Cost-Effectiveness of the Implantable Cardioverter-Defibrillator Versus Antiarrhythmic Drugs in Survivors of Serious Ventricular Tachyarrhythmias

Results of the Antiarrhythmics Versus Implantable Defibrillators (AVID) Economic Analysis Substudy

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Background—The implantable cardioverter-defibrillator (ICD) is an effective but expensive device. We used prospectively collected data from a large randomized clinical trial of secondary prevention of life-threatening ventricular arrhythmias to determine the cost-effectiveness of the ICD compared with antiarrhythmic drug (AAD) therapy, largely with amiodarone.

Methods and Results—Charges for initial and repeat hospitalizations, emergency room, and day surgery stays and the costs of antiarrhythmic drugs were collected on 1008 patients. Detailed records of all other medical encounters and expenses were collected on a subgroup of 237 patients. Regression models were then created to attribute these expenses to the rest of the patients. Charges were converted to 1997 costs using standard methods. Costs and life years were discounted at 3% per year. Three-year survival data from the Antiarrhythmics Versus Implantable Defibrillators trial were used to calculate the base-case cost-effectiveness (C/E) ratio. Six-year, twenty-year, and lifetime C/E ratios were also estimated. At 3 years, total costs were $71,421 for a patient taking AADs and $85,522 for a patient using an ICD, and the ICD provided a 0.21-year survival benefit over AAD treatment. The base-case C/E ratio was thus $66,677 per year of life saved by the ICD compared with AAD therapy (95% CI, $30,761 to $154,768). Six- and 20-year C/E ratios remained stable between $68,000 and $80,000 per year of life saved.

Conclusions—The ICD is moderately cost-effective for secondary prevention of life-threatening ventricular arrhythmias, as judged from prospectively collected data in a randomized clinical trial. (Circulation. 2002;105:2049-2057.)

Key Words: cost-benefit analysis ■ heart arrest ■ antiarrhythmia agents ■ defibrillation ■ tachyarrhythmias

The Antiarrhythmics Versus Implantable Defibrillators (AVID) trial has recently demonstrated the superiority of the implantable cardioverter-defibrillator (ICD) over therapy with amiodarone or sotalol for reducing all-cause mortality in survivors of ventricular fibrillation or hemodynamically compromising ventricular tachycardia.1 In addition, the Multicenter Automatic Defibrillator Implantation Trial (MADIT)2 and the Multicenter Unsustained Tachycardia Trial (MUSTT)3 have shown that prophylactic ICDs improve survival among selected patients with nonsustained ventricular tachycardia. As a result of such trials, use of the ICD continues to increase. Approximately 65,000 ICD systems were implanted in the United States in 2000. At a cost to the hospital of $18,000 to $25,000 per system, this translates into $1.2 to $1.6 billion per year for hardware alone.

Previous published estimates of ICD cost-effectiveness have varied, with base case estimates (in United States dollars) ranging from $17,100 to $138,800 per year of life saved.4–8 Applicability of these results is limited either because they rely on computer models and retrospective data4–6 or because of the very selective patient population studied7 or relatively small sample size.8

The AVID economic substudy was prospectively designed to determine the medical costs for patients with life-
threatening ventricular arrhythmias. It represents the largest prospective comparison performed of the costs of the ICD to those of antiarrhythmic drugs (mostly amiodarone) for these patients.

Methods

Clinical Trial and Economic Evaluation Design

The population recruited into the AVID trial has been previously described. Briefly, patients who either had been resuscitated from cardiac arrest or had experienced sustained ventricular tachycardia causing syncope or severe hemodynamic impairment and had an ejection fraction (EF) ≤0.40 were eligible for the study. Patients were randomized to receive an implantable cardioverter-defibrillator (ICD) or to receive antiarrhythmic drug (AAD) therapy. The primary endpoint was all-cause mortality. The trial was terminated early because ICD therapy was shown to be superior to AAD therapy. Of the 1016 participants in the AVID trial, 8 were excluded from the economic substudy because they had not completed their initial hospitalizations at the time of the trial termination. The average follow-up for all 1008 patients at the study’s end was 1.49 years. Data were collected on patients treated with ICDs for an additional year after study termination. This was not done for patients treated with AAD therapy, because many crossed over to treatment with ICD after the study’s results were made public.

