

SPECIAL ARTICLE

Cost-Effectiveness of Implantable Cardioverter–Defibrillators

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ABSTRACT

BACKGROUND

Eight randomized trials have evaluated whether the prophylactic use of an implantable cardioverter–defibrillator (ICD) improves survival among patients who are at risk for sudden death due to left ventricular systolic dysfunction but who have not had a life-threatening ventricular arrhythmia. We assessed the cost-effectiveness of the ICD in the populations represented in these primary-prevention trials.

METHODS

We developed a Markov model of the cost, quality of life, survival, and incremental cost-effectiveness of the prophylactic implantation of an ICD, as compared with control therapy, among patients with survival and mortality rates similar to those in each of the clinical trials. We modeled the efficacy of the ICD as a reduction in the relative risk of death on the basis of the hazard ratios reported in the individual clinical trials.

RESULTS

Use of the ICD increased lifetime costs in every trial. Two trials — the Coronary Artery Bypass Graft (CABG) Patch Trial and the Defibrillator in Acute Myocardial Infarction Trial (DINAMIT) — found that the prophylactic implantation of an ICD did not reduce the risk of death and thus was both more expensive and less effective than control therapy. For the other six trials — the Multicenter Automatic Defibrillator Implantation Trial (MADIT) I, MADIT II, the Multicenter Unsustained Tachycardia Trial (MUSTT), the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial, the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial, and the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) — the use of an ICD was projected to add between 1.01 and 2.99 quality-adjusted life-years (QALY) and between \$68,300 and \$101,500 in cost. Using base-case assumptions, we found that the cost-effectiveness of the ICD as compared with control therapy in these six populations ranged from \$34,000 to \$70,200 per QALY gained. Sensitivity analyses showed that this cost-effectiveness ratio would remain below \$100,000 per QALY as long as the ICD reduced mortality for seven or more years.

CONCLUSIONS

Prophylactic implantation of an ICD has a cost-effectiveness ratio below \$100,000 per QALY gained in populations in which a significant device-related reduction in mortality has been demonstrated.

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THE IMPLANTABLE CARDIOVERTER-defibrillator (ICD) can convert episodes of ventricular fibrillation and ventricular tachycardia to sinus rhythm, thus potentially averting sudden death from cardiac causes. Randomized trials clearly demonstrate that the implantation of an ICD reduces the subsequent risk of death among patients who have been resuscitated from a cardiac arrest.¹⁻³ However, because very few patients in the United States survive an out-of-hospital cardiac arrest, a strategy of implanting an ICD in patients at high risk for sudden death from cardiac causes has been proposed.

Eight clinical trials have randomly assigned patients at risk for sudden death due to left ventricular systolic dysfunction who have not had life-threatening ventricular arrhythmias to receive an ICD or an alternative therapy: the Defibrillator in Acute Myocardial Infarction Trial (DINAMIT), the Multicenter Automatic Defibrillator Implantation Trial I and II (MADIT I and MADIT II, respectively), the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial, the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial, the Multicenter Unsustained Tachycardia Trial (MUSTT), the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), and the Coronary Artery Bypass Graft (CABG) Patch Trial.⁴⁻¹¹ Several of these trials, most notably MADIT II and SCD-HeFT, have shown that prophylactic implantation of an ICD significantly reduced overall mortality.^{6,9} No such advantage was found in the DINAMIT and CABG Patch Trial, however.^{4,10}

The Centers for Medicare and Medicaid Services estimate that as many as 500,000 Medicare beneficiaries might be eligible to receive a prophylactic ICD in the United States.¹² Given the substantial cost of the ICD, the economic effect of this strategy must be considered. In this analysis, we evaluated the benefits, costs, and cost-effectiveness of the prophylactic implantation of an ICD in patients meeting the inclusion criteria of each of the eight primary-prevention trials.

METHODS

DESIGN OF THE STUDY

We used a decision model to estimate costs and survival among patients who received either an ICD for the primary prevention of sudden death from cardiac causes or control therapy (Fig. 1). We ad-

hered to recommendations for the conduct of cost-effectiveness analyses by using a societal perspective on health benefits and costs and applying a 3 percent annual discount rate.¹³ Although some of the individual trials from which we obtained data were supported by device manufacturers, none of the authors of this article had any association with the manufacturers of ICD devices.

