The Implantable Cardioverter Defibrillator : a Health Technology Assessment

KCE reports 58C

Federaal Kenniscentrum voor de Gezondheidszorg
Centre fédéral d'expertise des soins de santé
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EXECUTIVE SUMMARY

INTRODUCTION

Sudden cardiac death (SCD) is defined as a natural death due to cardiac causes, heralded by an abrupt loss of consciousness within one hour of the onset of acute symptoms. It is mostly initiated by a sudden inappropriate and extreme increase in heart rate (typically more than 200/min), eventually leading to a mechanical arrest of the heart. Virtually any cardiac disease can lead to this fatal arrhythmia but most commonly (up to 75%) the underlying disease is coronary heart disease. In about 20% of patients, the underlying heart disease is an idiopathic congestive cardiomyopathy and in <5%, SCD develops consequential to a primary electrical abnormality of the heart. SCD is among the most common causes of death in developed countries. It is estimated that in Belgium yearly 15 000 people die suddenly as a consequence of a sudden cardiac arrest.

Virtually all patients who develop a sudden cardiac arrest (SCA) eventually die 10 to 15 minutes later. The only way of preventing death is by delivering an external electrical shock (defibrillation) within minutes after the SCA took place. Considering that immediate defibrillation is only rarely available and that medical therapy to prevent the occurence of fatal arrhythmias barely offers any benefit, the hope for saving the life of victims of a SCA relies on prophylactically implanting a defibrillator, i.e. the "Implantable Cardioverter Defibrillator" or ICD, that provides an immediate shock in case a life threatening arrhythmia does occur. This means that one has to try to predict who is likely to develop a SCA and subsequently implant a device that will respond appropriately in case the expected fatal event takes place.

THE ISSUE

ICDs are battery-powered, implantable devices capable of monitoring heart rhythm and delivering an electric shock to restore normal rhythm when a life-threatening arrhythmia is detected. An ICD consists of a pulse generator, similar in size to a pacemaker, and one or more leads. Early devices required open chest surgery to be implanted but current ICDs are placed under the skin in the pectoral region with leads to the heart inserted via a vein whilst under local anaesthesia. After implant, a lifelong follow-up 2 to 4 times a year is needed and device replacement is required every 4 to 6 years.

The implantation of an ICD is a relatively safe procedure with a peri-operative mortality rate of 0.0 to 1.2%. The most often reported late adverse event is the occurrence of inappropriate shocks (14% of patients), i.e. firing of the device when there is no life threatening arrhythmia. Electronic malfunction leads to replacement in 2% of patients and the annual failure rate of the leads increases progressively with time. The survival rate of leads is 60%, eight years after implant.

The price of an ICD has been declining in recent years. Actually in Belgium reimbursement for the device is €15 708. The total cost for a first implant in primary prevention in Belgium is calculated to be €27 000, including the device, leads and all related procedures.

Estimating the propensity of patients to develop SCA relies on risk profiling, i.e. checking which and how many risk factors for developing a fatal arrhythmia a given person accumulates. Patients at highest risk for SCD are those who were lucky enough to survive a first cardiac arrest; they run a risk for a new fatal arrhythmia of 20% per year. The clinical effectiveness of the implantable cardioverter defibrillator (ICD) in these secondary prevention patients is generally considered as being established and is not discussed in this report.

In primary prevention ICD trials, risk profiling was mainly dependent on the nature of the underlying heart disease (coronary artery disease, idiopathic cardiomyopathy), the presence of a severely impaired pump function of the heart as indicated by a left ventricular ejection fraction (LVEF) of less than 30% and the presence of clinical heart failure (indicated by NYHA functional class). In early trials, risk estimation was further supplemented by an electrophysiological study in which the propensity of the heart to develop lifethreatening arrhythmias was investigated by means of electrical stimulation. Although this technique allows fairly accurately to predict the risk of SCA in high-risk patients, limitations are its invasive nature and the relatively high number of false negative results.

Most patients (80%) in whom an ICD is implanted never receive an appropriate shock from the device, indicating that risk stratification of patients prior to implant remains the Achilles heel of ICD-therapy. Although clinically classifying a certain patient in a given NYHA class and the calculation of the LVEF are subject to intra- and interobserver variability, and although these parameters are not constant over time, they are at present the best documented and currently most often used as noninvasive risk stratifiers. Yet, most patients thus selected for ICD implantation will never need a shock from the device.

CLINICAL EFFECTIVENESS

The clinical effectiveness of ICDs in the primary prevention of SCD has been studied in eight RCTs. In these studies, the ICD is compared with placebo (on top of optimal medical therapy for the underlying heart disease) or with amiodarone, an antiarrhythmic that, in certain patient subgroups, may reduce the incidence of SCD. The outcome data in terms of all-cause mortality in these trials is depicted in the table.

All-cause mortality in primary prevention trials.

RCT	Average follow-up (months)	ICD		CONTROL		HR	95% CI	ANNUAL DEATH RATE	
		n	N	n	N			ICD	CONTROL
MADIT I	27	15	95	39	101	0,46	0,26-0,82	0,06	0,17
CABG-PATCH	32	101	446	95	454	1,07	0,81-1,42	0,07	0,05
MADIT II	20	105	742	97	490	0,69	0,51-0,93	0,08	0,12
CAT	66	13	50	17	54	NS	NS	0,03	0,06
AMIOVIRT	24	6	51	7	52	NS	NS	0,07	0,06
DEFINITE	29	28	229	40	229	0,65	0,40-1,06	0,05	0,07
DINAMIT	30	62	332	58	342	1,08	076-1,55	0,07	0,06
SCD-HeFT	45,5	182	829	244	847	0,77	0,62-0,96	0,06	0,08

N: number at risk; n: number of deaths; HR: hazard ratio. See glossary for abbreviations of study acronyms. Shaded area relates to the trials with a statistically different all-cause mortality in ICD vs control patients. CI: confidence interval. RCT: ranomised controlled trial.

In three out of eight of these trials, a statistically significant reduction in all-cause mortality is obtained with ICD-therapy as compared to placebo. In a meta-analysis of all trials, the relative risk for all-cause mortality is estimated to be 0.75 (95% CI 0.59-0.96, p=0.025). There is considerable clinical heterogeneity between these trials, related to the nature of the underlying heart disease (ischaemic or nonischaemic), the time relation to a previous myocardial infarction or to a revascularisation procedure, additional risk stratifiers, etc….

MADIT II and SCD-HeFT are the studies to which current ICD clinical practice best corresponds.The MADIT II results present some peculiarities that are difficult to explain and that have raised some doubt about their applicability into clinical practice. In this trial that limited enrollment to patients with ischaemic heart disease, the mean time interval between the most recent AMI and enrollment was 6.5 years. During an average follow-up of 20 months, the mortality rates were 19.8% in the conventional-therapy group and 14.2% in the ICD group. Compared to other primary prevention ICD-trials, mortality in the placebo group was remarkably high and it was 50% higher than in the SCD-HeFT trial. This is counterintuitive since in SCD-HeFT apparently sicker patients were enrolled, the presence of heart failure being an inclusion criterium in it and not in MADIT II. Furthermore, in a post-hoc subgroup analysis of MADIT II, ICD-therapy did not benefit patients in whom the most recent AMI occured less than 18 months before ICD implant. These peculiarities suggest an important selection bias in this trial and may preclude its external validity.

So far, the SCD-HeFT trial seems to provide the best estimate of the effectiveness we may expect from ICD therapy. To be eligible for enrollment, patients had to have ischaemic or nonischaemic heart disease with a severely depressed left ventricular function (EF<36%) and clinical stable heart failure (NYHA class II or III) whilst under optimal medical therapy.

The median age of patients in this trial was 60 years and the median LVEF was 25%. As compared with placebo, ICD therapy was associated with a 23% decreased risk of death (HR 0.77; 97.5% CI 0.62-0.96) and an absolute decrease in mortality of 7.2% after five years or 1.8% per year. The results indicate that one has to treat between 13 and 128 patients to postpone one death beyond three years. In a post hoc subgroup analysis of the SCD-HeFT data, in patients older than 65 year, ICD was not better than placebo in reducing mortality during the trial.

There is evidence from clinical trials that early reperfusion, ß-blockers, statins and ACE-inhibitors reduce the risk of SCD in selected patients. Therefore, the appropriate use of these drugs and strategies in patients with a myocardial infarction or with heart failure is crucial, before proceeding to the expensive, invasive and less well documented ICD-therapy.

COST-EFFECTIVENESS

A literature review, limited to the assessment of the economic evaluations of ICD in primary prevention, was performed. Twelve economic evaluations of the use of ICD in primary prevention were retrieved. Three RCT-based economic evaluations of ICD overestimated the incremental cost-effectiveness ratio (ICER) (i.e. too high ICERs) since the long-term costs of non-ICD therapy and the long-term benefits of ICD use were not captured within the trial timeframe. The ICERs varied from €30,300 to €348,000 per life-year gained (LYG). If results were projected to longer time horizons, the reported cost-effectiveness ratios of ICD use became more favourable and ICERs varied from €17,700 to €60,200 per LYG. Key parameters driving the ICERs of the reviewed studies were: ICD cost, generator replacement periodicity, annual rate of all-cause mortality, ICD relative risk reduction and lifetime benefit extrapolation assumptions.

All these economic evaluations however, were performed in North America and Australia, where health care systems and health care costs may not directly compare to Belgium. Transferability of the current findings to Belgian settings could be problematic. Therefore, an analysis with Belgian health care costs was performed from the perspective of the Belgian health insurance system. The model simulates a hypothetical cohort of 1,000 SCD-HeFT-eligible patients comparing ICD implantation in primary prevention with conventional therapy. The observed 5-year SCD-HeFT trial data were extrapolated (three scenarios) to a patient's lifetime by the use of a Markov model with a monthly cycle length. For comparison with the base-case SCD-HeFT results, the model was also run using the hazard ratio and total mortality probabilities reported in the MADIT II trial. All cost inputs used in the model were derived from the Belgian ICD registry which is described in detail in chapter 7.

For the base case SCD-HeFT results, the ICERs of ICD versus conventional therapy was €60,000 (95% CI: 35,900 – 113,500) per LYG and €71,400 (40,200 – 134,600) per QALY gained in the most favourable scenario and €111,000 (63,900 – 214,800) per LYG and €132,100 (71,600 – 261,500) per QALY gained in the worst-case scenario. Using MADIT II data, the ICERs were more favourable and varied from €42,200 (28,400 – 74,900) to €106,500 (66,700 – 203,000) per LYG and from €50,300 (31,200 – 87,400) to €127,000 (74,600 – 237,900) per QALY gained, depending on the extrapolation scenario.

Next to probabilistic sensitivity analysis, the sensitivity of the results to variations in the discount rates and the frequency of battery replacement was assessed deterministically by the use of scenario analyses. If both the discount rates for costs and effects are equally set to 3%, as often recommended in international guidelines (instead of 3% for costs and 1.5% for benefits according to the Belgian guidelines) the ICERs increase from €60,000 to €70,200 per LYG and from €71,400 to €83,600 per QALY gained. With respect to the device replacement, if generators are replaced more frequently, the ICERs for the ICD patients become less favourable. Compared to the base-case (5-years replacement) on the other hand, if the battery life-duration is increased to 7 years, the cost-effectiveness ratio of ICD versus conventional therapy improves to €48,000 per LYG or €57,200 per QALY gained.

Finally, the yearly budget implication of an extension of the coverage for ICD implantation to primary prevention was estimated, relying on an anticipated number of 2000 new implants per year. Starting with an initial budget of €68,800,000 in 2007, the yearly ICD budget gradually increases in 2008-2011 due to the cumulated follow-up costs of the surviving patients and the yearly added 2000 new implants. In 2012, the foreseen budget rises sharply (up to €154,500,000) mainly due to the replacement of the primo-ICDs implanted 5-years earlier (in 2007) in combination with the yearly recurring new implants. In the ensuing years, the budget impact steadily rises due to a continuously increasing number of ICD patients to be followed. The net (incremental) cost (i.e. extracting the cost of conventional therapy for these patients) to the Health Authorities of extending the ICD indications to primary prevention (as defined in SCD-HeFT) is estimated to be more than €55 million in 2007, over €100 million in 2012 and to stabilize at about €156 million per year in 2022 if, c.p., 2000 new implants per year are considered. This long-term budget prognostication is important to consider since the cost of an ICD is more than a 'once-only' yearly expenditure. Especially replacement costs in surviving patients accrue periodically extra costs.

PATIENT ISSUES

ICD will not change dramatically the quality of life of the patients. On the one hand, no benefits are to be expected if no potentially lethal arrhythmia does occur in a given patient; on the other hand, the presence of the device, and the stress induced when the alarm is activated – rightly or wrongly – might impair quality of life.

The scientific literature on the subject is scarce and does not demonstrate any clear impact of ICD on patients' quality of life. What we know for sure is that the price the patient has to pay for eliminating a 2% annual risk of sudden death (in the best case scenario) is a surgical intervention (to be repeated every 5 year), increased medicalisation for the rest of his/her life, and the risk of complications. According to the literature ICD patients will experience some restrictions which might affect their own professional life or leisure activities, or have consequences for their relatives – for instance they might not be able to drive a car. These consequences of ICD are extremely important for the patients who must receive proper information and give an informed consent before a decision to intervene is taken.

ICD also raises the question of how would individuals prefer to die – in general, or in particular in end-of-life situations.

Finally the placement of an ICD raises ethical questions for the patient (for which patients should ICD be used, what information should be provided), but also for the society – should limited resources be spent on ICD? These questions were debated during a meeting with Belgian ethicists.

THE BELGIAN ICD REGISTRY

A description is given of the patients in whom an ICD was implanted in Belgium in the years 2001 and 2005. By linking claims data of the insurers to clinical and device data from the application forms at the RIZIV/INAMI, we were able to analyse population characteristics, hospitalisation data, health care consumption, delivery of medication, longevity of the implanted devices and mortality. Cost data thus retrieved were used to feed the model that was described higher.

The baseline characteristics of patients in the registry are comparable to those from other international registries: the average age of patients in 2005 was 62.8 years, 85% being males. In 66% of patients, the underlying heart disease was coronary heart disease and in 14% it was idiopathic dilated cardiomyopathy. In patients with ischaemic heart disease, 61% had an ejection fraction <36%. Unfortunately, due to lack of information, the functional status of patients could not be categorized. Most implants (80%) were for secondary prevention which is due to the fact that at present, reimbursement of ICDs in primary prevention is limited.

Eighteen hospitals have been implanting ICDs in Belgium. No clear difference in practice could be found by underlying heart disease, ejection fraction or the proportion of primary prevention indications but a reliable comparison of centres is often hampered by small numbers.

Guidant (Boston Scientific) and Medtronic have the highest penetration in Belgian hospitals with a market share of 46% and 49% in 2001 and of 39% and 35% in 2005 respectively. The longevity of the devices implanted in Belgium in 2001 are different between these two manufacturers with a considerable divergence of device survival curves at 4 years to the detriment of Guidant. Sufficient information is lacking to explain this difference.

In only 63% of patients with ischaemic heart disease, a statin was prescribed, which corresponds to figures reported in ICD trials but nevertheless is disappointing, given the fact that statins have shown to reduce all-cause mortality in patients with ischaemic heart disease. ß-blockers were prescribed in 74% of patients, which is in agreement with prescription practice in the ICD trials.

104 (32%) of 325 ICD-recipients in 2001 and 78 (8%) of 973 ICD-recipients in 2005, had died by the end of 2006. The cause of death was obtained by contacting the implant centres. In 2001, 33% of deaths were due to heart failure, 16% due to malignancy and 13% were sudden deaths. In 2005, these figures were 42%, 10% and 10% respectively. A considerable number of sudden deaths (19/161, 11.8%) do occur in patients in whom a device had been implanted to prevent SCD.

ORGANISATIONAL ISSUES

The Belgian cardiological community actually asks for the expansion of the reimbursement of ICDs in primary prevention towards the patient profiles described in the MADIT II and SCD-HeFT trials. This demand has been one of the driving forces to execute this HTA-report. From an organisational point of view, we were interested to estimate what could be the subsequent increase in the number of ICD implants in response to this. We extrapolated the effect of major ICD trials on the implant rate in neighbouring countries to Belgium. A rough estimate resulted in an expected increase in the annual number of new implants in Belgium of 2000 ICDs.

CONCLUSION

The evidence for implanting an ICD in primary prevention is robust only in selected high-risk patients, i.e. in patients with ischemic heart disease and severely depressed left ventricular function and symptomatic heart failure, not worse than NYHA class III.

Currently, most patients in whom an ICD is implanted never receive an appropriate shock from the device, stressing the need for a better pre-implant risk stratification.

Our economic study, based on the Belgian ICD Registry and results from the SCD-HeFT trial, provides a 95% CI for the base-case ICER of €40,200 to €134,600 per QALY and indicates that ICD use in primary prevention of sudden cardiac death is an inefficient therapy. From our model and a predicted yearly 2000 new ICD patients, we conclude that after a stabilisation period of 15 years after the extension of ICD reimbursement in primary prevention (SCD-HeFT patient profile), the projected net cost to the Health Authorities is huge and is estimated to amount to €156,000,000 per year.

An extension of the use of ICDs in clinical practice demands for a debate with all parties involved and should include a discussion on uncertainties in the effectiveness of ICDs, the repercussions of an implant on the patient's daily life and the enormous cost and budget impact of the device:

- Firstly, physicians should be encouraged to medically treat all myocardial infarction and heart failure patients according to evidence based best practice and to restrict implantation of ICDs in patients belonging to subgroups in whom their benefit is best demonstrated.
- Secondly, patients have to be fully involved in the decision making process and thoroughly informed about the potential benefits, risks and associated discomforts and the subsequent need for a lifelong requirement for maintenance and follow-up of the device.
- Thirdly, there should be a debate on a society level related to the willingness to pay for expensive devices that only very modestly prolong the life of patients.
- Finally, industry should improve the performance of ICDs, e.g. by prolonging battery life.

Taking these considerations into account may lead to a more efficient ICD reimbursement policy.

RECOMMENDATIONS

1. A further extension of the reimbursement of ICDs in the primary prevention of sudden cardiac death would result in an expansion of a technology towards an indication with an average ICER of €71 400 per QALY. An unrestricted ICD reimbursement for all patients meeting the criteria that have been used in pivotal clinical trials such as MADIT II and SCD-HeFT would result in inefficient use of resources. Long term annual budget impact would be enormous and is estimated at €156 million per year if 2000 new implants per year are considered from now on.
2. There is no evidence that ICDs incur more benefit than harm in the high elderly. It is unclear how this can be implemented into reimbursement criteria and whether the use of an age criterium would be acceptable from a societal point of view.
3. Longevity of the ICD is a major determinant of the cost-effectiveness of ICD therapy and increasing battery capacity would result in an improvement in efficiency. In a perfect world, longevity of an ICD should exceed a patient's life, obviating device replacement. Manufacturers should be encouraged to increase device longevity by imposing a longer device warranty period (five or more years).
4. The current Belgian reimbursement procedure (the so-called "convention") and the limitation of the number of implant centres has been responsible for preventing an unrestrained growth in the number in ICD implants. This procedure should be continued and the number of implant centres should remain limited in future years, leading to an optimal concentration of expertise and preventing an inappropriate increase in ICD implants consequent to a supply induced demand mechanism.
5. Investigating the RIZIV/INAMI application forms revealed some shortcomings. For later study and peer review of ICD practice in Belgium, a better application and registration procedure should be realized. Reporting baseline characteristics of patients, drug use, ejection fraction, NYHA class, co-morbid conditions, … should be mandatory. Application forms should be supplemented with a written informed consent of the patient.
6. Given the increasing use of device therapy in patients with heart failure, there is need to critically evaluate the clinical effectiveness and efficiency of cardiac resynchronisation therapy (CRT) in these patients as well as the incremental benefit of combined CRT plus ICD devices (CRT-D).

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GLOSSARY

ACC	American College of Cardiology
ACE-inhibitor	Angiotensin Converting Enzyme inhibitor
AHA	American Heart Association
AMI	Acute Myocardial Infarction
AMIOVIRT	Amiodarone Versus Implantable Cardioverter-Defibrillator Randomized Trial
AR	Absolute Risk
ARR	Absolute Risk Reduction
BWGCPE	Belgian Working Group on Cardiac Pacing and Electrophysiology
CABG-PATCH	Coronary Artery bypass Graft Patch Trial
CAT	Cardiomyopathy Trial
CHD	Coronary Heart Disease
CRT	Cardiac Resynchronisation Therapy
CRT-D	Cardiac Resynchronisation Therapy, combined with ICD
CRT-P	Cardiac Resynchronisation Therapy, combined with Pacing
CVD	Cardiovascular Disease
DEFINITE	Defibrillators in Non-Ischaemic Cardiomyopathy Treatment Evaluation
DINAMIT	Defibrillator in Acute Myocardial Infarction Trial
ECG	Electrocardiogram
EF	Ejection Fraction
EPS	Electrophysiologic Study
ESC	European Society of Cardiology
HF	Heart Failure
HR	Hazard Rate
HR-QoI	Health-Related Quality of Life
HTA	Health Technology Assessment
IHD	Ischemic Heart Disease
LVEF	Left Ventricular Ejection Fraction
MADIT	Multicenter Automatic Defibrillator Implantation Trial
MI	Myocardial Infarction
NNT	Number Needed to Treat
NYHA	New York Heart Association
QoL	Quality of Life
RCT	Randomized Controlled Trial
RR	Relative Risk
RRR	Relative Risk Reduction
SCA	Sudden Cardiac Arrest
SCD	Sudden Cardiac Death
SCD-HeFT	Sudden Cardiac Death in Heart Failure Trial
SR	Systematic Review
VPB	Ventricular Premature Beat

1 OBJECTIVE AND SCOPE

This HTA provides a systematic review of the clinical effectiveness and the cost-effectiveness of implantable cardioverter defibrillators (ICDs) compared with conventional therapy in people at risk of sudden cardiac death (SCD) due to ventricular tachyarrhythmias. Furthermore, the use of these devices is considered from a patient and a public health care perspective. A description will be provided of the current and past use of ICDs in Belgium.

Two broad categories of patients are generally considered with respect to ICDs: patients who have already experienced a symptomatic tachyarrhythmia (cardiac arrest, hypotension, syncope, …) and patients at high risk for developing a life threatening arrhythmia. Secondary prevention relates to patients in the first group and has been the most common area of application for the ICD so far. No new trials have been reported on secondary prevention since the year 2000. Several HTAs on secondary prevention have been published in the past, the most recent ones by the NHS HTA Programme [1] (2005) and the Swedish Council on Technology in Health Care [2] (2006). Since no new trials on secondary prevention have been reported after the year 2000, we will focus in this HTA report on the use of ICD in primary prevention, i.e. in patients who did not yet experience a serious arrhythmic event but who are considered being at high risk for it. As far as the use of ICDs in secondary prevention is concerned, this HTA report will only summarize the available evidence.

In primary prevention, patients at high risk for cardiac arrest can be distinguished into one of four different categories of heart disease: ischaemic cardiomyopathy, nonischaemic (or idiopathic) cardiomyopathy, electrical disease and (surgically corrected) congenital heart disease. Only a limited number of patients belong to the latter two categories and because of their specific nature, they will not be discussed in depth.

- **This HTA report refers to the use of implantable defibrillators in the primary prevention of sudden cardiac death in patients with ischaemic or nonischaemic cardiomyopathy.**

2 BACKGROUND

2.1 SUDDEN CARDIAC DEATH

Cardiac death essentially can occur either as sudden arrhythmic death (cardiac arrest) or as a consequence of pump failure (heart failure, cardiogenic shock).

Sudden cardiac death (SCD) is defined as a natural death due to cardiac causes, heralded by an abrupt loss of consciousness within one hour of the onset of acute symptoms. Pre-existing heart disease may have been known to be present, but the time and mode of death are unexpected.[3] Sudden cardiac death is among the most common causes of death in developed countries. It is estimated that yearly about 0.1 to 0.2% of the population dies suddenly. This means that in Belgium presumably 15 000 people die suddenly each year as a consequence of cardiac arrest. Approximately 50% of all coronary heart disease (CHD) deaths are sudden deaths and in approximately half of them, SCD is the first manifestation of the disease.[4]

An unexpected cardiac arrest is mostly caused by ventricular tachyarrhythmias, more specific sustained ventricular tachycardia or ventricular fibrillation. Virtually any cardiac disease can lead to these fatal arrhythmias but most commonly (75%)[5] the underlying disease is coronary heart disease, i.e. an acute or chronic deficient oxygen supply to the heart due to obstructed or narrowed coronary arteries. SCD is certainly not always caused by a massive heart attack. Depending on the author, acute infarction is estimated to be the triggering event in 20% to 50%[6] of SCDs.[5] In other cases, myocardial scarring results from one or more, sometimes subclinical, old infarctions. Apart from ischaemic heart disease most of the remaining cases of SCD are caused by cardiomyopathies (heart muscle anomalies) or result from primary electrical heart disease. Studies from the UK and the US estimate that 4% of SCDs fall into the latter category.[7]

Because sudden cardiac arrest (SCA) mostly occurs out-of-hospital and given the very short time interval (minutes) that is available to intervene, SCA mostly leads to SCD. The only way of restoring normal heart rhythm in these patients is by means of "defibrillation", the application of an electrical shock to the chest which depolarizes the heart and enables normal heart rhythm to resume. Only in rare instances, patients are lucky enough to develop a SCA in an environment where immediate advanced life support is available. This typically occurs in a hospital or in a public place where bystanders, trained in advanced life support can start resuscitation until the life-saving *external* defibrillation shock restores heart rhythm. Results from the Seattle cardiac-rehabilitation program showed that survival rate was almost 100% if patients with ventricular fibrillation are defibrillated immediately. After delays of 4 to 5 minutes, the survival rate decreases to 15 to 40%, and after 10 minutes or longer, 95% of the victims die.[8]

Thus, most cases of SCA are not amenable to treatment and one has to rely on preventive measures to reduce the enormous burden of fatalities due to SCA. It has been known for decades that patients at highest risk for SCA after an acute myocardial infarction (AMI) have substantial left ventricular dysfunction and frequent ventricular premature beats (VPB). Decades ago, prevention of cardiac arrest was empirically directed at "treating" these VPBs which were considered harbingers of SCD. The Cardiac Arrhythmia Suppression Trial (CAST) however made clear that treatment with the anti-arrhythmics encainide and flecainide induced, rather than prevented, the occurrence of cardiac arrest.[9]

In specific cases, such as following an AMI, ß -blocking agents and angiotensin converting enzyme (ACE) inhibitors were found to be helpful in preventing SCD. In broader categories of patients, amiodarone has been the most used anti-arrhythmic drug used in the prevention of SCD. A systematic review of 15 relatively small trials on the effects of amiodarone in patients at risk for SCD showed that it reduced total mortality by 10–19%. Amiodarone reduced risk similarly in patients after MI, with heart failure or with clinically evident arrhythmia.[10]

In the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) however, the largest trial ever on amiodarone for the prevention of SCD, amiodarone was associated with a similar risk of death as compared with placebo (HR 1.06; 97.5% CI 0.86-1.30).[11] Sotalol is a particular ß -blocker with antiarrhythmic properties comparable to amiodarone. It is effective in suppressing ventricular arrhythmias but is has greater proarrhythmic effects and has not been shown to provide a clear increase in survival. [4]

Considering that immediate external defibrillation is only rarely available in victims of SCA and that medical therapy to prevent the occurence of SCA barely offers any benefit, the hopes for saving those victims more and more relied on implanting a defibrillator that would provide an immediate defibrillation in case a life threatening arrhythmia occured.

- **It is estimated that yearly up to 15 000 people die suddenly in Belgium. Most of them have ischaemic heart disease. Many more patients are at high risk of developing sudden cardiac death and constitute the population amenable for an ICD.**

2.2 ARRHYTHMIAS IN ISCHAEMIC HEART DISEASE

The type of arrhythmia that is responsible for the SCA in ischaemic heart disease (IHD) depends on the temporal relation of the fatal arrhythmia and the myocardial infarction (MI). In the acute phase of a MI, the metabolic consequences of severe ischemia may trigger ventricular fibrillation, even though ventricular function was often normal before the event. This seems to be the most common mechanism responsible for SCD in patients with IHD but no previous MI.[12] As mentioned earlier, this mechanism may account for 20 to 50% of cases of SCA. The risk of SCD accompanying an AMI is greatest in the first few hours and declines rapidly thereafter. Many patients die before reaching a hospital. If they are succesfully defibrillated within minutes following the arrest, e.g. in a public area or in the emergency room of the hospital, recurrent VF occurs no more frequent than in a control AMI population without VF. Hence, treatment of these patients is no different from that of other patients following an AMI and there is no indication for an ICD to be implanted. In secondary prevention ICD-trials, patients succesfully resuscitated from SCA therefore were excluded from enrollment if the SCA took place within 72 hours following an AMI.[13, 14]

Myocardial scar formation after an infarction may lead to the development of a substrate for intramyocardial reentry, resulting in ventricular tachycardia, which, in turn, may precipitate SCA in the absence of acute ischemia. This type of ventricular tachycardia (usually monomorphic) may develop days or years after the index infarction.[6] The VALIANT study provides 21st century data on the temporal change of the risk of SCD in patients admitted to hospital with an AMI.[15] Solomon et al studied 14 609 patients admitted with an AMI, complicated by left ventricular dysfunction (defined as an EF ≤40%), heart failure or both. The median duration of follow-up was 24.7 months. The risk of SCA was highest within the first week and fell rapidly within the first month after the MI (1.4%/month) and gradually decreased to 0.50%/month in months 2-6 reaching a steady state at approximately 1 year (0.14 to 0.18% per month). The risk of SCD was greatest among patients with the lowest EF and reached 2.3% per month in patients with an EF ≤ 30%. In a Finnish study on 675 consecutive patients discharged from hospital after an AMI, and not selected by ejection fraction, a different picture emerged.[16] During a mean follow-up of 43 months, total mortality was 15.0%. Among the cardiac deaths (8.7%), 22 were sudden. The epidemiologic pattern of SCD was different from that reported in older studies. Arrhythmic events or SCDs did not concentrate early after the index event in this registry, but most of them occurred more than 18 months after the AMI.

Apart from acute and chronic ischemia, ventricular damage after one or more MIs and subsequent remodelling may lead to congestive heart failure which induces neural and humoral stimuli that may promote ventricular tachyarrhythmias in susceptible patients.

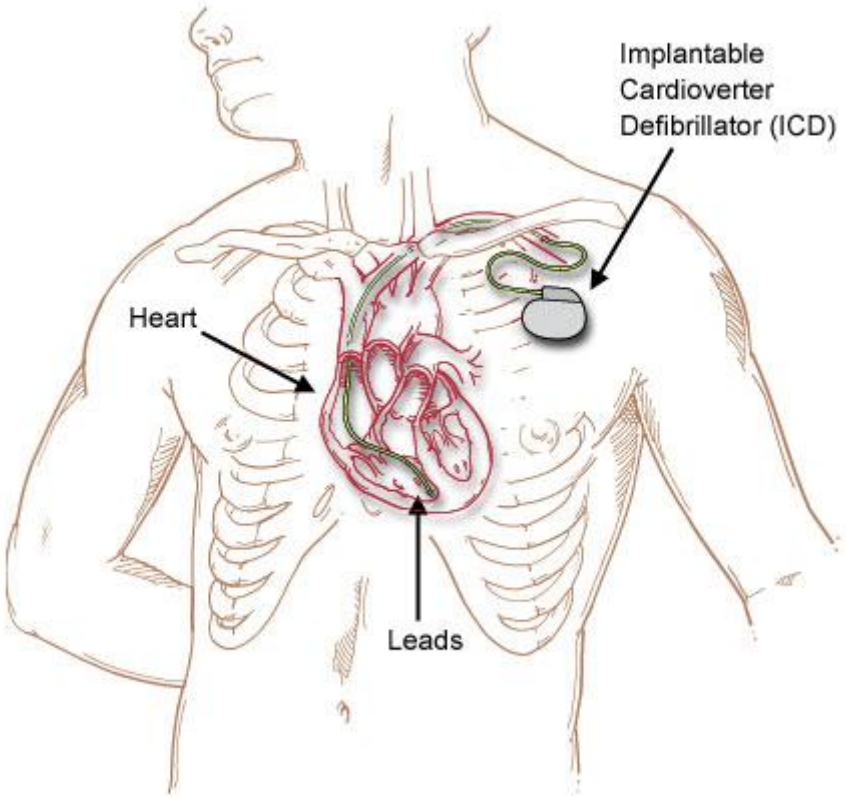
It has to be mentioned that, if obstructive coronary heart disease is complicated by ventricular arrhythmias, especially in patients with left main or proximal left anterior descending artery disease, there is a reasonable likelihood that revascularisation will reduce the frequency and complexity of the arrhythmias and, in some patients, will eliminate arrhythmias.[4]

- **The risk of SCD in patients admitted to hospital with an AMI is highest within the first week and falls rapidly during the first month. In high risk patients, SCD-risk in a recent study was 1.4% in the first month and gradually decreased, reaching a steady state after 1 year of 2% per year.**

2.3 THE IMPLANTABLE CARDIOVERTER DEFIBRILLATOR (ICD)

ICDs are battery-powered, implantable devices capable of monitoring heart rhythm and delivering an electric shock to restore normal rhythm when a life-threatening arrhythmia is detected. An ICD consists of two main parts: the defibrillator and the leads with electrodes. The defibrillator is a pulse generator, similar in size to a pacemaker and weighs about 80 grams. It can have one or more leads. Early devices required open chest surgery to be implanted but current ICDs are placed under the skin in the pectoral region with the leads into the heart inserted via a vein whilst under local anaesthesia (Figure 1)

Figure 1: The implantable cardiac defibrillator, connected to the heart with a single lead into the right ventricle.



Courtesy Boston Scientific (May 22, 2007).

The latest devices offer graded responses (so called "tiered therapy") to a sensed ventricular arrhythmia. Antitachycardia pacing, low-energy synchronised cardioversion and high-energy defibrillation shocks can be delivered successively via a transvenous lead, terminating the arrhythmia. Any ICD nowadays incorporates an antibradycardia pacemaker as well, for back-up pacing following a shock.

Device longevity has been gradually extended with advances in technology. They last from 5 to 8 years before replacement is required.

The ICD is supplemented with an external device, called the programmer, that can be used in the cardiologist's office to communicate with the ICD in order to change the settings of the device and to download stored information on arrhythmic events that have taken place and the way the device has responded to it.

The price of an ICD has been decreasing over time and may change from one country to another. In a recent Canadian HTA report, the device cost was estimated at C$19 500, i.e. €13 000.[17] In Australia, MSAC estimated the ICD price as AU$13 000 in public and AU$35 000 in private hospitals, i.e. €8 000 and €21 500 respectively[18]. Reimbursement in Belgium for an ICD actually is €15 708 (excl VAT) (Staatsblad, Moniteur Belge 11.07.2005).

2.4 HEART FAILURE

Heart failure (HF) is a complex syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the heart to function as a pump. Different conditions can affect this pumping ability and subsequently give rise to HF: coronary artery disease, arterial hypertension, cardiomyopathy, valvular malfunctions, ... Quantification of the systolic function of the heart (i.e. the pump function) typically relies on the calculation of left ventricular ejection fraction (LVEF). It is the percentage of blood the filled heart ejects with every beat. Normal values at rest are between 50 and 80%. The ejection fraction (EF) can be obtained by various invasive and non-invasive imaging techniques such as left ventricular angiography, echocardiography, MRI- or CT-scanning, nuclear imaging. The syndrome of HF is the clinical result of an impaired pump function of the heart (both emptying or filling of the heart can be defective) and is characterised by symptoms such as breathlessness and fatigue. Some authors wrongly use the term HF in asymptomatic patients with cardiac pumping dysfunction but HF is not equivalent to cardiomyopathy or left ventricular dysfunction, the latter terms merely describing an anatomical substrate, that in some patients leads to the development of HF. There is no single diagnostic test for HF, and diagnosis largely relies on clinical judgement based on a combination of history and physical examination completed with appropriate investigations.

Because of widely varying definitions, the epidemiology of HF is difficult to interpret. European estimates of the prevalence of HF in the general population range from 0.4 to 2%. The prevalence of HF increases rapidly with age, with a mean age of the HF population being 75 years, the elderly population being nearly 50% female. HF has a poor prognosis, as bad as most cancers. Half of patients carrying a diagnosis of HF will die within 4 years, and in patients with severe HF more than 50% will die within a year. HF is the most frequent cause of hospitalisation among people older than 65 years of age.

The functional status of patients with HF is traditionally encoded by means of the New York Heart Association (NYHA) classification. Subjective symptoms are used to rank patients according to their functional capacity into four classes as shown in Table 1.

Table 1: Ranking of functional status according to NYHA class.

NYHA Class	Patient Symptoms
Class I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnoea.
Class II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnoea.
Class III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnoea.
Class IV	Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.

In a study of CHD patients referred for nuclear imaging, in patients with LVEF≤35%, functional capacity was preserved (mean VO2 max 21.7±3.7 ml/kg/min) in 30%, moderately impaired (mean VO2 max 14.7±1.7 ml/kg/min) in 47% and severely impaired (mean VO_2 max 9.7±1.6 ml/kg/min) in 23%. Thus, 30% of patients with a severely depressed left ventricular function were considered as being in NYHA class I, while 70% were classified by the authors as NYHA class II or III[a].

The two most important risk factors for SCD are a low EF and heart failure. The risk of mortality related to EF is nonlinear, with a marked increase beginning when the EF falls below 40%. The mortality pattern in HF depends on the functional status of the patient. As one goes from NYHA class I to class IV, there is an increased annual risk of total mortality, whereas there is a decreased risk of SCD.[5] This is clearly illustrated in a post-hoc analysis of the MERIT-heart failure trial,[19] in which total mortality and mode of death in relation to NYHA class at randomisation was analysed. The results are depicted in Table 2 and indicate that the proportion of SCD decreases with increasing severity of HF according to NYHA class. Conversely, the proportion of patients who die from worsening HF increases with increasing severity of HF.

Table 2: Mode of death by NYHA class (%) and one-year mortality in the MERIT-heart failure trial.

	NYHA class II	NYHA class III	NYHA class IV		1-yr mortality in metoprolol arm (N=1990)
SCD	64	59	33		79 (4,0%)
HF	12	26	56		30 (1,5%)
Other	24	15	11		36 (1.8%)

- **Not all patients with a severely depressed left ventricular function develop heart failure.**
- **Patients with a NYHA functional class II or III are more prone to sudden death whereas patients in NYHA class IV are more likely to die from heart failure.**

a De Sutter, Personal Communication

2.5 CARDIAC RESYNCHRONISATION THERAPY (CRT)

It is beyond the scope of this HTA to study the effectiveness of CRT-D devices (i.e. CRT with an ICD incorporated in it) but since their expected broader application in clinical practice in the near future may influence the use of ICDs, the concept of CRT is briefly mentioned.

Patients with HF are traditionally treated by means of drugs, unless a surgical correctable underlying problem such as a valvular dysfunction is present or (in rare instances) cardiac transplantation is an option. In recent years a new mode of therapy for advanced HF has been introduced which is referred to as "cardiac resynchronisation therapy" (CRT). This implies the implantation of a specially designed (biventricular) pacemaker that stimulates both the right and left ventricle and enables an optimally synchronised contraction of both ventricles, resulting in a better cardiac output.

A subgroup of cardiac patients with a depressed left ventricular function and clinical HF have a combined problem of increased risk of SCD and intractable symptoms of HF, which make them candidate for CRT and an ICD alike. Combined devices for defibrillation and biventricular pacing, known as CRT-D are available for clinical use. The effectiveness of CRT and CRT-D as compared to medical treatment of patients with HF was studied in the COMPANION trial.[20] A total of 1520 patients who had advanced heart failure (NYHA class III or IV) due to ischaemic or nonischaemic cardiomyopathies and a QRS interval of at least 120 msec were randomly assigned to receive optimal pharmacologic therapy (diuretics, ACE-inhibitors, β-blockers, and spironolactone) alone or in combination with cardiac-resynchronization therapy with either a pacemaker (CRT-P) or a defibrillator (CRT-D). As compared with optimal pharmacologic therapy alone, CRT-P significantly decreased the risk of the combined end point of death from or hospitalization for heart failure (HR, 0.81), as did CRT-D (HR, 0.80). The difference in effect of CRT-P vs. CRT-D was not statistically significantly. The use of an ICD in combination with CRT should be based on the indications for ICD therapy.[21]

- **Cardiac resynchronisation therapy (CRT) represents a mode of treatment for heart failure that can be implemented in one single device that functions both as CRT and ICD, the so-called CRT-D.**

3 CLINICAL EFFECTIVENESS

3.1 DATA SOURCES

The main electronic databases were searched within a restricted time window from July, 1, 2003 to January, 8, 2007. Our search strategy is elaborated in appendix x. We were able to retrieve 4 RCTs, 4 SRs and 5 HTAs.

An excellent HTA was published in September 2005 and covered the literature until October 2003.[1] The most recent systematic review (SR) was published in 2006 and reviewed the literature until June, 2005.[22] During the preparation of this manuscript, an additional HTA was issued by the Canadian Agency for Drugs and Technologies in Health in March 2007.[17]

3.2 SECONDARY PREVENTION

After the year 2000, no new clinical trials on secondary prevention of sudden cardiac death that fulfilled our predefined inclusion criteria have been published. One randomized trial on secondary prevention published in 2004 compared empirical amiodarone treatment with electrophysiology guided therapy (drugs, revascularisation, ablation, aneurysmectomy, ICD) [23]. Another trial from 2003 was excluded from our review because of the idiosyncratic nature of the patients enrolled: young (mean age 40 years) South Asian men, predominantly with primary electrical heart disease, randomized to ICD or propranolol.[24]

A clinical review without formal meta-analysis of ICDs in both primary and secondary prevention of SCD has recently been published by Goldberger.[25] This review will be further discussed in the chapter on primary prevention. The meta-analysis by Desai on the use of ICDs in patients with nonischaemic cardiomyopathy also included both primary and secondary prevention trials.[26] Mäkikallio performed a SR of secondary and primary prevention studies but studied only the association between usage of a ß - blocker and benefit from ICD.[27]

The SRs that included both primary and secondary prevention patients and that were published within our predefined time window will be discussed in more detail in the chapter on primary prevention.

No SR restricted to secondary prevention has been published after the 2005 NHS HTA that discussed three RCTs and three SRs (Connolly[28], Ezekowitz[29] and Lee[30]) (Table 3).

Table 3: RCTs and SRs related to ICD use in secondary prevention of SCD included in the 2005 NHS HTA.[1]

YEAR	STUDY TYPE	STUDY / AUTHOR	CLINICAL CONTEXT
1997	RCT	AVID	SEC PREV
2000	RCT	CASH	SEC PREV
2000	RCT	CIDS	SEC PREV
2000	SR	CONNOLLY	SEC PREV
2003	SR	EZEKOWITZ	PRIM + SEC
2003	SR	LEE	PRIM + SEC

See text and glossary for abbreviations of different study acronyms.

