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Chapter 6

Cost-Effectiveness of Primary Prevention Implantable Cardioverter Defibrillator Treatment: Data from a Large Clinical Registry

Joep Thijssen, MD[1]; M. Elske van den Akker van Marle, PhD[2]; C. Jan Willem Borleffs, MD PhD[1]; Johannes B. van Rees, MD[1]; Mihály K. de Bie, MD[1]; Enno T. van der Velde, PhD[1], Lieselot van Erven, MD, PhD[1]; Martin J. Schalij, MD, PhD[1].

From [1] the Department of Cardiology and [2] the Department of Medical Decision Making, Leiden University Medical Centre, Leiden, the Netherlands.

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ABSTRACT

Background

Although randomized trials have shown the beneficial effect on survival of an implantable cardioverter defibrillator (ICD) as primary prevention therapy in selected patients, data concerning the cost-effectiveness in routine clinical practice remain scarce. Accordingly, the purpose of the current study was to assess the cost-effectiveness of primary prevention ICD implantation in the real world.

Methods

Patients receiving primary prevention single-chamber or dual-chamber ICD implantation at the Leiden University Medical Center were included in the study. Using a Markov model, lifetime cost, life years (LY), and gained quality-adjusted life years (QALY) were estimated for device recipients and control patients. Data on mortality, complication rates, and device longevity were retrieved from our center and entered into the Markov model. To account for model assumptions, one-way deterministic and probabilistic sensitivity analyses were performed.

Results

Primary prevention ICD implantation adds an estimated mean of 2.07 LYs and 1.73 QALYs. Increased lifetime cost for single-chamber and dual-chamber ICD recipients were estimated at €60,788 and €64,216 respectively. This resulted for single-chamber ICD recipients, in an estimated incremental cost-effectiveness rate (ICER) of €35,154 per QALY gained. In dual-chamber ICD recipients, an estimated ICER of €37,111 per QALY gained was calculated. According to the probabilistic sensitivity analysis, estimated cost per QALY gained are €35,837 (95% CI: €28,368 - €44,460) for single-chamber and €37,756 (95% CI: €29,055-€46,050) for dual-chamber ICDs.

Conclusion

Based on data and detailed costs, derived from routine clinical practice, ICD therapy in selected patients with a reduced LVEF appears to be cost-effective.

INTRODUCTION

Multiple randomized studies have demonstrated a survival benefit in selected groups of patients with ischemic and non-ischemic heart disease following implantable cardioverter defibrillator (ICD) implantation.[1-7]

With the recommendation of ICD therapy as prophylaxis for sudden cardiac death in patients with a depressed left ventricular ejection fraction (LVEF), worldwide implantation rates have increased significantly.[8, 9] Concomitantly, the costs associated with ICD treatment increased as well, putting a heavy cost burden on health care systems, making it essential to assess the cost-effectiveness of ICDs.[10, 11] Previously, several studies have assessed the cost-effectiveness of the primary prevention use of ICDs and demonstrated that ICDs may be cost-effective if current guidelines are followed.[12-18] However, it is difficult to extrapolate these results to routine clinical practice since these studies mainly used experts' opinions for complication rates, device longevity, and costs.

Since 1996, all patients receiving an ICD at the Leiden University Medical Center have been assessed and followed-up. This thoroughly screened cohort provided a unique opportunity to assess cost-effectiveness of primary prevention ICD implantation based on clinical data and detailed costs derived from routine clinical practice.

METHODS

Design of the study

The estimated lifetime cost and effects of primary prevention implantable cardioverter defibrillator (ICD) implantation were compared with conventional pharmacological therapy in patients with a reduced left ventricular ejection fraction (LVEF) using a Markov model. For the current analysis, a model initially developed by Sanders et al. and thereafter further adapted by Cowie et al was used.[13, 15] In this model, a hypothetical cohort of patients receiving ICD therapy or conventional pharmacological therapy were tracked using a 1-month cycle length. In each model cycle, patients from both cohorts were at risk for sudden cardiac death (SCD), heart failure death (HFD), other cardiac death (OCD), and non cardiac death (NCD). Also, patients receiving ICD therapy were at risk for ICD treatment related complications such as: operative death, implant associated complications, device associated complications and discontinuation of ICD therapy. Furthermore, associated medical costs were included in the model and therewith provide the opportunity to estimate the lifetime costs and effects of patients receiving ICD therapy or conventional pharmacological therapy.

