

# Use of Primary Prevention Implantable Cardioverter-Defibrillators in a Population-Based Cohort Is Associated With a Significant Survival Benefit

Ratika Parkash, MD, MSc, FRCPC; John L. Sapp, MD, FRCPC; Magdy Basta, MBBS, FRCPC; Steve Doucette, MSc; Kara Thompson, MSc; Martin Gardner, MD, FRCPC, FACC; Chris Gray, MD, FRCPC; Brenda Brownell, CCHRAA; Hena Kidwai, MBBS; Jafna Cox, MD, FRCPC

**Background**—Underuse of implantable defibrillators has been previously noted in patients at risk for sudden cardiac death, as well as for survivors of sudden cardiac death. We sought to determine the utilization rates in a primary prevention implantable cardioverter-defibrillator (ICD)-eligible population and mortality in this group compared with a group that had undergone implantation of this therapy.

**Methods and Results**—A retrospective cohort of patients from April 1, 2006, to December 31, 2009, was used to define a primary prevention ICD-eligible population. Two groups were compared on the basis of ICD implantation (no-ICD versus ICD). The primary outcome measure was mortality. Of the 717 patients found to be potentially eligible for a primary prevention ICD, 116 (16%) were referred. The remaining cohort of 601 patients were compared with an existing cohort of primary prevention ICD patients (n=290). A significant survival benefit was associated with primary prevention ICD implantation (hazard ratio, 0.46; 95% CI [0.33–0.64];  $P<0.0001$ ). When adjusted for prespecified variables known to be associated with overall mortality and propensity score, a similar survival benefit was seen (hazard ratio, 0.59; 95% CI [0.40–0.87];  $P=0.01$ ). Appropriate ICD therapy occurred in 26% of those in the ICD group, during a mean follow-up of 2.7 years.

**Conclusions**—A significant mortality benefit was observed for patients who underwent primary prevention ICD implantation compared with those who did not. Vigilance is required to ensure that patients eligible for primary prevention ICDs are appropriately referred and assessed to allow such patients to benefit from this life-saving therapy. (*Circ Arrhythm Electrophysiol.* 2012;5:706-713.)

**Key Words:** defibrillation ■ registries ■ sudden cardiac arrest ■ sudden death ■ survival

Evidence-based guidelines have extended the use of implantable defibrillators to a large population of patients who have not suffered a cardiac arrest or sustained malignant ventricular arrhythmias, but who are at identifiably high risk of sudden cardiac death.<sup>1,2</sup> This, along with a dramatic increase in the number of patients surviving myocardial infarction (MI) and heart failure, has obvious resource and cost implications associated with prophylactic implantable cardioverter-defibrillator (ICD) implantation.

for such therapies.<sup>13,14</sup> Evidence from clinical trials may not be generalizable in the real world because of several factors: access to resources, physician factors, patient factors, or overall resource allocation.

We sought to compare mortality of real-world patients eligible for prophylactic ICD implantation in those who did and did not receive this therapy.

## Methods

Institutional approval was obtained from the Capital District Health Authority Research Ethics Board to conduct the present study.

## Patient Selection

Two patient cohorts were identified for comparison: the ICD group and the no-ICD group. The no-ICD group was defined as those patients with candidacy for an implantable defibrillator based on current published guidelines, whereas the ICD group fulfilled the same criteria but had appropriately received an ICD.<sup>2</sup>

The no-ICD group was derived using the Improving Cardiovascular Outcomes in Nova Scotia (ICONS)/Cardiovascular Health of Nova

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These guidelines are based on several clinical trials that have demonstrated an important survival benefit with prophylactic ICD implantation.<sup>3–10</sup> Although these trials provide invaluable data on the effects of therapies, clinical trial populations are highly selected because of careful and restricted eligibility criteria<sup>11,12</sup> and may not accurately reflect mortality or morbidity outcomes in the population that may be eligible

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From the Department of Medicine, Queen Elizabeth II Health Sciences Center (R.P., J.L.S., M.B., K.T., M.G., C.G., B.B., H.K., J.C.) and the Department of Community Health and Epidemiology (S.D.), Research Methods Unit, Dalhousie University, Halifax, Nova Scotia, Canada.