Only one RCT reached a statistically significant overall mortality reduction with ICD.[31] In this study, the average unadjusted length of additional life associated with ICD was 2.7 months at 3 years. Three SRs reported a statistically significant survival benefit in ICD-treated patients, with a summary RR of all-cause mortality between 0.72 and 0.76. The absolute risk reduction of all cause mortality due to ICD therapy was between 3.5% and 7.0% per year in these SRs. Prolongation of life by an ICD was 2.1 months at 3 years and 4.4 months at 6 years.[1]

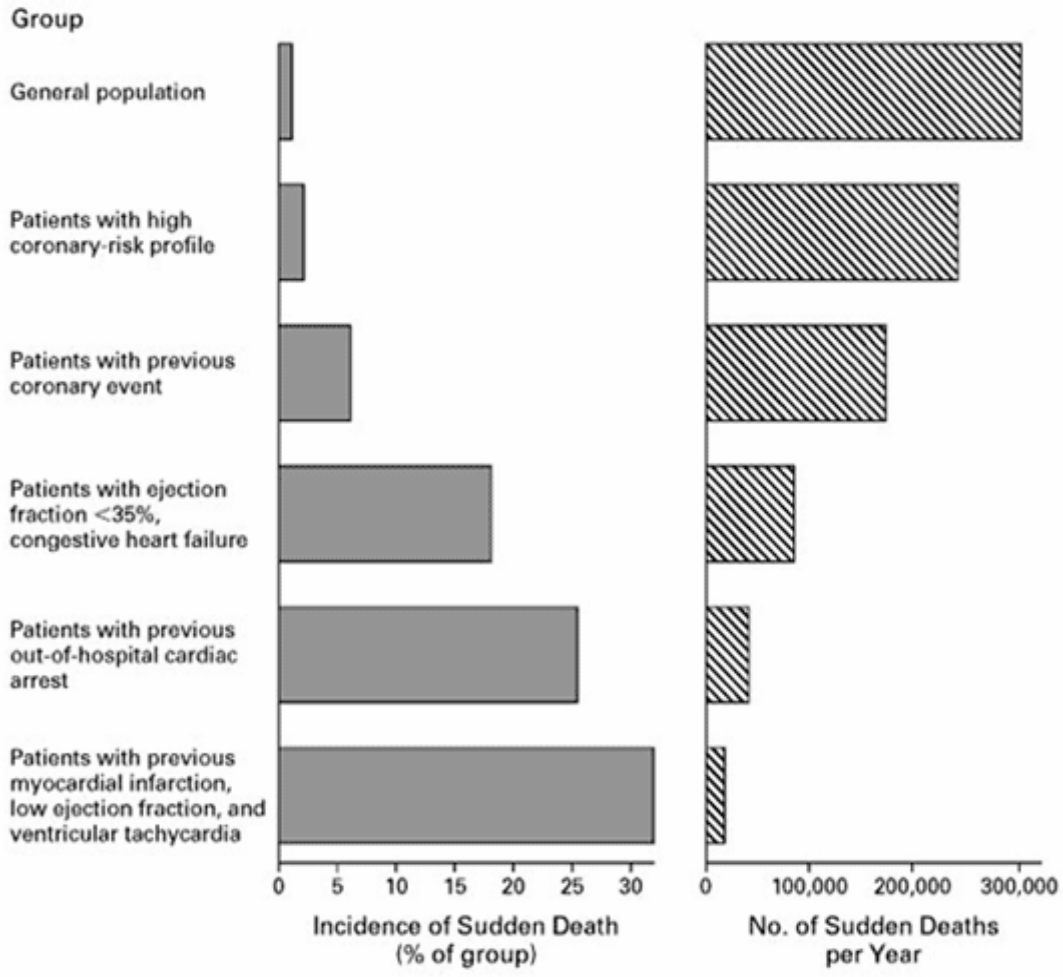
- **The absolute risk reduction of all cause mortality in secondary prevention studies is estimated in systematic reviews between 3.5% and 7.0% per year respectively and is accompanied by a very modest prolongation of life.**

3.3 PRIMARY PREVENTION

The efficacy of the ICD in secondary prevention of SCD is traditionally accepted. However, only a limited number of patients are lucky enough to take advantage of this technology because most out-of-hospital cardiac arrests lead to death. The overall survival rate of patients with out-of-hospital cardiac arrest is estimated to be lower than 5%.[32]

The most important challenge cardiologists are facing when considering the use of an ICD in primary prevention is in predicting which patients will benefit from an ICD. The overall incidence of SCD in Europe is estimated at 0.1 to 0.2% per year. This population contains a wide spectrum of patients with a variable preceding risk of SCD: patients at risk for developing an AMI, patients who survived a coronary event and patients at high risk for SCD, due to a poor left ventricular function or heart failure as well as a small number of survivors of a cardiac arrest. The large subgroup with the lowest risk of SCD, i.e. patients with a high coronary risk profile, constitute in absolute terms the group within which the most sudden deaths can be prevented. This is graphically displayed in the chart below (Figure 2).

Figure 2: Incidence of sudden death in specific populations and the corresponding annual numbers of sudden deaths.



Source: Huikuri, New England Journal of Medicine.[33]

The simple documentation of "benign" ventricular arrythmias on electrocardiogram (ECG) in a patient is a poor predictor of the occurence of "malign" arrhythmias. Several other techniques have been introduced to try to elucidate a propensity to cardiac arrest (i.e. ventricular fibrillation): longer term ECG-monitoring, abnormalities on a signal-averaged electrocardiogram, micro T wave alternans, depressed heart-rate variability or an elevated average 24-hour heart rate. So far, for none of these techniques the effectiveness has been proven in large RCTs.

Trials on primary prevention of SCD typically recrute patients with ischaemic or idiopathic cardiomyopathy with poor left ventricular function (EF<35%) and an annual risk of death between 10 and 20%. Early studies demanded the presence of spontaneous or inducible arrythmias (by electrophysiologic study - EPS) but later on, the presence of such arrythmias was no more mandatory and inclusion essentialy was based on left ventricular function (as estimated by EF), the presence of clinical HF and the underlying cardiac disease.

3.3.1 Randomized Controlled Trials on ICD in primary prevention

Table 4 shows a chronological list of the RCTs comparing ICD with non-ICD in both primary and secondary prevention, together with the underlying heart disease and ejection fraction.

Table 4: Chronological list of RCTs comparing ICD with non-ICD in primary and secondary prevention of SCD.

YEAR	SEC PREV	PRIM PREV	UNDERLYING HEART DISEASE	EJECTION FRACTION (%)
1996		MADIT I	ischaemic	25-27
1997	AVID		81% ischaemic	31-32
1997		CABG-PATCH	ischaemic	27
2000	CASH		70-77% ischaemic	44-47
2000	CIDS		82-83% ischaemic	33-34
2002		MADIT II	ischaemic	23
2002		CAT	nonischaemic	24-25
2003		AMIOVIRT	nonischaemic	22-23
2004		DEFINITE	nonischaemic	21-22
2004		DINAMIT	ischaemic	28
2005		SCD-HeFT	ischaemic + nonischaemic	24-25

Sec prev: secondary prevention. Prim prev: primary prevention. Ejection fraction values relate to mean EF in intervention – control group. Single number indicates overall study population mean. "81% ischaemic" denotes that 81% of the study population had ischaemic heart disease. See text or glossary for abbreviations of different study acronyms. Shaded area refers to trials published before the predefined time window of this review.

AMIOVIRT, DEFINITE, DINAMIT and SCD-HeFT are the RCTs that were published within the time window of the search procedure for this HTA. Two trials that are not mentioned in table 4, are included in some SRs on ICD: MUSTT and BEST-ICD. These trials have a mutually comparable yet complex design and randomised patients to anti-arrhythmic or EPS-guided therapy. Because no formal randomisation of patients to ICD or no-ICD was done, these studies do not meet the scope of this project and were not included in this review.

These RCTs will be discussed briefly.

3.3.1.1 MADIT

The Multicentre Automatic Defibrillator Implantation Trial was published in 1996 and was the first large RCT on ICD use.[34] In 2002 a second paper was published by the same author group, the so-called MADIT II study and since then, the first paper often is referred to as the MADIT I trial. The trial was totally supported by a research grant from CPI/Guidant Corporation that supplied the defibrillators. The study tested the hypothesis whether prophylactic implantation of an ICD in patients with CHD at high risk for ventricular arrhythmia could improve overall survival as compared to conventional medical therapy (which could include antiarhythmic drugs and was left to the discretion of the patient's attending physician). Over the course of five years, 196 patients from 32 (mostly US) hospital centres were enrolled. They were characterized by prior myocardial infarction; a NYHA functional class I, II, or III; a left ventricular ejection fraction ≤35%; a documented episode of asymptomatic unsustained ventricular tachycardia (VT); and inducible, nonsuppressible VT on electrophysiologic study. They were randomly assigned to receive an ICD (n=95) or conventional medical therapy (n=101). During an average follow-up of 27 months, there were 15 deaths in the defibrillator group and 39 deaths in the conventional-therapy group (HR for overall mortality, 0.46; 95 % CI 0.26-0.82). The authors concluded that in patients with a prior myocardial infarction who are at high risk for ventricular tachyarrhythmia, prophylactic therapy with an ICD leads to improved survival as compared with conventional medical therapy.

When this trial started in December 1990, only transthoracic implants were approved and transvenous devices were used from August, 1993 on. Eventually, 98 patients had a transthoracic and 98 had a transvenous device implanted.

Given the fact that 32 electrophysiology-centres needed five years to enroll 196 patients suggests a substantial selection bias in this study. Furthermore, there was a remarkable low use of β-blockers in this study on patients with a prior MI with a substantial difference between the two treatment groups. By the end of the study, 27% of ICD-patients and only 5% of conventionally treated patients were on β-blocking therapy. This may have influenced the occurence of SCA and could have exaggerated the perceived efficacy of the ICD.

In a substudy the authors looked at the survival benefit in relation to the underlying mortality risk, estimated by three different risk factors (ejection fraction, QRS duration, and history of heart failure requiring therapy.[35] The ICD was associated with a significant reduction in mortality only in high-risk subsets with EF <26%, QRS duration ≥0.12 second, and a history of heart failure requiring treatment. Patients with an EF between 26 and 35% did not have improved survival with an ICD.

3.3.1.2 CABG-Patch

The Coronary Artery Bypass Graft Patch Trial (CABG-PATCH)[36] investigated whether systematically implanting an ICD in high-arrhythmic-risk patients, scheduled for elective coronary bypass surgery (CABG) could improve overall survival. The trial was supported by grants from the NHLBI and CPI/Guidant. High risk status was defined in these patients as the presence of left ventricular dysfynction (EF<36%) and abnormalities on the signal averaged ECG. Over the course of five years, 37 clinical centres screened all patients who were scheduled for elective CABG. Of 1422 eligible patients, 1055 were enrolled, and 900 randomly assigned to therapy with an ICD (446 patients) or to the control group (454 patients). The primary end point of the study was overall mortality. During an average follow-up of 32±16 months, there were 101 deaths in the ICD group (71 from cardiac causes) and 95 in the control group (72 from cardiac causes). The hazard ratio for death from any cause was 1.07 (95% CI 0.81-1.42). The authors found no evidence of improved survival. They suggested that the absence of benefit could be related to the deleterious effect of the epicardial ICD implantation that augmented surgical risk and to the beneficial effect of the revascularization as such on the risk of SCD.

3.3.1.3 MADIT II

The second Multicentre Automatic Defibrillator Implantation Trial was a primary prevention trial in patients with a prior MI in which the presence of documented arrhythmias was not mandatory to be eligible for the study.[35] Patients could be enrolled if they had a MI one month or more before entry, and an EF of 30% or less (in MADIT I, the upper EF limit was 35%). There was no further requirement of risk stratification. Prescribing medication in borh groups was was left to the discretion of the patients' physicians. The appropriate use of ß-blockers, ACE-inhibitors and lipid lowering drugs was strongly encouraged in both study groups. Some patients were enrolled many years after the infarction and the mean time interval between the most recent AMI and enrollment was 81±78 months. During an average follow-up of 20 months, the mortality rates were 19.8% in the conventional-therapy group and 14.2% in the defibrillator group. The hazard ratio for the risk of death from any cause in the ICD group as compared with the conventional-therapy group was 0.69 (95% CI 0.51-0.93). The authors concluded that in patients with a prior MI and advanced left ventricular dysfunction, prophylactic implantation of an ICD improves survival.

A worrying finding in this trial was that new or worsened HF requiring hospitalization was slightly more frequent in the ICD group (19.9%) than in the conventional-therapy group (14.9%). Several possible explanations were forwarded by the authors: patients saved from malignant ventricular arrhythmias by the implantation of a defibrillator live longer than conventionally treated patients and would thus have more time for HF to develop, defibrillator shocks might contribute to rehospitalization and myocardial injury and backup right ventricular pacing may impair ventricular function.

In a remarkable post-hoc subgroup analysis, the hazard ratio for ICD benefit was only 0.98 for patients in whom the most recent AMI occurred less than 18 months before ICD implant. Later on there was a survival benefit that remained substantial up to more than 15 years following the AMI.[37]

3.3.1.4 CAT

The German Cardiomyopathy Trial investigated whether prophylactic implantation of an ICD in patients with nonischaemic symptomatic cardiomyopathy (NYHA class II or III) and an EF≤30% affected overall survival compared to conventional treatment.[38] One hundred four patients were enrolled in the trial: 50 were assigned to ICD therapy and 54 to the control group. Because the overall mortality rate was too low in this small trial, the study was stopped for futility after the pilot phase. After a mean follow-up of 5.5 years, 30 deaths had occurred (13 in the ICD group and 17 in the control group). Cumulative survival was not significantly different between the two groups (93% and 80% in the control group versus 92% and 86% in the ICD group after 2 and 4 years, respectively).

3.3.1.5 AMIOVIRT

The Amiodarone Versus Implantable Cardioverter-Defibrillator Randomized Trial (AMIOVIRT) investigated the effect on total mortality of an ICD versus amiodarone in patients with nonischaemic dilated cardiomyopathy and asymptomatic nonsustained ventricular tachycardia.[39] It was a small trial in which 103 patients were randomised to either ICD or amiodarone. Patients in NYHA class IV were excluded. 85% of patients were in NYHA class II or III. The percentage of patients surviving at one year (90% vs. 96%) and three years (88% vs. 87%) in the amiodarone and ICD groups respectively, were not statistically different.

3.3.1.6 DEFINITE

The Defibrillators in Nonischaemic Cardiomyopathy Treatment Evaluation (DEFINITE) investigators randomised 458 patients with nonischaemic cardiomyopathy, nonsustained VT or multiple ventricular premature beats (VPB) and a LVEF<36% to receive standard medical therapy or standard therapy plus an ICD.[40] All patients had a prior history of heart failure but they were excluded if they were in NYHA class IV. They were followed for a mean of 29 months.

There were 68 deaths: 28 in the ICD group, as compared with 40 in the standard-therapy group (HR, 0.65; 95% CI 0.40-1.06). The mortality rate at two years was 14.1% in the standard-therapy group and 7.9% in the ICD group. There were 17 SCDs: 3 in the ICD group, as compared with 14 in the standard-therapy group (HR, 0.20; 95% CI 0.06-0.71). The implantation of an ICD was associated with a nonsignificant reduction in the risk of death from any cause but significantly reduced the risk of SCD.

3.3.1.7 DINAMIT

The Defibrillator in Acute Myocardial Infarction Trial (DINAMIT) trial investigated the effectiveness of the prophylactic use of an ICD early after an acute MI.[41] 674 patients were enrolled and randomized to ICD or no-ICD therapy, 6 to 40 days following an acute MI. Eligible patients had a reduced LVEF (≤35 %) and impaired cardiac autonomic function (manifested as depressed heart-rate variability or an elevated average 24-hour heart rate on Holter monitoring). The primary outcome was mortality from any cause. Death from arrhythmia was a predefined secondary outcome. During a mean follow-up period of 30 months, there was no difference in overall mortality between the two treatment groups (HR for death in the ICD group,1.08; 95% CI 0.76-1.55). There were 12 deaths due to arrhythmia in the ICD group, as compared with 29 in the control group (HR in the ICD group, 0.42; 95% CI 0.22-0.83). In contrast, there were 50 deaths from nonarrhythmic causes in the ICD group and 29 in the control group (HR in the ICD group, 1.75; 95% CI 1.11-2.76). The exact cause of death of these patients is not reported but a postfactum analysis of the study results indicated that the increased risk of nonarrhythmic death was confined to patients who had received a shock from the ICD. It looks as if SCD in these patients is transformed to a nonarrhythmic death, e.g. death due to heart failure. An editorialst suggests that the propensity to SCA in these patients may simply be a harbinger of advanced heart failure.[42]

3.3.1.8 SCD-HeFT

The Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) investigators randomised 2521 patients with either ischaemic or nonischaemic heart disease to conventional therapy for heart failure plus placebo, conventional therapy plus amiodarone, or conventional therapy plus an ICD.[11] Conventional therapy was considered to include, when appropriate, a ß-blocker, an ACE-inhibitor, an aldosterone-blocker, aspirin, and a statin. Patients had to have NYHA class II or III heart failure and an EF of ≤35%. The ICD involved was a simple single-lead device, conservatively programmed in a "shock-only" mode. The primary endpoint was death from any cause. The median LVEF in patients was 25%; 70% were in NYHA class II, and 30% were in class III. The cause of HF was ischaemic in 52% and nonischaemic in 48%. The median follow-up was 45.5 months. As compared with placebo, amiodarone was associated with a similar risk of death (HR 1.06; 97.5% CI, 0.86-1.30) and ICD therapy was associated with a 23% decreased risk of death (HR 0.77; 97.5% CI 0.62-0.96) and an absolute decrease in mortality of 7.2% after five years in the overall population. The results were comparable in both the prespecified subgroups of ischaemic and nonischaemic heart failure. The hazard ratio for death from any cause with ICD compared to placebo was 0.79 (97.5% CI 0.60-1.04) in ischaemic heart failure and 0.73 (97.5% CI 0.50-1.07) in nonischaemic disease.

During 5 years of follow-up, 21% of the patients in the ICD group received a shock for rapid VT or VF. The average annual rate of appropriate shocks was 5.1%.[11]

This study is the largest ever that investigated the effectiveness of amiodarone and came to the conclusion that amiodarone does not improve survival among patients with mild to moderate heart failure. In a prespecified subgroup analysis of NYHA class, there was a 44% increase in the risk of death among the NYHA class III patients treated with amiodarone as compared to the placebo group. The interaction between ICD therapy and NYHA class was also significant. Whereas in NYHA class II patients, there was a 46% reduction in risk of death, patients in NYHA class III had no apparent reduction in the risk of death with ICD as compared with placebo.

3.3.1.9 Summary

Table 5 and Table 6 summarize the mortality rates and numbers needed to treat NNT) for three years calculated from the RCTs discussed above. Cumulative death rates at three years were either retrieved from the text or manually derived from the printed Kaplan-Meier curves. Yearly survival was obtained by calculating the cubic root of survival at three years, assuming a constant survival per year during the first three years. Confidence limits for NNT calculated according to Altman.[43, 44]

Table 5: Outcome data of the primary prevention trials.

RCT	AVERAGE FOLL-UP (MO)	ICD		CONTROL		HR	95% CI	ANNUAL DEATH RATE	
		n	N	n	N			ICD	CONTROL
MADIT I	27	15	95	39	101	0,46	0,26-0,82	0,06	0,17
CABG-PATCH	32	101	446	95	454	1,07	0,81-1,42	0,07	0,05
MADIT II	20	105	742	97	490	0,69	0,51-0,93	0,08	0,12
CAT	66	13	50	17	54	NS	NS	0,03	0,06
AMIOVIRT	24	6	51	7	52	NS	NS	0,07	0,06
DEFINITE	29	28	229	40	229	0,65	0,40-1,06	0,05	0,07
DINAMIT	30	62	332	58	342	1,08	076-1,55	0,07	0,06
SCD-HeFT	45,5	182	829	244	847	0,77	0,62-0,96	0,06	0,08

N number at risk; n number of deaths; HR hazard ratio.

Table 6: NNT to postpone one death beyond three years, as derived from the primary prevention trials.

RCT	average foll-up (mo)	NNT (3 years)			
		lower	NNT	upper	CI of NNT
MADIT I	27	3	5	16	(3 to 16)
CABG-PATCH	32	38	-104	-18	NNT (benefit) 38 to ∞ to NNT (harm) 18
MADIT II	20	7	12	55	(7 to 55)
CAT	66	4	11	-23	NNT (benefit) 4 to ∞ to NNT (harm) 23
AMIOVIRT	24				Insufficient info
DEFINITE	29	9	16	-98	NNT (benefit) 9 to ∞ to NNT(harm) 98
DINAMIT	30	26	-79	-12	NNT (benefit) 26 to ∞ to NNT (harm) 12
SCD-HeFT	45,5	13	22	128	(13 to 128)

NNT: number needed to treat. Confidence Intervals (CI) calculated according to Altman.[43, 44]

3.3.2 Systematic Reviews on ICD in primary prevention

As discussed earlier, our literature search resulted in the retrieval of four SRs. Two of these were strictly limited to primary prevention trials,[22] [45] one was related to nonischaemic cardiomyopathy,[26] and one included a CRT-D trial as well.[25] Table 7 lists these SRs chronologically. Asterisks indicate whether a primary study was included in the corresponding review. The shaded area refers to papers published before the predefined time window and are added for the sake of completeness.

Table 7: Systematic reviews of ICD in primary prevention, published after July 2003.

			UNDERLYING HEART DISEASE	NANTHAKUMAR (PP)	DESAI (PP+SP)	GOLDBERGER (PP+SP)	ABDULLA (PP)
	YEAR			2004	2004	2006	2006
1	1996	MADIT I	ischaemic	*		*	*
2	1997	CABG-PATCH	ischaemic	*		*	*
3	2002	MADIT II	ischaemic	*		*	*
4	2002	CAT	nonischaemic	*	*	*	*
5	2003	AMIOVIRT	nonischaemic	*	*	*	*
6	2004	DEFINITE	nonischaemic	*	*	*	*
7	2004	DINAMIT	ischaemic	*		*	*
8	2005	SCD-HeFT	ischaemic and nonischaemic	*	*	*	*

PP primary prevention; SP secondary prevention.

3.3.2.1 Nanthakumar

Nanthakumar et al pooled 10 primary prevention trials of which nine compared ICD vs. standard medical therapy and one trial, COMPANION,[20] compared CRT-P vs. CRT-D vs. medical therapy.[45] The latter trial is not a comparison between ICD and no-ICD, given the confounding effect on outcome due the resynchronisation device. This SR also includes the MUSTT trial[46] which compares an EPS guided strategy vs. empiric therapy. ICD use was not randomised in this trial. The remaining eight trials are those meeting the inclusion criteria of our review which are tabulated in Table 7.

When the deaths from the ten trials were pooled, there was a 25% relative reduction in all-cause mortality with the ICD (RR 0.75; 95% CI 0.63-0.91). All-cause mortality in the control group for the 10 studies was 26.4%, compared with 18.5% in the ICD group, i.e. an absolute mortality reduction of 7.9%. In a sensitivity analysis, when the results of the MUSTT trial was discarded, the RR was 0.81 (CI 0.69-0.95) instead of 0.75. Discarding the COMPANION study reportedly did not affect the estimated combined relative risk reduction and resulted in a RR of all-cause mortality of 0.74 (95% CI 0.60-0.92).

3.3.2.2 Desai

Desai et al. performed a meta-analysis of RCTs on the effect of ICD on all-cause mortality in patients with nonischaemic cardiomyopathy in both primary and secondary prevention.[26] They included five RCTs in their analysis, one of which was the COMPANION trial[20] that in essence was a study on CRT as discussed earlier. Their pooled analysis suggested a significant reduction in total mortality among patients randomized to ICD or CRT-D vs medical therapy (RR 0.69; 95% CI 0.55-0.87). Mortality reduction reportedly remained significant after elimination of CRT-D trials.

3.3.2.3 Goldberger

Goldberger and Lampert published a SR whithout formal meta-analysis.[25] They reviewed the literature on ICD in primary and secondary prevention, irrespective of the underlying heart disease. In primary prevention, they found a survival benefit (1) in patients with a history of MI and EF≤30% and (2) in patients with class II or III heart failure and an EF≤35%. They concluded that "ICD implantation is first-line therapy for primary prophylaxis in most patients with marked left ventricular dysfunction, regardless of etiology."

3.3.2.4 Abdulla

Abdulla et al present a review of the impact of CRT and prophylactic ICD on outcome.[22] The results of both interventions are analysed separately. The meta-analysis of the same eigth RCTs we have tabulated earlier resulted in an odds ratio for all-cause mortality of 0.75 (95% CI 0.59-0.96, p=0.025).

3.3.2.5 Summary

Table 8 shows an overview of the results from the SRs as discussed above. The paper by Goldberger is not mentioned in this table because it performed no formal meta-analysis.

Table 8: All-cause mortality (average follow-up: 20-48 months) in three systematic reviews.

SYSTEMATIC REVIEW	ICD INTERVENTION			CONTROL				RR (95% CI)	
	n	N	AR	n	N	AR	ARR	RR	95% CI
NANTHAKUMAR	652	3530	0,18	983	3723	0,26	7,9	0,75	0,63-0,91
DESAI	334	1754	0,19	439	1799	0,24	5,4	0,69	0,55-0,87
ABDULLA	512	2774	0,18	597	2569	0,23	4,8	0,75	0,59-0,96

N number at risk; n number of deaths. AR absolute risk. ARR absolute risk reduction. RR relative risk.

From these meta-analyses it is concluded that the ICD confers a reduction of all-cause mortality in primary prevention in patients at high risk of SCA. In only three of eight RCTs, including the two largest ones, a statistically significant mortality reduction was observed. The effect estimate in the SR with the highest ARR (Nanthakumar) is exaggerated due to the inclusion of the results from the MUSST trial that was not a RCT of ICD vs. no-ICD. The SR by Desai combines primary and secondary prevention studies in nonischaemic heart disease only. The effect estimate is influenced by the inclusion of a CRT trial. This estimate may not be transferable to patients with ischaemic heart disease. The meta-analysis by Abdulla best reflects the overall estimate of the effect of ICD as obtained from the trials corresponding to the criteria used in this HTA report. An ARR of 4.8% in all-cause mortality during an average follow-up of 20-48 months was calculated .

3.3.3 HTAs on ICD in primary prevention

Table 9 lists the HTAs we retrieved and indicates the primary ICD studies that were included. One HTA that was not yet available at the moment of our literature search was published later on by the Canadian Agency for Drugs and Technologies in Health in March 2007[17]. Because the HTA report from Ontario was outdated at the moment we produced our manuscript, we do not further report on it.

The uptake of the MUSTT and BEST-ICD trials in some of the HTAs is indicated for the sake of completeness, but as justified earlier, we did not include the results of these in our HTA report.

We will briefly summarize the most notable findings within these HTAs.

Table 9: HTA reports published after July 2003 and their corresponding RCTs.

RCTs			HTAs					
SEC PREV	**PRIMARY PREV**	**CLINICAL CONTEXT**	**ONTARIO (Canada)**	**ICSI (US)**	**BLUE CROSS (US)**	**NHS (UK)**	**MSAC (Australia)**	**CADTH (Canada)**
			2003	2005	2005	2005	2006	2007
	MADIT I	ischaemic	*	*	*	*	*	*
	CABG-PATCH	ischaemic	*	*	*	*	*	*
AVID						*		
CASH						*		
CIDS						*		
	MADIT II	ischaemic	*	*	*	*	*	*
	CAT	nonischaemic			*	*	*	*
	AMIOVIRT	nonischaemic			*			*
	DEFINITE	nonischaemic		*	*		*	*
	DINAMIT	ischaemic		*	*		*	*
	SCD-HeFT	isch + nonisch		*	*		*	*
	MUSTT	*ischaemic*	*		*	*	*	*
	BEST-ICD	*ischaemic*						*

MUSTT and BEST-ICD (italic) are included in the table but are not part of this review because in these trials allocation of patients to ICD or no-ICD was electrophysiology-study guided. The shaded area indicates trials that were published before the predefined time-window for this report. An asterisk indicates whether an HTA incorporated the corresponding RCT.

3.3.3.1 Clinical effectiveness

Treatment with an ICD in addition to conventional medical treatment significantly reduces the RR of all-cause death by 28% and of SCD by 67%, which corresponds to an absolute risk reduction of 6% for all-cause death and 7% for SCD.[17] Inconsistent results are obtained from subgroup analyses and no reliable conclusions can be made about the relative efectiveness of ICD on patients with varying ages, QRS-durations, ejection fractions, different rhyhtms or different causes of heart failure[18]. When the total RCTs study population of over 7000 patients was divided into an ischaemic and a nonischaemic group, the all-cause death risk reduction attributable to the use of ICD failed to reach statistical significance in both groups. The RRR for SCD with ICD was statistically significant but, as emphasized by the CADTH group, all-cause death is the more reliable clinical outcome because bias can be introduced if deaths are systematically misclassified, as is likely when studies (such as ICD studies) are not double-blind.[17]

3.3.3.2 Cost effectiveness

The summary of our review of the HTA-literature on cost effectiveness of ICD use will be discussed in chapter 4.

3.3.3.3 Patient issues

The most common psychological problems after ICD surgery are anxiety, depression, fear of shock, and fear of death. Some anxiety or depression is experienced by 24% to 87% of patients, and up to 38% will experience anxiety of sufficient intensity and duration to meet diagnostic criteria for an anxiety spectrum disorder. The frequency with which the ICD has fired and a recent shock are linked to anxiety.[17]

The available evidence on the impact of ICD on the quality of life (QoL) of patients is weak, especially for primary prevention applications.[47] However, we can hardly expect a preventive therapy to improve QoL.[17]

Moreover, because ICDs may prolong life, allowing more time for deterioration of the underlying cardiac disorder, in the long term ICDs may lead to a QoL decrement over time.

Patients should be well informed about the benefits and the potential harms of ICDs. Some may prefer not to undergo an operative procedure even when fully informed of the expected survival benefit. Patients with intractable heart failure e.g. may decline ICD implantation because of concerns regarding prolongation of a very poor quality of life. Others may be anxious towards defibrillation shocks. In addition, there are often competing risks of mortality due to comorbid conditions that must be considered by both the patient and the physician.

3.3.3.4 Public health issues

The introduction of ICD therapy poses important questions about the allocation of public health care resources, moreover because the use of ICDs in the future is likely to augment because of the increasing use of the device in primary prevention and in patients with heart failure. Theoretically, any patient with an EF<35% could be considered a candidate for an ICD. As a result of limited financial resources, cardiologists can be put into the difficult moral position when they have to decide whether or not to discuss the potential therapeutic benefit of an ICD and whether or not to proceed to implant an ICD.

3.3.3.5 Organisational issues

The implantation of an ICD should only be performed by physicians specifically trained in the procedure. Typically such physicians are cardiac electrophysiologists who sometimes need the help of a cardiothoracic surgeon for the surgical part of the procedure.[47] Implantation of ICDs should be performed in experienced centres, usually in the cardiac catheterization or electrophysiologic laboratory. A post-operative hospital stay is generally required and typically lasts about one to two days. However, successful outpatient placement of the device was performed in the SCD-HeFT study.[47]

- **In three out of eigth primary prevention RCTs, ICD therapy resulted in a statistically significant reduction of all-cause mortality.**
- **In a meta-analysis of the results of these eight primary prevention trials, the pooled estimate of the relative risk reduction of all-cause death was 25%, corresponding to an absolute risk reduction of 4.8% over a period of two to four years.**
- **Currently, high-risk status for SCD is mainly defined by left ventricular ejection fraction, the nature of the underlying heart disease and whether or not clinical heart failure is present.**
- **Most patients in whom an ICD is implanted will never receive an appropriate shock from the device. The average annual rate of appropriate shocks is 5%.**
- **There is urgent need to better define high-risk patients by additional noninvasive techniques.**

3.4 HARMS

The implantation of an ICD is a relatively safe procedure, with a perioperative mortality rate of 0.0 to 1.2%.[1, 47, 18] Adverse events are poorly reported in the RCTs but significant morbidity may occur in 1 to 3% of patients,[47] the most common complications being related to the surgical procedure, device failure and inappropriate shocks. The most frequently encountered early surgical complications are hematoma (3%) and hemothorax or pneumothorax (1 to 2%)[18]. Later on, infection at the site of the pocket sometimes occurs. In MSAC, infection is described with an overall rate of 2% within 30 days post-ICD implantation and 1% later on.

Lead dislodgement, if it occurs, usually happens within the first few months after implantation. Early dislodgement was documented in 17 papers with rates varying between 0.5 an 7.0%. The median rate of dislodgement was 1.5%. Median late lead problems occur in 2 to 7% of patients.[48] Along with an increase of the number of patients implanted for primary prevention, the mean survival of patients following implant will increase which may lead to a future increase of lead problems that are typically long-term complications. In a single-centre German study, 990 consecutive patients who underwent a first ICD implant between 1992 and 2005 were analysed in order to assess the annual rate of transvenous lead defects. Overall, 148 defibrillation leads (15%) failed during the follow-up. The estimated lead survival rates at 5 and 8 years after implantation were 85% and 60%, respectively. The annual failure rate increased progressively with time after implantation and reached 20% in 10-year-old leads. Lead defects affected newer as well as older models[49].

Other problems associated with ICD therapy include inappropriate shock discharge mostly for atrial fibrillation with rapid ventricular response, defibrillator storm with appropriate recurrent ICD discharge for recurrent ventricular tachyarrhythmias or inappropriate discharge for a multiplicity of reasons.[4] The occurrence of inappropriate shocks varies across studies, with rates varying between 0.5 and 19% within 30 days of implantation and an overall rate of 14% more than 30 days postimplantation.

Heart failure can exacerbate due to the ICD implant, when a high percentage of the heartbeats are paced from the right ventricular apex, especially when left ventricular function is already compromised.

Potential and actual ICD malfunctions caused by failure of generator components, once made public, are known as ICD advisories or recalls. The risk of failure (comparing the number of failures with the number of devices implanted) associated with current ICD advisories ranges from 0.009% to 2.6% of devices during a variable follow-up period that is typically less than 24 months.[50] Of 415 780 ICDs implanted in the USA during the years 1990 to 2002, 8489 were explanted due to malfunction. The rate per 1000 implants , after decreasing from 38.6 in 1993 to 7.9 in 1996, increased markedly later on during that period, peaking in 2001 at 36.4. Overall, the annual ICD malfunction replacement rate was 20.7 per 1000 implants.[51]

Gould recently reported a retrospective Canadian study in which complications associated with elective ICD generator replacement for device recalls were studied.[50] At the 17 surveyed centres, between October 2004 and October 2005, 2915 patients had recall devices, of whom 533 underwent replacement. During a mean of 2.7 months follow-up after ICD replacement, complications occurred in 43 patients (8.1%). Major complications attributable to advisory device replacement requiring reoperation occurred in 31 patients (5.8%), with death in 2 patients after extraction for pocket infection. Maisel et al. analyzed US FDA reports of ICD generator malfunctions from 1990 to 2002. They report that the three-year replacement rate of malfunctioning ICDs, from 2000 to 2002, was 26.8 per 1,000 implants, which is three times the replacement rate for the mid-1990s.[51, 17]

Apart from technical problems directly related to the device, the ICD also can affect the patient psychologically, the most common problems reported being anxiety, depression, fear of shock and fear of death.[17] It is worth contemplating the number of patients, enrolled in RCTs, in whom the device is deactivated or explanted during the course of the study. Table 10 lists the rate of cross-overs (in both directions) reported in different RCTs and clearly illustrates that in 1% to 9% of "ICD intervention patients" the device is turned of or explanted.

Table 10: Cross-overs as reported in different RCTs.

RCT	ICD explanted or deactivated			CONTROLS switched to ICD		
	n	N	AR	n	N	AR
MADIT I	2	95	0,02	11	101	0,11
CABG-PATCH	40	446	0,09	18	454	0,04
MADIT II	14	742	0,02	22	490	0,04
CAT	NA	50		NA	54	
AMIOVIRT	NA	51		8	52	0,15
DEFINITE	2	229	0,01	NA	229	
DINAMIT	NA	332		NA	342	
SCH-HeFT	32	829	0,04	188	1692	0,11

N: number at risk. n: number crossed over. AR: absolute risk for cross-over during trial.

In a French registry of 220 patients receiving an ICD for Brugada syndrome, a low incidence of arrhythmic events was found, with an annual event rate of 2.6% during a follow-up of >3 years, in addition to a significant risk of device-related complications. The complication rate was 28%, including inappropriate shocks, which occurred in 45 patients (20%). Inappropriate shocks were 2.5 times more frequent than appropriate ones.[52]

Patients in whom an ICD is implanted have to shoulder certain responsabilities. Careful monitoring of the functioning of the device is essential. Furthermore, some precautions have to be taken into consideration. Electrical interference, such as from metal detection devices used at airports and strong magnetic field, such as those from MRI machines, have to be avoided. Cellular phones may be used, but it is advised to keep the phone on the opposite side of the body from the ICD. Car driving can be prohibited temporarily or permanantly, depending on local legal regulations. These issues will be further elaborated in chapter 5.

- **The implantation of an ICD is a relatively safe procedure, with a perioperative mortality rate of 0.0 to 1.2%.**
- **The occurrence of inappropriate shocks varies across studies, with rates varying between 0.5 and 19% within 30 days of implantation and an overall rate of 14% beyond 30 days.**
- **The device malfunction rate per 1000 implants, increased markedly after 1999, peaking in 2001 at 36.4.**
- **The annual failure rate of leads increases progressively with time after implantation and reaches 20% in 10-year-old leads.**

3.5 CLINICAL EFFECTIVENESS: DISCUSSION

To determine which patient should have an ICD implanted, it sounds reasonable for clinicians to consider the inclusion and exclusion criteria that were required for enrolment of patients in the RCTs we discussed so far (Table 11). Different clinical characteristics of patients that were taken into consideration in these trials could have influenced the outcomes: the underlying heart disease (ischaemic vs. nonischaemic), ejection fraction, age, time relation to previous AMI or revascularisation, NYHA class, life expectancy, co-morbidity, etc. We will briefly discuss these criteria in relation to their applicability in daily practice.

Table 11: Inclusion and exclusion criteria for enrollment in RCTs.

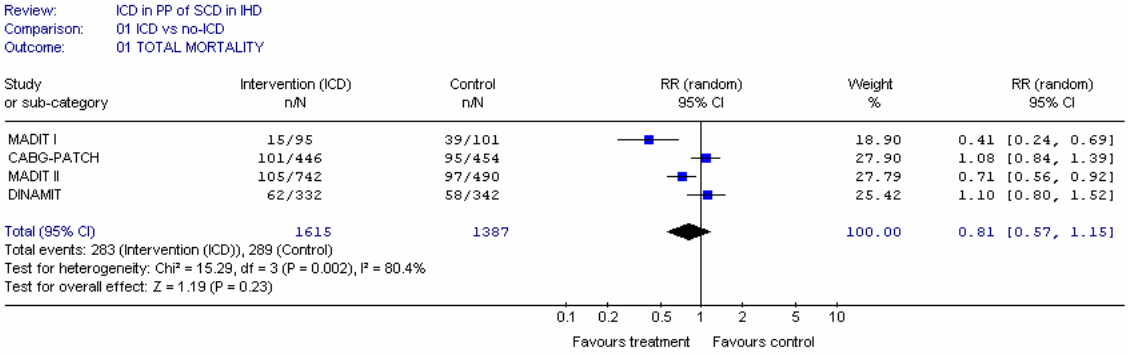
RCT	INCLUSION CRITERIA	EXCLUSION CRITERIA
MADIT I	CHD, AMI > 3 weeks; nonsust VT, unrelated to AMI; inducible, nonsuppresible tachyarrhythmia; EF ≤35%;	> 80 yr; accepted ICD indication; NYHA class IV; no indication for revascularisation; MI < 3 weeks; symptomatic hypotension; CABG < 2 mo; PCI < 3 mo; advanced cerebrovascular disease; reduced likelihood for survival for the duration of the trial;
CABG-PATCH	scheduled for CABG; EF≤35%; abnl SAECG;	>80 yr; accepted ICD indication; poorly controlled DM; previous or concomitant valve surgery; concomitant cerebrovas surgery; creat > 3 mg/dl; emergency CABG; expected survival < 2 years;
MADIT II	CHD, AMI>1 month; EF≤30%;	no upper age limit; accepted ICD indication; NYHA class IV; AMI< 1mo; revasc < 3mo; advanced cerebrovasc disease; high likelihood of death during trial;
CAT	symptomatic dilated CMP (NYHA class II or III); EF≤30%;	>70yr; accepted ICD indication; NYHA class I and IV; CHD; excessive alcohol;
AMIOVIRT	dilated CMP (NYHA class I to III); EF≤35%;	no upper age limit; accepted ICD indication; NYHA class IV;
DEFINITE	history of symptomatic CMP; EF≤35%; VPBs;	no upper age limit; accepted ICD indication; NYHA class IV;
DINAMIT	recent (6-40 days) AMI; EF≤35%;	>80 yr; accepted ICD indication; NYHA class IV - class I unclear; limited life expectancy; planned CABG; 3VD-PCI post-MI;
SCD-HeFT	stable HF (class II or III) and EF≤35%;	no upper age limit; NYHA class I or IV;

3.5.1 Underlying heart disease

3.5.1.1 Ischaemic heart disease

Ischaemic heart disease is estimated to be the underlying disease in 75% of patients developing SCD.[32] The effectiveness of ICD in reducing all-cause mortality in patients with ischaemic heart disease has been studied in 4 RCTs. One additional study, the SCD-HeFT included patients with both ischaemic (52%) and nonischaemic (48%) heart disease.The latter study did not provide the exact number of deaths in both groups. Of the four RCTs that restricted enrollment to patients with ischaemic heart disease, two obtained a relative risk that favoured treatment with ICD.[34, 35] When we combine the results of the four trials in a meta-analysis, the overall RR estimate (Figure 3) indicates that treatment with an ICD yields a statistically nonsignificant 19% (-43% to +15%) decrease in all-cause mortality (RR 0.81, ARR 3.3%) compared with control treatment.

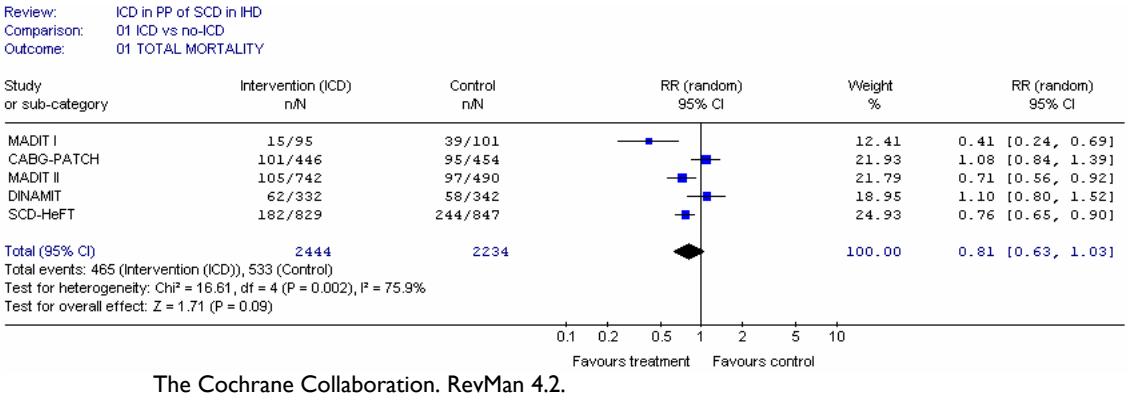
Figure 3: Relative risk for all-cause mortality in ICD trials in patients with ischaemic heart disease. Meta-analysis.



See text for abbreviations of different study acronyms. The Cochrane Collaboration. RevMan 4.2.

When we add the results of the SCD-HeFT trial, which included 48% nonischaemic heart disease patients, but reportedly obtained similar results in ischaemic and nonischaemic patients, the pooled estimate for all-cause death remains non-significant with a RR of 0.81 (95% CI 0.63-1.03) and an ARR of 4.9% (Figure 4).

Figure 4: Relative risk for all-cause mortality in ICD trials in patients with ischaemic heart disease + SCD-HeFT trial. Meta-analysis.



The Cochrane Collaboration. RevMan 4.2.

We opted for a random effects model to perform these analyses because of a marked statistical heterogeneity of the results, as reflected by the high X^2 score. There is also a clinical heterogeneity between the four trials in ischaemic heart disease as reflected by the inclusion criteria and the clinical characteristics of the patients enrolled in the trials. In the seminal MADIT I trial, many elements suggest that the trial population is highly selected and is not representative of nowadays patients considered for an ICD implant.

When the trial started in 1990, only transthoracic implants were approved and transvenous devices were used from August, 1993 on. Eventually, half of the patients had a transthoracic device and half had a transvenous device implanted. Thirty-two electrophysiology centres needed five years to enrol 196 patients, which suggest that highly selected patients were recruited. There was a very low use of ß-blockers with a substantial difference in use between the two treatment groups. By the end of the study, 27% of ICD-patients and only 5% of conventionally treated patients were on ß-blocking therapy. This may have influenced the occurence of SCA and could have exaggerated the perceived efficacy of the ICD.

The cumulative annual mortality rate in the control group of MADIT I was markedly higher than in later ICD trials: it was 17% in MADIT I compared to 8% in SCD-HeFT and 12% in MADIT II (Table 6). The fact that baseline risk in SCD-HeFT was much lower than in MADIT II is counterintuitive because in SCD-HeFT sicker patients were expected to be enrolled, the presence of heart failure being an inclusion criterium in SCD-HeFT and not in MADIT II. This also points towards a clinical heterogeneity of trials. When we omit MADIT I from the meta-analysis, the pooled estimate for all-cause death is non-significant with a RR of 0.88 (95% CI 0.71-1.09).

CABG-Patch showed that an ICD implantation at the time of elective CABG did not improve survival in patients considered at high risk of SCD. DINAMIT showed that prophylactic ICD implantation, 6 to 40 days after an AMI did not reduce overall mortality. Following the report of these trials, the implantation of ICDs in combination with CABG or in the acute phase of an AMI has been halted.

