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VALUE IN HEALTH

Cost-Benefit Analysis of Preventing Sudden Cardiac Deaths with an Implantable Cardioverter Defibrillator versus Amiodarone

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ABSTRACT

Objectives: To conduct a cost-benefit assessment of prevention of sudden cardiac deaths with an implantable cardioverter defibrillator (ICD) versus amiodarone from the perspective of the health-care systems in the UK and France.
Methods: Course after implantation with an ICD or taking amiodarone was modeled using discrete event simulation; 1000 pairs of identical patients were simulated 100 times for each analysis. Rates of life-threatening arrhythmia and death from other causes were assumed identical, but the case fatality of arrhythmia and hospitalization differ between treatments. Rates were based on published data, primarily from the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). Direct medical costs (in 2004 Euros) and lives saved were estimated over 5 years. The monetary value of a life (UK €2.1 million, France €2.0 million) was applied to this benefit and examined relative to the net investment required.
Results: ICDs decreased deaths during the 5 years from 37.0% to 29.7% at a net cost of €26,222 to €20,008 per patient, yielding cost-benefit ratios of 0.17 (UK) and 0.14 (France)—more than a 5 to 1 return on investment. Sensitivity analyses showed ICDs represent value for money whenever a life is valued at least at €274,000.
Conclusion: In these European countries where society values a life at more than €2 million, ICDs are a worthwhile investment compared with amiodarone for primary prevention of sudden cardiac deaths in patients with heart failure.
Keywords: cost-benefit analysis, ICD, implantable cardioverter defibrillator, sudden cardiac deaths.

Introduction

The implantable cardioverter defibrillator (ICD) is the most effective way to prevent a ventricular arrhythmia from being fatal [1]. It is a life-preserving device—without it few patients experiencing ventricular arrhythmias arrive in hospital soon enough to survive [2]. ICDs have been recommended for several years for patients with prior ventricular arrhythmias (so-called secondary prevention of sudden cardiac death [SCD]) [1,3]. Most recently, indications for ICD have been expanding as clinical trials have shown improved survival in patients with serious heart disease who have not yet suffered a ventricular arrhythmia (so-called primary prevention of SCD) [4]. The direct economic consequences of this expansion can be considerable, however. For example, the results of the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) led to the expansion of coverage in the United States, and it is expected that Medicare beneficiaries eligible for an ICD will increase by one-third, to nearly 500,000—an additional 25,000 patients will be implanted in the first year of coverage, and potentially up to 2500 lives will be prolonged [5].

Even before primary prevention was being considered, there was already evidence that ICDs have not been uniformly adopted, and that this is probably due to economic, as well as clinical, concerns [1,6]. Various cost-effectiveness analyses of ICD use have been completed [7–10] and have generally concluded that the cost-effectiveness of ICD use is borderline, except when patients are at high risk of SCD. This conclusion is largely due to the methods selected for the analyses: Cost-effectiveness studies use duration of life, often adjusted to reflect the average quality of life, as the measure of benefit. This leads, in our opinion and that of others [11], to undervaluing of the benefit when the intervention tends to be for more elderly patients, especially if they are chronically ill and thus likely to have their survival "quality-adjusted" downward. Although cost-effectiveness analyses are prevalent in health technology assessments, the morality of valuing a person's life less because they are older or ill is questionable. In this article, we provide a different view of the economic desirability of ICD use for primary prevention of SCD by carrying out a cost-benefit assessment compared with amiodarone in the UK and France. This

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method was chosen because it places an equal value on each life saved.

Methods

Data and Sources

Because no single data source provided all of the required age-dependent arrhythmia and mortality inputs, these were derived by combining data from two sources. The major source for inputs was the published results of the SCD-HeFT [4]—individual patient data were not made available to us. The SCD-HeFT was a randomized, controlled, primary prevention trial of 2521 patients with mild to moderate heart failure (New York Heart Association class II/III) and ejection fractions of 35% or less. All the patients were receiving optimal medical therapy before enrollment (beta-blocker, diuretic, statin, and ACE inhibitor). Patients were assigned to ICD (N = 829), amiodarone (N = 845), and placebo (N = 847); median follow-up was 3.8 years. The 5-year mortality in the placebo group was 36.1%. When amiodarone was compared with placebo, there was no significant difference, whereas those receiving an ICD had a 23% reduction in mortality, an absolute decrease of 7.2% after 5 years. Other information obtained from the trial was the initial age distribution and all-cause mortality over 5 years.

