



Clinical

EVIDENCE

ICD implantation benefit in primary prevention cohort

Mortality Benefit Among Primary Prevention Implantable Cardioverter-Defibrillator Recipients on Contemporary Heart Failure Treatment (Ahmed et al.)¹

The Role of ATP in Primary Prevention Patients

Assessment of primary prevention patients receiving an ICD – Systematic evaluation of ATP: APPRAISE ATP (Schuger et al.)^{2,3}

Safety and Performance of the Modular CRM (mCRM™) System

A Modular Communicative Leadless Pacing-Defibrillator System (Knops et al.)⁴



▶ **ICD implantation benefit in primary prevention cohort**

ICD Implantation significantly reduces mortality in primary prevention population.

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▶ **The Role of ATP in Primary Prevention Patients**

The value of ATP in the overall cohort of primary prevention patients who receive ICDs: APPRAISE ATP Trial.

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▶ **Safety and Performance of the Modular CRM (mCRM™) System**

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Summary

This Clinical Evidence is focused on patients with defibrillators implanted for the primary prevention of sudden cardiac death. Following the latest advances in medical and device therapy, Dr Ahmed *et al.*¹ investigated the persistence of the survival benefits of ICD implantation in patients with a primary prevention of sudden cardiac death (SCD). Recently, Dr Schuger³ has presented preliminary findings of the APPRAISE ATP trial, a multicentre, randomised study aimed at evaluating the role of ATP as a first-line therapy in this specific patient setting. Impressive results on the safety and performance of the EMPOWER leadless pacemaker, designed to provide pacing therapy and capable of offering a modular approach for S-ICD implanted patients, are finally available in the New England Journal of Medicine.⁴



Mortality benefit among primary prevention ICD patients

The implantable cardioverter-defibrillator (ICD) has significantly reduced sudden cardiac death (SCD) in high-risk populations. Landmark trials, such as MADIT-II⁵ and SCD-HeFT⁶, demonstrated an improved survival with ICDs compared to medical therapy or placebo. However, significant advancements in medical therapy and device technology in the last years suggest a need to reassess the survival impact of ICD implantation in contemporary populations undergoing heart failure (HF) treatment.

Ahmed *et al.*¹ used a large, contemporary, real-world data set to compare mortality rates between patients with a primary prevention (PP) indication for ICD implantation who did or did not receive treatment with an ICD.

The **endpoint** was **all-cause mortality**, and study follow-up began at 1-year after the indication date and extended to the date of death or last in-person evaluation.

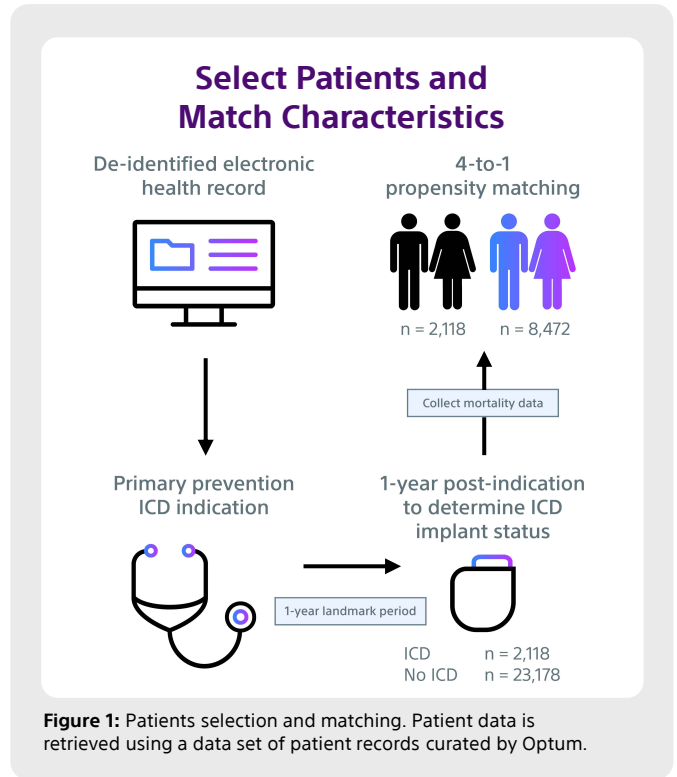


Figure 1: Patients selection and matching. Patient data is retrieved using a data set of patient records curated by Optum.

