ORIGINAL RESEARCH

Sex-Based Differences in Selected Cardiac Implantable Electronic Device Use: A 10-Year Statewide Patient Cohort

Kasun De Silva ^(b), MD;* Natasha Nassar, PhD;* Tim Badgery-Parker ^(b), PhD; Saurabh Kumar ^(b), PhD; Lee Taylor, MBBS; Pramesh Kovoor ^(b), PhD; Sarah Zaman ^(b), PhD; Andrew Wilson ^(b), PhD; Clara K. Chow ^(b), PhD

BACKGROUND: Cardiac implantable electronic devices (CIEDs) include pacemakers, cardioverter defibrillators, and resynchronization therapy. This study aimed to assess CIED implantation and outcomes by sex and indication.

METHODS AND RESULTS: This was a retrospective cohort study of adults with cardiovascular hospitalizations in New South Wales, Australia (2008 to 2018). CIED implantation in patients with arrhythmia, cardiomyopathy, and syncope were examined. Subcategories (complete heart block, atrial fibrillation/atrial flutter, ventricular tachycardia/ventricular fibrillation/cardiac arrest, sick sinus syndrome, and ischemic and nonischemic cardiomyopathy) were investigated. Primary outcome was implantation of CIEDs in men versus women adjusted for age and comorbidities. Secondary outcomes were trends over time, time to implant, length of stay, emergency status, and 30-day survival. Of 1 291 258 patients with cardiovascular admissions, 287 563 had arrhythmia, cardiomyopathy, or syncope and 29080 (2.3%) received a CIED (22 472 pacemakers, 6808 defibrillators, 3207 resynchronization therapy). Women with arrhythmia, cardiomyopathy, or syncope were less likely to have pacemakers (adjusted odds ratio [aOR], 0.78 [95% CI, 0.76–0.80]), defibrillators (aOR, 0.4, [95% CI, 0.40–0.45]) and resynchronization therapy (aOR, 0.66 [95% CI, 0.61–0.71]). Differences persisted across subcategories, including fewer pacemakers in complete heart block (aOR, 0.89 [95% CI, 0.80–0.98]) and syncope (aOR, 0.70 [95% CI, 0.63–0.79]); fewer defibrillators in ventricular tachycardia/ventricular fibrillation/cardiac arrest (aOR, 0.69 [95% CI, 0.61–0.77]); and less resynchronization therapy in cardiomyopathy (aOR, 0.62 [95% CI, 0.51–0.75]). Men and women receiving devices had higher 30-day survival compared with those who did not receive a device, and 30-day survival was similar between men and women receiving devices.

CONCLUSIONS: Lower CIED implantation was seen in women versus men, across nearly all indications, including complete heart block and ventricular tachycardia/ventricular fibrillation/cardiac arrest. The underuse of cardiac devices among women may arguably reflect a sex bias and requires further research.

Key Words: cardiac implantable electronic devices
cardiac resynchronization therapy
implantable cardioverter defibrillator
pacemaker
sex

Gincluding pacemakers, implantable cardioverter defibrillators (ICDs), and cardiac resynchronization therapy (CRT), are used for treating cardiac arrhythmias and cardiomyopathies and for prevention of sudden cardiac death. Randomized clinical trials have demonstrated that benefits of pacemakers on major adverse cardiovascular events are similar in men and women.¹ There is less evidence for ICDs and CRTs and an underrepresentation of women in ICD/CRT clinical trials has been observed.² International cardiology society guidelines do not have sex-specific recommendations for differential CIED implantation in men and women.^{3–6}

Correspondence to: Clara Chow, PhD, Department of Cardiology, Westmead Hospital, Westmead Applied Research Centre, University of Sydney, Darcy Road, Westmead, Sydney 2145, New South Wales, Australia. Email: clara.chow@sydney.edu.au

^{*}K. De Silva and N. Nassar are co-first authors and contributed equally.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.121.025428

For Sources of Funding and Disclosures, see page 10.

^{© 2022} The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- In a statewide cohort of patients presenting with cardiac arrhythmias, cardiomyopathy, and syncope, lower cardiac implantable electronic device use was seen in women compared with men independent of age and comorbidities.
- These sex-differences persisted across device type (pacemakers, defibrillators, and cardiac resynchronization therapy) and across implantation subdiagnoses including lower use of pacemakers for complete heart block and syncope, defibrillators for ventricular tachycardia, ventricular fibrillation and cardiac arrest, and cardiac resynchronization therapy for cardiomyopathy.
- This is the largest study to date to systematically examine implant rates for men versus women stratified by implant subdiagnosis and adjusting for age and comorbidities.

What Are the Clinical Implications?

- This is a contemporary population-level snapshot of a cohort of patients receiving cardiac implantable electronic device therapies, allowing an understanding of implantation trends and real-world practices.
- Although it is unclear if these observed sex differences are due to systematic sex bias, the broad array of reduced use of devices in women versus men across subdiagnoses such as complete heart block suggests the existence and persistence over time of sex-based disparities in cardiac implantable electronic device use in women.
- This research should provoke further examination of the reasons for these differences and ways to address them.

Nonstandard Abbreviations and Acronyms

CRT	cardiac resynchronization therapy
NSW	New South Wales

There has been recent increased interest in differences in cardiovascular management by sex globally. Women with cardiovascular disease are less likely to receive timely interventions and secondary prevention treatments.⁷⁻¹⁰ To date there is limited and conflicting evidence of sex differences in CIED implantation rates. Some studies have observed differences in implantation of selected CIEDs by sex,^{2,8,11} although few have adequately controlled for confounding comorbidities. Prospective registry-based studies have also suggested sex differences^{12,13}; however, these are generally limited to recruiting hospitals committed to quality improvement and may not be generalizable to real-world practice. Other studies have found no sexbased differences in device implantation.¹⁴

Understanding whether there are sex differences in implantation at a population level and subsequently obtaining information on whether this is related to reason for implantation, type of device, or comorbidities is important. The aim of this study was to assess CIED implant rates and outcomes by sex in a longitudinal cohort study of patients in New South Wales (NSW), Australia, with arrhythmia, cardiomyopathy, and syncope and to examine whether differences are related to age, demographics, and comorbidities.

METHODS

Data Sharing

All data relevant to the study are included within the article and the supplemental material. No additional data are available.

Study Population

The study population comprised all people aged 18 years and over residing in NSW, Australia, with an acute public or private hospital admission for cardiovascular conditions from July 1, 2008 to June 30, 2018. The state of NSW has the largest population in Australia; in June 2021 this was estimated to be 8.2 million residents (32% of Australia).

Data Source

Data were sourced from linked NSW Health Admitted Patient Data Collection, Emergency Department Data Collection, and death records from the Registry of Births, Deaths, and Marriages. The linked data set included a census of all inpatient admissions to public and private hospitals, public hospital emergency department presentations, and deaths registered in NSW. For each admission, sociodemographics, clinical diagnoses and procedures performed, and patient status at discharge were recorded. Clinical diagnoses and procedures were classified using the *International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10-AM)* and Australian Classification of Health Interventions, respectively.

From the study population, we identified all people who underwent a cardiac implant, and using the principal diagnosis, we selected conditions where >10% of individuals had a cardiac implant (Table S1). Individuals were then classified into 3 diagnostic groups, with (1) cardiac arrhythmia, (2) cardiomyopathy, and (3) syncope (Table S2). The cardiac arrhythmia cohort was

subcategorized into complete heart block, other heart block, atrial fibrillation/atrial flutter, ventricular tachycardia/ventricular fibrillation/cardiac arrest (VT/VF/cardiac arrest), sick sinus syndrome, and other arrhythmia. The cardiomyopathy cohort was subcategorized into ischemic and nonischemic cardiomyopathy.

Study Outcome Measures

The main study factor of interest was whether sex disparities existed in men versus women presenting to hospital with acute cardiovascular conditions who subsequently had a CIED implanted. Implantation of these devices was defined according to Australian Classification of Health Interventions procedure codes (Table S3). Implantation of a left ventricular lead was used to identify CIEDs with CRT capability.

The primary outcome was implantation rate of a CIED and secondary outcomes were implantation rates for pacemaker, ICD, or CRT in the arrhythmia, cardiomyopathy, and syncope cohorts (and subcategories). We examined if implantation varied over the 10-year period; and in emergency (based on care or treatment required within 24 hours, public hospitals only), versus nonemergency (elective) implantation. We also report by sex, median days from admission to implant, median number of admissions from diagnosis to implant, median length of stay for implant insertion (days), and mortality rate per 100 patients at 30 days.

Additional covariates included sociodemographics, age category (18–44, 45–64, 65–74, 75–84, 85+ years), geographical location (based on the postcode of residence and categorized into major cities, inner regional areas, and outer regional/rural/remote areas according to the Australian Statistical Geography Standard Remoteness Structure¹⁵), and comorbidities (determined using the Elixhauser classification.¹⁶).