The second major source—for mortality rates in five age groups and the probability of developing severe amiodarone toxicity—was a published meta-analysis of trials of amiodarone based on individual patient data [12,13]. Thirteen trials (N = 6252) were included in the meta-analysis, which evaluated the effect of prophylactic amiodarone on all-cause death and fatal arrhythmia after myocardial infarction or congestive heart failure (22%). The mean follow-up was 1.4 years.

Model

A discrete event simulation was designed to follow a patient's course after implantation with an ICD or initiation of amiodarone for primary prevention of SCD (Fig. 1). Individual patients were created by assigning unique characteristics to each one: For example, each patient was assigned an age based on the SCD-HeFT population [4], which had a median age of 60.1 years (25th percentile 51.7 years, 75th percentile 68.5 years). Then each patient was "cloned" to ensure comparison of identical cohorts. One clone received an ICD, the other amiodarone, and both also received optimal medical therapy (beta-blocker, diuretic, statin, and ACE inhibitor). The rate of life-threatening arrhythmia was the same for the clones. If a severe arrhythmia occurred, the model determined whether the patient survived the event and then whether a hospitalization occurred, and these consequences differed depending on which treatment the patient was on: The probabilities were lower with an ICD. Survivors of an event were exposed to a higher rate of life-threatening arrhythmia for the following 6 months. Each patient with an ICD may develop postimplantation complications (lead- and device-related), which may lead to hospitalization for a reoperation or revision. Patients on amiodarone may develop severe drug toxicity. A patient with amiodarone toxicity was assumed to be hospitalized and a probability of death was assigned. The age-dependent hazard of death from causes other than severe arrhythmia was the same for each of the treatments. When a patient died or reached the end of

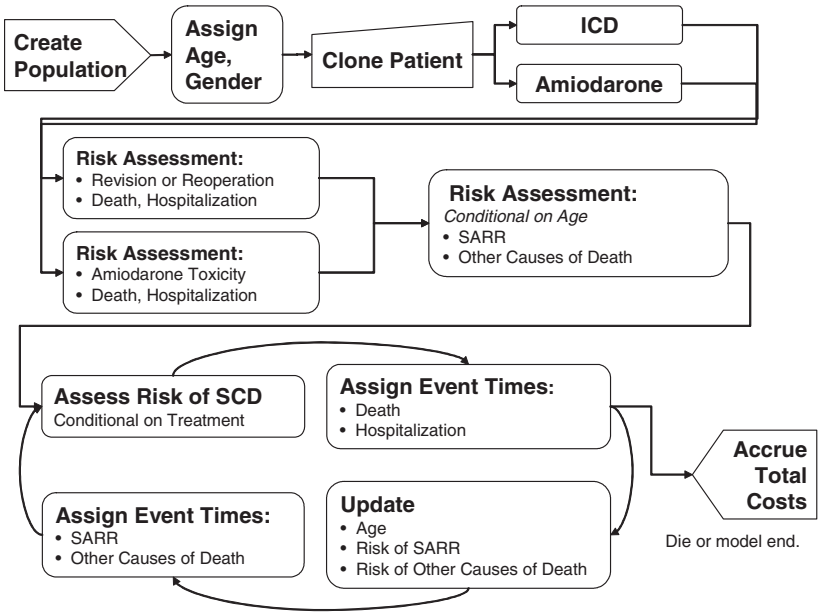

Figure 1 Schematic representation of model implemented as a discrete event simulation.

the time horizon (5 years), he or she was removed from the simulation. During the simulation, the number of deaths, revisions, and hospitalizations were counted, and their associated direct medical costs (given the health-care system perspective) were accrued according to the patient's assigned treatment. The simulation was carried out using ARENA v8.01 (Rockwell Software, Inc., Warrendale, PA) [14].