Economic data were collected prospectively as an integral part of the trial. For cost computations we used the methods for economic evaluation proposed by the United States Public Health Service Panel on the Cost Effectiveness Analysis in Health and Medicine. The perspective of the analysis was societal. Data were not collected on salary or time lost from work, costs of travel for medical care or AVID study participation, or other costs not directly incurred by medical treatment. The time horizon used for the primary analysis was the 3-year duration of the trial, because it provided unbiased empiric data for comparison purposes. Both life years and cost were discounted at 3%. Prices were standardized to 1997 United States dollars.

It became evident early in the trial that it would be impossible to collect all data on every health care encounter for >1000 patients. Thus, data collection was divided into 2 basic types. Data collected on all patients included hospital bills and antiarrhythmic drug use. All other data were collected on a subset of patients only. These patients were called the “shoebox patients” because of the way they often collected their receipts, bills, invoices, and charge slips.

Data Collected on All Patients

For each hospitalization (including emergency department, short stay, and overnight visits), its reason, the cardiac procedures performed, length of stay, and the hospital charges were collected by study coordinators. Hospital charges were unavailable for 21% of hospitalizations, usually because the patients were in a VA hospital or a health maintenance organization. In such cases, charges were imputed as described below.

Antiarrhythmic drug name (principally amiodarone) and daily dosage were collected at all follow-up visits, and costs were assigned directly using the average wholesale price (cost of drug to pharmacy). The average monthly wholesale price for 400 mg per day of amiodarone was $198.32.

Data Collected on the 237 Shoebox Patients Only

Generally, there were 4 shoebox patients at each site: the first patients with ventricular tachycardia (VT) and ventricular fibrillation (VF) randomized to ICD and the first patients with VT and VF randomized to AAD. Healthcare utilization data were collected for shoebox patients at least every 3 months, and many patients received monthly phone calls. The data included hospitalizations, outpatient services, physician, clinic, and laboratory visits, procedures and tests, medications, and ancillary support. Shoebox patients were also requested to provide copies of all bills and statements. Information abstracted from the bills included dates of service, service code, provider name, charges, and reimbursements. The data then were exhaustively reviewed by experienced nurse coordinators for consistency and completeness.

Extrapolating Data from the Shoebox Cohort to the Entire Trial Population

Using shoebox data, cost models were developed for clinical laboratory and physician office visits with associated procedures and testing, extended and home health care costs, nonantiarrhythmic medication costs, and physician fees for inpatient care. The models used patient characteristics, treatments, and tests done during outpatient visits as well as follow-up duration and year of treatment to impute costs for the nonshoebox patients.

Assignment of Costs to Physician, Clinic, and Laboratory Visits and Associated Tests

For physician and clinic visits, reimbursement rates (which averaged 80% of charges) were used as a surrogate for cost. Costs were ascribed to office or clinic visits based on Current Procedural Terminology codes. Costs for laboratory and tests were derived using reimbursement on the associated bills for reference.

Extended Care and Home Health Care Costs

From billing data we calculated a cost of $97.66 per hour for registered nurse home health care and $46.26 per hour for other home health care. For extended care, reimbursement averaged $252.49 per day.

Nonantiarrhythmic Medications

For shoebox patients, the minimum average wholesale price was assigned for each product name, formulation, and strength. Limited nonarrhythmic drug use was also tracked for all AVID patients by grouping medicines used into general therapeutic categories. Shoebox drug cost data were then used to provide per-patient nonarrhythmic drug cost estimates for nonshoebox patients.