Thus, MADIT II and SCD-HeFT are the trials that best reflect current ICD-practice. Both studies indicated an overall survival benefit of ICD-treated patients with a yearly ARR of 3.4% and 1.8% respectively in the study population. While MADIT II had shown a benefit of ICD therapy in patients with a previous MI and poor left ventricular function, SCD-HeFT extended these findings towards a much larger group of patients with heart failure from any cause. However, several questions remain unanswered such as the time dependency of the effectiveness of an ICD following an AMI or a revascularisation procedure, cut-off points for EF, the presence of clinical HF, the contribution of additional risk factors for life threatening arrhythmias in decision making,

3.5.1.2 Nonischaemic cardiomyopathy

Three RCTs have been published in patients with nonischaemic cardiomyopathy (CAT, AMIOVIRT and DEFINITE). In none of these, all-cause mortality differences between the ICD and control groups reached statistical significance, although the larger study, DEFINITE, showed a significant decrease in SCD. The two other studies included only a limited number of patients (≈50 in each group) and recorded a very limited number of fatal events after one year (2 to 7 in each group). The CAT trial enrolled only symptomatic patients with a NYHA class II or III and DEFINITE required a history of symptomatic HF for patients to be eligible for the trial. AMIOVIRT included a limited number of NYHA class I patients (Table 13). In the CADTH report, a meta-analysis indicated a pooled RR of all-cause mortality of ICD in nonischaemic patients of 0.76 (95% CI 0.54-1.06) corresponding to a non-significant reduction in absolute risk of 5%.[17] In the SR of Desai et al, five primary prevention trials were pooled and their meta-analysis suggested a significant reduction in total mortality among patients randomized to ICD vs medical therapy (RR 0.69; 95%CI 0.55-0.87).[26] This result was however biased by inclusion of the results from the COMPANION trial, in which medical therapy was compared to CRT-D instead of a stand-alone ICD.[20] In a subgroup analysis of the DEFINITE trial, a statistically significant difference in all-cause mortality was only reached for NYHA class III patients. These findings indicate that there is currently little evidence to support ICD implantation in asymptomatic patients with nonischaemic cardiomyopathy even those with a low EF.[53]

3.5.2 Ejection Fraction

Left ventricular ejection fraction has been an important characteristic of patients enrolled in RCTs because it has since long been known as a major risk factor for SCD. In MADIT I, the upper limit allowed for enrolment was 35%. However in a substudy the ICD was associated with a significant reduction in mortality only in high-risk subsets with an EF less than 26%. Patients with an EF between 26 and 35% did not have improved survival with an ICD.[54] This finding presumably was the reason why the same authors lowered the upper EF-limit for enrolment in MADIT II to 30%.

Table 12 lists the ICD trials with the corresponding mean EFs in patient groups. Average EF values in patients are substantially lower than the cut-off values required for enrolment. In survivors of cardiac arrest, such as the patients included in the secondary prevention trials, patients had a higher EF than in the primary prevention trials. This could indicate that patients with EFs higher than 30 or 40% also have a substantial risk of SCA. It could as well be the result of a selection bias in that patients with SCA and severely depressed left ventricular function have a lower chance being successfully resuscitated and included in a secondary prevention trial.

Table 12: ICD trials with the corresponding mean EF of intervention and control patients.

SEC PREV	PRIMARY PREV	PER PROTOCOL EF UPPER LIMIT	EF (INTERV / CONTROL)
	MADIT I	35	25-27
	CABG-PATCH	35	27
AVID		NA	31-32
CASH		NA	44-47
CIDS		NA	33-34
	MADIT II	30	23
	CAT	30	24-25
	AMIOVIRT	35	22-23
	DEFINITE	35	21-22
	DINAMIT	35	28
	SCD-HeFT	35	24-25

EF: ejection fraction. NA: not applicable (secondary prevention trials). When two numbers are given, the first relates to the intervention and the second to the control group.

Although EF is an important risk stratifier in ICD trials, considerable uncertainty remains as to the sensitivity and specificity of this parameter in predicting SCA. The risk of SCD is influenced by many other factors in addition to EF. This is illustrated by the fact that although the EF of patients in different primary prevention trials is comparable (21 to 27%) the total mortality in the respective control patients differs substantially: in MADIT II one-year mortality is 12% whereas in SCD-HeFT, in which one would expect a higher mortality because patients were required to have symptomatic heart failure, it was only 8% (Table 5).

An additional problem when using LVEF as risk stratifier is that in one patient, EF is not constant over time and can differ between observers. Gehi argues that the echocardiographic measurement of left ventricular dimensions can vary significantly in weekly repeated measurements in an individual patient. The limits of agreement may vary by as much as 8.5% above or below the mean calculated EF in repeated studies. There may also be differences in the calculated EF for the individual patient, depending on the method used to calculate it. Even using cutting-edge techniques of myocardial imaging, such as contrast echocardiography and cardiac magnetic resonance imaging, there can be a substantial difference in the EF between these studies in an individual patient.[55]

3.5.3 NYHA Class

Although not all RCTs required patients to have clinical heart failure to be eligible for inclusion, most patients did have a functional class II or III. Approximately two thirds of patients enrolled in trials in ischaemic disease had symptomatic heart failure (Table 13). The CABG-PATCH paper does not explicitly mention that NYHA class IV were not eligible, but we presume that no NYHA class IV patients would be selected to undergo elective bypass surgery.

In nonischaemic heart disease trials, a great majority of patients had clinical heart failure. In DEFINITE, CAT and SCD-HeFT, all patients had a history of heart failure whereas in AMIOVIRT a limited number of patients had a functional class I (13% in the amiodarone group and 18% in the ICD group).

Table 13: Functional class of patients enrolled in ICD trials.

Intervention/Control	NYHA I	NYHA II	NYHA III	NYHA IV
MADIT I	37/33	63/67		0/0
CABG-PATCH	29/26	71/74		0/0
MADIT II	35/39	35/34	25/23	5,0/4,0
CAT	0/0	67/64	33/36	0/0
AMIOVIRT	18/13	64/63	16/24	0/0
DEFINITE	25/18	54/61	21/21	0/0
DINAMIT	14/12,0	61/59	26/29	0/0
SCD-HeFT	0/0	70	30	0/0

Percentage of intervention/control patients in NYHA classes I to IV in corresponding RCT.

Thus, patients enrolled in clinical trials not only had a severely depressed left ventricular function but most of them did have clinical heart failure. As suggested by Gorgels, the logical clinical approach to prevent sudden death is to focus on the population with large infarctions, low ejection fractions and overt heart failure.[56] This is also in accordance with the joint ACC/AHA/ESC 2006 ICD guidelines that attribute for NYHA I-patients a recommendation class IIa ("it is reasonable") in ischaemic heart disease and class IIb ("it may be considered") in nonischaemic disease (appendix).[4] Medicare also limits coverage for ICDs in patients with NYHA class II or III (see appendix).[57]

The benefit of ICD therapy in patients with a NYHA functional class III is uncertain. As discussed earlier, the interaction between ICD therapy and NYHA class in the SCD-HeFT trial was significant. Whereas in NYHA class II patients, there was a 46% reduction in risk of death in this trial, patients in NYHA class III had no apparent reduction in the risk of death with ICD as compared with placebo.[11]

3.5.4 Age and Gender

In four out of eight RCTs, an upper age limit was imposed for patients to be acceptable for enrollment in the trial: patients had to be no older than 80 years in three trials and no older than 70 years in one (Table 14). When we compare the ages of patients enrolled in trials that imposed an age limit to these in trials with no age limit, we can see no difference. This suggests that even when no age limit is imposed, there is a strong tendency to avoid ICD implant in octagenarians, which seems sensible, given the very low or even absent increase of longevity that can be expected from ICD therapy in primary prevention in elderly people.

Table 14: Mean age of patients enrolled in RCTs.

RCT	Age in ICD group	Age in control group	Per protocol upper age limit
MADIT I	64	62	> 80
CABG-PATCH	64	63	> 80
DINAMIT	61,5	62,1	> 80
MADIT II	64	65	no
AMIOVIRT	58	60	no
DEFINITE	58,4	58,1	no
SCD-HeFT	60,1	59,7	no

no: no upper age limit was imposed in corresponding trial.

Henyan et al performed a meta-analysis to estimate the impact of gender on survival among patients treated with an ICD for primary prevention.[58] The ICD significantly reduced the risk of death from any cause by 26% in male patients who received an ICD compared to controls (HR 0.74; 95%CI 0.60–0.91) but not among female patients (HR 0.81; 95%CI 0.60–1.09). When the COMPANION trial was discarded from this analysis, results remained similar.

It is not clear whether the lack of a significant benefit in women is due to the relatively low number of female patients included in the trials (8 to 33%) or that pathophysiological mechanisms play a role. Presently, there is no evidence indicating that men or women should be treated differently as far as ICD therapy is concerned.

3.5.5 Non Cardiac co-morbidities

In the trials reported earlier, patients were excluded for enrolment for different reasons: advanced cerebrovascular disease, reduced likelihood for survival for the duration of the trial (i.e. 20 or 27 months in the MADIT trials), expected survival less than 2 years, excessive alcohol use (Table 11).

As discussed earlier, in most trials, an upper age limit of 80 years was imposed.

Currently in Belgium, reimbursement of an ICD is refused in (1) patients with severe psychiatric illness that could be aggravated by the implant or could preclude follow-up and in (2) patients with a life expectancy less than 6 months (see appendix).

In Sweden, before considering ICD implantation in primary prevention, patients should have an expected survival with ICD treatment of at least two years, which is in accordance with the exclusion criteria as used in RCTs.[2]

3.5.6 Indicators of Arrhythmic risk

As described earlier, LVEF is the most important risk stratifier used for selection of patients for ICD therapy. Gehi argues that it is unfortunate that current guidelines have reduced risk stratification for SCD to a single, potentially imprecise measurement because the risk for SCD is distributed across a spectrum rather than simply high or low.[55]

Several noninvasive methods have been investigated to try to better define the risk for SCD of individual patients: QRS-duration, long term ECG-monitoring, signal-averaged electrocardiogram, heart rate variability, baroreflex sensitivity, heart rate profile during and after exercise, maximum oxygen consumption during exercise, microvolt T-wave alternans, serum BNP level, ... So far, none of these techniques have in RCTs proven to be reliable risk stratifiers upon which decisions for ICD therapy can rely.

3.5.7 Time dependence of SCA in relation to AMI

As reported earlier, the risk of SCD is highest within the first few hours of an AMI. After the acute event, traditionally the period of highest risk was considered to be during the first 6 to 12 months after the infarction.[12] The natural history of SCD following AMI may however have changed, due to early reperfusion strategies and more widespread prescription of ß -blockers, ACE-inhibitors and statins. In patients with an AMI complicated by left ventricular dysfunction, heart failure or both, the VALIANT study indicated that the risk of SCA was highest within the first week and fell rapidly within the first month after the MI (1.4%/month) and gradually decreased reaching a steady state at approximately 1 year (0.14 to 0.18% per month).[15] In a population study on out-of-hospital SCA in the Netherlands, Gorgels et al reported on 492 cases of SCA.[56] In 224 SCA victims with a previous cardiac history, one or more previous MIs were present in 113. Data on the time interval between the first MI and SCA was available in 92 cases and was on average 9.7 with a median of 9.0 years and a range from 0 to 29 years. In a Finnish study on non-selected patients discharged alive from hospital after an AMI, SCDs did not concentrate early after the index event, but most of them occurred more than 18 months after AMI.[16]

When we add the results of the ICD trials to these somewhat incoherent epidemiological data, uncertainties become even more complicated. In MADIT I, MADIT II and in the MUSTT trial, the majority of patients were recruited more than one year after the index MI. In MADIT II the mean time from the most recent MI to enrollment in the study even was 6.5 years. In a post-hoc subgroup analysis of MADIT II, the hazard ratio for ICD benefit was only 0.98 for patients in whom the most recent AMI occured less than 18 months before ICD implant. Later on there was a survival benefit that remained substantial up to more than 15 years following an AMI.[37] According to some authors, this remarkable finding suggests a selection bias for enrollment into this trial.[12]

In the DINAMIT trial that investigated the effectiveness of an ICD implanted in the acute phase of a MI, there was no effect of the ICD on total mortality. Arrhythmic death was significantly reduced by the ICD but death from nonarrhythmic causes was higher in the ICD group, nihilating the effect of the ICD on all-cause mortality. Thus DINAMIT identified a subgroup of patients with risk factors for SCD in whom ICD therapy does not provide a survival benefit. This unexpected finding could be explained by the fact that the presence of markers of autonomic dysfunction (which was a prerequisite for enrollment) not only identified patients at risk for SCD but patients at risk from dying from HF as well. In other words, succesfully termination of a ventricular tachyarrhythmia may simply convert what would have been a SCD to a death from pump failure, without an effect on survival.[42]

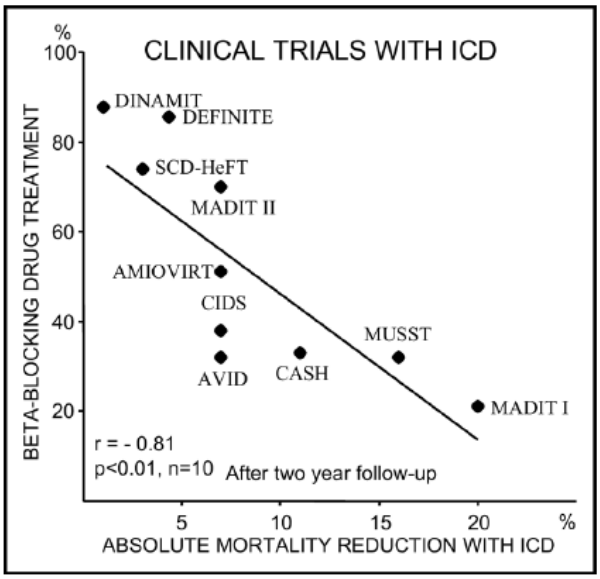
3.5.8 Concomitant Therapies

Early ICD trials have been performed in an era where medical therapy was markedly different from modern practice. In the MADIT I trial for example, that started enrollment of post MI patients in 1990, there was a remarkable low use of ß -blockers. Moreover, there was a substantial difference in ß-blocker use between the two treatment groups. By the end of the study, 27% of ICD-patients and only 5% of conventionally treated patients were on β -blocking therapy. ACE-inhibitors were used in only half of them. In SCD-HeFT, enrollment started in 1997 and 97% of patients took an ACE inhibitor or an ARB blocker, 69% took a β -blocker and 40 % a statin. Whereas β -blockers were contraindicated in most patients with heart failure in the early nineties, later on their benefit was clearly demonstrated, especially in patients with left ventricular dysfunction. As already indicated earlier, the mortality rate in the control group of these trials, indicating baseline risk, was remarkably different (Table 5).

The current high rate of prescription of β -blockers and other medication has changed the incidence of SCD in high risk patients and it is conceivable that consequently, the absolute mortality benefit of ICD therapy has decreased. This hypothesis was tested by Mäkikallio et al in a meta-analysis of RCTs on primary and secondary prevention of SCD.[27]

Although one can question the validity of this post hoc analysis, it indicated a strong negative association between the use of β -blocking medication and the 2-year mortality benefit of ICD therapy (r= -0.81) as depicted in Figure 5.

Figure 5: Absolute 2-year mortality benefit in relation to the use of ß-blockers in different RCTs.



From Mäkikallio and Huikuri in Am J Cardiol.[27]

The association between the use of angiotensin-converting enzyme inhibitors and the 2-year mortality benefit of ICD therapy was weaker (r = - 0.66).

The improvement of prognosis of post-MI patients due to changing medical therapy may explain why in a subgroup analysis of MADIT II, no survival benefit was seen in patients in whom the index infarction occurred less than 18 months before enrolment in the trial.[37] Gillis also argues that the unexpected results of DINAMIT could be explained by the same concept. Current medical therapy with ß -blockers, ACE inhibitors, and aldosterone blockers prevents or at least delays the adverse ventricular remodeling that occurs after MI and that contributes to the electrophysiological mechanisms of sudden death from cardiac causes. Thus, the benefits of ICD implantation for the prevention of sudden death may be delayed for months to years after a myocardial infarction.[42]

- **The effectiveness of ICDs has been best substantiated in patients with ischaemic heart disease with severely depressed left ventricular function and clinical heart failure (especially NYHA class II).**
- **Current standard medical therapy of MI patients in the acute phase and later on, has beneficial effects on subsequent SCD risk. Recruitment of patients in RCTs took place in an era when treatment of AMI was not optimal compared to 21st century standards. This may lead to an overestimation of the absolute mortality risk reduction attained by ICDs nowadays.**
- **MADIT II and SCD-HeFT are the trials that best reflect current ICD-practice. Both studies indicated an overall survival benefit of ICD-treated patients with a yearly ARR of 3.4% and 1.8% respectively.**
- **There remains uncertainty on how to best define patients at highest risk for sudden cardiac death. A low left ventricular ejection fraction (30-35%) has been most often used in trials for this purpose but most patients never receive an appropriate shock of the device.**
- **Some patients with an LVEF >35% may also be at considerable risk for SCD.**
- **A problem with LVEF as risk stratifier is that in one patient, LVEF is not constant over time and can substantially differ between observers.**

4 COST-EFFECTIVENESS: REVIEW OF THE LITERATURE

4.1 INTRODUCTION

Over the past two decades, there has been a great concern in determining the efficiency[b] of implantable cardioverter defibrillators (ICD) use and several economic evaluations on the topic were published. While early economic evaluations targeted secondary prevention, i.e. prevention of an additional life-threatening event in survivors of sudden cardiac arrest or patients with recurrent unstable rhythms, most recent publications focus on primary prevention, i.e prevention of a first life-threatening arrhythmic event. Therefore the current review was limited to the assessment of the economic evaluations of ICD in primary prevention. The evidence about ICD use in secondary prevention is still briefly described, mainly based on the existing literature reviews and health technology assessment (HTA) reports.

The research questions for the current review were:

- What is the evidence, based on full economic evaluations, on the efficiency of ICD versus non-ICD therapy in primary prevention?
- How does risk-stratification of patients affect the efficiency of ICD?
- Are there other key parameters (e.g. mortality rates, ICD costs…) driving the efficiency of ICD?

To answer those questions, electronic databases (HTA (CRD), DARE (CRD), NHS EED (CRD), Medline (Ovid), Econlit (Ovid), Embase) were searched up to the end of the year 2006 to identify all relevant HTA reports, systematic reviews and full economic evaluations measuring the efficiency of ICD. All returned references were assessed against pre-defined selection criteria (in terms of population, intervention, outcome and design) in a two-step procedure: initial assessment of the title and abstract; next full-text assessment. When no abstract was available or the reference was unclear or ambiguous, consideration of the reference was made on the basis of full-text assessment. There was no time restriction for the retrieval of full economic evaluations but HTAs and reviews were restricted to the period 2003-2006. Reference lists of papers retrieved were checked for additional relevant references. Selected HTAs were assessed with the INAHTA checklist. All full economic evaluation fulfilling the selection criteria were summarised in an in-house data extraction form. Finally, this whole literature search and selection procedure was replicated by a second reviewer to assess the quality of this process.

4.2 LITERATURE SEARCH AND SEARCH RESULTS

4.2.1 HTAs

The HTA (CRD) database was searched up to October 2006 with the following search term: "MeSH Defibrillators, Implantable". Of the 36 references identified, only those that fulfilled the following four criteria (Table 15) were retrieved:

[b] The evaluation of efficiency refers to how do the costs of health care programmes relate with their consequences[59].

Table 15: HTAs' selection criteria

	Inclusion criteria	*Exclusion criteria*
Population	Patients at risk of sudden cardiac death due to ventricular arrhythmia	Other population
Intervention	ICD	Other intervention: cardiac resynchronisation therapy …
Outcome	Assessment of at least efficacy / effectiveness, safety, and economic impact. Ethical and organisational issues should also be dealt with.	No or limited assessment of safety, efficacy/effectiveness or economic impact.
Design	HTA (at least secondary assessment of all items in the "outcome" criteria)	Non-HTA study: review, primary studies, guidance…

The flow diagram of the HTAs selection process is presented in appendix 1. The four selection criteria were primarily applied to the citations and abstracts of the 36 references identified. This resulted in the exclusion of 17 references among which 2 were discarded because they had been recently updated.

Nineteen studies were selected for full-text evaluation. The information contained in those studies was reviewed and 7 of them did not meet our outcome (3) and design (4) criteria. Another 7 studies were further excluded: 4 because of their foreign language and 3 because the full-text was not publicly available (private US company). The 5 selected studies were assessed with the INAHTA checklist (see appendix 2)[60-62, 1, 63]. Finally, with the aim to select only on the most recent information, the two eldest studies were discarded[60, 61].

4.2.2 Literature reviews

Relevant reviews of the literature on the efficiency of ICD versus drug therapy were searched in MEDLINE (Ovid). The search was performed up to October 2006 and the strategy used can be found in appendix 3. Of the 115 references identified, only those that met all the following criteria (Table 16) were kept:

Table 16: Literature reviews' selection criteria

	Inclusion criteria	*Exclusion criteria*
Population	Patients at risk of sudden cardiac death due to ventricular arrhythmia	Other population
Intervention	ICD	Other intervention: CRT…
Outcome	Formal assessment of the efficiency (i.e. economic evaluations) of ICD	Efficiency is not the focus of the study: article on efficacy, safety, organisational issues...
Design	Reviews of full economic evaluations (systematic review or not), i.e. secondary studies	Other type of studies: primary studies, HTAs, editorials…

The flow diagram of the reviews' selection process can be found in appendix 4. Based on their title and abstract, 91 studies did not meet our selection criteria. Of the 24 studies for which the full-text was scrutinized, 14 were excluded because the selection of economic evaluations reviewed was not comprehensive and the number of studies included rather limited (i.e. outcome criteria). Two additional studies were discarded because they were written in a foreign language.

Further exploration of the 83 and 13 unique references returned by Embase and DARE (CRD), respectively, did not reveal any additional relevant study (appendix 3). Eight reviews of economic evaluations were thus selected[64-71] of which 5 were considered outdated for our purpose[64-68].

4.2.3 Economic evaluations

A search in MEDLINE (Ovid) was performed up to November 2006 in order to identify the full economic evaluations of ICD. The search strategy is presented in appendix 5. Three hundred and twenty-four (324) unique citations were returned and assessed against our inclusion criteria (Table 17). Only full economic evaluations were retained, that is evaluations comparing at least two alternative treatments in terms of both their costs and outcomes (see classification of economic studies in appendix 6). The flow chart of the selection process is presented in appendix 7.

Table 17: Economic evaluations' selection criteria

	Inclusion criteria	*Exclusion criteria*
Population	Patients at risk of sudden cardiac death due to ventricular arrhythmia	Other population
Intervention	ICD	Other intervention: CRT…
Outcome	Formal assessment of the efficiency (i.e. economic evaluations) of ICD	Economics is not the focus of the study: article on efficacy, safety, organisational issues...
Design	Full economic evaluations: CEA, CUA, CBA or CMA[c], i.e. primary studies.	Other type of studies: RCT, HTA, guidance, editorials, cost description, cost comparison, cost outcome description …

Of the 324 citations returned, 283 did not meet our inclusion criteria based on title and abstract evaluation. Of the 41 citations retained for full-text assessment, 14 were excluded because of their inappropriate design, 1 because of the outcome criteria and one because of the intervention criteria. Another two studies had to be discarded because of their language. Twenty three full economic evaluations of ICD were thus retained with our search strategy. Further exploration of the 389, 12 and 3 unique references returned by Embase, Econlit (Ovid) and NHS EED (CRD), respectively, did not reveal any additional relevant study (appendix 5). One additional full economic evaluation was however identified after scrutiny of the HTA's reports content[18].

Twelve (12) of the 24 studies selected assessed the efficiency of ICD in secondary prevention[72-82, 63], the remaining assessing the efficiency of ICD in primary prevention[83-92, 18, 93]. The economic evaluations of ICD in primary prevention are summarised in appendix 8.

[c] CEA: cost-effectiveness analysis, CUA: cost-utility analysis, CBA: cost-benefit analysis, CMA: cost-minimisation analysis.

4.3 SUMMARY OF THE MAIN FINDINGS

4.3.1 Efficiency of ICD in secondary prevention

According to the selected HTAs[62, 1, 63] and reviews of the literature[69-71] on the efficiency of ICD, 11 full economic evaluations have assessed the use of ICD in secondary prevention (i.e. patients who were survivors of a previous cardiac arrest, or had already experienced an episode of ventricular tachycardia (VT) or ventricular fibrillation (VF))[72-82] Our literature search identified a twelfth economic evaluation performed in Buxton et al's HTA report[63]. These 12 full economic evaluations pertain to 11 different studies since the analysis of Sheldon et al.[79] is a risk-stratification extension of the analysis of O'Brien et al[78].

As illustrated in Table 18, the studies differ in many aspects. Three studies are performed alongside randomized controlled trials (RCT), while 7 studies are based on models and one study is derived from a single non-trial observational database. Only three evaluations are done in Europe, the remaining being done in North America. The comparator was Amiodarone in 7 studies and either "usual drug therapy" or "EP-guided therapy" (i.e. antiarrhythmic drug therapy) in the remaining 4 studies. All studies ignored the indirect costs of lost productivity and included only the direct costs of treatment. Early model-based studies (publication year before 1996) all include the cost of transthoracic implantation while most recent analyses reflect the transition to the less expensive transvenous mode of implantation. In their base-cases, the evaluations performed alongside clinical trials limited their estimates to the data observed within their follow-up periods (2 to 6 years time horizon). However, in their sensitivity analysis, O'Brien et al.[78] and Larsen et al.[80] extrapolated their estimates beyond their follow-up periods (i.e. to 12 and 20 years, respectively). Typically, model-based analyses had longer time horizon than RCT-based studies (from 6 years to lifetime time horizon). The two studies of Owens et al.[77, 81] are the only ones to provide cost-utility ratios, by adjusting their outcome for quality of life. In the first analysis of Owens et al.[77] and in Buxton et al.[63], it was assumed that there was no difference in utility between the Amiodarone and the ICD group (around 0.75). In their most recent model, Owens et al.[81] assumed there is a small advantage in utility for the ICD versus Amiodarone group (0.83 versus 0.80).

The main results of the studies, together with their assumptions about life expectancy in each treatment group, are presented in Table 19. For the ease of comparison, the results have been standardised to euros (reference year 2005) by inflating them with local consumer price indices and converting them with 2005 purchasing power parities[d].

Table 19 clearly shows a split between the results of the studies published in the period 1990-1995 and the studies published after 1996. The 4 economic evaluations published before 1995 predate all RCT evidence and inevitably had to rely on assumptions to estimate the relative effectiveness of ICD above drug therapy. Their results appear rather optimistic, with benefits of ICD ranging from 1.7 to 2.2 life years gained compared to conventional treatment and with relatively favourable cost-effectiveness ratios (from €26,650[72] to €45,010[73] per life-year gained). By contrast, based on RCT evidence, the 7 studies published after 1996 use more realistic and conservative values for the relative effectiveness of ICD versus conventional treatment, which shifts up the upper limit of the range of the base-case cost-effectiveness ratios (CERs) (from €29,930[77] to €172,380[78] per life-year gained). One exception is the study of Wever et al.[76] who are the only ones to conclude that ICD dominates drug therapy (i.e. is both more effective and less costly). The conclusions of this first published RCT-based economic evaluation need however to be treated with caution given the small sample size of the trial (n = 60 patients) and the reservations regarding the economic evaluation methodology[63].

[d] USA: ftp://ftp.bls.gov, Canada: http://www.statcan.ca, UK: http://www.statistics.gov.uk, Purchasing power parities: http://www.oecd.org/

Table 18: Main assumptions of the economic evaluations of ICD use in secondary prevention

Author	Publication year	Country	Comparator	Source of data	Method of implantation	Time horizon
Studies based on decision model						
Kuppermann et al.[72]	1990	USA	Usual drug therapy	Expert opinion	Transthoracic	Lifetime
O'Brien et al[74].	1992	UK	Amiodarone	Comparison case series	Transthoracic	20 years
Larsen et al.[73]	1992	USA	Amiodarone	Literature	Transthoracic	Lifetime
Kupersmith et al.[75]	1995	USA	EP-guided drug therapy	Assumptions	Transthoracic	6 years
Owens et al.[77]	1997	USA	Amiodarone	Various (including RCTs)	?	Lifetime
Owens et al.[81]	2002	USA	Amiodarone	Various (including RCTs)	Transvenous?	Lifetime
Buxton et al.[63]	2006	UK	Amiodarone	Various (including RCTs)	?	20 years
Studies alongside RCTs						
Wever et al.[76]	1996	Netherlands	EP-guided drug therapy	Trial	Transthoracic	2 years
O'Brien et al.[78] and Sheldon et al.[79]	2001	Canada	Amiodarone	CIDS	Transthoracic and transvenous	6 years
Larsen et al.[80]	2002	USA	Amiodarone	AVID	Transthoracic and transvenous	3 years
Studies based on observational database						
Weiss et al.[82]	2002	USA	Usual drug therapy	Medicare	Not stated	8 years

The RCT-based studies of O'Brien et al.[78] and Larsen et al.[80] illustrate the difficult task of estimating the long-term efficiency of ICD versus drug therapy. A key problem in RCT-based economic evaluation is indeed that of data truncation which requires extrapolation of data beyond the observation period of the trial. In O'Brien et al.[78], the cost-effectiveness ratio improves substantially when the results of the 6-year trial are extrapolated to a 12-year time horizon. In Larsen et al.[80], the ratio deteriorates when the 3-year RCT results are extrapolated to a 6-year time horizon, and then remains stable when extrapolated to a 20-year time horizon. In both studies the cost-effectiveness ratio are highly dependent on the assumptions made about the long-term survival rate.

Though not all studies were powered for subgroup analyses, there were substantial reductions in the cost-effectiveness ratios when patients were stratified by individual risk factor, i.e. left ventricular ejection fraction (LVEF), age and New York Health Association (NYHA) classification[78-80]. Other key parameters improving the cost-effectiveness of ICD versus drug therapy are the relative risk reduction in all-cause mortality[77], and the ratio of sudden to non-sudden cardiac death in the population[81].

Given the considerable variations in the estimated cost-effectiveness ratios of the studies published after RCT evidence was available, it seems hard to provide any firm conclusion on the efficiency of the use of ICD in secondary prevention. The reported CERs of ICD in secondary prevention, up to the trials' observation periods, vary from €70,990[80] to €172,380[78] per life year gained. When extrapolated to a lifetime horizon, the variations in cost-effectiveness ratios are even greater with a cost of €29,930[77] to €224,680[80]. This strengthens the need for longer-term patient follow-up data. The studies further showed that key parameters substantially influencing the cost-effectiveness ratios are patient stratification by risk factor and the underlying risk of sudden to non-sudden cardiac death. Even in secondary prevention, ICD may only be cost-effective in selected high-risk patients. None of the economic evaluations were based on Belgian data.

Table 19: Results of the economic evaluations of the use of ICD in secondary prevention

Author Costing year (Currency)	Life expectancy (y)			Strategy	ICER[a] as reported	ICER[a] in 2005 €
	ICD	Drug	Difference			
Studies based on decision model						
Kuppermann et al., 1990[72]						
1986 (US$)	5.10	3.20	1.90		17,100	26,650
O'Brien et al., 1992[74]						
1990 (UK£) [c]	-	-	1.70		15,400	30,050
Larsen et al., 1992[73]						
1989 (US$)	6.07	3.85	2.22	45-year-old patients	27,600	37,970
				55-year-old patients	29,200	40,290
				65-year-old patients	32,700	45,020
Kuppersmith et al., 1995[75]						
1993 (US$)	3.78	2.06	1.72		31,100	36,770
Owens et al., 1997[77]						
1995 (US$)	5.64	4.95	0.69	*High-risk patients (% of RRR[e])*		
				Cost per LYG (40%)	27,300	30,600
				Cost per QALY (40%)	37,300	41,810
				Cost per LYG (20%)	54,000	60,530
				Cost per QALY (20%)	74,400	83,400
				Intermediate-risk patients (% of RRR[e])		
				Cost per LYG (40%)	26,700	29,930
				Cost per QALY (40%)	36,300	40,690
				Cost per LYG (20%)	56,000	62,770
				Cost per QALY (20%)	76,800	86,090
Owens et al., 2002[81]						
1999 (US$)	5.24[b]	4.39[b]	0.85[b]	*Cost per QALY*		
				Base case	54,700	56,090
				SCD / NSCD = 4[g]	36,000	36,910
				SCD / NSCD = 0,25[g]	116,000	118,940
Buxton et al., 2006[63]						
2002 (£)	-	-	1.24	Base case	57,104	83,500
Studies alongside RCTs						
Wever et al., 1996[76]						
1993 (US$)	871[d]	676[d]	195[d]		ICD dominates	
O'Brien et al., 2001 (CIDS)[78]						
1999 (CAN$)	4.58	4.35	0.23	*6 years time horizon (trial data)*		
				Base case	213,500	172,380
				LVEF < 35%	108,500	87,600
				LVEF ≥ 35%	Amiodarone dominates	
				12 years time horizon (extrapolation)		

				Benefit continues	99,400	80,260
				Benefit equivalent	118,700	95,840
				Benefit declines	149,700	120,870
Sheldon et al., 2001 (CIDS)[79]						
1999 (CAN$)	4.58	4.35	0.23	*6 years time horizon (trial data)*		
				0 risk factors[f]	Amiodarone dominates	
				1 risk factor[f]	238,400	192,490
				2 risk factors[f]	96,700	78,080
				3 risk factors[f]	23,300	18,810
Larsen et al., 2002 (AVID)[80]						
1997 (US$)	2.48	2.27	0.21	*3 years time horizon (trial data)*		
				Base case	66,700	70,990
				LVEF ≤ 35%	60,900	64,820
				LVEF > 35%	536,100	570,590
				Extrapolations		
				6 years	79,300	84,400
				20 years: High benefit	68,400	72,800
				20 years: Low benefit	80,400	85,570
				Lifetime: High benefit	67,100	71,420
				Lifetime: Low benefit	211,100	224,680
Studies based on observational database						
Weiss et al., 2002[82]						
1999 (US$)	4.60	4.10	0.50	Base case	78,400	80,390
				At 3 years	133,500	136,890

a Incremental cost-effectiveness ratio, cost per LYG unless otherwise stated; b QALYs; c Estimated date for cost data collection; d mean survival in days; e Relative risk reduction in total mortality; f Risk factors are age ≥ 70 years, LVEF ≤ 35% and NYHA class III; g Ratio of sudden cardiac death to non-sudden cardiac death.

4.3.2 Efficiency of ICD in primary prevention

4.3.2.1 Characteristics of the economic evaluations

The main characteristics of the 12 economic evaluations of the use of ICD in primary prevention are summarized in Table 20. In comparison to the studies evaluating ICD in secondary prevention, those of ICD in primary prevention are much more recent with all but one article[83] published after the year 2000. With the exception of that early article, all studies incorporate the reduced cost of transvenous implantation. In Mushlin et al.[83] both transthoracic and transvenous implantation methods are used. Most studies evaluate ICD in survivors of myocardial infarction with impaired respiratory function, either with[83, 90] or without electrophysiologic study (EPS)[84, 86-88, 90, 91, 93]. Other targeted populations are congestive heart failure patients[85, 90, 94, 92] and patients with genetic disorders[89]. The comparator to ICD is Amiodarone in 3 studies[83, 84, 92] and conventional drug therapy with no or limited use of Amiodarone in all other articles.

Overall, there are 3 studies performed alongside RCT's and 9 modelling studies. Model-based studies adopt longer time horizons than RCT-based studies, with estimates for costs and effects usually extrapolated to lifetime. Though evaluations performed alongside RCTs provide estimates based on the data observed during the trial duration, estimates extrapolated beyond their observation period are also reported separately. Five studies are CEAs[83, 86, 89, 94, 93], 2 are CUAs[85, 91] and 5 include both metrics of effectiveness[84, 87, 88, 90, 92]. In all CUAs, the utility weights for patients receiving ICD and those receiving drug therapy remain unchanged (i.e. 0.71 in Chen et al.[85], 0.85 in Mark et al.[92] and 0.88 in Sanders et al.[84, 87, 90], Al-Khatib et al.[88] and Chan et al.[91]). In Chen et al.[85] however, there is allowance for a deterioration of the psychological dimension in the first year after ICD implantation (utility weights of 0.64 for ICD, 0.71 for drug therapy). Seven studies include only the direct medical costs of treatment[83, 86, 88, 90, 94, 92, 93]. Four studies adopt a broader perspective and include either direct non-medical costs (i.e. travel costs[84, 87]) or morbidity time costs (i.e. lost or impaired ability to work due to morbidity[91], time lost due to hospitalisations and visits[85]). In Goldenberg et al.[89], direct medical costs and mortality time costs (i.e. lost economic productivity due to death) seem to be included in the numerator of the ICER. As explained in Gold et al.[95] this leads to double-counting since mortality is already captured in the effectiveness measure (i.e. LYG). Gold et al.[95] further mention that mortality effects may well be expressed in monetary terms but this calculation should not be included in the ICER. Based on the figures reported in Goldenberg et al.[89], CERs have thus been recalculated excluding mortality time costs.

Table 20: Main assumptions of the economic evaluations of ICD use in primary prevention

Author	Publication year	Country	Comparator	Source of data	Patient population	Time horizon
Studies based on decision model						
Hancock et al.[94]	2006	Australia	Optimal pharmacologic treatment (no Amiodarone)	SCD-HeFT trial, expert opinion, literature	SCD-HeFT criteria	Lifetime
Chen et al.[85]	2004	USA	Standard drug therapy (limited use of Amiodarone)	Literature, expert opinion	NHYA class II or III	9 years
Chan et al.[91]	2006	USA	Conventional medical therapy	Database, MADIT II trial, literature	MADIT II criteria	Lifetime
Al-Khatib et al.[88]	2005	USA	Conventional medical therapy	Databases, MADIT II trial, literature	MADIT II criteria	Lifetime
Sanders et al.[87]	2004	USA	Conventional medical therapy	Databases, MADIT II trial, literature	MADIT II criteria	Lifetime
McGregor et al. [86]	2004	Canada	Conventional medical therapy	Literature, meta-analysis	MADIT II criteria	15 years
Sanders et al.[84]	2001	USA	Amiodarone	Patient registry, expert opinion	Past MI Non-sustained VT	Lifetime
Goldenberg et al.[89]	2005	USA	Surgery or drug treatment (no Amiodarone)	Literature	Genetic cardiac disorders: - Long QT syndrome - Hypertrophic cardiomyopathy	Lifetime
Sanders et al.[90]	2005	USA	Control therapy	Patient registries, literature, trial reports	DEFINITE, MADIT I, MADIT II, COMPANION, MUSTT, SCD-HeFT criteria	Lifetime
Studies alongside RCTs						
Mark et al.[92]	2006	USA	Conventional medical therapy (no Amiodarone)	SCD-HeFT	NYHA class II or III LVEF ≤ 35%	Lifetime
Zwanziger et al.[93]	2006	USA	Conventional medical therapy (limited use of Amiodarone)	MADIT II	MI 1 month or more before study LVEF ≤ 30% No NYHA class IV	3.5 years
Mushlin et al.[83]	1998	USA	Conventional medical therapy (mainly Amiodarone)	MADIT I	MI 3 weeks or more before study LVEF ≤ 35% Inducible VT at EPS Non-sustained VT	4 years

MI: myocardial infarction; VT: ventricular tachycardia; NYHA: New York Heart Association; LVEF: left ventricular ejection fraction; EPS: electrophysiologic study

4.3.2.2 *Results of the economic evaluations*

The studies results (standardised to Euros of the year 2005 with local consumer price indexes and purchasing power parities[d]) and reported effectiveness measures are summarised in Table 21. Two studies modelling ICD use in patients meeting MADIT II[84] and SCD-HeFT[85] criteria had to rely on expert opinion and (rather optimistic[85]) assumptions for ICD effectiveness since they pre-date the publication of the results of those two RCTs. Both studies have thus been discarded in the current discussion.

Table 21: Results of the economic evaluations of the use of ICD in primary prevention

Author Costing year (Currency)	Life expectancy (y)			Strategy	ICER[a] as reported	ICER[a] in 2005 €
	ICD	Drug	Difference			
Studies based on decision model						
Hancock et al., 2006[94]						
2005 (OZ$)	-	-	2.63	Public hospital		
				Lifetime (base-case)	39,900	25,283
				10 years time horizon	78,400	49,679
				5 years time horizon	127,700	80,919
				No benefit after 5 years	83,300	52,784
				Private hospital		
				Lifetime (base-case)	95,000	60,198
				10 years time horizon	154,300	97,774
				5 years time horizon	293,100	185,727
				No benefit after 5 years	200,900	127,303
Chen et al., 2004[85]						
2002 (US$)	2.90[b]	1.90[b]	1.00[b]	Cost per QALY	97,865	92,929
Chan et al., 2006[91]						
2004 (US$)	8.20[c]	6.70[c]	1.50[c]	Cost per QALY	55,800	50,461
Al-Khatib et al., 2005[88]						
2002 (US$)	10.88	8.26	2.62	*Time horizon*		
				Lifetime (Base-case)	50,500	47,953
				12 years	79,900	75,870
				6 years	167,900	159,432
				3 years (trial data)	367,200	348,681
				No benefit after 3 years	123,400	117,177
Sanders et al., 2004[87]						
2003 (US$)	9.60	7.01	2.59	Base case (cost / LYG)	36,700	34,073
				Cost per QALY		
				Base case	50,900	47,256
				No benefit after 3 years	112,600	104,539
				SCD / NSCD = 4[d]	37,900	35,187
				SCD / NSCD = 0.25 [d]	132,500	123,014
McGregor et al., 2004[86]						
2002(CAN$)	-	-	1.10	Base-case	47,460	35,583
				6 years time horizon	98,200	73,625
Sanders et al., 2001[84]						
1999 (US$)	7.08[c]	6.49[c]	0.57[c]	LVEF ≤ 30%		
				Cost per LYG	63,300	64,906
				Cost per QALY	71,800	73,622
				LVEF > 40%		

				Cost per LYG	501,500	514,225
				Cost per QALY	557,900	572,056
Goldenberg et al., 2005[89]						
2001 (US$)	58.8	48.7	10.1	LQTS patients – Males	37,856[e]	36,515
	61.0	45.7	15.4	LQTS patients – Females	29,082[e]	28,052
	57.4	33.6	23.7	HCM patients – Males	17,758[e]	17,129
	34.6	59.8	25.2	HCM patients – Females	18,356[e]	17,706
Sanders et al., 2005[90]						
2005 (US$)	7.70[c]	4.06[c]	3.64[c]	MADIT I	25,300	22,130
	8.86[c]	4.72[c]	4.14[c]	MUSTT	24,500	21,430
	8.20[c]	6.16[c]	2.04[c]	MADIT II	39,000	34,113
	11.8[c]	9.03[c]	2.72[c]	DEFINITE	36,800	32,189
	5.88[c]	4.01[c]	1.87[c]	COMPANION	36,500	31,926
	7.59[c]	6.19[c]	1.40[c]	SCD-HeFT	50,700	44,347
Studies alongside RCTs						
Mark et al., 2006[92] (SCD-HeFT)						
2003 (US$)	10.87	8.41	2.46	*Time horizon*		
				Lifetime (Base-case)	38,390	35,641
				12 years	58,510	54,321
				8 years	88,660	82,310
				5 years (trial data)	127,500	118,375
				No benefit after 5 years	98,770	91,700
				NYHA class II	29,870	27,733
				NYHA class III	ICD dominated	
				Age ≥ 65 years	43,950	40,804
				Age < 65 years	35,500	32,959
				QRS ≥ 120	40,100	37,229
				QRS < 120	37,250	34,583
Zwanziger et al,. 2006[93] (MADIT II)						
2001 (US$)	2.89[c]	2.72[c]	0.17[c]	*3.5 years time horizon (trial data)*		
				Base case	235,000	226,676
				Age ≥ 65 years	133,000	128,289
				Age < 65 years	870,000	839,185
				NYHA ≥ II	164,000	158,191
				NYHA I	366,000	353,037
				QRS ≥ 120	196,000	189,058
				QRS < 120	334,000	322,170
				12 years time horizon (extrapolation)		
				Benefit continues	78,600	75,816
				Benefit declines	91,300	88,066
				No benefit	114,000	109,962
Mushlin et al., 1998[83] (MADIT I)						
1995 (US$)	3.66	2.80	0.86	*Time horizon*		
				4 years (trial data)	27,000	30,265
				8 years (extrapolation)	16,900	18,943

a Incremental cost-effectiveness ratio, with both costs and effects discounted. Cost per LYG unless otherwise stated; b Discounted QALYs; c Discounted life expectancy; d Ratio of sudden cardiac death to non-sudden cardiac death; e Own computations.

Results for all patients groups

With health benefits and costs restricted to observed trials durations, two RCT-based economic evaluations report unattractive ICERs (over €118,000 per LYG)[92, 93]. By contrast, with a 0.86 gain in life-years over the 4-year MADIT I trial duration, Mushlin et al.[83] report a more favourable short-term trial-based ratio (€30,300 per LYG). Huge ICERs are also reported by modelling studies restricting their time horizon to the follow-up period of the trial they rest on, i.e. from €81,000[94] to €348,000[88, 96] per LYG. Model-based studies simulating survival over longer time periods (usually lifetime, i.e. on average from 65 years up to death) during which ICD benefit is assumed to continue, report much favourable though inconsistent ICERs ranging from €17,100[89] to €60,200[94]. Similarly, a significant degree of heterogeneity is found among the survival gains reported for a lifetime: from 1.1[86] to 4.14[90] life-years gained. Higher survival gains (up to 25 life-years gained) are reported in Goldenberg et al.[89] since they target young patients (from 10-year olds) with inherited cardiac disorders as opposed to adult patients (60- to 65-year olds) with acquired heart disease.