Results

There were 25,296 total patients who met all inclusion and no exclusion criteria. The propensity score matched 2,118 patients with ICD and 8,472 without ICD (Figure 1): patient characteristics, as age (63.4 years vs. 63.6 years; $p = 0.62$) and sex (75.0% vs. 75.3% male; $p = 0.76$), and history of heart failure (HF) medications are well balanced between the two groups.

The mean time from 1-year post-indication to last encounter or all-cause mortality was 2.1 ± 1.6 years for ICD patients and 2.0 ± 1.6 years for non-ICD patients.

Patients with PP indication without ICDs are more likely to experience death compared to patients with ICDs as shown in Figure 2.

The Cox proportional hazards model indicates that PP-indicated patients treated with an ICD have a **24.3% lower risk of all-cause mortality** compared to those PP-indicated patients without an ICD (Hazard Ratio (HR): 0.757; 95% CI: 0.68-0.85; $p < 0.001$).

At 5-year the all-cause mortality rate was 37.6% (95% CI: 33.2%-41.7%) for patients who received an ICD, whereas it was 44.7% (95% CI: 42.6%-46.7%) for those who did not receive an ICD.

The HR for ICD benefit was similar between ischemic and non-ischemic patients: it was 0.76 (95% CI: 0.68-0.85) for ischemic patients and 0.62 (95% CI: 0.34-1.15) for non-ischemic patients ($p = 0.50$).

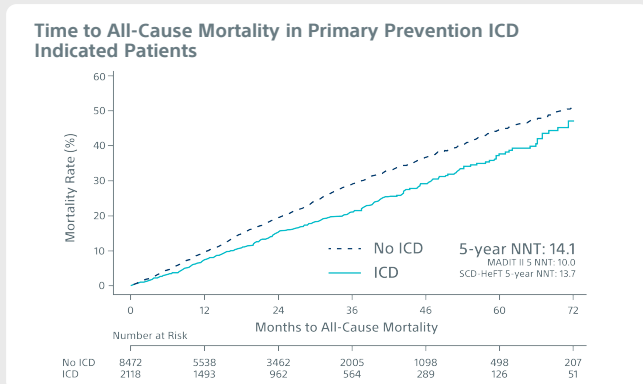


Figure 2: Time to all-cause mortality in patients with an indication for primary prevention ICD therapy.

"ICD implantation should continue to be offered as a life-saving intervention to the hundreds of thousands of patients at risk of SCD who meet current guideline indications."¹

These findings confirm that **ICD treatment of patients with a PP-indication is still associated with improved mortality**, even in the context of evolving adjunctive HF treatment.





Systematic evaluation of ATP: APPRAISE ATP

The APPRAISE ATP trial was a prospective, randomised, global, multicentre clinical study aimed at understanding the role of ATP in primary prevention (PP) patients who are currently indicated for ICD therapy.²

The trial enrolled 2,626 patients indicated for primary prevention ICDs from 134 centres across North America, Europe, and Asia. Preliminary findings were presented at HRS Congress by Dr C. Schuger.³

