.4; 95% CI: 0.4 to 0.5; p<0.0001 • **Dislodgement:** LP 1% versus TVP 3%; RR reduction 83%; p<0.0001 • **Device revisions:** LP 2%; RR reduction 94%; p<0.0001 • **Device removals:** LP 1%; RR reduction 83%; p<0.0001 • **CRT upgrades:** LP 2%, TVP 2%; p=0.3955 • **LP upgrade to TVP:** 1% (95% CI: 1% to 2%)

First author, date	Efficacy outcomes	Safety outcomes
		Additional Device-Related Outcomes: • **Embolism/thrombosis:** LP 0.2%, TVP 0.2%; HR: 1 (95% CI: 0.4 to 2.6); p=0.9015 • **Pericarditis:** LP 2%, TVP 2%; HR: 1 (95% CI: 0.7 to 1.3); p=0.6876 • **Hemothorax:** LP 1%, TVP 1%; HR: 1 (95% CI: 1 to 1.3); p=0.7931 • **Mechanical failure:** LP 1%, TVP 2%; RR reduction: 48%; p<0.0001 • **Device stenosis:** LP 1%, TVP 1%; RR reduction: 14%; p=0.4152 • **Pocket complications:** LP N/A, TVP 2% **All-cause Mortality (2-year):** • **LP:** 34% (95% CI: 33 to 35%) • **TVP:** 24% (95% CI: 23 to 24%) • **Statistical Comparison:** higher mortality in LP group (HR**:** 1.5; 95% CI: 1.4 to 1.6; p<0.0001). **Sensitivity Analyses:** • **Mortality conditional on survival at 6-months:** Higher mortality remained in LP (HR: 1.39; 95% CI: 1.3 to 1.5; p<0.0001). • **Subgroup analysis (people with AV block):** Mortality higher in LP (HR: 1.51; 95% CI: 1.4 to 1.6; p<0.0001).

First author, date	Efficacy outcomes	Safety outcomes
		• **Falsification test (hip fracture outcome):** LP had higher hip fracture rate (HR: 1.3; 95% CI: 1 to 1.6; suggesting residual confounding). **Subgroup Analyses (by comorbidities):** • **End-stage renal disease:** LP statistically significantly higher (14.9%) than TVP (2.0%); p<0.0001. • **CHF:** LP higher (41.4%) versus TVP (30.6%); p<0.0001. • Higher mortality consistently observed in LP group, attributed to baseline higher comorbidity burden.
Shah, 2023	**Primary Efficacy Outcomes:** • Implant success rate: 98% (62/63) • Capture threshold: <2 V in 96% • Mean R-wave amplitude: 10 SD 5.3 mV • Stable pacing impedances. **Capture Threshold**: • At Implant: 0.8 V (SD 0.5) (95% CI: 0.3 to 2.8 V) • 1 to 4 months: 0.7 V (SD 0.5) • 5 to 8 months: 0.7 V (SD 0.6)	**Complications**: • 16% (10/63) • Major complications (pericardial effusion, femoral venous thrombus, LP replacement for high pacing thresholds) • No deaths, LP infections, or device embolisations • Stable electrical parameters over follow-up **Secondary Outcomes:** • Follow-up of 9.5 (SD 5.3) months.

First author, date	Efficacy outcomes	Safety outcomes
	• 9 to 12 months: 0.7 V (SD 0.5) **Measured R-Wave Amplitude**: • At Implant: 10 mV (SD 5.3) (95% CI: 2.5 to 21.5 mV) • 1 to 4 months: 11 mV (SD 4.3) • 5 to 8 months: 11 mV (SD 4.2) 9 to 12 months: 10.8 mV (SD 4.9) **Pacing Impedance**: • At Implant: 710 ohms (SD 232) (95% CI: 480 to 1580 ohms) • 1 to 4 months: 641 ohms (SD 129) • 5 to 8 months: 603 ohms (SD 85) • 9 to 12 months: 601 ohms (SD 93) • **Device Longevity**: • Estimated more than 8 years in 90% of people at 5 to 8 months follow-up (using Monte-Carlo Methods)	• No device-related infections or embolisations. **Vascular Access Complications**: • Bleeding from femoral venous site resolved with manual compression • Nonocclusive right common femoral venous thrombus (treated with anticoagulation) **Long-Term Outcomes**: • Electrical performance remained stable in 3% (1 needing steroid treatment and 1 needing device replacement) **Procedural Complications (≤24 hours after Implant):**11% (7/63) **Pericardial effusion with tamponade**: 1, successfully treated with pericardiocentesis. **Unsuccessful LP implantation**: 1, device retrieval performed. **Femoral venous bleeding**: 3 (5%), resolved with manual compression. **Hematoma at femoral venous access site**: 1, resolved without intervention. **Right bundle branch block**: 1, resolved spontaneously after 1 week. **Arrhythmia/ECG changes**: 1.

First author, date	Efficacy outcomes	Safety outcomes
Strik, 2023	**Implantation Success:** 100% (35/35) **Primary Efficacy Endpoint (Low ≤2V & Stable Pacing Threshold at 6 Months):** 97% (34/35) **Baseline Pacing Threshold at Implantation:** Mean 2.75V **R-wave amplitude increases at 6 months:** +1.4 mV ($p < 0.01$) **Decreased impedance at 6 months:** -89 ohms (p<0.01) **Pacing threshold unchanged at 6 months:** -0.11V (p=0.3) **Pacing Threshold <1V at different time points:** • Hospital Discharge: 77% • 6 Months: 86% • 1 Year: 83% • 2 Years: 91% **People with >40% VP burden at 1 year:** 37% (13/35)	**Freedom from Major Complications at 6 Months:** 100% (35/35) **Freedom from Major Complications Over Follow-up (26 SD 15 months, range 6 to 60 months):** 100% **Deaths (non-device related, due to pre-existing conditions):** 3 **Device-related infections:** 0 **Device dislodgement:** 0 **LP Retrieval Needed:** 0 **1 case of pacemaker syndrome (resolved with reprogramming)** No perforations, telemetry failure No major complications during follow-up No radiographically visible device dislodgements or telemetry failures

First author, date	Efficacy outcomes	Safety outcomes
	Follow-Up Syncope Cases: 1 presyncope despite pacemaker implantation **Device interrogations and assessments conducted at multiple timepoints:** Baseline, Discharge, 1 Month, 6 Months, 1 Year, and Yearly Thereafter **Fluoroscopy Time for Implantation:** Mean 6 (SD 5) min (range: 1 to 29 min) **Final LP Position:** 89% in the septum, 6% in RV apex, 6% in RV infundibulum **Proportion of People Needing Multiple Deployments:** 74% first attempt, 11% second, 11% third, 1 needed 6 deployments	
Amrani, 2020	**Primary Efficacy Outcome:** • **Successful Implantation:** 40/41 (98%) in ≥90 years group; 87/88 (99%) in <90 years group (p=0.58). • **Less than 2 Repositions:** 39 (98%) in ≥90 years group; 80 (92%) in <90 years group (p=0.32). • **Procedure Time:** 26.1 (SD 11.6) minutes in ≥90 years group; 30.3 (SD 14.2) minutes in <90 years group (p=0.11).	**Procedure-Related Complications:** • **Major Complications:** 0% (no events) in ≥90 years group; 2% (2 events) in <90 years group. • **Incision Site Haematoma:** 0% in ≥90 years group; 2 (2%) in <90 years group. • **Pseudoaneurysm:** 0% in ≥90 years group; 1 (1%) in <90 years group. **Mortality Rates:**

First author, date	Efficacy outcomes	Safety outcomes
	• **Fluoroscopy Time:** 6.4 (SD 4.7) minutes in ≥90 years group; 7.2 (SD 4.9) minutes in <90 years group (p=0.41). • **Pacing Threshold less than1.0 V (0.24 ms):** 39 (98%) in ≥90 years group; 83 (95%) in <90 years group (p=0.55). • **R-wave Amplitude more than5 mV:** 93% in ≥90 years group; 92% in <90 years group (p=0.97). • **Impedance (400 to 1500 OHMS):** 100% in both groups. **Follow-up Pacing Outcomes:** • **1 month:** Continued stability in thresholds; 100% <1.5 V in both groups. • **3 to 12 months:** 100% of ≥90 years group-maintained threshold <1.5 V. • **24 months:** Stability observed in pacing thresholds, but specific data for ≥90 years group not provided. **Length of Hospital Stay:** • Median stay: 3.0 days (IQR: 2.0 to 5.5) in ≥90 years group; 3.0 days (IQR: 1.0 to 9.0) in <90 years group (p=0.95).	• **Total Deaths:** 13 (32%) in ≥90 years group; 16 (18%) in <90 years group. • **Non-cardiovascular Causes:** 93% of deaths in both groups. • **High Pacing Threshold more than1.5 V (0.24 ms):** 1 (1.5 V) in ≥90 years group; 2 (1.5 V, 4.0 V) in <90 years group.
Panico, 2024	**Primary Efficacy Outcome:** **Survival Probability at 2 Years:**	**All-Cause Mortality Rates:**

First author, date	Efficacy outcomes	Safety outcomes
	• LP was associated with lower all-cause mortality compared to TVP (HR=0.7, 95% CI: 0.5 to 1.0, p=0.045) **Complications at Follow-up:** **Device-related infections:** • LP: 0% (n=0), TVP: 9% (n=8) (HR=0.4, 95% CI: 0.2 to 0.8, p=0.0093). **Interventions on haemodialysis vascular access:** • LP: 19% (n=17), TVP: 33% (n=30) (HR=0.6, 95% CI: 0.4 to 1.1, p=0.09). **Annual rate of vascular interventions:** • LP: 4/10 py, TVP: 8.2/10 py (RR=0.49, 95% CI: 0.31 to 0.75, p=0.0014). **Thrombectomy/angioplasty on AVF:** • LP: 3/10 py, TVP: 6.3/10 py (RR=0.5, 95% CI: 0.3 to 0.8, p=0.0034). **First AVF creation:** LP: 0.30/10 py, TVP: 0.8/10 py (RR=0.4, 95% CI: 0.1 to 1.6, p=0.23). **Ulterior AVF creation:** • LP: 0.4/10 py, TVP: 0.8/10 py (RR=0.6, 95% CI: 0.1 to 2.1, p=0.43). **AVF closure/aneurysm resection:** • LP: 0.3/10 py, TVP: 0.3/10 py (RR=0.9, 95% CI: 0.1 to 5.5, p=0.91).	• **In-Hospital Mortality:** LP: 1.1% (n=1), TVP: 7.9% (n=7) (OR=0.13, 95% CI: 0.003 to 1.1, p=0.064). **Acute (<90 Days) Complications:** • **Cardiac arrest:** LP: 3.4% (n=3), TVP: 7.9% (n=7) (HR=0.4, 95% CI: 0.1 to 1.7, p=0.22). • **Hemopericardium:** LP: 1.1% (n=1), TVP: 0% (n=0). • **Endocarditis or device-related infections:** LP: 0%, TVP: 5% (n=4) (HR=0.4, 95% CI: 0.1 to 1, p=0.045) **Long-Term Complications (>90 Days):** • **Device-related infections:** LP: 0%, TVP: 9% (n=8) (HR=0.4, 95% CI: 0.2 to 0.9, p=0.0093). • **DVT/PE:** LP: 7.9% (n=9), TVP: 13% (n=11) (HR=1, 95% CI: 0.4 to 2.2, p=0.92). **Hospital Stay:** LP: 6.8 days (mean), TVP: 11.2 days (mean) (mean difference=-4.4 days, 95% CI: -8.2 to 0.6 days). **Surgical Interventions on Vascular Access:** **Total interventions:** LP: 27, TVP: 75 (RR=0.5, 95% CI: 0.3 to 0.8, p=0.0014).

First author, date	Efficacy outcomes	Safety outcomes
		Time before first intervention: HR=0.6, 95% CI: 0.4 to 1.1, p=0.09).
Molitor, 2024	**Baseline Pacing Threshold:** Not reported **Final Pacing Threshold:** 0.6 (SD 0.4) V at 0.2 ms (jugular) versus 0.5 (SD 0.3) V at 0.2 ms (femoral), p=0.722 **Baseline Sensing Amplitude:** Not reported **Final Sensing Amplitude:** 10 (SD 4.4) mV (jugular) versus 9.9 (SD 4.4) mV (femoral), p=0.799 **Baseline Impedance:** Not reported **Final Impedance:** 772.3 (SD 218.6) ohms (jugular) versus 705.8 (SD 142.3) ohms (femoral), p=0.011 **Pacing Threshold (Day 1):** 0.6 (SD 0.5) V at 0.2 ms (jugular) versus 0.5 (SD 0.4) V at 0.2 ms (femoral), p=0.446 **Sensing Amplitude (Day 1):** 10.9 (SD 4.2) mV (jugular) versus 10.8 SD 4.4 mV (femoral), p=0.865	**Complications (Total):** 2 (jugular) versus 16 (femoral), p<0.01 • **Pericardial Effusion:** 1 (jugular) versus 1 (femoral) • **Device Dislocation:** 1 (jugular) versus 0 (femoral) • **Arterial Injuries:** 0 (jugular) versus 2 (femoral) • **Major Groin Hematomas:** 0 (jugular) versus 13 (femoral) **Positioning Success Rate (First Attempt):** 70% (jugular) **Device Deployment Attempts:** Median 1 (range 1 to 8) (jugular) **No bailout femoral access needed in jugular group:** 100% success with jugular approach, no conversions **No significant procedural discomfort or vagal reactions observed in jugular group:** 0 reported

First author, date	Efficacy outcomes	Safety outcomes
	Impedance (Day 1): 695.7 (SD 205.6) ohms(jugular) versus 662.9 (SD 131.4) ohms (femoral), p=0.188 **Pacing Threshold (Day 14):** 0.6 SD 0.4 V at 0.2 ms (jugular) versus 0.6 SD 0.4 V at 0.2 ms (femoral), p=0.963 **Sensing Amplitude (Day 14):** 11.4 (SD 4.4) mV (jugular) versus 11.7 (SD 4.3) mV (femoral), p=0.771 **Impedance (Day 14):** 611.1 (SD 143.7) ohms (jugular) versus 605.6 (SD 96.7) ohms (femoral), p=0.675 **Electrical Parameters Stability:** No statistically significant changes over follow-up (14 days), jugular and femoral groups showed similar electrical behavior **Procedure Time:** 42.4 (SD 18.5) min (jugular) versus 48.94 (SD 21.04) min (femoral), p=0.02 **Fluoroscopy Time:** 4.7 (SD 5.2) min (jugular) versus 7.7 (SD 7.8) min (femoral), p=0.001	cases **No mortality reported in either group during follow-up:** 0 deaths in both groups **Faster participant mobilisation post-procedure compared to femoral approach:** Immediate mobilisation in jugular group, compared to delayed mobilisation in femoral group **Lower vascular complication risk with ultrasound-guided jugular puncture:** Ultrasound used in all jugular cases, reducing risk of access-site complications **Radiation Exposure:** Fluoroscopy time and radiation dose were statistically significant and lower in the jugular group, contributing to overall procedural safety

First author, date	Efficacy outcomes	Safety outcomes
	Fluoroscopy Dose: 828.7 (SD 1264.5) cG × cm² (jugular) versus 842.8 (SD 1006.3) cG × cm² (femoral), p=0.930	

Knops, 2023	**Atrial capture threshold**:
	• Baseline: Not provided
	• 90 Days: 0.8 (SD 0.7) V
	Atrial sensing amplitude (P-wave amplitude):
	• Baseline: Not provided
	• 90 Days: 3.6 (SD 1.9) mV
	AV synchrony success:
	• Baseline: Not applicable
	• 90 Days: 97% (95% CI: 95.4 to 99.3, p<0.001)
	Successful device implantation rate:
	• At Procedure: 98% (295/300)
	Mean atrial pacing capture threshold:
	• 90 Days: 0.8 (SD 0.7) V
	Mean P-wave amplitude:
	• 90 Days: 3.6 (SD 1.9) mV
	Mean AV synchrony percentage:
	• 90 Days: At least 95% across all postures and activities
	Overall AV synchrony across multiple postures and gaits:
	• Sitting: 98% (95% CI: 97 to 99%)
		Freedom from device- or procedure-related serious adverse events:
		• 90 Days: 90% (95% CI: 87 to 94%, p<0.001)
		Incidence of device- or procedure-related complications:
		• 90 Days: 10% (29 out of 300, 35 events total)
		Incidence of AF:
		• 90 Days: 3% (9), 5 people had prior history.
		Incidence of pericardial effusion:
		• 90 Days: 1% (2), 1 needed pericardiocentesis
		Incidence of device dislodgement (intraprocedural and postprocedural):
		  ○ Intraprocedural: 2% (5)
		  ○ Postprocedural: 2% (5), occurring at 26 SD 17 days after implantation.
		• Incidence of complete AV block at 90 Days: 1
		• Incidence of loss of implant-to-implant communication at 90 Days: 1

First author, date	Efficacy outcomes	Safety outcomes

	• Supine: 97% (95% CI: 95 to 98%)
	• Left lateral recumbent: 97% (95% CI: 96 to 99%)
	• Right lateral recumbent: 97% (95% CI: 96 to 99%)
	• Standing: 98% (95% CI: 98 to 99%)
	• Normal walk: 98% (95% CI: 98 to 99%)
	• Fast walk: 98% (95% CI: 97% to 99%)
		• Intermittent capture in the ventricular LP at 90 days: 1
		• Incidence of access site bleeding at 90 Days: 1
		• Incidence of retroperitoneal hematoma at 90 Days: 1
		• Incidence of heart failure at 90 Days: 1
		• Incidence of syncope at 90 Days: 1, resulted in distal phalanx fracture.
		• Incidence of pleural effusion at 90 Days: 1
		• Incidence of urinary retention at 90 Days: 3
		• Incidence of oral pain at 90 Days: 1, led to tooth extraction.
		• Device revision procedures (retrieval and reimplantation) at 90 Days: 8 revision procedures performed; 6 received new pacemakers.
		Mortality rate (all-cause deaths) at 90 Days: 4 deaths (1%)
		  • Causes: Cardiac arrest (2), malignancy (1), sepsis (1)
		  • None were device- or procedure-related.

Tjong, 2018	**HRQoL:** Evaluated using the Short-Form-36 (SF-36) questionnaire.	**Activity Restrictions:**

First author, date	Efficacy outcomes	Safety outcomes
	Baseline to 3 Months Improvement: • **Physical Functioning:** Mean increase: **6.2 points**; SD not specified. p-value**≤0.0001**. • **Role Physical:** Mean increase: **11.3 points**; SD not specified. p**≤0.0001**. • **Mental Health:** Mean increase: **4.7 points**; SD not specified. p**≤0.0001**. • Other domains showed significant increases (exact p-values and means for each domain are not detailed). **Baseline to 12 Months Improvement:** Continued improvements in SF-36 scores: • **Physical Component Scale:** Mean at baseline: **36.3; SD 9.0**. Mean at 3 months: **38.7; SD 9.1**; p<**0.001.** Mean at 12 months: **38.6; SD 9.4**; p<**0.001**. • **Mental Component Scale:** Mean at baseline: **47.3; SD 12.5**. Mean at 3 months: **50.9; SD 11.6**; p<**0.001**. Mean at 12 months: **50.7; SD 12.2**; p<**0.001**. **Implant Success Rate:**	• 49% rated discharge instructions as less restrictive than traditional pacemaker systems. • 47% rated them equally restrictive, and only 4% found them more restrictive.