Ethics

The study was approved by the University of Sydney Human Research Ethics Committee. As it was a retrospective study, informed consent was not required.

Statistical Analysis

Descriptive analyses were conducted to assess frequency and rate of cardiac implants by cardiac condition and sociodemographic characteristics of each condition subtype. Baseline characteristics of men and women were compared using chi-square tests. Adjusted odds ratios (aOR) for implantation of a device in women compared with men were obtained from logistic regression models adjusting for age in years (as restricted cubic spline with 4 degrees of freedom), and indicators for each Elixhauser comorbidity. Mortality rates were calculated using survival analysis and

log-rank test applied to compare 30-day mortality rates for those who did and did not have a pacemaker, ICD, or CRT implant by each cardiac condition and stratified by sex. Modeling of interaction of sex for each pacing group and diagnosis was performed. Time to implant was calculated by calculating median number of days of admissions before implant, and outcomes following implant including median length of stay in hospital were also determined and compared using Wilcoxon rank sum tests. Sex differences in emergent implantation of devices were compared using chi-square tests. All analyses were conducted in SAS V9.4 (Cary, NC) and R 4.0.2 (R Core Team, 2020). Authors T-BP, NN, and CKC had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

RESULTS

The study cohort consisted of 1 291 258 patients with an acute cardiovascular condition ("all patients"). Of these patients, 287 563 had a principal diagnosis of arrhythmia, cardiomyopathy, or syncope. Overall, less cardiovascular presentations were women (45.9%) compared with men (54.1%); however, with respect to arrhythmia, the proportion of male cardiovascular presentations due to arrhythmia (13.5%) were similar to the proportion of women (13.3%). Men were younger and had more comorbidities (Table 1).

There were some differences in arrhythmia and cardiomyopathy and syncope presentations by sex. As a proportion of all cardiovascular hospitalizations, men were more likely to present with complete heart block (0.60% [95% Cl, 0.58-0.62] versus 0.47% [95% Cl, 0.46-0.50], P<0.001), other heart block (0.61% [95% Cl, 0.59-0.63] versus 0.49% [95% Cl, 0.48-0.51], P<0.001), VT/VF/cardiac arrest (1.56% [95% Cl, 1.53-1.59] versus 0.77% [95% Cl, 0.74-0.79], P<0.001), other arrhythmias (1.37% [95% Cl, 1.35-1.40] versus 1.27% [95% CI, 1.24-1.30], P<0.001), and ischemic cardiomyopathy (0.45% [95% CI, 0.44-0.47] versus 0.36% [95% Cl, 0.34-0.38], P<0.001). In contrast, women were more likely to present with sick sinus syndrome (0.59% [95% CI, 0.57-0.61] versus 0.45% [95% CI, 0.44-0.47], P<0.001), atrial fibrillation/atrial flutter (9.84% [95% Cl, 9.76-9.91] versus 9.00% [95% Cl, 8.94-9.07], P<0.001), cardiomyopathy (2.10% [95% Cl. 2.07-2.14] versus 1.95% [95% CI, 1.91-1.98], P<0.001), and syncope (7.61% [95% Cl, 7.55-7.68] versus 6.17% [95% Cl, 6.13-6.24], P<0.001).

A CIED was implanted in 29080 (2.25% [95% CI, 2.23– 2.28]) patients (Table 1). Most devices were implanted in urban centers and a higher proportion of men received a CIED device (2.60% [95% CI, 2.57–2.65]) compared with women (1.84%, [95% CI, 1.80–1.887]) (*P*<0.001).

Table 1.	Characteristics of the Baseline Patient Population
----------	---

	Male sex No. (%; 95% CI)	Female sex No. (%; 95% Cl)	<i>P</i> value
All patients	698997 (100)	592261 (100)	<0.001
Arrhythmia	94449 (13.51; 13.43–13.59)	78721 (13.29; 13.21–13.38)	<0.001
Complete heart block	4192 (0.60; 0.58–0.62)	2840 (0.47; 0.46–0.50)	<0.001
Other heart block	4274 (0.61; 0.59–0.63)	2930 (0.49; 0.48–0.51)	<0.001
Sick sinus syndrome	3180 (0.45; 0.44–0.47)	3473 (0.59; 0.57–0.61)	<0.001
Atrial fibrillation/flutter	62941 (9.00; 8.94–9.07)	58253 (9.84; 9.76–9.91)	<0.001
Ventricular tachycardia/ventricular fibrillation/cardiac arrest	10914 (1.56; 1.53–1.59)	4533 (0.77; 0.74–0.79)	<0.001
Other arrhythmia	9609 (1.37; 1.35–1.40)	7511 (1.27; 1.24–1.30)	<0.001
Cardiomyopathy	13596 (1.95; 1.91–1.98)	12455 (2.10; 2.07–2.14)	<0.001
Ischemic	3167 (0.45; 0.44–0.47)	2130 (0.36; 0.34–0.38)	<0.001
Nonischemic	12427 (1.78; 1.75–1.81)	12 177 (2.06; 2.02–2.09)	0.111
Syncope	43242 (6.17; 6.13–6.24)	45 100 (7.61; 7.55–7.68)	<0.001
Cardiac device implant	18 191 (2.60; 2.57–2.64)	10889 (1.84; 1.80–1.87)	<0.001
Pacemakers	13052 (1.87; 1.84–1.90)	9420 (1.59; 1.56–1.62)	<0.001
Implantable cardiac defibrillators	5285 (0.76; 0.74–0.78)	1523 (0.26; 0.24–0.27)	<0.001
Cardiac resynchronization therapy	2076 (0.30; 0.28–0.31)	1131 (0.19; 0.18–0.20)	<0.001
Age, y			<0.001
18–44	83733 (11.98; 11.90–12.06)	64904 (10.96; 10.88–11.04)	<0.001
45–64	222007 (31.76; 31.65–31.87)	144593 (24.41; 24.30–24.52)	<0.001
65–74	160 191 (22.91; 22.82–23.02)	112977 (19.08; 18.96–19.18)	<0.001
75–84	154 441 (22.09; 2.00–22.19)	150480 (25.41; 25.30–25.52)	<0.001
85+	78625 (11.25; 11.17–11.32)	119307 (20.14; 20.04–20.25)	<0.001
Region			· · ·
Major cities	475 175 (67.98; 67.87–68.09)	405798 (68.52; 68.40-68.63)	<0.001
Inner regional	164729 (23.57; 23.47–23.67)	140232 (23.68; 23.57–23.79)	<0.001
Outer regional/remote	59093 (8.45; 8.34-8.52)	46232 (7.81; 7.74–7.87)	<0.001
Comorbidities			
Cancer	9595 (1.37; 1.35–1.40)	6706 (1.13; 1.11–1.16)	<0.001
Congestive heart failure	34870 (4.99; 4.94–5.04)	26851 (4.53; 4.48–4.57)	<0.001
Diabetes	127 763 (18.27; 18.19–18.37)	90881 (15.34; 15.25–15.44)	<0.001
Hypertension	137 794 (19.71; 19.62–19.81)	110409 (18.64; 18.54–18.74)	<0.001
Obesity	7689 (1.10; 1.08–1.12)	5777 (0.98; 0.95–1.00)	<0.001
Renal failure	47 457 (6.79; 6.73–6.85)	33727 (5.69; 5.64–5.75)	<0.001
Other comorbidity	286599 (41.00; 40.89-41.12)	228397 (38.56; 38.44–38.69)	<0.001

"All patients" are all patients aged over 18 years who presented with selected cardiovascular conditions to a hospital in New South Wales from 2008to 2018 (see Table S1 for *International Classification of Diseases, Tenth Revision, Australian Modification* codes). Percentages provided are of total men and total women included, respectively.

pacemakers were the most common device implanted (n=22472, 77.3% [95% Cl, 76.8–77.8] of all CIEDs) and men had higher implant rates than women (1.87% [95% Cl, 1.84–1.90] versus 1.59% [95% Cl, 1.56–1.62], P<0.001). ICDs (23.4% [95% Cl, 22.9–23.9] of all CIEDs) were also implanted at higher rates in men (0.76% [95% Cl, 0.74–0.78]) versus women (0.26% [95% Cl, 0.24–0.27]) (P<0.001). Similarly, CRTs (11% [95% Cl, 10.7–11.4] of CIEDs) were implanted at higher rates in men (0.30% [95% Cl, 0.28–0.31]) versus women (0.19% [95% Cl,

0.18–0.20]). Baseline data stratified by CIED type are presented in Table S4. The proportion of men versus women receiving pacemakers, ICDs, and CRTs did not change noticeably over the 10-year study period (Figure 1).