DECISION MODEL

We adapted a Markov model^{14,15} developed to assess the cost-effectiveness of the ICD¹⁶⁻¹⁸ (Fig. 1) using Decision Maker software (version 2002.7.2, Pratt Medical Group). The model tracked a cohort of patients who received either a prophylactic ICD or control therapy. Each month, patients in this Markov tree were at risk for sudden death from cardiac causes, nonsudden death from cardiac causes, and death from noncardiac causes.

We assumed that the probability of death was constant and matched the total rate of death from any cause among the control patients during the average follow-up period (range, 16 to 41 months). For extrapolation beyond the trial period, we assumed the annual rate of death from any cause observed during the trial period continued, but we also incorporated data from the U.S. general population to account for the increase in the age- and sex-specific rate of death from noncardiac causes as the cohort aged.¹⁹ Additional information is provided in the Supplementary Appendix, available with the full text of this article at www.nejm.org.⁴⁻¹¹

EFFICACY OF THE ICD

We modeled the efficacy of ICD therapy as a reduction in the relative risk of death from any cause on the basis of the hazard ratios reported by each clinical trial (provided in the Supplementary Appendix).^{4-11,16,20-30} The effectiveness of the ICD, as compared with control therapy, in reducing the hazard ratio for death varied among the trials in relation to their annual rate of death from any cause (correlation coefficient, -0.76) (Fig. 2). For our base-case analysis, we assumed that the benefit of the ICD would continue throughout the patient's lifetime and that the generator would be replaced every five years.²¹

QUALITY OF LIFE

The Markov model incorporated adjustments for the quality of life associated with age-specific current health, a history of myocardial infarction, and

with implantation of an ICD with the use of utilities. Utilities are a measure of the quality of life rated on a scale from 0 to 1, where 0 represents death and 1 ideal health. The model assumed that one year of life with left ventricular dysfunction equaled 0.88 year of optimal health on the basis on data from previous studies.^{27,29,31} This figure was then multiplied by age-specific weights based on data from the Beaver Dam Health Outcomes Study.²⁸ In our base-case analysis, we assumed that the quality of life did not change as a result of the implantation of an ICD. We assumed that patients who were hospitalized for lead infections received a quality-of-life decrement of 3.5 days (as shown in the Supplementary Appendix).

COSTS

Our analysis included the direct costs of medical care associated with inpatient and outpatient treatment (provided in the Supplementary Appendix). We included the costs of the initial ICD implantation; of ongoing therapy for both the control and ICD groups, including visits to physicians, laboratory tests, and rehospitalization; and of ICD generator or lead replacement. We updated all costs to 2005 U.S. dollars using the gross domestic product deflator.^{32,33} We based the cost of ICD implantation (\$27,975) and replacement (\$18,390) on the fiscal-year 2005 Medicare Inpatient Prospective Hospital Payment system (diagnosis-related groups 515 and 115) and professional fees (Current Procedural Terminology codes 33249 and 33240). We assumed that single-chamber ICDs were used in terms of both costs and complications. We obtained follow-up hospitalization costs unrelated to ICD implantation for both strategies from the Myocardial Infarction Triage and Intervention patient registry.^{34,35}

SENSITIVITY ANALYSES

We performed sensitivity analyses to account for important model assumptions and uncertainties. For clinical variables, our ranges for sensitivity analyses represent our judgment of the variation likely to be encountered in clinical practice on the basis of both the literature and discussion with experts. In sensitivity analyses that included all model variables, the incremental cost-effectiveness of the ICD as compared with control therapy was most sensitive to variation in five factors: the efficacy of the ICD in reducing mortality, the cost of ICD implantation, the frequency of generator replacement, the quality of life, and the time horizon used in the