Though they were not initially designed for this purpose, subgroup analyses were performed in Mark et al.[92] and Zwanziger et al.[93] In Zwanziger et al.[93], the reported ICERs are consistently more favourable in higher-risk subgroups (i.e. age ≥ 65 years, NYHA classes ≥ II, QRS ≥ 120, blood urea nitrogen > 25 mg/dl). This is however not confirmed by Mark et al.[92] in which reported ICERs remain constant or are less favourable in higher-risk subgroups (i.e. age ≥ 65 years, NYHA class III, QRS ≥ 120, LVEF ≤ 30%). In Chan et al.[91], the efficiency of stratifying MADIT II patients with microvolt T-wave alternans (MTWA) was assessed. Relative to medical therapy, providing ICD only to those with positive or undetermined MTWA test (i.e. patients associated with an increased risk of arrhythmic event) is more cost-effective (€44,100 per QALY) than providing ICD to all patients (€50,500 per QALY).

Results per patients group

Two studies report the results of cost-effectiveness analyses for ICD use in MADIT I patients[83, 90], that is patients with asymptomatic non-sustained ventricular tachycardia, a prior myocardial infarction, an ejection fraction ≤ 35% and an inducible ventricular tachycardia at electro-physiological testing not suppressed by Procainamide. Both economic evaluations report consistent and attractive ICERs of €22,000[90] and €30,000[83] per life-year gained. Further, Mushlin et al's[83] ICER would reduce to €25,700 per life-year saved if transvenous ICD were used instead of older devices. It is interesting to note that, among the primary prevention trials reviewed by Sanders et al.[90], MADIT I patients suffered the highest underlying mortality rate and had the lowest hazard ratio for death after ICD.

The efficiency of ICD in patients meeting MADIT II criteria is investigated as part of the MADIT II trial itself[93] and in 5 subsequent model-based evaluations[86-88, 90, 91]. Eligibility requirements for the MADIT II study included a previous myocardial infarction and a LVEF ≤ 30%, with no NYHA class IV patients and no electrophysiological test required. Lifetime ratios range from €34,000 per LYG[87] to €50,500 per QALY[91] while the trial-based ICER was over €200,000 per LYG. Though the authors' conclusions diverge regarding the attractiveness of ICD use in MADIT II patients, they all recognise that reducing the cost of ICD and leads, or increasing the periodicity of generator replacement substantially improves the cost-effectiveness ratio. Further, risk-stratification analyses in Zwanziger et al.[93] and Sanders et al.[87] suggest that ICERs become more favourable in higher-risk subgroups (i.e. rates of cardiac mortality and sudden cardiac death, age, QRS duration, NYHA).

The efficiency of ICD therapy in patients with NYHA class II or III congestive heart failure and a LVEF ≤ 35% was evaluated alongside the SCD-HeFT trial[92] and in 2 subsequent modelling studies[90, 94]. Within the trial duration, the ICER reaches over €118,000 per LYG. Over a lifetime, however, the incremental cost per LYG becomes more attractive but varies between €25,300[94] and €60,200[94]. By contrast with Mark et al.[92] and Sanders et al.[90], Hancock et al.[94] report that reducing the cost of ICD or increasing the generator's life only had a small impact on their base-case ICER.

Further note that in Mark et al.[92] and in Sanders et al.[90], the cost of single-chamber ICD was used in their base-case. Subgroup analyses in Mark et al.[92] did not significantly impact their base-case ICER, except for NYHA class II patients where ICD therapy appeared much more attractive (€27,700 per LYG) than for NYHA class III patients (ICD dominated).

Goldenberg et al.[89] is the only study assessing the cost-effectiveness of ICD therapy in young patients with inherited high-risk long QT syndrome (i.e. LQTS patients with recurrent syncope during beta-blocker therapy and/or QTc prolongation > 50 second) and hypertrophic cardiomyopathy (i.e. HCM patients with one of those risk factors: family history of HCM-related sudden death, extreme left ventricular hypertrophy, syncope, multi-repetitive, prolonged or non-sustained ventricular tachycardia on ECG, hypotensive blood pressure). ICD implantation in those patients is found to be attractive with a lifetime incremental cost per LYG around €17,500 for HCM patients, €28,000 for LQTS female patients and €36,500 for LQTS male patients (own computations including only direct medical costs). When the cost of the productive time gained due to avoided mortality is accounted for, ICD therapy becomes cost-saving for all HCM patients and for LQTS female patients. By contrast, ICD therapy in low-risk LQTS and HCM patients, i.e. patients without known risk-factors, is not cost-effective (ICER over €385,000 per LYG).

Discussion

Based on this review, there is some evidence that prophylactic implantation of ICD is attractive in MADIT I patients[83, 90] and in young high-risk patients with inherited cardiac disorders (LQTS, HCM)[89] Considering the small number of published economic evaluations targeting those specific populations, this should however be confirmed by additional studies. The case for prophylactic ICD implantation in other patient groups is less clear given the variability of the reported ICERs. Clearly, RCT-based economic evaluations of ICD overestimated the ICERs (i.e. too high ICERs). Indeed many ICD costs occur early while the long-term costs of non-ICD therapy and the long-term benefits of ICD use are not captured within the trial timeframe. Over the course of longer time horizons, the reported cost-effectiveness ratios of ICD use became more favourable. However, in the absence of robust long-term follow-up data, lifetime estimates of health benefits and ICERs are only speculative since they heavily depend on the assumptions taken to project survival in the ICD arm (i.e. projections of the hazard ratio).

All economic evaluations reviewed here were performed in North America and Australia, where the health care systems and health care costs may not directly compare to Belgium. Since July 2005, the cost of an ICD (single or dual chamber) in Belgium was set up by the health authorities at €16,650. This Belgian cost lies in the lower limit of the range of the ICD device costs reported by the reviewed US economic evaluations, (i.e. about €16,300[89, 92] for a single chamber ICD, and from €18,200 to €22,200 for a dual chamber ICD[83, 88, 89, 93]). Though this could translate into more attractive ICERs for ICD use in Belgium, other factors (such as a lower cost of medical treatment in Belgium versus the USA) may drive the ICER in the opposite direction. Transferability of the current findings to Belgian settings should therefore be done with great caution.

- **Secondary prevention. Trial duration time horizon: ICERs vary from €70,990 to €172,380 per LYG. Lifetime horizon: ICERs vary from €29,930 to €224,680 per LYG.**
- **Primary prevention. Trial duration time horizon: ICERs vary from €30,300 to €348,000 per LYG. Lifetime horizon: ICERs vary from €17,700 to €60,200 per LYG.**
- **ICD implantation in MADIT I patients (ICER < €25,700 per LYG) and in high-risk patients with long QT syndrome (€28,000 - €36,500 per LYG) and hypertrophic cardiomyopathy (~€17,500 per LYG) may well be cost-effective.**
- **There is conflicting evidence about the efficiency of prophylactic ICD implantation in other populations (MADIT II, SCD-HeFT).**
- **Patient stratification by age, NYHA class, LVEF and QRS criteria improves the ICER for MADIT II patients, but has no or a negative impact on the ICER for SCD-HeFT patients.**
- **Key parameters driving the ICERs of the reviewed studies were: ICD cost, generator replacement periodicity, annual rate of all-cause mortality, ICD relative risk reduction and lifetime benefit extrapolation assumptions.**

5 ECONOMIC EVALUATION OF ICD IMPLANTATION IN A BELGIAN SETTING

5.1 COST-EFFECTIVENESS ANALYSIS

5.1.1 Study design

5.1.1.1 Analytic technique

A Markov simulation model was developed in Excel in order to assess the efficiency of prophylactic ICD implantation. Both cost-effectiveness (with outcomes expressed in life-years gained) and cost-utility analyses (with life-years gained adjusted for quality of life) are performed. @Risk adds-on tool was used for probabilistic modelling and probabilistic sensitivity analyses. Half-cycle corrections were performed.

5.1.1.2 Target population

The model simulates a hypothetical cohort of 1,000 SCD-HeFT-eligible patients. The SCD-HeFT is a randomized, controlled, primary prevention trial including 2521 patients (median age 60 years) with moderately symptomatic heart failure (NYHA class II or III) and left ventricular dysfunction of 35% or less[11].

5.1.1.3 Perspective

The analysis is performed from the perspective of the Belgian health insurance system. Only the direct costs of medical care are included, excluding patients' out-of pocket payments. Since baseline employment rates are expected to be low in this population, indirect productivity costs were ignored.

5.1.1.4 Comparators

Two scenarios are compared (see Appendix 1):

- Conventional therapy for all patients. As in the SCD-HeFT trial, we modelled the possibility for patients in conventional therapy to receive an ICD should they survive an episode of life-threatening arrhythmia (i.e. secondary prevention).
- Prophylactic ICD implantation for all. ICD implantation in primary prevention.

5.1.1.5 Time horizon

Primary data in the SCD-HeFT trial are reported for a 5-year follow-up period[11]. These observed data were extrapolated to a patient's lifetime by the use of modelling.

5.1.1.6 Discounting

For the base-case, conform to the Belgian guidelines, future costs and benefits were discounted at a rate of 3% and 1.5%, respectively[97]. All results and tables are thus presented with both costs and effects discounted at those rates.

5.1.2 Efficacy data

The Markov model tracks a cohort of 1000 patients who receive either conventional therapy or prophylactic ICD. Each month (the length of a Markov cycle), patients are at risk of death (sudden cardiac death, non-sudden cardiac death and non-cardiac death altogether).

The probability of total death among conventional therapy patients was derived from the SCD-HeFT trial[11]. Assuming the reported probability of total death in the placebo group (36.1%) is constant over 5 years, this translated into an annual overall probability of death of 8.57%[e] or 0.74% per month (Table 22). For extrapolation beyond this period (i.e. from 65 year-old on), we assumed that the probability of total death among conventional therapy patients proportionally increases with the (gender-adjusted) all-cause mortality of the Belgian population of the same age.

The probability of total death among ICD patients was also derived from the SCD-HeFT trial[11]. Assuming the reported probability of total death among ICD patients (28.9%) is constant over 5 years, this corresponds to an annual overall probability of death of 6.59%[e] or 0.567% per month (Table 22). Given the uncertainty surrounding the long-term benefits of ICD, three scenarios were investigated for extrapolation beyond the trial period:

Extrapolation scenario 1: as for conventional therapy patients, the probability of total death among ICD patients is assumed to increase proportionally with the (gender-adjusted) all-cause mortality of the Belgian population of the same age.

Extrapolation scenario 2: the long-term probability of total death among ICD patients is derived by rising the long-term probability of survival among control patients of the same age to the power of the hazard ratio (0.77[11]) and by taking its complement[f].

Extrapolation scenario 3: under this "worst-case" scenario, it is assumed that the relative benefit of ICD versus conventional therapy disappears beyond the trial duration. Total mortality among ICD patients is thus set equal to total mortality among conventional therapy patients.

Five-year probabilities of total death for both conventional therapy and ICD patients were fitted with Beta distributions in order to assess these parameters' uncertainty. To reflect the significant improvement in total death for ICD patients compared to conventional therapy patients[11] and thus to avoid an overlap between the Beta distributions, these were truncated by excluding their lower and upper 1% tails. For the hazard ratio, a normal distribution on the natural log (whose exponent is taken afterwards) was chosen to reflect uncertainty[98].

5.1.3 Epidemiological and clinical data

The clinical and epidemiological data used in the base-case model, together with their range for the sensitivity analysis, are presented in Table 22 below:

Table 22: Clinical and epidemiological data (Base-case, SCD-HeFT)

Input variable	Base-case value	Range (95% CI[a])		Source
		Lower bound	Upper bound	
Characteristics of the population				
Start age of the cohort (years)	60	-	-	SCD-Heft (Bardy et al., 2005)
Median left ventricular ejection fraction	25,00%	-	-	SCD-Heft (Bardy et al., 2005)
Proportion female	23,66%	-	-	SCD-Heft (Bardy et al., 2005)
Conventional therapy				
5-year probability of total death	36,10%	*33,39%*	*38,85%*	SCD-Heft (Bardy et al., 2005)
Annual probability of total death (assumption of constant probability of death over 5 years)				
Years 1 - 5	8,57%	*7,80%*	*9,37%*	Own computations
Cross-over to ICD (%)	11,11%	*9,65%*	*12,65%*	SCD-Heft (Bardy et al., 2005)
ICD therapy				
5-year probability of total death	28,90%	*26,32%*	*31,54%*	SCD-Heft (Bardy et al., 2005)
Annual probability of total death (assumption of constant probability of death over 5 years)				
Years 1 - 5	6,59%	5,93%	7,30%	Own computations
Hazard ratio total mortality	0.77[b]	*0,64*	*0,93*	SCD-Heft (Bardy et al., 2005)
Operative death (%)	0,60%	*0,11%*	*1,09%*	Point 3.4 of the current report
Frequency of generator replacement (years)	5	Min: 1	Max: 10	Simulation scenarios
Utilities (annual)				
Control therapy	0,85	*0,66*	*0,99*	Mark et al., 2006
ICD therapy	0,85	*0,66*	*0,99*	Mark et al., 2006

e Annual probability of death = 1 – [(1 – 5-year probability of death) EXP (1/5)]

f Probability of death ICD $_t$ = 1 – [Probability of survival CT $_t$ EXP (hazard ratio)]

As in the SCD-HeFT trial, patients on conventional therapy have an 11.11% probability of receiving an ICD during their follow-up. We however made the simplifying assumption that cross-over could only occur once, i.e. at the reported median time of 26 months after randomization[11]. No additional life-saving benefits were attributed to cross-over patients other than those already accounted for in the control arm of the SCD-HeFT trial (i.e. intention to treat analysis). We further assumed that ICD implantation for primary prevention patients was associated with a perioperative mortality ranging from 0.0 to 1.2%[1, 47, 18] The base-case battery life was assumed to be 5 years (range for the scenario analysis: 1 to 10 years).

On the basis of data from a previous study[92], the model assumed that one year of life with heart failure equals 0.85 year (range 0.6 – 1) with optimal health and that the quality of life does not change as a result of the implantation of an ICD.

Utility parameters and probabilities for cross-over and perioperative mortality were fitted with Beta distributions to reflect uncertainty[98].

5.1.4 Cost data

All cost inputs used in the model were derived from the Belgian ICD registry (a thorough description of this registry is to be found in chapter 7 of this report). The Belgian ICD database is a merge between two datasets: first the dataset of the IMA / AMI (the Belgian sickness founds) that contains information on resource consumption and costs at the patient level; and second the dataset of the RIZIV / INAMI (the National Institute of Sickness and Invalidity Insurance) that contains some clinical information on ICD patients, such as primo- or replacement-implant, reason for ICD replacement (battery depletion or other), date of patient's death and the code for the initial ICD medical indication (see the list of codes in appendix to chapter 3: Belgian coverage for ICD in 2005). Data from the Belgian ICD registry were available for patients implanted with an ICD in the years 2001 and 2005. Both patients' groups were followed up to their death or December 2005. Follow-up costs were derived from the 2001 database, while implantation costs were derived from the 2005 database. The 2005 database was segmented based on whether patients had a primo- or a replacement-implant, and whether the initial medical indication for implantation was primary (code 3) or secondary prevention (codes 1.1, 1.2, 1.3, 2.1, 2.2, 2.3 and 2.4). In 2005, we could identify 112 patients implanted with a primo-ICD in primary prevention, 401 patients implanted with a primo-ICD in secondary prevention, 10 patients implanted with a replacement-ICD in primary prevention and 159 patients implanted with a replacement-ICD in secondary prevention. ICD-related follow-up costs (both inpatient and outpatient) were computed based on patients who received a primo-implantation in 2001 with an initial indication of secondary prevention. A total of 134, 121, 109 and 99 patients could be followed during the first, second, third and fourth year after the hospital discharge for ICD primo-implantation. Follow-up costs related to primary prevention patients could not be derived due to the limited number of such patients in the 2001 database. A list of the cost inputs obtained from each database is provided in Table 23.

Table 23: Cost inputs derived from the Belgian ICD registry

List of the cost inputs	Number of patients	Appendix
2001 database		
Annual outpatient ICD follow-up costs in secondary prevention	y1: 134 y2: 121 y3: 109 y4: 99	7
Annual inpatient ICD follow-up costs in secondary prevention		8
Annual follow-up costs of the underlying disease		-
2005 database		
Cost of ICD primo-implantation in primary prevention	112	3
Cost of ICD primo-implantation in secondary prevention	401	4
Cost of ICD replacement (battery depletion) in primary prevention	10	5
Cost of ICD replacement (battery depletion) in secondary prevention	159	6

In order to obtain resource consumption and cost estimates of all inputs listed above, a protocol for analysing the Belgian ICD registry was developed (appendix 2). As general principles, patient-level data for primo- or replacement-ICD were divided into three periods: pre-implant, implant and post-implant periods (see appendix 2 for a comprehensive definition of those periods). For each period, the protocol lists all relevant ICD-related nomenclature codes whose consumption and cost should be retrieved from the database. Individual nomenclature codes were classified into homogeneous procedure groups (e.g. echocardiography, 24-hour ECG…) for which the mean cost and resource consumption values, max, min and 95% confidence intervals were systematically reported (see appendix 3 – 6).

For the annual ICD-related follow-up costs and resource consumption of patients implanted in 2001, the protocol provides two lists of nomenclature codes to be considered: one for inpatient follow-up and the other for outpatient follow-up. Outpatient follow-up costs consisted in physician fees and ICD-related procedures temporarily associated with an ICD control (i.e. performed on the same day as an ICD control). Inpatient follow-up costs consisted in all resources consumed during a hospitalisation (from hospital admission to discharge) only if a nomenclature code for "device or electrode" could be identified during that hospitalisation. Individual nomenclature codes for the follow-up were also classified into homogeneous procedure groups for which the mean cost and resource consumption per patient, max, min and 95% confidence intervals were systematically reported (see appendix 7, 8).

Finally, as specified in the protocol, the follow-up costs of the underling disease (i.e. the cost for the treatment of the patients' heart disease, independent of the cost of their ICD) were computed by deducting all ICD-related follow-up costs (both inpatient and outpatient) from the aggregated total cost of the ICD patients. All computed annual mean follow-up costs per patient were divided by 12 to fit the model cycle.

The cost of a treatment with Amiodarone was computed based on the drug prices published by the Belgian Health Insurance System (INAMI/RIZIV), excluding the patients' share for the drug[99]. For the first month of treatment, we assumed that dosage would be 600 mg Amiodarone per day the first week, 400 mg per day the second week and 200 mg per day thereafter. For each following month, we assumed the dosage would be constant, at 200 mg per day.

The results of the analysis of the Belgian ICD registry are reported in Table 24. Details of the components of each cost input are to be found in the appendix. All costs are expressed in Euros from the year 2005. Costs from previous years were inflated to 2005 values with the Health Consumer Price Index[100]. In order to account for the uncertainty around the cost inputs, gamma distributions have been used. Gamma distributions were defined with the mean cost, min, max and 95% CI reported for each cost component (i.e. for each procedure group) of the above-listed cost inputs.

By lack of information on their 95% CI, yearly follow-up costs of the underlying disease were varied by 50% around their estimates and fitted with Beta distributions. After a run of 1,000 Latin Hypercube simulations, 95% CI on the total costs inputs could be retrieved (see Table 24).

Since patients characteristics from the Belgian ICD registry do not totally match the profile of the patients used for modelling, the impact of those differences between patients' groups on the costs of ICD implantation was assessed by regression analyses. The dependency of the costs of ICD implantation (primo-implantation in primary prevention, primo-implantation in secondary prevention and replacement in secondary prevention, all limited to the ICD-(re)implantation period) to the following variables was investigated: gender, age (per 10-year categories), LVEF (35% threshold), implantation centre and etiology (ischaemic, idiopathic cardiomyopathy, other). From the regressions' results (not shown), there was no significant association between those variables and the costs of ICD (re)implantation. No regression analysis could be performed for the cost of ICD replacement in primary prevention due to the small sample size (only 10 patients in that group).

Table 24: Cost inputs (all costs in Euro 2005)

Input variable	Base-case value	Range (95% CI[a]) Lower bound	Range (95% CI[a]) Upper bound	Source
ICD scenario				
ICD primo implantation costs, primary prevention				
Pre-ICD implantation period	2,175.23 €	*2,068.47 €*	*2,278.47 €*	IMA / RIZIV database
ICD implantation period	22,578.91 €	*21,817.34 €*	*23,331.79 €*	IMA / RIZIV database
Post-ICD implantation period	2,362.28 €	*2,103.96 €*	*2,609.45 €*	IMA / RIZIV database
Total	27,116.42 €	*26,289.59 €*	*27,921.25 €*	
ICD replacement costs, primary prevention				
Pre-ICD re-implantation period	3,152.01 €	*2,369.51 €*	*3,912.69 €*	IMA / RIZIV database
ICD re-implantation period	27,116.24 €	*20,472.00 €*	*34,086.30 €*	IMA / RIZIV database
Post-ICD re-implantation period	2,395.49 €	*1,812.20 €*	*3,040.76 €*	IMA / RIZIV database
Total	32,663.74 €	*25,907.07 €*	*39,829.70 €*	
Yearly outpatient ICD follow-up costs				
Year 1	369.83 €	*343.12 €*	*396.29 €*	IMA / RIZIV database
Year 2	299.45 €	*277.49 €*	*322.90 €*	IMA / RIZIV database
Year 3	270.32 €	*246.25 €*	*293.25 €*	IMA / RIZIV database
Year 4	286.39 €	*260.84 €*	*311.01 €*	IMA / RIZIV database
Yearly inpatient ICD follow-up costs				
Year 1	568.20 €	*215.16 €*	*1,162.97 €*	IMA / RIZIV database
Year 2	37.77 €	*4.87 €*	*122.41 €*	IMA / RIZIV database
Year 3	42.07 €	*19.81 €*	*78.72 €*	IMA / RIZIV database
Year 4	205.57 €	*38.30 €*	*531.07 €*	IMA / RIZIV database
Yearly follow-up costs of the underlying disease				
Year 1	7,412.77 €	*4,397.80 €*	*10,413.34 €*	IMA / RIZIV database
Year 2	4,109.69 €	*2,438.17 €*	*5,773.22 €*	IMA / RIZIV database
Year 3	4,091.41 €	*2,427.32 €*	*5,747.55 €*	IMA / RIZIV database
Year 4	4,959.72 €	*2,942.47 €*	*6,967.34 €*	IMA / RIZIV database
Conventional therapy scenario				
Cost of Amiodarone				
Month 1	7.99 €	-	-	www.cbip.be
Subsequent months	4.89 €	-	-	[Accessed 05/2007]
Yearly follow-up costs of the underlying disease				
Year 1	7,412.77 €	4,397.80 €	10,413.34 €	IMA / RIZIV database
Year 2	4,109.69 €	2,438.17 €	5,773.22 €	IMA / RIZIV database
Year 3	4,091.41 €	2,427.32 €	5,747.55 €	IMA / RIZIV database
Year 4	4,959.72 €	2,942.47 €	6,967.34 €	IMA / RIZIV database
ICD primo implantation costs, secondary prevention (cross-over)				
Pre-ICD implantation period	2,042.18 €	*1,981.71 €*	*2,103.86 €*	IMA / RIZIV database
ICD implantation period	21,975.05 €	*21,579.70 €*	*22,370.06 €*	IMA / RIZIV database
Post-ICD implantation period	3,243.91 €	*3,202.75 €*	*3,282.89 €*	IMA / RIZIV database
Total	27,261.14 €	*26,866.53 €*	*27,658.26 €*	
ICD replacement costs, secondary prevention (cross-over)				
Pre-ICD re-implantation period	2,455.52 €	*2,324.96 €*	*2,585.52 €*	IMA / RIZIV database
ICD re-implantation period	20,564.48 €	*19,606.60 €*	*21,516.39 €*	IMA / RIZIV database
Post-ICD re-implantation period	2,985.41 €	*2,107.24 €*	*3,857.59 €*	IMA / RIZIV database
Total	26,005.41 €	*24,716.41 €*	*27,370.38 €*	
Yearly outpatient ICD follow-up costs (cross-over)				
Year 1	369.83 €	*343.12 €*	*396.29 €*	IMA / RIZIV database
Year 2	299.45 €	*277.49 €*	*322.90 €*	IMA / RIZIV database
Year 3	270.32 €	*246.25 €*	*293.25 €*	IMA / RIZIV database
Year 4	286.39 €	*260.84 €*	*311.01 €*	IMA / RIZIV database
Yearly inpatient ICD follow-up costs (cross-over)				
Year 1	568.20 €	*215.16 €*	*1,162.97 €*	IMA / RIZIV database
Year 2	37.77 €	*4.87 €*	*122.41 €*	IMA / RIZIV database
Year 3	42.07 €	*19.81 €*	*78.72 €*	IMA / RIZIV database
Year 4	205.57 €	*38.30 €*	*531.07 €*	IMA / RIZIV database

a: 95% CI in italic style were retreived after 1000 simulations

In our model, each patient entering the ICD-implantation branch incurs the cost of ICD primo-implantation in primary prevention. Each subsequent month, surviving patients further incur inpatient and outpatient ICD follow-up costs. By lack of long-term data on patients in primary prevention, the ICD-related follow-up costs for those patients were assumed to be 90% that of ICD patients in secondary prevention. This assumption is however varied in the sensitivity analysis (range 80% to 100%, fitted with uniform distribution). Finally, each surviving patient in the ICD-group incurs the cost of ICD replacement in primary prevention every 5 year.

In the conventional therapy group, we assumed that 10% (range 0-20%, fitted with a Beta distribution) of patients would incur the cost of Amiodarone in the first and subsequent months[35]. Further, patients in the conventional therapy group crossing-over to ICD therapy were assigned the initial cost of ICD primo-implantation in secondary prevention, the monthly inpatient and outpatient follow-up costs in secondary prevention and the cost of ICD replacement in secondary prevention every 5-year if alive.

Beside this, we assumed that both conventional therapy and ICD surviving patients (primary prevention and cross-over) would incur the same annual treatment costs due to their heart disease (i.e. follow-up costs of the underlying disease), up to the end of their life.

5.1.5 Sensitivity analyses

Sensitivity analyses were performed to account for important model assumptions and uncertainties. First, to allow for a direct comparison with our base-case SCD-HeFT results, the model was run again using the hazard ratio and total mortality probabilities reported in the MADIT II trial. Second, the sensitivity of the results to variations in the discount rates and in the frequency of battery replacement was assessed deterministically, by the use of scenario analyses. Finally, the combined impact of uncertainty in the model's input parameters was assessed via probabilistic sensitivity analysis, with a run of 1,000 Latin Hypercube simulations. See above for the choice of distributions applied to the input parameters.

5.1.5.1 MADIT II scenario

For this scenario, the efficacy data reported in the MADIT II trial have been used, instead of that reported in the SCD-HeFT trial (our base-case). Assuming the probability of total death in the MADIT II conventional therapy group (31%) is constant over 3 years, we computed an annual overall probability of death of 11.63% (or 1.025% per month)[35]. For extrapolation beyond this period (i.e. from 68 year-old on), we assumed that the probability of total death among conventional therapy patients proportionally increases with the (gender-adjusted) all-cause mortality of the Belgian population of the same age.

Assuming the reported probability of total death in the MADIT II ICD-patients group (22%) is also constant over 3 years, this corresponds to an annual overall probability of death of 7.95% (or 0.687% per month). Extrapolations of the ICD benefits beyond the trial duration followed the same structure as specified above:

Extrapolation scenario 4: as for control therapy patients, the probability of total death among ICD patients is assumed to increase proportionally with the (gender-adjusted) all-cause mortality of the Belgian population of the same age.

Extrapolation scenario 5: the long-term probability of total death among ICD patients is derived by rising the long-term probability of survival among conventional therapy patients of the same age to the power of the hazard ratio (0.69^{35}) and by taking its complement.

Extrapolation scenario 6: under this "worst-case" scenario, it is assumed that the relative benefit of ICD versus conventional therapy disappears beyond the trial duration. Total mortality among ICD patients is thus set equal to total mortality among conventional therapy patients.

The data used for the MADIT II scenario are summarized in Table 25:

Table 25: Clinical and epidemiological data (MADIT II scenario)

Input variable	Base-case value	Range (95% CI[a]) Lower bound	Range (95% CI[a]) Upper bound	Source
Characteristics of the population				
Start age of the cohort (years)	65	-	-	MADIT II (Moss et al., 2002)
Mean left ventricular ejection fraction	23,00%	-	-	MADIT II (Moss et al., 2002)
Proportion female	15,00%	-	-	MADIT II (Moss et al., 2002)
Conventional therapy				
3-year probability of total death	31,00%	*27,58%*	*34,50%*	MADIT II (Moss et al., 2002)
Annual probability of total death (assumption of constant probability of death over 3 years)				
Years 1 - 3	11,63%	10,20%	13,15%	Own computations
Cross-over to ICD (%)	11,11%	*9,66%*	*12,65%*	SCD-Heft (Bardy et al., 2005)
ICD therapy				
3-year probability of total death	22,00%	*19,53%*	*24,56%*	MADIT II (Moss et al., 2002)
Annual probability of total death (assumption of constant probability of death over 3 years)				
Years 1 - 3	7,95%	6,99%	8,97%	Own computations
Hazard ratio total mortality	0,69	*0,51*	*0,93*	MADIT II (Moss et al., 2002)
Operative death (%)	0,60%	*0,11%*	*1,09%*	Point 3.4 of the current report
Frequency of generator replacement (years)	5	*Min: 1*	*Max: 10*	Simulation scenarios
Utilities (annual)				
Control therapy	0,85	*0,66*	*0,99*	Mark et al., 2006
ICD therapy	0,85	*0,66*	*0,99*	Mark et al., 2006

a: 95% CI in italic style were retreived after 1000 simulations

5.1.5.2 Discount rate

To assess the sensitivity of the results to the discount rates applied, different scenarios are presented in the sensitivity analysis: 0% or 3% or 5% for both benefits and costs and finally 0% for benefits combined with 5% or 3% for costs (Table 26).

Table 26: Scenarios for discounting

	Base-case	Discounting scenario 1	Discounting scenario 2	Discounting scenario 3	Discounting scenario 4	Discounting scenario 5
Cost	3%	3%	5%	5%	3%	0%
Outcome	1.5%	3%	5%	0%	0%	0%

5.1.5.3 Battery replacement frequency

The base-case battery-life duration (5 years) was varied between 1 to 10 years (1-year increment) to see the impact on the base-case results.

5.1.6 Results

5.1.6.1 Survival projections

Figure 6 and Figure 7 display the projected survival of the SCD-HeFT and the MADIT II trials for the conventional therapy group and the three ICD extrapolation scenarios described previously. Extrapolations start at age 65 and 68 for the SCD-HeFT and MADIT II trials, respectively. The slope of the survival curve in the MADIT II conventional therapy group is steeper than that of SCD-HeFT, which suggests a sicker population in MADIT II. Undiscounted mean life-expectancy after half-cycle correction was estimated to be 7.95 years for SCD-HeFT and 5.83 for MADIT II conventional therapy patients. As expected, extrapolation scenarios 3 and 6 (simulating no long-term ICD benefits) generated the smallest life-expectancy in ICD patients (mean life expectancies of 8.55 and 6.37 years for SCD-HeFT and MADIT II respectively). There was a small difference between MADIT II extrapolation scenarios 4 and 5 (mean ICD-patients' life expectancy of respectively 7.55 and 7.45 years). Similarly, for the SCD-HeFT trial, extrapolation scenario 1 (based on the proportional increase in conventional therapy mortality) generated about the same ICD-patients' life expectancy than scenario 2 (based on the hazard ratio), i.e. respectively 9.38 and 9.35 years. As such, the undiscounted gain in life-years is 1.43 years in the first scenario. Taking into account the discount rate, this becomes 1.22 years. Adjusting for QoL it decreases further to 1.03 years. For the fourth scenario, this respectively is 1.73, 1.51, and 1.29 years.

Figure 6: Projected survival (from 65 years on) of the 1000 SCD-HeFT patients.

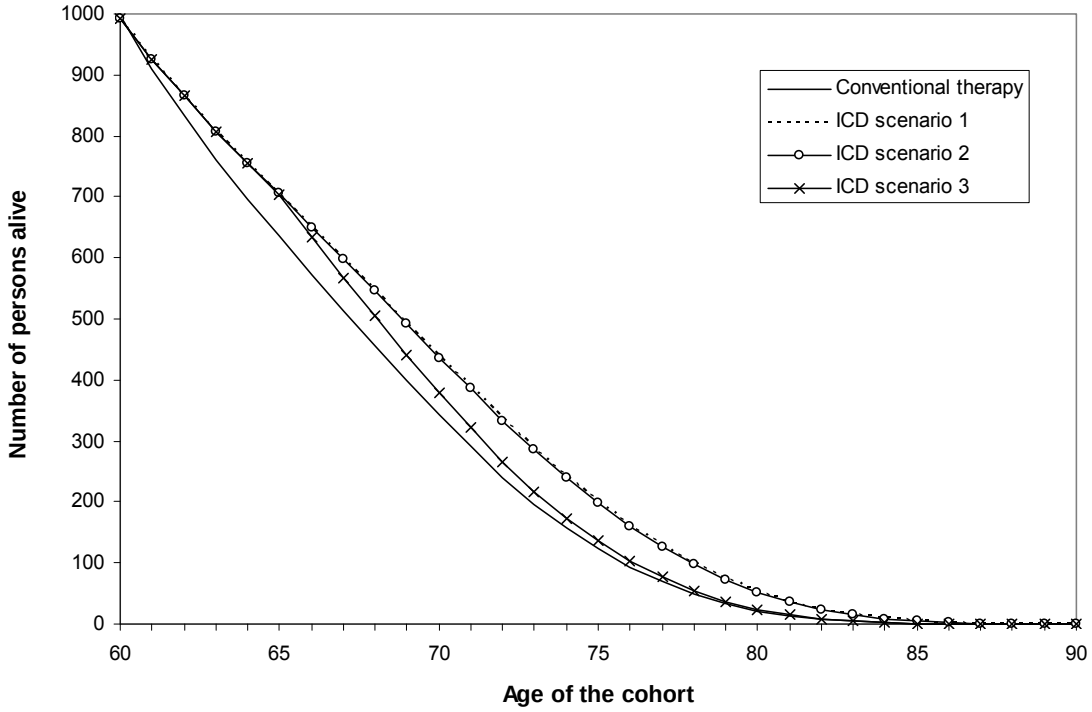
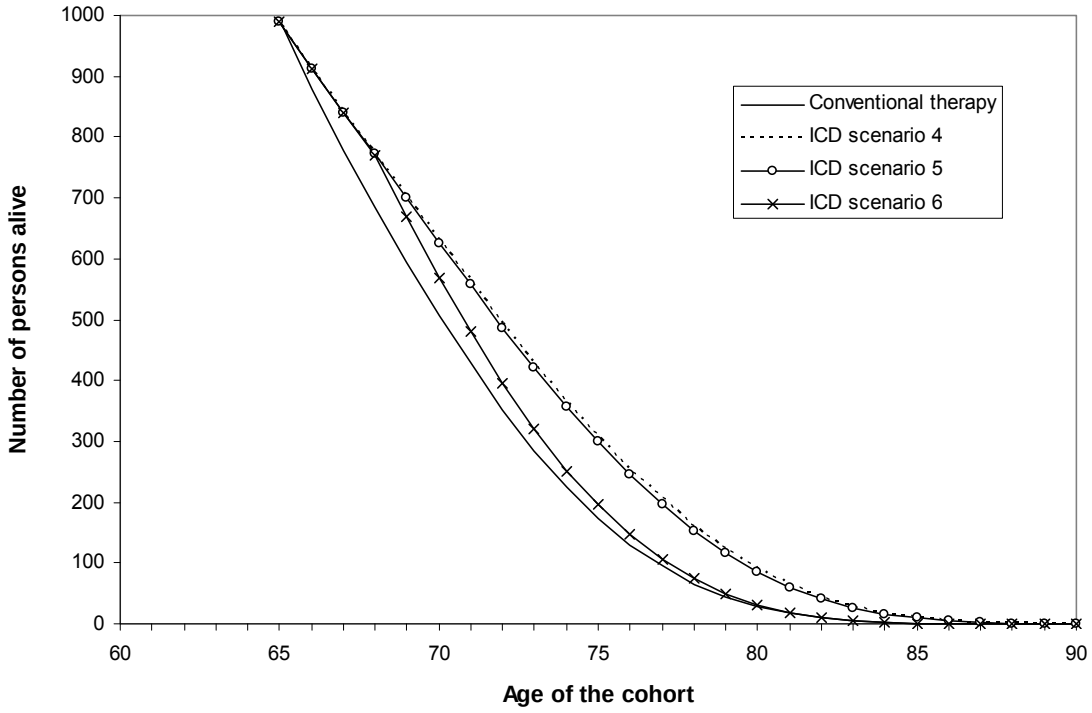


Figure 7: Projected survival (from 68 years on) of the 1000 MADIT II patients.



5.1.6.2 Cost-effectiveness analysis

The results of the 1000 Latin Hypercube simulations are presented in Table 27 and are illustrated on the cost-effectiveness planes below (Figure 8 and Figure 9). For the ease of comparison, the results of our base-case scenarios (SCD-HeFT) and of the corresponding MADIT II scenarios are presented together.

For the reference case, over a lifetime, ICD patients are expected to live from 0.5 to 1.2 discounted life-years (0.45 – 1 discounted QALYs) longer than conventional therapy patients, depending on the extrapolation scenario. When the benefits of ICD over conventional therapy are assumed to continue after 5 years, the ICERs are about €60,000 per LYG and €71,400 per QALY gained. Under the assumption that the benefits of ICD stop after the trial duration, the ICER reaches €111,000 per LYG and €132,100 per QALY gained.

Using MADIT II input data and over a lifetime, patients implanted with ICD have a gain in life-expectancy of 0.5 to 1.5 discounted LY (0.42 – 1.3 discounted QALYs) compared to patients in conventional therapy. The ICERs vary from €42,200 to €106,500 per LYG and from €50,300 to €127,000 per QALY gained.

Table 27: Incremental cost-effectiveness ratios and 95% CI of ICD compared to conventional therapy (All costs in Euro 2005)

Extrapolation scenarios	IC		IE (LYG)		IE (QALY gained)		ICER (€/LYG)		ICER (€/QALY gained)	
	Lower bound 95% CI	Upper bound 95% CI	Lower bound 95% CI	Upper bound 95% CI	Lower bound 95% CI	Upper bound 95% CI	Lower bound 95% CI	Upper bound 95% CI	Lower bound 95% CI	Upper bound 95% CI
SCD-HeFT data										
Extrapolation scenario 1	66.464 € 56.989 €	77.215 €	1,22 0,55	1,94	1,03 0,45	1,74	59.989 € 35.873 €	113.518 €	71.428 € 40.225 €	134.623 €
Extrapolation scenario 2	66.247 € 55.865 €	77.667 €	1,19 0,46	1,94	1,01 0,38	1,69	61.850 € 36.431 €	125.229 €	73.553 € 41.434 €	147.943 €
Extrapolation scenario 3	53.041 € 45.373 €	60.436 €	0,53 0,23	0,84	0,45 0,19	0,75	110.968 € 63.859 €	214.771 €	132.128 € 71.640 €	261.549 €
MADIT II data										
Extrapolation scenario 4	59.844 € 51.265 €	69.613 €	1,51 0,74	2,27	1,29 0,61	2,03	42.222 € 28.421 €	74.852 €	50.331 € 31.250 €	87.352 €
Extrapolation scenario 5	59.086 € 46.971 €	73.847 €	1,44 0,46	2,52	1,22 0,38	2,21	47.871 € 27.388 €	107.689 €	56.808 € 30.312 €	124.369 €
Extrapolation scenario 6	49.226 € 44.520 €	54.430 €	0,50 0,25	0,73	0,42 0,20	0,66	106.488 € 66.715 €	203.080 €	126.946 € 74.622 €	237.932 €

Figure 8 and Figure 9 illustrate the total uncertainty around the input parameters used in the model. For each trial, the dots in the plots represent the distribution of the difference in costs (ICD minus conventional therapy) and the difference in effectiveness (either LYs or QALYs gained) obtained from the 1000 simulations. On both graphs, only extrapolation scenarios 1 and 4 (e.g. ICD LT mortality proportional to CT mortality) are depicted. For the base-case, ICD implantation resulted in an incremental cost of €60,000 per LYG (95% CI: €35,900 - €113,500) and of €71,400 per QALY gained (95% CI: €40,200 - €134,600). ICERs for the MADIT II trial were more favourable with €42,200 per LYG (95% CI: €28,400 - €74,900) and €50,300 per QALY gained (95% CI: €31,200 - €87,400).

Figure 8: Cost-effectiveness plane (€ per QALY gained)

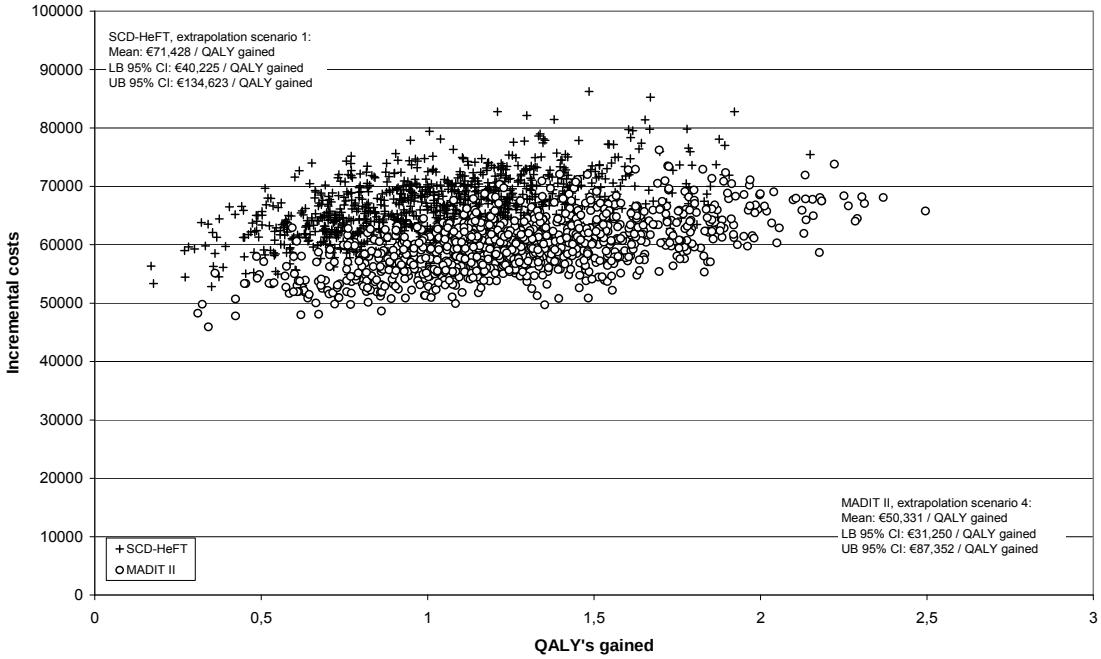
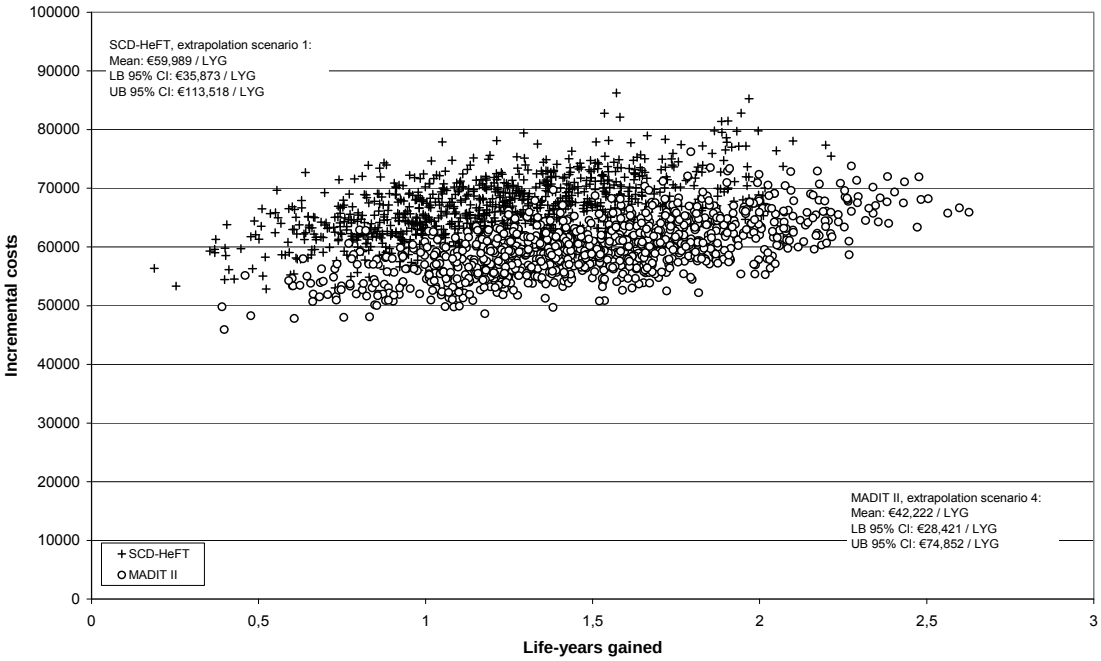


Figure 9: Cost-effectiveness plane (€ per LYG)



5.1.7 Sensitivity analyses

5.1.7.1 Discounting scenarios

The results of the six scenarios varying the discount rates for both costs and effects are presented in Table 28. Results were sensitive to variations in the effect discount rate with improved ICERs the further this rate decreased (i.e. improved discounted life expectancy). Variations in the discount rate for the costs side also had an impact on the results, less weight being given to the future costs of ICD replacement the higher the discount rate for costs.