First author, date	Efficacy outcomes	Safety outcomes
	• 720 successfully implanted out of 726 attempts (99% success rate).	
Cabanas-Grandío, 2020	**Physical Function at 6 months:** • LP group: 63; SD 27 • TVP group: 42; SD 26 • p<.001 **Role Physical at 6 months:** • LP group: 64; SD 43 • TVP group: 36; SD 45 • p=.004 **Mental Health at 6 months:** • LP group: 75; SD 22 • TVP group: 65; SD 23 • p=.017	**Chest discomfort at 6 months:** • LP group: 18% • TVP group: 39% • p=.032 **Restriction in physical activities due to chest discomfort at 6 months:** • LP group: 11% • TVP group: 37% • p=.004 **Discomfort in the area of intervention at 6 months:** • LP group: 13% • TVP group: 35% • p=.017
Ueyama, 2024	**In-Hospital (short-term) outcomes (part of primary outcomes):** **Length of stay (days)** • Median: Both 4.0 days • IQR: LPs: 2 to 8, TVPs: 2 to 7	**In-Hospital (short-term) outcomes (part of primary outcomes):** **Overall complications** • LPs: 7% • TVs: 10% • p=0.014

First author, date	Efficacy outcomes	Safety outcomes
	• Adjusted mean difference: 1 day (95% CI: 0.2 to 1.4) • p=0.005	**Device-related complications** • LPs: 1% • TVPs: 2% • p=0.015 **Other complications** (e.g. hematoma, cardiac arrest, pericarditis, etc.) • LPs: 3% • TVPs: 5% • p=0.014 **In-hospital death** • LPs: 2% • TVPs: 1% • p=0.17 **Long-term outcomes:** **All-cause death** • Adjusted HR: 1.1 • 95% CI: 1 to 1.3 • p=0.15 **Heart failure hospitalisation** • sdHR: 0.9 • 95% CI: 0.7 to 1.1 • p=0.24 **Infective endocarditis**

First author, date	Efficacy outcomes	Safety outcomes
		• sdHR: 1 • 95% CI: 0.4 to 2.2 • p=0.95 **Device-related complications** • sdHR: 0.4 • 95% CI: 0.2 to 0.6 • p<0.001 **Sensitivity Analyses** **LPs vs TVPs (AF cohort)** • All-cause death HR: 0.9 (95% CI: 0.7 to 1.2), p=0.57 • Device-related complications sdHR: 1 (95% CI: 0.4 to 2.4), p=0.97 **LPs vs TVPs (non-AF cohort)** • All-cause death HR: 1.2 (95% CI: 0.9 to 1.6), p=0.23 • Device-related complications sdHR: 0.2 (95% CI: 0.1 to 0.7), p=0.017

Procedure technique

Most procedures were done using femoral vein access, but jugular vein access was also used.

Final device positioning differed between groups in the RCT of 51 people (Garweg 2023). None of the LPs were placed at the ventricular apex, whereas 6 out of 24 (25%) TVPs needed apical placement because of inadequate pacing parameters in non-apical positions.

In the systematic review and meta-analysis (Oliveira 2023) of 21 studies, LP devices included the Micra (Medtronic, Minnesota) in 15 studies, Nanostim device in 2 studies, both Micra and Nanostim in 3 studies, while 1 study did not specify the LP device used.

Most studies used single-chamber LPs but the study by Knops (2023) used a dual-chamber LP. Dual-chamber LP may need alternative access strategies compared to single-chamber implantation. The Aveir DR i2i (Abbott Medical) dual-chamber LP system was implanted percutaneously via the femoral vein.

Efficacy

Successful Implantation

This outcome was reported in 10 studies and ranged from 98 to 100% for LPs.

A randomised controlled trial of 51 people reported a 100% implantation success rate in both LP and TVP groups. The first-attempt success rate was statistically significantly higher in the LP group (96%; 26 out of 27) compared to the conventional pacemaker group (63%; 15 out of 24, $p<0.001$). Despite this difference, the median total implantation time was similar between groups (LP: 35 minutes, IQR: 31 to 45; TVP: 35 minutes, IQR: 20.3 to 47.8, $p=0.999$). Venous access time was statistically significantly longer in the LP group (17 minutes,

IQR: 14 to 19) compared to the TVP group (7 minutes, IQR: 6 to 14, p<0.001), likely due to additional procedural steps needed for LP implantation, such as routine RV angiography and the use of temporary pacing guide wires in 18 people (Garweg 2023).

In the meta-analysis by Mhasseb (2025), the overall rate of successful implantation was 99% (95% CI 98 to 100%) in the LP group and 98% (95% CI 97 to 99%) in the TVP group (p=0.07). The authors noted that TVP implantation was associated with a higher rate of procedural complications, which contributed to early implantation failures.

The 5-year follow-up of the Micra PAR study (El-Chami 2024) reported a 99% implantation success rate, with the Micra VR successfully implanted in 1,792 out of 1,809 people. Similarly, in the PACES registry study by Shah (2023), which included 63 children and young people, the implantation success rate was 98% (62 out of 63).

A retrospective study of young adults (Strik 2023) involving 35 people aged 18 to 40 years reported a 100% successful implantation rate for the Micra VR LP, with no technical failures or abandoned procedures. Similarly, a prospective observational study (Amrani 2020) including 129 elderly people found no statistically significant difference in success rates between age groups, with implantation being successful in 98% (40 out of 41) of people aged 90 or above and 99% (87 out of 88) in people younger than 90 (p=0.58).

A propensity score-matched retrospective cohort study (Panico 2024) of people using haemodialysis reported implantation success rates of 99% for LPs and 100% for TVPs.

In a prospective study of 200 people (Molitor 2024), comparing jugular versus femoral vein approaches, the success rate was 100% (100 out of 100) with jugular vein access. Success rate in the femoral group was not reported.

For dual-chamber LP implantation, a prospective study (Knops 2023) of 300 people reported an implantation success rate of 98% (295 out of 300), based on achieving effective implant-to-implant communication.

In the prospective study of 720 people (Tjong 2018), 99% people had successful LP implantation.

Adequate Pacing Performance

The randomised controlled trial of 51 people comparing LPs with TVPs reported similar VP percentages at 12 months (LP: 58% versus TVP: 62%, p=0.744). However, paced QRS duration was statistically significantly shorter in the LP group (median 158 ms, IQR: 146 to 166) than in the conventional pacemaker group (164 ms, IQR: 158 to 178, p=0.024). Additionally, pacing efficiency was superior in the LP group, with a statistically significant lower mean pacing threshold at 12 months (0.4 V versus 0.7 V, p<0.001) and higher mean R-wave sensing (14.2 mV versus 10.4 mV, p=0.021), (Garweg 2023).

Similarly, a meta-analysis of 21 studies by Oliveira (2025) found that LPs demonstrated a statistically significant lower pacing capture threshold than TVPs, with a mean difference (MD) of -0.2 V (95% CI -0.2 to -0.2 V, p<0.01). No statistically significant difference in impedance was observed (MD 32.6 ohms, 95% CI -22.5 to 87.8 ohms, p=0.25).

The ability of LPs to achieve AV synchrony was specifically assessed in a systematic review and meta-analysis of 8 observational studies by Wu (2023). The pooled AV synchrony proportion across these studies was 79% (95% CI 72 to 86%), with individual study results ranging from 63% to 89%. Additionally, programming optimisation led to an 11% improvement in synchrony (95% CI 7 to 16%, p<0.01), demonstrating the adaptability of LPs in improving pacing performance over time.

Long-term observational studies further support these findings. The Micra PAR 5-year follow-up study (El-Chami 2024), involving 1,809 people, documented stable pacing capture thresholds, with initial values of 0.7 V at 0.2 ms at implant, which remained consistent at 0.7 at 0.2 ms at 60 months. Pacing impedance declined from 727 ohms at implantation to 533 ohms at 60 months, while sensing amplitude improved from 10.7 mV to 13.1 mV over the same period. Additionally, the Micra AV CED registry study (El-Chami 2024), which included 118,110 people, demonstrated that AV synchrony with LP ranged between 80% and 84%, over a 2-year follow-up period.

Findings from paediatric and younger adult populations also indicated stable electrical performance over time. The retrospective PACES study (Shah 2023) involving 63 children and young people reported that capture thresholds decreased over time, with an initial mean of 0.8 V at 0.2 ms, which declined to 0.7 V at 1 to 4 months, and 9 to 12 months. Similarly, in the retrospective study of young adults (aged 18 to 40 years) by Strik (2023), the pacing efficacy endpoint was met in 97% of people at 6 months, with 1 person having a pacing threshold above 2 V. Additionally, mean R-wave amplitude increased from baseline to 6 months (1.4 mV, $p<0.01$), while impedance decreased (-89 ohms, $p<0.01$), which was statistically significant. At 2 years, 91% of population maintained a pacing threshold below 1 V.

Among an elderly population, findings were similarly positive. The prospective observational study (Amrani 2020) reported that 99% of people aged 90 or above had a pacing threshold below 1.5 V at 0.2 ms, demonstrating electrical stability with no statistically significant differences compared to the younger cohort. The propensity score-matched retrospective cohort study of people on haemodialysis found that LPs maintained stable electrical parameters, with a mean pacing threshold of 0.5 V at implantation, remaining consistent over a median follow-up of 24 months (Panico 2024).

The impact of venous access approach on pacing performance was evaluated in a prospective study (Molitor 2024) of 200 people, comparing jugular and femoral approaches. Pacing thresholds for the jugular approach remained stable over time, measured at 0.6 V at implantation, Day 1, and Day 14. These values were comparable to those observed with the femoral approach, which showed thresholds of 0.5 V at implantation and Day 1, and 0.61 V at Day 14. Sensed amplitudes in the jugular group increased from 10.0 mV at implantation to 10.9 mV on Day 1 and 11.4 mV on Day 14, closely matching the femoral group, which recorded 9.9 mV, 10.8 mV, and 11.7 mV at the same time points. No deterioration in electrical performance was observed. Lead impedance was initially higher in the jugular group at 772.3 ohms; SD 218.6 ohms at implantation, compared to 705.8 ohms; SD 142.3 ohms in the femoral group (p=0.011), but differences diminished over time, with values of 695.7 ohms (SD 205.6) versus 662.9 ohms (SD 131.4) on Day 1 (p=0.188) and 611.1 ohms (SD 143.7) versus 605.6 ohms (SD 96.7) on Day 14 (p=0.675), indicating comparable long-term electrical performance between the 2 approaches.

The performance of dual-chamber LPs was assessed in a prospective single-group study (Knops 2023) of 300 people, evaluating atrial capture threshold and sensing amplitude. At 3 months, 90% of population met predefined criteria for adequate atrial capture threshold (less than or equal to 3.0 V at 0.4 ms) and atrial sensing amplitude (P-wave more than or equal to 1 mV) (95% CI 86.8 to 93.6, p<0.001). The mean atrial capture threshold was 0.8 V (SD 0.7), and mean P-wave amplitude was 3.6 mV (SD 1.9), indicating stable pacing function.

6 minute Walk Test (6MWT)

In the randomised controlled trial of 51 people, there was no significant decline in 6MWT distance over 12 months in either group (p=0.577), and the difference between LP and TVP groups at 12 months was also not statistically significant (p=0.088) (Garweg 2023).

Cardiac Function

A key finding from the RCT study (Garweg 2023) was the preservation of tricuspid valve function in LP population. Over the study period, tricuspid regurgitation statistically significantly worsened in the TVP group (p=0.001), whereas it remained stable in the LP group (p=0.195). By 12 months, there was no progression of tricuspid regurgitation in 58% of those in the LP group compared with 13% of those in the TVP group (p=0.009). Additionally, at 12 months, tricuspid regurgitation worsened in 70% of the TVP population but in only 31% of the LP group (p=0.009). The difference for mitral regurgitation was not statistically significant (p=0.304).

A notable difference was observed in NT-proBNP levels, a biomarker for heart failure progression. At baseline, levels were comparable between groups (LP: 1176 pg/dl, IQR: 603 to 2357; TVP: 907 pg/dl, IQR: 410.5 to 2345.8, p=0.355). By 12 months, NT-proBNP levels had increased in the TVP group but had decreased in the LP group. The final median NT-proBNP level was 970.0 pg/dl (IQR: 536.0 to 1453.5) in the LP group compared to 1394.0 pg/dl (IQR: 1030.0 to 2245.5) in the TVP group (p=0.041). Interaction analysis confirmed a statistically significant overall difference between groups (p=0.013).

Length of Hospital Stay

In the prospective study of 129 elderly individuals (Amrani 2020), hospital stay was similar across age groups, with a median of 3.0 days in both the people aged 90 and more and less than 90 years. The IQR was 2 to 5.5 and 1 to 9 days, respectively, with no significant difference (p=0.95).

In the propensity score-matched study of people on haemodialysis (Panico 2024), those who had LPs had a statistically significantly shorter hospital stay (mean: 6.8 days) compared to those with TVPs (mean: 11.2 days, p=0.0014).

The retrospective cohort study by Ueyama (2024) including 10,338 people who had TAVR reported that the median length of stay was 4 days for both LP and TVP groups. The IQR was slightly wider for LPs (2 to 8 days) compared to TVPs (2 to 7 days). The length of stay was significantly longer with leadless pacemakers compared to transvenous pacemakers (adjusted mean difference 0.8 days; 95% CI: 0.2 to 1.4; p=0.005).

Health-related Quality of Life

The prospective multi-centre clinical trial of 720 people (Tjong 2018) evaluated HRQoL using the Short-Form-36 (SF-36) questionnaire, revealing significant improvements from baseline to 3 months post-implantation of the LPs. Specifically, Physical Functioning improved by an average of 6.2 points ($p \leq 0.0001$), Role Physical increased by 11.3 points ($p \leq 0.0001$), and Mental Health rose by 4.7 points ($p \leq 0.0001$). Continued improvements were observed at 12 months, with the Physical Component Scale showing mean scores of 36.3 (SD 9.0) at baseline, 38.7 (SD 9.1) at 3 months ($p<0.001$), and 38.6 (SD 9.4) at 12 months ($p<0.001$). The Mental Component Scale recorded mean scores of 47.3 (SD 12.5) at baseline, 50.9 (SD 11.6) at 3 months ($p<0.001$), and 50.7 (SD 12.2) at 12 months ($p<0.001$).

In the retrospective study of 106 people (Cabanas-Grandio 2020), in terms of physical functioning, the LP group scored an average of 63 with a standard deviation of 27, while the TVP group had a lower average score of 42 (SD 26), yielding a statistically significant difference ($p<.001$). Similarly, for role physical, the LP group scored an average of 64 (SD 43) compared to 36 (SD 45) in the TVP group, with $p=.004$ indicating a statistically significant difference. Mental health scale for LP group had an average score of 75 (SD 22), contrasted with the TVP group's average of 65 (SD 23), resulting in a statistically significant p-value of .017. These metrics were assessed using the SF-36 questionnaire.

Device Durability

The RCT by Garweg (2023), reported higher impedance values in the LP group suggesting lower current drain and potentially extended battery longevity. At 12 months, pacing impedance was 661.2 ohms (SD 133.1) in the LP group versus 447.4 ohms (SD 121.8) in the TVP group ($p<0.001$). Furthermore, pacing thresholds remained statistically significantly lower in the LP group at all time points ($p<0.001$).

The meta-analysis by Mhasseb (2025) reported that LPs had a lower incidence of generator malfunction than TVPs (LogOR=-0.5, p=0.13). Battery longevity was also evaluated, with a median projected lifespan of 6.8 years, and a 12.1-year median battery life. Battery depletion was reported in less than 1% of LPs, indicating a high degree of durability.

Long-term observational data further support these findings. The Micra PAR 5-year follow-up study (El-Chami 2024) reported that at 5 years, the projected median battery longevity was 6.8 years, with 84% of people having at least 5 additional years of battery life remaining. Device durability remained high, with only 2% of devices needing replacement because of elevated pacing thresholds or battery depletion.

Among paediatric and younger populations, LPs also demonstrated favourable long-term performance. The Children PACES registry study (Shah 2023), which included 63 people, projected battery longevity using Monte Carlo methods, estimating that 90% of the 55 people with available follow-up data would exceed 8 years of battery life. The retrospective study (Strik 2023) of young adults undergoing LP implantation, with an average follow-up of 26 months; SD 15 months (range: 6 to 60 months), indicated stable device performance, with no reported instances of pacemaker failure, extraction, or retrieval during the study period.

The prospective study of 129 elderly individuals (Amrani 2020) reported that LPs had optimal electrical performance, with no reported device failures, dislodgements, migrations, or malfunctions over a 2-year follow-up period. During the 3-month follow-up after implantation, 93% of people aged less than 90 years and all people aged 90 or above maintained stable pacing thresholds of less than 1.5 V.

Safety

Cardiac perforation

The meta-analysis by Mhasseb (2025) reported that cardiac perforation was statistically significantly higher in the LP group than the TVP group. Among the 10 studies included in the analysis, 8 studies documented a greater risk of perforation in LPs (LogOR=1, $p<0.001$). However, Oliveira (2025), in a separate meta-analysis, found no statistically significant difference in myocardial perforation rates between LPs and TVPs (OR=1.8, 95% CI 0.5 to 6.5, $p=0.39$).

Findings from large observational studies support the low absolute incidence of cardiac perforation. The Micra PAR 5-year follow-up study (El-Chami 2024) reported 1 case of cardiac perforation among 1,809 people. Similarly, the retrospective PACES registry study (Shah 2023) recorded 1 case of cardiac perforation with pericardial effusion in a 7-year-old, 19 kg child, where the device had been deployed at the RV apex. This complication led to cardiac tamponade, which was successfully managed with pericardiocentesis, allowing the device to remain in place without further issues.

In elderly populations, the prospective study of 129 people (Amrani 2020) documented 1 case of cardiac perforation occurring in a person aged under 90 years. This complication was observed early in the implantation experience of the clinical team, suggesting that operator experience may play a role in procedural safety.

The propensity score-matched retrospective cohort study (Panico 2024) of people on haemodialysis found that cardiac perforation was not commonly reported in either LP or TVP groups. 1 case of haemopericardium was recorded in the LP group, potentially due to perforation, though no statistically significant difference was observed compared to the TVP group (0% incidence, p=0.07).

Cardiac tamponade

The meta-analysis by Mhasseb (2025) reported a 0.33% cumulative incidence of cardiac tamponade in those who had LPs, consistent with findings (0.33% cumulative incidence) from the Oliveira (2025) study, which found a statistically significantly increased risk in the LP group compared to the TVP group (OR 3.8, 95% CI 2.4 to 5.8, p<0.01). Observational data from the Micra PAR follow-up study (El-Chami 2024), included 6 cases of cardiac tamponade (less than 1%) among 1,809 people.

Pericardial effusion

The meta-analysis of 21 studies by Oliveira (2025) reported a statistically significantly higher risk of pericardial effusion in the LP group compared to the TVP group (OR 2.5; 95% CI 1.4 to 4.4, p<0.01). The systematic review and meta-analysis by Wu (2023) reported 4 cases of pericardial effusion in their study cohort (n=464).

The occurrence of pericardial effusion was consistently low across studies, with 1 case reported in each of the Micra PAR 5-year follow-up study (El-Chami 2024), the children PACES registry (Shah 2023), and both the jugular and femoral approach groups in a prospective study of 200 people (Molitor 2024). These findings suggest that pericardial effusion remains a rare complication, regardless of population or venous access approach.

In the prospective single-group study (Knops 2023) of 300 people who had dual-chamber LPs, pericardial effusion was reported in 2 people (1%), with 1 needing pericardiocentesis, while the other was managed conservatively.

Pulmonary oedema

In the Micra PAR 5-year follow-up study including 1,809 people (El-Chami 2024), there was 1 report of pulmonary oedema during the follow-up period.

Atrial Fibrillation (AF)

The Micra PAR 5-year follow-up study (El-Chami 2024) reported that AF was more common in people who had LPs compared to historical TVP cohorts, though precise incidence rates were not reported.

In a prospective study (Knops 2023) involving 300 people implanted with dual-chamber LPs, AF was the most common arrhythmic complication, occurring in 9 people (3%). Of these, 5 people had a prior history of atrial arrhythmias. In 8 people, AF occurred either during or immediately after implantation of the atrial LPs. All AF cases were successfully managed with pharmacological or electrical cardioversion.

Device failure (dislodgement, migration, embolisation, malfunction, battery issues)

The meta-analysis by Mhasseb (2025) reported that device dislodgement was lower in the LP group than in the TVP group. Among the 10 studies assessing this outcome, 8 documented a statistically significantly higher risk of dislodgement in TVPs (LogOR=-1.1, $p<0.001$). Lead dislodgement was less common in the LP group (0.1%) compared to the TVP group (1%, $p<0.001$) and there were a 70% lower odds of pacing failure due to lead dislodgement in the LP group compared to the TVP group (OR=0.3, 95% CI: 0.2 to 0.4). Additionally, generator malfunction was more frequent in TVPs (LogOR=-0.5, $p=0.13$), though this difference was not statistically significant. Similarly, a meta-analysis by

Oliveira (2025) found that people who had LPs were at lower risk of lead dislodgement compared to those with TVPs (OR 0.3, 95% CI 0.2 to 0.6, p<0.01), a finding attributed to the absence of transvenous leads in LPs. 1 case of device dislodgement was reported in the systematic review by Wu (2023).

