

# Sex Differences in the Use of Implantable Cardioverter-Defibrillators for Primary and Secondary Prevention of Sudden Cardiac Death

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**S**UDDEN CARDIAC DEATH IS A leading cause of mortality in the United States. Overall, the risk of sudden cardiac death increases with age and is higher in men than in women, although the sex difference narrows and eventually disappears after age 85 years.<sup>1</sup> Patients with significant left ventricular systolic dysfunction are at increased risk for sudden cardiac death, but the majority of events occur in the absence of overt heart disease.<sup>2</sup>

Evidence from the Multicenter Automatic Defibrillator Implantation Trial (MADIT I,<sup>3</sup> MADIT-II,<sup>4</sup> and the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT)<sup>5</sup> supports the use of implantable cardioverter-defibrillator (ICD) therapy for primary prevention of sudden cardiac death among patients with significant left ventricular systolic dysfunction. With the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial, the ICD became first-line therapy for patients who survive a life-threatening ventricular arrhythmia.<sup>6</sup> The efficacy of ICDs for second-

See also pp 1525 and 1564.

**Context** Previous studies of sex differences in the use of implantable cardioverter-defibrillators (ICDs) predate recent expansions in Medicare coverage and did not provide patient follow-up over multiple years.

**Objective** To examine sex differences in ICD use for primary and secondary prevention of sudden cardiac death.

**Design, Setting, and Participants** Analysis of a 5% national sample of research-identifiable files obtained from the US Centers for Medicare & Medicaid Services for the period 1991 through 2005. Patients were those aged 65 years or older with Medicare fee-for-service coverage and diagnosed with acute myocardial infarction and either heart failure or cardiomyopathy but no prior cardiac arrest or ventricular tachycardia (ie, the primary prevention cohort [n=65 917 men and 70 504 women]), or with cardiac arrest or ventricular tachycardia (ie, the secondary prevention cohort [n=52 252 men and 47 411 women]), from 1999 through 2005.

**Main Outcome Measures** Receipt of ICD therapy and all-cause mortality at 1 year.

**Results** In the 2005 primary prevention cohort, 32.3 per 1000 men and 8.6 per 1000 women received ICD therapy within 1 year of cohort entry. In multivariate analyses, men were more likely than women to receive ICD therapy (hazard ratio [HR], 3.15; 95% confidence interval [CI], 2.86-3.47). Among men and women alive at 180 days after cohort entry, the hazard of mortality in the subsequent year was not significantly lower among those who received ICD therapy (HR, 1.01; 95% CI, 0.82-1.23). In the 2005 secondary prevention cohort, 102.2 per 1000 men and 38.4 per 1000 women received ICD therapy. Controlling for demographic variables and comorbid conditions, men were more likely than women to receive ICD therapy (HR, 2.44; 95% CI, 2.30-2.59). Among men and women alive at 30 days after cohort entry, the hazard of mortality in the subsequent year was significantly lower among those who received ICD therapy (HR, 0.65; 95% CI, 0.60-0.71).

**Conclusion** In the Medicare population, women are significantly less likely than men to receive ICD therapy for primary or secondary prevention of sudden cardiac death.

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ary prevention of sudden cardiac death has been further established over the past decade.<sup>7</sup>

Medicare coverage of ICDs has expanded with the accumulating evidence, but many eligible beneficiaries still do not receive them. Previous studies have explored racial differences in the use of ICDs.<sup>8,9</sup> Previous studies also have documented important sex differences in ICD use, but those studies

predate recent expansions in coverage<sup>10,11</sup> or did not provide patient follow-up over multiple years.<sup>9,12</sup> There-

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fore, we examined sex differences in the use of ICD therapy for primary and secondary prevention of sudden cardiac death in a nationally representative, longitudinal sample of Medicare beneficiaries from 1999 through 2005.

## METHODS

### Data Sources

We analyzed a 5% national sample of Medicare inpatient, outpatient, and carrier standard analytic files and the corresponding denominator files. The inpatient files contain institutional claims for facility costs covered under Medicare Part A, and the outpatient files contain claims from institutional outpatient providers (eg, hospital outpatient departments, ambulatory surgery centers). The carrier files contain noninstitutional provider claims for services covered under Medicare Part B. The denominator files contain demographic data and information about program eligibility and enrollment. Race/ethnicity are reported by Medicare beneficiaries at the time of enrollment and recorded in the denominator files. In this analysis, we used the reported categories "white" and "black" and combined all others as "other/unknown."