Inpatient Physician Fees

Physician fees for each shoebox patient hospitalization were obtained from billing data. A regression model was developed to relate physician fees to total hospital charges and reason for admission. Physician fees for each nonshoebox patient hospital admission were then assigned. Using a survey of AVID sites’ physician reimbursement rates, costs were determined to be 50% of billed charges.

Extrapolating Hospital Cost Data to All Trial Patients

Hospital charges were converted to costs using provider-level cost-charge ratios from the Health Care Financing Authority. Models were then developed for both baseline and recurrent hospitalizations, which related costs to both hospitalization and patient factors using the 79% of hospitalizations with charge data. These models were then used to impute hospital costs for the other 21% of hospitalizations. The final models are shown in the Appendix.

Method of Analysis

The primary intention-to-treat cost-effectiveness analysis was restricted to data obtained by April 7, 1997, when trial enrollment was terminated, and additionally restricted to 3 years of follow-up because of the limited quantity of data beyond 3 years. The bootstrap procedure was used to obtain a 95% CI for the cost-effectiveness ratio.

Sensitivity Analyses

Several a priori subgroup analyses were performed on the premise that treatment effects or costs might differ among the subgroups. In particular, a trend found in the AVID trial toward improved survival in patients with EF >35% had been independently verified in the Canadian Implantable Defibrillator Study (CIDS). In addition, we performed 2 analyses using extended time frames. The combined AVID, CIDS, and Cardiac Arrhythmia Study Ham-
burg (CASH) database was used to obtain empirical estimates of survival differences out to 6 years, because the patients in CASH and CIDS were similar and follow-up was longer than in AVID. Collected cost data to 5 years for the ICD arm and 4 years for the AAD arm were used and then extrapolated to 6 years through curve fitting.

In the second analysis, we conducted 20-year and lifetime cost-effectiveness evaluations. We assumed that the yearly cost increase in the ICD arm would equal the differential seen from year 3 to year 4, or $8435. This is approximately one third the cost of generator replacement and hence implies no other differential costs between the 2 treatment groups except generator replacements, occurring at a 33.3% rate per year. We also assumed that the base cost per year for patients treated with AADs after 3 years was $3801 per year, the base cost in the fourth year of the trial.

In addition, we modeled 2 different assumptions about survival beyond 6 years. In the first, the survival curves of the 2 treatment groups remain approximately parallel from year 6 onward (relative hazard is 1). Thus, the relative survival advantage of the ICD group diminishes slowly over the ensuing years. In the second, survival beyond 6 years is modeled by Weibull distributions derived from empiric data out to 6 years (see Figure 2).

**Results**

**Patient Characteristics**

Selected characteristics for the 237 shoebox patients and the 771 nonshoebox patients are shown in Table 1. The two groups are similar clinically and had similar lengths of stay and initial hospitalization charges. The shoebox patients included a higher percentage of females and a higher percentage with ventricular fibrillation as their index arrhythmia (concern that patients with VT might be overenrolled led to strategies, later relaxed, stressing enrollment of patients with VF).

**Repeat Hospitalizations**

There were 1920 repeat hospitalizations among trial participants: 942 among patients treated with AAD and 978 among those randomized to the ICD (Table 2). Of these hospitalizations, 74% to 79% were for repeat inpatient admissions, whereas 21% to 26% represented emergency room or day surgery (“short stay”) admissions. Many patients had <3 years of follow-up, because follow-up was arbitrarily curtailed or censored when the trial ended early. After adjusting for this censoring, the estimated number of hospitalizations by 3 years was 1555 among the patients treated with AAD and 1582 among patients treated with ICD. Total inpatient hospital stays longer than 3 years were slightly shorter among patients treated with ICD than with AAD, 16.4 versus 18.9 days. During the trial, 58 patients treated with AADs (12% of all patients treated with AAD) crossed over to ICD therapy (3-year rate of 16%). Among patients treated with ICD, 110 (22%) received antiarrhythmic drugs (3-year rate of 32%). Only 7% (3-year rate of 18%) of patients treated with ICD underwent battery replacements before the trial ended.