In the previous model however, trial data were based on expert opinion and manufacturer data, while in the current study these inputs (i.e. complication rates, device longevity, and costs) were based upon actual data of routine clinical practice at the Leiden University Medical Center, the Netherlands.

Cost-effectiveness was calculated for both single-chamber and dual-chamber ICD devices. Data entered in the model was derived from 483 consecutive patients with a reduced LVEF (≤35%) who received a primary prevention single-chamber (n=45, 9%) or dual-chamber (n=438, 91%) ICD in the LUMC between January 1996 and September

2009. Eligibility for ICD implantation was based on international guidelines for primary prevention.[8, 9] Baseline characteristics for the complete group are summarized in Table 1. During a mean follow-up of 31.7±26.9 months, 22 single-chamber and 86 dual-chamber replacement devices were implanted. Eleven (2%) patients without data for the most recent 6 months prior to the end of the study were considered lost to follow-up, however included in the analysis as far as data was acquired.

Life years and quality-adjusted life years (QALY) gained were discounted at 1.5% per annum and costs were discounted at 4% per annum.[19-21]

Death probabilities

The overall mortality rate in patients with reduced LVEF who received primary prevention ICD implantation was founded on data from routine clinical practice. Since specific causes of death were unavailable in our center, modeling into different categories of death was predicated upon the meta-analysis of mortality rates from six primary prevention trials conducted by Cowie et al.[13] The overall mortality rate in ICD recipients from routine clinical practice was distributed over four different categories of death (SCD, HFD, OCD and NCD) in the same proportion as found in the pooled estimate derived from the meta-analysis. Non cardiac mortality was adjusted to age by incorporating the Dutch lifetable (statline.cbs.nl).

Table 1. Baseline patient characteristics.

	Total (n = 483)
Clinical characteristics	
Age (years)	61±11
Male (%)	409 (85)
Left ventricular ejection fraction (%)	27±7
QRS, mean (SD), ms	111±26
Renal clearance, mean (SD), ml/min	85±35
Ischemic heart disease (%)	399 (83)
History of atrial fibrillation/flutter (%)	96 (20)
Medication	
ACE inhibitors/AT II antagonist (%)	423 (88)
Aspirin (%)	239 (49)
Beta-blocker (%)	331 (69)
Diuretics (%)	328 (68)
Statins (%)	359 (74)
Antiarrhythmic medication *	
Amiodarone (%)	45 (9)
Sotalol (%)	57 (12)

*ACE = angiotensin-converting enzyme; AT = angiotensin; SD = standard deviation. * Patients could be treated with >1 antiarrhythmic drug.*

The efficacy of ICD therapy was defined as the relative risk of death for each type of mortality outcome in the ICD therapy group when compared with the control group. Given that mortality data of a reliable control group (i.e. without ICD therapy) from routine clinical practice was not available, the mortality rates of the control group were assessed by using the mortality rates of the ICD therapy group and the relative risks provided by the meta-analysis of Cowie et al.[13]

In our cohort 62 patients died during a mean follow-up of 31.7 months, resulting in a monthly death probability of 0.0043 for ICD patients in the current analysis. In the meta-analysis of Cowie et al., the monthly death probability for ICD patients was 0.0072 and for patients receiving conventional pharmacological therapy was 0.0105.[13] This resulted in an adjusted death probability for the hypothetical cohort of patients receiving conventional pharmacological therapy in the current analysis of 0.0063. According to the pooled estimate derived from the meta-analysis, these overall monthly death probabilities were then proportionally distributed over the four different categories of death (SCD, HFD, OCD and NCD) (Table 2). It was assumed that the benefit of ICD therapy was constant over time.