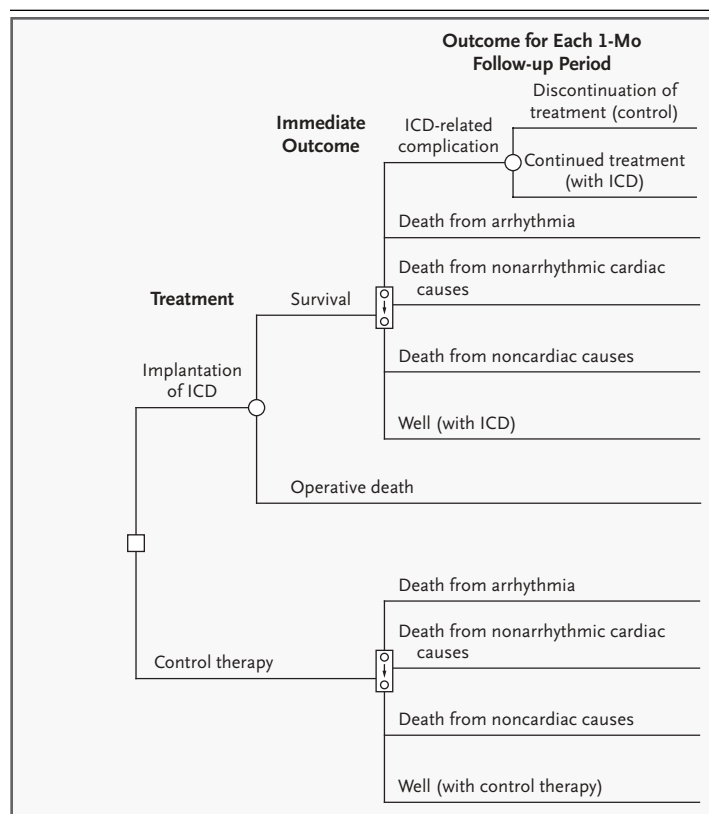


Figure 1. The Decision Model.

The square on the left represents a choice between alternative treatments: the implantation of an ICD or control therapy. Circles represent chance nodes. Patients who receive an ICD are at risk for death from the implantation procedure. Patients who do not die from the procedure and patients assigned to conventional (control) treatment enter the Markov tree (denoted by rectangles containing circles and an arrow). The Markov tree represents the clinical events that can occur during each one-month period as a patient is followed until death: a patient may die (from arrhythmia, nonarrhythmic cardiac causes, or noncardiac causes). If the patient survives, he or she remains well for the one-month period. Patients who have an ICD may have a lead infection or failure that may (or may not) cause them to discontinue treatment (and to switch to the control therapy).

analysis. We therefore explored these variables more extensively and assessed the range of potential effects.

RESULTS

VALIDATION OF THE MODEL

For the trial period, our Markov model predicted mortality rates associated with control therapy that were within 0.3 percentage point of those found in the individual trials. For the ICD strategy, our model matched the trial results within 1.6 percentage

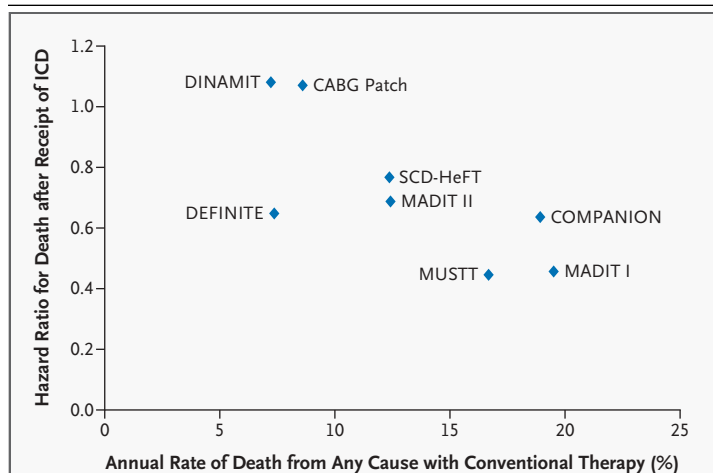


Figure 2. Hazard Ratios for the Risk of Death after the Implantation of an ICD, as Compared with Control Therapy, in Eight Primary-Prevention Trials.

The eight trials were as follows: the Defibrillator in Acute Myocardial Infarction Trial (DINAMIT), the Multicenter Automatic Defibrillator Implantation Trial I (MADIT I), MADIT II, the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial, the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial, the Multicenter Unsustained Tachycardia Trial (MUSTT), the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), and the Coronary Artery Bypass Graft (CABG) Patch Trial.⁴⁻¹¹

points except for those of MADIT I, for which our estimated mortality rate was 20 percent at 27 months, rather than the actual rate of 15.8 percent. The cause of this discrepancy is not clear.