We obtained research-identifiable files for 1991 through 2005 from the Centers for Medicare & Medicaid Services. We included persons living in the United States who were 65 years or older on the date of cohort entry, and we restricted the analysis to claims filed during periods of fee-for-service coverage. The institutional review board of the Duke University Health System approved the study.

### Study Population

We used diagnosis codes to identify primary and secondary prevention cohorts, focusing on patients who became eligible for ICD therapy between 1999 and 2005 because evidence supporting ICD use in these cohorts emerged in 1996 and 1997<sup>4,6</sup> and because we wanted to allow a lag period of adoption of at least 1 year.

In the primary prevention cohort, we included beneficiaries for whom a di-

agnosis of acute myocardial infarction (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] code 410 or 412) and either heart failure (428) or cardiomyopathy (425.4) were reported on an inpatient, outpatient, and/or carrier claim. Diagnoses may have been reported on separate claims (ie, claims from different files or different dates), although the date of cohort entry—defined as the date of the second qualifying diagnosis—must have occurred between 1999 and 2005. Beneficiaries with a prior diagnosis of cardiac arrest (427.5) or ventricular tachycardia (427.1, 427.41, and 427.42) were excluded. On subsequent diagnosis of cardiac arrest or ventricular tachycardia, 9864 beneficiaries (7.2%) in the primary prevention cohort progressed to the secondary prevention cohort.

The secondary prevention cohort included beneficiaries for whom a diagnosis of cardiac arrest or ventricular tachycardia was reported on a single inpatient, outpatient, or carrier claim between 1999 and 2005. We excluded patients with a diagnosis of cardiac arrest or ventricular tachycardia before 1999.

We identified receipt of ICD therapy by the presence of *Current Procedural Terminology* code 33245, 33246, or 33249 on a single carrier claim. New ICDs and upgrades to existing devices were combined for these analyses. We excluded beneficiaries who received a device before 1999 or before cohort entry (n=305).

### Statistical Analysis

We examined characteristics of patients in each cohort by sex. Categorical variables are presented as percentages, and continuous variables are presented as means with SDs. We identified comorbid conditions using the coding algorithms described by Birman-Deych et al<sup>13</sup> and Quan et al.<sup>14</sup> Specifically, we searched all inpatient, outpatient, and carrier claims for 365 days preceding the date of cohort entry for evidence of coronary heart disease (ICD-9-CM codes 410-414, 429.2, and V45.81), hypertension (401-405 and

437.2), cerebrovascular disease (362.34 and 430-438), dementia (290, 294.1, and 331.2), chronic pulmonary disease (416.8, 416.9, 490-505, 506.4, 508.1, and 508.8), diabetes mellitus (250), peripheral vascular disease (093.0 437.3, 440, 441, 443.1-443.9, 47.1, 557.1, 557.9, and V43), renal disease (403.01, 403.11, 403.91, 404.02, 404.036, 404.12, 404.13, 404.92, 404.93, 582, 583.0-583.7, 585, 586, 588.0, V42.0, V45.1, and V56), and metastatic solid tumor (196-199).

We used the cumulative incidence function to estimate the proportion of patients in each cohort who received ICD therapy. This approach accounts for both censoring and competing risks.<sup>15</sup> Censoring occurred when patients switched to managed care or reached the end of the study. Patients in the primary prevention cohort were subject to the competing risks of mortality and progression to the secondary prevention cohort. Patients in the secondary prevention cohort were subject to the competing risk of mortality. In any interval, the incidence of ICD use is the product of the ICD-specific hazard rate for that interval applied to the cumulative probability of being event-free at the beginning of that interval. The cumulative incidence is simply the accumulation of these quantities over time.

To examine the unadjusted relationships between study variables and the number of days from cohort entry to ICD therapy, we used a Cox proportional hazards model, which accounts for both censoring and competing risks. We also fit a multivariate Cox proportional hazards model using age, race, comorbid conditions, geographic region, and year of cohort entry to estimate the independent effect of sex on ICD use.

To examine the robustness of the findings, we replicated the analyses after stratifying by age (<75 years vs ≥75 years). We reasoned that any observed sex difference might simply reflect that women tend to be older when diagnosed with ischemic heart disease or cardiac arrest and thus may be less

likely to be recommended for ICD therapy. In addition, because not all forms of ventricular tachycardia require ICD therapy, we replicated the analysis after limiting the secondary prevention cohort to beneficiaries with only an incident cardiac arrest.