The simulation was controlled by two equations: the severe arrhythmia rate and other-cause mortality as functions of age; and two age-independent parameters: the case-fatality rates of a severe arrhythmia by treatment (Table 1). The equation for life-threatening arrhythmia was derived by combining SCD-HeFT results with the age-specific fatality data from the meta-analysis of amiodarone trials. The SCD-HeFT has not reported the arrhythmia-related deaths separately but indicated that "appropriate ICD shocks" were reported at an average hazard of 5.1% per year. The average hazard of dying from an arrhythmia in the trial was derived for amiodarone users by assuming that 90% [15–17] of the 5.1% would be fatal. This average estimate was translated to age-conditional hazards (h_{age}) by calibrating the equation derived from the amiodarone meta-analysis: $h_{age} = 2.0299E^{-4} \times Age + 4.7318E^{-5}$, ($R^2 = 0.98$). The calibration involved changing the intercept so that the derived hazard matched the average one from the trial at the median age of 61 years. Age-specific values of the death hazard were then derived, and the implied severe arrhythmia rates were estimated using the 90% case-fatality rate. The resulting severe arrhythmia hazard ($SARR_{age}$) for each 3-month period was therefore $SARR_{age} = 2.2555E^{-4} \times Age - 1.91062E^{-3}$, where *Age* is the current age. Survivors of a severe arrhythmia are, by definition, in a secondary prevention context. They are assigned a higher arrhythmia hazard (1.5-fold) for the following 6 months.

Because the SCD-HeFT trial reported the effect of an ICD on all-cause mortality only, the case-fatality rate with arrhythmia had to be derived. This was carried out by assuming that the entire reduction seen in the trial was due to prevention of arrhythmia deaths (i.e., no reason to assume ICD avoids deaths due to other causes). Thus, an estimate of the hazard of deaths due to other causes was needed, and this was obtained by subtracting from the all-cause death hazard of 8.9 per 100 person-years for amiodarone, the arrhythmia death hazard: $8.9 - (5.1 \times 0.9) = 4.31$ per 100 person-years. For patients with an ICD, the arrhythmia death hazard can now be obtained by subtracting this common other death hazard from the observed overall mortality of 6.8 per 100 person-years: $6.8 - 4.31 = 2.49$ per 100 person-years. This yields an estimate for the ICD case-fatality rate of 49% (2.49/5.1).

Because all-cause mortality increases with age but the proportion of deaths due to arrhythmia decreases [12], the rate of deaths due to other causes also increases with age. The age-specific other-cause mortality was derived by subtracting the age-specific arrhythmia mortality from the corresponding all-cause mortality. The latter was obtained by applying an age-specific cause ratio to the age-specific arrhythmia mortality. The cause ratio, CR_{age}, was estimated using the linear fit of the observed ratios of arrhythmia to the all-cause mortality reported in the meta-analysis of amiodarone trials [12]: $CR_{age} = -9.0139E^{-3} \times Age + 0.96165$ ($R^2 = 0.9$). The ratio equation was calibrated to SCD-HeFT by changing the intercept to 1.1016 to match the ratio calculated from the all-cause mortality observed in the trial and the derived arrhythmia-related mortality for the age of 61 years. The age-dependent all-cause mortality was then derived using the age-specific ratio given by this equation and the age-specific arrhythmia mortality derived for each of

Table 1 Source and derivation (given in {}) of main model inputs (in italics) relating to mortality and arrhythmia rates

Input	Source	Amiodarone	ICD
Severe arrhythmia rate (SARR)			
Mean	SCD-HeFT	Same as ICD	5.1%
Age-dependent	Meta-analysis*	2.2555 E^{-4} Age – 1.91062 E^{-3}	
Case-fatality rate (CFR)	[15–17], derived	90%	49% {ARM/SARR}
All-cause mortality (ACM)			
Mean	SCD-HeFT	0.089	0.068
Age-dependent	Meta-analysis	Age-dependent ARM/CR	
Arrhythmia mortality (ARM)			
Mean	Derived	0.0459 {SARR × CFR}	0.0249 {ACM – OCM}
Age-dependent	Meta-analysis	Age-dependent SARR × CFR	
Age-dependent cause ratio (CR)			
Mean	SCD-HeFT	51.57% {ARM/ACM}	36.62% {ARM/ACM}
Age-dependent	Meta-analysis*	– 9.0139 E^{-3} × Age + 1.1016	
Other-cause mortality (OCM)			
Mean	Derived	0.0431 {ACM – ARM}	Same as amiodarone
Age-dependent	Derived	Age-dependent ACM – ARM	

*Calibrated to the SCD-HeFT mean.
ICD, implantable cardioverter defibrillator; SCD-HeFT, Sudden Cardiac Death in Heart Failure Trial.