Also, if both the discount rates for costs and effects are equally set to 3%, as often recommended in international guidelines and so performed in other economic evaluations of ICD (see chapter 4), the ICER's increase to €70,200 per LYG and €83,600 per QALY gained.

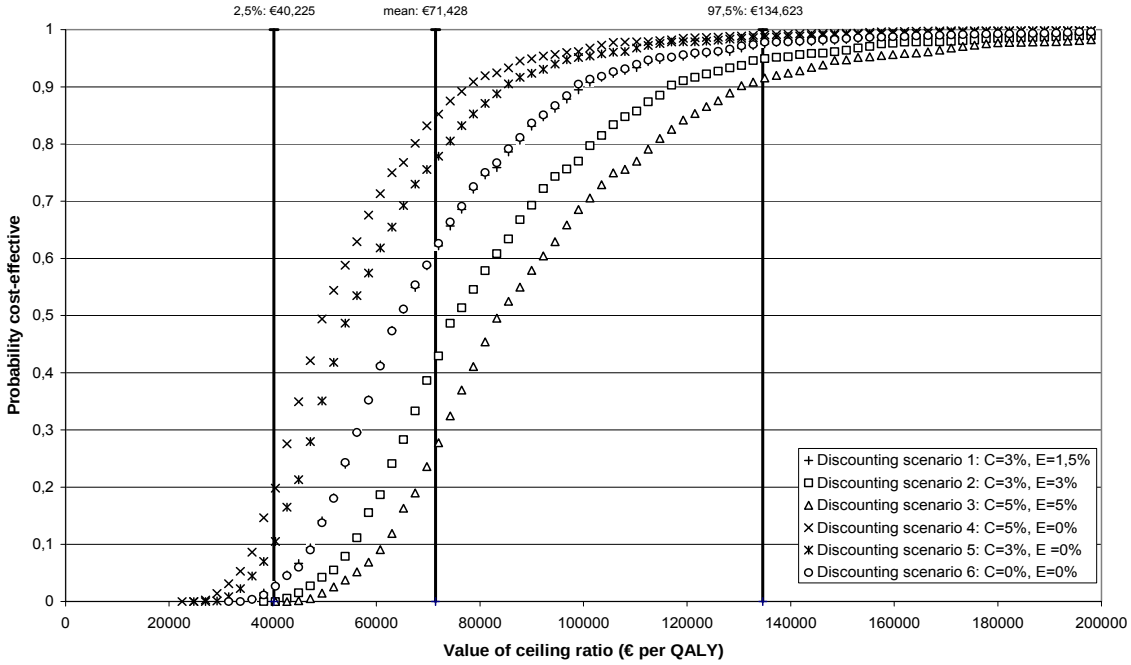
Table 28: Impact of the discount rates on the base-case results (SCD-HeFT, Extrapolation scenario 1) (All costs in Euro 2005)

Discounting scenario		IC		IE (LYG)		IE (QALY gained)		ICER (€/LYG)		ICER (€/QALY gained)	
		Lower bound 95% CI	Upper bound 95% CI	Lower bound 95% CI	Upper bound 95% CI	Lower bound 95% CI	Upper bound 95% CI	Lower bound 95% CI	Upper bound 95% CI	Lower bound 95% CI	Upper bound 95% CI
1	C: 3%	66.464 €		1,22		1,03		59.989 €		71.428 €	
	E: 1,5%	56.989 €	77.215 €	0,55	1,94	0,45	1,74	35.873 €	113.518 €	40.225 €	134.623 €
2	C: 3%	66.464 €		1,04		0,88		70.216 €		83.606 €	
	E: 3%	56.989 €	77.215 €	0,47	1,65	0,39	1,48	41.963 €	132.331 €	46.889 €	157.432 €
3	C: 5%	60.570 €		0,86		0,73		78.107 €		93.006 €	
	E: 5%	52.445 €	69.519 €	0,38	1,36	0,32	1,22	46.355 €	148.315 €	51.653 €	176.690 €
4	C: 5%	60.570 €		1,44		1,22		46.394 €		55.241 €	
	E: 0%	52.445 €	69.519 €	0,65	2,29	0,53	2,06	27.738 €	88.068 €	31.023 €	104.603 €
5	C: 3%	66.464 €		1,44		1,22		50.830 €		60.522 €	
	E: 0%	56.989 €	77.215 €	0,65	2,29	0,53	2,06	30.433 €	96.068 €	34.201 €	114.166 €
6	C: 0%	78.301 €		1,44		1,22		59.718 €		71.104 €	
	E: 0%	66.237 €	92.875 €	0,65	2,29	0,53	2,06	36.326 €	111.848 €	40.375 €	133.062 €

Figure 10 presents the cost-effectiveness acceptability curves for the 6 discounting scenarios. The curves represent, for each scenario, the probability that ICD implantation is cost-effective, depending on a given threshold value for a QALY. The mean ICER (€71,400 / QALY gained) and 95% CI (€40,200 - €134,600) for the base-case (i.e. with a discount rate of 3% for costs and 1.5% for effect according to the Belgian guidelines) are also reported on the graph. The two curves on the left represent the most favourable scenarios, i.e. scenarios where the benefits are not discounted.

The graph clearly shows that, under all plausible discounting scenarios, the probability that the ICER is below €30,000 per QALY is almost nil. Only 1.4% of the 1000 ICERS simulated for the fourth discounting scenario lied below this threshold. With a €45,000 per QALY threshold, the probability that ICD implantation is cost-effective was estimated at 6.7% for our base-case (discounting scenario 1) and 35% for the most optimistic scenario (scenario 4).

Figure 10: Cost-effectiveness acceptability curves for the 6 discounting scenarios (SCD-HeFT, extrapolation scenario 1)



5.1.7.2 Battery replacement frequency

The results of the 10 scenarios varying the frequency of device replacement are presented in Table 29. Due to the large cost of device replacement, if generators are replaced more frequently, the ICERs for the ICD patients become less favourable. Compared to our base-case (5-years replacement), however, if the battery life-duration is increased to 7 years, the cost-effectiveness ratio of ICD versus conventional therapy patients improves to €48,000 per LYG or €57,200 per QALY gained.

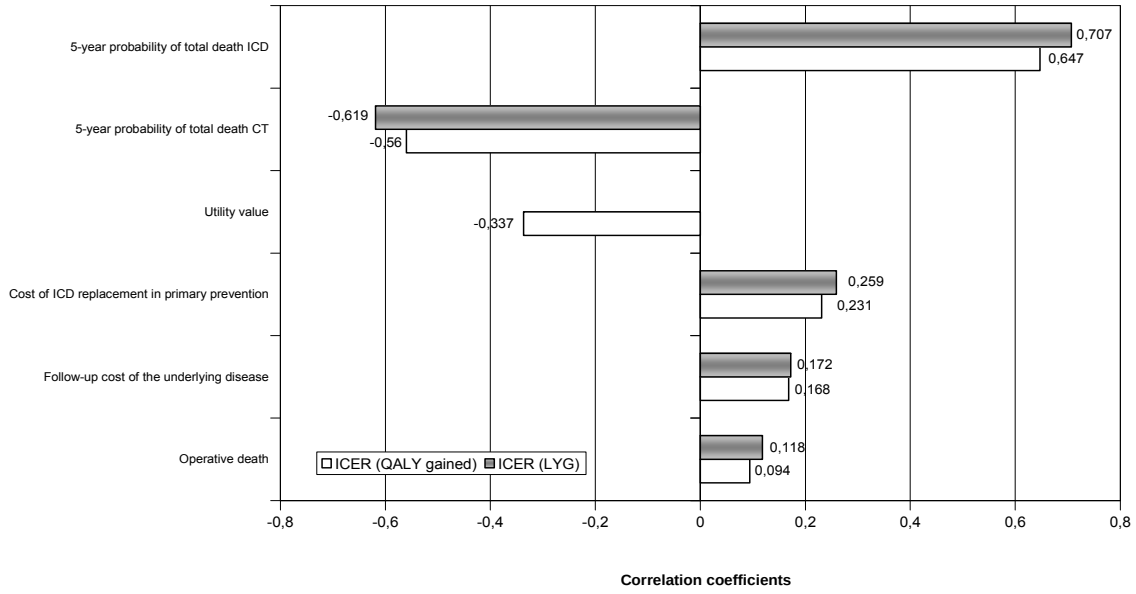
Table 29: Impact of battery replacement frequency on the base-case results (SCD-HeFT, extrapolation scenario 1) (All costs in Euro 2005)

Battery replacement ferquency	IC		IE (LYG)		IE (QALY gained)		ICER (€/LYG)		ICER (€/QALY gained)	
	Lower bound 95% CI	Upper bound 95% CI	Lower bound 95% CI	Upper bound 95% CI	Lower bound 95% CI	Upper bound 95% CI	Lower bound 95% CI	Upper bound 95% CI	Lower bound 95% CI	Upper bound 95% CI
every year	255.414 €		1,22		1,03		231.472 €		275.508 €	
	202.622 €	309.726 €	0,55	1,94	0,45	1,74	130.037 €	464.143 €	146.665 €	538.609 €
every 2 years	136.866 €		1,22		1,03		123.875 €		147.458 €	
	111.402 €	162.530 €	0,55	1,94	0,45	1,74	71.198 €	242.600 €	80.084 €	284.724 €
every 3 years	97.562 €		1,22		1,03		88.204 €		105.007 €	
	81.190 €	114.485 €	0,55	1,94	0,45	1,74	51.681 €	171.371 €	57.758 €	200.607 €
every 4 years	78.062 €		1,22		1,03		70.510 €		83.949 €	
	66.257 €	90.991 €	0,55	1,94	0,45	1,74	41.861 €	134.567 €	46.789 €	159.217 €
every 5 years	66.464 €		1,22		1,03		59.989 €		71.428 €	
	56.989 €	77.215 €	0,55	1,94	0,45	1,74	35.873 €	113.518 €	40.225 €	134.623 €
every 6 years	58.715 €		1,22		1,03		52.959 €		63.062 €	
	51.037 €	67.913 €	0,55	1,94	0,45	1,74	32.110 €	98.984 €	35.683 €	117.696 €
every 7 years	53.310 €		1,22		1,03		48.058 €		57.229 €	
	46.668 €	61.270 €	0,55	1,94	0,45	1,74	29.411 €	89.960 €	32.568 €	106.410 €
every 8 years	49.356 €		1,22		1,03		44.473 €		52.963 €	
	43.385 €	56.587 €	0,55	1,94	0,45	1,74	27.359 €	83.375 €	30.317 €	98.390 €
every 9 years	46.256 €		1,22		1,03		41.663 €		49.618 €	
	40.655 €	53.009 €	0,55	1,94	0,45	1,74	25.674 €	78.014 €	28.710 €	91.836 €
every 10 years	43.758 €		1,22		1,03		39.399 €		46.925 €	
	38.602 €	50.279 €	0,55	1,94	0,45	1,74	24.316 €	73.214 €	27.199 €	86.565 €

5.1.7.3 Probabilistic sensitivity analysis

The results of the probabilistic sensitivity analysis are illustrated in Figure 11. This graph shows which parameters contribute most to the uncertainty around the expected base-case ICER (€71,400 per QALY gained with 95% CI: €40,200 - €134,600; or €60,000 per LYG with 95% CI: €35,900 - €113,500). Only input parameters whose coefficient of correlation exceeds 0.1 are plotted. Both ICD and conventional therapy 5-year mortality rates were the most influential input parameters. ICD and conventional therapy total mortality rates act however in opposite direction: the higher the mortality in the conventional therapy group and the lower the mortality in the ICD group, the better (lower) the ICERs. Uncertainty in the utility values was also strongly negatively correlated with the uncertainty around the ICERs, higher estimates of the utilities being associated with a lower (better) ICER. The uncertainty around the cost estimates for ICD replacement in primary prevention and for the follow-up of the underlying disease also had a substantial contribution to the overall variability of the ICERs. All other input parameters (e.g. the proportion of patients on Amiodarone under conventional therapy, the ratio of the ICD-related follow-up costs in secondary versus primary prevention) only had a minor contribution to the uncertainty of the ICERs.

Figure 11: Probabilistic sensitivity analysis after 1,000 Latin Hypercube simulations (SCD-HeFT, extrapolation scenario 1)



5.2 BUDGET IMPACT ANALYSIS

Based on part 7 of the current report (Organisational issues), the extension of the indications for ICD implantation to primary prevention was estimated to lead to roughly 2000 new implants per year in Belgium. The impact on the 2007-2014 horizon budget of the Belgian Health Care payer of implanting 2000 new patients with an ICD instead of treating them by conventional therapy was evaluated and the results are reported in Table 30 and Table 31.

We assumed the number of new ICD implants would remain constant through years so that each cohort presented in the tables starts with 2000 primary prevention patients. Patients in the 2007 cohort are followed for 8 years (2007 up to 2014), patients in the 2008 cohort are followed for 7 years (2008 up to 2014), and so on. The same cost categories and assumptions as for the base-case cost-effectiveness analysis have been used.

All costs are expressed in Euros from the year 2005. For the yearly budget of ICD, the cost categories were ICD primo-implantation, ICD replacement, ICD follow-up (inpatient and outpatient) and the follow-up of the underlying disease. For the yearly budget of conventional therapy, the cost categories were Amiodarone, the follow-up of the underlying disease and the cross-over (primo-implantation, replacement and follow-up). The values (mean cost and 95% CI) presented in the tables were obtained after a run of 1000 simulations of the cost-effectiveness model, with a zero discount rate for costs.

The total per column in Table 30 represents the total yearly budget consumed if ICD implantation of 2000 new primary prevention patients starts in 2007 and is carried on each subsequent year. Starting with an initial budget of €68,800,000 in 2007, the yearly budget gradually increases in 2008-2011 due to the cumulated (ICD- and non-ICD-related) follow-up costs of the (still living) patients implanted in the preceding years. In 2012, the foreseen budget rises sharply (up to €154,500,000) to allow for the replacement of the primo-ICD's implanted 5-years ago (in 2007). In the years after, the budget steadily rises due the continuously increasing number of ICD patients to be followed.

The net cost to be paid by the Health Authorities for the 2000 primary prevention patients to switch from a conventional therapy to an ICD treatment was computed by subtracting the total yearly budget for ICD (Table 30) by the total yearly budget for conventional therapy (Table 31). The results are presented in Table 30. The net cost remains fairly stable in the first two years, i.e. at around €56,000,000. In 2009, the net budget drops as a result of the avoided cost of ICD primo-implantation in cross-over patients and reaches around €51,250,000. This net cost slightly increases over years due to the cumulated ICD-related follow-up costs of the surviving patients. As expected, the net cost almost doubles because of ICD replacement in the fifth year post primo-implant (€100,900,000 in 2012) and then drops again in 2014 (net cost of €99,950,000) due to the avoided cost of ICD replacement in cross-over patients.

Table 30: Budget impact of implanting 2000 new primary prevention patients with an ICD (Horizon 2007-2014) (All costs in Euro 2005)

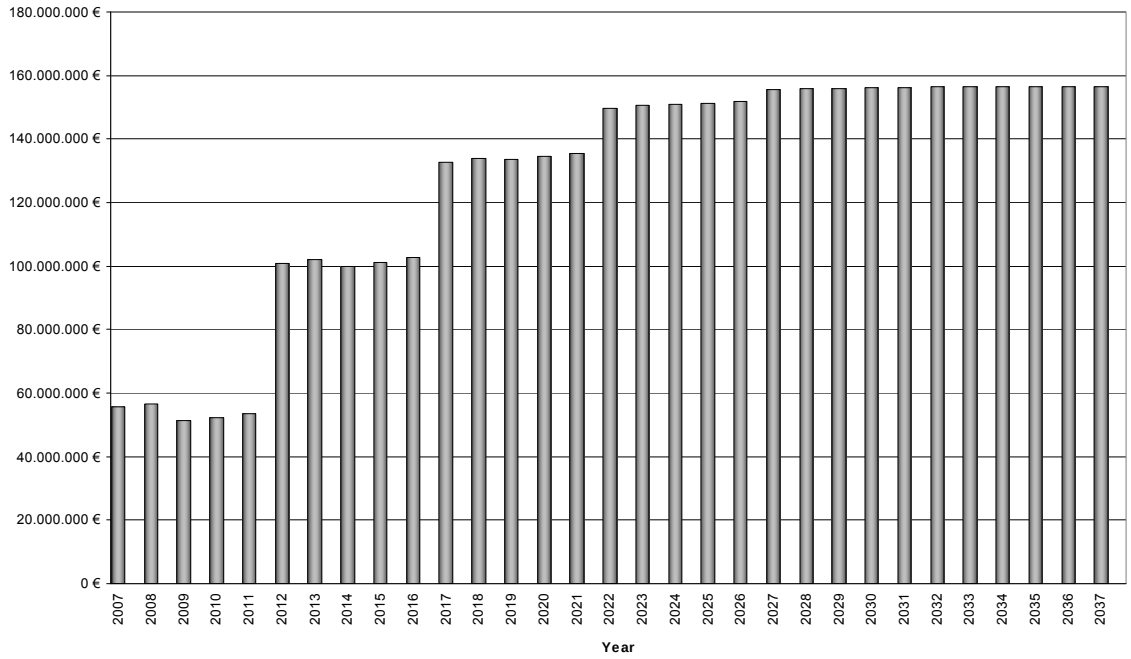
Cohort year	Cost categories	Costs (and 95% confidence interval) of the cohort in the follow-up year:									
		2007	2008	2009	2010	2011	2012	2013	2014		
2007	ICD primo-implantation in primary prevention	54,232,580 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €		
		52,558,640 € 55,805,600 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €		
	ICD replacement in primary prevention	0 €	0 €	0 €	0 €	0 €	46,179,380 €	0 €	0 €		
		0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	36,285,060 € 56,187,960 €	0 € 0 €	0 € 0 €		
	ICD follow-up in primary prevention	1,497,997 €	632,971 €	476,657 €	673,472 €	649,416 €	603,271 €	556,226 €	510,564 €		
		890,184 € 2,459,606 €	516,762 € 804,456 €	401,098 € 564,863 €	439,601 € 1,063,848 €	413,377 € 1,046,910 €	383,939 € 968,681 €	353,716 € 893,239 €	323,571 € 822,650 €		
	Underlying disease follow-up	13,057,310 €	7,908,676 €	6,881,714 €	7,672,056 €	7,275,910 €	6,758,860 €	6,231,728 €	5,720,108 €		
		7,758,914 € 18,346,086 €	4,699,072 € 11,100,732 €	4,088,418 € 9,607,876 €	4,557,378 € 10,745,728 €	4,321,450 € 10,206,314 €	4,011,364 € 9,510,442 €	3,690,780 € 8,761,708 €	3,389,276 € 8,064,376 €		
2008	ICD primo-implantation in primary prevention		54,232,580 €	0 €	0 €	0 €	0 €	0 €	0 €		
			52,558,640 € 55,805,600 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €		
	ICD replacement in primary prevention		0 €	0 €	0 €	0 €	0 €	46,179,380 €	0 €		
			0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	36,285,060 € 56,187,960 €	0 € 0 €		
	ICD follow-up in primary prevention		1,497,997 €	632,971 €	476,657 €	673,472 €	649,416 €	603,271 €	556,226 €		
			890,184 € 2,459,606 €	516,762 € 804,456 €	401,098 € 564,863 €	439,601 € 1,063,848 €	413,377 € 1,046,910 €	383,939 € 968,681 €	353,716 € 893,239 €		
	Underlying disease follow-up		13,057,310 €	7,908,676 €	6,881,714 €	7,672,056 €	7,275,910 €	6,758,860 €	6,231,728 €		
			7,758,914 € 18,346,086 €	4,699,072 € 11,100,732 €	4,088,418 € 9,607,876 €	4,557,378 € 10,745,728 €	4,321,450 € 10,206,314 €	4,011,364 € 9,510,442 €	3,690,780 € 8,761,708 €		
2009	ICD primo-implantation in primary prevention			54,232,580 €	0 €	0 €	0 €	0 €	0 €		
				52,558,640 € 55,805,600 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €		
	ICD replacement in primary prevention			0 €	0 €	0 €	0 €	0 €	46,179,380 €		
				0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	36,285,060 € 56,187,960 €		
	ICD follow-up in primary prevention			1,497,997 €	632,971 €	476,657 €	673,472 €	649,416 €	603,271 €		
				890,184 € 2,459,606 €	516,762 € 804,456 €	401,098 € 564,863 €	439,601 € 1,063,848 €	413,377 € 1,046,910 €	383,939 € 968,681 €		
	Underlying disease follow-up			13,057,310 €	7,908,676 €	6,881,714 €	7,672,056 €	7,275,910 €	6,758,860 €		
				7,758,914 € 18,346,086 €	4,699,072 € 11,100,732 €	4,088,418 € 9,607,876 €	4,557,378 € 10,745,728 €	4,321,450 € 10,206,314 €	4,011,364 € 9,510,442 €		
2010	ICD primo-implantation in primary prevention				54,232,580 €	0 €	0 €	0 €	0 €		
					52,558,640 € 55,805,600 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €		
	ICD replacement in primary prevention				0 €	0 €	0 €	0 €	0 €		
					0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €		
	ICD follow-up in primary prevention				1,497,997 €	632,971 €	476,657 €	673,472 €	649,416 €		
					890,184 € 2,459,606 €	516,762 € 804,456 €	401,098 € 564,863 €	439,601 € 1,063,848 €	413,377 € 1,046,910 €		
	Underlying disease follow-up				13,057,310 €	7,908,676 €	6,881,714 €	7,672,056 €	7,275,910 €		
					7,758,914 € 18,346,086 €	4,699,072 € 11,100,732 €	4,088,418 € 9,607,876 €	4,557,378 € 10,745,728 €	4,321,450 € 10,206,314 €		
2011	ICD primo-implantation in primary prevention					54,232,580 €	0 €	0 €	0 €		
						52,558,640 € 55,805,600 €	0 € 0 €	0 € 0 €	0 € 0 €		
	ICD replacement in primary prevention					0 €	0 €	0 €	0 €		
						0 € 0 €	0 € 0 €	0 € 0 €	0 € 0 €		
	ICD follow-up in primary prevention					1,497,997 €	632,971 €	476,657 €	673,472 €		
						890,184 € 2,459,606 €	516,762 € 804,456 €	401,098 € 564,863 €	439,601 € 1,063,848 €		
	Underlying disease follow-up					13,057,310 €	7,908,676 €	6,881,714 €	7,672,056 €		
						7,758,914 € 18,346,086 €	4,699,072 € 11,100,732 €	4,088,418 € 9,607,876 €	4,557,378 € 10,745,728 €		
2012	ICD primo-implantation in primary prevention						54,232,580 €	0 €	0 €		
							52,558,640 € 55,805,600 €	0 € 0 €	0 € 0 €		
	ICD replacement in primary prevention						0 €	0 €	0 €		
							0 € 0 €	0 € 0 €	0 € 0 €		
	ICD follow-up in primary prevention						1,497,997 €	632,971 €	476,657 €		
							890,184 € 2,459,606 €	516,762 € 804,456 €	401,098 € 564,863 €		
	Underlying disease follow-up						13,057,310 €	7,908,676 €	6,881,714 €		
							7,758,914 € 18,346,086 €	4,699,072 € 11,100,732 €	4,088,418 € 9,607,876 €		
2013	ICD primo-implantation in primary prevention							54,232,580 €	0 €		
								52,558,640 € 55,805,600 €	0 € 0 €		
	ICD replacement in primary prevention							0 €	0 €		
								0 € 0 €	0 € 0 €		
	ICD follow-up in primary prevention							1,497,997 €	632,971 €		
								890,184 € 2,459,606 €	516,762 € 804,456 €		
	Underlying disease follow-up							13,057,310 €	7,908,676 €		
								7,758,914 € 18,346,086 €	4,699,072 € 11,100,732 €		
2014	ICD primo-implantation in primary prevention								54,232,580 €		
									52,558,640 € 55,805,600 €		
	ICD replacement in primary prevention								0 €		
									0 € 0 €		
	ICD follow-up in primary prevention								1,497,997 €		
									890,184 € 2,459,606 €		
	Underlying disease follow-up								13,057,310 €		
									7,758,914 € 18,346,086 €		
Total costs per year		68,787,887 €	77,329,534 €	84,687,905 €	93,033,433 €	100,958,758 €	154,500,270 €	161,288,224 €	167,518,896 €		
Net cost per year		55,778,081 €	56,591,333 €	51,256,384 €	52,330,500 €	53,503,231 €	100,915,061 €	102,193,414 €	99,950,140 €		

Table 31: Budget impact on treating 2000 new primary prevention patients with conventional therapy (horizon 2007-2014) (All costs in Euro 2005)

Cohort year	Cost categories	Costs (and 95% confidence interval) of the cohort in the follow-up year:															
		2007		2008		2009		2010		2011		2012		2013		2014	
2007	ICD implantation in secondary prevention (cross-over)	0 €	0 €	0 €	0 €	6,058,086 €	6,905,872 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €
	ICD replacement in secondary prevention	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	3,550,604 €	4,137,138 €
	Amiodarone	11,886 €	14,204 €	10,301 €	12,324 €	9,418 €	11,276 €	8,612 €	10,341 €	7,874 €	9,497 €	7,148 €	8,661 €	6,425 €	7,816 €	5,741 €	7,039 €
	Follow-up (underlying disease and ICD)	12,997,920 €	18,241,642 €	7,718,094 €	10,849,552 €	6,625,816 €	9,310,510 €	7,262,800 €	10,196,378 €	6,744,720 €	9,420,806 €	6,122,534 €	8,586,358 €	5,503,176 €	7,727,472 €	4,917,602 €	6,922,662 €
2008	ICD implantation in secondary prevention (cross-over)			0 €	0 €	0 €	0 €	6,058,086 €	6,905,872 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €
	ICD replacement in secondary prevention			0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €
	Amiodarone			11,886 €	14,204 €	10,301 €	12,324 €	9,418 €	11,276 €	8,612 €	10,341 €	7,874 €	9,497 €	7,148 €	8,661 €	6,425 €	7,816 €
	Follow-up (underlying disease and ICD)			12,997,920 €	18,241,642 €	7,718,094 €	10,849,552 €	6,625,816 €	9,310,510 €	7,262,800 €	10,196,378 €	6,744,720 €	9,420,806 €	6,122,534 €	8,586,358 €	5,503,176 €	7,727,472 €
2009	ICD implantation in secondary prevention (cross-over)					0 €	0 €	0 €	0 €	6,058,086 €	6,905,872 €	0 €	0 €	0 €	0 €	0 €	0 €
	ICD replacement in secondary prevention					0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €
	Amiodarone					11,886 €	14,204 €	10,301 €	12,324 €	9,418 €	11,276 €	8,612 €	10,341 €	7,874 €	9,497 €	7,148 €	8,661 €
	Follow-up (underlying disease and ICD)					12,997,920 €	18,241,642 €	7,718,094 €	10,849,552 €	6,625,816 €	9,310,510 €	7,262,800 €	10,196,378 €	6,744,720 €	9,420,806 €	6,122,534 €	8,586,358 €
2010	ICD implantation in secondary prevention (cross-over)							0 €	0 €	0 €	0 €	6,058,086 €	6,905,872 €	0 €	0 €	0 €	0 €
	ICD replacement in secondary prevention							0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €
	Amiodarone							11,886 €	14,204 €	10,301 €	12,324 €	9,418 €	11,276 €	8,612 €	10,341 €	7,874 €	9,497 €
	Follow-up (underlying disease and ICD)							12,997,920 €	18,241,642 €	7,718,094 €	10,849,552 €	6,625,816 €	9,310,510 €	7,262,800 €	10,196,378 €	6,744,720 €	9,420,806 €
2011	ICD implantation in secondary prevention (cross-over)									0 €	0 €	0 €	0 €	6,058,086 €	6,905,872 €	0 €	0 €
	ICD replacement in secondary prevention									0 €	0 €	0 €	0 €	0 €	0 €	0 €	0 €
	Amiodarone									11,886 €	14,204 €	10,301 €	12,324 €	9,418 €	11,276 €	8,612 €	10,341 €
	Follow-up (underlying disease and ICD)									12,997,920 €	18,241,642 €	7,718,094 €	10,849,552 €	6,625,816 €	9,310,510 €	7,262,800 €	10,196,378 €
2012	ICD implantation in secondary prevention (cross-over)											0 €	0 €	0 €	0 €	6,058,086 €	6,905,872 €
	ICD replacement in secondary prevention											0 €	0 €	0 €	0 €	0 €	0 €
	Amiodarone											11,886 €	14,204 €	10,301 €	12,324 €	9,418 €	11,276 €
	Follow-up (underlying disease and ICD)											12,997,920 €	18,241,642 €	7,718,094 €	10,849,552 €	6,625,816 €	9,310,510 €
2013	ICD implantation in secondary prevention (cross-over)													0 €	0 €	0 €	0 €
	ICD replacement in secondary prevention													0 €	0 €	0 €	0 €
	Amiodarone													11,886 €	14,204 €	10,301 €	12,324 €
	Follow-up (underlying disease and ICD)													12,997,920 €	18,241,642 €	7,718,094 €	10,849,552 €
2014	ICD implantation in secondary prevention (cross-over)															0 €	0 €
	ICD replacement in secondary prevention															0 €	0 €
	Amiodarone															11,886 €	14,204 €
	Follow-up (underlying disease and ICD)															12,997,920 €	18,241,642 €
Total cost per year		13,009,806 €		20,738,201 €		33,431,521 €		40,702,933 €		47,455,527 €		53,585,209 €		59,094,809 €		67,568,756 €	

The projected net cost over the next 30 years is plotted in Figure 12. The graph illustrates that, due to their mortality, the cumulated yearly number of ICD patients alive will stabilize, so that the yearly incremental budget would finally reach equilibrium. This equilibrium is expected to occur 15 years after the start of the extension of the ICD indications (in 2022), time by which the net ICD implantation cost to the Health Authorities would stabilize at around €156,000,000 per year.

Figure 12: Projected yearly net cost of extending the indications for ICD implantation to primary prevention (All costs in Euro 2005)



5.3 CONCLUSION

This economic evaluation found that, in Belgium, ICD implantation in primary prevention is associated with a lifetime ICER ranging from €71,400 (95% CI: €40,200 - €134,600) to €132,000 (95% CI: €71,600 - €261,500) per QALY, depending on the extrapolation scenario. Even using the most optimistic extrapolation scenario, the ICER could only be decreased to €46,900 per QALY with a battery life of 10 years, to €50,300 per QALY using MADIT II data or to €55,200 per QALY with discount rates for costs and effects set at 5 and 0%, respectively.

Though a useful tool for decision-makers to distinguish between more efficient and less efficient health technologies, there are theoretical and pragmatic difficulties in eliciting a fixed ICER threshold below which a technology would automatically be defined as cost-effective[101]. In Belgium so far, no such ICER range was defined. In the UK however, based on previously assessed technologies, NICE has described ranges in which the probability of acceptance of a health intervention varies[102]:

- Cost per QALY < £20,000 (< €30,000): intervention likely to be accepted
- Cost per QALY between £20,000 and £30,000 (from €30,000 to €45,000): needs additional factors (e.g. the innovative nature of the technology, the particular features of the condition and population receiving the technology) to justify acceptance of the intervention
- Cost per QALY > £30,000 (> €45,000): the case on the additional factors have to be extremely strong to justify acceptance of the intervention.

If we appraise the most plausible ICERs found in our model against the NICE thresholds, we would need strong arguments, other than the cost-effectiveness estimates, for this technology to be accepted.

From the budget-impact analysis, it was estimated that extending the indications for ICD implantation to primary prevention (as defined in MADIT II and/or SCD-HeFT) would lead to 2000 new implantations per year in Belgium. After a stabilisation period, this was estimated to cost an additional €156,000,000 per year to the Health Authorities.

- **Compared with conventional therapy, prophylactic ICD implantation improves life-expectancy by 0.53 – 1.22 discounted years (0.45 – 1.03 discounted QALYs) at a cost of €71,400 (95% CI: €40,200 - €134,600) to €132,000 (95% CI: €71,600 - €261,500) per QALY gained, depending on the extrapolation scenario envisaged.**
- **After a stabilisation period, the net cost to the Health Authorities of extending the ICD indications to primary prevention was estimated at €156,000,000 per year.**

6 PATIENT ISSUES

Several RCTs have indicated the effectiveness of an ICD in reducing mortality in patients at high risk for sudden cardiac arrest. In this chapter, we will reflect further on the impact of implanting such a device on the well-being and the quality of life of the patient. The chapter focuses, as the entire report, on primary prevention indications of ICD implantation. Indeed, with the growing evidence on clinical effectiveness attention is shifting from the issue of mortality as an outcome towards the impact of ICD on quality of life. Questions can be raised about the particular issue of "assurance" for the patients and their peers but also on issues of mental, social and physical discomforts coming together with the use of the device.

In a first step, we will describe the issues that are mainly related to quality of life at the level of the individual patient. Next, we consider societal considerations (social justice) of introducing this technology.

6.1 METHODOLOGY

6.1.1 Literature

To describe implications for the patients in his/her life after an ICD implant for preventive purpose, we reviewed the literature from 1996 to 2007 in databases Medline, Embase, Psychinfo, Sociological abstract. Details are reported in appendices to this chapter.

We have also consulted the HTA reports identified in the clinical and economic part of the present report.

6.1.2 Patient organisations

To describe what the major problems or worries of ICD patients are, we have searched for patients' organizations in Belgium. As we have not identified a Belgian ICD-patients organisation, we visited the web-sites of the Dutch and French patient organisations. We have also contacted the French one by telephone.

6.1.3 Ethical issues

A roundtable meeting was organised with academic experts on "Ethical issues in patients eligible for implantation of an implantable cardioverter defibrillator (ICD)".

Eight experts were recruited in French and Flemish-speaking groups with a different normative cadre. They were philosopher, physician, sociologist or pharmacologist.

They were contacted by e-mail. Information on the technology, on the clinical effectiveness and very briefly on the patient issues as published in the literature were sent to them.

The discussion was intended to take place in a time frame of 3-hours.

After having received a brief oral description of the technology, participants were asked to reflect on two main questions:

- Informing the patient on decisions to implant an ICD: The health care-provider-patient relationship: what are the general ethical principles to be considered and what are the issues of ethical risk communication?
- Issues of social justice and equity in providing ICDs: What considerations should be taken into account and can limits be imposed from a policy point of view on the persons entitled to have an ICD implanted?

Some case reports have been distributed to be assessed individually by the ethical experts and discussed in the group in order to find out to what extent ethical issues are translated to policy recommendations in ICD (appendix).

Discussion were recorded for practical purpose but not typewritten. Two reporters have taken notes during the discussion group.

Each participant was asked to speak his/her mother tongue and to briefly explain the concepts they were using.

6.2 FINDINGS: THE PATIENT'S PERSPECTIVE

Studies related to patient issues of ICD implants for primary prevention are scarce. Most available studies focus on secondary prevention, probably because the evidence for the benefit of ICDs in primary prevention has emerged later. A very limited number of studies consider generic QoL in primary prevention alone while the literature on more specific items of QoL do not make a distinction between primary and secondary prevention. Furthermore, in the small number of studies that we could find concerning ICD in primary prevention, patients are not characterized by their presenting symptoms or functional status. This means that current evidence can only help in informing patients in a more generic way, irrespective of the medical indication for the implant or the functional status of the patient.

6.2.1 ICD and Quality of Life

We first discuss the literature on the impact of the ICD on quality of life (QoL) in general. Next we will focus on some more specific items related to QoL.

6.2.1.1 Generic Quality of Life measures

QoL is a concept that is related to many aspects of life, including a person's physical health, psychological state, level of independence, social relationships, personal beliefs and relationships to salient features of the environment. There is no consensus over a definition of QoL[103]. The meaning of the concept may change from one study to another. As a consequence, several tools are used to measure QoL, with different focus on one aspect or another: wellbeing, psychological disturbance, health outcomes, etc. Consequently, studies are difficult to compare.

Most reviews discussing QoL after an ICD implant combine both primary and secondary prevention studies[104, 61, 105, 63, 106, 107, 94]. Only one very recent Canadian HTA (2007) report analysed studies on primary prevention exclusively[17].

For the generic QoL issues we only discuss RCTs where ICD therapy is compared to another treatment and in which the results related to primary prevention issues could be isolated (Table 32). We have identified 4 studies. We excluded one (PainFREE RX II)[108] because it focused on different intervention modes of an ICD (pacing vs. shock), rather than comparing ICD vs. no-ICD.

We present the results of the selected studies in a narrative way. It is impossible to make a meta-analysis of the outcomes in the selected studies because of the diversity of the scales used to assess QoL.

Details of the studies have been described in a preceding chapter.

Table 32: Primary prevention trials of QoL in ICD patients

Study	Context	QoL measures	Follow-up	Results
CABG-Patch[109]	Primary prevention, Comparison between ICD (n= 446) and no ICD (n=454) in patients undergoing CABG.	- SF-36 (7 subscales) - Reported health transition - work status - body image	6 months	- Feeling that their health had improved during the preceding year more in control group than in ICD group - Lower level of psychological wellbeing in ICD patients but association with shocks received or not
AMIOVIRT[39]	Primary prevention In non-ischemic dilated cardiomyopathy. Amiodarone (n=219) vs ICD (n=219)	- Quality of Wellbeing Schedule - State trait anxiety Inventory	At baseline (randomization) and during follow up visits (every 4 months)	- No difference between amiodarone and ICD patients at baseline and at one year - No difference in both groups of Qol after 1 year follow-up
MADIT II[110]	Primary prevention, ischemic cardiomyopathy ICD (n=658) vs conventional treatment (n=431)	- Health Utility Index 3 (HUI3)	At baseline, 3,12,24,36 months	No difference in QoL

QoL is studied from different point of views: e.g. comparing QoL before vs. after implant, focusing on the occurrence of shocks or comparing patients treated medically vs. patients treated with an ICD.

CABG-Patch Trial: In the CABG-Patch Trial, QoL was collected at baseline (randomization) and then 6 months after CABG surgery[109]. To assess QoL, 3 measurement tools were used:

- generic health concepts as perceived by the patients is measured through 7 subscales of the SF-36 health survey i.e. (1) perception of general health status, (2) physical functioning, (3) physical role functioning, (4) bodily pain, (5) social functioning, (6) emotional role functioning and (7) mental health.
- Information about the patients' reported health transition by asking them to assess their current health status relative to 1 year earlier.
- Patients' work status.
- Perception of body.

The authors categorized indicators in 3 groups: perception of health status, ability to function and psychological wellbeing.

Sixty-eight percent of the 719 included patients did complete the instrument. Patients in the control group reported that they felt their health had improved more over the preceding year than patients in ICD group. They also felt that their day-to-day activities were limited less because of their medical condition. Regarding the psychological wellbeing, they had a higher score, though these differences disappeared when comparing non-ICD patients with ICD-patients that did not receive shocks. ICD shocks are therefore likely to explain ICD patients' lower mental health scores.

AMIOVIRT: This study compared the effects of amiodarone versus ICD in patients with a nonischemic dilated cardiomyopathy [39]. 219 patients were randomly enrolled in each group. No placebo group was included. In this study, two different tools were used to approach QoL:

- the Quality of Wellbeing Schedule
- the State Trait Anxiety Inventory.

The QoL was on average the same in both groups at baseline and at 1 year. The authors concluded that because neither amiodarone nor ICD did affect the QoL of the patients, the therapeutic choice between amiodarone or ICD should not to be influenced by QoL issues for this patient population.

MADIT II: This study enrolled 1232 high-risk patients for SCD in US and Europe. The study compares an ICD implant to medical treatment. In order to weight the survival benefit of ICD with the quality of life based on patient preferences, health-related quality of life (HRQoL) was assessed in a sub-sample of 1089 subjects in the US[110]. The self-administered Health Utility Index 3 was used to measure HRQoL for 8 attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain and discomfort. Years gained measured in the study were weighted by this score to convert the benefit of both treatments in QALYs. Since the measured QoL decreases over time in the ICD group, the benefit of years gained is gradually reduced (corrected) over time. Authors conclude that there is no difference in QALYs gained between ICD-implanted patients and conventional treated patients after 3 years. This conclusion remains when QALYs are calculated only in patients alive (difference=-0.037 QALYs, p=0.64).

In conclusion, there are not many studies that looked at QoL in the context of primary prevention. Findings tend to argue that, for this indication, QoL, as it is measured in the selected studies, is not affected by ICD implant. However, the measure of QoL is not standardized through the 3 studies and cover different aspects of it. A general conclusion on QoL is therefore difficult to draw.

6.2.1.2 Selected aspects of Quality of Life

We have identified 9 reviews and 1 HTA-report that pointed out specific aspects of QoL or wellbeing of ICD patients(Table 33). The quality of the reviews was assessed using criteria proposed by the Dutch Cochrane Centerg111}. For the HTA report, we used the INHATA checklist to assess quality112. We did not find literature specifically related to selected aspects of Quality of Life among patients implanted for primary prevention. We additionally used primary (qualitative) studies to illustrate some findings.

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g The Dutch Cochrane grid[111] suggest to assess if the effect is clinically pertinent, if the clinical question is clear, if results are clearly given in a table, is the confidence interval mentioned, is the search strategy adequate, is publication bias examined, what are the inclusion exclusion criteria for studies, is the quality of the studies examined, is outcome assessment blinded or double blinded? We have qualified a review as 'good' if the score is >=7/8.5 – fair between 4-6.5/8.5 and poor under 4/8.5.

Table 33: reviews about impact of ICD on the patient

Reviews	Context	issues	Results for QoL related issues	Quality of the review
Gallagher, 1997[104]	Review on QoL and ICD	-psychological issues -physical function -work and social function -coping strategies - implications for research	-fear of shocks -sources of anxiety but same level than non-ICD SCA patients -contradictory findings about change in activities -modification in employment status -coping strategies: optimism, evasion, denial, overprotectiveness	Poor
Sears, 2002[113]	Review of the published literature on QoL and psychological functioning of ICD patients	- QoL - Return to work - Incidence and impact of psychological issue - Effect of shocks on QoL - implications	- no change in QoL but younger and female have worse QoL. -return to work is possible -relation between shocks, psychological distress and QoL	Poor
Sears 2003[114]	Review on the published literature on shocks and storm in ICD patients	-medical and psychological aspect of of ICD shocks and storm description of a model of biopsychosocial management for patients following the experience of ICD storms	Interdisciplinary management of patients with multiple shocks or with experience with ICD storm is advised	Poor
McCready, 2003[115]	Impact of ICD on psychological wellbeing and QoL (Recent large randomized trials)	- psychological effect - QoL	Stress anxiety Mood disturbance Sexual dysfunction sense of loss of control	Poor
Burke, 2003[105]	To identify key psychological characteristics associated with ICD implantation – meta analysis	- QoL - Mood	No evidence of effect of ICD implant on QoL or mood, neither regarding shocks received	Good
Shea, 2004[116]	Review of published studies on the impact on QoL with regard to driving, occupational concerns and recreational issues	-QoL - driving - occupational concerns - recreational issues -implication for nursing	-driving restrictions are probably too conservative for most patients -ICD has consequences for several employments - several recreational activities have to be restricted	Poor

Sola, 2005[117]	Review of the studies addressing post implant psychological disturbance	- Link with psychological theories - Patterns and prediction of psychopathology after ICD implant - Demographics - Personal psychology - Social and family context - Experiences with ICD QoL	- After an ICD implantation, anxiety, depression, specific fears regarding device firing and fear of death are described - Recovery of QoL at 1 year after a decline in the post-implant period -younger patients show increased anxiety disorder	fair
Thomas, 2006[118]	Review the research on psychological status and QoL of patients with ICD	- QoL - Psychological distress - Shocks - Age - Time since implantation	- No clear conclusion on psychological distress after ICD implant - Difference in QoL according to shock status seem to be due to both time since implant and shocks status	fair
Groenveld, 2006[107]	Review of studies on healthcare costs and QoL effects of ICD	- QoL - Effect of shocks on QoL - Psychological issue - Driving and social relations - Sexuality - Work and leisure activities	Little independent effect of shocks on QoL Driving restriction is correlated with decrease in self-efficacy and patients frequently resumed to drive despite restrictions - ICD has impact on patient sexuality (decrease in sexual interest, regain after 2 years)	fair
Ho, 2007[17]	HTA report on ICD for primary prevention	-clinical efficacy -cost-effectiveness -psychosocial issues	- More study is needed regarding QoL and ICD implant for primary prevention - it is difficult to pinpoint causality between health status, QoL and ICD shocks - the most common psychological issue reported in secondary reviews are anxiety and depression	Good

As was the case for general quality of life issues, many reviews point the lack of evidence due to methodological flaws such as small sample size, low response rate and the retrospective design of the studies. More, they concern specific patients that already have symptoms. Results have therefore to be read with caution. We summarize the findings here:

Psychological issues

The psychological adjustment after an ICD implantation seems to be a major point in the literature, including depression and anxiety. Nevertheless, we have identified no study approaching this problem in the context of primary prevention.