Complications of ICD therapy

Patients with reduced LVEF who received primary prevention ICD implantation were at risk for device associated complications. The following complications were included in the model: operative death, device infection, lead dislodgement, inappropriate shocks, discontinuing ICD therapy following inappropriate shock, and lead failures requiring replacement. The probability of experiencing such complications was based on data from routine clinical practice in our center and is presented in Table 3. Complication rates were calculated for the complete group of devices (i.e. all single-chamber and dual-chamber devices). The effect of different complication rates was tested in the sensitivity analysis. Mean device longevity was based on data from our center, and was 4.6 years in single-chamber and 4.7 years in dual-chamber ICD devices.

Table 2. Estimated mortality rates for different categories of death based on data from a meta-analysis of 6 primary prevention trials and the all-cause mortality rate of the Leiden ICD population.

	Meta-analysis†		Current study	
One-month death probability	ICD therapy	Conventional therapy	ICD therapy	Conventional therapy
Sudden cardiac death	0.0015	0.0042	0.0009*	0.0025*
Heart failure death	0.0029	0.0029	0.0017*	0.0018*
Other cardiac death	0.0004	0.0002	0.0002*	0.0001*
Non-cardiac death	0.0024	0.0031	0.0014*	0.0019*
All-cause	0.0072	0.0105	0.0043	0.0063*

** Estimated values; †Meta-analysis of mortality rates from the following primary prevention trials: AMIOVIRT, MADIT I, MADIT II, SCD-HeFT, CAT, and DEFINIT.*

Table 3. Base case model inputs.

Model inputs
One month death probability single-chamber ICD cohort
Sudden cardiac death
Heart failure death
Other cardiac death
Non-cardiac death
All cause
Initial implant operative death probability
Mean follow-up (months)
Mean age (years)
Gender (% male)
One-month probability of inappropriate shocks
One-month probability of discontinuing ICD after inappropriate shocks
Monthly probability of a right atrial lead replacement due to failure following initial implant
Monthly probability of a right ventricular lead replacement due to failure following initial implant
Monthly probability of a right atrial lead replacement due to failure following replacement implant
Monthly probability of a right ventricular lead replacement due to failure following replacement implant
Probability of a lead infection at initial implant
Probability of a lead infection at replacement ICD implant
Probability of a lead dislodgement at initial implant
Probability of a lead dislodgement at replacement ICD implant
Initial device + leads cost(€) (2010)
Replacement device cost (€) (2010)
Atrial lead replacement cost per event (lead failure) (€) (2010)
Right ventricular lead replacement cost per event (lead failure) (€) (2010)
Lead infection cost (€) (2010)
Lead dislodgement cost (€) (2010)
Inappropriate shocks cost (€) (2010)
Monthly long term inpatient and outpatient cost (€) (2010)
ICD additional monthly follow-up cost (€) (2010)
Mean device longevity (years)
Duration of ICD benefit
Utility of heart failure patient annual
Utility of ICD complications state (annual)
Discount rate outcomes (%)
Discount rate costs (%)

ICD therapy single-chamber	ICD therapy dual-chamber	Conventional therapy	Data sources
0.000916	0.000916	0.002538	Clinical data /Cowie et al.[13]
0.001743	0.001743	0.001752	Clinical data /Cowie et al.[13]
0.000224	0.000224	0.000102	Clinical data /Cowie et al.[13]
0.001439	0.001439	0.001890	Clinical data /Cowie et al.[13]
0.004322	0.004322	0.006283	Clinical data /Cowie et al.[13]
0.00207	0.00207	Not applicable	Clinical data
31.7	31.7	28	Clinical data/Cowie et al.[13]
60.8	60.8	61.1	Clinical data/Cowie et al.[13]
84.7	84.7	79.5	Clinical data/Cowie et al.[13]
0.00538	0.00538	Not applicable	Clinical data
0.00000	0.00000	Not applicable	Clinical data
Not applicable	0.00017	Not applicable	Clinical data
0.00127	0.00127	Not applicable	Clinical data
Not applicable	0.00083	Not applicable	Clinical data
0.00234	0.00234	Not applicable	Clinical data
0.02277	0.02277	Not applicable	Clinical data
0.03704	0.03704	Not applicable	Clinical data
0.00828	0.00828	Not applicable	Clinical data
0.00000	0.00000	Not applicable	Clinical data
19,600	22,150	Not applicable	Clinical data
17,000	19,000	Not applicable	Clinical data
Not applicable	2,845	Not applicable	Clinical data/Hakkaart et al.[23]
4,895	4,895	Not applicable	Clinical data/ Hakkaart et al.[23]
29,561	32,111	Not applicable	Clinical data/ Hakkaart et al.[23]
4,895	4,895	Not applicable	Clinical data/ Hakkaart et al.[23]
132	132	Not applicable	Clinical data/ Hakkaart et al.[23]
197	197	197	RIVM 2008
43	43	Not applicable	Clinical data/ Hakkaart et al.[23]
4.6	4.7	Not applicable	Clinical data
Lifetime	Lifetime	Not applicable	Assumption
0.85	0.85	0.85	Mark et al.[14]
0.75	0.75	Not applicable	Sanders et al.[15]
1.5	1.5	1.5	CVZ 2006[19]
4.0	4.0	4.0	CVZ 2006[19]