BASE-CASE ANALYSIS

The health and economic outcomes varied greatly among the trial populations (Table 1). In each population, prophylactic implantation of an ICD was more expensive than control therapy, with the increase in estimated lifetime discounted costs ranging from \$55,700 in the CABG Patch Trial to \$101,500 in MUSTT. In six of the eight populations, implantation of the ICD improved life expectancy relative to control therapy, with the discounted increment ranging from 1.40 to 4.14 years (undiscounted range, 2.12 to 6.21) or from 1.01 to 2.99 quality-adjusted life-years (QALY) (undiscounted range, 1.53 to 4.47). The incremental cost-effectiveness ratios based on these trials ranged from \$24,500 to \$50,700 per life-year added and from \$34,000 to \$70,200 per QALY added (Table 1). In two trials (DINAMIT and CABG Patch), the life expectancy of the patients who received an ICD was less than that of the patients who received control

therapy, so the ICD was both more expensive and less effective than control therapy.

SENSITIVITY ANALYSES

The incremental cost-effectiveness of the ICD as compared with control therapy became more favorable as the efficacy of the ICD increased within the 95 percent confidence interval for the reduction in the risk of death from any cause that was calculated in each trial (Table 1 and Fig. 3A). Since the efficacy of the ICD is, in general, related to the estimated annual mortality rate in the patient population studied (Fig. 2), the incremental cost-effectiveness of the ICD tended to be more favorable in higher-risk patients.

Lowering the estimated cost of the ICD improved cost-effectiveness. If the cost of the ICD were reduced from \$27,975 to \$10,000, the incremental cost-effectiveness of ICD therapy would improve from \$70,200 to \$52,400 per QALY gained in SCD-HeFT and from \$34,000 to \$27,900 per QALY gained in MUSTT. Conversely, if the cost of the device were increased to \$60,000, the incremental cost-effectiveness of the ICD would be less favorable, ranging from \$44,700 per QALY gained in MUSTT to \$101,800 per QALY gained in SCD-HeFT.

If ICD generators were replaced more frequently than every five years, the cost-effectiveness of ICD therapy would be less economically favorable (replacement every three years yields an incremental cost-effectiveness of between \$41,200 and \$88,600 per QALY gained for the clinical trials in which prophylactic implantation of an ICD was found to be better than control therapy). However, if the generators were replaced every seven years, the cost-effectiveness of ICD implantation relative to control therapy would improve to between \$30,800 and \$62,300 per QALY gained (Fig. 3B).

We initially assumed that the prophylactic implantation of an ICD would not further change the patients' quality of life, but if the patients' quality of life were decreased by prophylactic ICD implantation, the cost-effectiveness of this approach would be much less favorable (Fig. 3C). For example, in SCD-HeFT, if a patient in the control group has a utility of 0.88 and a patient with an ICD has a utility of 0.72 or less, then the control therapy is associated with both lower costs and better outcomes than the implantation of an ICD. Such an ICD-associated decrease in the quality of life might be anticipated, for example, in a patient who received numerous shocks from the device.³⁶ However, as long as the

Table 1. Health and Economic Outcomes of the Prophylactic Implantation of an ICD as Compared with Control Therapy.*

Trial and Strategy	Cost	Increase in Cost Related to ICD	Life Expectancy	Increase in Life Expectancy Related to ICD	QALY	Increase in QALY Related to ICD	Incremental Cost-Effectiveness of ICD†			
							\$/Life-Yr	Baseline Efficacy	High Efficacy	Low Efficacy
	\$			year					\$/QALY	
MADIT I										
Control	38,300		4.06		2.98					
ICD	130,400	92,100	7.70	3.64	5.62	2.64	25,300	34,900	27,000	96,600
CABG Patch										
Control	78,600		8.41		6.13					
ICD	134,400	55,700	8.01	(0.40)	5.84	(0.29)	Dominated	Dominated	84,200	Dominated
MUSTT										
Control	44,300		4.72		3.46					
ICD	145,800	101,500	8.86	4.14	6.45	2.99	24,500	34,000	28,800	47,600
MADIT II										
Control	57,500		6.16		4.51					
ICD	136,900	79,400	8.20	2.03	5.98	1.47	39,000	54,100	37,200	213,900
DEFINITE										
Control	84,400		9.03		6.57					
ICD	184,900	100,500	11.75	2.73	8.53	1.96	36,800	51,300	34,500	Dominated
DINAMIT										
Control	88,300		9.44		6.87					
ICD	147,200	58,800	8.96	(0.48)	6.53	(0.34)	Dominated	Dominated	70,900	Dominated
COMPANION										
Control	37,800		4.01		2.95					
ICD	106,100	68,300	5.88	1.87	4.31	1.36	36,500	50,300	36,100	123,800
SCD-HeFT										
Control	57,800		6.19		4.53					
ICD	128,800	71,000	7.59	1.40	5.54	1.01	50,700	70,200	45,600	368,800