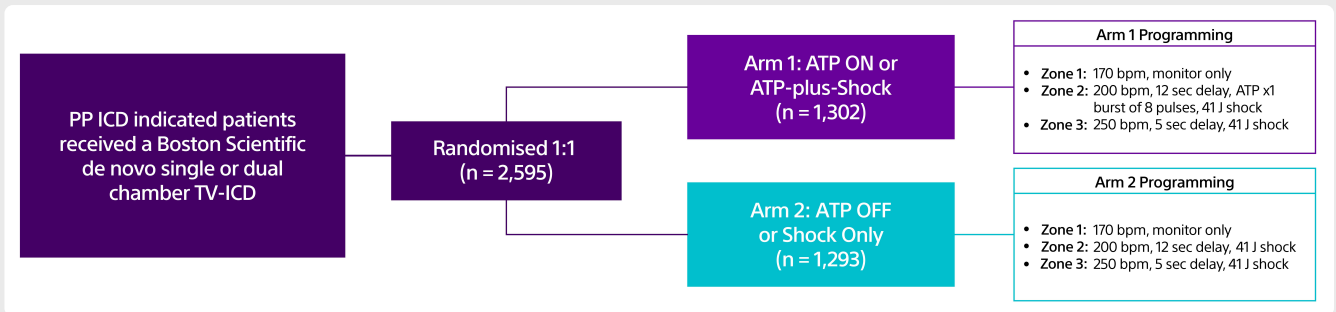


Figure 3: Patients received either a single- or dual-chamber transvenous ICD (TV-ICD), and 2,595 of them were randomised 1:1 into different therapy programming groups in an equivalence study design, with sequential superiority analysis conducted for each group.

Results

The percentage of patients free from all-cause shocks at 1-year was 95.7% for ATP-plus-shock arm vs. 94.7% for the shock-only arm.

At 5-years, the percent of patients free from all-cause shocks was 85.4% for the ATP-plus-shock arm vs. 80.6% for the shock-only arm.

- A single burst of ATP prior to shock in the VT zone (200-249 bpm) resulted in a relative risk reduction of all-cause shock by 28% (HR 0.72, CI 0.57-0.92, p = 0.005), representing an **absolute reduction of 1% per year** for the study population.
- **No significant interactions between any prespecified patient subgroup** and the primary endpoint were found, implying that all PP patients responded similarly to their assigned study arm.

- **The total shock burden per 100 subjects was not statistically different** (HR 0.86, CI 0.63-1.19, p = 0.38).
- **The burden of VT/ VF storm events was significantly greater in the ATP-plus-shock arm** (HR 2.39, CI 1.29-4.44, p = 0.006).
- Although not statistically significant, there were **numerically more deaths in the ATP-plus-shock arm** (HR: 1.15, p = 0.184) and the composite endpoint of all-cause shocks and death was non-significant (HR: 0.92, p = 0.284).



Given an absolute all-cause shock reduction of 1% per year in PP patients with a TV-ICD, the benefit of ATP should be discussed with PP patients who are eligible for an S-ICD during **shared decision-making**. This should be compared to the lifetime risk associated with having a lead in the heart with a TV-ICD.⁷⁻⁹

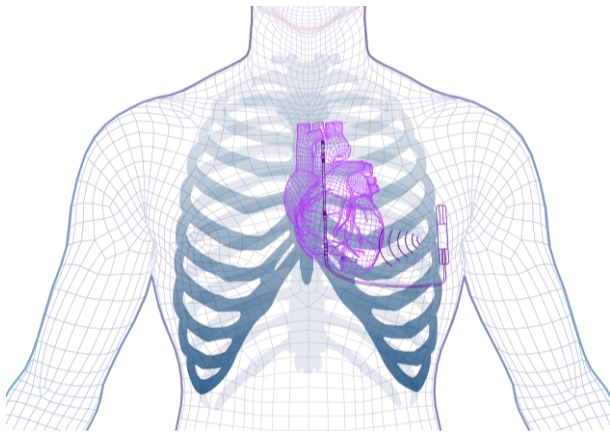




New Horizons for Leadless Therapy: First Results of the Pivotal MODULAR ATP Trial

The MODULAR ATP trial is an on-going prospective, non-randomised, single-arm global study designed to assess the safety, performance, and effectiveness of an **investigational modular pacing-defibrillator system** comprising a subcutaneous ICD coupled with a leadless pacemaker (LP).⁴

From July 2021 through January 2024, 293 patients were implanted with the EMBLEM™ S-ICD and EMPOWER™ LP System in 38 centres, 162 subjects* were followed for 6 months.