The Micra PAR 5-year follow-up study (El-Chami 2024) of 1,809 people documented 2 cases of device dislocation without embolisation (less than 1%) and 1 case of embolisation during implantation. Additionally, battery depletion in the presence of elevated thresholds was reported in 12 people. In the larger Micra AV CED registry study (El-Chami 2024) of 118,110 people, device-related complications were statistically significantly lower in LP population (219 out of 7,552; 3%) compared to TVP population (7,518 out of 110,558; 7%, p<0.0001). Dislodgement was observed in 1% (38 out of 7,552) of LP population versus 3% (3,095 out of 110,558) of TVP population (p<0.0001), and mechanical failure occurred in 1% (60 out of 7,552) versus 2% (1,658 out of 110,558) (p<0.0001).

The propensity score-matched retrospective study of people on haemodialysis found that lead-related complications were higher in the TVP population (Panico 2024). Lead fractures and dislodgements were observed exclusively in those who had TVPs (9%), whereas no cases of lead dislodgement, migration, embolisation, or battery malfunction were reported in the LP group (HR 0.4, 95% CI 0.2 to 0.9, p=0.0093). The prospective study (Molitor 2024) of 200 people comparing venous access sites reported only 1 case of device dislocation in the jugular approach group, which was the only device-related complication documented in that study. In the retrospective cohort study of 10,338 people who had TAVR as well as pacemaker implantation (Ueyama 2024), in-hospital device-related complications were 1% for LPs and 2% for TVPs (p=0.015), with fewer long-term device-related complications (sdHR 0.4; 95% CI: 0.2 to 0.6; p<0.001) and the differences in groups were statistically significant. In the AF cohort, device-related complications were not statistically significant between LPs and TVPs

(sdHR 1; 95% CI: 0.4–2.4; p=0.97). The non-AF cohort showed fewer complications with LPs compared to TVPs (sdHR 0.2; 95% CI: 0.1 to 0.7; p=0.017) and the difference was statistically significant.

In the prospective single-group study of 300 people evaluating the safety and performance of dual-chamber LPs, there were 6 cases of intraprocedural dislodgement (5 atrial and 1 ventricular pacemaker) (Knops 2023). Additionally, postprocedural dislodgement was observed in 5 cases, all involving the atrial LPs, at an average of 26 days: SD 17 days (range, 0 to 40 days) after implantation. In 4 of these cases, the device migrated outside the right atrium to the right ventricle (n=3) or the right pulmonary artery (n=1). All dislodged devices were successfully retrieved, and in 3 cases, reimplanted.

Repeat surgery (for device retrieval and revisions)

The meta-analysis by Mhasseb (2025) found that reintervention rates were significantly lower in the people who had LPs than in those with TVPs. Among the 19 included studies, 7 specifically examined reintervention outcomes, all of which reported a higher likelihood of device revision or extraction in the TVP group (LogOR=-0.7, p<0.001). The primary reasons for reintervention in TVPs included lead-related complications and system failures.

The Micra PAR 5-year follow-up study (El-Chami 2024) of 1,809 people reported an all-cause system revision rate of 5% (95% CI: 4% to 6%) over 5 years. The primary drivers of system revision were device upgrades (41%) and elevated pacing thresholds (31%). Similarly, the Micra AC CED study (El-Chami 2024), which included 118,110 people, found that device-related reinterventions were lower in LP population (264 out of 7,552; 4%) compared to TVP population (6,191 out of 110,558; 6%) (p<0.0001), which was statistically significant. Furthermore, device removals occurred in 53 out of 7,552 LP population (less than 1%), while the rate of upgrade from LP to a TVP pacemaker was 1% (106

out of 7,552), indicating that while LPs need fewer system revisions overall, device upgrades still occur in a small proportion.

The retrospective study of 63 children and young people (aged 21 and under; Shah 2023) reported 1 case of device retrieval and replacement due to high pacing thresholds at 1-month post-implantation. The retrospective cohort study of people on haemodialysis (Panico 2024) found that repeat procedures were more common in those who had TVP because of lead-related complications. Reinterventions for lead dysfunction occurred in 9% of people with TVPs compared to 0% of those with LPs (HR 0.4, 95% CI 0.2 to 0.9, p=0.0093).

The prospective single-group study of 300 people implanted with dual-chamber LPs, reported 8 revision procedures within 90 days (Knops 2023). Of these, 6 involved successful percutaneous retrieval followed by new pacemaker implantation, while 2 people did not have a replacement atrial pacemaker at the investigator's discretion.

Venous thromboembolism

The meta-analysis by Mhasseb (2025) indicated a higher risk of thromboembolic events in people who had LPs with a LogOR of 0.5 (95% CI: -0.3 to 1.2; 6 studies; I^2=97%). However, this association did not reach statistical significance. The Micra PAR study (El-Chami 2024) reported 2 cases of venous thrombosis (less than 1%) among 1,809 people, comprising 1 case of deep vein thrombosis (DVT) and 1 case of pulmonary embolism (PE). The Micra AV CED registry study (El-Chami 2024), which included 118,110 people, found comparable rates of embolism and thrombosis between LP recipients (15 out of 7,552; 0.2%) and TVP population (221 out of 110,558; 0.2%), with no statistically significant difference between the groups (p=0.9015).

The retrospective multicentre study of 63 children and young people (Shah 2023) reported 1 case of a non-occlusive femoral venous thrombus identified post-

implantation. This was successfully treated with enoxaparin for 2 months, with complete resolution confirmed on follow-up imaging.

A propensity score-matched retrospective cohort study (Panico 2024) of people on haemodialysis reported that VTE incidence was slightly higher in the people who had TVPs (13%) compared to those who had LPs (8%). This difference was not statistically significant (HR 1, 95% CI 0.4 to 2.2, p=0.92).

In the prospective study of 300 people who had dual-chamber LP implantation, a single case of pulmonary embolism occurred 28 days post-implantation. This event was excluded from the primary safety analysis as it was attributed to COVID-19 rather than the pacemaker itself.

Vascular complications

The Micra PAR 5-year follow-up study (El-Chami 2024) reported a low incidence of vascular complications, with 12 cases (0.7%) of groin puncture-related issues, including AVF (less than 1%), vascular pseudoaneurysm (less than 1%), and vessel puncture site haematoma (less than 1%). Similarly, the retrospective study of young adult population by Strik (2023) found minimal vascular complications, with no major adverse events reported.

The prospective observational study (Amrani 2020) of an elderly population reported a 2% incidence of vascular complications (n=2), comprising a single case of femoral pseudoaneurysm and 1 haematoma, both of which were deemed unrelated to the LP device itself. Similarly, the retrospective cohort study of a propensity score-matched haemodialysis population (n=384) found that vascular complications were more common in TVP population than in LP population, with 8 cases (9%) occurring in the people who had TVP implantation compared to 2 cases (2%) in the LP population (HR 4.25, 95% CI 0.88 to 20.39, p=0.07).

The prospective study of 200 individuals reported that the femoral approach was associated with a higher rate of complications, with 2 people having femoral artery injury (2%) and 13 major groin haematomas (13%). No vascular complications were observed in the jugular approach group (Molitor 2024).

In the prospective single-arm study of 300 people with dual-chamber LPs, there was 1 report each of vascular access site bleeding and retroperitoneal haematoma (Knops 2023).

Bleeding

The RCT of 51 people by Garweg (2023) reported a single case of pocket haematoma in the TVP group, which led to prolonged hospitalisation. The Micra PAR study of 1,809 people (El-Chami 2024), reported 1 case of retroperitoneal haemorrhage. The Children PACES registry study (Shah 2023) reported minor bleeding at the femoral venous access site in 3 people (5%), all of which resolved with manual compression. 1 person developed a femoral haematoma that needed no further intervention.

The retrospective propensity score-matched study of people on haemodialysis (Panico 2024) reported similar rates of bleeding events in both LP and TVP groups. 6 cases (7%) were recorded in the people who had TVPs, compared to 4 cases (5%) in the LP population (HR 0.7, 95% CI 0.2 to 2.4, p=0.52). In the prospective study of 300 individuals implanted with dual-chamber LPs, bleeding-related complications were minimal, with 1 case of access site bleeding and 1 case of retroperitoneal haematoma (Knops 2023).

Infections

The meta-analysis by Mhasseb (2025) assessed infection rates across 11 studies and found that while infection risk was lower in those who had LPs compared to those with TVPs, the difference did not reach statistical significance (LogOR=-0.6, p=0.27). Similarly, Oliveira (2025) conducted a separate meta-

analysis evaluating infection rates and found no statistically significant difference between LPs and TVPs (OR 0.5, 95% CI 0.2 to 1.4, p=0.18).

In the Micra PAR 5-year follow-up study (El-Chami 2024), infection rates remained low, with 9 cases reported among 1,809 people. Of these, 5 were classified as major complications, including sepsis, abdominal wall infection, and catheter site infection, all of which were managed successfully with antibiotic therapy. No cases needed device removal because of infection. In the Micra AV CED study (El-Chami 2024), which analysed data from 7,552 LP recipients, 45 device-related infections were documented (1%). This rate was lower than that observed in the dual-chamber TVP cohort (p<0.0001). Furthermore, device-related infections were statistically significantly lower in the LP group (1%; 45 out of 7,552, p<0.0001). The impact of pacemaker type on infection risk has also been examined in high-risk populations. In a retrospective propensity score-matched study of people on haemodialysis, Panico (2024) reported a statistically significantly higher infection rate among the people who had TVP implantation. Device-related infections occurred in 9% of TVP population, whereas no infections were documented in the LP population (HR 0.4, 95% CI 0.2 to 0.9, p=0.0093).

Mortality

The RCT by Garweg (2023) reported 3 deaths during the study period between 9 and 11 months after implantation—1 in the LP group and 2 in the TVP group. These deaths were attributed to non-cardiac causes (2 due to cancer and 1 due to pulmonary infection) and were not related to the device itself.

The systematic review and meta-analysis by Inoue (2024) demonstrated a statistically significantly higher pooled mortality rate among people who had simultaneous LP implantation and CIED removal (23%, 95% CI: 16% to 32%, I^2=0%, p=0.72) compared to post-extraction LP implantation (9%, 95% CI: 4% to 16%, I^2=21%, p=0.27), with a statistically significant difference between these

groups (p=0.008). Temporal trends indicated an estimated 1-month mortality rate of 3%, which was lower than the 7% observed in the simultaneous implantation population. By 186 days, mortality increased to 9% in the post-extraction implantation group, compared to 21% in the simultaneous implantation population.

The impact of pacemaker type on all-cause mortality has also been evaluated in meta-analyses. The meta-analysis by Mhasseb (2025), analysing 13 of 19 included studies, found a higher risk of mortality associated with TVPs, but this did not reach statistical significance (Cohen's d=-0.1, 95% CI: -0.2 to 0.01). Similarly, found no statistically significant difference in overall mortality between the people who had LPs and TVPs, with ORs and HRs consistently non-significant across different analytical approaches: overall analysis (OR 1.4, 95% CI 0.7 to 3.2, p=0.35), multivariate-adjusted analysis (OR 1.3, 95% CI 0.7 to 2.8, p=0.43), and time-to-event analysis (HR 1.1, 95% CI 0.9 to 1.3, p=0.53). This review also documented 1 death following LP implantation; however, the cause was not specified, making it unclear whether the event was device- or procedure-related.

The Micra PAR 5-year follow-up study (El-Chami 2024) reported 676 deaths among 1,809 people, corresponding to a 5-year mortality rate of 40%. Notably, 5 procedure-related deaths were identified, including 2 attributed to cardiac perforation. In a broader cohort analysis, the Micra AV CED study (El-Chami 2024) involving 118,110 people reported statistically significant higher all-cause mortality in LP population (2,567 of 7,552; 34%) compared to TVP population (26,305 of 110,558; 24%), yielding a HR of 1.5 (95% CI: 1.4 to 1.6, p<0.0001). A sensitivity analysis adjusting for 6-month survival confirmed persistence of this increased mortality risk (adjusted HR: 1.4, 95% CI: 1.3 to1.5).

The retrospective study of young adult people (n=35) recorded 3 deaths over a mean follow-up of 26 months, however none were related to LP implantation or

the device (Strik 2023). There were 2 deaths in people with severe pre-existing conditions needing intubation and sedation, while the third resulted from malignancy. In the prospective observational study of an elderly population (Amrani 2020), 29 deaths were reported, with a mortality rate of 32% among those aged more than 90 years (n=13) compared to 18% in those younger than 90 years (n=16). Importantly, all deaths in this cohort were attributed to non-cardiovascular causes, with no device-related mortality reported.

In the propensity score-matched cohort study of people on haemodialysis (Panico 2024), the HR for mortality in the LP population compared to TVP was 0.7 (95% CI: 0.5 to 1, p=0.045), indicating a statistically significant reduction in mortality risk.

The prospective study of 300 people with dual-chamber LPs reported 4 deaths during follow-up, occurring between 46- and 86-days post-implantation (Knops 2023). The mean age of these people was 74 years. Causes of death included cardiac arrest (n=2), malignancy (n=1), and sepsis (n=1), with none attributed to the device or implantation procedure. In the retrospective cohort study of 10,338 people who had TAVR as well as pacemaker implantation (Ueyama 2024), there were no statistically significant differences in groups regarding all-cause death, with an adjusted HR of 1.1 (95% CI: 1 to 1.3; p=0.15) and in-hospital death (2% versus 1%; p=0.17). In the AF cohort, there was no statistically significant difference in all-cause death between LPs and TVPs (HR 0.9; 95% CI: 0.7 to 1.2; p=0.57). Similarly, in the non-AF cohort, LPs and TVPs showed no statistically significant difference in all-cause death (HR 1.2; 95% CI: 0.9 to 1.6; p=0.23).

Pacemaker syndrome

In the large prospective registry study, El-Chami (2024) followed 1,809 people with LPs over 5 years and reported pacemaker syndrome incidence of less than 1% (n=7). Similarly, in a retrospective study of 35 young adults by Strik (2023),

1 person experienced pacemaker syndrome, presenting with intermittent chest discomfort and light-headedness, attributed to retrograde P-wave conduction during VP. This issue was managed successfully by lowering the lower rate limit of the pacemaker without necessitating device removal or replacement.

Cardiomyopathy

In the large prospective registry study of 1,809 people by El-Chami (2024) pacing-induced cardiomyopathy occurred in 5 people over 5 years.

Pericarditis

The Micra AV CED study, also led by El-Chami (2024), evaluated a larger cohort of 7,552 LP population compared to 110,558 TVP population. Pericarditis was reported in 2% of LP population and 2% of TVP population (p=0.6876), indicating no significant difference.

Overall complication rate

The systematic review and meta-analysis by Oliveira (2025) reported overall complications were significantly lower in the comparison group, with an OR of 0.6 (95% CI: 0.5 to 0.8; p<0.01). Procedure-related adverse events were assessed in a systematic review by Wu (2023), which included 7 studies and reported an overall complication rate of 6%. The Micra AV CED study by El-Chami (2024), evaluated a larger cohort of 7,552 LP population compared to 110,558 TVP population. In this study, overall complication rates were statistically significantly lower in the LP population (5% versus 10%, p<0.0001), with fewer device-related complications such as dislodgement and infections. The retrospective cohort study of 10,338 people who had TAVR and pacemaker implantation (Ueyama 2024) reported that overall complication rates were statistically significant between LP and TVP groups (7% versus 10%; p=0.014).

Activity Restrictions

In the prospective multi-centre clinical trial of 720 people (Tjong 2018), it is reported that 49% of people rated them as less restrictive compared to TVPs. Additionally, 47% of people felt that the discharge instructions were equally restrictive, while only a small minority of 4% found them to be more restrictive.

At six months post-implantation in the retrospective study of 106 people (Cabanas-Grandio 2020), only 11% of people in the LP group reported restrictions in physical activities due to chest discomfort, compared to 37% in the TVP group. This difference (p=.004) was statistically significant.

Other device- or procedure-related adverse events

The RCT of 51 people by Garweg (2023) reported a statistically significant higher radiation dose in the LP group because of the use of biplane RV angiography, with reported values of 334.9 mGy (IQR: 219.6 to 444.9) compared to 9.2 mGy (IQR: 3 to 28.3) in the conventional group (p<0.001).

The meta-analysis by Mhasseb (2025) reviewed various complications, including pneumothorax, haemothorax, and haematoma. While the odds of major complications were lower for LPs than for TVPs (LogOR=-0.3), this difference was not statistically significant (p=0.14). Similarly, Oliveira (2025) found no significant difference between LPs and TVPs in terms of tricuspid regurgitation (OR 1.2, 95% CI 0.6 to 2.3, p=0.69) or haematoma (OR 1, 95% CI 0.6 to 1.9, p=0.96). The study found that pneumothorax was statistically significantly lower in the LP group compared to the TVP group (OR 0.3, 95% CI 0.2 to 0.5, p<0.01).

The systematic review by Wu (2023), which included 7 studies and reported 1 case of elevated pacing threshold, 2 cases of atrial undersensing, and 5 unspecified complications. The review also identified ventricular pause and oversensing-induced tachycardia as potential synchrony algorithm-related complications, though only 2 cases were reported across the entire dataset.

In the Micra AV CED study (El-Chami 2024), which evaluated a larger cohort of 7,552 LP population compared to 110,558 TVP population, the rate of upgrades to cardiac resynchronisation therapy (CRT) was similar between the 2 groups (1.6% versus 1.7%, p=0.40).

The PACES children registry study of 63 people reported a complication rate of 16%. Among these complications, 1 person developed right bundle branch block post-implantation, which resolved spontaneously within a week, while another experienced attenuation of measured R waves 4 days post-implantation, improving after a 5-day course of oral steroids. There were no reported cases of worsening tricuspid valve regurgitation, thromboembolic events, or arrhythmias beyond those previously described.

The retrospective cohort study by Panico (2024) examined a propensity score-matched population of 384 hemodialysis population implanted with either LPs or TVPs. The study found that central venous stenosis and vascular access complications were more common in those who had TVPs. Interventions related to haemodialysis vascular access were needed in 33% of TVP population compared to 19% of LP population (HR 0.6, 95% CI 0.4 to 1.1, p=0.09), which was not statistically significant.

The prospective single-group study (Knops 2023) assessing the safety and efficacy of dual-chamber LPs in 300 people reported 35 device- or procedure-related serious adverse events occurring in 29 people (10%). The primary safety endpoint was met in 271 people (90%; 95% CI, 87 to 94%; p<0.001), exceeding the predefined safety threshold of 78%. The retrospective cohort study by Ueyama (2024) including 10,338 people who had TAVR reported that there were no statistically significant differences between those who had LPs and those who had TVPs in heart failure hospitalisation (sdHR 0.9; 95% CI: 0.7 to 1.1; p=0.24) or infective endocarditis (sdHR 1; 95% CI: 0.4 to 2.2; p=0.95).

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional society or royal college. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they had never happened (theoretical).

They listed the following theoretical adverse events:

- Rapid battery depletion due to high pacing thresholds or exit block
- Long-term difficulty or inability to extract chronically implanted devices

10 professional expert questionnaires for this procedure were submitted. Find full details of what the professional experts said about the procedure in the specialist advice questionnaires for this procedure.

Validity and generalisability

- Sample sizes varied widely, from small studies like Garweg's RCT (n=51) and a young adult study (n=35) to large analyses such as Oliveira's meta-analysis (n=47,229). Smaller studies lacked statistical power, while larger ones included heterogeneous populations.
- Only the 5-year Micra PAR study includes UK data (El-Chami 2024). The rest are from the US, France, Switzerland, the Netherlands, or other non-UK European and North American centres.
- Follow-up durations ranged from 90 days (dual-chamber LP study) to over 5 years (Micra PAR), providing some insight into long-term outcomes. Long-term data are particularly valuable for this procedure.
- Bias was common, with most studies being observational. Meta-analyses by Inoue and Mhasseb found publication bias, especially regarding

adverse events. Many studies, such as the Micra AV CED and Micra PAR, were industry-funded, raising concerns about conflict of interest despite transparency in methodology.

- Procedural variation was also notable. While Garweg's RCT used standard protocols, others, like the jugular vs femoral study, tested alternative access routes. Device differences (Micra, Nanostim, Abbott dual-chamber LP) made direct comparisons difficult due to varying algorithms and fixation methods.
- Results were often conflicting—LPs were associated with reduced infection risk in some studies, but not consistently across pooled data. Reported AV synchrony for LP also varied, with lower rates in real-world settings than in trials, likely due to differences in programming and population selection.
- Key evidence gaps remain in long-term outcomes beyond 5 years, LP retrieval and replacement, and patient-reported outcomes. Ongoing trials may help address these gaps, particularly for new dual-chamber LPs and alternative implantation techniques, focusing different subgroups.