Device Implants by Type, Primary Diagnosis in Men Versus Women

Most CIEDs implanted for arrhythmia and syncope were pacemakers, whereas for VT/VF/cardiac arrest and

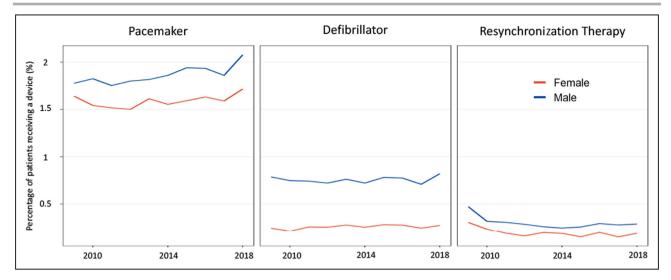


Figure 1. Trends in insertion of cardiac devices for men vs women by device type.

Percentage of patients receiving CIEDs stratified by sex and device type over study period (2008–2018). Denominator is all men or women, respectively, aged over 18 years who presented with selected cardiovascular conditions to a hospital in New South Wales in each year from 2008 to 2018 (see Table S1 for *International Classification of Diseases, Tenth Revision, Australian Modification* codes). Implant rates have not been adjusted for number and type of presentation, age, or comorbidities. CIED indicates cardiac implantable electronic device and ICD, implantable cardioverter defibrillator.

cardiomyopathy the main implanted device was an ICD (Table 2).

For each device and cardiac diagnosis subcategory, women consistently had lower implant rates versus men (Table 2). These sex differences persisted after adjusting for age and comorbidities (Figure 2, Table S5), with women less likely to have pacemaker implantation (aOR, 0.78 [95% CI, 0.76–0.80]), ICD implantation (aOR, 0.43 [95% CI, 0.40–0.45]), and CRT implantation (aOR, 0.66 [95% CI, 0.61–0.71]).

Differences persisted in clinically significant subcategories. For pacemakers, odds of implantation were lower for women compared with men for those diagnosed with cardiac arrhythmia (aOR, 0.72 [95% Cl, 0.69-0.74]). The differences were consistent across subcategory indications of complete heart block (aOR, 0.89 [95% CI, 0.8-0.98]), atrial fibrillation/atrial flutter (aOR, 0.65 [95% Cl, 0.6-0.7]). Pacemaker implant rates were also lower in women for cardiomyopathy (aOR, 0.62 [95% CI, 0.5-0.77]), and syncope (aOR, 0.70 [95% CI, 0.63-0.79]). Similarly, for ICDs, women were less likely to receive devices for cardiac arrhythmia (aOR, 0.43 [95% CI, 0.4-0.47]). The differences were consistent for specific indications: VT/VF/cardiac arrest (aOR, 0.69 [95% Cl, 0.61-0.77]), cardiomyopathy (aOR, 0.41 [95% CI, 0.37-0.45]), ischemic cardiomyopathy (aOR, 0.33 [95% Cl, 0.26-0.42]), and for nonischemic cardiomyopathy (aOR, 0.44 [95% CI, 0.3-0.62]). For CRT where the primary diagnosis is cardiomyopathy, odds of implant were lower for women (aOR, 0.62 [95% Cl, 0.51-0.75]). This persisted in the subcategories of ischemic cardiomyopathy (aOR, 0.39 [95% Cl, 0.22-0.64]) and nonischemic cardiomyopathy (aOR, 0.70 [95% Cl, 0.56-0.86]).

Acuity and Clinical Outcomes of Implantation of Cardiac Devices in Men Versus Women

Women compared with men were more likely to require emergency pacemaker implantation (66.8% versus 62.3%, P<0.01) and emergency CRT implantation (58.4% versus 50.7%, P<0.001). There were no sex differences in emergency ICD implantations (women 49% versus men 49.8%, P=0.614). Although there were statistical differences for men and women in median length of time from admission to implant, diagnosis to implant and length of stay for implant insertion, absolute differences in these categories were small (Table S6).

Mortality at 30 Days in Men Versus Women

Mortality rates (at 30 days) are presented in Table 3. Patients receiving CIED had lower 30-day mortality rates compared with patients not receiving devices. There was a significant interaction for any device by sex on 30-day mortality in the overall cohort (P<0.001) with higher mortality in men. In this cohort there was also a significant sex interaction for pacemaker use (P<0.001) with higher mortality in men. However, there were no other significant sex interactions for mortality when stratified by specific diagnosis and pacing groups (with smaller sample sizes in these groups).

	Male sex				Female sex			
	No CIED (%)	Pacemaker (%)	ICD (%)	CRT (%)	No CIED (%)	Pacemaker (%)	ICD (%)	CRT (%)
All patients (n=1 291 258)	97.40 (97.36–97.43)	1.87 (1.84–1.90)	0.76 (0.74–0.78)	0.30 (0.28–0.31)	98.16 (98.13–98.20)	1.59 (1.56–1.62)	0.26 (0.24–0.27)	0.19 (0.18–0.20)
Arrhythmia (n=173 170)	86.33 (86.11–86.55)	11.26 (11.06–11.46)	2.52 (2.42–2.62)	1.30 (1.23–1.38)	89.69 (89.48–89.90)	10.05 (9.84–10.26)	0.89 (0.82–0.96)	0.99 (0.92–1.06)
Complete heart block (n=7032)	30.03 (28.66–31.44)	67.96 (66.53–69.36)	2.31 (1.90–2.81)	5.92 (5.24–6.67)	34.79 (33.06–36.56)	64.12 (62.34–65.86)	1.44 (1.07–1.95)	5.95 (5.14–6.88)
Other heart block (n=7204)	46.46 (45.05–47.89)	51.04 (49.61–52.46)	2.90 (2.46–3.42)	4.76 (4.19–5.41)	48.91 (47.10–50.72)	49.39 (47.58–51.20)	1.98 (1.53–2.55)	4.16 (3.50–4.95)
Sick sinus syndrome (n=6653)	33.05 (31.44–34.70)	65.50 (63.83–67.14)	1.89 (1.47–2.42)	5.82 (5.06–6.69)	33.60 (32.05–35.19)	65.53 (63.94–67.10)	0.95 (0.68–1.33)	6.22 (5.46–7.07)
Atrial fibrillation/flutter (n=121 194)	96.58 (96.44–96.72)	2.89 (2.76–3.02)	0.55 (0.50–0.61)	0.38 (0.33–0.43)	97.30 (97.17–97.43)	2.56 (2.43–2.69)	0.15 (0.13–0.19)	0.21 (0.18–0.26)
Ventricular tachycardia/ ventricular fibrillation/ cardiac arrest (n=15447)	83.79 (83.09–84.47)	1.99 (1.74–2.27)	14.57 (13.19–15.24)	1.59 (1.38–1.85)	88.84 (87.89–89.72)	1.99 (1.62–2.43)	9.51 (8.69–10.40)	1.15 (0.88–1.50)
Other arrhythmia (n=17 120)	76.95 (76.10–77.80)	20.81 (20.01–21.64)	2.34 (2.06–2.66)	2.44 (2.15–2.76)	81.67 (80.78–82.53)	17.41 (16.57–18.29)	1.00 (0.78–1.25)	1.85 (1.57–2.18)
Cardiomyopathy (n=26051)	86.83 (86.25-87.39)	2.07 (1.85–2.33)	11.48 (10.96–12.03)	2.65 (2.39–2.93)	95.17 (94.78–95.54)	1.11 (0.94–1.31)	3.83 (3.51–4.18)	1.28 (1.09–1.49)
Ischemic (n=5297)	81.62 (80.24–82.93)	2.31 (1.84–2.89)	16.64 (15.38–17.98)	3.13 (2.57–3.79)	94.93 (93.91–95.78)	1.13 (0.76–1.67)	4.00 (3.24–4.91)	0.80 (0.50–1.27)
Nonischemic (n=24604)	74.68 (73.91–75.44)	1.71 (1.49–1.95)	8.36 (7.88–8.86)	2.12 (1.88–2.38)	81.26 (80.56–81.94)	0.97 (0.81–1.16)	3.24 (2.94–3.56)	1.17 (0.99–1.34)
Syncope (n=88342)	97.92 (97.78–98.05)	1.78 (1.66–1.91)	0.32 (0.27–0.38)	0.17 (0.13–0.21)	98.72 (98.61–98.82)	1.19 (1.10–1.30)	0.10 (0.07–0.13)	0.10 (0.08–0.14)

Table 2. Implant Rates by Device, Sex, and Primary Diagnosis

J Am Heart Assoc. 2022;11:e025428. DOI: 10.1161/JAHA.121.025428

"All patients" are all patients aged over 18years who presented with selected cardiovascular conditions to a hospital in New South Wales from 2008 to 2018 (see Table S1 for *International Classification of Diseases*, *Tenth Revision, Australian Modification* codes). Percentages provided are of total men and total women included in each diagnosis category (rows), respectively. CIED indicates cardiac implantable electronic device; CRT, cardiac resynchronization therapy; and ICD implantable cardioverter defibrillator.