Substantial evidence indicates that patients with an ICD experience psychological distress,[118] most commonly anxiety, specific fears regarding the device firing and fear of death.[117] Gallagher reported that, anxiety in ICD patients was similar to survivors of SCA-non-ICD patients. However, ICD-recipients express that worries about shocks, activity, work, body image, heart condition, medication, driving, costs and follow up visits, sexual activities and social support may have contributed to their anxiety[104].

Younger patients seem to suffer more psychological distress[118], probably because they do not see the device as potentially prolonging their life, but rather as imposing dramatic lifestyle changes, decreasing independence and because of concerns with body image.[117].

Studies about gender-related susceptibility are inconclusive. Samples are often mainly composed of males.[117]

The link between psychological distress and the QoL has been studied in 2 studies which indicate that higher anxiety is associated with poorer QoL ([119] cited by [118]). Moreover, it appears that anxious and depressed patients had poorer QoL than other ICD patients ([120]cited by [118]).

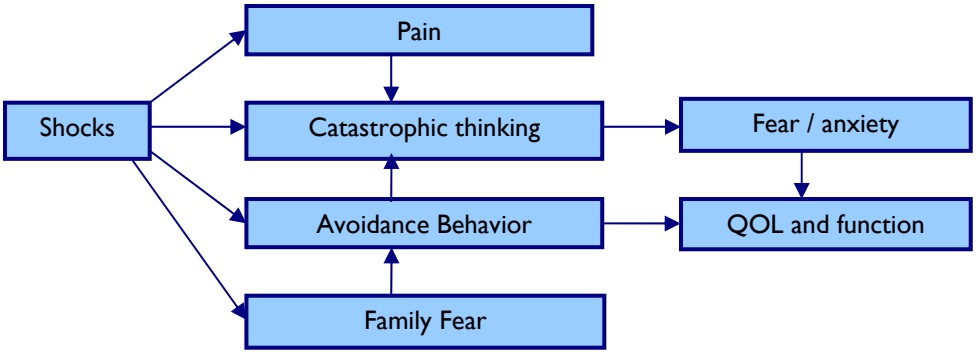
Determining whether psychological disturbance is caused by or associated with ICD is challenging but impossible to answer so far. Moreover, poor psychosocial outcome in ICD patients may result from the underlying cardiac condition, rather than as a response to the implantation of the device as such [17]. The lack of evidence is due to the use of invalid diagnostic instruments, the size of the samples in the studies, the study-design and the potential presence of co-morbid conditions that are potential confounders[115]. These elements make it difficult to determine whether poor psychological adjustment results from the ICD implant, the experience of shocks or the underlying cardiac condition[105].

Several authors relate psychological issues and shocks and particularly focus on the impact of the shocks on the patient's wellbeing. In the CABG-Patch study, it is clearly demonstrated that psychological wellbeing has been worsened if the patient has received shocks[109]. This could be due to the fact that shocks may reinforce a sense of illness, and therefore decrease the perceived QoL. Unpredictability of the shocks is a stressor[121] and post shock anxiety is a serious adverse side effect of the ICD therapy[122]. According to Gallagher et al[104], people fear shocks because they are unpredictable, painful, induce loss of control or because they could be unsuccessful. On the other hand, it has been noticed that shocks can be reasuring as the first experience of shock provides confirmation that the device works[123].

An increased frequency of shocks results in greater anxiety and depression[118]. The occurrence of an ICD storm (2 or more shocks in 24 hours) that affects 10 to 20% of ICD patients is particularly alarming for the patients because they feel helpless and it causes distress in families. They have thus to be managed from a medical point of view as well as from a psychological point of view[114].

Sears[113] proposes a hypothetic model on the interrelationship between shocks, psychological adjustment and QoL (Figure 13).

Figure 13: Hypothesised interrelationship between shocks, psychological distress and quality of life (QoL)[113]



But the association between shocks and a deteriorated QoL could reflect more an effect of the time since implant[105] or to both time since ICD implantation and shock status[118].

Impact on the lifestyle, social relationships and family

ICD patients report subtle changes in their lifestyle, since they have to adapt to the new situation [123]. Several topics are relevant for the patient lifestyle: driving restriction, employment, activity level, kind of leisure activities and sexual activities. Modifications in the familial and social relationship are also reported.

A major source of concern to patients are the **driving restrictions** that are imposed on them[124]. The ICD "labels" a person as being at risk for a SCA. The loss of consciousness as such is not necessarily prevented by the shock. Moreover, some ICD patients may experience inappropriate shocks that can induce temporary loss of control. Driving restrictions induce significant lifestyle adjustments for most ICD patients: it impacts personal freedom, eligibility for continued employment and overall QoL[116]. Social isolation is also reported in a UK sample[124]. The time to wait before being authorized to drive again was found to be difficult by the patient and his partner. The driving restriction is also a source of conflicts when it leads to changing driving roles between partners[124]. Several authors[104, 125, 107] report that the restrictions seem to be poorly respected.

In the US, the 1996 guideline imposed permanent driving restriction for commercial purpose and 6 months for personal use (if no shock was received during this period). The guideline was just updated (2007) because of the evolution of the ICD technology and the expansion of the indication for primary prevention. At present, patients who received an ICD for prophylactic purpose are restricted from driving a private vehicle for at least one week. In absence of symptoms, they are then allowed to resume driving[126]. In Canada, a consensus conference has recommended that patients with an ICD implant for primary prevention are restricted from driving during 4 weeks after surgery. Commercial driving remains forbidden[127]. Patients who have declined the ICD while recommended have no restriction for private driving but is disqualified for commercial driving. In the United Kingdom, asymptomatic patients who have been ICD implanted for prophylactic purpose can drive from one month after the placement of the device[128]. In the Netherlands the duration is 2 months[129] and in France, they could resume driving on medical advice[130].

Living with an ICD could also influence the **employment** status. The ICD implant restricts the execution of certain professional activities. Shea documents that occupations that include commercial driving, operating heavy machinery, and exposure to excessive heights or the use of motorized saws can be risky because inappropriate shocks could result from electromagnetic interference. The exclusion from professional tasks can have financial and emotional impact on the patient with an ICD[116].

Sears et al concluded that the majority of ICD patients who wish to return to work are capable of doing so[113]. Gallagher recalls that employment rates after ICD implant also depend on pre-existing cardiac disorder, unemployment, preceding SCAs, voluntary retirement and age of recipient[104].

Regarding the **activity level** in general, results of studies are difficult to compare because of methodological differences[104]. Some studies reported major effects while others found only minor impact. Shea adds that some patients reported to have 'anticipatory anxiety' before taking up commonplace activities[116]. Receiving shocks could lead to avoidance of activities that are associated with ICD firing[114, 131].

Some activities have to be undertaken with caution and after authorization of the physician because they increase the risk of injury (for the patient himself or for the others) in case of sudden incapacity: mountain biking, skiing, snorkelling, scuba diving, parachuting, boating[116]. Moreover, there are certain activities that could endanger the integrity of the implant: rowing or repetitive upper-body exercises. In this matter, Shea tells that younger patients in particular have concern about anxiety or fear to resume lifestyle adjustment after ICD implant.

However, interpreting the studies about lifestyle modifications is difficult[107]. Indeed, many if not most ICD patients have also significant heart disease that by itself may limit activities.

Sexual activities seem also to be influenced after an ICD implant[107]. Gallagher et al report that recipients of ICD fear that sexual activity could induce a shock and therefore reduce or totally abstain from sexual activity[104]. Several studies report patients receiving shocks during sexual intercourse. They reported also anxiety and apprehension and sometimes decrease in sexual activity or in sexual interest[132].

ICD-patients report about **Excessive family involvement** in patient issues **and inadequate social support** [104, 117]. After ICD shocks, certain family members express hypervigilance, helplessness, uncertainty and overprotection. The relationship with the partner sometimes become strained. Patients seek social support as a coping strategy but it seems that they have difficulties to find it[104].Otherwise, isolation is undesirable because being unmarried and a low social support contribute to reducing overall QoL[117].

A series of inconveniences in the daily life due to the **electromagnetic interference** are reported[133]. Several devices have to be used with caution. Hazards might interfere with airport security scanners, doorways with electronic theft-detection, magnetic items (stereo), cellular telephones, and microwaves[134, 124]. Patients should not undergo MRI procedure.

Medical consumption changes

Besides the surgery, at least three times a year, non-invasive clinical follow-up is mandatory to check the integrity and functionality of the device [134]. Adverse events such as malfunction or infection may occur as discussed in a previous chapter, and induce additional medical consumption. Modern devices have to be renewed after 5 years [133]. In recent years many advisories from manufacturers have led to premature re-interventions in some patients. [50, 51]

6.2.2 ICD and "Quality of Death"

Several issues have to be discussed related to the process of dying and end-of life issues.

First of all there is the issue of adequate information to the patient and their peers. Stevenson argues that circumstances in which it could be desirable to turn off the device have to be explained to the patient, e.g. because of the progression of heart failure or of another terminal disease[135]. Patients should also be informed that turning off the device would not lead to immediate death: it is not 'life support'.

Moreover, information has to be provided on the fact that the defibrillator could also fire after death. This issue should be discussed with the patient and his/her family [136], even before the implantation[137].

Secondly there is a very difficult "quality of death" issue, related to the use of ICD. Quality of death implies a minimization of pain and suffering and a maximization of the autonomy of the patient's wishes, along respecting the sancticity of life. Quality of death" is related to the ultimate cessation of life after medical care has been deemed futile, with full engagement of patients and family desire [136].

Technologies (ß -blockers, thrombolysis, ACE-inhibitors, statins, primary PCI,…) have led to a better survival of victims of the acute phase of a myocardial infarction. This led to an increase of the number of patients with severe left ventricular dysfunction and patients with heart failure. These patients die later on because of a fatal arrhythmia, heart failure or a non-cardiac disease. The ICD can prevent SCD but the other causes of dying are evidently not influenced by the ICD. According to Stevenson, "many patients who realize the risk of sudden death do not appreciate the likelihood of other modes of death"[135], maybe longer and more painful.

Thirdly, particular questions concern the deactivation of the device. The issue is related to the question of the "do-not-resuscitate" authorization as ICD is by nature a device to resuscitate. If such an authorisation is obtained, the device has to be disabled.[137] Berger identified 3 categories of concerns that could stimulate discussion around ICD deactivation: (a) some patients value no longer continued survival, (b) for others, the ICD no longer offers the prospect of increased survival and (c) for still another group, the implant impedes active dying. Berger argues that QoL assessments could be better made by the patients than by a physician[137].

Several authors discuss the necessity for developing guidelines related to end-of-life issues.

Sears proposes a palliative care decision-making tree in an effort to enhance quality of death experience[136]. Globally, when a terminal illness is identified, one should firstly discuss the "Do Not Resuscitate" statement including a discussion with the patient's wishes about the ICD therapy. Then, when death is imminent (< 6 months) the patient should be given the choice between ICD left on or hospice care that will lead to the device deactivation.

About the issue of hospice care, Ballentine[138] proposes to extend the guidelines proposed by Quill et al[139] for life-sustaining treatment: in summary, these guidelines are advocating to assess the rationality and consistency of the patient, his/her condition must be fully understood, alternatives should be explored, depression and other disorders that distort judgement should be excluded, specific plans should be made for how to proceed once treatment is discontinued and second opinion should be obtained.

6.2.3 Patient organisations

We could not identify an ICD patients' organisation in Belgium. Such groups do exist in the neighbouring countries France and The Netherlands. Theoretically, Belgian patients could address themselves to one or the other according to their mother tongue.

In general, the mission of the patients' organizations is to represent the interest of ICD patients, their partners and people around them and to inform and support them. They specifically aim to dialogue with the insurances companies, the caregivers and the government, organise information meetings, contact with fellow-suffers and the information about issues that are of specific interest for ICD patients. In France they also encourage the prevention of sudden cardiac death.

For example, the most recent issues that had to be tackled in France were:

- To have the ICD reimbursed by the social insurance,
- To impede the project of law that intended to totally prohibit driving for patients with an ICD implant,
- To permit access to (real estate) property and consumption to patients by obliging the insurance companies to at least consider the loan applications of these people

Patient groups also deliver psychological support to their members. Questions and worries often raised by ICD-patients are related to inappropriate shocks, why they received implant (Brugada syndrome), lack of information before surgery (practically no information from the physician before implantation and few after but mainly from the nursing staff). This last point has also been mentioned in a UK qualitative study[124]. Another problem frequently encountered seems to be that certain patients do not understand that an ICD could save their life but is not curing the underlying disease.

The biggest part of the demand for psychological help occurs 15 days before the surgery and during the 6 following months.

6.2.4 Discussion

We have tried to assess the impact of ICD on QoL issues in primary prevention as it is reported in the literature in order to review thematics that have to be discussed with patients before implantation.

We had to state that primary prevention patients eligible for ICD differ from the secondary prevention patients in terms of severity of illness, functional status, expectations towards medical intervention and outcome. However many studies or systematic reviews do not clearly make a distinction between primary or secondary prevention. It is thus only based on a limited number of studies that issues of quality of life can be introduced in the debate of ICD.

Based on these studies, no clear association exists between QoL and ICD implant in patients. Nevertheless, several important methodological flaws have been mentioned regarding among others, measures, definitions and design. Several potentially negative outcomes or changes in daily life are well described in the literature but they are not documented specifically for primary prevention. The most common potentially negative outcome of the ICD implant is linked to the risk of receiving inappropriate shocks, i.e. the needless delivery by the device of a shock to the heart. This can for example be provoked by a (sudden) increase in heart rate due to a normal physiologic trigger (exercise) or due to a (benign) supraventricular arrhythmia. Inappropriate shocks represent up to one third of the shocks received. The shocks do not appear having and impact on overall QoL. However insecurity due to the unpredictability of shocks, when and where it will occur is a stressor[121]. They risk causing psychological distress by fragile patients: they could have an impact on anxiety and depression. More, they could lead some patients to avoid doing certain activities. They could also reinforce the patient's perception that he/she is ill.[109]

Even if there is discussion in the literature on the clear association between shocks and QoL, this aspect has to be considered before to implant a patient. Nevertheless, the potential impact of the ICD on psychological functioning and QoL continues to evolve with technological advances[115]. Newer devices are able to better differentiate benign from malign arrhythmias.

ICD could also have an impact on lifestyle, regardless of the potential shocks: Regarding the problem of the driving licence, today in Belgium, patients who have received a first ICD implant are not allowed to drive during the 6 months following surgery. They are allowed to resume driving if they have not received a shock during this period of time. For the replacement of the device there is no restriction in driving[8]. These restrictions are stricter than what exist in other countries and should be updated. Commercial driving is totally and permanently restricted. One may question whether these restrictions are appropriate for patients in whom an ICD is implanted for primary prevention? If the probability of ICD discharge is small, could driving (for private use) not be allowed? If patients experience ICD shocks during follow-up, they should be advised not to drive during the following six months. This recommendation was proposed after an evaluation of the risk of road accidents due to a shock in secondary prevention[125]. For the time being, driving is not allowed during at least 6 month, even if the ICD was implanted for a primary preventive purpose. The question of fitness to drive is pertinent in the ICD problematic but concerns every disease that could lead to a loss of consciousness that is difficult to predict.

8 Arrêté Royal du 23 mars 1998

The question of the fitness to drive of patients at risk of sudden death who have refused to get an ICD remains.

Literature reports also impact on employment, leisure activities, familial and social functioning. Regarding the employment status and leisure activities, consequences of the ICD implant should be discussed with the patient in advance.

Regarding modifications in well-being as well as the management of the impact on the family, they could probably be improved with appropriate interventions. There are some examples in the medical literature but for this report we did not thoroughly search for the results of interventions and cognitive therapy to help psychological adjustment. These are designed for ICD-patients in general and not specific for primary prevention. Thus, in the CABG-Patch trial, patients were advised not to participate in self-support groups, because these focused mainly on secondary prevention patients and may not be indicated for prophylactic implanted persons because it might create confusion[109].

The ICD implant raises also the question of the end-of-life and quality of death. Patients have to be informed that with the ICD their life can be prolonged but their illness with all the suffering associated to it as well. Moreover, patients have to be aware of the possibility to deactivate the implant in certain circumstances related to the end-of-life.

To summarize, primary prevention patients receive an ICD because they are considered to be at high risk of SCD, mostly because they have IHD and a severely depressed left ventricular function. Within this group, two different types can be considered, representing the extremes of a broad continuum: people with a reduced left ventricular function that lead a quasi normal life and people for whom the left ventricular dysfunction is complicated by symptomatic heart failure.

If a patient is a candidate for an ICD for primary prevention, along with the positive aspect of the ICD, he should be informed about the potential negative implications, including those on QoL and restrictions in daily life activities. Ideally, the information provided should take into account the health status and the QoL of the patient at baseline.

Any discussion on patient-issues in primary prevention should distinguish between these patient groups. Indeed, in nearly asymptomatic patients the main question is: what is the benefit of the device at what 'cost'?
In patients with heart failure problems questions are more related to the issues of co-morbidities and the competing risk of dying from heart failure. In some of these patients, an ICD transforms suddenly dying from a cardiac arrest into a progressively deterioration of physical capabilities, characterised by repeated hospital admissions for heart failure, ultimately leading to death. The question of "*quality of death*" arises in patients with end-stage heart failure, as is also the case in any ICD-patient with a limited life expectancy, making a global reflection on the 'end-of-life' of ICD-implanted patients worthwhile.

Unfortunately, no QoL-studies have been performed that consider symptomatic and asymptomatic primary prevention patients separately. For patients who are considered at risk for SCD but who otherwise lead a 'normal' life (NYHA functional class I), we could argue that the QoL would at best be unchanged or could in some cases even decrease after an ICD placement. With an ICD implanted, the patient runs the risk of receiving inappropriate painful shocks (unexpected during daily life, when having sexual intercourse or doing sport), he will be faced with driving restrictions that can lead to modification in working status and could impact freedom, he/she will have an increase of the 'medicalisation' of life with more medical consultations and more explicitly being considered as ill, possibly leading to overprotection within the family. On the other hand, ICD-patients could positively experience the fact that the implant is a safety net that is able to prolong life, especially in the context of secondary prevention. The sum of the perceived benefit and the potential negative impact on daily life could lead to a perceived deterioration of QoL after an ICD implant.

It should also be noticed that for symptomatic heart failure patients, an ICD is not intended to change the symptoms of heart failure. They may become aware of their additional risk of SCA, thus they could maybe better perceive the potential benefit of the ICD than asymptomatic people. On the other hand, an ICD can prolong life of patients with heart failure by preventing a sudden death that however could be replaced by a more painful way of dying.

Finally, regarding QoL, it seems that younger ICD-patients have more psychological distress and worse QoL after the ICD implant. With the trend to implant more patients for a primary prevention purpose, the average age of patients will be younger and the patient issues will probably take another dimension (more frequent, more consequent in daily life).

For the moment, there is no patients group in Belgium but people can take contact with the French or Dutch organisations.

In conclusion, more research is needed in patients implanted for primary prevention purposes about QoL in general and on specific issues that could potentially affect the quality of their life. Studies should take into account the baseline functional status of the patients before implantation, in order to incorporate these results in discussions with patients prior to implant.

- **ICD in primary prevention has no clear impact on generic QoL as it is measured in the available studies.**
- **We miss primary prevention studies that relate QoL changes induced by an ICD depending on functional status of the patients.**
- **Driving restrictions are of major concern in patients, affecting different lifestyle modalities. Long term driving restrictions imposed to patients implanted for primary prevention reasons can be questioned.**
- **Thorough information of patients before and after an ICD implant has to be further studied and consequently improved.**
- **The possibility not to implant a device or to deactivate it because of medical reasons, particularly in the context of end-of-life, has to be discussed early with the patient.**

6.3 RESULTS OF THE EXPERT PANEL INTERVIEW

6.3.1 General comments on the workshop

The aim of the expert panel session was to make an inventory of ethical considerations to be taken into account when developing policy-recommendations on the future use if the ICD. Finally, due to the agenda, six academic experts participated to the round table. They were coming from different moral or ethical theoretical backgrounds (or "schools"). Four members of the KCE participated in the session. One person took the role of moderator, two persons took the role of observers and reporters. The director participated in the discussions. The KCE-members did bring in supplementary information in the course of the discussion. We have stated that all of the experts present to the meeting were linked with the national committee of bioethics.

The discussions took place within a time frame of 3 hours.

The participants were informed their task was limited to bring in general expertise on ethical issues related to ICD. It was explained that this project aims not at making an in depth analysis of different theoretical moral groundings on the problem: the aim was gathering information on moral or ethical principles for developing recommendations and/or using ICD. It was explicitly stated, that we did not want to initiate a fundamental debate on the "ethical-theoretical" groundings of each individual expert. Participants knew they would not be quoted on personal terms, and that the reporting would be limited to a generalised thematic organisation of the themes addressed during the meeting.

As the invited experts know each other from different academic and policy contexts, people were quite aware of the moral and ethical backgrounds of each other. The reflection process during the meeting was very constructive and interactive, in which the confrontation of different opinions lead to the development of arguments. If appropriate, the results section describes different perspectives and opinions related to an issue.

The interactive discussion ended in identifying ethical considerations to be taken into account when addressing the issue of ICD.

The discussion evolved along the following lines:

The discussion with the six ethical experts evolved around two major themes, classified in this chapter as "ethics related to the patient–provider" relationship and "social ethics" related to issues of distributive and social justice. As described in the methodology-section, the moderator did steer the experts to address both these topics in a sequential way.

After the short introduction on the technology a general round was held in which the experts could raise informative questions on the technology and the clinical context of use of the device. During this round, the experts raised a lot of questions on the efficacy of the device (expressed in numbers), on the use context of the device in Belgium, and on available knowledge of patients issues related to the ICD.

The experts first discussed issues of patient-physician relationships. The question was raised on informing the patient about emerging technologies, and on the clinical decision making to implant and ICD. In the second part of the discussion, the reflection was steered towards issues of policy recommendations related to the use of public resources and issues of distributive justice.

6.3.2 Patient-physician relationship

Concerning the use of ICD in primary prevention, some basic moral principles have to steer the patient physician relationship

6.3.2.1 The patient has the right to be informed

It can be expected from an ethical perspective that the patient has the right on information on the availability of the ICD technology. Even in conditions that making this information available to a patient could induce new problems, there is moral right for the patient to be informed on available interventions, in this case an ICD.

However it was clearly raised that it can also be morally expected that each patient being informed, should receive information about all relevant aspects related to the technology (benefits, clinical as well as personal side effects, issues of follow-up, costs, etc…). Although that in our current health care organisation model it becomes more and more difficult to develop an extensive communication process, one can expect that a patient gets an overall picture of advantages and disadvantages of the technology.

Physicians have a professional responsibility in this issue of information providing. The issue was mentioned that this information process could perhaps be put in hands of a multidisciplinary team.

6.3.2.2 The autonomy of the patient

Putting forward the right to be informed is directly related to the acceptance of the autonomy of the patient. There was a general consensus in the group that –as a general principle- each individual should be approached as a person capable of deciding about the course of action to be taken, if the necessary information is being provided. Accepting the patient as an autonomous being, capable to take decisions is a very important moral principle[9].

[9] The particular issue of physically or mentally unable patients was mentioned during the meeting as a particular problem, but was not elaborated.

However, different moral perspectives do exist on this issue of autonomy.

- a perspective called "radical autonomy", implying that in any circumstance a person has the absolute right on full information.
- In contrast to this approach an argument was developed for "parentalism", which is still considered as paternalism by opponents of this approach. It was argued that in some circumstances physicians (or more general health care providers) should have the right to secrecy about certain issues, if the health care provider assesses the situation as too disturbing, or not really relevant for the patient
- A slightly different approach was called "situational ethics": from this perspective one should consider the issue of adequacy of information: providing information should be adapted to the particular situation and context. It was said that, although the right on information is not absolute, it should al least be an ethical principle to consider the situation and circumstances in which information is provided. The example was given that it would be debatable to provide information on a technology, if it is not readily available.

Informing the patient is thus certainly not a clear cut or simple yes or no issue. Several practical circumstances, related both the physician and patient can hamper the process of informing. Implementing the principle requires a context-sensitive approach.

One of the major issues affecting the provision of information is the power relationship between providers-patients. The power relationship is in any physician-patient relationship by nature asymmetric. These differences in power are affecting the information sharing roles. In a health care relationship, patients find themselves in a vulnerable position. Patients do expect to be guided, but also have an opportunity to consider and decide in clinical issues. The trust relationship is fundamental in this perspective, and it can be expected that providers have a moral obligation to develop this trust relationship on true grounds. Moreover, the deontological codes of conduct for health care providers hold the principle that they should not harm the patient

A person is more than a rational actor: emotional factors also play a role, and the use of information is not just a rational weighing of instrumental information.

6.3.2.3 (Societal) Responsibility of the physician

The physician has a primary responsibility to take best clinical choices, based on a clear assessment of the condition of a patient. It is expected that this decision is taken based on information on the expected benefit and harms of a technology.

One can assume that this assessment of the condition is not only based on strict biomedical criteria limited to a particular organ (in this case the functioning of the heart), but also other patient characteristics as his general health status for example.

Moreover, based on their clinical responsibility, physicians have the moral responsibility to judge/assess the patients situation beyond the conditions of reimbursement determined by RIZIV. One cannot expect that in a clinical relationship, clinical interventions judged as necessary (see also further on necessity of care) can be abstained from people because of administrative regulations.

The basic principles of the clinical relationship can be complemented. It could also be expected that a physician takes at least the societal perspective in account when taking decisions. The participants stressed the importance of not develop a reductionist biomedical perspective on a problem, especially in those cases where the assessment of necessary care is at stake.

Replying to a very particular question of the moderator, the remark was made that one cannot develop standardised external government regulations defining conditions guiding the clinical practice of ICD-implants. Since ICD can reduce the risk for SCD, but that also other patient issues are important, it would be difficult to frame the clinical decision making in regulations. Making clinical decisions is part of the moral responsibility of the physicians' profession.

But there is a moral responsibility for doctors to go beyond a reductionist approach. However, this statement does not exclude the fact that decision-makers have the responsibility to develop frameworks.

6.3.2.4 It is non-ethical if a physician has an established relationship with industry

It is judged unethical that a physician with links with the industry guides the decision of a patient. This ethical principle is closely related to the expectation of a trust relationship and to the issue of the power positions of both provider and patient. If there is a link with industry, there is an obvious problem of conflicts of interest in the decision making process.

6.3.3 Social ethics

In the second part of the discussion, the attention was shifted to issues of policy making and social justice. The major question we raised was: " *if recommendations have to be developed on the role of policy makers, what ethical or moral considerations should be taken into account*".

6.3.3.1 It can be expected that policymakers set boundaries for use of technologies

From a collective point of view, there are good (moral or ethical) grounds, enabling the policy makers to define conditions for the use of the technology. Based on the fact that the use of a technology is always related to the use of collective (public) scarce means, a government has to develop a framework to develop criteria for the use of technology. Developing such frameworks is directly related to issues of social justice.

There could be potential paradoxes in combining in a non-flexible way the ethics of physician-patient relations and social ethics. Integrating both perspectives is not a simple exercise Therefore it should be clear that decision-makers decide on the health care organisation conditions within which the individual patient-provider relationship takes form. It was emphasised that setting priorities and allocation of collective resources, should not determine in an absolutist way the individual provider-patient relationship.

The development of such frameworks has to be related to some other prerequisites:

Transparency in decision making (and criteria used for social redistribution)

In the current Belgian system the lack of transparency in the decision making procedures is criticised. There is a potential democratic deficit in current decision making processes about technologies. From ethical and democratic considerations one would expect that procedures and working practices leading to e.g. reimbursement decisions are to be clarified.

Evidence based policy

Evidence based policymaking is an ethical prerequisite. For those technologies lacking conclusive evidence about benefits and harms, strategies should be developed to have at least a follow up of the use of the technology (by means of developing appropriate information of benefits and harms of the technology)

Clearly identified and multiple criteria (clinical, economic, social)

In developing frameworks for allocating public means against the background of distributive justice, it is required to apply not solely clinical, but also social and economical and ethical criteria. Related to the previous issue, transparency is improved if information is available on the multiple criteria and the weighing of these criteria. There is a need for an "ethics of proportionality" (éthique de proportionalité)

From the social redistribution perspective technologies should be compared to other technologies (including other preventive technologies/interventions)

The assessment of a technology and developing criteria of use and reimbursement should always be done in a comparative perspective. This comparison should not only be limited to the available alternatives for a particular bio-medical problem, but should be broadened to the impact of other interventions and health problems (e.g. primary prevention of the cardiac diseases). It is directly related to the problem of "necessary care".

6.3.3.2 Always question "necessity" of an intervention or technology

One of the important ethical principles that should guide the allocation of resources to interventions is the issue of medical necessity. This question is important both at the individual patient-provider level as on the social ethics level.

Due to the current lack of transparency in the decision making process the whole idea of necessary care remains

The idea of necessary care should directly be related to the available evidence. The use of ICD in primary is recognised a good example to show that the available clinical an economic evidence is not always sufficient to decide on this issue of necessary care

7 THE BELGIAN ICD REGISTRY

7.1 PREFACE

The objective of this chapter is to describe the characteristics of the patients that received an ICD in Belgium in 2001 and in 2005. For that purpose the patient claims data of the different Belgian sickness funds (IMA/IAM) were linked with the data (application forms with clinical data) from the RIZIV/INAMI (National Institute of Sickness and Invalidity Insurance) in order to analyse the following items: mortality, population characteristics, hospitalisation data, health care consumption, delivery of cardiac medication. The two databases could be linked to a unique individual patient code, generated by an irreversible encryption algorithm by a third party, hiding the identity and protecting the privacy of the individual. Approval was obtained from the «Sectoraal comité van de sociale zekerheid» / «Comité sectoriel de la sécurité sociale» on Jan 17, 2007.

Ever since 1987 ICDs have been reimbursed by the Belgian sickness insurance based on a model convention concluded between the implant centre and the RIZIV. On February 1st, 2002 a revised contract of this model convention became effective. The most important change of the convention contract considered the condition that a device, in order to qualify for reimbursement, had to be registered by the Insurance Committee of the RIZIV on proposal by the Technical Committee for Implants instead of the former acceptance by the Board of Senior Medical Officers of the sickness funds (and after positive advice of the Convention Commission with the suppliers of implants). The indications were extended and also the contraindications were added. These were based upon the guidelines of the American College of Cardiology and the American Heart Association. These guidelines were published by circular in 1998. Also the conditions the institution, called "centre for implantable heart defibrillators" in the new convention text, has to comply with are enlarged. Here also is referred to international and national guidelines. In this model convention the number of new implants that could be approved annually was increased to the fixed quotum of 520 ICDs in 2002. In 2005 the fixed quotum attained more than 800 first implantation-devices. By the end of 2006, the Insurance Committee of the RIZIV has signed a convention with 17 hospitals (ICD-centres). A hospital is eligible for ICD-accreditation if it has an accredited heart centre (interventional cardiology, cardiac surgery and electrophysiology), 6 FTE cardiologists, 2 FTE electrophysiologists and performs on average 15 ICD procedures per year. A yearly report of the total number of ICD implants to the RIZIV/INAMI as well as peer review submission are mandatory.

In order to control a justifiable volume of reimbursable devices and to establish the indications for an intervention, a consultative body, the so-called Agreement Council ("Akkoordraad", "Conseil d'accord"), was created from the start as an essential element of the model convention with the participating centres. This council consists of cardiologists, specialised in electrophysiology, of the conventioned centres and of members of the Board of Senior Medical Officers. The chairmanship is filled by the Chairman of the Board of Senior Medical Officers. The agreement council convenes for instance each time when the Board of Senior Medical Officers established that the annually fixed quotum of expected first implants will be exceeded. Also for the execution of the peer review tasks of the agreement council, the Board of Senior Medical Officers will transmit to the other members-cardiologists the anonymised essential data of each first implant for which an intervention was granted.

The current study started with the IMA claims data of all patients in whom an ICD was implanted in 2001 and in 2005 and these were linked with RIZIV data (application forms). Matching was based gender, year of birth, hospital reference, NIS-code (National Institute of Statistics code) and date of implantation and the following results were obtained:

- For 2005:

After validating the IMA data (regularizations, clearly incorrect costs and 8 hospitals that did not belong to the list of the 17 contracted centres performing such interventions) we ended up with a file of 1043 interventions with ICD-implantation. Of these, 974 could be successfully matched (93%), the percentage differing from one centre to another (73% up to 100%).

- For 2001:

After validating the IMA data, 458 records resulted. Of these 327 could be successfully matched with the data of the RIZIV (71%). The percentage of matching according to the centres varies considerably more than in 2005: from 17% up to 100%. The poor number of matching data in 2001 is mainly due to insufficient RIZIV data. There is no evidence for a systematic error in the acquisition of records. Data were produced from the mandatory application forms the hospital has to fill in. The lack of information was concentrated in mainly 4 hospitals, but registration was not yet mandatory in 2001. A considerable improvement in registration quality and completeness since 2001 is noted. This explains the far better match up to 93% of the 2005 data. Differences in completeness, detail and quality of data registration explain the limitation in the inclusion rate of all patient files in efficiency studies of ICD-therapy nonwithstanding the availability of a national ICD-database and may necessarily lead to an imperfect picture of the actual need and use of ICDs in a specific country.[63]

The indications for implantation were more restrictive and less detailed in 2001. In order to get a comparable group of ICD-patients all the indications for ICD-implantation of the 2001 patients were "translated" to the list of accepted indications that were valid in 2005 (see appendix).

7.2 NOMENCLATURE AND ICD CENTRES

7.2.1 Nomenclature codes

In 2005 a distinction in nomenclature (official list of reimbursed health provisions) was made between a first device implantation (77% of cases) and a replacement (23% of cases). Two different codes for replacement were introduced in the nomenclature: 687971: outpatient-based implantation and 687982 hospitalised patient-based implantation.

Table 34: Nomenclature of ICD-codes applicable in 2001 and 2005

	2001	%	2005	%
686302 first implantation 2005			753	77
687971 replacement ambulatory 2005			28	3
687982 replacement hospitalised 2005			192	20
772380 (first) implantation 2001	325	100		
TOTAL	**325**		**973**	

7.2.2 ICD centres

In 2001, twelve hospitals with a RIZIV convention performed ICD-implantation; in 2005 the number of accredited centres increased to 17. In one hospital ICD-implantations were discontinued after 2001 (nr.12). The total numbers of ICDs implanted in 2005 are generally larger in the ICD-centres that adhered to the convention already in 2001 since a considerable replacement-population had been built up.

List of ICD centres:

- U.Z. Gent
- U.Z. Antwerpen

- U.Z. Leuven – Gasthuisberg
- C.H.U. de Liège
- Hôpital Erasme – U.L.B.
- C.H.U. Brugman
- Cliniques Universitaires U.C.L. de Mont-Godinne
- O.L.Vrouwkliniek Aalst
- A.Z. Sint-Jan
- A.Z. Middelheim
- C.H.R. de la Citadelle
- Hartcentrum van het Virga Jesseziekenhuis
- H. Hartziekenhuis Roeselare
- A.Z. Maria Middelares Gent
- Ziekenhuis Oost-Limburg – Campus Sint-Jan
- Centre Hospitalier Régional Namur
- Cliniques Universitaire Saint-Luc

Table 35: Number of implants per hospital

Anonymous hospital number	2001	%	2005	%
1	56	17%	93	10%
2	20	6%	67	7%
3	82	25%	59	6%
4	4	1%	29	3%
5	14	4%	29	3%
6	34	10%	123	13%
7	13	4%	98	10%
8	51	16%	152	16%
9	20	6%	42	4%
10	6	2%	74	8%
11	18	6%	38	4%
12	7	2%	0	0%
13	0	0%	35	4%
14	0	0%	31	3%
15	0	0%	46	5%
16	0	0%	38	4%
17	0	0%	13	1%
18	0	0%	6	1%
Total	**325**		**973**	

7.3 DEMOGRAPHIC, SOCIO-ECONOMIC, GEOGRAPHICAL AND ADMISSION DATA

The distribution of age and gender are shown in Table 36 and Table 37, and in Fig. 1. To constitute a comparison basis a sample of the general population with almost the same distribution of age and gender as the ICD-patient population of 2005 was randomly selected. In Table 37 the data of the 2005 ICD-population are compared with those of the at random selected population ("2005 ref"). There is an overwhelming male majority among the ICD-patient population and further comparison with the normal arrhythmia risks and prevalence among the male and female population has to be carried out.

7.3.1 Gender

The majority of the patients are male.

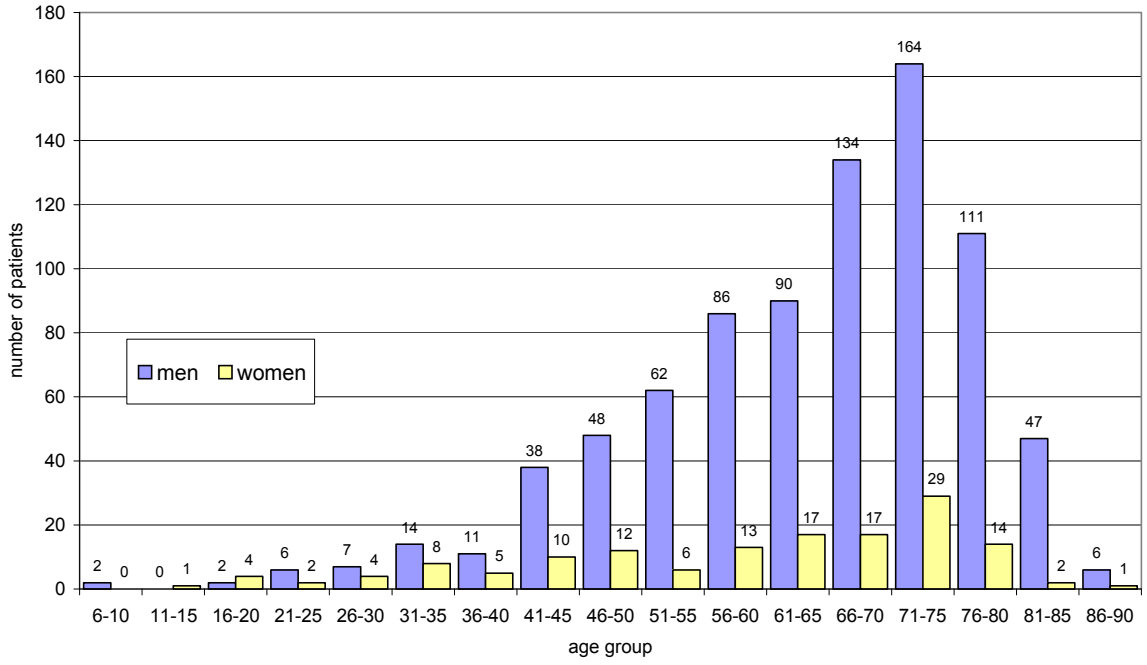
Table 36: Sex distribution of ICD recipients in the Belgian Registry.

	2001	%	2005	%
Men	261	80%	828	85%
Women	64	20%	145	15%
Total	**325**		**973**	

7.3.2 Age

In 2001, the average age of the ICD-patients in 2005 was 62,8 years. This is slightly different from the mean patient age at implantation of 63,4 years in 2001. The median value of patient age is 66 years and 67 years in 2001 and 2005 respectively. The age-sex distribution in 2005 is shown in the figure below.

Figure 14: Age-sex distribution of ICD recipients in the Belgian Registry in 2005.



7.3.3 Comparison age-sex distribution ICD population 2005 with reference population 2005

Table 37: Comparison age-sex distribution in 2005 ICD recipients and reference population 2005

AGE	ICD 2005					REF 2005				
	Men	Women	Row%	Total	Col%	Men	Women	Row%	Total	Col%
6-10	2	0	0%	2	0%	10	6	38%	16	0%
11-15	0	1	100%	1	0%	11	9	45%	20	0%
16-20	2	4	67%	6	1%	11	13	54%	24	0%
21-25	6	2	25%	8	1%	29	9	24%	38	1%
26-30	7	4	36%	11	1%	42	29	41%	71	1%
31-35	14	8	36%	22	2%	69	11	14%	80	2%
36-40	11	5	31%	16	2%	57	16	22%	73	1%
41-45	38	10	21%	48	5%	188	47	20%	235	5%
46-50	48	12	20%	60	6%	243	61	20%	304	6%
51-55	62	6	9%	68	7%	316	30	9%	346	7%
56-60	86	13	13%	99	10%	438	65	13%	503	10%
61-65	90	17	16%	107	11%	461	85	16%	546	11%
66-70	134	17	11%	151	16%	664	91	12%	755	15%
71-75	164	29	15%	193	20%	856	137	14%	993	20%
76-80	111	14	11%	125	13%	555	77	12%	632	13%
81-85	47	2	4%	49	5%	238	13	5%	251	5%
86-90	6	1	14%	7	1%	32	5	14%	37	1%
Total	**828**	**145**	**15%**	**973**	**100%**	**4220**	**704**	**14%**	**4924**	**100%**

7.3.4 Social Security Status

About 90% of the patients are salaried workers vs only 10% independent workers. This reflects grosso modo the distribution of the general population. Belgian sickness insurance provides two different categories: the general workers, salaried people working on a wage basis, and independent workers. The independent workers have a different system of income based contribution to the social security (pension, unemployment and health care). For some specific care provisions (ambulatory care) and for some drugs they have larger co-payment rates.

Table 38: Status of sickness insurance of ICD recipients, compared to reference population.

	2001	%	2005	%	2005 ref	%
General	290	91%	866	89%	4378	90%
Independent	30	9%	106	11%	490	10%
Total	**320**		**972**		**4868**	

7.3.5 Preferential tariff

One in four ICD-patients benefits from a preferential low co-payment in health care. This is only slightly more in the population ICD-patients than in the general reference population. In both systems (salaried and independent workers) the Belgian sickness insurance provides a lower co-payment for the socio-economically weaker population. These patients (selected on criteria as total income, unemployment, working incapacity, age) have a lower co- payment called preferential tariff.

Table 39: Number of ICD patients with preferential tariff.

	2001	%	2005	%	2005 ref	%
No preferential tariff	236	73%	744	76%	4010	81%
Preferential tariff	89	27%	229	24%	914	19%
Total	**325**		**973**		**4924**	

7.3.6 Social Security Qualification

One in four patients are 'active', which means that they are not retired (1 in 2 patients) or disabled (1 in 7 patients). The group of disabled includes handicapped persons and invalids as well. After a period of continued working incapacity during at least one year, the status of invalidity is attributed by the RIZIV. Patients defined as disabled in Table 40 were already handicapped or invalid when they receive their device.

Table 40: Social Security Qualification of ICD-patients and reference population.

	2001	%	2005	%	2005 ref	%
Improtected	7	2%	15	2%	141	3%
Active	88	27%	277	28%	1759	36%
Disabled	50	15%	114	12%	181	4%
Retired	168	52%	540	55%	2739	56%
Widow	12	4%	27	3%	99	2%
Total	**325**		**973**		**4919**	

7.3.7 Criterion "120 days of hospitalization"

This criterion is one of the medical dependancy parameters a patient must fulfill to be entitled to the lump sum-payment benefit for chronically ill patients. The 120 days of hospitalization are counted during the running calendar year or the year before the implantation date. This lump-sum payment benefit is meant to cover for complementary health care costs, that for this category of insurees are proved to be considerably more important in relation to their poorer health status. In 2001 more patients with an ICD fulfilled this criterion of 120 days of hospitalization than in 2005, so the 2001 ICD-population was generally of poorer health. This could be the result of the more limitative indication criteria for ICD-therapy and also of the more restrictive selection of implantation candidates by the cardiologists. Differences in 2001 vs 2005 cost-consciousness among the cardiologists about the use of highly expensive devices may also play a role. In 2001 8 % of the ICD-patients were attributed the status of chronically ill. This percentage drops to 3% in 2005. The different indications for reimbursement prevailing in 2001 and 2005 are given in appendixes 1 and 2.

Table 41: Number of ICD patients hospitalized more than 120 days.