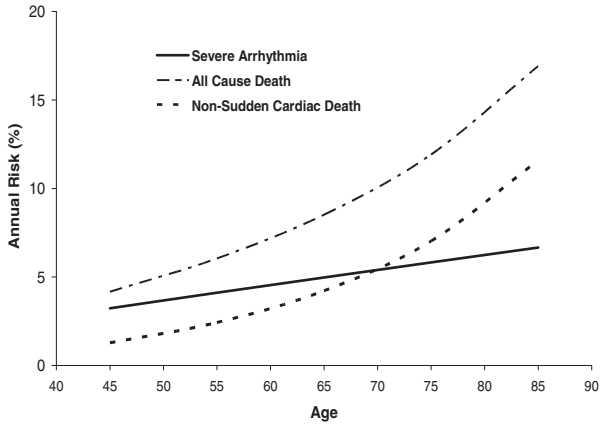

Figure 2 Age-specific risks derived using data from the Sudden Cardiac Death in Heart Failure Trial and the meta-analysis.

the simulated amiodarone users. The resulting age-dependent functions are illustrated in Figure 2.

Adverse Events

In the SCD-HeFT, all devices were inserted as an outpatient procedure, and ICD-related complications were experienced by 5% of the patients at the time of the implantation. Outpatient insertion of the ICD is not currently routine practice, however, so in the simulation all patients were admitted to hospital for the procedure. Thus, complications arising during the implant procedure do not change the cost of the hospital stay. Annual lead and device complication risks, 0.9% and 0.2%, respectively, were estimated from data provided by Medtronic [18], which are consistent with recent reports [19]. When a complication arises, half are assumed to lead to reoperation and the rest to a revision procedure. The risk of pulmonary toxicity with amiodarone (1% per year) was obtained from a published meta-analysis [13]. The probability of dying from pulmonary toxicity was set at 10% [20].

Value of a Life

Each life "saved" was assigned a monetary value developed by government authorities using the willingness-to-pay (WTP) approach. In the simplest form of this, the subject is asked how much he or she is willing to pay to obtain a given reduction in the risk of death. Because this direct approach is subject to many biases and measurement problems, more sophisticated methods have been developed to elicit WTP [21]. These establish the value of intangibles such as a "life" by creating an imaginary market and asking representatives of the society to carry out hypothetical trades in that market [22]. Those contingency trades are then taken to reveal the value of the intangible at issue.

The monetary value of a prevented fatality recommended by the UK government for cost-benefit analyses of scenarios involving accidental and near immediate loss of life was based on research conducted by the Department of Transport [23]. Since 1993, the UK Department of Transport has based their valuation of preventing road traffic fatalities on a WTP approach, and their estimate has been reviewed in the contexts of rail transport, domestic fires and public fires, and similar values elicited [24]. The monetary value of a life used for the UK analyses was from a recent Department of Transport report [24] (£1,312,260, 2003 GBP) inflated to 2004 (£1,445,000, €2.1 million) [25]. The French government commissioned a study that recommended transport investment decisions be made using a value of €2.0 million (2000) [26]. Consistent with the principles of cost-benefit analysis, the value of a life was not adjusted to take into account the age of the beneficiaries nor their illness [24].

Costs

Details of the cost inputs and sources are provided in Table 2 [27–34]. Costs are reported in 2004 Euros. These include hospitalization, ICD, and medication costs. Where necessary, the costs were inflated using the appropriate price index to 2004 [26]. Each patient in the ICD cohort accrues an initial hospitalization and ICD cost (including the lead and device costs). All postoperative complications were assumed to lead to a revision and accrue a cost. When a reoperation was required, then both the revision and replacement device costs were assigned.

For patients on amiodarone, there is an initial cost when therapy is started, and the daily cost of treatment. When severe amiodarone toxicity occurs, the patient accrues a hospital cost. Optimal medication costs were assigned to each patient in addition to the ICD or amiodarone costs. The probability of hospitalization after a severe arrhythmia was estimated (Table 3). Without the ICD, these arrhythmias are almost always fatal so it was assumed that 100% of the survivors on amiodarone are hospitalized. Most patients with an ICD who receive an "appropriate shock" and survive the arrhythmic event do not need to be hospitalized (Medtronic, pers. comm.). No cost was assigned to a death from other causes.