Any ongoing trials

- Danish Randomized Trial on Leadless vs Transvenous Pacing (DANVERS) (NCT05856799); RCT; Denmark; n=80; completion date August 2025

- The leadless MICRA AV versus DDD pacing study (LEAVE DDD) (NCT05498376); RCT (open label); Switzerland; n=100; completion date December 2027

- Aveir VR coverage with evidence development post-approval study (CED) (NCT05336877); observational (case-control); US; n=8,744; completion date January 2028

- Aveir DR i2i Study (NCT05252702); interventional (single group assignment); worldwide; n=550; completion date November 2025

- The leadless II IDE Study for the Aveir VR leadless pacemaker system (NCT04559945); interventional (single group assignment); worldwide; n=326; completion date August 2023

- Longitudinal coverage with evidence development study on Micra leadless pacemakers (Micra CED) (NCT03039712); observational (cohort); US; n=37,000; completion date June 2027

- Key factors of leadless pacemaker implantation with implantation site, complications and prognosis (NCT05761821); observational (cohort); China; n=300; completion date December 2024

- Micra transcatheter pacing system post-approval registry (NCT02536118); observational (cohort, patient registry); worldwide; n=3100; completion date August 2025

- International leadless pacemaker registry (i-LEAPER) (NCT05528029); observational; Belgium, Italy, Switzerland; n= 2000; completion date December 2024

- Aveir AR coverage with evidence development (CED) study (ARRIVE) (NCT06100770); observational; US; n=586; completion date January 2031

- A Safety and Effectiveness Monitoring in France for AVEIR VR LP and AVEIR AR LP (France LEADLES) (NCT06262295); observational (patient registry); France; n=600; completion date September 2028

- Aveir dual-chamber leadless pacemaker real-world evidence post-approval study; observational; USA; n= 1805; completion date January 2030

- Aveir single-chamber leadless pacemaker real-world evidence post-approval study (NCT05270499); observational (patient registry); US; n= 2100; completion date February 2034

Existing assessments of this procedure

- UK Expert Consensus Statement for the Optimal Use and Clinical Utility of Leadless Pacing Systems on Behalf of the British Heart Rhythm Society. A UK expert panel used a modified Delphi method to assess how LPs can be better utilised. They developed 36 survey statements and distributed them to LP implanters. The consensus process required a 25% response rate and at least 75% of statements meeting a 66% agreement threshold. 31 statements reached consensus, with 23 gaining 90% and above agreement. Based on these results, seven recommendations were proposed to help expand LP use and improve population outcomes.

- British Heart Rhythm Society Standards for Implantation and Follow-up of Cardiac Rhythm Management Devices in Adults: January 2024 Update. LP may be recommended for people at high risk of infection, those with end-stage renal disease, previous device infections, anatomical barriers to transvenous systems, immunocompromised population, those on biological or immunosuppressive therapies, or receiving radiotherapy near the device site. It may also be considered for people with congenital heart disease or those under 40 years of age, particularly when atrioventricular synchrony is clinically important.

Related NICE guidance

Interventional procedures

- Laser sheath removal of pacing leads (2004) NICE interventional procedure guidance 63 (Recommendations: recommended only in people for whom standard methods of removal are ineffective)

Clinical guidelines

- AF: diagnosis and management (2021) NICE guideline NG196

Technology appraisals

- Implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure (review of TA95 and TA120) (2014) NICE technology appraisal guidance TA314
- Dual chamber pacemakers for symptomatic bradycardia due to sick sinus syndrome without AV block (part review of technology appraisal guidance 88) (2014) NICE technology appraisal guidance TA324
- Dual-chamber pacemakers for symptomatic bradycardia due to sick sinus syndrome and/or AV block (2005) NICE technology appraisal guidance 88

Professional societies

- British Heart Rhythm Society (BHRS)
- British Cardiovascular Intervention Society
- British Cardiovascular Society.

Evidence from people who have had the procedure and patient organisations

NICE received 2 submissions from patient organisations about LPs and 1 patient commentary from a person who had this procedure.

The views of patient organisations were consistent with the published evidence and the opinions of the professional experts.

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 2 completed submissions. These were considered by the interventional procedures technical team, and any relevant points have been taken into consideration when preparing this overview.

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Appendix A: Methods and literature search strategy

Methods and literature search strategy

NICE has identified studies and reviews relevant to LP implantation for bradyarrhythmias from the medical literature.

Search strategy design and peer review

This search report is informed by the Preferred Reporting Items for Systematic reviews and Meta-Analyses literature search extension (PRISMA-S).

A NICE information specialist ran the literature searches on 17 January 2025. See the search strategy history for the full search strategy for each database. Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The principal search strategy was developed in MEDLINE ALL (Ovid interface). It was adapted for use in each of the databases listed in table 4a, taking into account the database's size, search functionality and subject coverage. The MEDLINE ALL strategy was quality assured by a NICE senior information specialist. All translated search strategies were peer reviewed to ensure their accuracy. The quality assurance and peer review procedures were adapted from the Peer Review of Electronic Search Strategies (PRESS) 2015 evidence-based checklist.

Review management

The search results were managed in EPPI-Reviewer version 5 (EPPI-R5). Duplicates were removed in EPPI-R5 using a 2-step process. First, automated deduplication was done using a high-value algorithm. Second, manual deduplication was used to assess low probability matches. All decisions about inclusion, exclusion and deduplication were recorded and stored.

Limits and restrictions

The CENTRAL database search removed trial registry records and conference material. The Embase search excluded conference material.

English language limits were applied to the search when possible, in the database. This is standard NICE practice for review topics.

The limit to remove animal studies in the searches is standard NICE practice, which has been adapted from Dickersin K, Scherer R, Lefebvre C (1994) Systematic Reviews: Identifying relevant studies for systematic reviews. BMJ 309(6964): 1286

Main search

Table 4a Main search results

Database	Date searched	Database platform	Database segment or version	Number of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	17/01/2025	Wiley	Issue 01 of 12, January 2025	13
Cochrane Database of Systematic Reviews (CDSR)	17/01/2025	Wiley	Issue 01 of 12, January 2025	0
Embase	17/01/2025	Ovid	1974 to January 16, 2025	768
INAHTA International HTA Database	17/01/2025	https://database.inahta.org/	-	11
MEDLINE ALL	17/01/2025	Ovid	1946 to January 16, 2025	628

MEDLINE ALL search strategy

1 arrhythmias, cardiac/ or bradycardia/ or heart block/ or AV block/ or bundle-branch block/ or sick sinus syndrome/ or AF/ 180361

2 (bradycardia* or bradyarrhythm*).tw. 27494

3 ((cardiac* or heart* or AV*) adj2 (arrhythmia* or block*)).tw. 44907

4 (abnormal* adj2 (heart* or cardiac* or AV*) adj2 rhythm*).tw. 593

5 ((heart* or cardiac* or AV*) adj2 rhythm* adj2 (disease* or disorder*)).tw. 1705

6 (Atrial adj2 Fibrillat*).tw. 100250

7 Bundle* branch* block*.tw. 10944

8 ((slow* or reduc* or low*) adj2 (heart* or cardiac*) adj2 (rate* or beat* or rhythm*)).tw. 10925

9 ((sinus* or sinotrial*) adj2 (syndrome or dysfunction* or disease*)).tw. 10418

10 or/1-9 272016

11 Cardiac Pacing, Artificial/ or Pacemaker, Artificial/ 46791

12 (leadless or wireless).tw. 24704

13 11 and 12 837

14 LPMS.tw. 237

15 ((leadless or wireless) adj4 (pacemak* or pacin*)).tw. 1212

16 ((leadless or LP*) adj2 implant*).tw. 508

17 or/13-16 1643

18 10 and 17 517

19 (micra* adj4 leadless adj4 pacemaker*).tw. 148

20 (micra* adj4 pacemaker* adj4 implant*).tw. 84

21 (micra* adj4 transcatheter adj4 pacing).tw. 104

22 (Aveir* adj4 leadless adj4 pacemaker).tw. 27

23 (Aveir* adj4 (AR or VR or DR)).tw. 28

24 or/19-23 269

25 18 or 24 657

26 limit 25 to english language 628

Embase search strategy

1 heart arrhythmia/ or bradycardia/ or heart block/ or AV block/ or heart bundle branch block/ or sick sinus syndrome/ or AF/ 430409

2 (bradycardia* or bradyarrhythm*).tw. 40864

3 ((cardiac* or heart* or AV*) adj2 (arrhythmia* or block*)).tw. 63468

4 (abnormal* adj2 (heart* or cardiac* or AV*) adj2 rhythm*).tw. 886

5 ((heart* or cardiac* or AV*) adj2 rhythm* adj2 (disease* or disorder*)).tw. 2122

6 (Atrial adj2 Fibrillat*).tw. 179782

7 Bundle* branch* block*.tw. 17516

8 ((slow* or reduc* or low*) adj2 (heart* or cardiac*) adj2 (rate* or beat* or rhythm*)).tw. 15265

9 ((sinus* or sinotrial*) adj2 (syndrome or dysfunction* or disease*)).tw. 15317

10 or/1-9 515425

11 heart pacing/ or artificial heart pacemaker/ 48312

12 (leadless or wireless).tw. 29115

13 11 and 12 624

14 LPMS.tw. 296

15 ((leadless or wireless) adj4 (pacemak* or pacin*)).tw. 2098

16 ((leadless or LP*) adj2 implant*).tw. 928

17 or/13-16 2631

18 10 and 17 1050

19 (micra* adj4 leadless adj4 pacemaker*).tw,dm,dv. 365

20 (micra* adj4 pacemaker* adj4 implant*).tw,dm,dv. 222

21 (micra* adj4 transcatheter adj4 pacing).tw,dm,dv. 245

22 (Aveir* adj4 leadless adj4 pacemaker).tw,dm,dv. 40

23 (Aveir* adj4 (AR or VR or DR)).tw,dm,dv. 65

24 or/19-23 658

25 18 or 24 1382

26 (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 6126021

27 25 not 26 813

28 limit 27 to english language 768

Cochrane Library (CDSR and CENTRAL) search strategy

#1 MeSH descriptor: [Arrhythmias, Cardiac] explode all trees 14039

#2 MeSH descriptor: [Bradycardia] explode all trees 708

#3 MeSH descriptor: [Heart Block] explode all trees 793

#4 MeSH descriptor: [AV Block] explode all trees 140

#5 MeSH descriptor: [Bundle-Branch Block] explode all trees 255

#6 MeSH descriptor: [Sick Sinus Syndrome] explode all trees 198

#7 MeSH descriptor: [AF] explode all trees 7522

#8 (bradycardia* or bradyarrhythm*) 9308

#9 ((cardiac* or heart* or AV*) near/2 (arrhythmia* or block*)) 11190

#10 (abnormal* near/2 (heart* or cardiac* or AV*) near/2 rhythm*) 140

#11 ((heart* or cardiac* or AV*) near/2 rhythm* near/2 (disease* or disorder*)) 198

#12 (Atrial near/2 Fibrillat*) 17629

#13 Bundle* branch* block* 1050

#14 ((slow* or reduc* or low*) near/2 (heart* or cardiac*) near/2 (rate* or beat* or rhythm*)) 3510

#15 ((sinus* or sinotrial*) near/2 (syndrome or dysfunction* or disease*)) 1361

#16 {or #1-#15} 41287

#17 MeSH descriptor: [Cardiac Pacing, Artificial] explode all trees 1944

#18 MeSH descriptor: [Pacemaker, Artificial] explode all trees 1018

#19 #17 or #18 2446

#20 (leadless or wireless) 1642

#21 #19 and #20 18

#22 LPMS 8

#23 ((leadless or wireless) near/4 (pacemak* or pacin*)) 46

#24 ((leadless or LP*) adj2 implant*) 19

#25 {or #21-#24} 83

#26 #16 and #25 29

#27 (micra* near/4 leadless near/4 pacemaker*) 8

#28 (micra* near/4 pacemaker* near/4 implant*) 6

#29 (micra* near/4 transcatheter near/4 pacing) 4

#30 (Aveir* near/4 leadless near/4 pacemaker) 0

#31 (Aveir* near/4 (AR or VR or DR)) 0

#32 {or #27-#31} 12

#33 #26 OR #32 33

#34 "conference":pt or (clinicaltrials or trialsearch):so 801159

#35 #33 NOT #34 13

INAHTA HTA Database search strategy

1 "Arrhythmias Cardiac"[mh] 60

2 "Bradycardia"[mh] 13

3 "Heart Block"[mh] 5

4 "AV Block"[mh] 2

5 "Bundle-Branch Block"[mh] 1

6 "Sick Sinus Syndrome"[mh] 4

7 "AF"[mh] 156

8 (bradycardia* or bradyarrhythm*) 24

9 ((cardiac* or heart* or AV*) and (arrhythmia* or block*)) 145

10 (abnormal* and (heart* or cardiac* or AV*) and rhythm*) 16

11 ((heart* or cardiac* or AV*) and rhythm* and (disease* or disorder*)) 19

12 (Atrial and Fibrillat*) 183

13 Bundle* branch* block* 3

14 ((slow* or reduc* or low*) and (heart* or cardiac*) and (rate* or beat* or rhythm*)) 213

15 ((sinus* or sinotrial*) and (syndrome or dysfunction* or disease*)) 26

16 #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1 532

17 "Cardiac Pacing Artificial"[mh] 47

18 "Pacemaker Artificial"[mh] 61

19 (leadless or wireless) 50

20 #18 OR #17 81

21 #20 AND #19 12

22 LPMS 0

23 ((leadless or wireless) and (pacemak* or pacin*)) 12

24 ((leadless or LP*) and implant*) 11

25 #24 OR #23 OR #22 OR #21 19

26 #25 AND #16 9

27 (micra* and leadless and pacemaker*) 5

28 (micra* and pacemaker* and implant*) 2

29	(micra* and transcatheter and pacing)	5
30	(Aveir* and leadless and pacemaker)	0
31	(Aveir* and (AR or VR or DR))	0
32	#31 OR #30 OR #29 OR #28 OR #27	6
33	#32 OR #26	11

Inclusion criteria

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events not available in the published literature.
- People with bradyarrhythmias.
- Intervention or test: leadless cardiac pacemakers.
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in Appendix B: Other relevant studies.

Find out more about how NICE selects the evidence for the committee.

Appendix B: Other relevant studies

Other potentially relevant studies that were not included in the main evidence summary (tables 2 and 3) are listed in table 5 below.

Observational studies with fewer than 30 people were excluded.

Table 5 additional studies identified

Study	Number of people and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Afzal MR, Daoud EG, Cunnane R, et al. (2018) Techniques for successful early retrieval of the Micra transcatheter pacing system: A worldwide experience. Heart Rhythm 15(6): 841–846	n=40 (29 with full procedural details) Follow-up duration for delayed retrievals: median 46 days (range 1 to 95 days)	Early retrieval of LP is feasible and safe. All retrievals (immediate and delayed) were successful with no serious complications. Most common reasons were elevated pacing thresholds and infections.	Only successful retrievals were included; limited generalisability due to small sample size, retrospective nature, and absence of a comparator group.
Alhuarrat M, Kharawala A, Renjithlal S, et al. (2023) Comparison of in-hospital outcomes and complications of leadless pacemaker and traditional transvenous pacemaker implantation.	n=35,430 admissions; LP group: n=7780; TVP group: n=27,650; in-hospital outcomes only	LP population had significantly higher in-hospital mortality (aOR 1.6), vascular complications (aOR 7.5), venous thromboembolism (aOR 3.7), cardiac complications (aOR 1.8), device thrombus (aOR 5.0), and transfusion need (aOR 1.5) compared to TVP population. TVP population was	Covered in systematic reviews included in evidence summary.

EP Europace 2023; euad269.		more likely to experience pulmonary complications (aOR 0.7) and device revisions (aOR 0.4). Differences may reflect higher comorbidity burden in LP group.	
Ando K, Inoue K, Harada T, et al. (2023) Safety and Performance of the Micra VR Leadless Pacemaker in a Japanese Cohort – Comparison with Global Studies Circulation Journal 87(12): 1809–1816	n=300 Follow-up: mean 7.23; SD 2.83 months	Micra VR implantation was highly successful with a low acute (30 day) major complication rate of 3%, consistent with global trial data. No procedure- or device-related deaths occurred. Frailty scores improved post-implantation.	Limited to a non-randomised observational study with a relatively short follow-up period. More robust evidence from randomised controlled trials or meta-analyses was prioritised for the main summary.
Arps K, Li B, Allen JC Jr, et al. (2023) Association of leadless pacing with ventricular and valvular function. J Cardiovasc Electrophysiol 34(11):2233–2242.	n=54; median follow-up echocardiogram at 8.9 months (IQR 4.5 to 14.5)	LP implantation was not associated with worsening tricuspid regurgitation in the short term. There was a significant decline in LVEF (mean decrease: 52% to 48%, p=0.0019) and TAPSE (1.8 cm to 1.6 cm, p=0.0437), indicating a reduction in biventricular function. 24% of people experienced a 10% or more drop in LVEF, consistent with known effects of RV pacing.	Small, single-center cohort with short-term follow-up; observational nature limits ability to determine causality for observed ventricular function decline.

Bahbah A, Sengupta J, Kapphahn-Bergs M, et al. (2024) A comparison of procedure-related adverse events between two right ventricular leadless pacemakers. Journal of Cardiovascular Electrophysiology 35(12): 2397–2401	n=10,940 (Micra VR), n=5,990 (AVEIR VR) Follow-up duration not specified; adverse events reviewed from 2022 to 2024	Micra VR and AVEIR VR showed similar rates of major adverse clinical events (p=0.387) and procedure-related complications (including death and perforation). However, AVEIR VR had a higher rate of device dislodgement (p<0.001), while Micra VR had more unacceptable pacing thresholds requiring replacement (p=0.001). Design-related differences may account for these outcomes.	The study is based on retrospective analysis of adverse event reports from the MAUDE database, which may be subject to reporting biases and lacks the controlled conditions of prospective clinical trials. Therefore, more robust, randomised controlled studies were prioritised in the main evidence summary.
Bahbah A, Sengupta J, Witt D, et al. (2024) Device dislodgement and embolization associated with a new leadless pacemaker. Journal of Cardiovascular Electrophysiology 35(12): 2483–2486	n=5,990 (AVEIR VR, over 21 months) n=72,237 (Micra VR, over 8 years) Follow-up: Device approval periods: AVEIR VR (Apr 2022 to Dec 2023), Micra VR (2016 to Apr 2024)	Dislodgement and/or embolisation (D/E) occurred in less than 1% of both AVEIR VR cases and Micra VR cases (p<0001). Most AVEIR D/E events (60%) occurred during implantation, commonly due to release mechanism or fixation issues.	Data based on passive post-market surveillance (MAUDE), with known limitations in voluntary reporting accuracy and absence of clinical adjudication or comparator control.
Beccarino NJ, Choi EY, Liu B, et al. (2023) Concomitant leadless pacing in pacemaker-dependent patients undergoing transvenous	n=86, undergoing LP implantation at the time of transvenous lead extraction for active CIED infection; median follow-up 163 days (IQR 57 to 403)	Concomitant LP implantation during TLE for active infection was associated with no procedural complications and no recurrent infections during follow-up. Despite a 29%	Covered by systematic reviews included in main evidence summary.

lead extraction for active infection: Mid-term follow-up. Heart Rhythm 20(6): 853–860.		mortality rate, most deaths were unrelated to infection.	
Bertelli M, Toniolo S, Ziacchi M, et al. (2022) Is Less Always More? A Prospective Two-Centre Study Addressing Clinical Outcomes in Leadless versus Transvenous Single-Chamber Pacemaker Recipients. J Clin Med 11(20): 6071.	n=344 (LP: n=72; TVP: n=272); follow-up duration not explicitly stated but included both acute and long-term complications	No statistically significant difference in complication rates between LP and TVP groups. Higher mortality in the TVP group attributed to older age and comorbidities. LP implantation was preferentially used in people with higher bleeding/infection risk, difficult venous access, or active lifestyle.	Covered by systematic review included in the main evidence summary.
Bhatia NK, Kiani S, Merchant FM, et al. (2021) Life cycle management of Micra transcatheter pacing system: Data from a high-volume center. Journal of Cardiovascular Electrophysiology 32(2): 484–490	n=302 Follow-up: mean 1105.5; SD 529.3 days (3 years)	LP was durable with low complication rates over long-term follow-up. 6% of people required system modification—either extraction (n=11) or abandonment (n=12)—mainly due to CRT upgrade, threshold issues, or battery depletion. All extractions and abandonments were successful without long-term complications.	Study focuses on long-term device management rather than long-term safety and efficacy outcomes and includes a limited number of extraction/abandonment cases.
Bodin A, Clementy N,	n=42,315 total (LP: 1487; TVP: 40,828); matched cohort:	LP recipients had lower all-cause and cardiovascular	Covered by systematic review

Bisson A, et al. (2022) Leadless or Conventional Transvenous Ventricular Permanent Pacemakers: A Nationwide Matched Control Study. J Am Heart Assoc 11(16): e025339.	n=1344 per group; mean follow-up 6.2; SD 8.7 months	mortality within 30 days post-implantation compared to TVP recipients. During midterm follow-up, there were no significant differences between LP and TVP groups in all-cause mortality, cardiovascular death, or infective endocarditis after matching for baseline comorbidities.	included in the main evidence summary.
Bongiorni MG, Della Tommasina V, Barletta V et al. (2019) Feasibility and long-term effectiveness of a non-apical Micra pacemaker implantation in a referral centre for lead extraction. EP Europace 21(1): 114–120.	n=52 Follow-up: mean 13; SD 9 months	LP implantation was successful in 52 people, with 60% receiving non-apical implants. Non-apical placement was feasible and had no adverse impact on electrical performance. Pacing thresholds remained optimal in 94% of people. No device-related adverse events occurred during follow-up, demonstrating safety and long-term stability even in high-risk population.	Relatively small sample size and single-centre design More comprehensive, multicentre studies with larger cohorts and randomised controlled designs were prioritised in the main evidence summary.
Breeman KTN, Oosterwerff EFJ, de Graaf MA, et al. (2023) Five-year safety and efficacy of leadless pacemakers in a Dutch cohort.	n=179 (93 Nanostim, 86 Micra VR) Follow-up: mean 44; SD 26 months (3.7 years); up to 5 years	LPs demonstrated good long-term safety and performance. The 5-year major complication rate was 4% when excluding Nanostim advisory-related events, and 27% when including them.	Includes people implanted with the discontinued Nanostim device; results may not reflect outcomes relevant to currently used LPs.