* The following eight trials were evaluated: the Defibrillator in Acute Myocardial Infarction Trial (DINAMIT), the Multicenter Automatic Defibrillator Implantation Trial I (MADIT I), MADIT II, the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial, the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial, the Multicenter Unsustained Tachycardia Trial (MUSTT), the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), and the Coronary Artery Bypass Graft (CABG) Patch Trial.⁴⁻¹¹ Numbers in parentheses correspond to a decrease in the value and thus to an increase in the risk of death among patients who received an ICD. Costs and life expectancy are discounted at an annual rate of 3 percent. QALY denotes quality-adjusted life-year.

† Low efficacy and high efficacy correspond to the results obtained with the use of 95 percent confidence intervals for the efficacy of prophylactic ICD implantation as compared with control therapy in each clinical trial, except in the case of SCD-HeFT, which reported 97.5 percent confidence intervals. The term “dominated” means that the prophylactic implantation of an ICD was both more expensive and less effective than control therapy.

utility associated with having an ICD exceeded 0.84, the cost-effectiveness would be less than \$100,000 per QALY gained. Recent clinical trials suggest that the implantation of an ICD may in fact improve the average quality of life.^{36,37} In SCD-HeFT, if the ICD utility were increased to 0.95 (base-case utility, 0.88), then the cost-effectiveness of the implantation of an ICD would improve to less than \$50,000 per QALY gained.

Because patients with nonischemic cardiomyopathy might have a lower quality of life than those with ischemic heart disease, we also explored the effect of decreasing patients' utility on the basis of the presence of left ventricular dysfunction (for both the ICD and control strategies) from our base-case value of 0.88 to 0.75, as suggested in one study.³⁸ In the clinical trials in which prophylactic implantation of an ICD was found to be better than control

therapy, the cost-effectiveness of the ICD would range from \$39,800 to \$82,400 per QALY gained. Because such patients might also have higher inpatient costs, we also explored increasing monthly inpatient costs. Our results were not sensitive to these changes; increasing these monthly inpatient costs by 50 percent (for both treatment strategies) would change the incremental cost-effectiveness of the implantation of an ICD from \$70,200 to \$73,500 per QALY gained in SCD-HeFT and from \$34,000 to \$37,300 per QALY gained in MUSTT.

EXTRAPOLATION AND THE TIME HORIZON

Our base-case analyses used a time horizon that encompassed the lifetime of the patient, and we assumed that the costs and benefits associated with the ICD in reducing the risk of sudden death from cardiac causes would continue for the entire period. If we used a lifelong horizon but assumed that ICD efficacy ceased after the first three years, the cost-effectiveness of the ICD as compared with control treatment became much less favorable, ranging from \$70,200 per QALY gained in MUSTT to \$171,800 per QALY gained in SCD-HeFT (Fig. 4A). As long as the ICD retained its effectiveness for at least seven years, the cost-effectiveness of this approach as compared with control therapy was less than \$100,000 per QALY gained in all trials in which prophylactic implantation of an ICD was found to be better than control therapy (Fig. 4A).

We also evaluated the costs and benefits of the implantation of an ICD as compared with control therapy for various time horizons (Fig. 4B). In these analyses, both costs and benefits were included in the simulation through the use of a specified time horizon (for example, three years), and neither costs nor benefits that occurred after that time frame were included. Cost-effectiveness became substantially more favorable as the time horizon increased (Fig. 4B). Therefore, a cost-effectiveness analysis limited to a shorter time horizon would result in a less favorable estimate of cost-effectiveness than would an analysis with a longer time horizon.

DISCUSSION

Our analysis demonstrates that under most assumptions, the prophylactic implantation of an ICD has a cost-effectiveness ratio below \$100,000 per