Correspondence to Ratika Parkash, MD, MSc, Queen Elizabeth II Health Sciences Center, HI Site, 1796 Summer St, Room 2501D, Halifax, NS B3H 3A7, Nova Scotia, Canada. E-mail parkashr@cdha.nshealth.ca

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Scotia (CVHNS) registry. ICONS was a 5-year study (October 1997–April 2002; population, 932 402 [1997]; 935 015 [2001])<sup>15</sup> that aimed to determine whether management of patients with an acute coronary syndrome, congestive heart failure (CHF), or atrial fibrillation could be improved through a multilateral healthcare stakeholder effort using a disease management strategy. The study enrolled all patients admitted to any hospital throughout the province (primary, secondary, and tertiary care institutions) with an acute coronary syndrome or CHF. The methodology of the present study has been described previously.<sup>16</sup> After the study ended in 2002, the CVHNS, a branch of the Department of Health, continued to maintain a registry of all consecutive patients hospitalized province-wide with the same diagnoses (CVHNS registry). Cases contained in the registry were identified using daily patient lists at all provincial institutions that provided inpatient hospital care. Detailed clinical information was abstracted by trained abstractors and entered into the ICONS/CVHNS registry. Once identified, patients were automatically followed up for repeat hospitalizations and linkage with the vital statistics registry to confirm deaths. Further clinical information garnered at follow-up from repeat hospitalizations was also obtained for analysis. Nova Scotia has a closed healthcare system with universal access for all provincial residents, thus ensuring completeness of follow-up, as well as linkage with vital statistics.

The no-ICD cohort was derived from the ICONS/CVHNS provincial registry. Patients who were admitted to a hospital between April 1, 2006, and December 31, 2008, were included. This period was chosen as it reflected a time period in which contemporary medical and interventional therapies would have been used to manage these patients and to have a minimum of 1-year follow-up.

Based on current guidelines, patients in the no-ICD cohort were identified for inclusion in the present study if they had either (1) ejection fraction (EF)  $\leq 35\%$  and an admission for heart failure or (2) EF  $\leq 30\%$  and documented coronary artery disease.<sup>17</sup> Patients were excluded if they had a prior or subsequent ICD implantation, a prior ventricular tachycardia/ventricular fibrillation arrest, or a documented follow-up EF  $\geq 35\%$ . All available follow-up EFs were examined to ensure that subsequent measurements remained below 35%. They were also excluded if they were nonresidents, died within the index hospital admission, lived in a chronic care facility with a terminal illness or had dementia, metastatic cancer, or renal failure requiring hemodialysis.

The ICD group was derived from a comprehensive prospective ICD registry at the Queen Elizabeth II Health Sciences Center, the only defibrillator implant center of the region. This registry was established in April 2006 and has been prospectively collecting data on all patients referred or implanted with an implantable defibrillator in the Nova Scotia province. All patients who were implanted with an ICD before this date have been entered into a separate retrospective registry, which has been rolled into the prospective registry. Follow-up is thus available for the entire population of patients with ICDs in the Nova Scotia province. The follow-up schedule for these patients conforms to the guidelines for ICD follow-up<sup>18</sup> (ie, every 6 months). Unscheduled visits may occur if an ICD therapy or other event occurs. Any patient followed up at a satellite ICD center continues to have in-clinic visits at the Queen Elizabeth II Health Sciences Center yearly. Any ICD event that may have occurred in the interim is obtained via email or fax from the satellite follow-up center. For the present study, the ICD cohort was comprised of patients who were implanted with a primary prevention ICD between April 1, 2006, and December 31, 2009. Patients who underwent primary prevention ICD implantation for only ischemic cardiomyopathy (EF  $\leq 30\%$  and documented coronary artery disease) or nonischemic cardiomyopathy (EF  $\leq 35\%$  and New York Heart Association II or greater heart failure) were included in the study. Patients who underwent primary prevention ICD implantation for arrhythmogenic ventricular cardiomyopathy, ion channelopathies, hypertrophic cardiomyopathy, infiltrative cardiomyopathy, or other indications were excluded from this analysis, as were nonresidents of Nova Scotia. All therapies (shocks and antitachycardia pacing) from the implantable defibrillator were adjudicated for appropriateness by 2 cardiac electrophysiologists. Any

disagreement between the 2 interpretations was resolved by review with a third electrophysiologist.

Mortality data were obtained through linkage with the provincial vital statistics registry. This linkage is highly reliable as each patient in Nova Scotia must have a death certificate filed with the provincial vital statistics registry; linkage was accomplished through a health card number that is provided to each Nova Scotian resident at no charge and is a requirement to obtain any medical care. Baseline clinical and demographic information on the no-ICD group were collected through the ICONS/CVHNS registry, whereas matching data were available for the ICD group within the Queen Elizabeth II ICD registry.