Heart Rhythm 20(8): 1128–1135		Capture threshold was less or equal to 2 V and stable in 98% of people. No infections or late complications occurred.	
Cantillon DJ, Exner DV, Badie N, et al. (2017) Complications and Health Care Costs Associated with Transvenous Cardiac Pacemakers in a Nationwide Assessment. JACC: Clinical Electrophysiology 3(11): 1296–1305.	n = 72,701 (mean age 75; SD 12 years; 55% men) Follow-up: Mean 1.5; SD 1.1 years; outcomes tracked up to 3 years	TVP complications were more frequent than previously reported, with an overall 3-year complication rate of 15 to 16%. Key findings include: Acute complications (within 30 days): 8% in single-chamber TVP, 9% in dual-chamber TVP Most common: thoracic trauma (4%, cost: $70,114), lead revision (4%, cost: $9,296), and infection (1%, cost: $80,247) Long-term complications (1 to 36 months): 6% (single-chamber) and 6% (dual-chamber)	Focused on health systems and healthcare costs.
Cantillon DJ, Dukkipati SR, Ip JH, et al. (2018) Comparative study of acute and mid-term complications with leadless and transvenous	n=718 LP (LEADLESS II) vs. n=1436 TVP (matched); complications assessed at less than or at 1 month (short-term) and between 1 to 18 months (mid-term).	LP recipients had significantly fewer overall complications (HR 0.4; 95% CI 0.3 to 0.6), with reduced short-term (6% vs 9%) and mid-term (1% versus 5%) complications. LCPs had higher rates of pericardial effusion	Covered in systematic review included in the main evidence summary.

cardiac pacemakers. Heart Rhythm 15(7): 1023–1030.		(2% versus 0.3%; p=.005) but fewer infectious, lead-related, and pocket-related events. No thoracic trauma events occurred in the LP group.	
Chinitz L, Ritter P, Khelae SK, et al. (2018) Accelerometer-based atrioventricular synchronous pacing with a ventricular leadless pacemaker: Results from the Micra atrioventricular feasibility studies. Heart Rhythm 15(9): 1363–1371.	n=64 across 12 centers in 9 countries; median 6 months post-implant (range 0 to 41.4 months); evaluation over 30 minutes of pacing.	Accelerometer-based atrial sensing algorithm achieved high atrioventricular synchrony (AVS) during pacing: 87% average AVS overall, 80% in high-degree AV block, and 94% in intrinsic conduction. AVS was significantly better during AV algorithm pacing than VVI pacing in high-degree block (p<.001).	Covered in systematic review included in the main evidence summary.
Chinitz LA, El-Chami MF, Sagi V, et al. (2023) Ambulatory atrioventricular synchronous pacing over time using a leadless ventricular pacemaker: Primary results from the AccelAV study. Heart Rhythm 20(1): 46–54.	n=152 enrolled; primary analysis subset: n=54 with complete AV block and normal sinus function; follow-up at 1 and 3 months	In people with complete AV block and normal sinus function, LP achieved mean resting AVS of 85% and ambulatory AVS of 75% at 1 month. Optimisation improved ambulatory AVS to 83% (p<.001). AVS remained stable at 3 months, and quality of life improved significantly (p=.031). No device upgrades were needed during the follow-up.	Covered by systematic review included in the main body evidence summary.
Crossley GH, Piccini JP,	n=6,219 (LP n=2,202; TVP	LP recipients had lower adjusted 3-year	Covered by systematic review

Longacre C, et al. (2023) Leadless versus transvenous single-chamber ventricular pacemakers: 3 year follow-up of the Micra CED study. J Cardiovasc Electrophysiol 34(4): 1015–1023.	n=4,017); 3-year follow-up	risks of chronic complications (HR 0.8, 95% CI 0.7 to 0.9; p<.001), device-related reintervention (HR 0.5, 95% CI 0.4 to 0.7; p<.001), and device-related infection (HR 0.4, 95% CI 0.2 to 0.8; p=.005) compared with TVP recipients. No significant difference in 3-year all-cause mortality was observed (HR 1, 95% CI 0.9 to 1.1; p=.73).	included in the main evidence summary.
Crossley GH, Longacre C, Higuera L, et al. (2024) Outcomes of patients implanted with an atrioventricular synchronous leadless ventricular pacemaker in the Medicare population. Heart Rhythm 21(1): 66–73.	n=7471 LP recipients; n=107,800 dual-chamber TVP recipients; outcomes assessed at 30 days and 6 months	LP recipients had higher comorbidity burden (mean Charlson Index 4.9 versus 3.8) but similar unadjusted 30-day complication rates (9% vs 9%). After adjustment, LP was associated with significantly lower 30-day (9% versus 11%) and 6-month complication rates (HR 0.5; 95% CI 0.4 to 0.6) and reinterventions (HR 0.5; 95% CI 0.4 to 0.6). Higher mortality in LP group attributed to baseline health differences.	Covered by Mhasseb (2025) systematic review included in the main evidence summary.
Darlington D, Brown P, Carvalho V, et al. (2022) Efficacy and safety of leadless	18 studies included n=2,496 (LP recipients) Follow-up duration varied across studies	LPs demonstrated high implant success rates (96 to 100%) with low adverse event rates. Device/procedure-related death rate	More updated and comprehensive studies have been included in the main evidence summary.

pacemaker: A systematic review, pooled analysis and meta-analysis. Indian Pacing and Electrophysiology Journal 22(2): 77–86		was less than 1%; overall complication rate 3%; pericardial tamponade 1%. Other complications such as pericardial effusion, dislodgement, revision, malfunction, infection, and access site complications occurred in less than 1% of people. No significant differences found between LPs and TVPs for: • Haematoma (RR 0.7, 95% CI 0.2 to 2.2) • Pericardial effusion (RR 0.6, 95% CI 0.2 to 2.3) • Device dislocation (RR 0.3, 95% CI 0.1 to 1.7) • Any complication (RR 0.4, 95% CI 0.2 to 1.1) • Death (RR 0.5, 95% CI 0.2 to 1.4)	
Defaye P, Klug D, Anselme F, et al. (2018) Recommendations for the implantation of leadless pacemakers from the French Working Group	Not applicable (guideline document); consensus formed based on expert experience and early clinical trials.	Recommended cautious use of LPs due to limited long-term data and complication risk. Identified groups most suitable for LP: those with no venous access, high infection risk, prior	Not an empirical study; guideline based on expert consensus rather than original research data.

on Cardiac Pacing and Electrophysiology of the French Society of Cardiology. Archives of Cardiovascular Disease 111(1): 53–58.		endocarditis, or cosmetic preferences. Advocated for implantations only in high-expertise centers with cardiac surgery facilities. Advised that only board-certified electrophysiologists with sufficient volume (more than 20 LPs/year) perform these procedures. Highlighted risks: tamponade, vascular injury, device migration, and lack of extraction experience. Stressed mandatory surveillance via national registry and outlined minimum training and implantation volumes to ensure safety.	
Denman RA, Lee G, Phan K, et al. (2018) Leadless Permanent Pacing: A Single Centre Australian Experience. Heart, Lung and Circulation 28(11): 1677–1682	n=79 Follow-up: median 355 days (range; 9 to 905 days)	Implantation was successful in 96% of people. Electrical performance remained excellent over follow-up with a median R-wave of 11.2 mV, capture threshold of 0.5 V at 0.2 ms, and impedance of 754 ohm. No people required revision or were readmitted for device-related complications. 1 case of acute dislodgement was successfully managed. 5 deaths	Single-centre study with small sample size and limited generalisability; lacks comparator arm or stratification across different risk groups.

		(7%) occurred, all unrelated to the device.	
Doshi RN, Ip JE, Defaye P, et al. (2024) Chronic wireless communication between dual-chamber leadless pacemaker devices. Heart Rhythm, published online ahead of print on October 19, 2024.	n=399 Follow-up: at implant, discharge, 1, 3, and 6 months	Aveir DR dual-chamber LPs demonstrated more than 90% success in implant-to-implant (i2i) wireless communication (A-to-V and V-to-A) throughout 6 months. People with less than 70% success at implant showed marked improvement by 1 month, decreasing to only 5% by 6 months. Improvements were linked to reprogramming and post-implant device adaptation.	The study focuses on device communication metrics rather than clinical outcomes such as complications, mortality, or pacing efficacy; thus, it is not directly comparable with safety and performance endpoints in the main summary.
Duray GZ, Ritter P, El-Chami M, et al. (2017) Long-term performance of a transcatheter pacing system: 12-Month results from the Micra Transcatheter Pacing Study. Heart Rhythm 14(5): 702–709	n=726 (Micra) Follow-up: 12 months for safety, 24 months for electrical performance	At 12 months, freedom from major complications was 96% (95% CI: 92 to 97; p<0.0001), meeting the prespecified performance goal. The risk of major complications was 48% lower than with TVPs (HR 0.5; 95% CI: 0.6 to 0.8; p=0.001). Device performance remained stable through 24 months with projected battery life of 12.1 years.	Earlier results already incorporated into broader summaries; this study includes historical comparator data and device-specific outcomes rather than direct head-to-head comparison within a randomised framework.
El-Chami MF, Soejima K, Piccini JP et al. (2019)	n=720 (Micra) n=16 developed 21 serious infectious events (SIEs)	Serious infections (bacteraemia or endocarditis) occurred in 2% of	Focused specifically on rare post-implant infectious events; small number of

Incidence and outcomes of systemic infections in patients with leadless pacemakers: Data from the Micra IDE study. Pacing and Clinical Electrophysiology 42(8): 1105–1110.	Follow-up after SIE: mean 13.1; SD 9.1 months	people (16/720), on average 4.8 months post-implant. All events were adjudicated as unrelated to the device or procedure. Most infections involved gram-positive organisms and resolved with antibiotics, with no persistent bacteraemia observed.	cases limits generalisability and does not evaluate broader safety or efficacy outcomes of the device.
El-Chami MF, Johansen JB, Zaidi A, et al. (2019) Leadless pacemaker implant in patients with pre-existing infections: Results from the Micra postapproval registry. J Cardiovasc Electrophysiol 30(4): 569–574.	n=105 people with prior CIED infection who underwent Micra implant attempt less than or at 30 days after device explant; mean follow-up 8.5; SD 7.1 months	LP was successfully implanted in 99% of people with recent CIED infection. No LP removals due to infection were reported. Most people received IV antibiotics pre-implant (91%) and/or post-implant (42%). 2 persons died from sepsis, but no reinfections involved the LP system.	Covered by systematic review included in the main evidence summary.
El-Chami MF, Bonner M, Holbrook R, et al. (2020) Leadless pacemakers reduce risk of device-related infection: Review of the potential mechanisms.	More than 3000 (across clinical trials referenced); follow-up durations vary across studies included	LPs demonstrate a markedly lower rate of infection compared to TVPs (0.00% versus 1 to 2% in trials with over 3000 people). Proposed mechanisms include absence of subcutaneous pocket and leads, minimal skin/glove contact during implantation, smaller size, implantation in a	Narrative review — not a primary study or systematic review/meta-analysis; mechanism-focused without formal comparative data analysis.

Heart Rhythm 17(8): 1393–1397.		lower-flow cardiac environment, and biocompatible materials.	
El-Chami MF, Garweg C, Iacopino S et al. (2022) Leadless pacemaker implant, anticoagulation status, and outcomes: Results from the Micra Transcatheter Pacing System Post-Approval Registry. Heart Rhythm 19(2): 228–234.	n=1,795 (with documented anticoagulation status) Follow-up: 30 days post-implant	implantation was safe across all perioperative anticoagulation (AC) strategies: non-AC (n=585), interrupted AC (n=795), and continued AC (n=415). Major complication rates were 3%, 3%, and 2% respectively. Implant success exceeded 99% in all groups. Vascular or pericardial effusion events did not significantly differ among AC strategies, suggesting continued AC does not increase procedural risk.	Focused specifically on procedural safety relative to anticoagulation management, rather than overall clinical outcomes or long-term device performance.
El-Chami MF, Clementy N, Garweg C et al. (2019) Leadless pacemaker implantation in hemodialysis patients: Experience with the Micra transcatheter pacemaker. JACC: Clinical Electrophysiology 5(2): 162–170.	n=201, on hemodialysis (7% of 2,819 total) Follow-up: mean 6.2 months (range 0 to 26.7 months)	LP implantation was successful in 98% (197/201) of people having haemodialysis. The median procedure time was 27 minutes. There were 4 implant failures and 3 procedure-related deaths. No device-related infections or removals occurred. People included in this study had multiple comorbidities, and 72% were deemed unsuitable for TVPs.	A more recent study including people on haemodialysis has been included in table 2.

El-Chami MF, Bockstedt L, Longacre C et al. (2022) Leadless vs. transvenous single-chamber ventricular pacing in the Micra CED study: 2-year follow-up. European Heart Journal 43(12): 1207–1215.	n=6,219 (LP) vs. n=10,212 (TVP) Follow-up: 2 years	LP group had significantly fewer reinterventions (adjusted HR 0.6, 95% CI 0.5 to 0.9, P=0.003) and chronic complications (adjusted HR 0.7, 95% CI 0.6 to 0.8, P<0.0001) compared to TVP population. Adjusted all-cause mortality did not differ (HR 1, 95% CI 0.9 to 1, P=0.4).	A more recent publication from the same study has been included in the main evidence summary.
El-Chami MF, Al-Samadi F, Clementy N et al. (2018) Updated performance of the Micra transcatheter pacemaker in the real-world setting: a comparison to the investigational study and a transvenous historical control. *Heart Rhythm* 15(12): 1800–1807.	n=1817 (Micra PAR); mean follow-up 6.8; SD 6.9 months Comparators: n=726 (IDE study) and n=2667 (TVP control group)	The major complication rate in Micra PAR was 3% at 12 months (95% CI 2% to 3%). Compared to TVPs, LPs had a 63% lower risk of major complications (HR 0.4, 95% CI 0.3 to 0.5, p<0.001). There were no battery or telemetry issues, and pacing thresholds remained stable.	A more recent publication from PAR study has been included in the main evidence summary.
Fagerlund BC, Harboe I, Giske L et al. (2018) The Micra™ Transcatheter Pacing System, a leadless pacemaker, in patients indicated for single-chamber	Clinical review included data from 3 large multi-site trials (total n=1,575) and 3 smaller case series. Follow-up: up to 24 months (efficacy), 10-year horizon for cost-effectiveness model.	LP achieved satisfactory pacing thresholds in 93 to 97% of people at 12 to 24 months. Major complications occurred in 2 to 4% of people, with 4 reported device/system-related deaths.	More recent systematic reviews have been included in the main evidence summary.

ventricular pacemaker implantation: a single technology assessment. Norwegian Institute of Public Health.		Compared to historical controls, LPs had a lower complication rate, but evidence was rated low to very low certainty due to study design (single arm) and indirectness.	
Gangannapalle M, Monday O, Rawat A, et al. (2023) Comparison of Safety of Leadless Pacemakers and Transvenous Pacemakers: A Meta-Analysis. Cureus 15(9): e45086	This meta-analysis encompassed 17 studies comparing LPs and TVPs. The total number of people and specific follow-up durations varied across the included studies.	LPs were associated with a lower risk of total complications, device-related complications, pneumothorax, endocarditis, and need for reintervention compared to TVPs. However, the risk of pericardial effusion was significantly higher in the LP group.	Comprehensive and more recent meta-analyses have been included in the main evidence summary.
Garg A, Koneru JN, Fagan DH, et al. (2020) Morbidity and mortality in patients precluded for transvenous pacemaker implantation: Experience with a leadless pacemaker. Heart Rhythm 17(12): 2056–2063	n=2,817, undergoing Micra implantation; 546 (19%) were precluded from TVP implantation Follow-up: 36 months	People precluded from TVP had higher acute mortality (3% vs 1%, p=0.022) and 36-month mortality (38% vs 21%, p<0.001) than no precluded people.	Although informative for high-risk subpopulations, the comparative arm is not randomised, and the elevated mortality likely reflects baseline comorbidities rather than device performance, limiting its applicability for general evidence synthesis.
Garg J, Shah K, Bhardwaj R et al. (2023) Adverse events associated with Aveir™ VR	n=64 adverse event reports included (from post-FDA approval until January 2023) No follow-up	Most common complications included high threshold/noncapture (28%), stretched helix (17%), and	Brief communication: this study is based on voluntarily reported adverse events from a regulatory database

leadless pacemaker: a Food and Drug Administration MAUDE database study. Journal of Cardiovascular Electrophysiology 34(9): e15932.	duration specified; real-world device surveillance study	device dislodgement (16%). Serious adverse events included 5 cases of pericardial effusion requiring pericardiocentesis and 2 deaths (3%). The study highlights rare but serious safety concerns with the Aveir™ VR LP.	without denominator data or follow-up, limiting its comparability to prospective clinical trials or registries.
Garweg C, Chinitz L, Marijon E, et al. (2024) A leadless ventricular pacemaker providing atrioventricular synchronous pacing in the real-world setting: 12-Month results from the Micra AV post-approval registry. Heart Rhythm 21(10): 1939–1947	n=801 (LP), with 12-month follow-up Comparison: Historical cohort of 2667 people with TVPs	LP showed a significantly lower major complication rate at 12 months compared to transvenous dual-chamber pacing (4% vs 9%; HR 0.4, 95% CI 0.3 to 0.6 p<0.001) and a lower system revision rate (2% vs 6%; HR 0.3, 95% CI 0.13 to 0.5; p<0.001). Median AV synchrony index was 79% in high burden paced population.	This real-world observational registry lacks a direct comparator group within the study itself, limiting its suitability for inclusion in the main evidence summary prioritising controlled or randomised studies.
Garweg C, Vandenberk B, Jentjens S, et al. (2020) Bacteraemia after leadless pacemaker implantation. Journal of Cardiovascular Electrophysiology 31(9): 2440–2447	n=155, with LP implantation Median follow-up after bacteraemia: 263 days (range: 15 to 1134)	Bacteraemia occurred in 15 people (10%) at a median of 226 days post-implantation. FDG PET/CT in 6 people showed no evidence of infection involving the pacemaker. No cases of LP related endocarditis were identified, and all	Small single-centre retrospective study with a limited number of events and lack of control group; not prioritised for inclusion in main evidence summary focused on broader or comparative outcomes.