Subgroup				OR	95% Cl
Pacemaker		1			
Complete heart block				0.89	(0.8-0.98)
Other heart block			_	0.98	(0.89-1.08)
Sick sinus syndrome		-	-	1.02	(0.92-1.13)
Atrial fibrillation / atrial flutter		-		0.65	(0.6-0.70)
Syncope				0.7	(0.63-0.79)
All patients		•		0.78	(0.76-0.80)
Defibrillator		I			
VT / VF / Cardiac arrest				0.69	(0.61-0.77)
Ischemic cardiomyopathy				0.33	(0.26-0.42)
Nonischemic cardiomyopathy		-		0.49	(0.43-0.55)
All patients		•		0.43	(0.4-0.45)
Resynchronization Therapy		1			
Ischemic cardiomyopathy		_ _		0.39	(0.22-0.64)
Nonischemic cardiomyopathy				0.7	(0.56-0.86)
All patients		-		0.66	(0.61-0.71)
	0	0.5 1	1.5	2	
		Lower in women	Lower in men		

Figure 2. Odds of implantation of devices for women compared with men for selected conditions, adjusted for age and comorbidities.

Odds ratio with 95% CIs for pacemaker, implantable cardioverter defibrillator, and cardiac resynchronization therapy implantation in women versus men, adjusted for age and comorbidities. Odds ratio<1 suggests lower implant rates in women versus men. Additional odds ratio for other subcategories are presented in Table S5. OR indicates odds ratio; VF, ventricular fibrillation; and VT ventricular tachycardia.

The absolute differences in mortality between sexes were small and not clinically significant.

DISCUSSION

This is the largest study to systematically examine implant rates for cardiac devices (pacemakers, ICDs, and CRTs) in men versus women, stratified by implant diagnosis and adjusted for age and comorbidities. There were 4 important findings. First, primary diagnosis leading to device implantation differed by sex. Men were more likely to be treated for complete heart block, VT/VF/cardiac arrest, and ischemic cardiomyopathy, and women for sick sinus syndrome, atrial fibrillation/atrial flutter, and syncope. Second, implant rates for all 3 major cardiac devices (pacemakers, ICDs, and CRTs) were lower in women than men, across nearly all major indications when adjusted for age and comorbidities. Importantly, sex differences were seen in complete heart block, VT/VF/cardiac arrest, and ischemic cardiomyopathy. Third, sex differences in implantation rates remained unchanged over the 10-year study period. Finally, 30-day mortality rates were higher (for both men and women) in patients who did not receive a device compared with those who did, and this was consistent across indications.

Lower Implantation Rates of Pacemakers, ICDs, and CRT in Women

Few studies have compared CIED implant rates by sex and those that have yielded conflicting results. In German pacemaker registries, a lower proportion of devices were implanted in men than in women¹⁷ but such a difference could be because of inherent differences in arrhythmia burden, age, and comorbidities that were not explored in detail in that analysis. An older US study (1989–1990) with similar methodology to ours found that the odds of pacemaker insertion (adjusted for age and comorbidities) were 28% higher in men and similar to our own study (22% lower odds of pacemaker insertion in women).¹⁸ Noting that this study is now more than 30 years old, we also note that this study did not stratify by implantation diagnosis. This is important as our study and others have shown that the prevalence of arrhythmias and cardiomyopathy differs in men and women.⁸

From our study, differences in odds of pacemaker implantation for women seem particularly concerning for the indications of complete heart block (11% lower odds), atrial fibrillation (35% lower odds), and syncope (30% lower odds). We acknowledge that there is considerable clinical heterogeneity in treatment of atrial fibrillation and syncope, with these conditions not always requiring devices (for example, vasodepressor

	Male sex				Female sex			
	No CIED	Pacemaker	ICD	CRT	No CIED	Pacemaker	ICD	CRT
All conditions [†]	0.02 (0.02-0.02)	0.01 (0.01-0.01)	0.01 (0.01-0.01)	0.01 (0.01-0.01)	0.02 (0.02-0.02)	0.01 (0-0.01)	0.01 (0.01-0.01)	0.01 (0-0.01)
Arrhythmia	0.02 (0.02-0.02)	0.01 (0.01–0.01)	0.01 (0.01–0.02)	0 (0-0.01)	0.01 (0.01-0.01)	0.01 (0-0.01)	0.01 (0.01-0.01)	0 (0-0.01)
Complete heart block	0.06 (0.05-0.07)	0.01 (0.01–0.02)	0.04 (0-0.09)	0.02 (0-0.03)	0.05 (0.04-0.06)	0.01 (0.01-0.01)	0.03 (0-0.07)	0.01 (0-0.02)
Other heart block	0.01 (0.01–0.02)	0.01 (0.01–0.01)	0.01 (0-0.03)	0.02 (0-0.03)	0.01 (0.01-0.01)	0.01 (0-0.01)	0.01 (0-0.02)	0.01 (0-0.02)
Sick sinus syndrome	0.02 (0.01-0.02)	0.01 (0.01–0.01)	(00) 0	0 (0-0.01)	0.01 (0.01–0.02)	0.01 (0-0.01)	(0-0) 0	0 (0-0.01)
Atrial fibrillation/atrial flutter	0.01 (0.01–0.01)	0.01 (0-0.01)	0.01 (0-0.02)	0 (0-0.01)	0.01 (0.01–0.01)	0.01 (0-0.01)	0.01 (0-0.02)	0 (0-0.01)
Ventricular tachycardia/ ventricular fibrillation/cardiac arrest	0.07 (0.06–0.07)	0.01 (0-0.02)	0.01 (0-0.01)	0-0) 0	0.05 (0.05-0.06)	0.01 (0-0.01)	0.01 (0-0.01)	(0-0) 0
Other arrhythmia	0.01 (0.01–0.02)	0 (0-0.01)	0.01 (0-0.03)	0.01 (0-0.01)	0.01 (0.01–0.01)	0 (0-0.01)	0.01 (0-0.02)	0. (0-0.01)
Cardiomyopathy	0.05 (0.05–0.05)	0.01 (0-0.03)	0.01 (0-0.01)	0.01 (0-0.03)	0.04 (0.04–0.04)	0.01 (0-0.02)	0.01 (0-0.01)	0.01 (0-0.02)
Ischemic cardiomyopathy	0.07 (0.06–0.08)	0.02 (0-0.06)	0.01 (0-0.02)	0.01 (0-0.04)	0.06 (0.05–0.06)	0.02 (0-0.05)	0.01 (0-0.02)	0.01 (0-0.04)
Nonischemic cardiomyopathy	0.05 (0.04-0.05)	0.01 (0-0.02)	0.01 (0-0.01)	0.01 (0-0.03)	0.04 (0.03-0.04)	0.01 (0-0.02)	0 (0-0.01)	0.01 (0-0.02)
Syncope	0.01 (0.01–0.01)	0.01 (0.00-0.01)	(0-0) 0	0 (0-0)	0.01 (0.01–0.01)	0.00 (0-0.01)	0-0) 0	0 (0-0) 0
"All patients" are all patients aged over 18 who presented with selected cardiovascular conditions to a hospital in New South Wales from 2008 to 2018 (see Table S1 for International Classification of Diseases, Tenth	d over 18 who presente	d with selected cardiov	ascular conditions to a	hospital in New South	Wales from 2008 to 20	18 (see Table S1 for <i>In</i>	ternational Classificatio	n of Diseases, Tenth

Table 3. Adjusted* Mortality Rates (95% CI) at 30 Days After Cardiac Implantation for Men Versus Women Stratified by Condition

J Am Heart Assoc. 2022;11:e025428. DOI: 10.1161/JAHA.121.025428

Revision, Australian Modification codes). CIED indicates cardiac implantable electronic device; CRT cardiac resynchronization therapy; and ICD implantable cardioverter defibrillator.

"Pates are adjusted for age and presence of Elixhauser comorbidities. There was a significant sexinteraction for use of any device and for use of pacemaker in all conditions cohort (P<0.001 for both). There were no other significant sex interactions for other subgroups or pacing groups.

syncope). In this indication, lower pacemakers could be related to underlying differences in diagnosis by sex. However, indications for pacing in complete heart block are more definite,³ suggesting pacemaker underuse and arguably, a sex bias in implantation for women.

In contrast to pacemakers, sex disparities between ICD and CRT implant rates, particularly in the context of heart failure, have been more extensively studied, although findings are still conflicting. Early US Medicare studies using discharge coding (without adjustment for confounders) found that women were less likely to receive ICDs for the prevention of sudden cardiac death^{13,19} and less likely to receive CRT for heart failure.²⁰ Subsequent studies in the United States and Canada using similar methodology but adjusting for age and comorbidities demonstrated that women were ≈3 times less likely to receive ICD therapy for primary or secondary prevention of sudden cardiac death.^{21,22} In comparison to these data, prospective multicenter registries such as GWTG (Get With the Guidelines)) allow a complementary, granular understanding of indications and use of ICDs and CRT with provision of ECG criteria (including left bundle-branch block) and left ventricular ejection fraction. El Chami found that female sex was associated with reduced implantation of all devices for patients with a left ventricular ejection fraction <40%,¹¹ and Al Khatib similarly demonstrated that these sex differences have persisted over time despite the intentions of the GWTG quality improvement project.¹² Our study complements these prospective registries (which may be biased as the GWTG program likely attracts hospitals committed to guality improvement) as well as the older Medicare studies by including the broadest array of device types and indications in a contemporary population.