## Definitions

Ischemic heart disease was defined as the presence of coronary disease on coronary angiogram, with at least 70% stenosis in  $\geq 1$  epicardial vessels, previous MI documented as a rise in cardiac enzymes or wall motion abnormality on an echocardiogram, or previous revascularization. Assessment of EF from one of the following methods was accepted: echocardiogram, wall motion study, or left ventriculography. Previous revascularization was defined as documented percutaneous coronary intervention or coronary artery bypass grafting. A history of heart failure in the no-ICD group was defined as having had an admission for heart failure at any time during or before the study period and on history as obtained through data abstraction in the ICONS/CVHNS database. In the ICD group, heart failure was defined in a similar fashion.

## Statistical Analysis

The primary outcome was all-cause mortality. Baseline characteristics were summarized as mean  $\pm$  SD or prevalence (percentage), where appropriate. Categorical variables were compared using the  $\chi^2$  test and continuous variables using the 2-independent sample *t* test in each of the 2 groups. Survival analysis was performed using the Kaplan–Meier method, comparing patients who received an ICD to those who did not. A propensity analysis was performed to control for confounding by indication.<sup>19–21</sup> This technique accounts for the nonrandom assignment to each group, mitigates potential confounding factors and selection biases, and increases statistical efficiency. A propensity score for ICD use was developed using a multivariable logistic regression. This score represents the probability that a patient would receive an ICD.

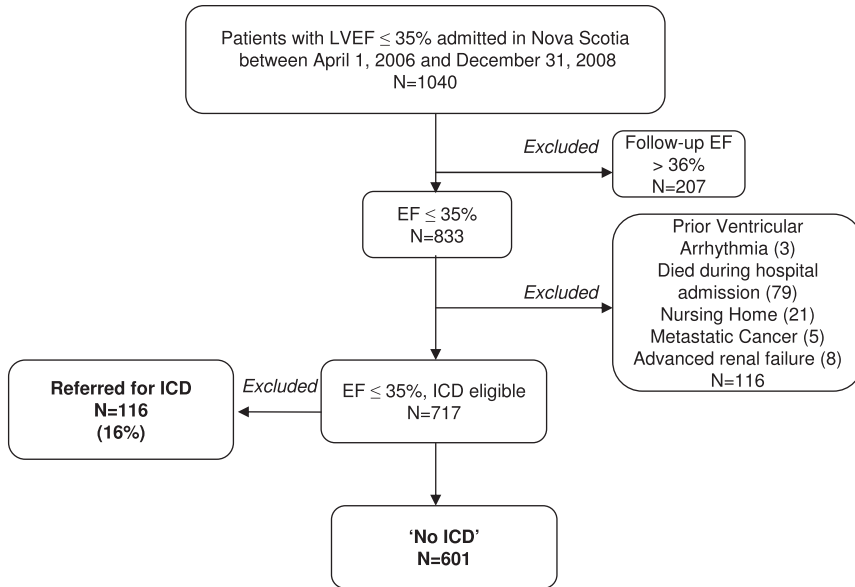
The variables that were entered into the propensity score were gender, age, creatinine, EF, diabetes mellitus, hypertension, peripheral vascular disease,  $\beta$ -blocker, and use of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers. These variables were chosen based on prior analyses demonstrating these as being predictors for mortality in comparable patient populations.<sup>3,5</sup> Propensity scores were used to match patients who received an ICD to a control patient who did not, using a SAS macro (SAS Institute Inc, Cary, NC). A greedy matching procedure selected match pairs initially identical to 5 decimal places of probability.<sup>17,22</sup> If no match existed at 5 decimal places, then matching would occur at 4 decimal places, and so on. If no match existed at 1 decimal place, then that patient receiving an ICD was excluded from the study.

Once the groups were identified, the remaining variables were examined for differences, as described above. Kaplan–Meier analysis was performed to assess mortality in a comparable population. Hazard ratios (HRs) were calculated for mortality. The log-rank test was used to test for significance in mortality between the 2 groups.  $P < 0.05$  was considered statistically significant. All analyses were conducted using SAS version 9.2.

## Results

### Patient Characteristics in the Unmatched Groups

The patient flow in each cohort is shown in Figures 1 and 2. Mean follow-up was 2.7 years in the entire cohort. The ICD cohort was derived using patients from the Queen Elizabeth



**Figure 1.** Flow of patients in the no-ICD cohort. LVEF indicates left ventricular ejection fraction; EF, ejection fraction; ICD, implantable cardioverter-defibrillator.