		infections resolved with antibiotics.	
Garweg C, Vandenberk B, Foulon S, et al. (2020) Leadless pacemaker for patients following cardiac valve intervention. Arch Cardiovasc Dis 113(12): 772–779.	n=170 LPs (54 post-valve intervention vs 116 controls); Median follow-up: 12 months	LP implantation was successful in all people, including the 54 with prior cardiac valve interventions (aortic, mitral, or multiple valves). No major procedural complications occurred. Both valve intervention and control groups showed similar reduction in LVEF over 12 months, which correlated with the amount of right ventricular pacing.	Broader registry study has been added in the main summary evidence.
Garweg C, Vandenberk B, Foulon S, et al. (2019) Leadless pacing with Micra TPS: A comparison between right ventricular outflow tract, mid-septal, and apical implant sites. Journal of Cardiovascular Electrophysiology 30(10): 2002–2011	n=133 Mean follow-up: 13; SD 11 months	LP implantation was successful in all. across RV outflow tract (n=45), mid-septal (n=58), and apical (n=30) sites. RVOT pacing was associated with the narrowest QRS duration (142 ms vs. 159 ms mid-septal vs. 181 ms apical; $p<0.001$). No pericardial effusion occurred. 2 major complications were reported in the apical group. Electrical performance (pacing threshold, R-wave amplitude) was stable across all positions.	This single-centre, non-randomised observational study with modest sample size offers valuable insights into implantation site differences but lacks comparative clinical outcomes beyond electrical parameters, limiting its inclusion in the main evidence summary.
Garweg C, Ector J, Voros G, et al. (2018)	n=66 Follow-up: mean 10.4; SD 6.1	LP was successfully implanted in 99% of people, with stable electrical	Single centre with small sample size and non-comparative design

Monocentric experience of leadless pacing with focus on challenging cases for conventional pacemaker. Acta Cardiologica 73(5): 459–468	months (range 1 to 23 months)	performance at follow-up. Mean pacing capture threshold was 0.6 V, impedance 580 Ohms, and R-wave sensing 10.6 mV. 1 major and 3 minor adverse events were reported. No dislodgement, infection, or pericardial effusion occurred. The device was also effective in anatomically challenging population.	limits generalisability and strength of evidence compared to larger multicentre or controlled trials.
Grubman E, Ritter P, Ellis CR, et al. (2017) To retrieve, or not to retrieve: System revisions with the Micra transcatheter pacemaker. Heart Rhythm 14(12): 1801–1806.	n=989 (LP group) vs. n=2667 (TVP group); up to 24 months follow-up	The 24-month revision rate for LP was 1%, statistically significantly lower than the 5% revision rate in the TVP group (75% relative risk reduction; p<0.001). No LP revisions were due to dislodgement or device-related infection. Most LP devices were disabled and left in situ; percutaneous retrieval was successful up to 14 months post-implant.	Broader registry studies have been included in the main evidence summary.
Gul EE, Baudinaud P, Waldmann V, et al. (2024) Leadless pacemaker implantation following tricuspid interventions: multicenter	n=40 with prior tricuspid valve interventions. Mean follow-up: 10 months	All people successfully received LPs after tricuspid valve surgery or intervention. No acute complications were observed. Electrical parameters (pacing threshold: 1.4; SD 1.2 V, impedance: 772; SD	Broader registry study has been prioritised in the main body evidence.

collaboration of feasibility and safety. J Interv Card Electrophysiol 67(5): 1241–1246.		245 Ohm, R-wave: 6.9; SD 5.4 mV) remained stable through follow-up. There were 4 deaths, not procedure related.	
Gulletta S, Schiavone M, Gasperetti A, et al. (2023) Peri-procedural and mid-term follow-up age-related differences in leadless pacemaker implantation: Insights from a multicenter European registry. Int J Cardiol 371:197–203.	n=1154; 2 cohorts: younger (50 or less in years, 6%) and older (more than 50 years); mid-term follow-up duration not explicitly stated	In younger people, LPs were primarily chosen due to preference (47% versus 6%, p<0.001), while in older population, infectious (68%) and vascular concerns (16%) were more common indications. Periprocedural complication rate was 4% with no significant age-related difference. Younger people had higher pacing thresholds at discharge and follow-up (0.6 V versus 0.5 V, p=0.004), though device performance remained acceptable in both groups.	Age-based subgroup analysis with limited representation of younger people (6% of cohort).
Haddadin F, Majmundar M, Jabri A, et al. (2022) Clinical outcomes and predictors of complications in patients undergoing leadless pacemaker implantation.	n=7,821 Follow-up: In-hospital and 30-day outcomes	Immediate procedure-related complications occurred in 8% of people. Specific complications included pericardial effusion (2%), pericardiocentesis (1%), vascular complications (2%), and device dislodgment.	Shorter follow up duration might not capture long term safety and efficacy outcomes. Studies with longer follow up period have been assessed in the main evidence summary.

Heart Rhythm 19(8): 1289–1296			
Hai JJ, Fang J, Tam CC, et al. (2019) Safety and feasibility of a midseptal implantation technique of a leadless pacemaker. Heart Rhythm 16(6): 896–902	n=51 Follow-up: Median 218.7 days	Midseptal LP implantation was successfully achieved in 90% of people using fluoroscopic guidance (RAO, LAO, and lateral views).	Small, single-centre feasibility study with a short follow-up duration and limited generalisability; primarily technical in nature rather than focused on comparative safety or efficacy outcomes.
Hauser RG, Gornick CC, Abdelhadi RH, et al. (2021) Major adverse clinical events associated with implantation of a leadless intracardiac pacemaker. Heart Rhythm 18(7): 1132–1139	n=363 major adverse clinical events (MACE) for Micra (LP) vs. n=960 MACE for CapSureFix (TVP) Timeframe: 2016–2020 (retrospective database review; no population-level follow-up duration)	LPs was associated with significantly more serious events: deaths (26% versus 2%), tamponade (79% versus 23%), and rescue thoracotomies (27% versus 5%) compared to TVPs (all p<0.001).	Although highlighting critical safety signals, this study is based solely on voluntary manufacturer-reported adverse event data from the MAUDE database, which lacks denominator data, standardised event adjudication, and clinical detail, limiting its reliability for inclusion in formal evidence summaries.
Hindricks G, Doshi R, Defaye P, et al. (2024) Six-month electrical performance of the first dual-chamber leadless pacemaker. Heart Rhythm 2024;21(1):66–73.	n=381; follow-up duration: 6 months post-implant	The Aveir DR dual-chamber LP showed stable and improving electrical performance over 6 months. Capture thresholds significantly decreased in both atrial (2.4 V to 0.8 V) and ventricular (0.8 V to 0.6 V) devices. Sensed amplitudes increased (atrial: 1.8	Short-term follow-up (6 months) in an early experience cohort; long-term outcomes and comparative effectiveness data with dual LP has been included in the main evidence summary.

		mV to 3.4 mV; ventricular: 8.8 mV to 11.7 mV). Impedance remained stable in the atrial device and decreased in the ventricular device. Performance did not vary by implant location. These results suggest robust and reliable pacing and sensing for dual-chamber LPs.	
Huang J, Bhatia NK, Lloyd MS, et al. (2023) Outcomes of leadless pacemaker implantation after cardiac surgery and transcatheter structural valve interventions. J Cardiovasc Electrophysiol 34(11): 2216–2222.	n=78; mean follow-up: 1.3; SD 1.1 years	LPs were successfully implanted in post-surgical and post-transcatheter valve intervention group, with device electrical performance over medium-term follow-up. Mean RVP burden decreased significantly (from 74% to 48%; p<.001). LVEF showed a modest decline (from 55% to 52%; p<.001). 6 people (8%) required conversion to TVPs—four due to need for cardiac resynchronisation and two for dual-chamber pacing. No device-related safety issues were highlighted.	Broader registry study has been added in the main summary evidence.
Huang J, Bhatia NK, Lloyd MS, et al. (2024) Impact of omitting the	n=621 LP implantations; 326 with heparin bolus, 243 without, 52 excluded due to	No statistically significant differences were observed between heparin bolus and	Operators chose anticoagulation strategy, possibly reflecting population-

intravenous heparin bolus on outcomes of leadless pacemaker implantation. J Cardiovasc Electrophysiol 35(6):1212-1216.	unknown status; median follow-up: 14.3 months	no-bolus groups in terms of procedural complications (hematoma, pseudoaneurysm, cardiac perforation, thrombus formation), 30-day readmission or mortality, or implant electrical parameters.	level confounders not fully adjusted.
Hofer D, Regoli F, Saguner AM, et al. (2023) Efficacy and Safety of Leadless Pacemaker Implantation in Octogenarians. Cardiology 148(5): 441–447	n=220 (of which 124 were 80 years or more) Follow-up: Not explicitly stated; included procedural and post-implant follow-up measurements	Implantation in octogenarians was found to be safe and effective, with a high success rate (99%) and a low major complication rate (3%). Procedural time and radiation exposure were slightly higher in people more or equal to 80 years, but post-procedural outcomes and device performance were comparable to younger people.	While relevant for older adults, the study's retrospective design, limited follow-up duration, and non-comparative structure reduce its strength for informing this evidence summaries.
Ip JE, Rashtian M, Exner DV, et al. (2024) Atrioventricular Synchrony Delivered by a Dual-Chamber Leadless Pacemaker System. Circulation 150(6): 439–450	n=464 enrolled; n=384 evaluable (83%) Follow-up: 3 months post-implantation	Achieved a mean atrioventricular (AV) synchrony of 98% across all evaluated beats and postures, outperforming atrial-to-ventricular and ventricular-to-atrial i2i communication success rates (both 94%; p<0.001). AV synchrony more than 95% was maintained consistently across various postures (sitting, standing, supine, lateral recumbency), activity	The study's follow-up period was limited to 3 months, which may not capture long-term performance and safety outcomes, which restricts its inclusion in evidence summaries prioritising long-term comparative data from randomised or controlled observational studies.

		levels (walking, fast walking), implantation indications, AV event types, and heart rates including more than 100 bpm.	
Jelisejevas J, Regoli F, Hofer D, et al. (2024) Leadless Pacemaker Implantation in Patients with a Prior Conventional Pacing System. CJC Open 6(4): 649–655	n=257 • Group 1: n=233 (no prior CPS) • Group 2: n=24 (prior CPS, 20 required lead extraction) Follow-up: Mean 12.5; SD 9.3 months	Implantation was successful and safe in people with prior conventional pacing systems (CPS). There were no major complications in the prior CPS group, including those who underwent lead extraction due to infection. No infections were recorded post-LP implantation, even when LP implantation followed device-related infection. Electrical parameters at implant and follow-up were comparable between groups. Major complications occurred in 3% of the full cohort (none in the prior CPS group).	Despite its relevance, the study's small subgroup size for prior CPS people (n=24), retrospective design, and limited generalisability restrict its inclusion in main evidence summaries prioritising large-scale or prospective comparative studies.
Jelisejevas J, Regoli F, Hofer D, et al. (2023) Leadless Pacemaker Implantation, Focusing on Patients With Conduction System Disorders Post-Transcatheter Aortic Valve Replacement: A	n=257 (26 with post-TAVR bradycardia; 231 non-TAVR controls); follow-up duration not explicitly reported, but complications assessed within 30 days post-implantation.	The implantation success rates were 100% in TAVR and 99% in non-TAVR groups. No significant differences were found in pacing parameters (sensing, impedance, and threshold) at implantation or during follow-up. The major complication	Broader registry study has been prioritised in the main summary evidence.

Retrospective Analysis. CJC Open 6(2Part A): 96–103.		rate was similarly low (4% in TAVR versus 3% in non-TAVR).	
Jelisejevas J, Breitenstein A, Hofer D, et al. (2021) Left femoral venous access for leadless pacemaker implantation: patient characteristics and outcomes. Europace 23(9): 1456–1461	n=143 (125 right femoral access, 18 left femoral access) Follow-up: Mean 15; SD 11.5 months	Left femoral venous access for LP implantation was safe and effective, with procedural success and device parameters comparable to the conventional right-sided approach. All 5 major complications (4%) occurred with right-sided access. Left-sided access was more commonly used following transfemoral TAVI (42% versus 8%, P=0.003).	While informative, the small sample size for left-sided access (n=18) and single-centre retrospective design limit generalisability
Katsuki T, Nagashima M, Kono H, et al. (2022) Clinical outcome for heart failure hospitalizations in patients with leadless pacemaker. Journal of Arrhythmia 38(5): 730–735	n=929 (368 LPs vs. 561 TVPs) Median follow-up: 1.7 years (IQR 0.8–2.6 years)	People with LPs had a significantly higher risk of heart failure hospitalisation than those with conventional pacemakers (adjusted HR 1.7; 95% CI 1.1 to 2.6; p=0.01).	The study's retrospective design and observational nature limit the ability to establish causality between pacemaker type and heart failure hospitalisation. Additionally, the median follow-up duration of 1.7 years may not be sufficient to capture long-term outcomes associated with different pacemaker types.
Kempa M, Mitkowski P, Kowalski O, et al. (2021)	Not applicable (policy and guidance document; no population cohort analysed)	Endorsed LPs as a safe and effective alternative to traditional TVPs, particularly when	This is an expert consensus document providing recommendations for clinical practice in

Expert opinion of a Working Group on Leadless Pacing appointed by the National Consultant in Cardiology and the Board of the Heart Rhythm Section of the Polish Cardiac Society. Kardiologia Polska 79(5): 604–608.		infection risk or venous access issues exist. Highlighted positive outcomes from international clinical trials confirming LP safety and efficacy. Provided Polish-specific guidance including - indications and contraindications for LP use, emphasis on procedural expertise and proper center accreditation for implantation and called for formal reimbursement frameworks in Poland to increase access.	Poland, not an original empirical study with a population cohort.
Khan MZ, Nguyen A, Khan MU, et al. (2024) Association of chronic kidney disease and end-stage renal disease with procedural complications and inpatient outcomes of leadless pacemaker implantations across the United States.	n=29,005 LP implantations (CKD: n=5,245 [18.1%]; ESRD: n=3,790 [13.1%]) In-hospital outcomes only (no post-discharge follow-up)	CKD and ESRD were significantly associated with increased inpatient mortality.	Focused only on in-hospital outcomes.
Khan MZ, Nassar S, Nguyen A, et al. (2024) Contemporary trends of leadless	Data from 2016–2020, showing growth from 3,230 LP implants (2016–2017) to 11,815 implants (2020) Follow-up: In-	LP implantations steadily increased in the US over the study period. Adjusted in-hospital mortality significantly declined (2018: aOR	Trend study, not aligned with the objective of this overview.

pacemaker implantation in the United States. Journal of Cardiovascular Electrophysiology 35(7): 1351–1359	hospital outcomes only	0.6; 2019: aOR 0.5; 2020: aOR 0.5, all p<0.01) compared to 2016 to 2017.	
Kiani S, Black GB, Rao B, et al. (2019) Outcomes of Micra leadless pacemaker implantation with uninterrupted anticoagulation. Journal of Cardiovascular Electrophysiology 30(8): 1313–1318	n=170 (OAC group: n=26; Off-OAC group: n=144) Follow-up: Not explicitly stated, complete in-hospital and procedural data	Implantation with uninterrupted anticoagulation (OAC) was safe and feasible. The composite complication rate was similar between OAC and Off-OAC groups (4% versus 1%; P=0.761), with no significant difference in length of stay (1.3; SD 2.6 vs 2.3; SD 3.4 days; P=0.108).	Focused on a specific subset of population, also the sample size is smaller.
Kiani S, Black GB, Rao B, et al. (2019) The Safety and Feasibility of Same-Day Discharge After Implantation of MICRA Transcatheter Leadless Pacemaker System.	n=167 (Same-day discharge [SD] group: n=25; Hospitalised overnight [HD] group: n=142) Follow-up: 45 days	Same-day discharge after LP implantation was safe and feasible. No major complications occurred in the SD group vs. 4% in the HD group (P=1.00), with similar rates of individual complications such as access site issues, pericardial effusion, dislodgement, or device revision.	The study did not capture long term safety and efficacy outcomes.
Kiblboeck D, Blessberger H, Ebner J, et al. (2024) Feasibility, timing and	n=48, undergoing CIED extraction (38 for infection, 10 for dysfunction); median follow-up 15	LP implantation was feasible in 98% of people undergoing CIED extraction, with 67% receiving the LP in a single procedure.	Covered in the systematic review included in the main evidence body.

outcome of leadless cardiac pacemaker implantation in patients undergoing cardiac implantable electronic device extraction. Clin Res Cardiol 2024 Aug 12. doi: 10.1007/s00392-024-02516-0	months (IQR 12 to 41)	Complete CIED removal was achieved in 92% overall and 97% of infected cases. In-hospital mortality was 6%, and 1-year survival was 85%. No LP-related mortality or recurrent infections occurred during follow-up.	
Knops RE, Tjong FVY, Neuzil P, et al. (2015) Chronic performance of a leadless cardiac pacemaker: 1-year follow-up of the LEADLESS trial. Journal of the American College of Cardiology 65(15): 1497–1504	n=31 (implanted with LPs) Follow-up: 12 months	Demonstrated stable electrical performance at 6 and 12 months, with mean pacing thresholds of 0.40; SD 0.3 V (6 months) and 0.43; SD 0.3 V (12 months), R-wave amplitudes of 10.6; SD 2.6 mV and 10.3; SD 2.2 mV, and impedance of 625; SD 205 ohms and 627; SD 209 ohms, respectively.	Small sample size and single-arm design without comparator group limits generalisability and prevents comparative assessment with conventional pacing systems.
Kowlgi GN, Tseng AS, Tempel ND, et al. (2022) A real-world experience of atrioventricular synchronous pacing with leadless	n=56 with LP implants; minimum follow-up 3 months	65% of people achieved atrial synchronous ventricular pacing (AVP) equal or more than 70%. Higher AV synchrony was associated with lower BMI, fewer comorbidities (e.g.,	Covered by systematic review included in the main evidence summary.

ventricular pacemakers. J Cardiovasc Electrophysiol 33(5):982–993.		heart failure), and prior cardiac surgery.	
Lenormand T, Abou Khalil K, Bodin A et al. (2023) Comparison of first- and second-generation leadless pacemakers in patients with sinus rhythm and complete atrioventricular block. Journal of Cardiovascular Electrophysiology 34(8): 1730–1737.	n=93 (45 first-generation Micra VR, 48 second-generation Micra AV) Follow-up: At least 1 year	Second-generation Micra AV pacemakers achieved atrioventricular synchrony (median AV-synchronous beats: 78%) and were associated with significantly lower incidence of pacemaker syndrome (0% versus. 11% in Micra VR group, *p*=0.02).	Focused on head-to-head comparison between device generations rather than broader safety/effectiveness outcomes. Small sample size and short-term follow-up limit generalisability.
Lenormand T, Abou Khalil K, Bodin A et al. (2023) Leadless cardiac pacing: Results from a large single-centre experience. Archives of Cardiovascular Disease 116(6-7): 316–323.	n=400 (328 Micra VR, 72 Micra AV) Follow-up: Median 16 months (694 person-years)	Implantation success was 100%. At 30 days, perioperative complication rate was 4%, and 88% of people were discharged the next day.	Single-centre retrospective study without a comparator group or stratified outcome data; limits generalisability.
Li B, Allen JC, Arps K, et al. (2022) Leadless pacemaker implantation after lead	n=39; mean follow-up 24.8; SD 14.7 months	LP implantation following extraction of infected cardiac devices was associated with low complication rates and no recurrence of	Covered in systematic review included in main evidence summary.

extraction for cardiac implanted electronic device infection. J Cardiovasc Electrophysiol 33(3): 464–470.		infection during the 2-year follow-up. Among 3 major complications (8%), none were infections.	
Loring Z, North R, Hellkamp AS, et al. (2020) VVI pacing with normal QRS duration and ventricular function: MOST trial findings relevant to leadless pacemakers. Pacing and Clinical Electrophysiology 43(12): 1545–1553.	n = 1284 (subset of the original 2010 MOST participants) Inclusion: LVEF more than 35%, QRS duration less than 120 ms, no prior ICD or ventricular arrhythmias Follow-up: 4 years	VVIR pacing, typical of most LPs, does not increase the risk of death, stroke, or heart failure hospitalisation compared to DDDR pacing. However, it significantly increases the risk of new-onset AF, especially in people without a history of AF.	Focused on pacing mode effects in LP-eligible populations, particularly highlighting the AF risk tradeoff with VVIR mode pacing typical in current LP devices.
Mararenko A, Udongwo N, Pannu V, et al. (2023) Intracardiac leadless versus transvenous permanent pacemaker implantation: Impact on clinical outcomes and healthcare utilization. J Cardiol 82(5):378–387.	n=21,782 (mean age 81.1 years, 46% female); follow-up focused on 30-day readmissions and in-hospital outcomes	No significant difference in 30-day readmission (HR 1.1, 95% CI 0.9 to 1.4) or inpatient mortality (HR 1.4, 95% CI 0.7 to 2.6) between LP and TVP groups. Length of stay was slightly longer for LP recipients (0.5 days; p<0.001).	Covered in systematic review included in main evidence summary.
Martínez-Sande JL, García-Seara J, Rodríguez-	n=30 (65 years or more); Mean follow-up: 5.3; SD 3.3 months	Successful implantation was achieved in all. Electrical pacing and	Small single-centre study with limited follow-up duration and generalisability.