**Outpatient Encounters: Shoebox Patients**

Table 3 shows data on ambulatory medical encounters among these 237 patients, including home care visits, extended care stays (in rehabilitation units or nursing homes), and clinic or laboratory visits. The various types of outpatient visits were not mutually exclusive, so patients could have clinic visits, blood tests, or other tests at the same time. Although the total clinic visits were similar, patients treated with ICD underwent 749 ICD checks compared with only 88 for patients treated...
with AADs, whereas treated with AADs had more blood and pulmonary function tests. The expected number of clinic visits over 3 years was just higher than 36, an average of 1 per month.

**Total Costs Per Patient Over 3-Year Follow-Up**

Per-patient costs adjusted for censoring (in 1997 dollars, but not discounted) for hospitalizations and physician fees are shown in Table 4. The total for a patient treated with ICD was $87 479, representing $16 611 more in total costs than the $73 564 for a patient treated with drugs. The difference can be explained by the higher costs for ICD patients’ initial hospitalization expenses ($41 192 hospital costs + $4306 physician fees=$45 498) than those for patients treated with AADs ($21 646+$2236=$23 882), which largely reflect the added expense of ICD and implantation costs. These initial differences were partially offset over time by somewhat higher costs for rehospitalizations and for antiarrhythmic drugs among patients treated with AADs.

Most expenses associated with the care of these complex patients come from inpatient encounters (Table 4). Initial plus repeat hospitalization costs make up 73% of all costs for patients assigned to AAD treatment and 84% of all costs for patients treated with the ICD.

**Cost-Effectiveness of the ICD**

Table 5 shows the base-case cost-effectiveness ratio for the ICD compared with AAD among all AVID trial patients and among several subgroups after costs and survival had been discounted at 3% per year over the life of the trial.

**Base Case Analysis**

At 3 years of follow-up, the expected survival for patients treated with the ICD was 0.21 years longer than for AAD at an incremental cost of $14 101, yielding a cost-effectiveness ratio of $66 677 per year of life saved by the ICD over AAD. The 95% bootstrap confidence limits were broad, ranging from $30 761 to $154 768.

**Subgroup Analyses**

The C/E ratio for a patient with VF was $27 721 less than for a patient with VT ($55 163 versus $82 884), because the ICD provided a greater 3-year survival benefit among patients with VF than among patients with VT (0.27 versus 0.17 years).

Patients with ejection fractions ≤0.35 randomized to receive AAD had the lowest average survival (2.15 years) of all the groups listed in Table 5, whereas those treated with an ICD gained the largest relative survival benefit, 0.29 years. However, because total costs were high for both drug- and device-treated patients, the cost per year of life saved by the ICD over AAD in this group ($60 967) was only modestly less than that for the AVID population as a whole. In contrast, there was little survival benefit of the ICD over drug therapy among patients with ejection fractions over 35%, only 0.02 years. Costs of care among both drug- and device-treated patients in this subgroup were the lowest of all the groups evaluated ($64 548 versus $73 126). None of these differences was statistically significant.

The negative cost-effectiveness ratio (−$9513) for the small subgroup of patients without coronary heart disease...
implies that the ICD saved both lives and costs compared with AAD therapy. In addition, cost-effectiveness ratios were similar for the younger, middle, and older age categories.

**Implications of Shorter Initial Hospitalization Length of Stay**

Initial hospital lengths of stay (LOS) for AVID-type patients are now shorter than the ∼13 days shown during the AVID trial. LOS declined even during the AVID trial, from almost 15 days at the beginning of the trial to 10 days at the end. Other investigators have described lengths of stay <5 days among survivors of ventricular arrhythmias who received pectorally implanted ICDs. Projecting from the hospitalization cost model (Appendix 1), reducing the baseline hospitalization stay might save $1328 per day. Thus, differential change of one day’s LOS would alter the cost-effectiveness ratio by $6281 ($1328 differential costs/0.21 years, the survival differential). If, for example, the mean LOS for patients with ICD dropped 3 days compared with patients treated with AAD, the cost-effectiveness ratio would fall from $66 677 to $47 834.