We used landmark analysis to explore the effect of ICD therapy on all-cause mortality at 1 year after the landmark date.<sup>16</sup> Patients in the primary prevention cohort who were alive at 180 days after cohort entry were classified according to receipt of ICD therapy at 180 days. This landmark generally reflects the recommendation to defer ICD therapy for 1 to 3 months after myocardial infarction or a revascularization procedure and until the patient is receiving optimal medical therapy.<sup>17</sup> Patients in the secondary prevention cohort who were alive at 30 days after cohort entry were classified according to receipt of ICD therapy at 30 days.

For each cohort, we explored the effect of ICD use on survival using inverse-weighted Cox proportional hazards models, with weights based on the probability of treatment.<sup>18</sup> In each prevention cohort, we estimated the probability of receiving ICD therapy using logistic regression models that included year of cohort entry, age, sex, race, and comorbid conditions and risks documented in the prior year (ie, myocardial infarction, congestive heart failure, hypertension, chronic pulmonary disease, cerebrovascular disease, dementia, diabetes mellitus, metastatic solid tumor, peripheral vascular disease, and renal disease). We estimated the overall effect of receiving ICD therapy on mortality, as well as sex-specific effects.

We used SAS version 9.1.5 (SAS Institute Inc, Cary, North Carolina) for all analyses;  $P < .05$  was considered statistically significant.

## RESULTS

TABLE 1 shows baseline characteristics of the primary and secondary prevention cohorts. In the primary prevention cohort (n=136 421 [65 917 men, 70 504 women]), women were

**Table 1.** Baseline Characteristics by Prevention Cohort and Sex

Characteristic	Primary Prevention Cohort (n = 136 421)		Secondary Prevention Cohort (n = 99 663)	
	Men (n = 65 917)	Women (n = 70 504)	Men (n = 52 252)	Women (n = 47 411)
Age, mean (SD), y	78 (7.0)	80 (7.7)	77 (7.1)	79 (7.8)
Race, %				
Black	6.1	8.9	8.8	12.4
White	90.4	87.4	87.8	84.1
Other/unknown	3.5	3.7	3.4	3.6
Comorbid conditions, %				
Cerebrovascular disease	34.3	36.0	33.3	34.9
Chronic pulmonary disease	44.2	41.8	44.8	40.9
Coronary heart disease	96.7	95.6	74.1	63.3
Dementia	8.3	12.9	8.5	13.7
Diabetes mellitus	39.4	40.3	36.4	36.1
Hypertension	81.0	87.7	76.4	82.5
Metastatic solid tumor	3.9	2.9	5.1	4.3
Peripheral vascular disease	34.3	33.5	32.4	31.1
Renal disease	16.7	14.3	18.4	15.8
Geographic region, %				
Midwest	27.3	27.2	26.4	24.7
Northeast	20.3	22.0	20.1	21.1
South	38.8	38.8	39.9	41.6
West	13.5	12.1	13.7	12.7

more likely than men to have hypertension or dementia in the year before cohort entry but less likely to have renal disease. Over the course of follow-up, 5761 men (8.7%) and 4103 women (5.8%) progressed to the secondary prevention cohort; 27 719 men (42.1%) and 32 851 women (46.6%) died; and 1938 men (2.9%) and 2162 women (3.1%) switched to managed care. In the secondary prevention cohort (n=99 663 [52 252 men, 47 411 women]), women were less likely than men to have ischemic heart disease or chronic pulmonary disease and more likely to have hypertension or dementia. From 1999 through 2005, 31 322 men (59.9%) and 30 058 women (63.4%) died, and 915 men (1.8%) and 930 women (2.0%) switched to managed care.

### Cumulative Rates of ICD Use

TABLE 2 shows the cumulative rates of ICD use by cohort, sex, and year of cohort entry. The outermost diagonal of the table shows the cumulative incidence of ICD use in each cohort by the end of the study period. From 1999 through 2005, there was a 4-fold in-

crease in the 1-year cumulative incidence of ICD use among men, and there was steady subsequent growth in these rates for men across all years of cohort entry. Although the pattern was similar among women, absolute rates of ICD use were approximately 75% lower than those for men at each point for each entry cohort.

In the secondary prevention cohort, rates of ICD use among men within a year of the qualifying diagnosis more than doubled from 1999 through 2004. Rates of ICD use increased steadily across all years of cohort entry, with later cohorts having cumulative rates that were markedly higher than those in earlier cohorts. Absolute rates were again much lower among women. In contrast to the pattern among men, the rate of use among women who entered the cohort in 2000 or later increased only slightly after the first year.