Mañero M et al. (2017) The Micra Leadless Transcatheter Pacemaker. Implantation and Mid-term Follow-up Results in a Single Center. Revista Española de Cardiología (English Edition) 70(4): 275–281.	(range up to more than 1 year in 4 people)	sensing parameters remained stable from implantation through follow-up. 1 moderate pericardial effusion occurred without tamponade; otherwise, no severe complications were observed.	Also, concurrent procedures were assessed.
Martinez-Sande JL, Garcia-Seara J, Gonzalez-Melchor L, et al. (2021) Conventional single-chamber pacemakers versus transcatheter pacing systems in a "real world" cohort of patients: A comparative prospective single-center study. Indian Pacing Electrophysiol J 21(2):89–94.	n=443 (LP: n=198, TVP: n=245); mean follow-up 22.3; SD 15.9 months	LP recipients had significantly fewer overall complications compared to TVP groups (HR 0.4, 95% CI 0.2 to 1; p=0.013), with a 96% probability of lower risk in Bayesian analysis. No significant differences in major complications (LP 3% versus TVP 6%; p=0.1761) or mortality.	Covered in systematic review included in the main body evidence.
Mitacchione G, Schiavone M, Gasperetti A, et al. (2023) Sex differences in leadless pacemaker implantation: A	n=1179 (64% male); after matching, n=738 (1:1 matched); median follow-up: 25 months (IQR 24 to 39)	There were no statistically significant sex differences in major complication rates (HR 2.03; 95% CI 0.7 to 5.8; p=.190) or all-cause mortality (HR 1; 95% CI 0.4 to	While sex-specific findings are valuable, the analysis was exploratory and not powered to detect small differences in adverse outcomes.

propensity-matched analysis from the i-LEAPER registry. Heart Rhythm 20(10):1429–1435.		2.4; p=.96). LP performance was similar between men and women, although women had slightly higher pacing impedance at implant and follow-up (670 ohms vs 616 ohms at 24 months; p=.014), remaining within acceptable ranges. Women were underrepresented among LP recipients.	No impact on safety or efficacy was observed despite impedance variation.
Molina-Lerma M, Cózar-León R, García-Fernández FJ, Calvo D. (2024) Spanish pacemaker registry. 21st official report of Heart Rhythm Association of the Spanish Society of Cardiology (2023). Rev Esp Cardiol (Engl Ed) 77(11):947–956.	112 hospitals participated 24,343 LP implantations reported in 2023 No specific population-level follow-up data provided	Marked 48% increase in reported device implantations compared to 2022. LPs saw an 18% rise, with 963 devices implanted. AV block remained the top indication; atrial tachyarrhythmia with slow ventricular response ranked second for the first time.	This is a national registry report summarising implantation trends and system use in Spain, not a clinical trial or comparative study measuring population outcomes.
Molina-Linde JM, Díaz-Infante E, Tercedor-Sánchez L, et al. (2023) The VR leadless pacemaker: Results of an expert panel using the	Involved expert evaluation of 256 clinical scenarios, 64 for people with AF, 192 for people in sinus rhythm. Follow-up not applicable; no population-level outcome data	The panel created appropriateness criteria for VR LP implantation. Limitation of vascular access via the superior vena cava was the strongest predictor for recommending LPs in both groups. Additional relevant variables included:	It provides expert-based recommendations rather than empirical outcome data.

RAND/UCLA method. Pacing Clin Electrophysiol 46(5):358–364.		life expectancy, risk of infection, presence of prosthetic valves, LVEF and population mobility and exercise capacity.	
Nair DG, Exner DV, Hadadi C et al. (2024) Early real-world implant experience with a helix-fixation ventricular leadless pacemaker. Journal of Interventional Cardiac Electrophysiology 67: 1539–1545.	n=167 Follow-up: 30 days post-implant	Implantation of the helix-fixation Aveir VR was successful in 99% of cases, with 98% free from acute adverse events.	Short-term follow-up (30 days), limited to initial commercial rollout without comparator group, and focused only on procedural outcomes.
Neuzil P, Exner DV, Knops RE, et al. (2025) Worldwide Chronic Retrieval Experience of Helix-Fixation Leadless Cardiac Pacemakers. J Am Coll Cardiol 85(11):1111–1120.	n=233 subjects with 234 retrieval attempts (mean retrieval time = 3.2 years, range 0.2 to 9 years post-implant)	The chronic retrieval success rate for helix-fixation LPs was 88% (205/234). Failures were mostly due to inability to access the docking button (86%). Retrieval-related complications occurred in 4% of people (9/233), with 11 total complications. Time since implantation (up to 9 years) did not statistically significantly affect retrieval success (p=0.71).	Focused on device retrieval safety and feasibility rather than on comparative effectiveness or long-term pacing outcomes of LPs versus TVPs.
Ngo L, Nour D, Denman RA et al. (2021)	36 studies included Micra: n=1608 (90-day data), n=3194 (1-year data) Nanostim: variable,	LPs showed a low pooled complication rate (less than 1% at 90 days and 2% at 1 year) and excellent	More recent systematic reviews with inclusion of studies with longer follow up duration

Safety and Efficacy of Leadless Pacemakers: A Systematic Review and Meta-Analysis. Journal of the American Heart Association 10(13): e019212.	fewer studies Follow-up: up to 1 year	pacing capture threshold maintenance (99% with less than or equal to 2V at 1 year).	have been covered in the main evidence summary.
Nicosia A, Iacopino S, Nigro G et al. (2022) Performance of transcatheter pacing system use in relation to patients' age. Journal of Interventional Cardiac Electrophysiology 65(1): 103–110.	n=577 Follow-up: Not explicitly stated; electrical parameters and safety outcomes assessed at implant and last follow-up	LP implantation was found to be safe and effective across all age groups (less than 70, 70 to77, 78 to83, and 83 and above years). Procedural complications were rare (less than 1%) and did not differ significantly by age group, despite greater frailty in older people. No cases of cardiac tamponade were reported. Electrical performance remained stable and comparable across all ages.	A larger study with similar subgroup of people was included in the main evidence summary.
Noor TA, Rana MOR, Kumari S et al. (2023) Outcomes of primary leadless pacemaker implantation: A systematic review. Annals of Noninvasive Electrocardiology 28(6): e13084.	n=1276 across 4 included studies Follow-up duration not consistently reported across all studies	LPs had shorter procedure and fluoroscopy times compared to temporary or TVPs in some studies. Major complications and mortality were not significantly different, and pacing parameters (threshold, impedance, sensing)	More recent systematic reviews have been included in the main evidence summary.

		were comparable. Hospital stay was generally shorter with LPs. The review suggests LPs may be an effective and safer alternative even in urgent/emergency pacing situations.	
Oates CP, Breeman KTN, Miller MA, et al. (2024) Long-Term Safety and Efficacy of Intraoperative Leadless Pacemaker Implantation During Valve Surgery. JACC: Clinical Electrophysiology 10(10): 2224–2233.	n=100; median follow-up duration: 10.6 months (IQR: 2 to 22.7 months)	Intraoperative LPs implantation during valve surgery was successful in all, with no device-related complications during follow-up. At 12 months, 95% of people maintained acceptable pacing thresholds (2.0 V or lower at 0.24 ms). The cohort included 99% with tricuspid valve involvement and 78% undergoing multivalve surgery.	Broader registry study has been included in the main evidence summary.
Oates CP, Basyal B, Whang W, et al. (2024) Trends in safety of catheter-based electrophysiology procedures in the last 2 decades: A meta-analysis. Heart Rhythm 21(9): 1718–1726.	n=43,914 across 174 studies Includes: • AF ablation: n=24,057 (126 studies) • Ventricular tachyarrhythmia ablation: n=1,781 (25 studies) • LP: n=8,896 (21 studies) • Left atrial appendage occlusion: n=9,180 (18 studies) Follow-up duration not	Vascular complication rates remained unchanged. Results suggest that procedural safety of catheter-based electrophysiology, including LP implantation, has improved over time despite increased usage.	It included multiple other procedures alongside LPs.

	uniformly reported		
Pagan E, Gabriels J, Khodak A, et al. (2020) Safety of leadless pacemaker implantation in the very elderly. Heart Rhythm 17(12):2023–2028.	n=302, aged 85 years or more (LP: n=183; TVP: n=119); follow-up not specified; focused on in-hospital procedural outcomes	LP implantation in very elderly people was successful in 98% and associated with similar procedure-related complication rates compared to TVP (3% vs 6%, p=0.276). LP group had significantly shorter procedure times (35.7; SD 23 minute versus 62.3; SD 31.5-minute, p<0.001). No significant differences in pericardial effusion, hematoma, or lead dislodgement rates.	Covered in systematic review included in the main evidence summary.
Palmisano P, Guido A, Panico V, et al. (2021) Leadless pacemaker versus transvenous single-chamber pacemaker therapy: peri-procedural aspects, utilization of medical resources and patient acceptance. Expert Review of Medical Devices 18(5): 483–491.	n=154 (77 matched pairs: LP versus TVP) Follow-up: baseline, 1 week, 3 months, and 6 months	L-PM implantation was associated with longer procedural time (42.2;SD 16.3 vs. 28.9;SD 11.9 minutes; *p*<0.001) but lower intra- and post-operative pain, shorter hospitalisation (3.2;SD 0.5 vs. 3.5;SD 1.1 days; *p*=0.034), greater acceptance (FPAS score: 58.7;SD 7.1 vs. 40.5;SD 4.1; *p*<0.001), and better quality of life on physical and mental health scales at all timepoints.	Single-centre study with a relatively small sample size; findings may not be generalisable to broader populations. Outcomes such as complication rates and long-term device performance were not the primary focus.

Palmisano P, Iacopino S, De Vivo S, et al. (2022) Leadless transcatheter pacemaker: Indications, implantation technique and peri-procedural patient management in the Italian clinical practice. International Journal of Cardiology 365: 49–56.	n=782 Median follow-up: 20 months	Implantation of L-PMs was primarily chosen due to high infection risk (30% of people). The implantation success rate was 99%, with 90% of devices implanted septally.	Focused on per-procedural patient management.
Palmisano P, Facchin D, Ziacchi M, et al. (2023) Rate and nature of complications with leadless transcatheter pacemakers compared with transvenous pacemakers: results from an Italian multicentre large population analysis. EP Europace 25(1):112–120.	n=2669 total (LP: n=665; TVP: n=2004); matched cohort: n=884 (442 LP versus 442 TVP); median follow-up: 39 months	LP group had significantly lower 12-month device-related complication rate (1% versus 2%, p=0.009). In the matched analysis, LP was associated with fewer late complications (more than 30 days; p=0.031), while early complication risk was similar (p=1.000). All LP complications occurred early, whereas 75% of TVP complications were lead- or pocket-related.	Covered in the systematic review included in the main evidence summary.
Piccini JP, Stromberg K, Jackson KP, et al. (2017) Long-term outcomes in leadless Micra transcatheter	LP cohort: n=711 Capture (TVP) cohort: n=538 Follow-up: up to 6 months	12% LP populations had an initial pacing threshold more than 1 V at 0.2 ms pulse width. Thresholds statistically significantly decreased over time	Primarily focuses on threshold behavior post-implant rather than broader clinical outcomes or direct device comparisons, might be informative

pacemakers with elevated thresholds at implantation: Results from the Micra Transcatheter Pacing System Global Clinical Trial. Heart Rhythm 14(5):685–691.		(p<.001), with 87% of those with high thresholds (1 to 1.5 V) and 85% of those with very high thresholds (more than 1.5 V) showing improvement by 6 months. Only 18% of people with an initial threshold more than 2 V achieved a threshold at 1 V or less at 6 months.	for procedural decision-making.
Piccini JP, Stromberg K, Jackson KP, et al. (2019) Patient selection, pacing indications, and subsequent outcomes with de novo leadless single-chamber VVI pacing. Europace 21(11):1686–1693.	n=720, successfully implanted with LP; 228 (32%) had non-AF indications; follow-up: 24 months	The study found that 32% of LP implants were for non-AF-related indications, mainly due to expectations of infrequent pacing (66%) or advanced age (27%). Non-AF people had significantly lower VP needs (median 13%) compared to AF people (68%; p<0.001). The 24-month risk of the composite outcome (cardiac failure, pacemaker syndrome, or syncope) was low (2%) and similar between groups (HR 1.4; 95% CI 0.5 to 4.2; p=0.59), supporting the safety and feasibility of leadless pacing in selected non-AF population.	The analysis was limited to the Micra IDE cohort and lacked direct comparisons with transvenous pacing or atrioventricular synchronous pacing outcomes
Piccini JP, El-Chami M,	n=15,408 (LP: n=5746; TVP: n=9662); acute	LP recipients had higher unadjusted acute complication	Covered by the systematic review

Wherry K, et al. (2021) Contemporaneous Comparison of Outcomes Among Patients Implanted with a Leadless vs Transvenous Single-Chamber Ventricular Pacemaker. JAMA Cardiol 6(10):1187–1195.	outcomes at 30 days and complications at 6 months	rates (8% versus 7%; p=.02) and more pericardial effusions/perforations (1% vs 0.4%; p=.004). However, after adjusting for population characteristics, the overall acute complication rate was similar (8% vs 7%). LP recipients had significantly fewer 6-month complications than TVP recipients (adjusted HR 0.8; 95% CI, 0.6 to 1; p=.02).	included in the main evidence summary.
Reddy VY, Exner DV, Cantillon DJ, et al. (2015) Percutaneous implantation of an entirely intracardiac leadless pacemaker. New England Journal of Medicine 373(12): 1125–1135.	n=526 enrolled; primary cohort: n=300, with 6-month follow-up	Successfully implanted in 96% of people. In the primary cohort, the combined efficacy endpoint (maintaining an acceptable pacing threshold less or equal to 2 V at 0.4 msec and R-wave amplitude more or equal to 5.0 mV through 6 months) was met in 90% of people, and the safety endpoint (freedom from device-related serious adverse events) was met in 93% of people.	The study evaluated the Nanostim LP, which is no longer available due to safety concerns, limiting the applicability of its findings to current clinical practice.
Reddy VY, Knops RE, Sperzel J et al. (2014) Permanent leadless cardiac	n=33 Follow-up: 3 months	Implant success rate was 97% (32/33). 1 person experienced right ventricular perforation and died following a stroke;	The small sample size, Nanostim device inclusion and short follow-up period limit the

pacing: results of the LEADLESS trial. Circulation 129(14): 1466–1471.		the overall complication-free rate was 94%. Pacing parameters remained stable or improved over the 3-month period.	generalisability of the findings.
Reynolds D, Duray GZ, Omar R, et al. (2016) A Leadless Intracardiac Transcatheter Pacing System. New England Journal of Medicine 374(6):533–541.	n=725 enrolled; n=719 (99%) received successful implantation; primary safety and efficacy assessed at 6 months	LPs met both prespecified safety (96% free from major complications; p<0.001 versus goal of 83%) and efficacy (98% with low, stable pacing thresholds; p<0.001 versus goal of 80%) targets. No device dislodgements occurred. Post hoc comparison with a TVP cohort (n=2667) showed a statistically significantly lower major complication rate (HR 0.5; 95% CI, 0.3 to 0.8; p=0.001).	Covered in the systematic review included in the main evidence summary.
Regoli FD, Saguner AM, Auricchio A, et al. (2023) Peri-Procedural Management of Direct-Acting Oral Anticoagulants (DOACs) in Transcatheter Miniaturized Leadless Pacemaker Implantation. J Clin Med 12(14):4814.	n=392, undergoing LP implantation; 282 on anticoagulation, including 192 on DOACs. No specific long-term follow-up duration stated—focused on peri-procedural outcomes.	A standardised DOAC management approach—skipping 1 dose before the procedure and resuming 6 to 24 hours afterward—was used in 115 people (Group 1A) and compared to alternative strategies in 77 (Group 1B). The incidence of major peri-procedural complications was low and similar in both groups (3% in 1A vs 4% in 1B; p=0.685). Group 1A people were more	While relevant for procedural safety, the study focused on anticoagulation strategy rather than comparing pacemaker systems or long-term device-related outcomes.

		likely to undergo elective implantation and had better overall clinical profiles. No significant increase in bleeding or thromboembolic events was observed with the standardised DOAC protocol.	
Ritter P, Duray GZ, Steinwender C, et al. (2015) Early performance of a miniaturized leadless cardiac pacemaker: the Micra Transcatheter Pacing Study. European Heart Journal 36(37): 2510–2519.	n=140 Follow-up: Mean 1.9; SD 1.8 months; 3-month outcomes reported in 60 people	Met both safety and efficacy endpoints. No unanticipated serious adverse device events were reported. Among 60 people with 3-month follow-up, all had pacing thresholds less than 2 V, with a mean threshold of 0.5; SD 0.2 V. 1 case of pericardial effusion occurred without tamponade.	Short follow-up period and limited 3-month data on a subset (n=60) reduce confidence in long-term outcomes.
Roberts PR, Clémenty N, Mondoly P, et al. (2023) A leadless pacemaker in the real-world setting: Patient profile and performance over time. Journal of Arrhythmia 39(1): 1–9.	n=928 Mean follow-up: 9.7; SD 6.5 months	Confirmed a high implant success rate (100%) and a low 30-day major complication rate (3%) for LPs, consistent with earlier IDE and PAR studies. Electrical performance was stable through 12 months, with a mean pacing threshold of 0.6; SD 0.4 V.	Broader real-world studies with larger sample size have been emphasised in main evidence summary.
Roberts PR, Clementy N, Al Samadi F, et al. (2017) A leadless pacemaker in	n=795 (implant success in 792; 99.6%) Follow-up: 30 days post-implant	100% implant success rate and a low 30-day major complication rate of 1.5%. Key complications	The short follow-up period limits the assessment of long-term safety and efficacy outcomes.

the real-world setting: The Micra Transcatheter Pacing System Post-Approval Registry. Heart Rhythm 14(9): 1375–1379.		included cardiac effusion, device dislodgement, and sepsis.	
Roberts PR, Pepper C, Rinaldi CA, et al. (2019) The use of a single chamber leadless pacemaker for the treatment of cardioinhibitory vasovagal syncope. Int J Cardiol Heart Vasc 23:100349.	n=32 Follow-up: mean 404; SD 237 days (range: 63 to 928 days)	Implantation was successful in all people, with a major complication rate of 3%. After follow-up, 87% of people were symptom-free, suggesting good efficacy. The study supports the feasibility and potential benefit of leadless pacing in this younger syncope population.	Limited sample size and observational design without a control group limit the generalisability and strength of conclusions regarding efficacy compared to conventional pacemakers or other management strategies.
Russo V, D'Andrea A, De Vivo S, et al. (2021) Single-Chamber Leadless Cardiac Pacemaker in Patients Without Atrial Fibrillation: Findings from Campania Leadless Registry. Frontiers in Cardiovascular Medicine 8: 781335.	n=140 Mean follow-up: 606.5; SD 265.9 days	No significant difference in perioperative complications (5%), cardiac hospitalisation (5%), syncope (4%), or all-cause mortality (8%) was observed between AF and non-AF groups. No pacemaker syndrome was reported in either group.	Evidence with larger sample size have been prioritised in main evidence summary.
San Antonio R, Chipa-Ccasani	n=107 (consecutive people receiving	Among 107 people, 43 (40%) received	Single-centre study with a modest

F, Apolo J, et al. (2019) Management of anticoagulation in patients undergoing leadless pacemaker implantation. Heart Rhythm 16(12):1849–1854.	LPs between 2014 and 2018)	anticoagulation. Anticoagulation was managed via temporary discontinuation or continuation. Only 2 people experienced complications: 1 haemorrhagic pericardial effusion and 1 saphenous vein thrombosis (not on anticoagulants).	sample size and no comparator group limits the generalisability of conclusions regarding anticoagulation safety across broader populations or different procedural techniques.
Sanchez R, Nadkarni A, Buck B, et al. (2021) Incidence of pacing-induced cardiomyopathy (PICM) in pacemaker-dependent patients is lower with leadless pacemakers compared to transvenous pacemakers. Journal of Cardiovascular Electrophysiology 32(2):477–483.	n=198 pacemaker-dependent people (TVP: n=131; LP: n=67) with baseline LVEF equal or more than 50%; mean follow-up: TVP 592; SD 549 days, LP 817; SD 600 days	PICM (equal and more than10% LVEF reduction) occurred more often in TVP recipients (14%) than LP recipients (3%; p=0.02). TVP was an independent predictor of PICM (OR: 1.1), while older age reduced the risk (OR: 0.9). Nearly all people responded to CRT, including both LP cases that developed PICM.	Covered by systematic review included in the main evidence summary.
Sasaki K, Togashi D, Nakajima I, et al. (2022) Clinical outcomes of non-atrial fibrillation bradyarrhythmias treated with a ventricular demand leadless	n=193 total; matched cohort: n=116 (58 in each group with LP or TVP); median follow-up 733 days (IQR: 395 to 997)	Although late device-related adverse event rates were not statistically significantly different (0% versus 4%; p=0.155), people receiving LP had statistically significantly higher HF-related readmission (29% versus 2%; p=0.001)	Covered in the systematic review included in the main body evidence.

pacemaker compared with an atrioventricular synchronous transvenous pacemaker: A propensity score-matched analysis. Circulation Journal 86(8):1283–1291.		and a trend toward higher all-cause mortality (28% versus 4%; p=0.059) compared to TVP recipients.	
Schiavone M, Gasperetti A, Mitacchione G, et al. (2022) Leadless Pacemaker Implantation in the Emergency Bradyarrhythmia Setting: Results from a Multicenter European Registry. Medicina 59(1): 67.	n=1154 with 6% presenting from emergency departments (ED+) Periprocedural outcomes only (no long-term follow-up reported)	Implantation for urgent bradyarrhythmias (ED+) was feasible and did not significantly increase the rate of major complications compared to elective implantations (ED−) (7% vs. 4%, p=0.244).	Short-term outcomes only; limited sample size for the emergency group and no follow-up beyond the procedural period.
Semlitsch T, Loder C (2020) Leadless pacemaker for right ventricle pacing (Update 2020). Decision Support Document 97 / Update 2020. Austrian Institute for Health Technology	n=2,976 across 16 new documents (3 ongoing multicentre single-arm studies, 1 multicentre case-control study, 5 monocentre case series)	The update identified limited evidence for comparative efficacy versus conventional pacemakers. However, LP showed consistent safety advantages, particularly in avoiding complications related to subcutaneous pockets and transvenous leads.	Evaluated as a policy-level update and synthesis of ongoing observational evidence rather than a new clinical study with direct comparative outcomes.