Quality-of-life

Based on the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), an utility score of 0.85 for both the ICD and the conventional therapy group was applied in the current model.[14] Furthermore, it was assumed that ICD implantation had no effect on the quality of life.[14, 22] If patients were exposed to ICD-related complications (e.g. device infection, inappropriate shocks, and lead replacement) a utility score of 0.75 during a period of one month was assumed.[15]

Costs

Cost analyses were performed from the health care perspective. Costs of health care associated with inpatient and outpatient treatment were included. Device and lead costs were based on average contractual price agreements between the Dutch hospitals and manufacturers (expert's opinion). For all routine procedures and ICD treatment related complications requiring hospital admission, the exact average duration of hospital stay, based on the clinical data available, was calculated and then multiplied with the standard cost per hospital day.[23] Procedural costs of device system implantation, device replacement, and lead replacement were derived in a micro cost analysis including personnel costs, diagnostic test, costs of consumables used during the procedure, depreciation of the radiology equipment and catheterization laboratory, and overhead costs.[23] For routine ICD and unexpected ICD check-up (i.e. following an appropriate or inappropriate shock), cost of an outpatient visit were applied.[23] All prices were converted to the price level of 2011 according to the general Dutch consumer price index (statline.cbs.nl, accessed January 2011). Results of other studies, reported in US dollars, were also converted to euros using the purchasing power parity index with a ratio of $1 = €0.8382 (stats.oecd.org, accessed December 2011).

In the current analysis, a cost-effectiveness ratio below €40,000 per gained QALY was assumed to be acceptable according to the current Dutch economic threshold.[24, 25]

Sensitivity analyses

To account for important model assumptions, one-way deterministic sensitivity analyses were performed. Ranges of the variables were established on current literature or on expert's opinion if literature was lacking.

Probabilistic sensitivity analysis (PSA) was performed to evaluate the combined uncertainty of individual input variables on the model's outcome of cost and effects. To achieve this, probability distributions for death and complication rates as well as the utilities scores associated with different states were defined and 10,000 simulations were undertaken.

RESULTS

Base-Case analysis

Following primary prevention ICD implantation, all-cause mortality decreased resulting in an increased life-expectancy of 2.07 years as compared with patients receiving conventional therapy. With an estimated utility score of 0.85 per life-year saved and 0.75 if patients were exposed to ICD-related complications, incremental QALYs were 1.73 years for ICD recipients.

With respect to single-chamber ICDs, implantation is associated with an average additional lifetime cost of €60,788 per patient when compared with conventional therapy. Consequently, both the lifetime costs and the effectiveness (i.e. life expectancy) were higher in single-chamber ICD recipients as compared with patients receiving conventional therapy. Accordingly, this resulted in an estimated cost-effectiveness of €29,369 per life year gained and €35,154 per QALY gained for patients with a mean age of 61 years receiving single-chamber ICD therapy as compared with patients receiving conventional therapy (Table 4).

Regarding primary prevention dual-chamber ICD implantation, average additional lifetime cost of €64,216 per patient were calculated. With an increased life-expectancy of 2.07 and a incremental QALY of 1.73, estimated cost-effectiveness of €31,025 per life year gained and €37,111 per QALY gained for patients with a mean age of 61 years receiving dual-chamber ICD therapy compared to patients receiving conventional therapy was assessed (Table 4).