**Extended Time Horizons**

Measured cumulative costs up to 4 (for patients treated with AAD) and 5 (for patients treated with ICD) years are shown in Figure 1. The cost differential at 3 years is $11 681 and at 4 years is $20 156. Survival to 6 years (based on the combined AVID/CASH/CIDS data) is shown in Figure 2. Over a 6-year time horizon, patients in the ICD and AAD arms survived an average of 4.66 and 4.29 years, respectively; a difference of 0.37 years. The hazard for the ICD arm appears approximately constant out to 6 years, whereas the hazard for the AAD arm appears approximately constant (and greater than the hazard for the ICD arm) out to 4 years and then begins to decrease.

Cost-effectiveness estimates for various time horizons and various survival assumptions are shown in Table 6 using the cost and survival assumptions described in the Methods section. Out to 6 years, the costs and survival differences using either survival model are the same, because both are based on the same empiric data for the first 6 years. Thus, the C/E ratio ($79 291) is the same. From 6 years to 20 years, however, the estimated C/E ratios differ slightly, from $68 378 to $80 358, depending on which survival assumptions are used. When lifetime survival is projected, the equal hazards model predicts that the C/E ratio will drop by $12 160, whereas the Weibull survival estimates, which predict a lessening of mortality in the AAD group in later years and thus a lessening relative benefit of the ICD, yield a lifetime C/E ratio of $200 000 per year of life saved. These unstable estimates in later years reflect inevitable uncertainty about the long-term survival of patients treated with antiarrhythmic drugs.

**Discussion**

The AVID economic substudy of 1008 patients represents the largest analysis to date of the costs of secondary prevention for survivors of cardiac arrest and hemodynamically unstable ventricular tachycardia. It has shown that the largest expense in the care of these patients is inpatient care, which makes up between 73% (for patients with AAD) and 84% (for patients with ICD) of total costs. It has demonstrated that over the 3-year time frame of the AVID trial, the cost to save 1 year of life with the ICD compared...
TABLE 4. Per-Patient Costs of Care for 3 Years

<table>
<thead>
<tr>
<th>Item</th>
<th>Patient Taking AADs</th>
<th>Patient With ICD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial hospitalization†</td>
<td>$21 646</td>
<td>$41 192</td>
</tr>
<tr>
<td>Repeat hospitalization†</td>
<td>$25 062</td>
<td>$22 761</td>
</tr>
<tr>
<td>Emergency/short stay visits‡</td>
<td>$645</td>
<td>$1007</td>
</tr>
<tr>
<td>Physician fees§</td>
<td>$2236</td>
<td>$4306</td>
</tr>
<tr>
<td>Total for hospitalizations</td>
<td>$53 453</td>
<td>$73 413</td>
</tr>
<tr>
<td>AAD§</td>
<td>$3986</td>
<td>$678</td>
</tr>
<tr>
<td>Medications (not AADs)§</td>
<td>$3300</td>
<td>$4319</td>
</tr>
<tr>
<td>Total for medications§</td>
<td>$7196</td>
<td>$4997</td>
</tr>
<tr>
<td>Other costs§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinic visits (physician contact)</td>
<td>$1765</td>
<td>$1896</td>
</tr>
<tr>
<td>Home care visits</td>
<td>$4321</td>
<td>$1533</td>
</tr>
<tr>
<td>ICD interrogation</td>
<td>$131</td>
<td>$675</td>
</tr>
<tr>
<td>Laboratory tests</td>
<td>$2516</td>
<td>$1668</td>
</tr>
<tr>
<td>Extended care</td>
<td>$4280</td>
<td>$2491</td>
</tr>
<tr>
<td>Physical therapy</td>
<td>$34</td>
<td>$37</td>
</tr>
<tr>
<td>Total other costs§</td>
<td>$12 914</td>
<td>$9070</td>
</tr>
<tr>
<td>Total</td>
<td>$73 564</td>
<td>$87 479</td>
</tr>
</tbody>
</table>

All values in 1997 dollars, not discounted. Ambulance charges ($459 for a patient treated with AADs; $410 for a patient treated with ICD) were not included in the cost computations.