	2001	%	2005	%	2005 ref	%
No 120 days hospitalized	298	92%	945	97%	4892	99%
120 days or more hospitalized	27	8%	28	3%	32	1%
Total	**325**	**100%**	**973**	**100%**	**4924**	**100%**

7.3.8 Criterion "more than 6 hospital admissions"

This criterion is also one of the medical criteria a patient must fulfill in order to have the right to receive the abovementioned lump sum-payment for chronically ill patients. The 6 hospitalizations are counted during the running calendar year or during the year before the attributed status. Similarly, in 2001 twice as many patients fulfilled the criterion of 6 or more hospitalizations than in 2005. Note that in the reference population of 2005 only 2% fulfill this criterion compared to 10% of the 2005 ICD-population, confirming that the ICD-population is generally of poorer health.

Table 42: Number of patients with more than 6 hospital admissions during the year of hospitalization or the year before

	2001	%	2005	%	2005 ref	%
No 6 hospitalizations	260	80%	873	90%	4839	98%
6 or more hospitalizations	65	20%	100	10%	85	2%
Total	**325**	**100%**	**973**	**100%**	**4924**	**100%**

7.3.9 Residence

In 2005, five percent of the patients came from the Brussels region, 65% were patients from Flanders and 29% were patients from Wallonia.

Table 43: Region of residence of ICD recipients.

	2001	%	2005	%	2005 ref	%
Flanders	225	72%	635	65%	2909	61%
Brussels	17	5%	52	5%	368	8%
Wallonia	70	22%	285	29%	1487	31%
Total	**312**	**100%**	**972**	**100%**	**4764**	**100%**

The lower percentage of ICD-implantations in Wallonia in 2001 may be due to a lack of sufficient data, since only 71 % of the patients could be matched and an important variability in registration between the centres was observed.

After standardization for age and gender, regional differences become less pronounced as depicted on Figure 16. Because of insufficient basline data it is difficult to explain the regional differences in implant rate. The density in implant centres in Flanders being more important than elsewhere might have influenced implant rate because of easier accessibility to ICD-therapy for the patient and referring cardiogists.

The incidence is lowest in Brussels (6,1), Walloon-Brabant (6,4) and Flemish-Brabant (7,8). For calculating these incidences, we used the matched and the non-matched ICDs in order to be as complete as possible.

Figure 15: Crude number of ICD-patients per 100.000 inhabitants

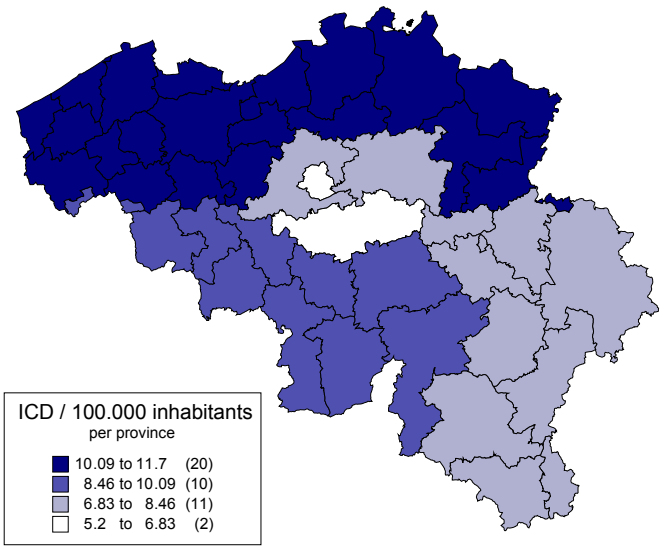
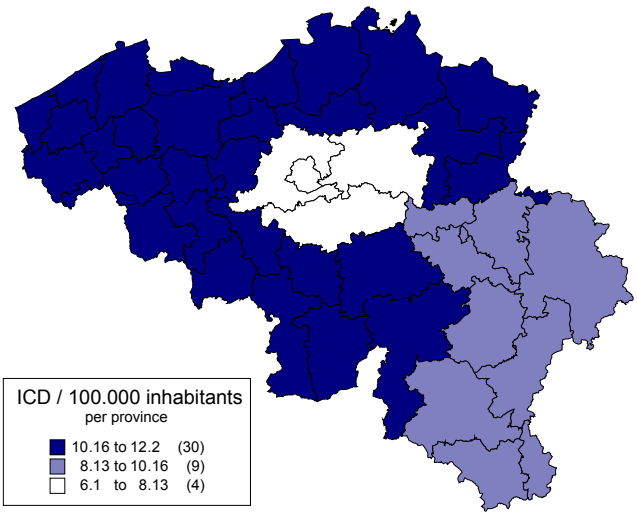


Figure 16: Age & gender standardized number of ICD-patients per 100.000 inhabitants



7.4 CLINICAL DATA

7.4.1 Underlying heart disease

Table 44 shows the underlying heart disease, which led to the indication of an ICD implantation.

Table 44: Underlying heart disease in ICD recipients.

	2001	%	2005	%
Ischaemic heart disease	188	67%	601	66%
Idiopathic cardiomyopathy	35	13%	129	14%
Primary electrical	30	11%	80	9%
Other	26	9%	94	10%
Total	279	100%	904	100%
NA	46	14%	69	7%

7.4.2 Manufacturer

This table shows the market share of the different suppliers for ICD-devices. The market share in the different hospitals is shown in the appendix to this chapter.

Table 45: Market share of different ICD manufacturers.

	2001	%	2005	%
Biotronik	5	2%	69	7%
Ela Medical	2	1%	7	1%
Guidant	128	46%	374	39%
Medtronic	135	49%	340	35%
St. Jude Medical	7	3%	181	19%
Total	**277**	**100%**	**971**	**100%**
NA	48	15%	2	0%

7.4.3 Replacement

The figures in Table 46are based on RIZIV data. The table shows the number of first implants versus replacements. The replacement market in Belgium is naturally growing for each centre in relation with their individually different total period of, and experience in ICD-therapy that in Belgium started in 1988. Over time this is dependent on the longevity of the power source and the corresponding increase in mandatory renewal period before reimbursement.

Table 46: Numbers of first implants and replacements.

	2001	%	2005	%
Primo-impl	276	85%	707	73%
Replacement	49	15%	264	27%
Total	**325**		**971**	
NA	0	0%	2	0%

7.4.4 Indication

In order to get a uniform group of patients, the reimbursement indications (further in the text referred to as "indication category #") of patients implanted in 2001 were "translated" to the list of accepted reimbursement indications used in 2005 as listed below:

1. Cardiac arrest
2. Caused by:
    a. Ventricular fibrillation or tachycardia, not linked to a temporary or reversible cause (acute myocardial infarction, electrolyte disturbance, drugs, trauma)
3. Or due to supposed ventricular fibrillation:
    b. When the clinical condition is a contraindication for electrophysiological testing
    c. When during electrophysiological testing no major ventricular arrhythmia can be provoked
4. Spontaneous sustained ventricular tachycardia with hypotension
    d. No electrophysiology has been performed
    e. Not inducible during electrophysiological testing
    f. Inducible during electrophysiological testing
    g. Spontaneously occurring despite treatment with class 3 antiarrhythmic (sotalol or amiodarone)
5. Nonsustained ventricular tachycardia following a previous myocardial infarction, without reversible ischemia, with a ejection fraction below 40%, with inducible sustained ventricular arrhythmia during electrophysiologic testing, at earliest 7 days after the AMI, not suppressed by anti-arrhythmic.
    h. Symptomatic nonsustained ventricular tachycardia in patients waiting for heart transplant, and who do not stay permanently in the hospital
    i. Symptomatic sustained ventricular tachycardia in patients waiting for heart transplant and who do not stay permanently in the hospital (mention the delay for possible heart transplant (e.g.: already on the active waiting list vs. candidate for future transplant)
6. Syncope due to tachyarrhythmia:
    j. Inducible sustained ventricular arrhythmia during electrophysiological testing
    k. Prolonged and hemodynamic compromising nonsustained ventricular tachycardia during electrophysiological testing
    l. Aetiology otherwise specified
7. Familial or genetic disorders with a known associated risk for ventricular arrhythmias, and with a elaborated motivated high risk for sudden cardiac death of the patient based on spontaneous or inducible ventricular arrhythmia, or suspected familiar causes:
    m. Long QT syndrome
    n. Brugada syndrome
    o. Hypertrophic cardiomyopathy
    p. Arrhythmogenic right ventricular dysplasia

Table 47: Implant indications in 2001 and 2005

Indication category #	2001	%	2005	%
1	0	0%	1	0%
1.1	48	22%	217	23%
1.2	1	0%	1	0%
1.3	26	12%	4	0%
Total 1	**75**	**34%**	**223**	**23%**
2	0	0%	1	0%
2.1	12	5%	10	1%
2.2	16	7%	35	4%
2.3	60	27%	268	29%
2.4	0	0%	35	4%
Total 2	**88**	**39%**	**349**	**38%**
Total 3	**34**	**15%**	**124**	**13%**
Total 4	**3**	**1%**	**22**	**2%**
4.1	1	0%	20	2%
4.2	2	1%	2	0%
Total 5	**12**	**5%**	**151**	**16%**
5.1	11	5%	135	14%
5.2	0	0%	8	1%
5.3	1	0%	8	1%
Total 6	**10**	**4%**	**69**	**7%**
6	0	0%	3	0%
6.1	3	1%	8	1%
6.2	6	3%	30	3%
6.3	1	0%	16	2%
6.4	0	0%	12	1%
Total	**222**	**100%**	**938**	**100%**
Non accepted indication	18	6%	0	0%
NA	85	26%	35	4%

In order to calculate the total number of primary prevention implants, we summed the patients with indication category #3, and those in whom an ICD was implanted for primary preventive indications in genetic disorders (indication category #6). Table 48 presents indication categories, reflecting in shorthand current Belgian coverage criteria.

Table 48: Shorthand description of current Belgian coverage criteria.

Indication category #	Considered as …	Shorthand description
1	secondary prevention	Cardiac arrest, VF
2	secondary prevention	Symptomatic sustained VT
3	primary prevention	IHD + nonsustained VT + EPS
4	secondary prevention	Symptomatic VT + bridge to transplant
5	secondary prevention	Syncope, attributed to tachyarrhythmia
6	primary prevention	(Asymptomatic) genetic disorders

Comprehensive description of indications described earlier in the text and available from appendix. Abbreviations: see glossary.

In 2001 18 ICDs were implanted on a medical indication that could not possibly be linked to one of the accepted indications of 2005. In 85 files due to incomplete registration the indication was not available. In 2005 still 35 application forms of the at the RIZIV introduced files did not mention the indication. Primary prevention is the indication in 20% of the patients, whereas secondary prevention is the indication in 80% of the patients. Although the total number of implants increases, the proportion of primary preventive ICD-therapy remains remarkably stable during the 2001-2005 period. This ratio varies considerably between the implantation centres (see below).

Table 49: Primary and secondary prevention ICD indications in Belgian Registry.

	2001	**%**	**2005**	**%**
Primary prevention	44	20%	193	21%
Secondary prevention	178	80%	745	79%
Total	**222**		**938**	

In a previous study exposed at the last meeting of the agreement council in 2006 and carried out by the RIZIV a similar distribution is observed:

Figure 17: Proportion of ICD indications 2001 and 2005 / RIZIV data

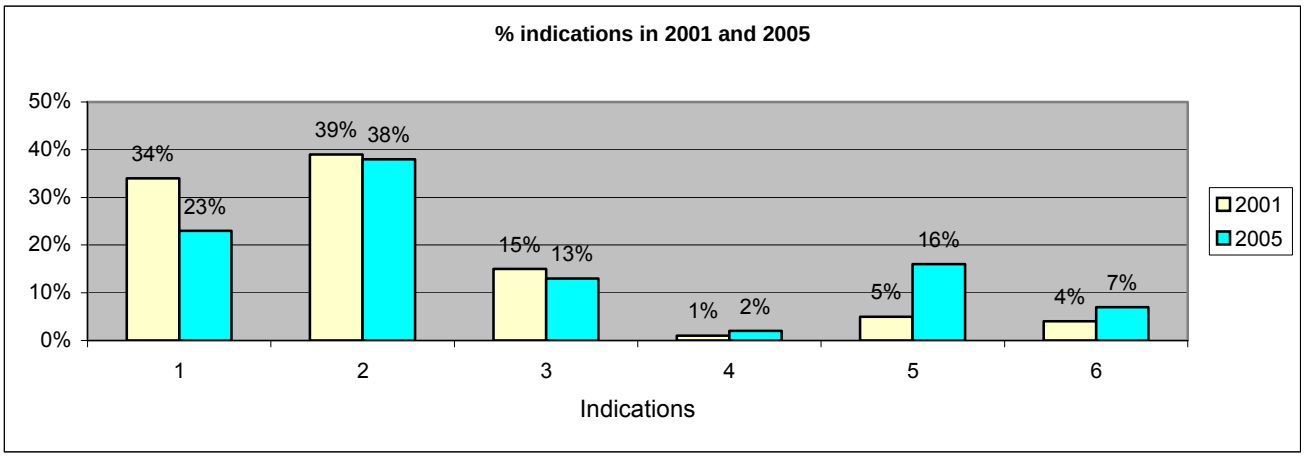
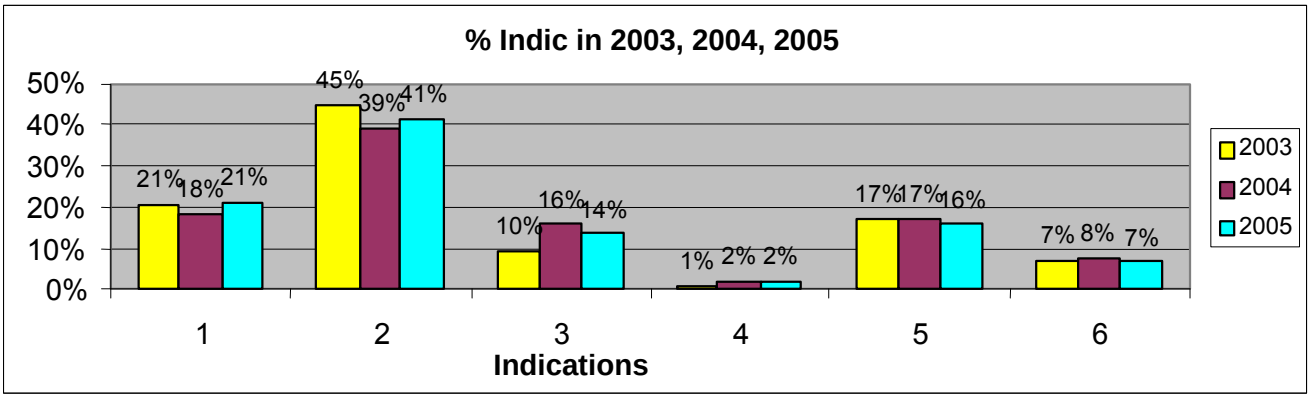


Figure 18: Proportion of ICD indications 2003, 2004 and 2005 / RIZIV data



7.4.5 ICD-device classes

Table 50: Distribution of different classes of ICD devices.

	2001	%	2005	%
Class 2	-	-	595	61%
Class 3-2el	-	-	256	26%
Class 3-3el	-	-	120	12%
Total	-	-	971	100%
Missing	**325**	**100%**	**2**	**0%**

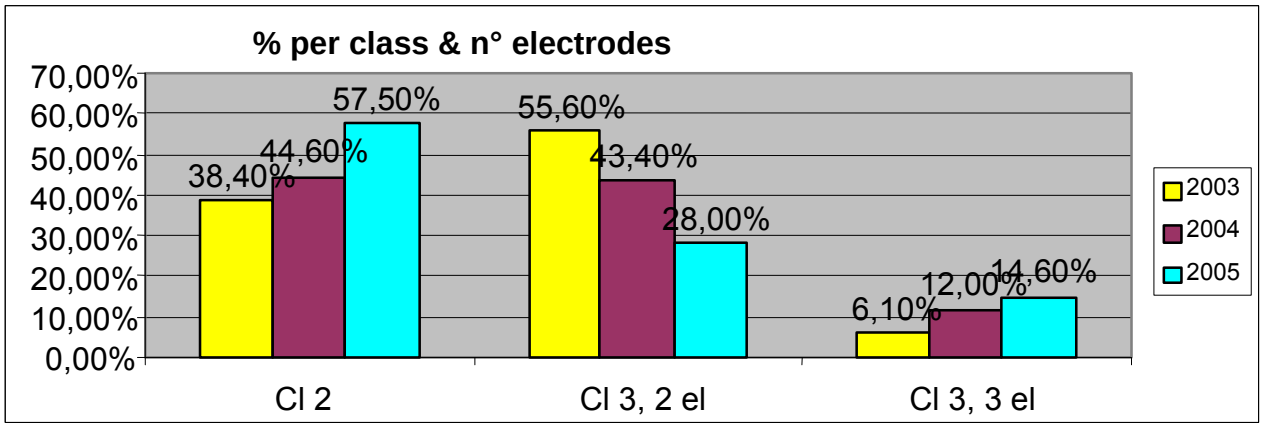
Not applicable in 2001

There are three different "administrative" classes of ICD approved in Belgium:

- Class 1: Prophylactic (shock only)
- Class 2: Classic single or dual chamber ICD
- Class 3: CRT-D

Currently, in Belgium there is no consistent coverage policy for CRT devices. CRT-P is not reimbursed in contrast with CRT-D, that is reimbursed as far as the patient meets criteria for implantation of an ICD. In the Belgian registry, CRT-D implants are referred to as "class 3" indications which are further subdivided into two subgroups depending on whether a left ventricular electrode is installed ("class 3-3") or the connection intended for this electrode is simply plugged and left available for an upgrade later on ("class 3-2"). Classic ICDs are referred to as "class 2" devices and "class 1" refers to shock-only devices which have almost never been used. In 2005, 61% of devices were class 2 and 39% were class 3 with somewhat more than 50% in class 3-2. From 2003 to 2005, a progressive switch from class 3-2 to class 3-3 devices is noted. The number of ICDs in the different classes as shown are those communicated during the last meeting of the agreement council in 2006.

Figure 19: Distribution of ICD classes / RIZIV data



7.4.6 Ejection Fraction

Table 51: Ejection fraction in ICD recipients in 2001 and 2005.

	2001	%	2005	%
< 31%	52	36%	231	45%
31-35%	20	14%	77	15%
36-50%	41	28%	130	25%
> 50%	32	22%	75	15%
Total	**145**	**100%**	**513**	**100%**
NA	180	55%	460	47%

NA: not availbale.

Of all patients that received an ICD in 2001 and in whom LVEF data were available (n=145) 72 (50%) had a low ejection fraction (</=35%). This subpopulation with low EF increased in the ICD patient group of 2005 (308 of 513 or 60%). About a quarter of the ICD-patients had an ejection fraction between 36 and 50%. Unfortunately, the functional status of these patients in terms of NYHA-class is unknown.

7.5 HOSPITAL CHARACTERISTICS

For the comparison of practice variability between ICD-centers the data of the ICD-subpopulations 2001 and 2005 are analysed together. Hospitals with less than 30 ICD-patients during the selected 2 year period were excluded. In this part only three topics are discussed: etiology (underlying heart disease), indication (according to reimbursement criterium) and LVEF. The hospital characteristics linked with other items such as age and gender distribution, different social security qualification, status and preferential tariff, chronically ill patient character, type of device and replacements are showed in an appendix.

7.5.1 Underlying heart disease

The explanation for this rather equal distribution in ICD patient selection based on etiology of the underlying heart disease is found in the limited reimbursement criteria that were set in the agreement between teh RIZIV and the implantation center. Therefore this distribution of indication does not necessarily reflect the actual prevalence and distribution of ICD-related cardiac pathology among the total Belgian population.

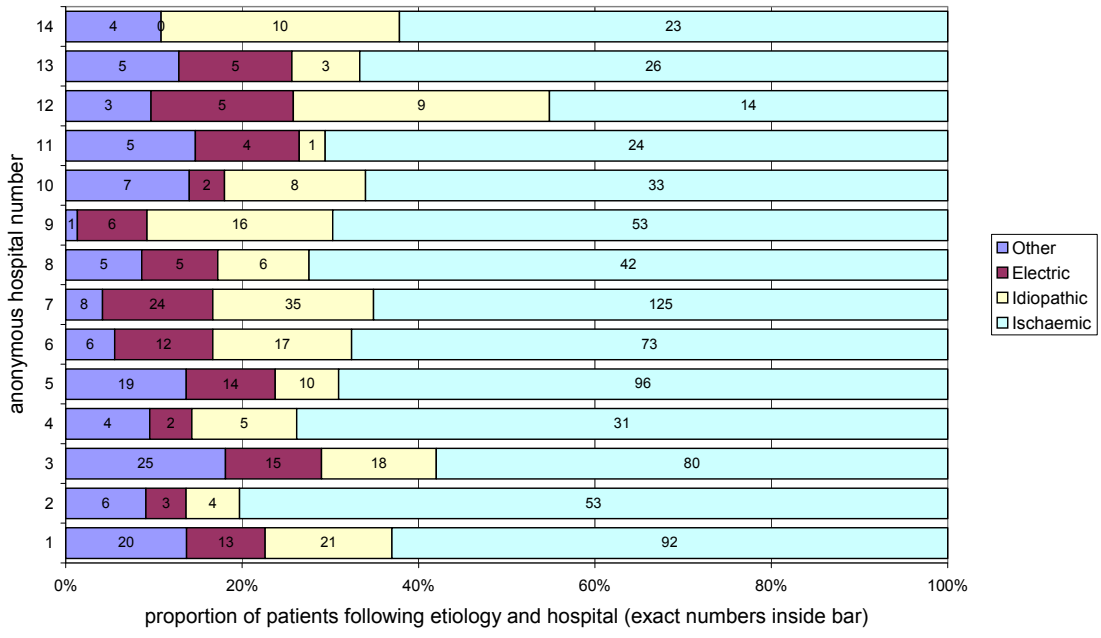
There was one hospital (nr. 4) with information lacking on the underlying heart disease.

Table 52: Underlying hearty disease in ICD recipients categorized in primary electrical disease, idiopathic cardiomyopathy, ischaemic heart disease and "other"

Hospital #	Other	%	Elect	%	Idio	%	Isch	%	Total
1	20	14%	13	9%	21	14%	92	63%	146
2	6	9%	3	5%	4	6%	53	80%	66
3	25	18%	15	11%	18	13%	80	58%	138
4									4
5	4	10%	2	5%	5	12%	31	74%	42
6	19	14%	14	10%	10	7%	96	69%	139
7	6	6%	12	11%	17	16%	73	68%	108
9	8	4%	24	13%	35	18%	125	65%	192
10	5	9%	5	9%	6	10%	42	72%	58
11	1	1%	6	8%	16	21%	53	70%	76
13	7	14%	2	4%	8	16%	33	66%	50
15	5	15%	4	12%	1	3%	24	71%	34
16	3	10%	5	16%	9	29%	14	45%	31
17	5	13%	5	13%	3	8%	26	67%	39
18	4	11%	0	0%	10	27%	23	62%	37
Total	119	10%	110	9%	163	14%	768	66%	1160

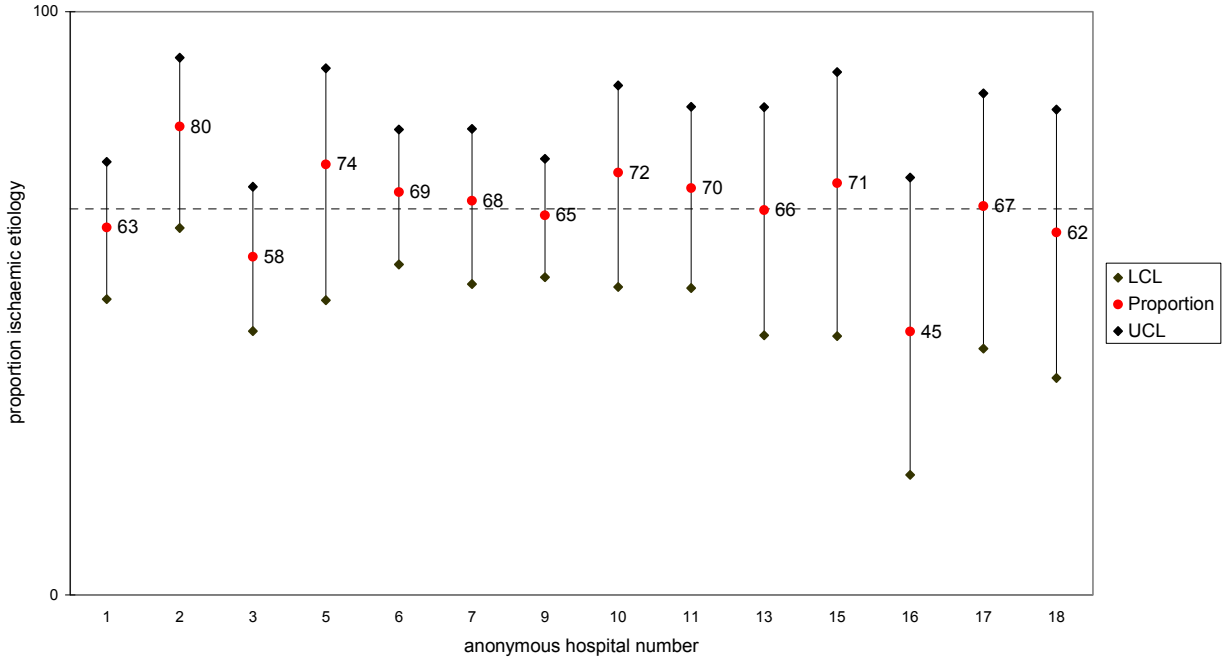
This table is depicted graphically in the next chart:

Figure 20: Underlying heart disease by centre.



The next figure represents for each hospital the proportion of ICD-patients with ischaemic heart disease, with their exact binomial confidence intervals (after Bonferroni correction). The dotted line is the mean proportion of all hospitals. There are no hospitals that differ significantly from the mean.

Figure 21: Proportion ischaemic heart disease per hospital



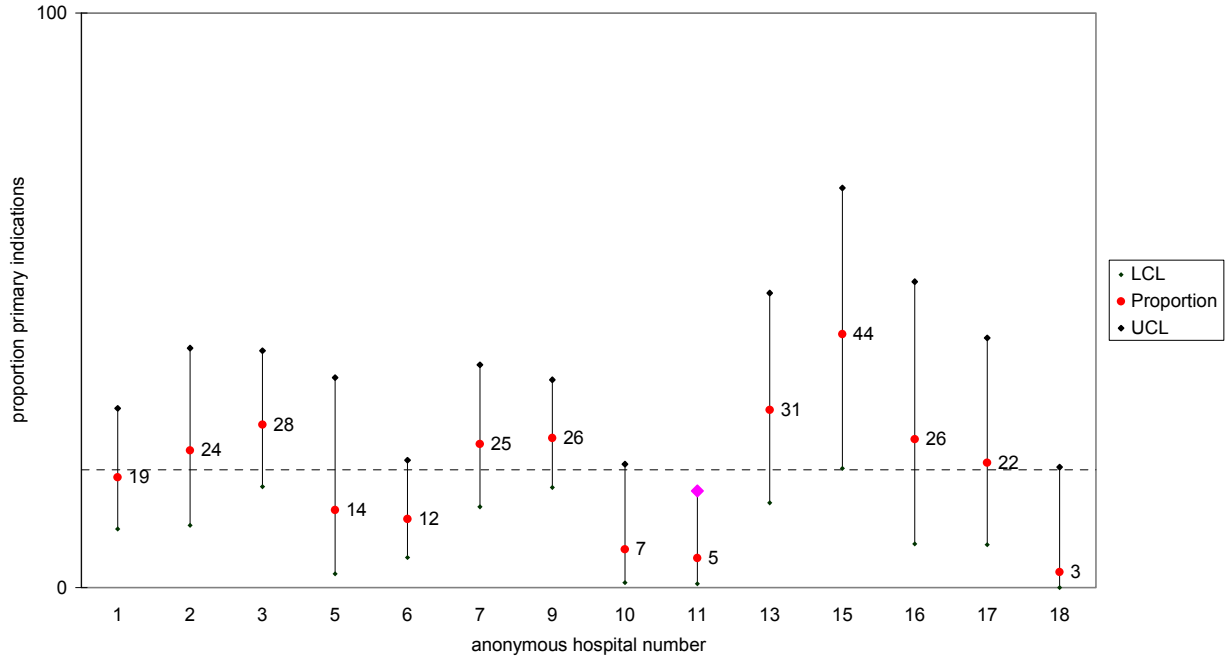
7.5.2 Implant indication

Table 53: Proportion of primary and secondary prevention indication per hospital number

Hosp	Sec Pr	%	Prim Pr	%	Total
1	101	81%	24	19%	125
2	51	76%	16	24%	67
3	91	72%	36	28%	127
4					4
5	32	86%	5	14%	37
6	118	88%	16	12%	134
7	81	75%	27	25%	108
9	142	74%	50	26%	192
10	56	93%	4	7%	60
11	74	95%	4	5%	78
13	38	69%	17	31%	55
15	19	56%	15	44%	34
16	23	74%	8	26%	31
17	36	78%	10	22%	46
18	36	97%	1	3%	37
Total	902	79%	233	21%	1135

The following figure shows for each hospital the proportion of primary indication and the exact confidence intervals (after Bonferroni correction). There is only one hospital (nr. 11) that has a significantly lower proportion of primary prevention indications, but total ICD-implant numbers are small.

Figure 22: Proportion of patients with ischaemic heart disease as underlying heart disease per hospital.



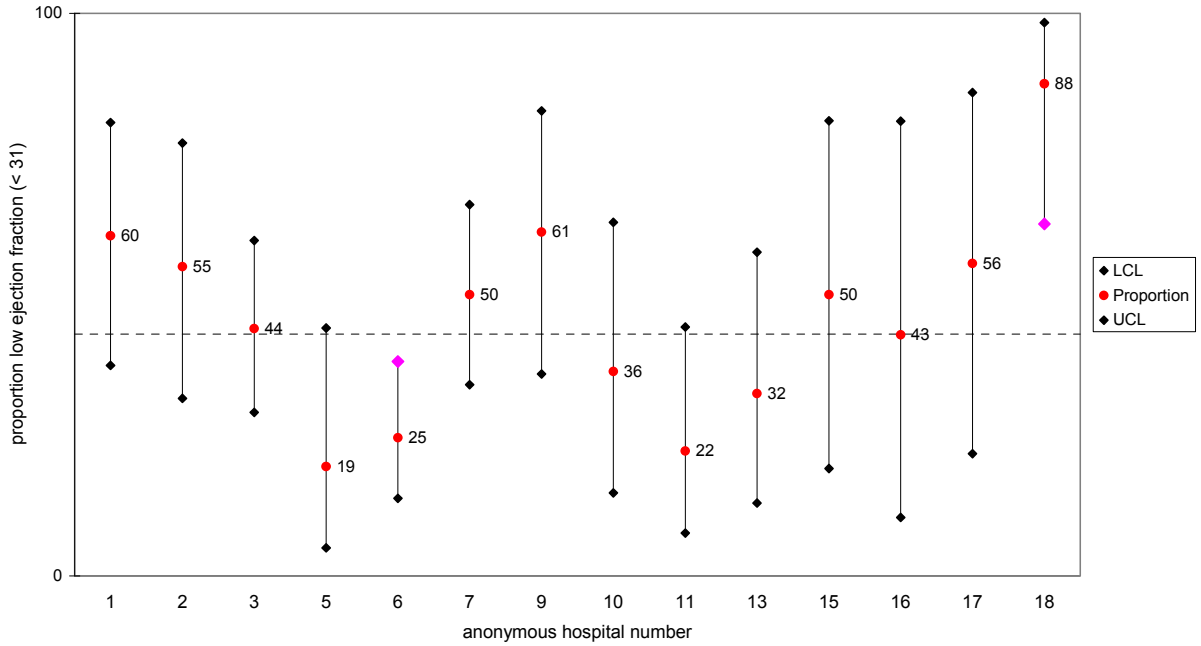
7.5.3 Ejection Fraction

Table 54: ICD patient ejection fraction per hospital

Hosp	< 31%	%	31-35%	%	36-50%	%	> 50%	%	Total
1	26	60%	3	7%	6	14%	8	19%	43
2	22	55%	8	20%	5	13%	5	13%	40
3	40	44%	12	13%	23	25%	16	18%	91
4	2	67%	0	0%	1	33%	0	0%	3
5	7	19%	5	14%	16	44%	8	22%	36
6	27	25%	17	15%	39	35%	27	25%	110
7	42	50%	13	15%	23	27%	6	7%	84
9	22	61%	7	19%	4	11%	3	8%	36
10	12	36%	1	3%	10	30%	10	30%	33
11	10	22%	2	4%	16	36%	17	38%	45
13	12	32%	11	30%	12	32%	2	5%	37
15	10	50%	5	25%	3	15%	2	10%	20
16	6	43%	4	29%	4	29%	0	0%	14
17	10	56%	3	17%	3	17%	2	11%	18
18	28	88%	2	6%	1	3%	1	3%	32
Total	276	43%	93	14%	166	26%	107	17%	642

One hospital (nr.5) has a significantly lower proportion of patients with low EF (< 31%) and another hospital (nr.18) has a significantly higher proportion of patients with low EF. All other hospitals vary around the mean proportion of 43% patients with lowest LVEF for ICD-implantation.

Figure 23: Proportion of ICD-patients with LVEF<35% by implant centre and 95% confidence intervals.



7.6 PATIENT CHARACTERISTICS BASED ON ETIOLOGY

The following tables show the differences between the ICD-population according to etiology: ischaemic, idiopathic and "other". Here patients with "primary electrical disease" are also included in the group "other". More detailed information about etiology linked with nomenclature codes (provisions), hospital, status, preferential tariff, social security classes, residence, number of replacements and type of device can be found in appendix .

7.6.1 Gender

Table 55: Underlying heart disease by gender in ICD patients.

	Other	%	Idio	%	Isch	%
Men	163	16%	119	12%	712	72%
Women	67	35%	45	24%	77	41%
Total	230	19%	164	14%	789	67%

Idio: idiopathic cardiomyopathy; Isch: ischemic heart disease.

7.6.2 Age

Table 56: Underlying heart disease by age group

	Other	%	Idio	%	Isch	%
1-5	1	100%	0	0%	0	0%
6-10	2	100%	0	0%	0	0%
11-15	1	100%	0	0%	0	0%
16-20	8	89%	1	11%	0	0%
21-25	10	91%	1	9%	0	0%
26-30	13	93%	1	7%	0	0%
31-35	17	71%	7	29%	0	0%
36-40	16	64%	5	20%	4	16%
41-45	31	61%	9	18%	11	22%
46-50	29	40%	9	13%	34	47%
51-55	21	24%	17	19%	50	57%
56-60	20	17%	24	20%	77	64%
61-65	21	15%	17	12%	104	73%
66-70	13	7%	26	14%	144	79%
71-75	19	8%	24	10%	191	82%
76-80	6	4%	22	15%	121	81%
81-85	2	4%	1	2%	50	94%
86-90	0	0%	0	0%	3	100%
Total	230	19%	164	14%	789	67%

Idio: idiopathic cardiomyopathy; Isch: ischemic heart disease.

7.6.3 Province

Table 57: Underlying heart disease by province of residence

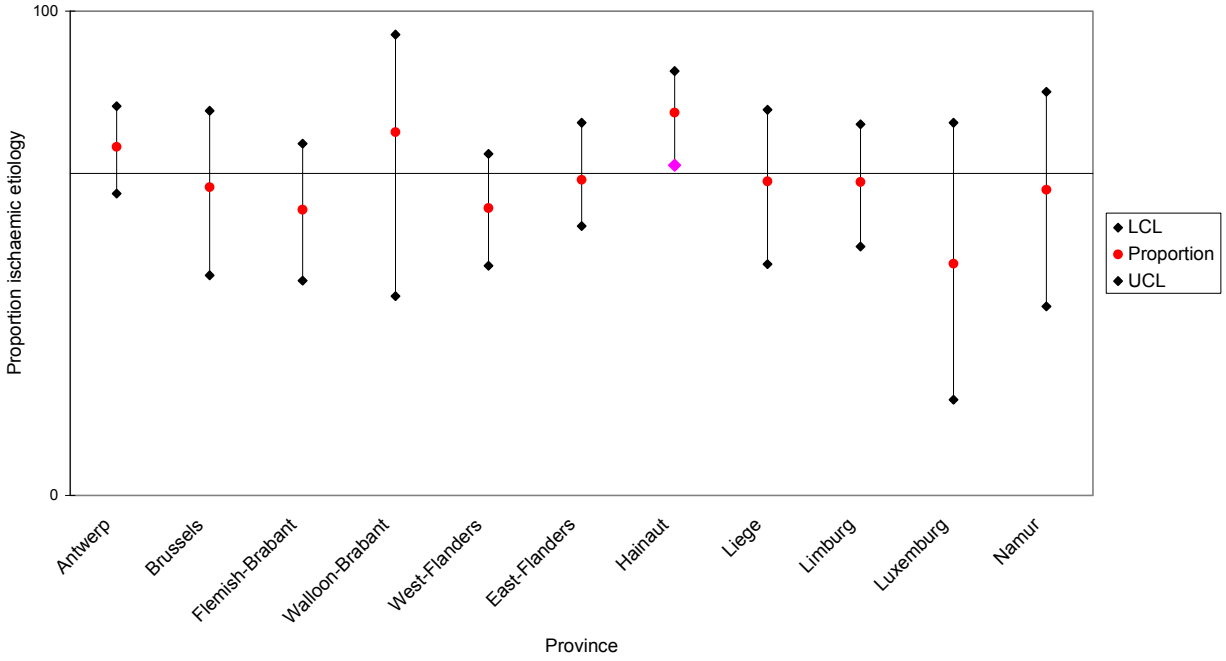
	Other	%	Idio	%	Isch	%
Antwerpen	31	15%	27	13%	149	72%
Brussels	12	18%	12	18%	42	64%
Vlaams Brabant	25	25%	16	16%	59	59%
Brabant Wallon	4	20%	1	5%	15	75%
W-Vl	35	23%	26	17%	89	59%
O-Vl	44	20%	34	15%	146	65%
Hainaut	20	14%	11	7%	117	79%
Liège	18	24%	8	11%	48	65%
Limburg	26	22%	16	13%	77	65%
Luxembourg	8	35%	4	17%	11	48%
Namur	6	16%	8	21%	24	63%
Total	229	20%	163	14%	777	66%

Idio: idiopathic cardiomyopathy; Isch: ischemic heart disease.

Although large differences in prevalence of specific arrhythmogenic cardiac disease between the provinces were expected based on some previous studies no major distinctions could be established.

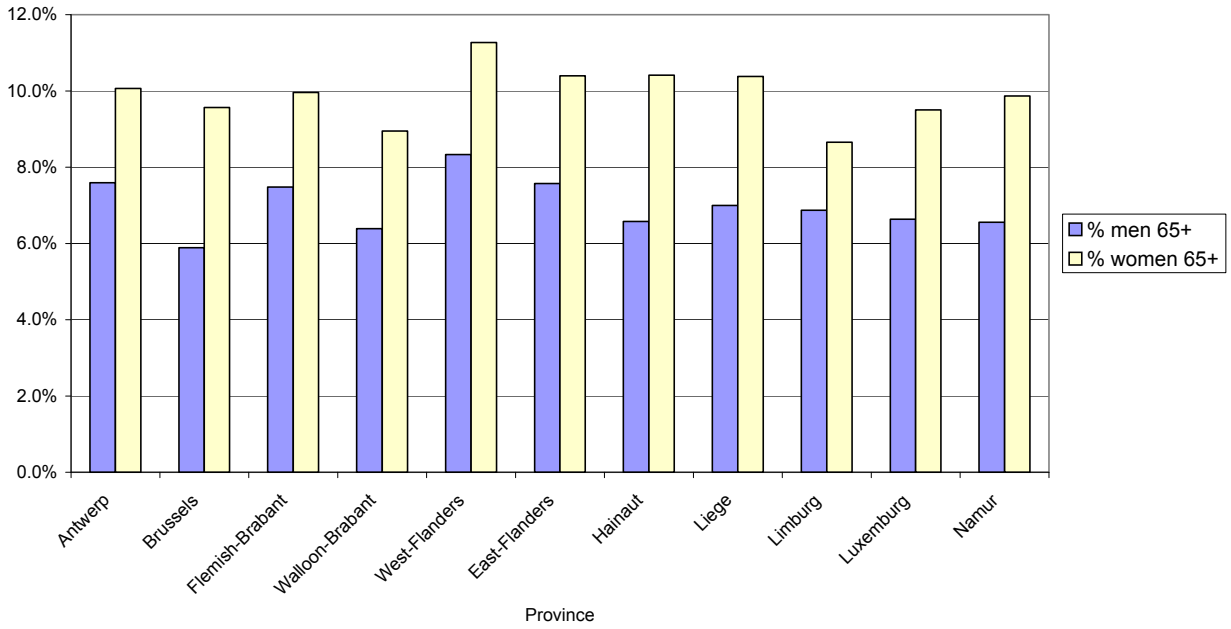
Only in the province of Hainaut the proportion of patients with IHD as underlying heart disease differs significantly from the average values. This finding corresponds to the result of other registries (cfr. Ghent-Charleroi study on AMI prevalence). In all other provinces the proportion does not differ from the mean percentage of ischaemic indication for ICD-implantation as can be seen in the following figure.

Figure 24: Proportion of IHD as underlying heart disease by province and 95% confidence intervals.



No important differences between the provinces with regard to the age and gender distribution among ICD-patients are found. In Figure 25 the proportion of men and women of 65 years and older is shown for each province.

Figure 25: Age and gender in total population per province



7.6.4 Ejection fraction

Table 58: LV Ejection fraction by underlying heart disease

	Other	%	Idio	%	Isch	%
< 31%	9	3%	58	21%	215	76%
31-35%	3	3%	9	9%	85	88%
36-50%	3	2%	24	14%	144	84%
> 50%	56	53%	6	6%	43	41%
Total	**71**	**11%**	**97**	**15%**	**487**	**74%**

Idio: idiopathic cardiomyopathy; Isch: ischemic heart disease.

The next figure represents the distribution of the ICD-patients in the ejection fraction categories according to the underlying heart disease. Overall 44% of the patients with ischaemic heart disease have an ejection fraction below 31 %.

Figure 26: Ejection fraction categories by underlying heart diseaseIndication

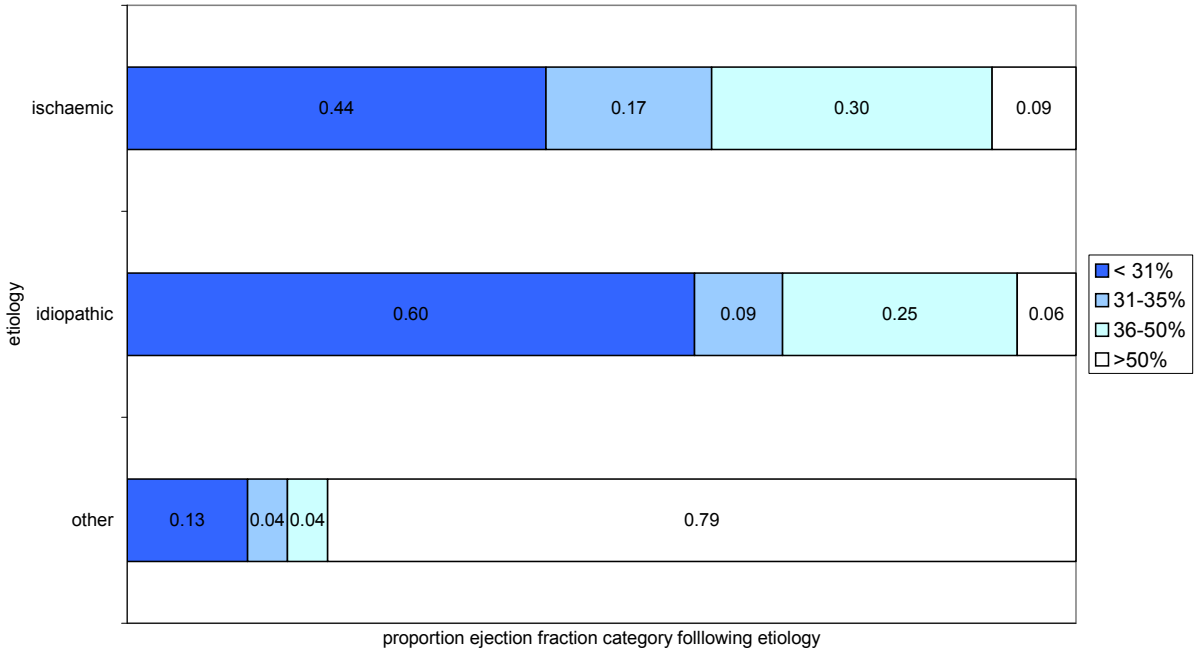


Table 59: Underlying heart disease by indication category

Indication category #	Other	row	col	Idio	row	col	Isch	row	col
1	**75**	27%	35%	**38**	14%	25%	**168**	60%	22%
2	**43**	10%	20%	**62**	15%	40%	**320**	75%	43%
3	**2**	1%	1%	**2**	1%	1%	**151**	97%	20%
4	**1**	4%	0%	**16**	70%	10%	**6**	26%	1%
5	**20**	13%	9%	**34**	21%	22%	**105**	66%	14%
6	**76**	96%	35%	**2**	3%	1%	**1**	1%	0%
total	**217**	**19%**	**100%**	**154**	**14%**	**100%**	**751**	**67%**	**100%**
Not accepted indication	8			8			1		

Indication categories: cf table 38

7.6.5 Type of prevention

Table 60: Type of prevention by underlying heart disease

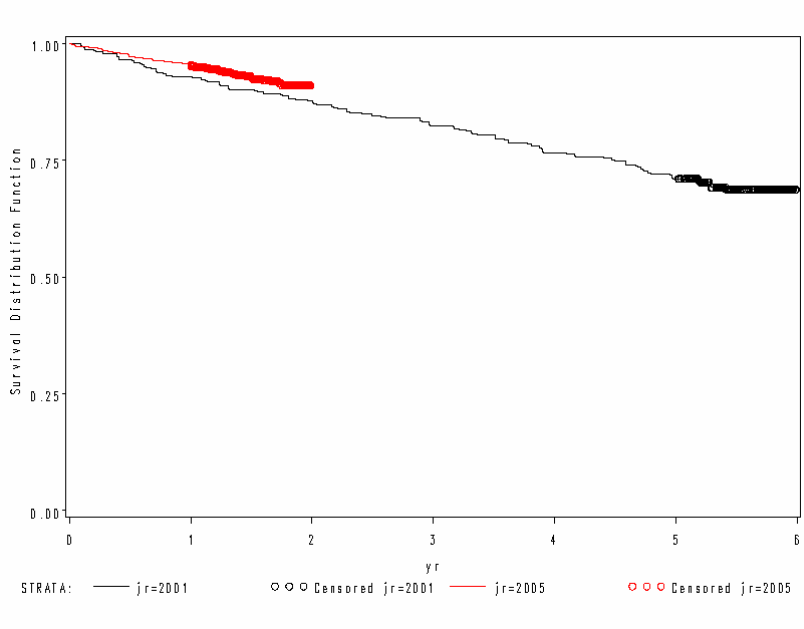
	Other	%	Idio	%	Isch	%
Secondary prevention	139	16%	150	17%	599	67%
Primary prevention	78	33%	4	2%	152	65%
Total	217	19%	154	14%	751	67%

7.7 SURVIVAL ANALYSIS

7.7.1 Patient survival

Mortality data of the patients are available till the end of 2006. The first patients of 2005 can thus be followed during maximum two years.