Analyses

Lives prolonged and the associated monetary value assigned to this benefit were estimated over 5 years. The direct medical costs of ICD implantation, complications (revision, reoperation), amiodarone treatment, hospitalization to manage toxicity, and optimal medication (beta-blocker, diuretic, or ACE inhibitor) were also estimated. Benefits and costs were discounted at 3.5% for the UK and 3% for France [35,36]. At the end of the simulation, the monetary value of the health benefit was applied and the cost-benefit ratio was calculated as the net direct cost of ICD versus amiodarone

Table 2 Direct medical cost inputs (in 2004 Euros)

Item	Unit	UK	France
Implantable cardioverter defibrillator			
Lead and device*		23,575	15,500
Hospital stay	Initial implant	7,184	4,984
	Revision	5,192	4,580
Amiodarone			
Initiation of treatment†		4,294	75
Hospital stay‡	Severe toxicity	252	2,942
Medication§	Per Diem	0.33	0.37
Optimal medication‖	Per Diem		
Beta-blocker		0.03	0.21
Diuretic		0.06	0.07
Statin		1.20	1.06
ACE inhibitor		0.32	0.65
Severe arrhythmia	Hospital stay	7,184	4,984

Cost estimates were derived from the following sources:
*ICD (Medtronic, pers. comm.).
†Amiodarone initiation presumed to be during a hospital stay in the UK [27], and at an outpatient visit with appropriate procedures in France [28].
‡Hospital stay for severe toxicity in the UK [27], France [29,30].
§Amiodarone UK [31], France [32].
‖Optimal medications UK [33], France beta-blocker [34], diuretic [32], statin [32], ACE inhibitor [34].

treatment divided by the monetary value of the number of lives saved. The ratio and the net difference between the value of the health benefit and the investment required were derived. The ratio represents the amount invested to obtain one monetary unit of benefit; if it is less than one it indicates a good result because it implies that the value of the benefits exceeds the net direct costs.

Sensitivity analyses were conducted on all key parameters, including age, case-fatality rates, arrhythmia rates, and the probability of hospitalization. Uncertainty in the base case estimates was examined using 100 model replications. Each replication simulated the experience of 1000 patients with each treatment.

Validation. Technical verification of the model was assessed by extensive extreme value analyses, internal testing, and "debugging," and by a careful review of the model calculations by a modeler not involved in the initial programming. Face validity was assessed by presentation of the model to clinical experts. The consistency of the model's predictions against the SCD-HeFT results was verified. The SCD-HeFT reported a 5-year mortality in the placebo group (36.1%), it was not significantly different for amiodarone, and a significantly lower risk (hazard ratio [HR] 0.77) for the ICD treatment group. The model predicts 36.9% 5-year mortality without the ICD, and 29.6% with the ICD (HR 0.76).

Table 3 Model inputs

Parameter	ICD	Amiodarone
Severe arrhythmia		
Annual risk, range (%)*	3.3–6.9	3.3–6.9
Hospitalization		
Survivors (%)	5	100
Fatal (%)	17	17
Death from other causes		
Annual risk, range (%)*	1.3–12.3	1.3–12.3
Adverse events		
Annual risk (%)	Lead—0.9 Device—0.2	Toxicity—1

*Age-dependent estimates.
ICD, implantable cardioverter defibrillator.

Results

The model predicts that 37.0% of the patients receiving amiodarone will die within 5 years of the start of treatment, compared with 29.7% of those who receive an ICD, a relative reduction of 19.7% and an absolute decrease of 7.3%. Thus, ICD use in 1000 patients is predicted to prevent 73 premature deaths over 5 years. The resulting net additional direct medical cost over 5 years for implanting an ICD in the 1000 patients compared with using amiodarone alone was €26,222 per patient in the UK and €20,008 in France (Table 4).