### Predictors of ICD Use

TABLE 3 shows univariate and multivariate predictors of ICD use. The results of the univariate and multivariate

ate analyses were largely consistent. Controlling for comorbid conditions, geographic region, and year of cohort entry, men in the primary prevention cohort were more likely than women to receive ICD therapy (hazard ratio [HR], 3.15; 95% confidence interval [CI], 2.86-3.47). Black patients were less likely than white patients to receive ICD therapy (HR, 0.85; 95% CI, 0.71-1.00). White men were most likely to receive ICDs (HR for black men, 0.77; 95% CI, 0.62-0.95; other men, 0.88; 95% CI, 0.68-1.15; white women, 0.31; 95% CI, 0.28-0.35; black women, 0.32; 95% CI, 0.24-0.42; and other women, 0.24; 95% CI, 0.15-0.39). De-

mentia and a diagnosis of metastatic solid tumor in the year before cohort entry were negatively associated with ICD use.

In the secondary prevention cohort, men were more likely than women to receive ICD therapy (HR, 2.44; 95% CI, 2.30-2.59), and black patients were less likely than white patients to receive ICD therapy (HR, 0.71; 95% CI, 0.64-0.79). White men were most likely to receive ICDs (HR for black men, 0.71; 95% CI, 0.62-0.80; other men, 0.78; 95% CI, 0.65-0.93; white women, 0.41; 95% CI, 0.38-0.44; black women, 0.29; 95% CI, 0.24-0.35; and other women, 0.33; 95% CI, 0.25-0.45).

Coronary heart disease and diabetes mellitus were independently and positively associated with ICD use, whereas dementia, renal disease, and metastatic solid tumor documented in the year before cohort entry were independently and negatively associated with ICD use.

Sex differences persisted when we stratified the multivariate analysis by age and adjusted for race, comorbid conditions, and geographic region. Among patients in the primary prevention cohort younger than 75 years (n=41 125), men were more likely than women to receive ICD therapy (HR, 2.61; 95% CI, 2.30-

**Table 2.** Cumulative Rates of Implantable Cardioverter-Defibrillator (ICD) Use by Year of Cohort Entry

Sex and Year of Cohort Entry	No. of ICDs by December 31, 2005	Cumulative Rate of ICD Use <sup>a</sup>						
		Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
<b>Primary Prevention Cohort</b>								
Men								
1999 (n = 9449)	276	7.6	10.8	13.8	19.1	23.2	27.7	31.0
2000 (n = 9364)	266	7.8	12.5	17.6	21.9	26.9	30.7	
2001 (n = 9288)	276	11.0	15.7	20.9	26.6	33.3		
2002 (n = 9411)	313	17.0	23.6	30.2	36.1			
2003 (n = 9756)	315	19.8	27.9	36.0				
2004 (n = 9568)	299	25.6	36.2					
2005 (n = 9081)	242	32.3						
Women								
1999 (n = 10 071)	56	1.8	2.5	2.9	3.8	4.4	5.0	6.0
2000 (n = 10 130)	73	2.3	3.1	3.7	5.1	6.8	7.6	
2001 (n = 9995)	93	3.2	4.7	6.1	7.9	10.6		
2002 (n = 10 248)	89	4.3	5.8	7.2	10.1			
2003 (n = 10 300)	104	5.8	8.7	10.9				
2004 (n = 10 238)	75	6.3	8.2					
2005 (n = 9522)	65	8.6						
<b>Secondary Prevention Cohort</b>								
Men								
1999 (n = 7124)	484	51.0	54.3	56.3	60.1	63.9	66.7	70.1
2000 (n = 7185)	551	57.7	61.5	65.4	69.3	74.6	79.1	
2001 (n = 7117)	645	74.2	78.2	83.0	89.2	92.8		
2002 (n = 7592)	838	95.7	101.5	107.1	113.0			
2003 (n = 7917)	868	99.1	106.8	113.3				
2004 (n = 7770)	864	107.4	116.0					
2005 (n = 7547)	721	102.2						
Women								
1999 (n = 6855)	156	16.9	17.8	19.3	20.2	21.3	22.1	23.4
2000 (n = 6747)	146	18.1	19.2	19.6	20.7	21.3	22.5	
2001 (n = 6617)	160	20.0	22.0	23.4	24.1	24.3		
2002 (n = 6780)	241	30.7	32.4	34.9	36.3			
2003 (n = 6806)	251	34.3	35.9	37.5				
2004 (n = 6843)	246	34.4	37.2					
2005 (n = 6763)	240	38.4						

<sup>a</sup>Values shown are per 1000 Medicare beneficiaries. Values in outermost diagonal indicate the cumulative incidence of ICD use in each cohort by the end of the study period.