Characteristics	n = 162
Male, n (%)	135 (83.3)
Age, years (SD)	60±12
Primary Prevention, n (%)	87 (53.7)
Left Ventricular Ejection Fraction (%)	33.1±12.6
Ischemic Cardiomyopathy, n (%)	99 (66.1)

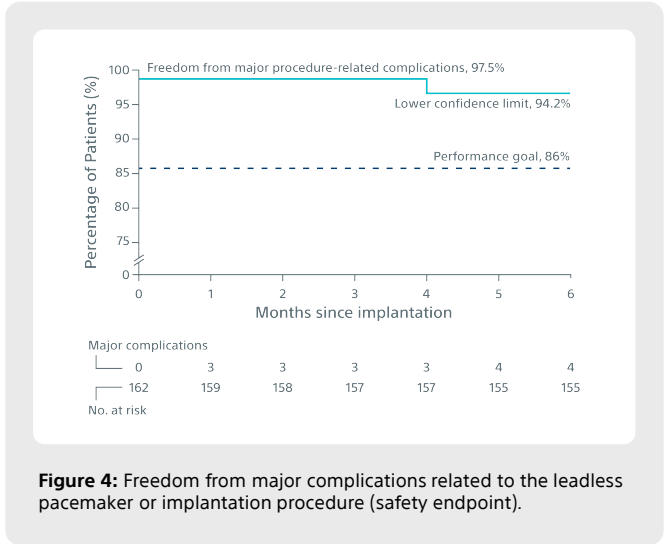
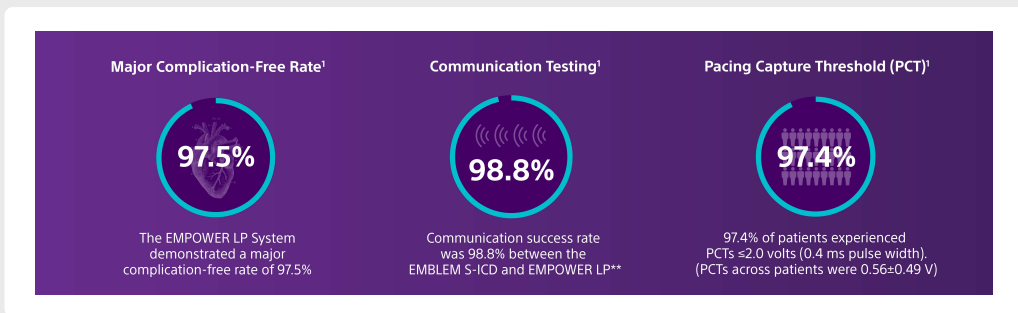


Figure 4: Freedom from major complications related to the leadless pacemaker or implantation procedure (safety endpoint).

Results

- The percentage of patients who **were free from leadless pacemaker-related major complications** was **97.5%**, which exceeded the prespecified performance goal (86%).
- Wireless-device communication was successful in **98.8%** of communication tests, which exceeded the prespecified goal (88%).
- Of 151 patients, 147 (97.4%) had pacing thresholds of 2.0 V (0.4ms) or less, which exceeded the prespecified goal (80%).
- ATP was delivered in 13 patients and **successfully terminated 61.3% of the episodes**. Appropriate therapy (ATP or shock) was delivered in 9.3% of patients. No instance of failure of therapy delivery caused by failure of device communication occurred.