Table 4. Costs, life years, quality-adjusted life years, and incremental cost-effectiveness ratios for implantable cardioverter defibrillator compared with control therapy.

	Cost (€)	LY	QALY	ICER (€/LY)	ICER (€/QALY)
Single-chamber					
Discounted					
ICD therapy	79,914	11.62	9.84	29,369	35,154
Control therapy	19,126	9.55	8.11		
Difference	60,788	2.07	1.73		
Undiscounted					
ICD therapy	104,428	13.24	11.21	31,282	37,641
Control therapy	25,299	10.70	9.09		
Difference	79,642	2.55	2.12		
Dual-chamber					
Discounted					
ICD therapy	83,342	11.62	9.84	31,025	37,111
Control therapy	19,126	9.55	8.11		
Difference	64,216	2.07	1.73		
Undiscounted					
ICD therapy	109,132	13.24	11.21	32,928	39,583
Control therapy	25,299	10.70	9.09		
Difference	83,833	2.55	2.12		

ICD = implantable cardioverter defibrillator; ICER = incremental cost-effectiveness ratio; LY = life years; QALY = quality-adjusted life years.

Deterministic sensitivity analysis

With all model variables included in the sensitivity analysis, incremental cost-effectiveness of ICD therapy compared with conventional therapy demonstrated to be most sensitive to variation in the following five factors: device longevity, device and lead costs, quality of life, discount rates, and mortality rates (Figure 1).

Device longevity in the current analyses (i.e. a mean of 4.6 years for single-chamber and 4.7 years for dual-chamber ICDs) was based on data from our own center. However, it is conceivable that device longevity varies according to the device settings and the generation of devices used per center. Accordingly, adaptation of the mean device longevity to 4 years resulted in an incremental cost-effectiveness of €38,123 and €40,746 per QALY for single-chamber and dual-chamber devices respectively. When the mean device longevity was increased to 10 years, incremental cost-effectiveness improves to €23,744 and €25,273 per QALY for single-chamber and dual-chamber devices respectively. As a result, the factor device longevity demonstrated to have the largest effect on the total costs and cost-effectiveness of all factors in the deterministic model.

With respect to device and lead costs, a 25% lowering in prices would affect incremental cost-effectiveness by 19%. Outcomes ranged from €26,392 to €38,817 per QALY for single-chamber devices and from €28,638 to €42,487 per QALY for dual-chamber devices.

Variation in the patients' quality of life to 0.75 in both therapy groups (i.e. ICD and conventional therapy) resulted in an incremental cost-effectiveness of €36,376 per QALY for single-chamber and of €39,675 per QALY for dual-chamber ICD therapy. Consequently, if it was assumed that the patients' quality of life was 0.75 in the conventional therapy group and 0.80 in the ICD therapy group, incremental cost-effectiveness improved to €26,644 per QALY and €29,060 per QALY for single and dual-chamber ICDs respectively.

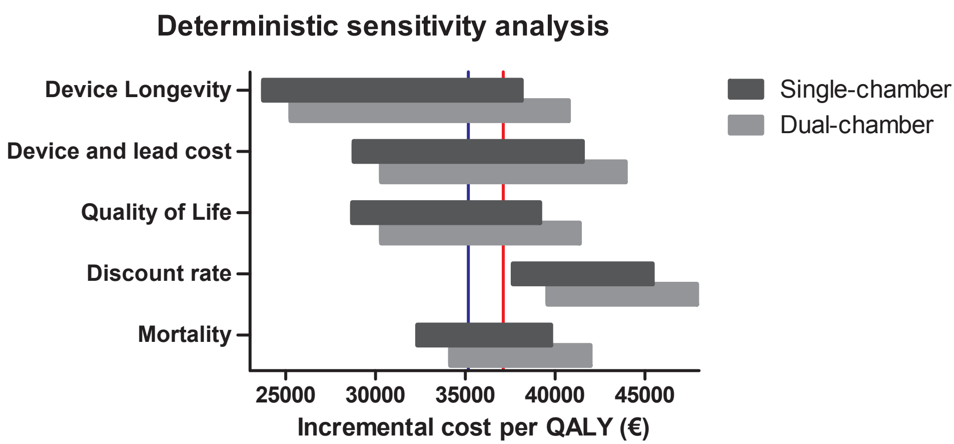

Figure 1. Tornado diagram of the deterministic sensitivity analysis representing the five most sensitive factors with regard to the incremental cost per QALY of ICD therapy compared with conventional therapy. The estimated cost per QALY based on the base case analyses are demonstrated for both single-chamber (blue line) and dual-chamber (red line) ICDs.