Table 4 Cost-benefit assessments over 5 years for the UK and France for 1000 patients (discounted at 3.5% for the UK and 3% for France)

Parameter	UK	France
Cost*		
ICD	33.5 million (262,808)	23.7 million (363,070)
Amiodarone	7.3 million (66,799)	3.7 million (316,350)
Net	26.2 million	20.0 million
Value of lives saved†	153.1 million	135.5 million
Cost-benefit ratio‡	0.17	0.14

*Cumulative costs in Euros (€) over 5 years for 1000 patients. Results are the mean (SD) of 100 replications.
†ICD use was predicted to prevent 73 premature deaths over 5 years for 1000 patients. Value of lives saved = Number of lives saved × Monetary value assigned to a life.
‡Cost-benefit ratio = Net costs/Value of lives saved.
ICD, implantable cardioverter defibrillator.

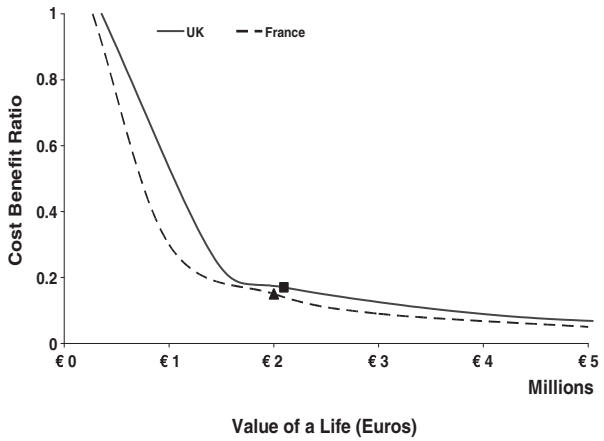

Figure 3 Cost-benefit ratio versus value of life in the UK (base case symbol ■) and France (base case symbol ▲).

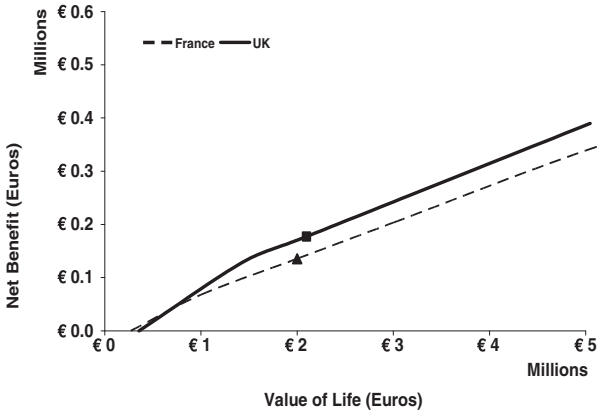

Figure 4 Net benefit (value of lives saved – net cost) versus value of life in the UK (base case symbol ■) and France (base case symbol ▲).

According to the value currently assigned to a life in each country, the benefit of preventing 73 deaths is valued at €153 million in the UK and at €135.5 million in France. Comparing this with the additional direct medical costs yields a cost-benefit ratio of 0.17 for the UK and of 0.14 for France. In other words, the health benefit gained is more than five times as valuable to these societies as the net amount that has to be invested. The net benefit (value of lives saved – net cost) was valued at €127 million in the UK and €115 million in France.

The monetary value assigned to a life is a key input in this simulation and so changes in this parameter affect the results considerably. Therefore, in the sensitivity analysis, the relation of the cost-benefit ratio to monetary values assigned to a life was examined (Figs. 3 and 4). The breakeven point (i.e., the value of a life at which the benefits just equal the net costs) was found to be €359,210 for the UK and €274,083 for France. Thus, ICD treatment is a very worthwhile investment as long as these societies assign a value to a life that is above these thresholds. Other sensitivity analyses are reported in Table 5. Varying these other parameters did not have a major impact on the ratios predicted. Another key input in the simulation is the rate of arrhythmia, and hence the risk of a sudden cardiac death. The arrhythmia rates are lower for younger patients, so the ratio is slightly less favorable in this age

Table 5 Univariate sensitivity analysis

		Total deaths			Cost-benefit ratio	
Parameter	Value	Amiodarone	ICD	NET	UK	France
Base case		370	297	73	0.17	0.14
Age group						
	40–50	234	167	67	0.19	0.15
	50–60	314	237	77	0.17	0.13
	60–70	416	340	76	0.16	0.13
	70–80	538	467	71	0.17	0.14
Case-fatality rate						
	Amiodarone 80% ICD 39%	372	299	73	0.17	0.14
	Amiodarone 95% ICD 54%	369	297	72	0.17	0.14
Hospitalization rates						
Amiodarone	Survive 80% Fatal 10%	369	297	72	0.18	0.14
	Survive 90% Fatal 25%	368	300	68	0.18	0.15
ICD	Survive 0% Fatal 10%	367	296	71	0.18	0.14
	Survive 10% Fatal 25%	369	298	71	0.18	0.14
Severe arrhythmia rate						
	3%*	379	313	66	0.19	0.16
	8%*	363	286	78	0.16	0.12