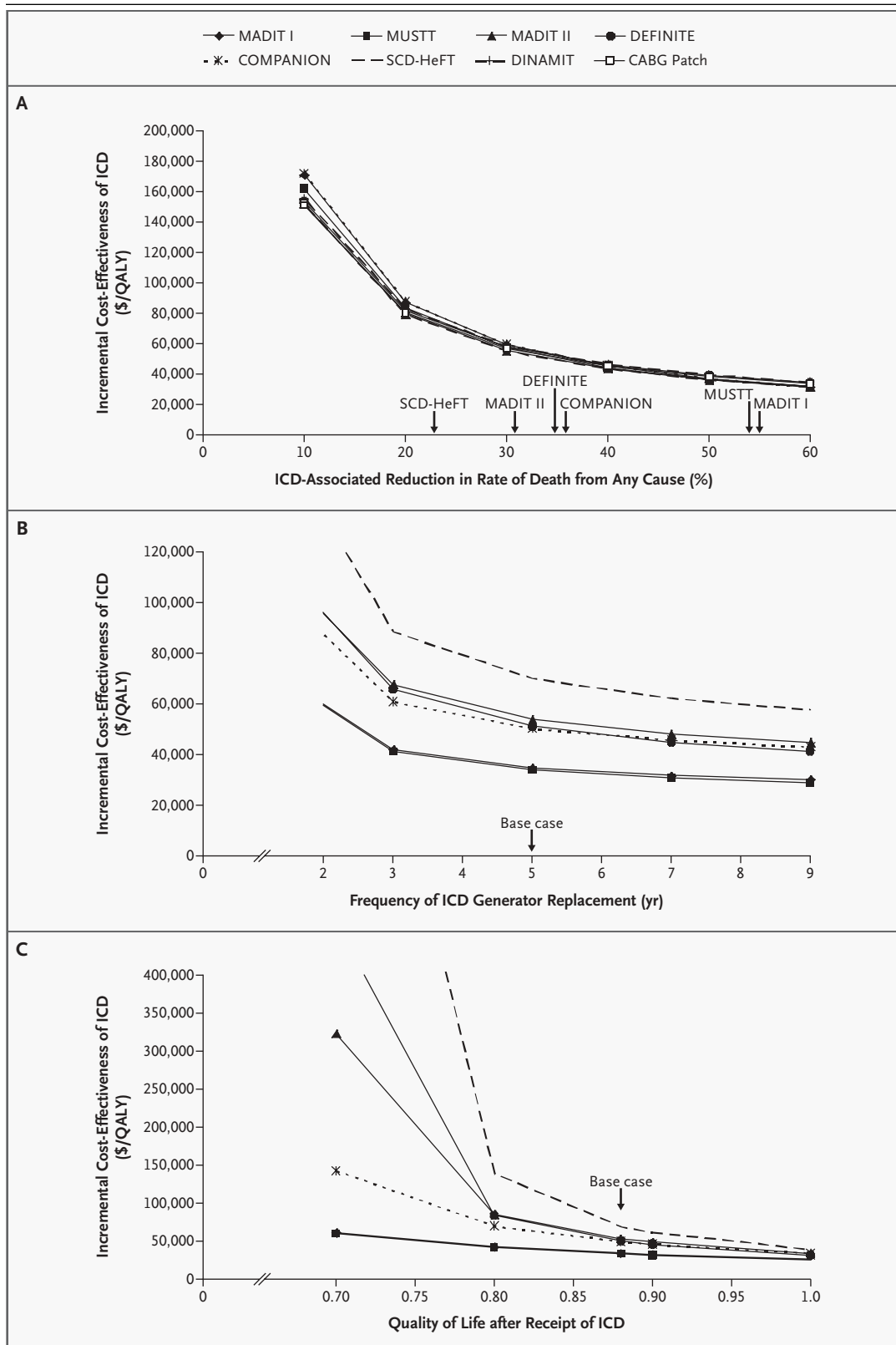
Figure 3 (facing page). Sensitivity Analysis of the Incremental Cost-Effectiveness of Prophylactic Implantation of an ICD, as Compared with Control Therapy, with Respect to Efficacy (Panel A), the Frequency of Generator Replacement (Panel B), and the Quality of Life (Panel C).