2.97). Among patients aged 75 years or older (n=95 296), men were more likely than women to receive ICD therapy (HR, 3.73; 95% CI, 3.24-4.29). Similarly, among patients in the secondary prevention cohort younger than 75 years (n=35 282), men were more likely than women to receive ICD therapy (HR, 2.19; 95% CI, 2.01-2.38). Among patients aged 75 years or older (n=64 381), men were more likely than women to receive ICD therapy (HR, 2.66; 95% CI, 2.45-2.90). When the secondary prevention cohort was restricted to survivors of cardiac arrest, men were more likely than women to receive ICD

therapy (HR, 1.96; 95% CI, 1.66-2.31).

### Relationship Between ICD Use and Mortality

At 180 days after entry into the primary prevention cohort, 47 729 men (72.4%) and 49 261 women (69.9%) were alive and not censored (TABLE 4). Overall, the unadjusted hazard of mortality for the subsequent year was 17% lower among patients who received ICD therapy in the first 180 days, although the difference was not statistically significant (HR, 0.83; 95% CI, 0.68-1.01). Unadjusted stratified analyses suggested a significant survival ben-

efit for women. After adjustment for age, comorbid conditions, year of cohort entry, and the probability of treatment, the hazard of mortality at 1 year after the landmark date was not significantly lower among those who received ICD therapy in the first 180 days (HR, 1.01; 95% CI, 0.82-1.23). Although unadjusted analyses suggested a significant survival benefit among women, the adjusted association was not statistically significant for either men or women.

Of the 99 663 patients in the secondary prevention cohort, 54 342 (54.5%) were alive and not censored 30 days after cohort entry. Overall, the hazard of