Reasons for These Sex-Based Disparities

The underlying cause of these sex differences is unclear. Importantly, it is difficult from the nature of this study to determine if the sex differences described are truly a result of deviation from good clinical care. Although this population-level snapshot allows an understanding of implantation trends and real-world practices, implantation diagnoses based on clinical coding do not have the granularity to optimally determine eligibility for each CIED. For example, although this study used ICD-10-AM coding for cardiomyopathy and VT/VF/cardiac arrest to identify the population that may receive ICDs and CRTs, the authors did not have access to ECGs or echocardiograms to determine if patients met criteria for CRT use, nor the angiographic data to determine if there was an ischemic cause for VT/VF/cardiac arrest that might preclude need for an ICD. Thus, in comparison to prospective studies, it is difficult to conclude that the observed sex differences are a result of sex-based disparities or purely differing eligibility between the 2 sexes.

In fact, it could be that these observed differences in CIED use are a result of clinician recognition of inherent differences in arrhythmia risk and cardiomyopathy presentations between men and women. For example, heart failure with preserved ejection fraction may contribute to a larger proportion of women than men with cardiomyopathy.^{23,24} Further, women with heart failure have a lower risk of sudden cardiac death than men but a higher risk of acute complications from CIED implant.²⁵⁻²⁷ It is possible that the sex differences observed are because of the treating physician responding appropriately to these clinical differences. However, although this may explain specific scenarios of lower ICD and CRT use in cardiomyopathy, it cannot explain the broad array of inequity in device provision across nearly all indications, including complete heart block and VT/VF and cardiac arrest. That is, it seems unlikely that misclassification due to clinical eligibility would be so consistent to result in women consistently having lower rates of implants across all diagnoses for devices.

In fact, there is convincing evidence in the literature of sex bias affecting CIED implantation. Although a random survey of 1210 American College of Cardiology physicians demonstrated that they reported being willing to offer ICDs equally to men and women,²⁸ in realworld observational analyses (with the GWTG-Heart Failure quality improvement project) Hernandez et al.²⁹ found that <40% of eligible hospitalized patients with heart failure received ICDs, with reduced odds of implantation for White women (0.62) and Black women (0.56) compared with White men. Women were less frequently counseled than men about ICD implantation.³⁰ This is concerning as some studies indicate women may be more anxious about implantation and more likely to refuse device implantation.³¹

It is likely that, similar to causes of sex differences in the treatment of coronary artery disease, where women with ST-segment–elevation myocardial infarction are less likely to receive invasive management, revascularization, or preventative medications compared with men,^{9,10,32} the observed sex differences in our study are secondary to a complex combination of biological differences and sex bias.³³ Regardless of cause, these findings contribute to a growing global awareness of the need to address these disparities.³⁴

Survival After CIED Implantation

In the current study, 30-day mortality (adjusted for age and comorbidities) was higher in both men and women who did not receive a device, compared with those who did, possibly reflecting selection bias for

Sex-Based differences in CIED use

device insertion. Our data suggested a sex interaction for mortality rates at 30 days for any pacing use and pacemaker use (the largest group of any pacing) with higher mortality in men; however, absolute differences were small. In a recent survival analysis of a pacemaker registry, survival rates for men and women were similar for pacemaker and ICD but significantly improved for women receiving CRT-defibrillator and CRT-pacemaker compared with men.³⁵

Study Limitations

This study has several limitations. First, using an administrative database reliant on hospital discharge coding, uncoded and confounding variables may have existed that were evident to the clinician making the selection of pacing system but that we cannot consider in our analysis. For example, although controlling for comorbidities, this study cannot account for differences in frailty and functional capacity between sexes that may have affected clinician decision-making. Previous studies suggest that this administrative coding has reasonable accuracy compared with registries.³⁶ Second, with regard to implant numbers, no differentiation is made between generator changes for end-of-life battery and new implantation of a device and hence actual number of devices performed in NSW may have been lower than described. Nevertheless, these data allow a reasonable estimate of the relative percentage and implant rates of the device types.

CONCLUSIONS

This analysis of a large-scale, real-world and contemporary data set confirms the existence, and persistence over time, of underuse of CIEDs in women. With increasing use of cardiac devices globally, this research should provoke further examination of the reasons for these concerning sex differences as well as ways to address them.

ARTICLE INFORMATION

Received February 25, 2022; accepted June 13, 2022.

Affiliations

Department of Cardiology, Westmead Hospital, Sydney, New South Wales, Australia (K.D.S., S.K., P.K., S.Z., C.K.C.); Westmead Applied Research Centre (K.D.S., N.N., S.K., S.Z., C.K.C.), Menzies Centre for Health Policy, Sydney School of Public Health, Faculty of Medicine and Health (N.N.,T.B.-P., A.W.); and Children's Hospital at Westmead Clinical School, Faculty of Medicine and Health (N.N.), University of Sydney, New South Wales, Australia; Centre for Health Systems and Safety Research, Australian Institute of Health Innovation, Macquarie University, Sydney, New South Wales, Australia (T.B.-P.); and Centre for Epidemiology and Evidence, New South Wales Ministry of Health, Sydney, New South Wales, Australia (L.T.).

Sources of Funding

This work was funded by the New South Wales Ministry of Health as part of the Co-Creating Evidence from High Value Public Health Data initiative, in

which researchers and policy makers co-create policy relevant evidence and insights using linked administrative health data. Andrew Wilson is co-director of the Australian Prevention Partnership Centre, which is jointly funded by the National Health and Medical Research Council (NHMRC), the ministries of health of the Australian, NSW, ACT, and Tasmanian governments, Victoria Health, and Cancer Council Australia. Clara K Chow is supported by an NHMRC Investigator grant (APP1195326). Saurabh Kumar is supported by a National Heart Foundation Fellowship.

Disclosures

None.

Supplemental Material

Tables S1-S6

REFERENCES

- Dêbski M, Ulman M, Zabek A, Haberka K, Lelakowski J, Malecka B. Gender differences in dual-chamber pacemaker implantation indications and long-term outcomes. *Acta Cardiol.* 2016;71:41–45. doi: 10.1080/AC.71.1.3132096
- Linde C, Bongiorni MG, Birgersdotter-Green U, Curtis AB, Deisenhofer I, Furokawa T, Gillis AM, Haugaa KH, Lip GYH, Van Gelder I, et al. Sex differences in cardiac arrhythmia: a consensus document of the European heart rhythm association, endorsed by the Heart Rhythm Society and Asia Pacific Heart Rhythm Society. *Ep Europace*. 2018;20:1565–1565ao. doi: 10.1093/europace/euy067
- Kusumoto FM, Schoenfeld MH, Barrett C, Edgerton JR, Ellenbogen KA, Gold M, Goldschlager NF, Hamilton RB, Joglar JA, Kim RJ, et al. 2018 ACC/AHA/HRS guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay: executive summary: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines, and the Heart Rhythm Society. *Circulation*. 2019;140:e333–e381. doi: 10.1161/CIR.000000000000627
- 4. Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, Elliott PM, Fitzsimons D, Hatala R, Hindricks G, et al. 2015 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: the task force for the Management of Patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC) endorsed by: association for European Paediatric and Congenital Cardiology (AEPC). *Ep Europace*. 2015;17:1601–1687. doi: 10.1093/ europace/euv319
- Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA, Cleland J, Deharo JC, Delgado V, Elliott PM, et al. 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy: the task force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European heart rhythm association (EHRA). *Eur Heart J.* 2013;34:2281–2329. doi: 10.1093/eurheartj/eht150
- Al-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, Deal BJ, Dickfeld T, Field M, Fonarow GC, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines and the Heart Rhythm Society. *Circulation*. 2018;138:e272–e391. doi: 10.1016/j.hrthm.2017.10.036
- Walli-Attaei M, Joseph P, Rosengren A, Chow CK, Rangarajan S, Lear SA, AlHabib KF, Davletov K, Dans A, Lanas F, et al. Variations between women and men in risk factors, treatments, cardiovascular disease incidence, and death in 27 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. *Lancet.* 2020;396:97– 109. doi: 10.1016/S0140-6736(20)30543-2
- Ehdaie A, Cingolani E, Shehata M, Wang X, Curtis AB, Chugh SS. Sex differences in cardiac arrhythmias: clinical and research implications. *Circ Arrhythm Electrophysiol.* 2018;11:e005680. doi: 10.1161/ CIRCEP.117.005680
- Hay M, Stehli J, Martin C, Brennan A, Dinh DT, Lefkovits J, Zaman S. Sex differences in optimal medical therapy following myocardial infarction according to left ventricular ejection fraction. *Eur J Prev Cardiol.* 2021;27:2348–2350. doi: 10.1177/2047487319900875