*Age-dependent estimates applied, assuming these values for patients aged 61 years.
ICD, implantable cardioverter defibrillator.

group because fewer patients benefit from the ICD. In this simulation the risk of death from other causes besides arrhythmia is assumed to increase, and so slightly less favorable results are observed for patients more than 70 years old.

Discussion and Conclusion

This cost-benefit study estimates that policies allowing ICDs to be implanted for primary prevention of SCDs in patients with heart failure will lead to an additional direct medical cost of between €20,000 and 26,000 per patient but will prolong 73 lives per 1000 implants. From an economic viewpoint, it is expected that investment in ICD will be considered worthwhile whenever a society values a life at more than about €274,000. This is a level of investment that is well below what has been judged acceptable for other lifesaving interventions, such as vaccination programs, and also for regulatory policies adopted for injury prevention, such as rear-seat belts, air bags, or decreasing environmental pollution [37–40], although in the United States somewhat different criteria have been applied in different sectors of American society, with lower levels of investment often expected for medical interventions [41].

Several cost-effectiveness analyses of ICD for primary prevention of SCD have been published as each additional clinical trial was completed [7–10]—where the value of saving lives is expressed in terms of expected gains in either length or quality of life. For example, recently Sanders et al. [8] developed a Markov model incorporating the efficacy of ICD as the relative risk of death based on each of the hazard ratios reported in six primary prevention trials—the Multicenter Automatic Defibrillator Implantation Trial (MADIT)-I, MADIT-II, the Multicenter Unsustained Tachycardia Trial, the Defibrillators in Non-ischemic Cardiomyopathy Treatment Evaluation trial, the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure trial, and the SCD-HeFT. Over a lifetime use of an ICD was predicted to add between 1.01 and 2.99 quality-adjusted life-years (QALYs), with net costs between $68,300 and $101,500, and the cost-effectiveness estimates of the ICD compared with control therapy ranged widely from $34,000 to $70,200 per QALY gained.

As the benefit in a cost-effectiveness study is defined in terms of the expected longevity as well as quality of life, lifesaving treatment among older or sicker individuals will lead to less favorable QALY gains and higher cost-effectiveness ratios than for younger or healthier patients [11,42]. Those analyses are assuming a particular utilitarian framework, where the goal is to maximize QALYs within a society, and in the health sector this approach has been found to work well to assess treatments that relieve pain or disability but perhaps should not be the only approach when the treatment prevents premature deaths. The utilitarian approach of cost-effectiveness analyses ignores the ethical and equity issues that arise when lifesaving interventions are not extended to particular groups on the basis that they are mostly older or sick patients. Although there may be a sense that allocation of scarce resources should be preferential toward younger or healthier people, there are equally compelling arguments that fairness (especially in the context of taxpayer supported health care) dictates that the system should allocate based on need. Products such as ICDs are a particularly difficult problem for health-care decision-makers responsible for allocating resources, because denial of access to this care conflicts with the widely accepted "rule of rescue," that is the imperative we all feel to try to save the life of an identified person [43,44]. For example, when the Oregon Health Services Commission tried to prioritize health-care services based on cost per QALYs, public outcry led to lifesaving treatments being placed in a special high-priority category with no link to their cost-effectiveness [45]. Hadorn [44] felt that the experience in Oregon reflected a fundamental conflict between results of cost-effectiveness analyses and the powerful human impulse to save a life. In any case, there is little evidence that the inequity that results from the use of the QALY correctly reflects any discrimination the society wishes to incorporate in its decision-making.