II ICD registry during the chosen time period. A total of 732 patients had received ICDs during this period. Exclusion of patients based on the province of residence (n=178), secondary prevention indications (n=183), or other (n=81) resulted in a final ICD population of 290 patients. The no-ICD cohort was derived from the ICONS/CVHNS registry. After exclusion for nursing home residency (n=21), metastatic cancer (n=5), renal failure requiring dialysis (n=8), death in hospital (n=79), or improved EF at follow-up (n=207), 717 patients remained during the period examined in both the groups. Of these, 116 were referred or later received an ICD, such that there was an overall ICD referral/implantation rate of 16% from this cohort of identified patients. A total of 601 patients remained in the no-ICD group for analysis. The discharge diagnosis in the no-ICD group was CHF in 47%, acute MI in 21%, both CHF and acute MI in 24%, unstable angina or atrial fibrillation in 4%, and unknown in 3.8%. All baseline EF measurements were made during the hospital admission or within 1 year of discharge. Further follow-up EFs were available in 12%, but 33% were confirmed to have persistent heart failure beyond the index admission.

Baseline characteristics within each group are presented in Table 1. The no-ICD group contained more women (34%

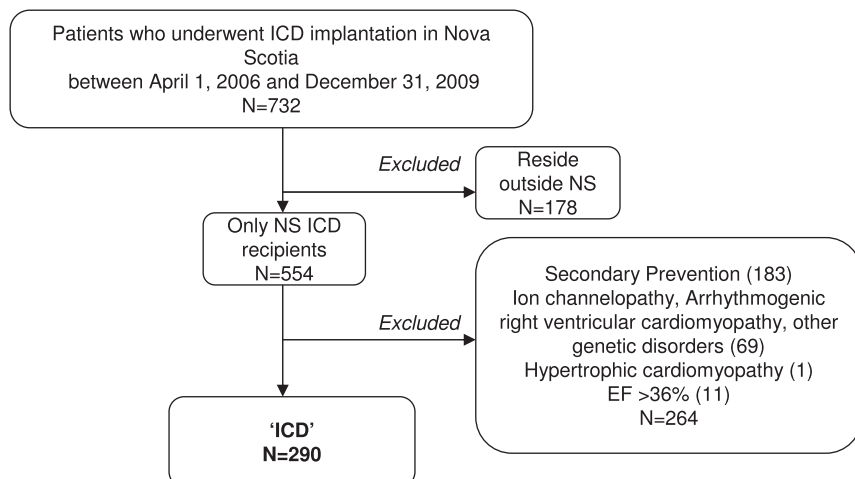
versus 15%), was slightly older (69±13 versus 65±11 years), had a higher EF (26% versus 24%), had a higher incidence of hypertension (59% versus 51%), and lower use of β-blockers (88% versus 98%) and angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers (74% versus 98%) at the time of assessment.

### Mortality in the Unmatched Groups

The 5-year survival rate in the ICD group was 78.6% (95% CI, 71.1–84.3) versus 61.2% (95% CI, 56.4–65.6) in the no-ICD group. Survival analysis in the ICD group versus the no-ICD group demonstrated a survival benefit in the former group (HR, 0.46; 95% CI [0.33–0.64];  $P < 0.0001$ ; Figure 3). There were, however, significant differences between the two groups, as noted previously.

### Patient Characteristics and Mortality in the Propensity-Matched Groups

To adjust for the differences in the 2 populations, a propensity analysis was performed. When adjusted for propensity quintile, the mortality in the ICD-matched group remained



**Figure 2.** Flow of patients in the ICD cohort. ICD indicates implantable cardioverter-defibrillator; NS, Nova Scotia; and EF, ejection fraction.