- Stehli J, Martin C, Brennan A, Dinh DT, Lefkovits J, Zaman S. Sex differences persist in time to presentation, revascularization, and mortality in myocardial infarction treated with percutaneous coronary intervention. *J Am Heart Assoc.* 2019;8:e012161. doi: 10.1161/JAHA.119.012161
- El-Chami MF, Hanna IR, Bush H, Langberg JJ. Impact of race and gender on cardiac device implantations. *Heart Rhythm*. 2007;4:1420–1426. doi: 10.1016/j.hrthm.2007.07.024
- Al-Khatib SM, Hellkamp AS, Hernandez AF, Fonarow GC, Thomas KL, Al-khalidi HR, Heidenrich PA, Hammill S, Yancy C, Paterson ED, et al. Trends in use of implantable cardioverter-defibrillator therapy among patients hospitalized for heart failure: have the previously observed sex and racial disparities changed over time? *Circulation*. 2012;125:1094– 1101. doi: 10.1161/CIRCULATIONAHA.111.066605
- Gauri AJ, Davis A, Hong T, Burke MC, Knight BP. Disparities in the use of primary prevention and defibrillator therapy among blacks and women. *Am J Med.* 2006;119(167):e17–e21. doi: 10.1016/j.amjmed.2005.08.021
- MacFadden DR, Crystal E, Krahn AD, Mangat I, Healey JS, Dorian P, Birnie D, Simpson CS, Khaykin Y, Pinter A, et al. Sex differences in implantable cardioverter-defibrillator outcomes: findings from a prospective defibrillator database. *Ann Intern Med.* 2012;156:195–203. doi: 10.7326/0003-4819-156-3-201202070-00007
- Australian Bureau of Statistics for the Commonwealth of Australia. Australian Statistical Geography Standard (ASGS): Volume 5 - Remoteness Structure. 2018. Available at https://www.abs.gov.au/websitedbs/d3310 114.nsf/home/remoteness+structure. Last accessed December 2021.
- Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care*. 1998;36:8–27. doi: 10.1097/00005650-199801000-00004
- Nowak B, Misselwitz B, Erdogan A, Funck R, Irnich W, Israel CW, Olbrich HG, Schmidt H, Sperzel J, Zegelman M. Do gender differences exist in pacemaker implantation?—Results of an obligatory external quality control program. *Europace*. 2010;12:210–215. doi: 10.1093/ europace/eup312
- Giacomini MK. Gender and ethnic differences in hospital-based procedure utilization in California. Arch Intern Med. 1996;156:1217–1224. doi: 10.1001/archinte.1996.00440100115013
- ChanPS, BirkmeyerJD, KrumholzHM, SpertusJA, NallamothuBK. Racial and gender trends in the use of implantable cardioverter-defibrillators among Medicare beneficiaries between 1997 and 2003. *Congest Heart Fail.* 2009;15:51–57. doi: 10.1111/j.1751-7133.2009.00060.x
- Alaeddini J, Wood MA, Amin MS, Ellenbogen KA. Gender disparity in the use of cardiac resynchronization therapy in the United States. *Pacing Clin Electrophysiol.* 2008;31:468–472. doi: 10.1111/j.1540-8159.2008.01016.x
- Curtis LH, Al-Khatib SM, Shea AM, Hammill BG, Hernandez AF, Schulman KA. Sex differences in the use of implantable cardioverterdefibrillators for primary and secondary prevention of sudden cardiac death. JAMA. 2007;298:1517–1524. doi: 10.1001/jama.298.13.1517
- MacFadden DR, Tu JV, Chong A, Austin PC, Lee DS. Evaluating sex differences in population-based utilization of implantable cardioverterdefibrillators: role of cardiac conditions and noncardiac comorbidities. *Heart Rhythm.* 2009;6:1289–1296. doi: 10.1016/j.hrthm.2009.05.017
- Bursi F, Weston SA, Redfield MM, Jacobsen SJ, Pakhomov S, Nkomo VT, Meverden RA, Roger VL. Systolic and diastolic heart failure in the community. *JAMA*. 2006;296:2209–2216. doi: 10.1001/ jama.296.18.2209

- Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. *N Engl J Med.* 2006;355:251–259. doi: 10.1056/ NEJMoa052256
- Rho RW, Patton KK, Poole JE, Cleland JG, Shadman R, Anand I, Maggioni AP, Carson PE, Swedberg K, Levy WC. Important differences in mode of death between men and women with heart failure who would qualify for a primary prevention implantable cardioverterdefibrillator. *Circulation*. 2012;126:2402–2407. doi: 10.1161/CIRCU LATIONAHA.111.069245
- Moore K, Ganesan A, Labrosciano C, Heddle W, McGavigan A, Hossain S, Horton D, Hariharaputhiran S, Ranasinghe I. Sex differences in acute complications of cardiac implantable electronic devices: implications for patient safety. *J Am Heart Assoc.* 2019;8:e010869. doi: 10.1161/ JAHA.118.010869
- Kim SK, Bennett R, Ingles J, Kumar S, Zaman S. Arrhythmia in cardiomyopathy: sex and gender differences. *Curr Heart Fail Rep.* 2021;18:274–283. doi: 10.1007/s11897-021-00531-0
- Al-Khatib SM, Sanders GD, O'Brien SM, Matlock D, Zimmer LO, Masoudi FA, Peterson E. Do physicians' attitudes toward implantable cardioverter defibrillator therapy vary by patient age, gender, or race? Ann Noninvasive Electrocardiol. 2011;16:77–84. doi: 10.1111/j.1542-474X.2010.00412.x
- Hernandez AF, Fonarow GC, Liang L, Al-Khatib SM, Curtis LH, LaBresh KA, Yancy CW, Albert NM, Peterson ED. Sex and racial differences in the use of implantable cardioverter-defibrillators among patients hospitalized with heart failure. *JAMA*. 2007;298:1525–1532. doi: 10.1001/ jama.298.13.1525
- Hess PL, Hernandez AF, Bhatt DL, Hellkamp AS, Yancy CW, Schwamm LH, Pterson ED, Schulte PJ, Fonarow GC, Al-khatib SM. Sex and race/ ethnicity differences in implantable cardioverter-defibrillator counseling and use among patients hospitalized with heart failure: findings from the get with the guidelines-heart failure program. *Circulation*. 2016;134:517– 526. doi: 10.1161/CIRCULATIONAHA.115.021048
- Horton HL, Marinchak RA, Rials SJ, Kowey PR. Gender differences in device therapy for malignant ventricular arrhythmias. *Arch Intern Med.* 1995;155:2342–2345. doi: 10.1001/archinte.1995.00430210092014
- Khan E, Brieger D, Amerena J, Atherton KK, Chew DP, Ilton M FA, Juergens CP, Kangaharan N, Rajaratnam R, et al. Differences in management and outcomes for men and women with ST-elevation myocardial infarction. *Med J Aust.* 2018;209:118–123. doi: 10.5694/ mja17.01109
- Stehli J, Duffy S, Burgess S. Sex disparities in myocardial infarction: biology or bias? *Heart Lung Circ.* 2021;30:18–26. doi: 10.1016/j. hlc.2020.06.025
- Vogel B, Acevedo M, Appelman Y. The *Lancet* women and cardiovascular disease commission: reducing the global burden 2030. *Lancet*. 2021;397:2385–2438. doi: 10.1016/S0140-6736(21)00684-X
- Varma N, Mittal S, Prillinger JB, Snell J, Dalal N, Piccini JP. Survival in women versus men following implantation of pacemakers, defibrillators, and cardiac resynchronization therapy devices in a large, nationwide cohort. J Am Heart Assoc. 2017;6:e005031. doi: 10.1161/ JAHA.116.005031
- Henderson T, Shepheard J, Sundararajan V. Quality of diagnosis and procedure coding in ICD-10 administrative data. *Med Care.* 2006;44:1011–1019. doi: 10.1097/01.mlr.0000228018.48783.34

SUPPLEMENTAL MATERIAL

Table S1. International Classification of Diseases 10th revision Australian Modification