Assessment (AIHTA).			
Shantha G, Brock J, Singleton MJ, et al. (2023) A comparative study of the two leadless pacemakers in clinical practice. Journal of Cardiovascular Electrophysiology 34(9): 1896–1903.	n=50 (25 AVEIR-VR, 25 MICRA-VR) with 8 weeks of follow-up	Both devices had 100% implant success and stable pacing parameters. AVEIR-VR had more single-attempt deployments (80% versus 60%), a higher rate of ventricular arrhythmias (20% versus 0%; *p*=.043), and a significantly longer estimated battery life (15 versus 8 years; *p*=.047). No significant procedural complications or dislodgements occurred.	Small sample size and short follow-up period; initial experience rather than long-term outcomes.
Sharma P, Guleria VS, Bharadwaj P et al., (2020) Assessing safety of leadless pacemaker (MICRA) at various implantation sites and its impact on paced QRS in Indian population. *Indian Heart Journal* 72(5): 376–382.	n=35 with mean follow-up of 1.4 years	Mid-septal LP implantation resulted in the narrowest paced QRS duration (139.3 ms), while apical placement had the broadest (166.6 ms). Left ventricular ejection fraction and pacing thresholds remained stable across all groups. 2 minor complications were reported (pericardial effusion and diaphragmatic pacing).	The small sample size and single-centre design may limit the generalisability of the findings.
Shtembari J, Shrestha DB, Awal S, et al. (2023) Comparative assessment of	17 studies included population numbers varied (exact pooled n not reported); follow-up duration	LPs had 42% lower odds of overall complications compared to TVPs (OR 0.6, 95% CI 0.4 to 0.8). LPs showed	More comprehensive systematic reviews and meta-analyses have been covered in the main evidence summary.

safety with leadless pacemakers compared to transvenous pacemakers: a systematic review and meta-analysis. Journal of Interventional Cardiac Electrophysiology 66(12): 2165–2175.	not uniformly stated across studies	significantly lower risks for device dislodgment (OR 0.3), re-intervention (OR 0.5), and pneumothorax (OR 0.1). However, LPs were associated with higher odds of pericardial effusion (OR 2.7). All included studies were observational.	
Soejima K, Asano T, Ishikawa T, et al. (2017) Performance of leadless pacemaker in Japanese patients vs. rest of the world: Results from a global clinical trial. Circulation Journal 81(11): 1589–1595.	n=38 Japanese people (total global cohort not specified here); 12-month follow-up	Japanese people had no major complications and low, stable pacing thresholds over 12 months. Despite smaller body size and different procedural practices (e.g., anticoagulation, length of stay), their outcomes were comparable to people from outside Japan. Freedom from major complications at 12 months was 100% in Japanese people vs. 96% in the rest of the world (P=0.211).	The limited sample size of the subgroups may restrict the generalisability of the findings to the entire population.
Sperzel J, Burri H, Gras D, et al. (2018) Primary safety results from the LEADLESS Observational Study. Europace 20(9): 1491–1497.	n=470 (safety endpoint evaluated in 300 post-pause people); follow-up at discharge, 90 days, 180 days, and every 6 months	Freedom from serious adverse device effects (SADEs) at 6 months was 95% (95% CI: 91 to 97%) in the 300 post-pause cohort, exceeding the predefined performance goal of 86% (P<0.0001). The	Nanostim device is no longer in use due to market withdrawal, limiting current clinical applicability of findings.

		most common SADEs included cardiac perforation (1%), device dislodgement, and vascular complications (1%). Cardiac perforation and dislodgement decreased significantly following protocol amendments and additional training during the study pause.	
Steinwender C, Khelae SK, Garweg C, et al. (2020) Atrioventricular synchronous pacing using a leadless ventricular pacemaker: Results from the MARVEL 2 study. JACC: Clinical Electrophysiology 6(1):94–106.	n=75 enrolled; n=40 with sinus rhythm and complete AV block included in the primary efficacy analysis; algorithm performance assessed over a 5 hour download period	In people with sinus rhythm and complete AV block, AV synchronous pacing using the enhanced accelerometer-based algorithm resulted in 70% or more AV synchrony in 95% of participants versus 0% during pacing ($p<0.001$). Mean AV synchrony rose from 27% to 89%. No pauses or oversensing-induced tachycardia episodes occurred in the full cohort.	Covered in the systematic review included in the main evidence summary.
Steinwender C, Lercher P, Schukro C, et al. (2020) State of the art: leadless ventricular pacing: A national expert consensus of the Austrian	Not a clinical study; no people enrolment or follow-up Based on pooled evidence, expert opinion, and national practice experience in Austria	This consensus document presents recommendations from a panel of Austrian experts on indications for LP vs TVP, infection management, operator training requirements and technical standards for LP implantation	This was a consensus-based expert opinion rather than a clinical or observational study with original population data or comparative outcomes.

Society of Cardiology. J Interv Card Electrophysiol 57(1):27–37.		It emphasises that LPs can be safely implanted with low complication rates if technical and clinical guidance is adhered to.	
Sultan A, Scheurlen C, Wörmann J et al. (2024) First long-term outcome data for the Micra VR™ transcatheter pacing system: data from the largest perspective German cohort. Clinical Research in Cardiology 113(7): 1443–1450.	n=188; mean follow-up of 723.4; SD 598 days	Among 188 people, predominantly with AV block III° in AF (85%), LPs demonstrated excellent long-term safety and performance. No infections or device failures were reported. Electrical parameters remained stable over time despite increased RV pacing demand (from 17% to 87%). Battery status declined as expected (3.2 V to 3 V), consistent with longevity estimates.	Broader real-world registry studies have been covered in main evidence summary.
Tachibana M, Banba K, Matsumoto K, et al. (2020) The feasibility of leadless pacemaker implantation for superelderly patients. Pacing Clin Electrophysiol 43(4):374–381.	n=62, aged more than 85 years (TVP group: n=35; LP group: n=27); follow-up duration up to 3 months	Despite a higher proportion of dementia in the LP group (63% versus 37%, p=.04), complication-free rates were similar between LP and TVP groups (87% versus 93%, p=.68). LP implantation had higher initial pacing thresholds (p<.01), but these improved over 3 months. Procedure and hospitalisation durations were	Covered in the systematic review included in the main body evidence.

		shorter in the LP group.	
Tam MTK, Cheng YW, Chan JYS, et al. (2024) Aveir VR real-world performance and chronic pacing threshold prediction using mapping and fixation electrical data. Europace 26(3): euae051.	n=123 Aveir VR implant attempts (122 successful, 99%) n=88 reached 3-month follow-up. Comparison with retrospective cohort of 139 LP people.	3-month PCT correlated with impedance during mapping and tethering (p<0.001), but not with post-fixation PCT (P>0.05). High intraoperative impedance (more than 470 ohms) predicted excellent chronic PCT with 88% sensitivity and 71% specificity. Despite higher initial high PCT rates for Aveir (12%) vs Micra (2%; P=0.004), the 3-month high PCT rates were similar (Aveir 2% vs Micra 3%; P=1.000). Complication rate was low (1.6%).	Focuses primarily on procedural and electrical performance characteristics (PCT prediction) of the Aveir VR device rather than direct comparative long-term safety or clinical effectiveness outcomes between different device types.
Tan MC, Tan JL, Tay ST, et al. (2023) A Systematic Review of Short-Term Outcomes of Leadless Pacemaker Implantation After Transvenous Lead Removal of Infected Cardiac Implantable Electronic Device.	n=253; mean follow-up 11.3; SD 10.6 months	LP implantation after transvenous lead removal (TLR) of infected cardiac devices was feasible and safe, with low complication (4%) and reinfection (less than 1%) rates. The most common infection pathogen was *Staphylococcus aureus*. Concomitant LP implantation during TLR was performed in 42% of cases. Few short-term complications were noted, including	Focused specifically on post-infection TLR scenarios, limiting generalisability to broader LP use cases.

American Journal of Cardiology 203: 444–450.		hematoma, femoral AV fistula, and pericardial effusion. 1 LP-related infection occurred during follow-up.	
Tjong FVY, Knops RE, Udo EO, et al. (2018) Leadless pacemaker versus transvenous single-chamber pacemaker therapy: A propensity score-matched analysis. Heart Rhythm 15(9):1387–1393.	n=440 (LP; n=220; TVP; n=220); median follow-up 800 days	When excluding PM advisory-related events, LPs had fewer complications than TVPs (1% versus 5%, p=.02). However, when including advisory-related complications, LPs had a higher total complication rate (11% versus 5%, p=.063), negating the initial advantage.	Covered in the systematic review included in the main evidence summary.
Togashi D, Sasaki K, Okuyama K, et al. (2023) Two-year Outcomes of Ventricular-demand Leadless Pacemaker Therapy for Heart Block After Transcatheter Aortic Valve Replacement. J Innov Card Rhythm Manag 14(6): 5491–5498.	n=39 (17 LPs, 22 TVPs); 2-year follow-up	Post-procedural complication rates were low and similar across groups, people with LPs had significantly higher all-cause mortality (41% versus 5%, p<.01) and more heart failure rehospitalisations (24% versus 0%, p=.01) compared to those with TVPs after TAVR. No significant differences were observed in late device-related adverse events or new-onset AF.	Broader registry study with larger sample size has been prioritised in the main body evidence
Tokavanich N, Machado C,	n=67; follow-up at 3 and 6 months	Micra VR had significantly shorter electrophysiology lab	Focused on comparative implant parameters and

Banga S, et al. (2023) Implant efficiency and clinical performance of Aveir™ VR and Micra™ VR leadless pacemaker: A multicenter comparative analysis of 67 patients. Pacing and Clinical Electrophysiology 46(8): 827–832.		time (41; SD 12 vs. 55; SD 11.5 min, p=.008) and fluoroscopy time (6.5; SD 2.2 vs. 11.5; SD 4.5 min, p<.001) compared to Aveir VR. Aveir VR showed higher initial pacing thresholds (0.7; SD 0.3 mA vs. 0.5; SD 0.18 mA, p<.001) but matched performance at 3 and 6 months. No significant differences in sensing, impedance, or pacing percentage were observed. Projected battery longevity was significantly greater in the Aveir™ VR group (18.8; SD 4.3 versus 7.7; SD 0.8 years, p<.001). Procedural complications were rare in both groups.	early performance, not long-term safety or effectiveness outcomes.
Tolosana JM, Guasch E, San Antonio R, et al. (2020) Very high pacing thresholds during long-term follow-up predicted by a combination of implant pacing threshold and impedance in leadless transcatheter pacemakers.	n=110 (LP implants from 2014 to 2018); 108 successful implants Follow-up: up to 48 months (mean 24; SD 16 months)	Only 4% of people developed very high pacing thresholds (VHPT: more than 2 V/0.2 ms). People who developed VHPT had higher implant pacing thresholds (1; SD 0.3 V vs 0.6; SD 0.3 V; p=.003) and lower implant impedance (580; SD 59 ohms vs 837; SD 232 ohms; p=.03).	While valuable for hypothesis generation and identifying predictors, further validation is needed before routine clinical application.

Journal of Cardiovascular Electrophysiology 31(4):868–874.			
Tonegawa-Kuji R, Kanaoka K, Mori M, et al. (2022) Mortality and 30-Day Readmission Rates After Inpatient Leadless Pacemaker Implantation: Insights from a Nationwide Readmissions Database. Canadian Journal of Cardiology 38(11): 1697–1705.	n=137,732 total pacemaker implantations (including 5,986 LP implantations); 30-day follow-up for readmissions	The in-hospital mortality rate for LP implantations was 5%, with an overall in-hospital complication rate of 16%, and a 30-day readmission rate also at 16%. Notably, in-hospital mortality declined from 11% in early 2017 to 4% by late 2019 (P<0.001), and overall complications decreased from 21% to 13% in the same period (P<0.001).	Focused on administrative database outcomes and trends rather than device-specific performance or prospective clinical trial data.
Tam TK, Chan YS, Chan GCP, et al. (2022) Effect of Low Body Mass Index in Outcome of Micra Leadless Pacemaker Implantation. Journal of the Hong Kong College of Cardiology 30(2): 43–52.	n=147, who underwent Follow-up duration extended to 12 months post-implantation.	The composite procedure safety and efficacy outcome was achieved in 93% of people.	The study's single-centre, retrospective design and focus on a specific population subgroup may limit the generalisability of its findings.
Vaidya VR, Dai M, Asirvatham SJ, et al. (2019) Real-world experience with	n=90 LP recipients (73 Micra, 17 Nanostim) matched 1:1 with 90 TVP recipients; median	LPs showed comparable safety to TVPs in terms of major (0% versus 1%) and minor (8%	Covered in the systematic review included in the main body evidence.

leadless cardiac pacing. Pacing Clin Electrophysiol 42(3): 366–373.	follow-up 62 days (IQR 28 to 169).	versus 3%) complications (p>0.05). LP group had significantly lower rates of device-related revision or extraction (0% versus 5%, p=0.028) and endocarditis (0% versus 3%, p=0.04), and no significant worsening of tricuspid regurgitation (0% versus 19%, p=0.017). Estimated device longevity was longer in the LP group (12 versus 10 years, p<0.0001).	
Valiton V, Graf D, Pruvot E, et al. (2019) Leadless pacing using the transcatheter pacing system (Micra TPS) in the real world: initial Swiss experience from the Romandie region. Europace 21(2): 275–280.	n=92; 1-year follow-up	Implantation success rate was high (98%), and pacing thresholds remained low and stable over time (median 0.4 V/0.2 ms). However, serious perioperative adverse events occurred in 7% (n=6), including 1 death, and 3 additional major events (3%) occurred during follow-up (including ventricular tachycardia and device explantation), resulting in an overall 10% major complication rate.	Limited by small sample size and regional data; initial real-world experience only, without comparator arm or long-term evaluation.
Vincent L, Grant J, Peñalver J, et al. (2022) Early trends in leadless pacemaker	Nationally representative cohort: exact sample size not specified in	LP use increased among older and more acutely ill people over time. From 2017 to 2019, LP-related	Covered in the systematic review included in the main body evidence.

implantation: Evaluating nationwide in-hospital outcomes. Heart Rhythm 19(8): 1334–1342.	abstract; in-hospital outcomes only.	procedural complications decreased significantly (11% to 8%; p<.001), and in-hospital mortality declined (8% to 4%; p<.001). Compared to TVP, LP had fewer procedural complications (9% versus 11%) but higher in-hospital mortality (5% versus 1%; p<.001).	
Wherry K, Stromberg K, Hinnenthal JA, et al. (2020) Using Medicare Claims to Identify Acute Clinical Events Following Implantation of Leadless Pacemakers. Pragmatic and Observational Research 11: 19–26.	n=230 dually enrolled people; 30-day follow-up for acute complications	95% agreement in identifying 30-day acute complications between Medicare administrative claims (Micra CED) and physician-adjudicated registry data (Micra PAR). Disagreements in reporting were limited to specific low-frequency complications such as arteriovenous fistula (50%), pulmonary embolism (67%), haemorrhage/hematoma (75%), and deep vein thrombosis (100%). No disagreements occurred in adjudicated event identification.	Focus was on data validation and agreement between administrative claims and registry data rather than direct clinical outcomes or safety/effectiveness of the device.
Xu F, Meng L, Lin H, et al. (2024) Systematic review of	Included 28 studies published between 2015 and 2023, covering a total of 13,129, who underwent LP	The review highlights that LPs significantly reduce complications associated with traditional TVPs, especially those	More robust systematic reviews have been covered in the main evidence summary.

leadless pacemaker. Acta Cardiologica 79(3): 284–294.	implantation. Follow-up durations ranged from 3 months to 5 years across included studies.	related to leads and pacemaker pockets.	
Yan L, Zhang Y, Liu Q, et al. (2024) Efficacy and safety of leadless ventricular pacemaker: a single-center retrospective observational study. Cardiovascular Diagnosis & Therapy 14(2): 878–889.	n=112, who had LP implantation between 2020 and 2023. The average follow-up period was 12.4; SD 3.7 months.	Success rate was 100%. Procedure-related complications occurred in 5% of included people, including 2 cases of pericardial effusion and 3 of vascular access complications. No lead-related or pocket infections were reported. Mean pacing threshold remained stable throughout follow-up (0.5; SD 0.2 V at implant vs. 0.5; SD 0.2 V at final follow-up, P=0.72).	Although informative, this study represents a single-centre retrospective series with limited generalisability, thus was excluded from the main summary table prioritising larger or multicentre datasets.
Zucchelli G, Tolve S, Barletta V, et al. (2021) Comparison between leadless and transvenous single-chamber pacemaker therapy in a referral centre for lead extraction. J Interv Card Electrophysiol 61(2):395–404.	n=200 (100 LP, 100 TVP); median follow-up: 12 months	LP implantation was associated with a lower acute complication rate (0% vs 7%, p=0.02) and fewer system revisions (0% vs 6%, p=0.038) compared to TVP. Both groups showed stable electrical performance, but LP demonstrated longer estimated battery longevity. 1 systemic infection occurred in the TVP group.	Covered in systematic review included in the main evidence summary.
Zucchelli G, Barletta V, Della	n=83 total (Group 1: 23 post-extraction; Group 2: 60 naïve); median follow-up:	LP implantation was feasible and safe in post-TLE people, with no significant	Covered in systematic review included in the main evidence summary.

Tommasina V, et al. (2019) Micra pacemaker implant after cardiac implantable electronic device extraction: feasibility and long-term outcomes. EP Europace 21(8):1229–1236.	18 months (IQR 1 to 24 months)	differences in fluoroscopy time, delivery success, or electrical performance at implant and 12-month follow-up compared to naïve people. No device-related events occurred during follow-up. Majority of implants achieved non-apical placement (72%) with no significant group differences.	