A less favorable incremental cost-effectiveness ratio will result if discount rates for both outcomes and cost are assumed to be equal. The effect of the variation of discount rates between 0% (i.e. undiscounted) and the more internationally accepted 3% for both outcomes and costs on the incremental cost-effectiveness of primary prevention ICD therapy is illustrated in Figure 1.

Another important factor determining the incremental cost-effectiveness of ICD therapy is the mortality rate of patients applicable for primary prevention ICD implantation. Based on the outcomes of the deterministic sensitivity analysis, the incremental cost-effectiveness tended to be more favorable in patients with an increased annual mortality. This outcome could be explained by the fact that in the current model a higher mortality is associated with an increased number of sudden cardiac deaths and therewith an improved beneficial effect of ICD therapy. This results in a higher number of incremental life years added for the ICD cohort as compared with the conventional pharmacological therapy cohort.

Probabilistic sensitivity analysis

Based on the PSA, the incremental cost-effectiveness of single-chamber ICDs compared with conventional therapy resulted in a mean estimate of €35,837 per QALY (95% CI: €28,368 - €44,460 per QALY). For dual-chamber ICDs, the PSA resulted in a mean estimate of the incremental cost-effectiveness of €37,756 per QALY (95% CI: €29,055-€46,050 per QALY) when compared with conventional therapy. The cost-effectiveness acceptability curve in Figure 2 shows the probability that single-chamber and dual-chamber ICDs are cost-effective compared with conventional therapy for different values of the willingness to pay. According

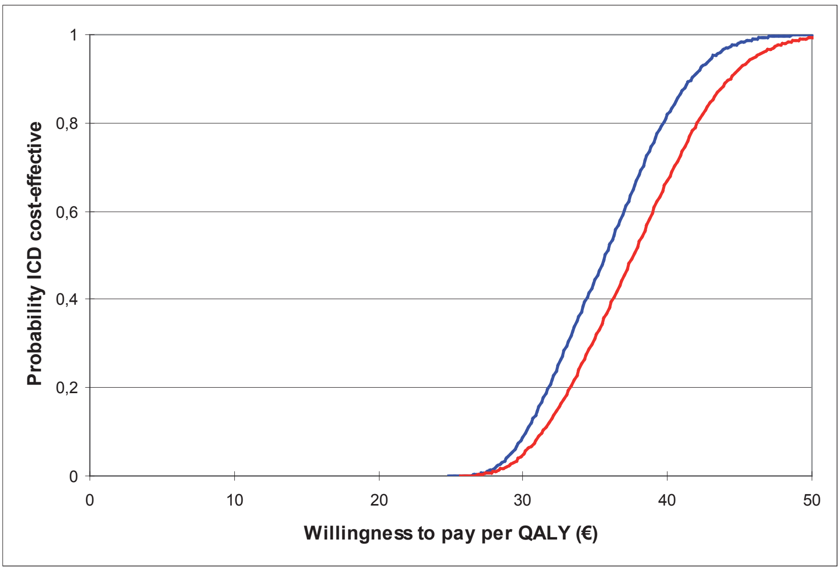

Figure 2. Cost-effectiveness acceptability curve for single chamber (blue line) and dual chamber (red line) ICD therapy compared to conventional therapy.

to the Dutch threshold of €40,000 per QALY, the probability that ICD therapy is cost-effective was estimated at respectively 81% for single-chamber ICDs and 67% for dual-chamber ICDs.