ICD10AM	ICD10AM description		
Code			
B33.2	Viral carditis		
E11.53	Type 2 diabetes mellitus with diabetic cardiomyopathy		
107.1	Tricuspid insufficiency		
108.1	Disorders of both mitral and tricuspid valves		
108.3	Combined disorders of mitral, aortic and tricuspid valves		
I10	Essential (primary) hypertension		
120.0	Unstable angina		
I20.1	Angina pectoris with documented spasm		
120.8	Other forms of angina pectoris		
120.9	Angina pectoris, unspecified		
I21.0	Acute transmural myocardial infarction of anterior wall		
I21.1	Acute transmural myocardial infarction of inferior wall		
I21.2	Acute transmural myocardial infarction of other sites		
I21.3	Acute transmural myocardial infarction of unspecified site		
I21.4	Acute subendocardial myocardial infarction		
I21.9	Acute myocardial infarction, unspecified		
I23.8	Other current complications following acute myocardial infarction		
I25.10	Atherosclerotic heart disease, of unspecified vessel		
I25.11	Atherosclerotic heart disease, of native coronary artery		
I25.5	Ischaemic cardiomyopathy		
I25.8	Other forms of chronic ischaemic heart disease		
125.9	Chronic ischaemic heart disease, unspecified		
130.9	Acute pericarditis, unspecified		
133.0	Acute and subacute infective endocarditis		
I34.0	Mitral (valve) insufficiency		
135.0	Aortic (valve) stenosis		
135.1	Aortic (valve) insufficiency		
135.9	Aortic valve disorder, unspecified		

(ICD10AM) codes for all patients included in the study

I42.0	Dilated cardiomyopathy
I42.1	Obstructive hypertrophic cardiomyopathy
I42.2	Other hypertrophic cardiomyopathy
I42.4	Endocardial fibroelastosis
I42.6	Alcoholic cardiomyopathy
I42.7	Cardiomyopathy due to drugs and other external agents
I42.8	Other cardiomyopathies
I42.9	Cardiomyopathy, unspecified
I43.0	Cardiomyopathy in infectious and parasitic diseases classified elsewhere
I44.0	Atrioventricular block, first degree
I44.1	Atrioventricular block, second degree
I44.2	Atrioventricular block, complete
I44.3	Other and unspecified atrioventricular block
I44.4	Left anterior fascicular block
I44.7	Left bundle-branch block, unspecified
I45.1	Other and unspecified right bundle-branch block
I45.2	Bifascicular block
I45.3	Trifascicular block
I45.4	Nonspecific intraventricular block
I45.5	Other specified heart block
I45.6	Pre-excitation syndrome
I45.8	Other specified conduction disorders
I45.9	Conduction disorder, unspecified
I46.0	Cardiac arrest with successful resuscitation
I46.9	Cardiac arrest, unspecified
I47.1	Supraventricular tachycardia
I47.2	Ventricular tachycardia
I47.9	Paroxysmal tachycardia, unspecified
I48	Atrial fibrillation and flutter
I48.0	Paroxysmal atrial fibrillation
I48.1	Persistent atrial fibrillation
I48.2	Chronic atrial fibrillation
I48.3	Typical atrial flutter

I48.4	Atypical atrial flutter
I48.9	Atrial fibrillation and atrial flutter, unspecified
I49.0	Ventricular fibrillation and flutter
149.2	Junctional premature depolarization
I49.3	Ventricular premature depolarization
I49.4	Other and unspecified premature depolarization
I49.5	Sick sinus syndrome
I49.8	Other specified cardiac arrhythmias
I49.9	Cardiac arrhythmia, unspecified
150.0	Congestive heart failure
I50.1	Left ventricular failure (if secondary diagnosis is coronary heart disease)
I50.1	Left ventricular failure (with secondary diagnosis of no coronary heart disease)
150.9	Heart failure, unspecified
151.6	Cardiovascular disease, unspecified
I51.7	Cardiomegaly
I51.8	Other ill-defined heart diseases
I51.9	Heart disease, unspecified
I63.3	Cerebral infarction due to thrombosis of cerebral arteries
163.4	Cerebral infarction due to embolism of cerebral arteries
163.9	Cerebral infarction, unspecified
164	Stroke, not specified as hemorrhage or infarction
195.1	Orthostatic hypotension
195.9	Hypotension, unspecified
I97.1	Other functional disturbances following cardiac surgery
197.8	Other intraoperative and postprocedural disorders of circulatory system, not elsewhere
	classified
O99.4	Diseases of the circulatory system in pregnancy, childbirth and the puerperium
Q24.6	Congenital heart block
R00.0	Tachycardia, unspecified
R00.1	Bradycardia, unspecified
R00.2	Palpitations
R00.8	Other and unspecified abnormalities of heart beat
R06.0	Dyspnea

R07.3	Other chest pain
R07.4	Chest pain, unspecified
R29.6	Tendency to fall, not elsewhere classified
R41.0	Disorientation, unspecified
R42	Dizziness and giddiness
R55	Syncope and collapse
R56.8	Other and unspecified convulsions
R57.0	Cardiogenic shock
R94.3	Abnormal results of cardiovascular function studies
S06.02	Loss of consciousness of brief duration [less than 30 minutes]
S06.5	Traumatic subdural hemorrhage
S06.6	Traumatic subarachnoid hemorrhage
T82.1	Mechanical complication of cardiac electronic device
T82.5	Mechanical complication of other cardiac and vascular devices and implants
T82.6	Infection and inflammatory reaction due to cardiac valve prosthesis
T82.7	Infection and inflammatory reaction due to cardiac and vascular devices, implants and
	grafts, not elsewhere classified
T82.8	Other specified complications of cardiac and vascular devices, implants and grafts
T86.2	Heart transplant failure and rejection
Z45.0	Adjustment and management of cardiac device

Abbreviations: ICD10AM International Classification of Diseases 10th revision Australian

Modification.

Table S2. International Classification of Diseases 10th revision Australian Modification

(ICD10AN	A) codes for the arrhyt	hmia, cardiomyopathy,	and syncope cohorts
Cohort	Sub-category	ICD10AM Code	ICD10AM description

Cohort	Sub-category	ICD10AM Code	ICD10AM description
Arrhythmia	Complete heart block	I44.2	Atrioventricular block, complete
	Other heart block	I44.0	Atrioventricular block, first degree
		I44.1	Atrioventricular block, second degree
		I44.3	Other and unspecified atrioventricular block
		I44.4	Left anterior fascicular block
		I44.7	Left bundle-branch block, unspecified
		I45.1	Other and unspecified right bundle-branch block
		I45.2	Bifascicular block
		I45.3	Trifascicular block
		I45.4	Nonspecific intraventricular block
		I45.5	Other specified heart block
		I45.8	Other specified conduction disorders
		I45.9	Conduction disorder, unspecified
	Sick sinus syndrome	I49.5	Sick sinus syndrome
	Atrial fibrillation / atrial flutter	I48	Atrial fibrillation and flutter
		I48.0	Paroxysmal atrial fibrillation
		I48.1	Persistent atrial fibrillation
		I48.2	Chronic atrial fibrillation
		I48.9	Atrial fibrillation and atrial flutter, unspecified
	VT/VF/Cardiac arrest	I46.0	Cardiac arrest with successful resuscitation
		I47.2	Ventricular tachycardia
		I49.0	Ventricular fibrillation and flutter
	Other arrhythmia	I49.2	Junctional premature depolarization
		I49.8	Other specified cardiac arrhythmias
		I49.9	Cardiac arrhythmia, unspecified
		Q24.6	Congenital heart block
		R00.1	Bradycardia, unspecified
Cardiomyopathy	Ischaemic	I25.5	Ischaemic cardiomyopathy

	150.1	Left ventricular failure (if any secondary diagnosis
		is coronary heart disease)
Non-ischaemic	E11.53	Type 2 diabetes mellitus with diabetic
		cardiomyopathy
	I42.0	Dilated cardiomyopathy
	I42.1	Obstructive hypertrophic cardiomyopathy
	I42.2	Other hypertrophic cardiomyopathy
	I42.6	Alcoholic cardiomyopathy
	I42.7	Cardiomyopathy due to drugs and other external
		agents
	I42.8	Other cardiomyopathies
	I42.9	Cardiomyopathy, unspecified
	I43.0	Cardiomyopathy in infectious and parasitic diseases
		classified elsewhere
	I50.1	Left ventricular failure (with no secondary diagnosis
		of coronary heart disease)
Syncope	R55	Syncope and collapse

Abbreviations: ICD10AM International Classification of Diseases 10th revision Australian

Modification, VF ventricular fibrillation, VT ventricular tachycardia.