*Adjusted for censoring.
†Based on a t test of approximately normalized data or Wilcoxon rank sum.
‡Data collected on all patients.
§Based on shoebox patient data (117 AAD and 120 ICD patients).
| Average for all patients, based on shoebox patient data but corrected by regression modeling for differences between shoebox and nonshoebox patients.

with treatment with (predominantly) amiodarone is moderately expensive, $66 677 per life year, compared with “economically attractive” therapies with C/E ratios between $50 000 and $100 000, and “economically unattractive” therapies with C/E ratios >$100 000. Six- and 20-year C/E ratios remained stable between $68 000 and $80 000 per year of life saved as various cost and survival estimates were evaluated. Subgroup analysis suggests that the ICD is relatively more cost-effective among patients presenting with ventricular fibrillation and relatively less cost-effective in patients with EF >0.35. The high C/E ratio for the latter group is fragile, however, because of the tiny life expectancy difference between patients treated with ICD and AAD. The negative cost-effectiveness ratio for patients without coronary heart disease is intriguing, but because of the relatively small number of patients in the noncoronary disease subgroup, this C/E ratio is likely attributable to the play of chance.

Comparison With Other Studies
Five other studies have evaluated the cost-effectiveness of the implantable defibrillator. Four of the 5 analyses used models and literature-derived survival and cost data from nonrandomized reports to simulate lifetime therapy costs and treatment ratios between $50 000 and $100 000, and “economically uncertain” therapies with C/E ratios between $50 000 and $100 000, and “economically unattractive” therapies with C/E ratios >$100 000. Six- and 20-year C/E ratios remained stable between $68 000 and $80 000 per year of life saved as various cost and survival estimates were evaluated. Subgroup analysis suggests that the ICD is relatively more cost-effective among patients presenting with ventricular fibrillation and relatively less cost-effective in patients with EF >0.35. The high C/E ratio for the latter group is fragile, however, because of the tiny life expectancy difference between patients treated with ICD and AAD. The negative cost-effectiveness ratio for patients without coronary heart disease is intriguing, but because of the relatively small number of patients in the noncoronary disease subgroup, this C/E ratio is likely attributable to the play of chance.

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TABLE 5. Incremental Cost-Effectiveness Over a 3-Year Horizon of ICD Compared With Drug Therapy