**Table 3.** Predictors of Implantable Cardioverter-Defibrillator Use by Prevention Cohort

Variable	HR (95% CI)			
	Primary Prevention Cohort		Secondary Prevention Cohort	
	Univariate Model	Multivariate Model <sup>a</sup>	Univariate Model	Multivariate Model <sup>a</sup>
Age, per y	0.92 (0.91-0.92) <sup>b</sup>	0.93 (0.93-0.94) <sup>b</sup>	0.94 (0.94-0.94) <sup>b</sup>	0.95 (0.95-0.95) <sup>b</sup>
Male sex	3.84 (3.50-4.22) <sup>b</sup>	3.15 (2.86-3.47) <sup>b</sup>	3.19 (3.01-3.39) <sup>b</sup>	2.44 (2.30-2.59) <sup>b</sup>
Race				
Black	0.78 (0.66-0.92) <sup>c</sup>	0.85 (0.71-1.00)	0.62 (0.56-0.69) <sup>b</sup>	0.71 (0.64-0.79) <sup>b</sup>
White	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Other/unknown	0.83 (0.66-1.05)	0.85 (0.68-1.08)	0.75 (0.65-0.88) <sup>c</sup>	0.79 (0.67-0.92) <sup>c</sup>
Comorbid conditions				
Cerebrovascular disease	0.79 (0.73-0.87) <sup>b</sup>	0.91 (0.83-0.99) <sup>d</sup>	0.96 (0.91-1.01)	0.97 (0.92-1.03)
Chronic pulmonary disease	0.93 (0.86-1.01)	0.89 (0.82-0.97) <sup>b</sup>	1.09 (1.04-1.15) <sup>c</sup>	0.98 (0.93-1.03)
Coronary heart disease	3.92 (2.70-5.69) <sup>b</sup>	3.11 (2.14-4.51) <sup>b</sup>	6.19 (5.61-6.83) <sup>b</sup>	5.33 (4.82-5.89) <sup>b</sup>
Dementia	0.18 (0.13-0.24) <sup>b</sup>	0.29 (0.21-0.41) <sup>b</sup>	0.21 (0.18-0.25) <sup>b</sup>	0.32 (0.27-0.38) <sup>b</sup>
Diabetes mellitus	1.13 (1.05-1.22) <sup>c</sup>	1.02 (0.94-1.11)	1.30 (1.23-1.36) <sup>b</sup>	1.10 (1.04-1.16) <sup>c</sup>
Hypertension	0.81 (0.73-0.89) <sup>b</sup>	0.85 (0.77-0.94) <sup>c</sup>	1.16 (1.09-1.24) <sup>b</sup>	1.04 (0.97-1.11)
Metastatic solid tumor	0.59 (0.42-0.83) <sup>c</sup>	0.57 (0.41-0.80) <sup>c</sup>	0.35 (0.28-0.43) <sup>b</sup>	0.36 (0.29-0.44) <sup>b</sup>
Peripheral vascular disease	0.90 (0.82-0.98) <sup>d</sup>	0.94 (0.86-1.02)	1.07 (1.01-1.12)	0.96 (0.91-1.01)
Renal disease	1.01 (0.90-1.15)	0.98 (0.86-1.11)	1.04 (0.97-1.12)	0.90 (0.84-0.97) <sup>c</sup>
Region				
Midwest	1.12 (0.98-1.29)	1.17 (1.02-1.34) <sup>d</sup>	1.26 (1.15-1.37) <sup>b</sup>	1.22 (1.12-1.33) <sup>b</sup>
Northeast	1.04 (0.90-1.20)	1.19 (1.03-1.38) <sup>d</sup>	1.10 (1.00-1.20) <sup>d</sup>	1.10 (1.01-1.20) <sup>d</sup>
South	1.12 (0.98-1.27)	1.14 (1.00-1.30)	1.11 (1.02-1.20) <sup>d</sup>	1.09 (1.00-1.18)
West	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Year of incidence				
1999	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
2000	1.17 (1.00-1.37)	1.19 (1.02-1.39) <sup>d</sup>	1.13 (1.02-1.26) <sup>d</sup>	1.15 (1.03-1.28) <sup>d</sup>
2001	1.53 (1.31-1.79) <sup>b</sup>	1.57 (1.34-1.84) <sup>b</sup>	1.38 (1.24-1.53) <sup>b</sup>	1.38 (1.24-1.53) <sup>b</sup>
2002	2.12 (1.81-2.48) <sup>b</sup>	2.24 (1.91-2.62) <sup>b</sup>	1.85 (1.67-2.04) <sup>b</sup>	1.81 (1.64-2.01) <sup>b</sup>
2003	2.79 (2.38-3.27) <sup>b</sup>	2.92 (2.49-3.42) <sup>b</sup>	1.99 (1.80-2.20) <sup>b</sup>	1.94 (1.76-2.15) <sup>b</sup>
2004	3.37 (2.85-3.98) <sup>b</sup>	3.59 (3.04-4.24) <sup>b</sup>	2.05 (1.86-2.27) <sup>b</sup>	2.04 (1.85-2.26) <sup>b</sup>
2005	4.59 (3.84-5.47) <sup>b</sup>	4.88 (4.09-5.83) <sup>b</sup>	2.02 (1.82-2.24) <sup>b</sup>	2.05 (1.85-2.28) <sup>b</sup>

Abbreviations: CI, confidence interval; HR, hazard ratio.

<sup>a</sup>Multivariate models include all variables listed.

<sup>b</sup>P < .001.

<sup>c</sup>P < .01.

<sup>d</sup>P < .05.

**Table 4.** Unadjusted and Adjusted Mortality at 1 Year by Cohort

	No. of Patients at Risk	No. of Deaths/Total No. (%) of Patients With ICD	No. of Deaths/Total No. (%) of Patients Without ICD	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
<b>Primary Prevention Cohort (ICD Use Within 180 Days of Cohort Entry)</b>					
Overall	96 990	97/931 (10.4)	12 881/96 059 (13.4)	0.83 (0.68-1.01)	1.01 (0.82-1.23)
Men	47 729	80/714 (11.2)	6167/47 015 (13.1)	0.91 (0.73-1.14)	1.05 (0.81-1.36)
Women	49 261	17/217 (7.8)	6714/49 044 (13.7)	0.62 (0.38-0.99) <sup>a</sup>	0.93 (0.67-1.29)
<b>Secondary Prevention Cohort (ICD Use Within 30 Days of Cohort Entry)</b>					
Overall	54 342	511/4673 (10.9)	8344/49 669 (16.8)	0.63 (0.57-0.69) <sup>b</sup>	0.65 (0.60-0.71) <sup>b</sup>
Men	29 333	396/3604 (11.0)	4502/25 729 (17.5)	0.60 (0.54-0.67) <sup>b</sup>	0.62 (0.55-0.69) <sup>b</sup>
Women	25 009	115/1069 (10.8)	3842/23 940 (16.0)	0.66 (0.55-0.79) <sup>b</sup>	0.71 (0.62-0.81) <sup>b</sup>

Abbreviations: CI indicates confidence interval; HR, hazard ratio; ICD, implantable cardioverter-defibrillator.