DISCUSSION

In the current analysis, primary prevention ICD implantation in addition to optimal pharmacologic therapy (i.e. conventional therapy) in patients with an increased risk for sudden cardiac death as a result of a reduced LVEF was assessed with the use of a Markov model. Based on the deterministic analysis, both single- and dual-chamber ICD implantation had an incremental cost-effectiveness ratio below the accepted threshold of €40,000 per QALY gained.[24, 25] The probabilistic sensitivity analyses confirms these results, as both single and dual chamber ICD therapy have a high probability of being cost-effective.

However, variation in specific model factors demonstrated to have major impact on the cost-effectiveness of ICD therapy. For example, an increased device longevity due to improved device batteries would have a considerable beneficial effect on the cost-effectiveness and should therefore be one of the main incentives of device manufacturers in the development of new generation ICDs. Furthermore, significant higher prices for ICD and leads, with respect to base case prices currently used, could easily result in less favorable or even unfavorable cost-effectiveness. Another important model factor with major impact on the cost-effectiveness is the quality of life. In the current study, the quality of life is based on data derived from the SCD-HeFT trial in which all patient received devices unable to deliver ATP.[14] However, nowadays almost all patients receive ICDs capable of ATP and as demonstrated by the PainFREE trial may experience a higher quality of life then reported in the SCD-HeFT trial.[26] Although exact data hereof remains unclear, the deterministic sensitivity analysis demonstrated that an improved quality of life in ICD recipients could have a large, namely beneficial, impact on the actual cost-effectiveness reported in the current study. Although exact data hereof remains unclear, the deterministic sensitivity analysis demonstrated that an improved quality of life in ICD recipients could have a large, namely beneficial, impact on the actual cost-effectiveness reported in the current study. Other factors with noteworthy effects on the cost-effectiveness were discount rates, mortality rates, and ICD efficacy.

Furthermore, worth mentioning is the relatively minor effect that most device related complications had on the cost-effectiveness. Although complications such as lead infections requiring complete replacement of the device and leads are associated with extremely high costs, the relatively low incidence significantly reduces the effect on total cost-effectiveness.

Comparison with different ICD cost-effectiveness analyses

Currently, cost-effectiveness analyses of primary prevention ICD therapy in patients with a reduced LVEF using data from real clinical practice are scarce. However, based on analysis and meta-analysis of the major primary prevention trials of ICD therapy several cost-effectiveness analyses have been published. Results from the SCD-HeFT trial demonstrated a comparable cost-utility ratio (discounted at 3%) of $41,530 (€34,810) per QALY for single-chamber ICDs as compared with medical therapy alone.[14] Of note is that, likewise the current analysis, Mark et al. assumed that the benefits of ICD therapy were constant over time and outcomes became economically attractive if benefits persist for at least 8 years, which was beyond the empirical 5-year trial data of the SCD-HeFT. Sanders et al. projected the cost-effectiveness of eight randomized trials in which primary prevention ICD implantation among patients who are at risk for sudden cardiac death due to a reduced LVEF was evaluated.[15] In two of those trials, primary prevention ICD implantation did not reduce the risk of death, and thus was both more expensive and less effective than control therapy. Since in these two trials primary prevention ICD implantation occurred in selected patients who are not included in the current analysis, comparison with these outcomes is less appropriate**.** Regarding the six other trials included by Sanders et al., primary prevention single-chamber ICD implantation was projected to add between 1.01 and 2.99 QALYs and the incremental cost-effectiveness (discounted at 3%) ranged from $34,000 (€28,500) to $70,200 (€58,842) per QALY gained. Results of the current study regarding the added life years and incremental costs per QALY are for both single-chamber and dual-chamber ICDs amidst these outcomes of Sanders et al (Table 5).

In the meta-analysis by Cowie et al., consisting out of 6 primary prevention trials with inclusion criteria matching ACC/AHA/ESC Class I or IIa recommendations, direct medical costs were estimated using Belgian national references and complications rates were based on experts opinion.[13] In this analysis, primary prevention single-chamber ICD implantation was projected to add 1.88 LY and the estimated mean lifetime costs per QALY gained were €29,530 and €31,717 according to the deterministic and probabilistic sensitivity analysis respectively. These outcomes are comparable with outcomes of the current analyses, indicating that single-chamber and dual-chamber ICDs are, based on clinical data and detailed costs derived from routine clinical practice, cost-effective as primary prevention therapy in patients with a reduced LVEF (≤35%).