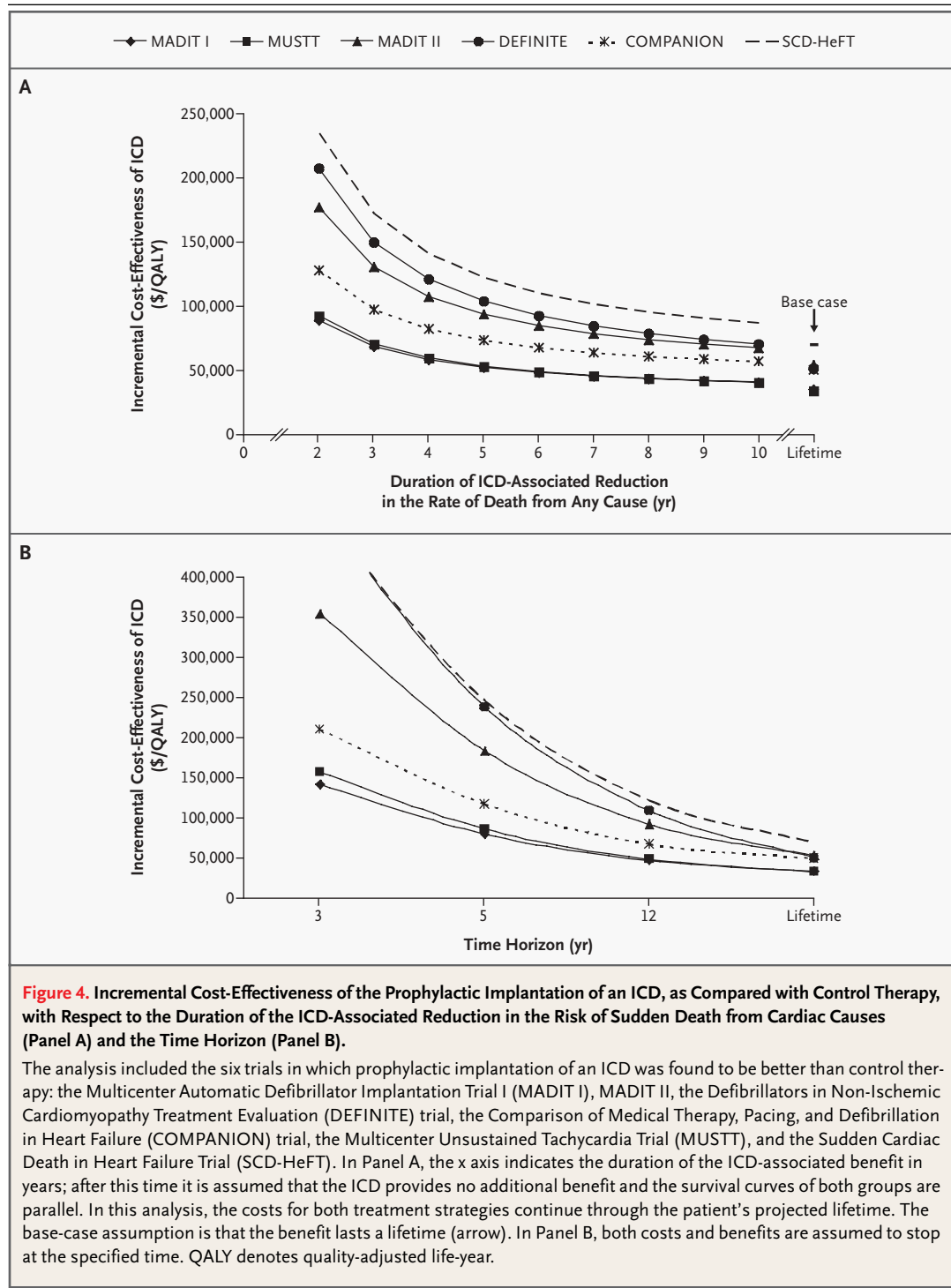
Eight trials were analyzed: the Defibrillator in Acute Myocardial Infarction Trial (DINAMIT), the Multicenter Automatic Defibrillator Implantation Trial I (MADIT I), MADIT II, the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial, the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial, the Multicenter Unsustained Tachycardia Trial (MUSTT), the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), and the Coronary Artery Bypass Graft (CABG) Patch Trial.⁴⁻¹¹ Panel A reflects the efficacy of the ICD in reducing the risk of death from any cause. The arrows indicate the efficacy of the ICD in reducing the risk of death from any cause in the individual trials. The arrow in Panel B indicates the base-case estimate of replacing the generator every five years. The arrow in Panel C indicates the base-case estimate of the quality of life with an ICD of 0.88. For this analysis, the assumed quality of life with control therapy remains constant at 0.88. QALY denotes quality-adjusted life-year.

QALY gained in patients at increased risk for sudden death as the result of a reduced left ventricular ejection fraction. The weight of evidence from eight randomized trials is that the prophylactic implantation of an ICD reduces the rate of death from any cause; in the six trials that showed a mortality benefit, we project that the implantation of an ICD adds between 2.12 and 6.21 undiscounted years of life. This increment in life expectancy is substantial as compared with that provided by many other medical interventions, and the incremental cost-effectiveness of the ICD, in appropriately selected patients, is similar to that of other interventions often accepted as cost-effective.