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>N</th>
<th>Cost, $</th>
<th>Survival, y</th>
<th>∆ Cost, $</th>
<th>∆Survival, y</th>
<th>C/E Ratio, $/y</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>1008</td>
<td>85 522</td>
<td>2.48</td>
<td>71 421</td>
<td>2.27</td>
<td>14 101</td>
<td>0.21</td>
</tr>
<tr>
<td>VF</td>
<td>453</td>
<td>81 401</td>
<td>2.46</td>
<td>66 610</td>
<td>2.19</td>
<td>14 791</td>
<td>0.27</td>
</tr>
<tr>
<td>VT</td>
<td>555</td>
<td>89 258</td>
<td>2.50</td>
<td>75 243</td>
<td>2.33</td>
<td>14 015</td>
<td>0.17</td>
</tr>
<tr>
<td>EF≤35%</td>
<td>695</td>
<td>92 358</td>
<td>2.44</td>
<td>74 581</td>
<td>2.15</td>
<td>17 777</td>
<td>0.29</td>
</tr>
<tr>
<td>EF&gt;35%</td>
<td>306</td>
<td>73 126</td>
<td>2.57</td>
<td>64 548</td>
<td>2.56</td>
<td>8578</td>
<td>0.02</td>
</tr>
<tr>
<td>Age &lt;60 y</td>
<td>266</td>
<td>86 432</td>
<td>2.59</td>
<td>69 930</td>
<td>2.37</td>
<td>16 502</td>
<td>0.23</td>
</tr>
<tr>
<td>Age 60–69 y</td>
<td>374</td>
<td>79 656</td>
<td>2.54</td>
<td>65 704</td>
<td>2.36</td>
<td>13 952</td>
<td>0.18</td>
</tr>
<tr>
<td>Age ≥70 y</td>
<td>368</td>
<td>90 741</td>
<td>2.33</td>
<td>76 873</td>
<td>2.11</td>
<td>13 886</td>
<td>0.21</td>
</tr>
<tr>
<td>CAD</td>
<td>822</td>
<td>87 802</td>
<td>2.45</td>
<td>70 672</td>
<td>2.22</td>
<td>17 130</td>
<td>0.23</td>
</tr>
<tr>
<td>Other cause</td>
<td>186</td>
<td>75 659</td>
<td>2.60</td>
<td>76 754</td>
<td>2.49</td>
<td>−1095</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Apparent calculation errors are attributable to rounding of survival years to 2 decimal points.
*Costs and survival discounted at 3% per annum.
effects, making them particularly difficult to compare with clinical trials that provide follow-up of only 3 to 6 years.

Of the clinical trials, MADIT\(^7\) and CIDS\(^8\) have reported cost-effectiveness analyses. The difference in average costs between the ICD-treated and the drug-treated patients was somewhat higher in MADIT than in the AVID trial, $21,580 over 4 years in MADIT compared with $14,101 over 3 years in AVID. However, because the survival difference was 3.6 times greater in MADIT than in AVID, the cost-effectiveness ratio (corrected to 1997 dollars) in MADIT was less than half that found in AVID, $30,337 versus $66,677. This survival difference, much more than cost differences, led to the substantial difference in cost-effectiveness ratios in the 2 studies.

In contrast, both a smaller survival benefit and an increased cost difference between ICD- and amiodarone-treated patients seem to have produced the relatively high C/E ratio seen in the recently reported CIDS cost-effectiveness analysis.\(^8\) Converted to United States dollars with the formula of $1 in Canadian dollars being equal to $0.65 in United States dollars, the CIDS base-case cost-effectiveness ratio over 6.3 years of follow-up was $138,803, roughly twice as high as the AVID trial. Costs of care for amiodarone-treated patients over 6.3 years were remarkably low in CIDS, only $25,909 per patient compared with >$70,000 per patient (United States dollars) over 3 to 4 years in the AVID trial and MADIT. Likewise, costs for patients with ICD were also lower than in the AVID trial and MADIT, $57,015 compared with $85,522 to $97,560. However, the $31,925 cost difference between amiodarone and ICD-treated patients in CIDS was much higher than in AVID and MADIT. This may in part reflect the fact that 34% of ICD patients in CIDS underwent ICD battery replacements during the 6.3 years of trial follow-up compared with only 7% of ICD patients in AVID during 3 years of follow-up. Comparison with AVID is made more problematic, because the 0.23-year survival benefit shown in CIDS did not achieve statistical significance.\(^12\)

**Limitations**

**Selective Data Collection**

Not all characteristics of the 237 shoebox patients, who were used to collect outpatient, laboratory, and physician bills, exactly matched the rest of trial participants (Table 1), including a higher frequency of ventricular fibrillation and larger proportion of women. As much as possible, regression modeling was used to account for baseline differences. In addition, outpatient care, medication costs, and physician billings together accounted for a relatively small proportion of total resource consumption when compared with the costs of inpatient hospital care.