The EMPOWER leadless pacemaker, capable of wireless communication with an S-ICD, **exceeded performance goals** in multiple aspects: freedom from major complications associated with the leadless pacemaker, successful communication between the leadless pacemaker and the S-ICD, and achieving a pacing threshold of up to 2.0 V (at a 0.4-msec pulse width) in a significant percentage of patients at 6 months.

*The study design included a pre-specified early analysis of the safety endpoint once 134 patients were implanted with the EMBLEM S-ICD and EMPOWER LP System and followed for 6 months. Because of variability in the 6-month follow up appointments, 162 patients were in this group for this early analysis of the safety endpoint.



“Implantation of a novel insertable cardiac monitor: preliminary multicenter experience in Europe”¹⁰

Fareh S. et al.

The LUX-Dx™ is a small (1.2 cm³) insertable cardiac monitor (ICM) designed to monitor, record, and store data related to cardiac arrhythmias. It is embedded with remote programming capabilities. The implantation kit includes an incision tool and a single-piece insertion tool pre-loaded with the ICM. The system also included two app: the LUX-Dx Clinic Assistant app and myLUX-Dx™ Patient app are designed to activate and interrogate ICM, to apply programming changes and to transmit data.

This analysis aimed to detail the LUX-Dx implantation experience in Europe during its first year of commercial use. 368 patients were included at 23 European centres. Operators collected implantation data and completed a questionnaire to measure satisfaction and provide feedback on the procedure and system. An anonymous patient survey gathered data on patient experience.



Breaking News
Discover the preliminary LUX-Dx European experience.

What are the main findings?

Implantation Procedure

- The most frequent indications for ICM implantation were **syncope** (64%) and **cryptogenic stroke** (9%).
- The median time from skin incision to suture was **4 min**.
- **ICM repositioning** was performed in 9 (**2%**) patients.
- **No procedural complications**.

LUX-Dx ICM

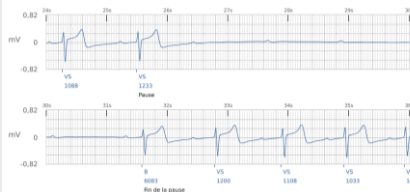


Incision and Insertion Tools



Signal Quality

- The mean **R-wave** amplitude was **0.39 ± 0.30 mV** at **implantation** and **0.41 ± 0.31 mV** before patient **discharge** (p = 0.052).
- **P-wave visibility** was **91 ± 20%** at **implantation** and remained **stable** before discharge (p = 0.790).



Operators and Patients Feedback

Operators Feedback	Excellent
Device and kit packaging	97%
Incision tool	92%
Insertion tool	96%
Ease of use of the app	89%
Ease of use of the remote management system	91%
Patient Experience	No
Pain during implantation	91%
Paresthesia after implantation	98%
Pain at discharge	98%
Paresthesia at discharge	99%

LUX-Dx implantation appears efficient and straightforward, with favourable post-implantation sensing values and associated with positive feedback from operators and patients.





Key Messages

- **ICD implantation benefit in primary prevention cohort:** The analysis by Dr Ahmed *et al.*¹ confirmed that ICD implantation in a primary prevention patients remains a valuable intervention over time to prevent SCD and is associated with significantly lower all-cause mortality compared to similar patients who did not receive an ICD
- **The Role of ATP in Primary Prevention Patients:** APPRAISE ATP, the largest head-to-head trial of ATP in primary prevention patients, has evaluated the true value of ATP. The study demonstrated superiority with a 28% relative risk reduction in time to first all-cause shock for the ATP ON arm compared to the ATP OFF arm, with an absolute all-cause shock reduction in 1% of primary prevention ICD indicated patients per year.³
- **Safety and Performance of the Modular CRM (mCRM™) System:** The MODULAR ATP Trial achieved all pre-specified safety and effectiveness 6-month endpoints which included major complication free rate (97.5%), communication success rate (98.8%) and pacing capture threshold (97.4% PCTs_< = 2.0V) in the mCRM system.⁴

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