**Table 1. Baseline Characteristics of Province-Wide Registry-Based Population**

Variable	ICD (n=290)	no-ICD (n=601)	P Value
Women, n (%)	43 (14.8)	206 (34.3)	<0.0001
MI, n (%)	179 (61.7)	339 (56.4)	0.13
Age, mean y (SD)	64.9 (10.9)	69.4 (13.0)	<0.0001
Creatinine, mean mmol/L (SD)	111.2 (38.4)	116.7 (61.3)	0.11
EF, mean % (SD)	23.8 (6.0)	26.0 (7.2)	<0.0001
Previous PCI, n (%)	65 (22.4)	91 (15.1)	0.007
Previous CABG, n (%)	109 (37.6)	61 (10.2)	<0.0001
History of heart failure, n (%)	263 (90.7)	473 (78.7)	<0.0001
Diabetes mellitus, n (%)	111 (38.3)	189 (31.5)	0.04
Hyperlipidemia, n (%)	199 (68.9)	249 (41.4)	<0.0001
Hypertension, n (%)	148 (51.0)	353 (58.7)	0.03
TIA/CVA, n (%)	25 (8.6)	60 (10.0)	0.52
History of atrial fibrillation, n (%)	105 (36.2)	83 (13.8)	<0.0001
Chronic obstructive pulmonary disease, n (%)	49 (16.9)	122 (20.3)	0.23
Peripheral vascular disease, n (%)	31 (10.7)	66 (11.0)	0.90
Previous malignancy, n (%)	29 (10.0)	67 (11.2)	0.60
β-Blocker, n (%)	282 (97.6)	528 (87.9)	<0.0001
ACEi/ARB, n (%)	275 (94.8)	443 (73.7)	<0.0001
Spironolactone, n (%)	94 (32.5)	53 (8.8)	<0.0001
Loop diuretic, n (%)	209 (72.0)	358 (59.6)	0.0003
Warfarin, n (%)	134 (46.4)	184 (30.6)	<0.0001
Digoxin, n (%)	103 (35.6)	149 (24.8)	0.0008
Amiodarone, n (%)	23 (8.0)	22 (3.7)	0.006

ICD indicates implantable cardioverter-defibrillator; MI, myocardial infarction; EF, ejection fraction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; TIA, transient ischemic attack; CVA, cerebrovascular accident; ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers.

lower (HR, 0.55; 95% CI [0.38–0.78]; *P*=0.007; Figure 4). The 5-year survival rate was 78.8% (95% CI, 71.1–84.7) in

the ICD group versus 66.5% (95% CI, 58.4–73.3) in the no-ICD group. Adding adjustment for age, EF, creatinine, use of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers and β-blockers, hypertension, diabetes mellitus, atrial fibrillation, and propensity score, the mortality difference persisted (HR, 0.57; 95% CI [0.39–0.82]; *P*=0.01).

Subjects from each group were then matched based on the propensity analysis. There were 252 patients from each group that met these criteria, and their baseline characteristics are shown in Table 2. The most significant difference that remained after matching was a history of heart failure, present in 91% in the ICD group versus 75% in the no-ICD group. There were significant differences in the use of loop diuretics, spironolactone, and digoxin. After matching patients on these criteria, mortality remained significantly higher in the no-ICD group (HR, 0.59; 95% CI [0.40–0.87]; *P*=0.01; Figure 3).

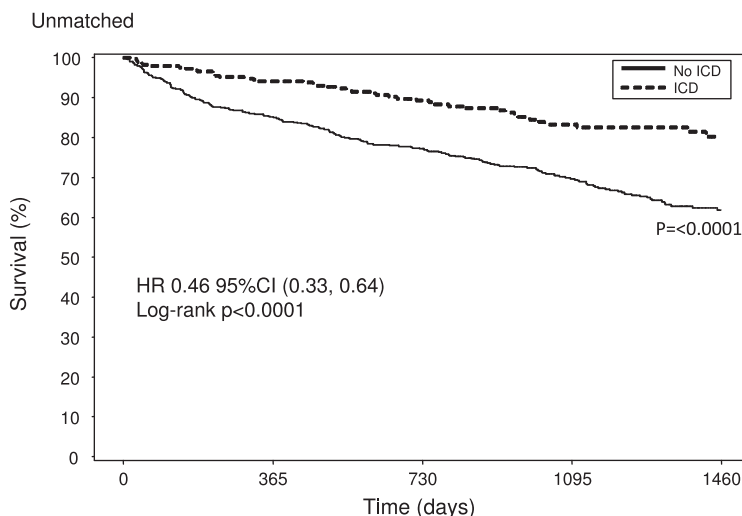
**Appropriate Therapy in the ICD Group**

The patients in the implanted group were examined for appropriate therapy from their ICD, during a mean follow-up of 2.7 years. Seventy-four of 290 (26%; 9.6% per year) patients had received appropriate therapy from their ICD. This included anti-tachycardia pacing in 34% and an appropriate shock in 66%.