The cost-benefit approach was used instead of the more common cost-effectiveness analysis because it was felt to be a preferable alternative way to assess the value of a lifesaving intervention such as the ICD, which is designed to preserve a life when a severe arrhythmia occurs but has no other day-to-day health benefit—in this it is like a seat belt, a helmet, and so on. The approach adopted here does not discriminate by assigning a lower value to the lives of older people (who have a lower life expectancy and, thus, less life-years to be gained) or of those who are irreversibly ill with heart failure (and, thus, gain less QALYs because their quality is already compromised permanently). Although medical practice may triage care toward younger individuals (e.g., in the UK children are assigned priority for receiving a renal transplant) [46], the morality of age-based rationing has been a matter of some debate [42,45,47,48], and not everyone agrees with the premise that society should place a lower value on the lives of the elderly or the ill. For example, Johri et al. [48] reported that for a lifesaving scenario, although 57% preferred allocating resources to a program serving 35-year-olds, more than a third disagreed with this concept (38% were age-neutral, and 4% of respondents preferred allocating resources to the program serving the elderly). Because the adjustments involved in estimating QALYs, or life-years gained, are discriminatory, especially in the context of this type of

intervention, our study contributes to the discussions by providing a different viewpoint to that already given by the cost-effectiveness studies. Moreover, in cost-benefit assessments the resource use and the health gains are valued in monetary units, and so both the investment and the return are measured on the same scale. This can be a particularly helpful approach because it avoids the awkward and unresolved problem of deciding how much money per QALY is acceptable.

Cost-benefit analysis has often been used to improve decision-making in many aspects of government spending on lifesaving interventions other than health care. Although to some people the monetary valuation of human life may appear immoral, in the UK, there is a policy requiring consideration of the costs and benefits of government proposals [49]. The Department of Transport value of preventing a fatality has been used in cost-benefit studies conducted by the Home Office, Health and Safety Executive, Environment Agency, Food Standards Agency, and other UK government departments [23]. In none of these situations was consideration given to the age or health status of the individuals affected. The values of a life for both France and the UK were about €2 million, somewhat higher than the €1 million (range €0.65–€2.5 million, 2000) used in Europe for cost-benefit analyses of environmental policies [50], but consistent with recent studies in Italy and Spain [51,52]; higher values have also been estimated [54–57]. The threshold value estimated in these analyses is well below all of these, however, indicating that regardless of which estimate is used, the cost-benefit ratio for ICD use is favorable. This holds even if one were to adjust downward the value of these patients' lives to reflect their age and illness.

If a severe arrhythmia arises, death is frequently so quick [2] that the majority are not hospitalized. Fewer patients with an ICD will need to be hospitalized (10%); however, the impact on the total direct medical cost is small because the severe arrhythmia rates are relatively low (ICDs fired at about 5% per year in the SCD-HeFT), and consequently not many hospitalizations are avoided. The largest component of the 5-year cost estimate is the ICD and hospitalization for implantation, which was estimated at 90% of the 5-year costs in each country. In the SCD-HeFT, all devices were inserted as an outpatient procedure, but because this is not yet routine practice, in the simulation all were assumed to be admitted to hospital. Each ICD implanted in the SCD-HeFT was a single-chamber device programmed with a simple pre-established programming for shock therapy (detection rate for tachyarrhythmias of 187 beats per minute or more), and no rate responsive pacing was allowed. Some ICDs have additional features, e.g., biventricular pacing, but the potential impact of these additional features on costs and outcomes has not been established. Such information could be of interest, because improvements in heart failure symptoms and reductions in hospitalizations can be achieved using cardiac-resynchronization therapy, which when combined with an ICD significantly reduces mortality [57].

A key assumption of this model is that the death rates derived from combining data from the SCD-HeFT and the meta-analysis of amiodarone trials are appropriate. Published data from the SCD-HeFT were used and a series of assumptions was made to derive the severe arrhythmia rate and the fatality rate with an ICD. The relationship between death risks and age was developed from a meta-analysis of amiodarone trials and assumed to apply to the candidates for ICD. This assumption is reasonable for a simulation because it is calibrated to reflect the death rate observed in the SCD-HeFT, and the results are consistent with the SCD-HeFT published results.

The use of ICD rather than amiodarone to manage severe arrhythmic events can be anticipated to prolong lives. Although cost-benefit analyses can facilitate comparison of health-care decisions, they do not address affordability. Nevertheless, the breakeven value of a life estimated here suggests that investment in ICDs is worthwhile in European societies. This supports clinical arguments for a greater investment to provide patients access to this life-prolonging treatment.

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