<sup>a</sup> $P < .01$ .

<sup>b</sup> $P < .001$ .

mortality was 37% lower among patients who received ICD therapy within 30 days of cohort entry (HR, 0.63; 95% CI, 0.57-0.69). After adjustment for age, comorbid conditions, year of cohort entry, and the probability of treatment, the hazard of mortality remained significantly lower among patients who received ICD therapy within 30 days. The association was consistent for men (HR, 0.62; 95% CI, 0.55-0.69) and women (HR, 0.68; 95% CI, 0.60-0.78).

## COMMENT

In a nationally representative sample of 236 084 Medicare beneficiaries, we found significant sex differences in the use of ICD therapy for the prevention of sudden cardiac death. Among patients with prior myocardial infarction and either cardiomyopathy or heart failure (ie, the primary prevention cohort), men were 3.2 times more likely than women to receive ICD therapy. Among patients with a prior diagnosis of cardiac arrest or ventricular tachycardia (ie, the secondary prevention cohort), men were 2.4 times more likely than women to receive ICD therapy.

We did not find that sex differences in the use of ICDs are becoming less pronounced. In an analysis of National Hospital Discharge Survey data from 1996 through 2001, Voigt et al<sup>12</sup> reported that 23.6% of women and 35.4% of men received ICD therapy but that the disparity disappeared by 2001. In our analysis of Medicare beneficiaries from 1999 through 2005, although rates of ICD use increased sub-

stantially for both men and women, sex differences persisted within and across prevention cohorts and by year of cohort entry.

Our findings are generally consistent with a 2002 analysis of Medicare beneficiaries with ischemic cardiomyopathy. Without adjustment for comorbidity and excluding ICD implantation performed on an outpatient basis or in subsequent years, Gauri et al<sup>9</sup> found that men were 2.9 times more likely than women to receive an ICD. In addition, we found a steady increase in the cumulative incidence of ICD use in the years after initial diagnosis.

Sex differences in the use of ICDs may reflect a variety of factors. Because women were older than men at presentation, physicians may have been less likely to recommend ICD therapy. Current guidelines recommend ICDs for patients who "have reasonable expectation of survival with good functional status for more than 1 year."<sup>17</sup> However, our stratified analysis provides solid evidence that age alone does not explain the observed difference. Among beneficiaries younger than 75 years, men were twice as likely as women to receive ICD therapy for either primary or secondary prevention of sudden cardiac death.

Women also may differ from men by having clinical characteristics that make them inappropriate candidates for ICD therapy. For example, in primary prevention trials, the survival benefit of prophylactic ICD therapy has been shown only among patients with sig-

nificant left ventricular dysfunction. Women are more likely than men to have isolated diastolic congestive heart failure (57% vs 43% in Olmsted County, Minnesota<sup>19</sup>), so rates of ICD use may be justifiably lower in women but probably not by the magnitude we observed. Medicare claims data contain no information on left ventricular ejection fraction, so we could not examine this explanation. However, this explanation would not apply to the secondary prevention cohort. The prevalence of ventricular tachycardia or ventricular fibrillation from reversible causes is only slightly higher among women,<sup>20</sup> so it would not account for the significant sex difference in rates of ICD use for secondary prevention.

Moreover, relatively few women were included in the landmark trials that established the survival benefit of ICD therapy, so physicians may perceive differential benefit between men and women. However, in the Multicenter Unsustained Tachycardia Trial (MUSTT), Russo et al<sup>21</sup> found no significant differences between men and women with respect to the percentage of patients for whom ICD therapy was recommended (62% of women vs 51% of men;  $P = .25$ ). Moreover, there were no significant differences in refusal rates between men and women for whom ICD therapy was recommended,<sup>21</sup> which suggests that sex differences in patient preferences do not explain our findings.