Table S3. Australian Classification of Health Interventions (ACHI) codes to define

Device	Block	ACHI code	ACHI description				
Pacemaker	648	38350-00	Insertion of permanent transvenous electrode into other				
			heart chamber(s) for cardiac pacemaker				
	649	38470-00	Insertion of permanent epicardial electrode for cardiac				
			pacemaker via thoracotomy or sternotomy				
	649	38473-00	Insertion of permanent epicardial electrode for cardiac				
			pacemaker via subxyphoid approach				
	649	38654-00	Insertion of permanent left ventricular electrode for				
			cardiac pacemaker via thoracotomy or sternotomy				
	650	38353-00	Insertion of cardiac pacemaker generator				
Defibrillator	648	38390-02	Insertion of permanent transvenous electrode into other				
			heart chamber(s) for cardiac defibrillator				
	649	38390-00	Insertion of patches for cardiac defibrillator				
	649	38470-01	Insertion of permanent epicardial electrode for cardiac				
			defibrillator via thoracotomy or sternotomy				
	649	38473-01	Insertion of permanent epicardial electrode for cardiac				
			defibrillator via subxyphoid approach				
	649	38654-03	Insertion of permanent left ventricular electrode for				
			cardiac defibrillator via thoracotomy or sternotomy				
	653	38393-00	Insertion of cardiac defibrillator generator				
Cardiac resynchronisation	648	38368-00	Insertion of permanent transvenous electrode into				
therapy			left ventricle for cardiac pacemaker				
	648	38390-01	Insertion of permanent transvenous electrode into				
			left ventricle for cardiac defibrillator				

pacemakers, defibrillators, and cardiac resynchronisation therapy

Abbreviations: ACHI Australian Classification of Health Interventions.

Table S4. Characteristics of men vs women receiving cardiac implantable electronic

devices

	Male				Female				
	No	PPM	ICD	CRT	No pacing	PPM	ICD	CRT	
	pacing								
Age									
18-44	82986	247	512	76	64505	202	199	37	
	(99.1%)	(0.3%)	(0.6%)	(0.1%)	(99.4%)	(0.3%)	(0.3%)	(0.1%)	
45-64	218475	1600	1978	474	143201	872	540	179	
	(98.4%)	(0.7%)	(0.9%)	(0.2%)	(99%)	(0.6%)	(0.4%)	(0.1%)	
65-74	155423	3167	1645	589	110689	1847	453	253	
	(97%)	(2%)	(1%)	(0.4%)	(98%)	(1.6%)	(0.4%)	(0.2%)	
75-84	148114	5333	1027	660	146428	3777	290	420	
	(95.9%)	(3.5%)	(0.7%)	(0.4%)	(97.3%)	(2.5%)	(0.2%)	(0.3%)	
85+	75808	2705	123	277	116549	2722	41	242	
	(96.4%)	(3.4%)	(0.2%)	(0.4%)	(97.7%)	(2.3%)	(0%)	(0.2%)	
Region									
Major Cities	461746	9637	3898	1514	397536	7209	1097	848	
	(97.2%)	(2%)	(0.8%)	(0.3%)	(98%)	(1.8%)	(0.3%)	(0.2%)	
Inner Regional	161312	2502	943	397	138338	1605	296	210	
	(97.9%)	(1.5%)	(0.6%)	(0.2%)	(98.6%)	(1.1%)	(0.2%)	(0.1%)	
Outer Regional/ Remote/ Very	57748	913	444	165	45498	606	130	73	
Remote	(97.7%)	(1.5%)	(0.8%)	(0.3%)	(98.4%)	(1.3%)	(0.3%)	(0.2%)	
Comorbidities									
alcohol	19984	128	123	29	4850	21	10	4	
	(98.8%)	(0.6%)	(0.6%)	(0.1%)	(99.4%)	(0.4%)	(0.2%)	(0.1%)	
anemia	7495	155	42	21	8196	142	19	14	
	(97.5%)	(2%)	(0.5%)	(0.3%)	(98.1%)	(1.7%)	(0.2%)	(0.2%)	
cancer	9488	85	23	13	6655	47	4	4	
	(98.9%)	(0.9%)	(0.2%)	(0.1%)	(99.2%)	(0.7%)	(0.1%)	(0.1%)	
cardiac arrhythmia	94841	5141	1946	795	72388	3911	536	413	
	(93.1%)	(5%)	(1.9%)	(0.8%)	(94.2%)	(5.1%)	(0.7%)	(0.5%)	

chronic pulmonary disease	19825	301	151	65	15501	151	37	29
	(97.8%)	(1.5%)	(0.7%)	(0.3%)	(98.8%)	(1%)	(0.2%)	(0.2%)
congestive heart failure	32628	967	1305	397	25795	718	352	159
	(93.6%)	(2.8%)	(3.7%)	(1.1%)	(96.1%)	(2.7%)	(1.3%)	(0.6%)
depression/psychosis	5665	67	45	14	5660	75	17	8
	(98.1%)	(1.2%)	(0.8%)	(0.2%)	(98.4%)	(1.3%)	(0.3%)	(0.1%)
diabetes	123943	2735	1122	427	88919	1695	281	211
	(97%)	(2.1%)	(0.9%)	(0.3%)	(97.8%)	(1.9%)	(0.3%)	(0.2%)
hypertension	134029	2684	1114	406	107914	2235	273	264
	(97.3%)	(1.9%)	(0.8%)	(0.3%)	(97.7%)	(2%)	(0.2%)	(0.2%)
obesity	7537	91	60	22	5688	74	17	7
	(98%)	(1.2%)	(0.8%)	(0.3%)	(98.5%)	(1.3%)	(0.3%)	(0.1%)
renal failure	46102	1006	366	170	32970	679	88	81
	(97.1%)	(2.1%)	(0.8%)	(0.4%)	(97.8%)	(2%)	(0.3%)	(0.2%)
other comorbidity	127174	2502	1107	405	114489	2079	363	251
	(97.3%)	(1.9%)	(0.8%)	(0.3%)	(97.9%)	(1.8%)	(0.3%)	(0.2%)

Abbreviations: CRT cardiac resynchronisation therapy, ICD implantable cardioverter defibrillator, PPM permanent pacemaker.

Table S5. Odds of implantation of devices for women compared with men for all

	PPM	ICD	CRT
All conditions	0.78 (0.76–0.80)	0.43 (0.40-0.45)	0.66 (0.61–0.71)
Arrhythmia	0.72 (0.69–0.74)	0.43 (0.40-0.47)	0.68 (0.62–0.75)
Complete heart block	0.89 (0.80–0.98)	0.70 (0.47-1.01)	1.03 (0.84–1.26)
Other heart block	0.98 (0.89–1.08)	0.74 (0.54–1.02)	0.90 (0.72–1.13)
Sick sinus syndrome	1.02 (0.92–1.13)	0.55 (0.35-0.84)	1.07 (0.87–1.32)
Atrial fibrillation/flutter	0.65 (0.60-0.70)	0.32 (0.25-0.41)	0.46 (0.37–0.58)
VF/VT/cardiac arrest	1.03 (0.80–1.32)	0.69 (0.61-0.77)	0.81 (0.59–1.11)
Other arrhythmia	0.79 (0.73–0.85)	0.49 (0.37–0.63)	0.77 (0.62–0.95)
Cardiomyopathy	0.62 (0.50-0.77)	0.41 (0.37–0.46)	0.62 (0.51-0.75)
Ischaemic	0.63 (0.38–1.01)	0.33 (0.26-0.42)	0.39 (0.22–0.64)
Non-ischaemic	0.64 (0.51–0.81)	0.49 (0.43–0.55)	0.70 (0.56–0.86)
Syncope	0.70 (0.63-0.79)	0.44 (0.30-0.62)	0.70 (0.47–1.01)

conditions, adjusted for age and comorbidities

Odds ratio with 95% confidence intervals for PPM, ICD, and CRT implantation in women versus men, adjusted for age and comorbidities. Odds ratio < 1 suggests lower implant rates in women versus men.

Abbreviations: CRT cardiac resynchronisation therapy, ICD implantable cardioverter defibrillator, PPM permanent pacemaker, VF ventricular fibrillation, VT ventricular tachycardia.

	Male			Female			P for difference		
							by sex§		
	PPM	ICD	CRT	PPM	ICD	CRT	РР	IC	CR
							М	D	Т
Emergent*	8130	2631	1052	6291	747	660	< 0.0	0.6	<0.0
	(62.3%)	(49.8%)	(50.7%)	(66.8%)	(49%)	(58.4%)	01	14	01
Median [†] days from admission	1 (0-5)	0 (0-8)	0 (0-7)	1 (0-5)	0 (0-7)	0 (0-12)	< 0.0	0.0	0.00
to implant [‡]							01	91	4
Median admissions from	1 (1-3)	2 (1-3)	1 (1-3)	1 (1-3)	2 (1-3)	2 (1-3)	< 0.0	0.9	0.58
diagnosis to implant							01	66	1
Median LOS for implant	3 (1-7)	3 (1-10)	2 (1-8)	4 (1-8)	2 (1-	3 (1-9)	< 0.0	0.9	0.01
insertion (days)					10)		01	16	0

Table S6. Procedural status of cardiac device implantation for men vs women

* Emergent (based on care or treatment required within 24 hours (public hospitals only)), versus non-emergent (elective) implantation.

† Medians are presented with interquartile range.

‡ For the admission where the device inserted.

§ χ^2 test for emergent proportion; Wilcoxon rank sum test for medians.

Abbreviations: CRT cardiac resynchronisation therapy, ICD implantable cardioverter defibrillator, LOS length of stay, PPM permanent pacemaker, SD standard deviation.