Van Brabandt et al. criticized the fact that Cowie et al. based their results on a meta-analysis of 6 primary prevention trials rather than using data from the SCD-HeFT alone.[27]

Table 5. Results of increased costs, increased life years, increased quality-adjusted life years, and incremental cost-effectiveness ratios for implantable cardioverter defibrillators compared with control therapy in different primary prevention ICD trials and the current analysis for both single-chamber and dual-chamber devices.

	Increase in Cost (€)	Increase in LY	Increase in QALY	ICER (€/LY)	ICER (€/QALY)
MADIT I [6, 15]	77,200	3.64	2.64	21,207	29,254
MUSTT [3, 15]	85,080	4.14	2.99	20,536	28,500
MADIT II [7, 15, 18]	66,555	2.03	1.47	32,690	45,348
DEFINITE [15, 29]	84,241	2.73	1.96	30,847	43,001
COMPANION [15, 30]	57,251	1.87	1.36	30,595	42,163
SCD-HeFT [2, 15]	59,514	1.40	1.01	42,498	58,842
Study single-chamber†	60,788	2.07	1.73	29,369	35,154
Study dual-chamber†	64,216	2.07	1.73	31,025	37,111

† *Converted to euros using the purchasing power parity index with a ratio of $1 = €0.8382 (stats.oecd.org, accessed December 2011).*
ICER = incremental cost-effectiveness ratio; LY = life years; QALY = quality-adjusted life years.

According to the results from the deterministic sensitivity analyses of the current study were ICD effectiveness was based on results from the SCD-HeFT alone, the incremental cost-effectiveness per QALY was €41,837 for single-chamber devices and €44,182 for dual-chamber devices. Consequently, it can be concluded that ICDs would be approximately borderline cost-effective if effectiveness is based on results from the SCD-HeFT trial alone.

Limitations

In the current study, mortality rates of the control group were assessed by using mortality rates of the ICD therapy group and the relative risks provided by the meta-analysis of randomized clinical trials by Cowie et al.[13] This was based on the assumption that the efficacy of ICD therapy in clinical practice is similar to the efficacy of ICD therapy demonstrated in the randomized clinical trials. In addition, the overall mortality rate of the ICD group and control group over the four different categories of death were distributed in a similar proportion as the pooled estimate derived from the meta-analysis. Furthermore, although clinical follow-up data was limited to a mean of 31.7 months, cost and benefits were projected to a lifetime horizon. Also, the current analysis was performed in a relatively small cohort of 483 patients with a low proportion of single chamber ICDs. Finally, the long enrolment time may has resulted in heterogeneity regarding clinical management and device technology within the study cohort. Importantly, all the above study limitations could have resulted in an over- or underestimation of the beneficial effects of ICD therapy, consequently over- or underrating the cost-effectiveness of ICD therapy in clinical practice.

Implications for society

In the current analyses, primary prevention ICD implantation has demonstrated to have a favorable effectiveness versus acceptable costs in patients with a reduced LVEF in the long term. However, despite existing guidelines supporting primary prevention implantation of ICDs in these patients, implementation hereof is currently far from complete as is demonstrated with the widely varying implantation rates across Europe.[9, 28] This might be the result of the high upfront cost of ICD therapy following implantation and the large patient population in which it may be applied.[11] Consequently, wide penetration of ICD therapy in selected patients forms an absolute challenge to health policymakers, since healthcare expenditure for ICDs in Europe could easily exceed several billion Euros per year. On the other hand, a saving effect might be expected due to an increased addition (i.e. work, consumption) to the general economy.

Furthermore it is worth mentioning that the current analysis reflected only the cost-effectiveness of primary prevention ICD therapy without resynchronization therapy in heart failure patients. Since patients, eligible for combined defibrillator and resynchronization therapy, are characterized by a more deteriorated form of heart failure, results of the current analysis do not apply for these patients.

CONCLUSION

Based on data from routine clinical practice, primary prevention single-chamber and dual-chamber ICD therapy in selected patients with a reduced LVEF appears to be cost-effective.

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