In the six randomized trials that showed a reduction in mortality associated with the implantation of an ICD,^{5-9,11} we found a cost-effectiveness ratio of less than \$51,000 per additional life-year and less than \$71,000 per QALY gained. In the two studies that found a higher mortality rate among patients who received an ICD than among patients who received control therapy, the ICD strategy was associated with higher costs and worse outcomes.

A quantitative overview²⁰ of the eight primary-prevention ICD trials showed a significant degree





of heterogeneity among these trials in the effectiveness of the ICD in reducing the rate of death from any cause. The disparity in results among these studies is probably a consequence of several factors, including the differing characteristics of the popu-

lations, the differing quality of the non-ICD medical therapy given to the control groups, and the differing competing risks of death from causes not affected by ICD implantation. The two trials in which patients assigned to ICD therapy had a higher

mortality rate were composed of patients who were undergoing concomitant bypass surgery (CABG Patch) or who had had an acute myocardial infarction (DINAMIT). Prophylactic implantation of an ICD in such patients may have reduced efficacy owing to the specific characteristics of the patient population, competing causes of death, or both. Whatever the reason, this heterogeneity in the effectiveness of prophylactic implantation of an ICD highlights the need for appropriate, evidence-based selection of patients.

Because the clinical results of the prophylactic implantation of an ICD vary substantially depending on the patient population, we did not pool the results of available trials to estimate an overall cost-effectiveness ratio. Indeed, cost-effectiveness is not an inherent property of any particular therapy but depends on the patient population in which the therapy is used. When the clinical effectiveness of a therapy varies according to the population selected, its cost-effectiveness will vary as well.³⁹

Prophylactic implantation of an ICD poses a difficult challenge to health policymakers owing to the high cost of the device and the large patient population in which it may be applied.⁴⁰ Even if this approach is used only in patient populations in which it has been shown to be cost-effective, the aggregate expenditure in the United States for ICDs could easily exceed several billion dollars per year. If clinicians extend the prophylactic use of ICDs to lower-risk patients in whom the efficacy is lower and cost-effectiveness less favorable, the societal cost will rise further. On the other hand, within the population of patients with low ejection fractions, it may be possible to identify subgroups that have a characteristically greater or lesser benefit. The Center for Medicare and Medicaid Services has announced plans for the prospective collection of data to assist in identifying such subgroups.¹² There is not yet, however, a consensus as to how such patients might be identified.

Recently, the SCD-HeFT investigators presented results from their trial-specific cost-effectiveness analysis.⁴¹ Their base-case analysis estimates that the ICD costs \$33,200 per life-year more than does medical management (as compared with our estimate of \$50,700 per life-year). Although we do not

have access to all their assumptions, incorporating into our model the lower ICD-implantation cost used in their analysis (\$17,500) would result in a cost-effectiveness ratio of \$43,200 per life-year.

Our study has several limitations. We used only summary data from each trial, so our projections may not match the more detailed results of prospective economic studies that may have been done within the individual trials. We also made lifetime projections of the clinical and economic outcomes of the prophylactic implantation of an ICD — an approach that required some assumptions. Our analysis demonstrates that as long as the mortality benefit associated with the prophylactic implantation of the ICD (as compared with control therapy) exceeds seven years, the ICD costs less than \$100,000 per QALY gained in the trials showing that the ICD implantation reduced the risk of death. We cannot, however, be certain that longer-term follow-up of the trials might indicate the need for some adjustments in our analyses. Nevertheless, in view of the substantial reductions in mortality seen during medium-term follow-up in these trials, these adjustments are not likely to change our major conclusions.

Our analysis is limited to ICDs and cannot be extrapolated to the newer devices that include a cardiac-resynchronization capability. The added cost and complexity of these combined devices suggest that their cost-effectiveness may be quite different from that of ICDs alone. By contrast, our findings are probably applicable to lower-cost ICDs that may omit noncritical features to reduce expense. Future price competition that lowers the costs of these devices would also enhance the cost-effectiveness of ICDs. In conclusion, our analysis suggests that the prophylactic implantation of an ICD has a cost-effectiveness ratio below \$100,000 per QALY gained in populations in which a significant device-associated reduction in mortality has been demonstrated.

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