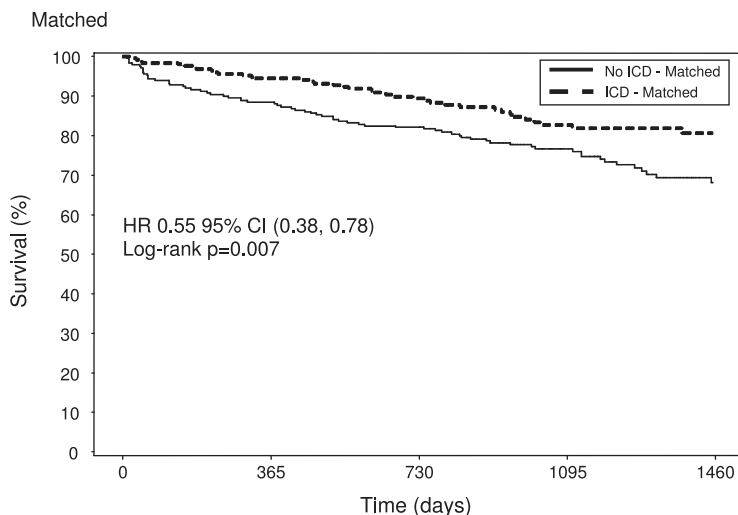
**Discussion**

We found that in a real-world cohort of patients, the use of a primary prevention ICD was associated with a significant survival benefit. Using a propensity analysis, the benefit of a primary prevention ICD remained significant, after controlling for confounding variables that may affect the decision to refer a patient for an ICD.

There are many factors that contribute to all-cause mortality in this population; however, the absolute risk of sudden cardiac death in this population remains 7.5% to 10% over 5 years.<sup>3,5</sup> The ICD group was found to have a 26% rate of appropriate therapy, with 66% of these events requiring a shock to terminate them. The mortality benefit in the ICD group may well be derived from the potential life-saving therapies from their implantable defibrillator. There is no doubt that the competing risk of nonsudden death factors into the benefit derived from



**Figure 3.** Unadjusted survival in the implantable cardioverter-defibrillator (ICD) vs no-ICD groups. HR indicates hazard ratio.



**Figure 4.** Survival in the matched cohorts: implantable cardioverter-defibrillator (ICD) vs no-ICD. HR indicates hazard ratio.

an ICD.<sup>23</sup> After matching patients on prespecified criteria so as to compare groups that were as homogeneous as possible in the context of a real-world population, one with an ICD versus one without, a significant mortality difference remained.

This is the first study to examine the potential benefit of primary prevention ICDs in a population-based cohort. The evidence for this therapy stems from rigorous clinical trials with homogeneous populations. The present study provides further evidence that the clinical trial evidence translates into practice and that the real benefit may actually be larger in the real world, than in the clinical trials. The 5-year mortality rate in our study in the no-ICD group was 33% versus 21% in the ICD group, resulting in a 43% relative risk reduction in total mortality. Although the mortality rates in the placebo arm of the Sudden Cardiac Death in Heart Failure Trial study (36%) and Multicenter Automatic Defibrillator Implantation Trial II (43%) are similar to the no-ICD group, the ICD group in our study demonstrated a comparatively improved survival over what was observed in each of these 2 studies, 29% in Sudden Cardiac Death in Heart Failure Trial and 33% in Multicenter Automatic Defibrillator Implantation Trial II, thereby resulting in an overall lower relative risk reduction in the clinical trial setting (23% and 31%, respectively).<sup>3,5,24</sup> A meta-analysis of 10 randomized trials of primary prevention ICDs revealed a 25% reduction in all-cause mortality.<sup>25</sup> The magnitude of benefit in the real world appears to be exaggerated, beyond what is seen in the clinical trials.

Some of the reasons for this may include the longer term follow-up in the present study, compared with the clinical trials where follow-up was frequently limited to <24 months.<sup>3,4,6-10</sup>; Sudden Cardiac Death in Heart Failure Trial had the longest follow-up, which was 44.5 months, with the exception of the Cardiomyopathy Trial study where follow-up was 5.5 years but only included 104 patients.<sup>7</sup> In this real-world cohort, the mean follow-up is 2.7 years, which may have resulted in a larger effect size, consistent with prior studies that have demonstrated the time dependence of benefit from primary prevention ICDs.<sup>26</sup>

Prior reports of ICD use in population-based cohorts have been reported in the secondary prevention ICD group,<sup>27,28</sup> but only recently have they been reported in primary prevention