Other findings from our study are also noteworthy. Controlling for measured confounders, black patients in both pre-

vention cohorts were 30% less likely than white patients to receive ICD therapy during the study period. This finding is consistent with those of other reports<sup>9,11,12</sup> and may reflect many factors, including physician attitudes, patient preferences, and differential access to medical resources and facilities.<sup>22,23</sup>

In both prevention cohorts, the rates of ICD use were low among both men and women, although there was steady growth in the cumulative rates of ICD use over time. These patterns reflect the expansion of Medicare coverage for ICD therapy, including reimbursement for prophylactic use in patients with ischemic cardiomyopathy. With the expansion of coverage, the Centers for Medicare & Medicaid Services requires that detailed clinical data be reported on all patients receiving an ICD.<sup>24</sup> The American College of Cardiology National Cardiovascular Data Registry will serve as the repository for these data and, when linked with claims data, will provide an important tool for exploring sex differences in the effectiveness of ICDs. However, the registry will not include data for all persons eligible to receive ICD therapy. Consequently, claims data will remain an important, albeit imperfect, source of information regarding differences in care.

In our observational analysis of survival, we found a significant survival benefit of ICD therapy in the secondary prevention cohort, overall and by sex. The results did not suggest a significant mortality benefit of ICD therapy in the primary prevention cohort. However, ICD therapy was not randomly assigned, and information on left ventricular ejection fraction—a critical variable likely related both to receipt of ICD therapy and to mortality—was not available. To the extent that ICDs are implanted selectively in patients who have low ejection fraction (and are therefore at high risk of mortality), the results may suggest that ICDs have improved the survival of high-risk patients so that their survival is now similar to that of low-risk patients. Without key clinical data, however, we cannot test that hypothesis. At best, the re-

sults provide a glimpse—albeit a crude one—of the effectiveness of ICD therapy for primary and secondary prevention of sudden cardiac death in elderly patients.

Our analysis has several limitations. First, administrative data lack important clinical information, such as data on ventricular function, the nature of the ventricular tachycardia, and the severity of comorbid conditions. Thus, the primary prevention cohort likely included beneficiaries with preserved systolic function, and the secondary prevention cohort likely included individuals with nonsustained ventricular tachycardia—groups in which a survival benefit from ICD therapy has not been demonstrated. The higher proportion of women with heart failure and preserved systolic function may explain some of the observed difference in the primary prevention cohort, but it is unlikely to account for the entire disparity. In addition, the results were similar in the sensitivity analysis in which only survivors of cardiac arrest were included in the secondary prevention cohort.

Second, no claims are filed when a beneficiary moves to managed care, so we missed all ICD implantations that occurred during periods of managed-care coverage. Thus, we may have understated the cumulative incidence of ICD use, although an effect on the sex difference is unlikely because there were no sex differences in selection to managed care.

Third, we observed patients only from the time at which they became eligible for Medicare, so ICD use before age 65 years was not included in the analysis. Because the average age at qualifying diagnosis exceeded 77 years in both cohorts and because we have data from 1991 forward, the impact of this limitation is unlikely to be significant. Moreover, by limiting the analysis to the Medicare population, we reduced the influence of sex differences in access to care.

Fourth, we have no information regarding patient preferences for ICD therapy, so we cannot account for pos-

sible sex differences in refusal rates. Finally, ICD therapy was not randomly assigned, and the decision to use ICDs may be related to unmeasured confounders. Therefore, the mortality results should be interpreted with caution.

## CONCLUSIONS

In this longitudinal analysis of Medicare beneficiaries at high risk for sudden cardiac death, we found significant sex differences in the use of ICD therapy from 1999 through 2005. Our findings in this cohort of elderly patients differ from an earlier study that suggested a narrowing of the gap between men and women, and they highlight the need for an improved understanding of sex differences in patterns of care. Moreover, it is essential that these findings be verified in data sets that include left ventricular ejection fraction and robust measures of comorbidity.

**Author Contributions:** Dr Curtis had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Curtis, Al-Khatib, Hernandez.

**Acquisition of data:** Curtis, Shea.

**Analysis and interpretation of data:** Curtis, Al-Khatib, Shea, Hammill, Hernandez, Schulman.

**Drafting of the manuscript:** Curtis.

**Critical revision of the manuscript for important intellectual content:** Curtis, Al-Khatib, Shea, Hammill, Hernandez, Schulman.

**Statistical analysis:** Curtis, Shea, Hammill.

**Obtained funding:** Curtis.

**Administrative, technical, or material support:** Shea, Schulman.

**Study supervision:** Al-Khatib, Schulman.

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