**Lack of Complete Hospital Billing Data**

Twenty-one percent of the 2928 hospitalizations in the AVID trial were at either government or health maintenance organization facilities, which did not produce hospital bills. An estimate of charges for both baseline and repeat hospitalizations was imputed for each patient enrolled from one of these hospitals using regression models. The imputed cost estimates, although imperfect, were computed similarly for both arms of the trial and were thus unlikely to introduce significant bias into the final analyses.
Short Analytical Time Frame
The costs of therapy with the ICD cannot be fully appreciated until the costs of generator replacement are accounted for. These costs were not a significant part of health care utilization in AVID, where only 7% of patients randomized to ICD therapy had undergone generator replacements at trial termination (3-year rate of 18%). Nevertheless, our initial modeling efforts, accounting for generator replacement costs in the ICD cohort and using 2 different assumptions about survival, suggest that our base case C/E ratio estimate is quite stable out to 20 years of follow-up.

Changes in ICD Management
More than half of the patients treated with ICD in the AVID trial underwent baseline electrophysiologic studies and almost all underwent predischarge ICD testing. Presently most ICDs are pectoral implants and are implanted by cardiologists in the cardiac catheterization laboratory under intravenous sedation only. Routine predischarge testing may no longer be indicated. All of these practice changes reduce costs and length of stay. Alternatively, the use of newer, dual-chamber ICDs may increase costs without increasing survival. Thus, the AVID analysis may either overstate or understate ICD costs (and cost-effectiveness) to some extent.

Conclusion
The AVID economic substudy base-case cost-effectiveness ratio of $66,677 suggests that a year of life saved by ICD implantation compared with AAD therapy (largely with amiodarone) is moderately cost-effective by conventionally accepted standards of “cost-attractive” therapies. However, most costs associated with the treatment of both groups were for in-hospital care. Changes in management that reduce hospital days of care or reduce hospitalizations entirely should substantially reduce the costs of care for these high-risk, difficult-to-treat patients. Analyses with longer follow-up will provide more insight into the effect of ICD battery longevity on the cost-effectiveness of the ICD.

Appendix

Rehospitalization Costs: Regression Model (1997 $)

<table>
<thead>
<tr>
<th>Coefficients</th>
<th>Covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>2934</td>
<td>Ablation</td>
</tr>
<tr>
<td>13,664</td>
<td>CABG</td>
</tr>
<tr>
<td>50,949</td>
<td>Heart transplant</td>
</tr>
<tr>
<td>4753</td>
<td>Pacemaker procedure</td>
</tr>
<tr>
<td>19,330</td>
<td>Valve repair/replacement</td>
</tr>
<tr>
<td>22,637</td>
<td>ICD explantation then generator replacement and lead replacement or repositioning (performed on separate days)</td>
</tr>
<tr>
<td>18,648</td>
<td>Generator and lead replacement</td>
</tr>
<tr>
<td>18,550</td>
<td>Original generator and lead implantation</td>
</tr>
<tr>
<td>11,896</td>
<td>Lead repositioning/replacement, explantation without replacement</td>
</tr>
<tr>
<td>11,535</td>
<td>Generator only implantation/replacement</td>
</tr>
<tr>
<td>786</td>
<td>High-cost region (Northern, mid-Atlantic, Pacific)</td>
</tr>
<tr>
<td>–581</td>
<td>Overnight stay (not associated with emergency department admission)</td>
</tr>
<tr>
<td>4351</td>
<td>Death in hospital</td>
</tr>
<tr>
<td>1072</td>
<td>LOS</td>
</tr>
</tbody>
</table>

Acknowledgments
This work was funded by National Heart, Lung and Blood Institute contract No. N01-HC-25117.

References
of left ventricular dysfunction who have survived malignant ventricular arrhythmias. J Am Coll Cardiol. 1999;34:1090–1095.
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Circulation. 2002;105:2049-2057; originally published online April 15, 2002;
doi: 10.1161/01.CIR.000015504.57641.D0

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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