ICD recipients.<sup>29,30</sup> Reports in both groups have demonstrated lower ICD implant rates than would be indicated by published guidelines. Prior studies have reported on the overall implant rates but have not been able to directly compare mortality in a broad population of patients who had not appropriately received this therapy. Shah et al<sup>30</sup> reported overall ICD use of 20% in participants of the Get With The Guidelines—Heart Failure registry. A small study performed in post-MI patients in southern Israel found that the ICD implantation rate was 14% in patients with a left ventricular EF≤35% and that the mortality in those patients who did not undergo ICD implantation was 19.7% versus 4.5%.<sup>29</sup> This is consistent with the findings in our study in which the estimated utilization rate was 16% and mortality in the no-ICD group was 18% at 2 years versus 10% in the ICD group. In a study from the Italian Network on CHF, Boriani et al<sup>31</sup> found that approximately half of the patients fulfilled criteria for primary prevention ICDs. The 1-year mortality in this group was higher when compared with the control population of the clinical trials supporting the notion that the real-world population is different from those entering clinical trials. These data are consistent with our findings that the real-world population may be at higher risk for mortality and provide an approximation of the low use of primary prevention ICDs. It is possible that those patients included in the final no-ICD group may have improved their EF to some extent, as in some cases, the EF used as an entry criterion for the no-ICD group may have been measured in the setting of an acute MI. After clinical recommendations, such patients would have had a repeat measure of their EF 1-month post-MI. In the present study, it was not possible to obtain this measurement in all patients; however, if a follow-up EF was available (26% did have a follow-up EF performed; however, 33% were confirmed to have ongoing heart failure), patients were excluded if their EF was >35%; in the absence of this data, we may have overestimated eligibility for a primary prevention ICD. A repeat assessment of EF may have resulted in an improved EF, precluding eligibility. Such patients would most likely be associated with a reduction in all-cause mortality and would result in an overall better prognosis. This may have led to an overestimate of survival in the no-ICD population and an underestimate of the referral rate and implantation

**Table 2. Baseline Characteristics of Matched Groups (1:1)**

Variable	ICD-Matched (n=252)	no-ICD-Matched (n=252)	P Value
Women, n (%)	41 (16.3)	45 (17.9)	0.64
MI, n (%)	158 (62.7)	143 (56.8)	0.17
Age, mean y (SD)	65.5 (10.7)	65.1 (12.8)	0.67
Creatinine, mean mmol/L (SD)	112.6 (39.2)	110.6 (54.4)	0.64
EF, mean % (SD)	24.2 (5.8)	24.1 (7.6)	0.81
Previous PCI, n (%)	52 (20.6)	43 (17.1)	0.31
Previous CABG, n (%)	97 (38.5)	24 (9.5)	<0.0001
History of heart failure, n (%)	230 (91.3)	190 (75.4)	<0.0001
Diabetes mellitus, n (%)	97 (38.5)	91 (36.1)	0.58
Hypertension, n (%)	132 (52.4)	132 (52.4)	1.00
TIA/CVA, n (%)	19 (7.5)	23 (9.1)	0.52
History of atrial fibrillation, n (%)	95 (37.7)	31 (12.3)	<0.0001
Chronic obstructive pulmonary disease, n (%)	42 (16.7)	44 (17.5)	0.81
Peripheral vascular disease, n (%)	26 (10.3)	27 (10.7)	0.88
Previous malignancy, n (%)	29 (11.5)	23 (9.1)	0.38
$\beta$ -Blocker, n (%)	245 (97.2)	245 (97.2)	1.00
ACEi/ARB, n (%)	238 (94.4)	240 (95.2)	0.69
Spironolactone, n (%)	84 (33.3)	26 (10.3)	<0.0001
Loop diuretic, n (%)	177 (70.2)	148 (58.7)	0.007
Warfarin, n (%)	117 (46.4)	94 (37.3)	0.04
Digoxin, n (%)	88 (34.9)	61 (24.2)	0.008
Amiodarone, n (%)	23 (9.1)	9 (3.6)	0.01

ICD indicates implantable cardioverter defibrillator; MI, myocardial infarction; EF, ejection fraction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; TIA, transient ischemic attack; CVA, cerebrovascular accident; ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers.

rate. Despite these limitations, it is clear that the group that is identified as no-ICD has a clearly poorer prognosis compared with the ICD group and that the utilization rate remains low.

It is evident from our data and others that there is lack of adherence to published guidelines.<sup>32</sup> There are many reasons to account for this: system factors, physician factors, and patient factors. System factors include such things as lack of access to appropriate investigations such as echocardiography, decreased access to specialist care in rural areas, delay between published guidelines and adoption into clinical practice, inadequate knowledge translation of the guidelines. Physician factors include bias in the application of therapy, insufficient resources to follow such patients, or the absence of a mechanism to trigger appropriate follow-up. Patient factors may include inadequate education on the risks and benefits of this therapy, refusal based on other issues, inability to reach an urban center because of socioeconomic status. Prior studies have attempted to explore each of these issues. Birnie et al<sup>28</sup> found that in a study of out-of-hospital cardiac arrest survivors in Ontario, Canada, patients were 3 times more likely to receive an ICD if admitted to a teaching hospital compared with a nonteaching hospital. Gravelin et al<sup>33</sup> found that implementation of a simple screening tool that queried EF resulted in a significantly increased referral compared with without one.

Our study encompassed a consecutive series of all eligible patients posthospitalization for a cardiovascular cause in an

entire healthcare system, which is truly a population-based sample of patients eligible for primary prevention ICDs during the period of the study. Although there are patients in the Nova Scotian healthcare system who were not hospitalized during this period and may still have been candidates for an ICD, the vast majority of patients who are referred for prophylactic ICD implantation have been hospitalized in the 12 months before referral.<sup>34</sup> In our own registry of ICD patients, 76% of those referred for prophylactic ICDs had undergone hospitalization in the year before referral. All patients in the registry have had a hospitalization event for a cardiovascular reason in the past. Patients included in a registry are not randomized, and it is unknown to what extent healthcare providers considered ICD referral but did not proceed on grounds not identifiable within registry data fields. We performed a propensity analysis to minimize these effects. Finally, undocumented patient characteristics may have exerted a significant influence on outcomes.

Our population was derived from a hospital-based network, which may have resulted in a bias toward increased mortality at inclusion, although rates of heart failure hospitalization before enrolment were not specified in reports of clinical trials. However, efforts were made to limit this effect. For example, patients who would not have been included in clinical trials such as those with severe renal dysfunction, residents of chronic care facilities with terminal illness, those with

dementia or malignancy or those who were excluded from our comparison group as well. Some of the more potent predictors of mortality, such as EF and presence of CHF, were equivalent or less frequent in the registry-based population and would likely favor an overall lower risk of death.

Increasing use of cardiac interventions,<sup>35</sup> coupled with increasing survival post-MI, and a growing number of heart failure survivors and the burgeoning elderly population<sup>36</sup> have all combined to increase the population of patients eligible for implantation of prophylactic ICDs. This increases the importance of understanding the magnitude of benefit that may be expected and the importance of appropriately applying this therapy. It is projected that the heart failure population will double by the year 2025 such that the absolute number of patients eligible to receive an ICD for primary prevention will likely rise accordingly. Recent studies have further expanded indications for cardiac resynchronization therapy, which has been found to have significant reduction in mortality in mild-to-moderate heart failure.<sup>37,38</sup> This is a significantly increased burden on a healthcare system, whose budget may not be expected to expand at the same rate. The resource implications are not the only consideration in the broader use for these devices. ICDs can have a significant impact on quality of life because of both appropriate and inappropriate shocks.<sup>39,40</sup> The recent increase of device advisories may also pose an additional risk in an ICD recipient.<sup>41,42</sup>

Our findings suggest that clinical trials evidence of the survival benefit from primary prevention ICDs translates to real-world benefit. Patients who have suffered heart failure and MI should be followed up for eligibility for ICD implantation. Identification of those at highest risk is important to provide the best quality of care to the burgeoning population patients with severe ventricular dysfunction.

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### CLINICAL PERSPECTIVE

Primary prevention implantable cardioverter-defibrillators (ICDs) are well established to provide significant mortality reduction in patients with persistently low ejection fraction post–myocardial infarction and with heart failure. We sought to determine utilization rates in a primary prevention ICD-eligible population and mortality in this group compared with a group that had undergone ICD placement. Using 2 comprehensive provincial registries, a primary prevention ICD-eligible cohort was derived from patients who had hospital admission for acute coronary syndrome (including myocardial infarction) or congestive heart failure. The primary prevention ICD population was derived from a prospective, provincial ICD registry. The primary outcome was mortality, derived through linkage with vital statistics. Our study estimated a low rate of utilization for primary prevention ICDs in a contemporary population at risk for sudden death. We found that in a real-world cohort of patients, the use of a primary prevention ICD was associated with a significant survival benefit. Using a propensity analysis, the benefit of a primary prevention ICD remained significant, after controlling for confounding variables that may affect the decision to refer a patient for an ICD. Our findings suggest that clinical trials evidence of the survival benefit from primary prevention ICDs translates to real-world benefit. Patients who have suffered heart failure and myocardial infarction should be followed up for eligibility for ICD implantation. Identification of those at highest risk is important to provide the best quality of care to the burgeoning population of patients with severe ventricular dysfunction.