Kaplan-Meier survival curves of Belgian registry patients.

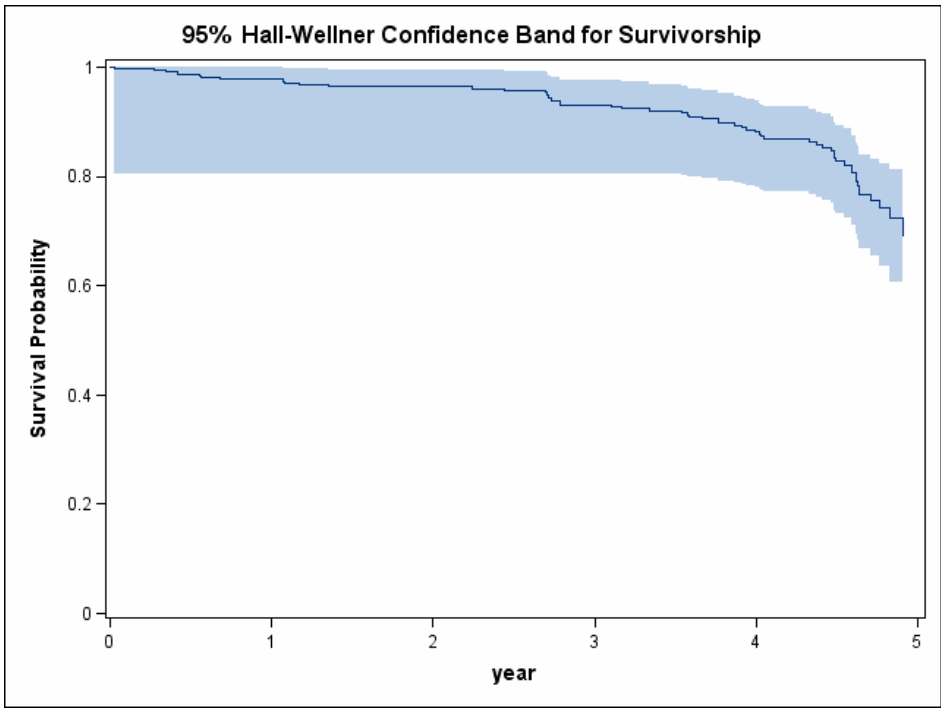


7.7.2 ICD Longevity

Mean survival of the ICD-device is 4,56 years. In the new convention contract text a 3 year warranty for ICD will be requested. The sudden decrease in survival could be explained by survival characteristics of the patient population and to a lesser extent by reimbursement criteria of ICD replacement.

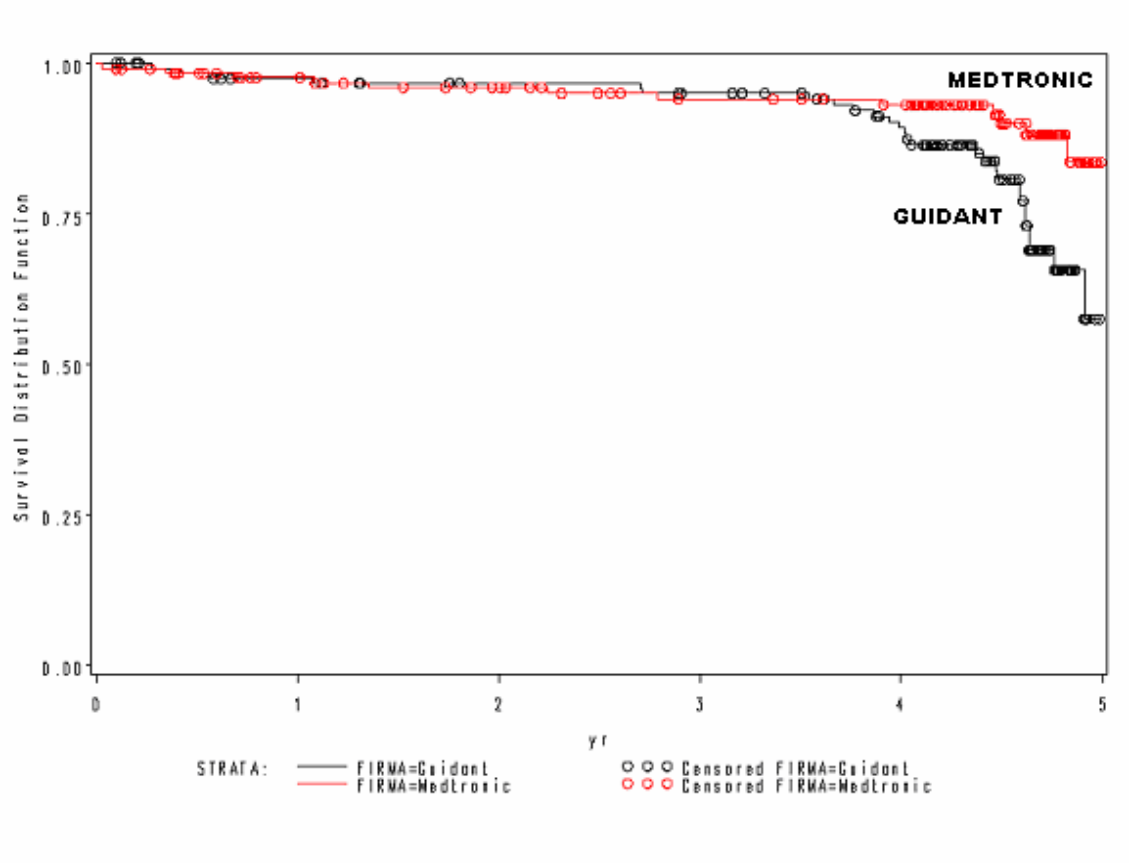
As will be discussed later, the longevity of the ICD device could be an important parameter in the selection of devices that are considered for reimbursement. Since there are considerable differences in power source and thus in longevity between ICDs on the market, a reimbursement policy rewarding the manufacturer that produces devices with best longevity has to be contemplated.

Figure 27: Kaplan-Meier survival curves of 2001 ICDs



7.7.3 ICD longevity according to manufacturer

Figure 28: Kaplan-Meier survival curves of ICDs by manufacturer (2001)



The differences in survival of the ICD devices of the 2 leading suppliers in 2001 are statistically significant (Log-rank test, p = 0.01). The indications for initial ICD implant according to these 2 suppliers in 2001 were not different, as can be seen in the following table. Other parameters that contribute to device survival in order to better explain the observed results were not available.

Table 61: ICD implant indication by manufacturer

Indication category #	Guidant	%	Medtronic	%
1	28	34%	36	37%
2	32	39%	38	39%
3	14	17%	11	11%
4	1	1%	2	2%
5	4	5%	6	6%
6	4	5%	5	5%
total	83	100%	98	100%
NA	45	35%	37	27%

Indication categories: cf table 38

7.8 DELIVERY OF MEDICATION AFTER IMPLANTATION IN 2005

The information on this part is based on the ambulatory (public pharmacy) delivery of medication, which is registered in Farmanet. We only looked at the patients with an ICD implanted in 2005 and considered a patient as using a specific group of pharmaceuticals if during a period of 6 months after implantation at least 2 packages of this medication had been delivered. Therefore we did not include the patients with an implant after July 1, 2005 (since these patients could at the moment of data selection not yet have been followed over a 6 months period). We also excluded the independents because of incompleteness of the Farmanet data for this specific group due to their insurance status.

The following table shows the percentage of patients consuming different groups of medication after implantation. The definition of these groups are based on ATC-codes.

Table 62: Percentage of patients consuming different groups of medication after implantation

	% of patients using a drug belonging to the ATC group as indicated after ICD implant
Anti-arrythmics NOT amiodarone/sotalol	31%
Amiodarone and sotalol	12%
Statins	33%
ß-blockers	73%
ACE-inhibitors	69%
Calcium-antagonists	12%
Anti-depressives	13%
Diuretics	49%
Antidiabetics	14%

In the following tables, consumption of some of these drugs groups according to the underlying heart disease and ejection fraction are shown.

7.8.1 Statins

From December 1st 2003 on, reimbursement of statins has been extended. Generic statins were already available in 2005 without specific conditions; the other statins were subject to a previous agreement.

75% of the costs are reimbursed, 85% for people who benefit from the preferential tariffs. It is nevertheless remarkable that only 63% of patients suffering from ischemic heart disease are using these statins.

7.8.1.1 By etiology

Table 63: Use of statins after ICD implant by underlying heart disease

Underlying heart disease	After ICD implant			Total
	No	Yes	%	
Ischaemic	96	161	63%	257
Idiopathic	40	17	30%	57
Other	77	15	16%	92
Total	**213**	**193**	**48%**	**406**
NA = 33				

7.8.2 ß-blockers

7.8.2.1 By etiology

Table x: Use of ß-blocker after ICD implant by underlying heart disease

Etiology	after			Total
	no	yes	%	
ischaemic	68	189	74	257
idiopathic	10	47	82	57
Other	29	63	68	92
Total	**107**	**299**	**74**	**406**
NA = 33				

7.8.2.2 By ejection fraction

Table x: Use of ß-blocker before and after ICD implant by ejection fraction.

ejection fraction	before	after	%	Total
< 31%	25	77	75	102
31-35%	7	18	72	25
36-50%	21	48	70	69
> 50%	10	33	77	43
Total	**63**	**176**	**74**	**239**
NA = 200				

7.9 MORTALITY ANALYSIS

Of the matched 325 ICD-implanted patients in 2001 a total number of 104 (32 %) and of the 973 matched ICD implanted patients in 2005 78 (8 %) had died by the end of 2006.

To carry out a mortality analysis on these patients all 18 implant centres in Belgium that performed ICD implantations in resp. 2001 and 2005 under ICD-convention agreement with the RIZIV, were contacted individually in order to explain the context of the research mission and to assure their optimal cooperation in the determination of the cause of death.

Subsequently a file with the deceased patients who received an ICD in 2001 and/or in 2005 was sent to the leading electrophysiologist/cardiologist of each centre. The file contained the name, ID-number, date of ICD-implantation and date of exitus for every deceased ICD-patient. Within two weeks after the mailing the implantation centres that had not yet responded received a phone call or another mail as a reminder.

Taking into account that some centres had performed ICD-therapy on request of other cardiac hospital centres not accreditated by the RIZIV but taking care of the follow up, that several of the high age patients lived in elderly homes and presented follow up barriers for the centre, and finally that in 2001 it was not mandatory by the RIZIV-convention agreement for the centre to keep a detailed registry for all ICD-patients, the responses are surprisingly complete.

Over a period of five weeks an overall response suggesting the cause of death was received for 161 (88 %) of the 182 patient files. For the 104 ICD patients that received their implant in 2001 and that had died, a response was given in 82 % (n = 90) and for the 78 deceased ICD-patients implanted in 2005 information was obtained in 91 % (n = 71) of the cases, suggesting the effect of better registry conditions imposed by the RIZIV since 2002.

In Table 64 en Table 65 the implant data and the mortality data for each centre are compared with the total number of ICD-implantations in 2001 and in 2005 (nr. 13-18 had no ICD-therapy in 2001). ICD-centres that did not have a RIZIV-convention approval for reimbursement of ICD-therapy in 2001, show only mortality data for the 2005 population.

In the 2001 ICD-population there is considerable variability in the mortality rate between centres with almost the same number of ICD-implants: one centre (nr. 5) noted 14 ICD-patients (4,3 % of all ICD-implantations) with 50 % mortality (2,15 % of all 2001 ICD-patients) and another centre (nr. 7) noted 13 ICD-patients (4 % of all 2001 implantations) with 15,4 % mortality (0,62 % of all 2001 ICD-patients). However these inter-centre differences are not statistically significant due to the relatively small numbers.

For the 2005 population the follow up period is limited to maximum 2 years and mortality figures in toto and per centre are considerably smaller.

Since there probably is no clear relationship between the total number of yearly implantations and the mortality rate per centre an important variability in patient selection as candidates for ICD-therapy is assumed. This could explain the far more favourable survival in some centres, a phenomenon that can be present in both 2001 and 2005 series (e.g. centre nr. 9). However the interpretation of mortality is rather complex and depends highly on the selection of the candidates for ICD-implantation.

In several studies reported in the literature the importance of NYHA-score as expression of the functional status on survival is strongly emphasized. Unfortunately, we did not have access to these data in our registry.

Table 64: Mortality study of 2001 ICD implanted patients (Belgian ICD-registry)

centre	mortality		total impl.		% mortality/ all ICD	% mortality/ centre
1	19	18,3%	56	17,2%	5,8%	33,9%
2	6	5,8%	20	6,2%	1,8%	30,0%
3	27	26,0%	82	25,2%	8,3%	32,9%
4	1	1,0%	4	1,2%	0,3%	25,0%
5	7	6,7%	14	4,3%	2,2%	50,0%
6	14	13,5%	34	10,5%	4,3%	41,2%
7	2	1,9%	13	4,0%	0,6%	15,4%
8	15	14,4%	51	15,7%	4,6%	29,4%
9	3	2,9%	20	6,2%	0,9%	15,0%
10	2	1,9%	6	1,8%	0,6%	33,3%
11	6	5,8%	18	5,5%	1,8%	33,3%
12	2	1,9%	7	2,2%	0,6%	28,6%
13	0	0,0%	0	0,0%	0,0%	0,0%
14	0	0,0%	0	0,0%	0,0%	0,0%
15	0	0,0%	0	0,0%	0,0%	0,0%
16	0	0,0%	0	0,0%	0,0%	0,0%
17	0	0,0%	0	0,0%	0,0%	0,0%
18	0	0,0%	0	0,0%	0,0%	0,0%
all	104	100,0%	325	100,0%		

Table 65: Mortality study of 2005 ICD implanted patients (Belgian ICD-registry)

centre	mortality		total impl.		% mortality/ all ICD	% mortality/ centre
1	7	9,0%	93	9,6%	0,7%	7,5%
2	8	10,3%	67	6,9%	0,8%	11,9%
3	2	2,6%	59	6,1%	0,2%	3,4%
4	0	0,0%	29	3,0%	0,0%	0,0%
5	2	2,6%	29	3,0%	0,2%	6,9%
6	13	16,7%	123	12,6%	1,3%	10,6%
7	12	15,4%	98	10,1%	1,2%	12,2%
8	11	14,1%	152	15,6%	1,1%	7,2%
9	0	0,0%	42	4,3%	0,0%	0,0%
10	9	11,5%	74	7,6%	0,9%	12,2%
11	6	7,7%	38	3,9%	0,6%	15,8%
12	0	0,0%	0	0,0%	0,0%	0,0%
13	1	1,3%	35	3,6%	0,1%	2,9%
14	3	3,8%	31	3,2%	0,3%	9,7%
15	3	3,8%	46	4,7%	0,3%	6,5%
16	0	0,0%	38	3,9%	0,0%	0,0%
17	1	1,3%	13	1,3%	0,1%	7,7%
18	0	0,0%	6	0,6%	0,0%	0,0%
all	78	100,0%	973	100,0%		

In Table 66 the mortality distribution per centre is given for the male and female patient population that received an ICD in 2001 or 2005 and that had died by the end of 2006. There is a very similar gender distribution for the total patient group with ICD implantation as for the deceased patient group: in 2001 for the total ICD-patients 80,3 % were men and 19,7 % women, and a 85,6 % male vs. 14,4 % female distribution among the deceased is found. In 2005 there is almost a complete identical distribution 85% male vs. 15% female patients and 85,6 % male vs. 14,1 % female mortality. Global survival chances are therefore apparently equal for male and female patients.

Table 66: Mortality distribution per centre of 2001 and 2005 ICD implanted patients

	2001			2005		
centre	Men	Women	Total	Men	Women	total
1	14	5	19	6	1	7
2	6	0	6	7	1	8
3	24	3	27	1	1	2
4	1	0	1	0		0
5	6	1	7	1	1	2
6	12	2	14	9	4	13
7	2	0	2	10	2	12
8	11	4	15	11		11
9	3	0	3	0		0
10	2	0	2	8	1	9
11	6	0	6	6		6
12	2	0	2	0		0
13	0	0	0	1		1
14	0	0	0	3		3
15	0	0	0	3		3
16	0	0	0	0		0
17	0	0	0	1		1
18	0	0	0	0		0
	89	15	104	67	11	78
	85,6%	14,4%	100,0%	85,9%	14,1%	100,0%

In order to evaluate the cause of death for the 2001 and 2005 population of ICD-treated patients that had died by the end of 2006 the death causes reported by the centres, were regrouped in cardiac versus non-cardiac death and further subdivided in death due to heart failure, sudden cardiac arrest or other for the cardiac causes and in malignancy and other for the non-cardiac causes (Table 67 and Table 68). Only two death causes in 2001 and three in 2005 could not be classified due to insufficient information. Note that death by heart failure with 33 % (2001) to 40,5 % (2005) is the most important cause of mortality, whereas global cardiac cause of death accounts for 53 % (2001) to almost 60 % (2005). Nevertheless a considerable number of deaths are due to sudden cardiac death a cause that the ICD-therapy in fact is meant to prevent.

Sudden cardiac arrest seems to be a more likely cause of death in male ICD-patients, but the small number does not permit a statistically valid conclusion.

Concerning the non-cardiac mortality the fatal malignancy pathology risk for male ICD-patients increasing with total follow up time seems also significantly higher, but again comparison of hazard ratio for cancer morality in an age-adjusted general population sample has to be carried out to confirm this.

Table 67: Mortality distribution for cardiac and non-cardiac cause of death of 2001 and 2005 ICD implanted patients

	2001				2005			
	Men	Women	Total		Men	Women	total	
cardiac								
heart failure	24	6	30	33,33%	26	4	30	42,25%
sudden death	11	1	12	13,33%	7		7	9,86%
other	5		5	5,56%	4	2	6	8,45%
subtotal	40	7	47		37	6	43	
non-cardiac								
malignancy	14		14	15,56%	7		7	9,86%
other	22	5	27	30,00%	18	3	21	29,58%
subtotal	36	5	41		25		28	
not available	1	1	2	2,22%	0	0	0	0,00%
Total	77	13	90	100,00%	62	6	71	100,00%
	85,56%	14,44%			87,32%	8,45%		

Table 68: Mortality distribution per cause of death and per ICD-centre of 2001 and 2005 ICD implanted patients

	2001									
		cardiac				non-cardiac			not available	total
centre	total deaths	HF	SCD	other	total	malignancy	other	total		
1	19	5	5	1	11	3	4	7	1	19
2	6	1	0	0	1	2	3	5	0	6
3	27	13	3	0	16	4	6	10	1	27
4	1	0	1	0	1	0	0	0	0	1
5	7	1	0	1	2	3	2	5	0	7
6	14	0	0	0	0	0	0	0	0	0
7	2	1	0	0	1	1	0	1	0	2
8	15	6	2	1	9	0	6	6	0	15
9	3	0	0	0	0	1	2	3	0	3
10	2	1	0	0	1	0	1	1	0	2
11	6	2	1	1	4	0	2	2	0	6
12	2	0	0	1	1	0	1	1	0	2
13	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0
	104	30	12	5	47	14	27	41	2	90
		33,3%	13,3%	5,6%	52,2%	15,6%	30,0%	45,6%	2,2%	100,0%
	2005									
		cardiac				non-cardiac			not available	total
centre	total deaths	HF	SCD	other	total	malignancy	other	total		
1	7	3	1	0	4	2	1	3	0	7
2	8	1	0	0	1	1	6	7	0	8
3	2	2	0	0	2	0	0	0	0	2
4	0	0	0	0	0	0	0	0	0	0
5	2	1	0	0	1	1	0	1	0	2
6	13	1	2	3	6	0	3	3	0	9
7	12	8	1	2	11	0	1	1	0	12
8	11	5	1	1	7	1	3	4	0	11
9	0	0	0	0	0	0	0	0	0	0
10	9	2	0	0	2	1	3	4	3	9
11	6	3	1	0	4	0	2	2	0	6
12	0	0	0	0	0	0	0	0	0	0
13	1	1	0	0	1	0	0	0	0	1
14	3	2	0	0	2	0	1	1	0	3
15	3	0	1	0	1	1	1	2	0	3
16	0	0	0	0	0	0	0	0	0	0
17	1	1	0	0	1	0	0	0	0	1
18	0	0	0	0	0	0	0	0	0	0
	78	30	7	6	43	7	21	28	0	71
		42,3%	9,9%	8,5%	60,6%	9,9%	29,6%	39,4%	0,0%	100,0%

In next two tables below, the cause of death of the 2001 and 2005 ICD-population is related to the age of the patients. The 2001 ICD-population counted 104 deaths in 12 centres, where in 88 cases the cause of death could be determined. The mean age at death was 72,4 y for all causes, for cardiac vs. non-cardiac causes the mean age was 72,7 y vs. 73,4 y. There is no significant difference in mean age at death between the subgroups heart failure and sudden cardiac death, but the patients with other cardiac death were globally younger of age.

The variability among the individual centres is not statistically significant. The 2005 ICD-population in Table 70 shows a mean age at death of 71,6 y for all causes and for cardiac vs. non-cardiac causes the mean age was 71,1 y vs. 71,8 y. In this group of ICD-patients the mean age at death for heart failure is 71,7 y and for SCD is 66,9 y. The data per centre again are relatively small and do not permit formal conclusions on patient selection for ICD-therapy. However it is noteworthy that the difference in age at death with an older population dying from heart failure and a younger one from sudden cardiac death (arrythmias) can only be established during a limited follow up period, during which the majority dies of heart failure at a clearly higher age.

With longer follow up period ICD-patients continue to die from SCD also at higher age and also the original age differences between the heart failure and the sudden cardiac populations are progressively reversed.

Table 69: Mortality by age and cause of death for 2001 ICD implanted patients (Belgian ICD-registry)

	AGE AT DEATH 2001							CAUSE OF DEATH 2001						
	cardiac				non-cardiac			cardiac				non-cardiac		
centre	HF	SCD	other	total	malign..	other	total	HF	SCD	other	total	malign	other	total
1	75,4	76,8	77,0	76,211	77,0	70,5	73,3	5	5	1	11	3	4	7
2	81,0			81,0	71,5	68,0	69,4	1	0	0	1	2	3	5
3	68,1	77,0		69,8	74,0	69,8	71,5	13	3	0	16	4	6	10
4		73,0		73,0				0	1	0	1	0	0	0
5	70,0		41,0	55,5	61,7	78,0	68,2	1	0	1	2	3	2	5
6								0	0	0	0	0	0	0
7	80,0			80,0	72,0		72,0	1	0	0	1	1	0	1
8	76,2	73,5	79,0	75,9		75,8	75,8	6	2	1	9	0	6	6
9					73,0	68,0	69,7	0	0	0	0	1	2	3
10	77,0			77,0		70,0	70,0	1	0	0	1	0	1	1
11	77,5	63,0	65,0	70,8		59,5	59,5	2	1	1	4	0	2	2
12			74,0	74,0		84,0	84,0	0	0	1	1	0	1	1
13								0	0	0	0	0	0	0
14								0	0	0	0	0	0	0
15								0	0	0	0	0	0	0
16								0	0	0	0	0	0	0
17								0	0	0	0	0	0	0
18								0	0	0	0	0	0	0
	72,7	74,8	67,2	72,7	71,4	71,3	71,3	30	12	5	47	14	27	41

Table 70: Mortality by age and cause of death for 2005 ICD implanted patients (Belgian ICD-registry)

	AGE AT DEATH 2005							CAUSE OF DEATH 2005						
	cardiac				non-cardiac			cardiac				non-cardiac		
centre	HF	SCD	other	total	malign..	other	total	HF	SCD	other	total	malign	other	total
1	68,3	58,0		65,8	77,0	75,0	76,3	3	1	0	4	2	1	3
2	76,0			76,0	75,0	67,7	68,7	1	0	0	1	1	6	7
3	62,5			62,5				2	0	0	2	0	0	0
4								0	0	0	0	0	0	0
5	74,0			74,0	55,0		55,0	1	0	0	1	1	0	1
6	80,0	66,5	74,0	72,2		74,7	74,7	1	2	3	6	0	3	3
7	66,8	73,0	76,0	69,0		85,0	85,0	8	1	2	11	0	1	1
8	73,8	67,0	68,0	71,7	81,0	71,7	74,0	5	1	1	7	1	3	4
9								0	0	0	0	0	0	0
10	74,0			74,0	76,0	66,5	69,7	2	0	0	2	1	3	4
11	83,0	61,0		75,7		75,5	75,5	3	1	0	4	0	2	2
12								0	0	0	0	0	0	0
13	76,0			76,0				1	0	0	1	0	0	0
14	72,5			72,5		70,0	70,0	2	0	0	2	0	1	1
15		76,0		76,0	80,0		80,0	0	1	0	1	1	1	2
16								0	0	0	0	0	0	0
17	87,0			87,0				1	0	0	1	0	0	0
18								0	0	0	0	0	0	0
	71,7	66,9	73,6	71,1	74,4	70,8	71,8	30	7	6	43	7	21	28

8 ORGANISATIONAL ISSUES

In forthcoming years an increase of the number of ICD implantations is very likely to occur due to an expansion of the use of these devices towards primary prevention and due to an increasing use of device therapy in heart failure. In this chapter, we try to quantitatively estimate this growth.

8.1 EXPANSION OF COVERAGE TO PRIMARY PREVENTION

Up to now, most ICD implants in Belgium have been for secondary preventive reasons. Reimbursement for ICDs in primary prevention from the year 2002 on was limited to MADIT I-criteria: patients with IHD and nonsustained VT in whom inducible and non-suppressible ventricular tachyarrhythmias are present on electrophysiologic study. In the original MADIT I study, LVEF had to be lower than 36% and patients were excluded if they had an AMI within three weeks from enrollment or if they had undergone coronary artery surgery within the past two months or coronary angioplasty within the past three months. In the current Belgian coverage definition, MADIT I criteria were slightly modified with an upper limit of LVEF of 39%, a minimal time span between a previous AMI of 7 days and no limitations imposed on the timing of revascularisation procedures.

As explained in the previous chapter, in order to calculate the total number of primary prevention implants, we summed the patients meeting the modified MADIT I criteria (indication category #3), and those in whom an ICD was implanted for primary preventive indications in genetic disorders (indication category #6). Strictly speaking, there was no reimbursement for ICDs in primary prevention in 2001, but on investigating the administrative patient files, 15% of implants evidently were primary prevention indications. Of 938 patients implanted in 2005 and for whom reliable clinical data were available, 193 (21%) received an ICD for a primary prevention indication and 745 (79%) for secondary prevention. In 2001, the corresponding numbers were 20% and 80% respectively when we applied the 2005 reimbursement criteria to the clinical data we were able to retrieve from the patient files (cf chapter 6). In 2005 the ratio primary/secondary prevention was 0.21/0.79=0.27.

The Belgian cardiological community actually asks for the expansion of the reimbursement of ICDs in primary prevention. In January 2006, the Belgian Working Group on Cardiac Pacing and Electrophysiology (BWGCPE) proposed an extension of reimbursement of ICDs based on the results from MADIT II, SCD-HeFT, MUSTT and on the criteria imposed by Medicare in the US:

- Ischaemic heart disease and LVEF 36-40%: spontaneous nonsustained VT, inducible tachyarrhythmia, >1 month following AMI and >3 months following revascularisation.
- Ischaemic heart disease and LVEF < 36%: >40 days following AMI and >3 months following revascularisation.
- Nonischaemic heart disease: LVEF <36%, NYHA class II or III in spite of at least 3 months of optimal medical therapy.

From an organisational point of view, it is essential to estimate what could be the resulting increase in the number of ICD implants in response to these expanded coverage rules. In a discussion we had with the "Akkoordraad", a Belgian commitee that groups the Belgian ICD implant centres and representatives of the government and insurers, it was promulgated that the extension of coverage of ICDs in Belgium to the new criteria, would only result in an increase of the number of implants with 20%.[i] Although the size of the target group for ICD treatment aimed at primary prevention is difficult to estimate, referring to an increasing use of ICDs in neighbouring countries, we expect a much larges increase in our country.

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i Akkoordraad ICD – Conseil d'accord ICD, June 21, 2006.

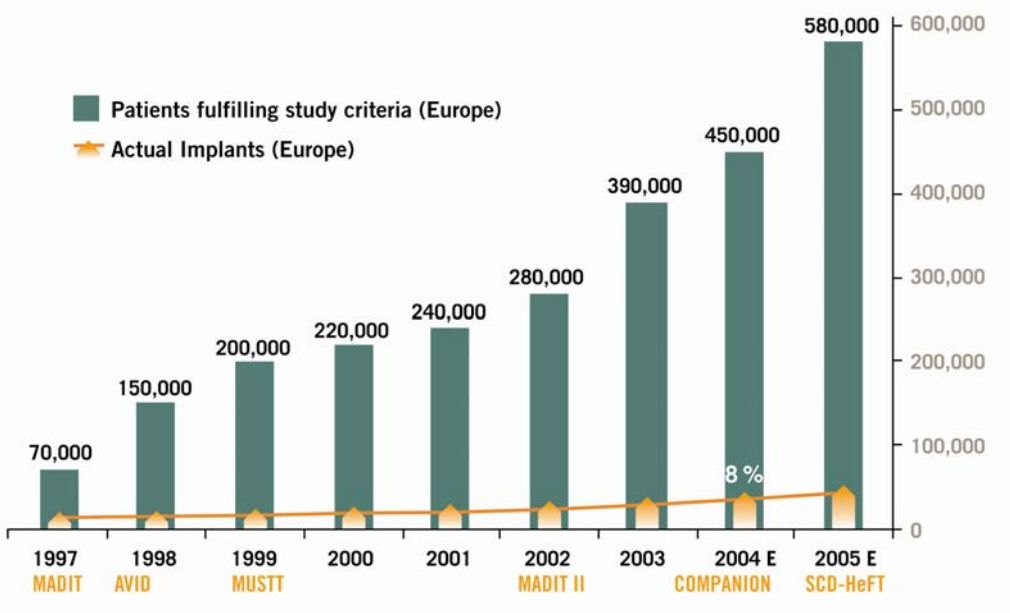
A rough estimate by the Swedish HTA agency predicts for primary prevention a yearly ICD implant rate of 111 to 167 per million.[2] It is not clear from the English language summary report whether replacements are included into this number. The target group for ICD treatment aimed at secondary prevention currently in Sweden, is approximately 44 to 56 per million per year. Combining the estimates for primary and secondary prevention for Sweden would result in 150 to 220 implants per million inhabitants with a primary/secondary ratio of 2.8.

In Denmark, in 2004 the large majority of ICD implants were for secondary prevention. MADIT I criteria were adopted the year before. Of 414 first implants (81/million) 89% were for secondary prevention.[140] In May 2006, indications were extended to patients with a LVEF <31% and NYHA II or III. In 2006, of 600 first implants (111/mio), 74% were for secondary prevention (ratio primary/secondary=0.35).[141]

In the 2005 Italian ICD Registry, 42% of patients were implanted for primary prevention (ratio=0.72) while in the USA, during the same period, the majority (82%) of implants were for primary prevention (ratio=4.6).[142]

In a simulation by Guidant[143] it was estimated that in the year 2005, 580 000 people in Europe fulfilled the inclusion criteria of SCD-HeFT. According to Guidant, only 8% of the clinically eligible patients actually received an ICD. For the US the potential was estimated as 857 181 patients with an actual implant rate of 66%. According to the Guidant estimations, compared to MADIT I, four times more patients meet the MADIT II and eight times more the SCD-HeFT criteria.

Figure 29: European patient population estimated by Guidant to fulfill trial criteria vs. actual implant rate.[143]



Courtesy Boston Scientific (May 22, 2007).

One might expect that the future increase in implantation rate will be largely accounted for by an increase in primary prevention implants, as a dramatic increase in survival following out of hospital cardiac arrest is not likely to occur.[144] In Belgium and Denmark, when primary prevention reimbursement was restricted to MADIT I patients, only 20% of patients were treated for primary prevention. In Italy in 2005, 42% of patients were implanted for primary prevention.

Schalij presented for the Netherlands an algorithm to predict the yearly need of ICDs in his country and estimated that in the forthcoming years, 10 500 units (de novo plus replacements plus CRT-D) would be needed (644/million).[145]

The Dutch "Gezondheidsraad", in its 2007 report on cardiac interventions, made a more conservative prediction for The Netherlands and expects the number of ICD and CRT to double during the next few years (from 2 100 in 2005 to 4 500 in 2010, i.e. 129 and 276 units/mio respectively).[146]

In Canada, it is estimated that 85 000 untreated Canadians are candidates for an ICD, i.e. 2631/mio that meet current primary preventive implantation guidelines. Every year, an additional 3 700 prophylactic cases (115/mio) are expected.[17]

Figure 30 depicts the evolution of the number of first ICD implants in The Netherlands from 1995 to 2005.[147] The number of 2 100 new implants in The Netherlands has been added by us (indicated by NL), as well as all new implants in Belgium in the years 2001 through 2005 (red dots annotated with BEL). Although a drastic facilitation of reimbursement has been implemented in The Netherlands in recent years, it is clear that ICD use in this country has been driven largely by the results of RCTs. In the mid-nineties ICD therapy was restricted to secondary prevention of SCD. MADIT I initiated a first increase by expansion of coverage towards the highest risk primary prevention patients. A second increase was initiated by the combined effect of MADIT II and COMPANION and a third wave is to be expected by the implementation of SCD-HeFT criteria into clinical practice. A similar increase of implant rate is depicted in the chart produced by Guidant as discussed earlier (Figure 29)

Belgium, as far as the number of ICD implants is considered, is lagging behind this trend with 75 new implants/mio/year in 2005. Since 2002, ICD reimbursement in primary prevention is limited to patients with "modified" MADIT I characteristics. Nevertheless, an increase in the number of ICDs is noticed, probably due to a more or less flexible application of reimbursement rules. The current implant rate in Belgium is rather low, not only compared to The Netherlands (129/mio) but also in comparison with the current implant rate in e.g. Denmark (111/mio) or Sweden (185/mio). The latter countries expect a continuing increase in the number of implants, due to a second wave of growth in accordance with the SCD-HeFT data. Adopting the Guidant prediction that estimated an eightfold increase in the population at risk in MADIT I as compared to SCD-HeFT and taking an unchanging number of secondary prevention implants to the Belgian 2005 data, would roughly lead to 2000 new implants per year in Belgium. We can reasonably expect that by expanding the implantation coverage of ICDs towards MADIT II and SCD-HeFT type patients, the total yearly number (de novo plus replacements) of implants will more than double to 200-250/mio in the forthcoming years.

Figure 30: Evolution of yearly number first ICD implants per million population in The Netherlands (NL) and in Belgium (BEL).

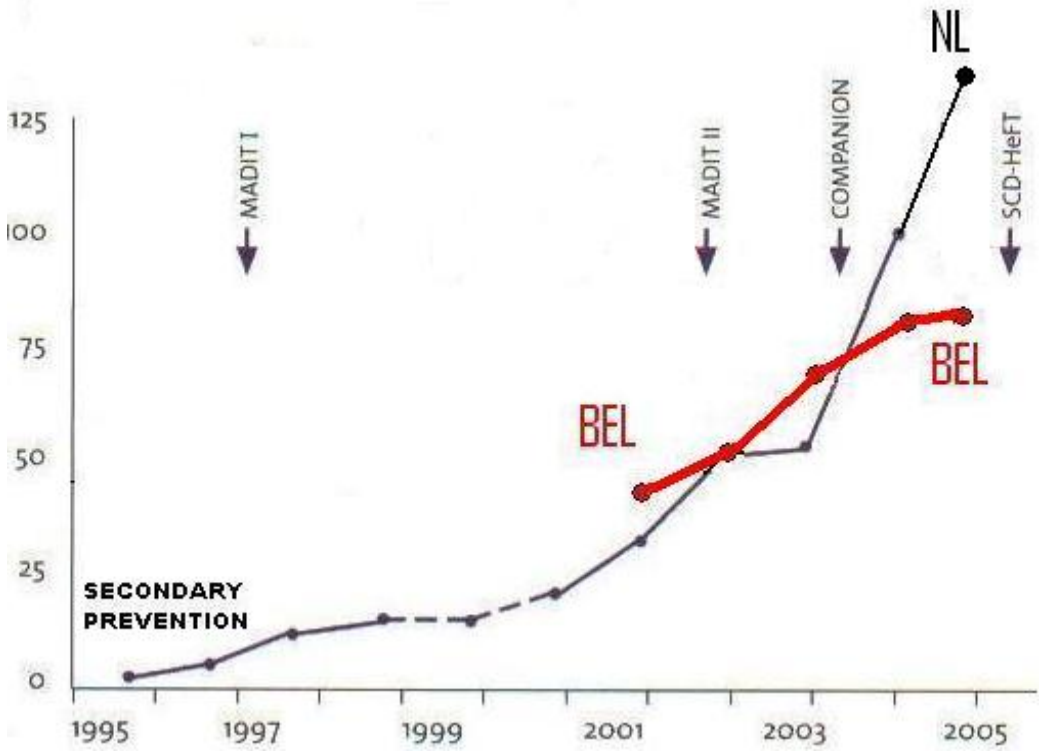


Chart adapted from Jordaens.[147] Belgian data from Belgian ICD Registry (2001 and 2005) and Akkoordraad-data (approximations). "Secondary prevention" relates to time window when ICD implants were exclusively performed for secondary preventive reasons.

8.2 EMERGING INDICATIONS FOR CRT-D.

Currently available data indicate that the use of an ICD in combination with CRT (CRT-D) should be based on the indications for the ICD therapy.[21] [20] Consequently, patients with a clinical indication for an ICD who have medically intractable HF, can be considered to be treated with a CRT-D. The other way round, there is a grey area of indications for implanting a CRT-D in patients with a severely depressed left ventricular function and clinical HF for whom a CRT device is considered by the cardiologist. It can be assumed that clinicians can become inclined to implant a CRT-D in this kind of patients with HF, reasoning that they also are at risk of SCD.

The increased use of CRT will inevitably lead to an increase of the use of defibrillators incorporated within the same CRT-D device. In Denmark, in 2006, 25% of all ICDs were CRT-Ds. Schalij expects for the near future in The Netherlands, of a total of 10 500 devices, 4000 will be CRT-Ds.[145]

At the moment, in Belgium there is no consistent coverage policy for CRT devices. CRT-P, i.e. CRT with only pacing facilities, is not reimbursed in contrast with CRT-D, that is reimbursed as far as a patient meets criteria for implantation of an ICD. When a CRT-P is implanted, it is registered as a traditional right ventricular anti-bradycardia pacemaker. Because of the disparate registration of CRT devices, their current use in Belgium is unknown.

8.3 ICD IMPLANT CENTRES

By the end of 2006, 17 centres were approved for ICD implantation in Belgium, a country with 10.4 million inhabitants. In The Netherlands, a neighbouring country with 16.3 mio inhabitants and 16 ICD centres and a presently much higher penetration of ICD use compared to Belgium, the Dutch Gezondheidsraad expected the number of ICDs and CRTs to double during the next few years and the existing 16 centres have reportedly sufficient capacity to accommodate this growth. In order to ensure high quality care, specific requirements for centres where cardiac arrhythmias are treated, have been set in The Netherlands. In addition to the presence of heart surgeons who specialise in antiarrhythmic surgery, at least four cardiologists-electrophysiologists must be available, and the centre must conduct at least 60 ICD/CRT implantations and 60 catheter ablations per year.[146] Imposing a minimal activity level for ICD implants is reasonable, not so much for the surgical procedure involved, but also for the essential technical skills and know-how for patient selection, electrophysiological studies and patient follow-up. In a post hoc analysis of data from 9 854 Medicare benificiaries in whom an ICD had been implanted by 1 672 physicians from 1999 to 2001, Al-Kathib et al investigated the relationship between patients' outcomes and the volume of ICD implantation procedures.[96] Ninety-day mortality did not differ between patients who had their ICD implanted by physicians with the highest volume of implants and those who had their ICD implanted by physicians with the lowest volume of implants (6.2% vs. 5.9%). On the other hand, patients who had their ICD implanted by high-volume physicians had lower rates of mechanical complications and ICD infection than patients who had their ICD implanted by low-volume physicians. These findings suggest that ICD implantation should be directed towards high-volume physicians.

Following hospital discharge after ICD implantation, patients need a lifelong follow-up of their defibrillator in the ICD clinic 3 to 4 times a year. On top of this, unscheduled visits occur, e.g. after (appropriate or inappropriate) discharges. Some patients will need more intensive follow-up with reprogramming, adaptation of drug therapy, psychological and social support while others will have the device as a stand-by and need only minimal technical and clinical check-ups. Therefore, the workload for an electrophysiology department will increase over the next decade, not only because of an increasing number of surgical procedures but also because of an accumulation of patients that need a check-up of the device.

New technology allows device interrogation wirelessly, allowing patients to be followed by "home monitoring". By means of radiofrequency, the ICD sends information to a receiver unit installed at the home of the patient and by using GSM technology, the information is transmitted to a central station. From there it is sent to the physicians by fax or SMS or it can be accessed on a server via internet. Although telemonitoring technology seems promising, its effectiveness and efficiency has not yet been clearly demonstated.[148]

9 GENERAL DISCUSSION

ICDs reduce all-cause mortality in specific subgroups of patients. Their use in secondary prevention is not expected to increase substantially and the future growth will presumably be found in the larger group of primary prevention patients with ischaemic and nonischaemic cardiomyopathy and severely depressed left ventricular function. Referring to the above mentioned discussion, we can expect an important expansion of the number of ICDs implanted in Belgium in forthcoming years.

Given the huge costs involved and the limitation of available resources, an efficient organisation and planning of ICD therapy is imperative. Cost-effectiveness can be improved by reducing cost or increasing effectiveness. Reducing the cost of the device (and the related follow-up procedures) and avoiding implantations in patients who subsequently will never need a shock, can help to achieve this goal. In this respect, the estimation of the risk of SCD and the life expectancy of a given potential patient is of utmost importance. Patients with IHD can be at low risk of SCD and hence may never develop ventricular fibrillation. On the other hand, they may have considerable cardiac or non-cardiac comorbidity, leading to death before ventricular fibrillation ever develops.

For risk stratification, the physician has to rely on efficacy data resulting from RCTs, the assessment of the external validity of these data and on clinical judgement. Left ventricular contractile function (ejection fraction) and a patient's functional status (NYHA class) are the parameters that are typically used in selecting patients. In addition to the evaluation of functional status, physicians have to rely on clinical judgement in order to take into account clinical elements that are more difficult to assess: (biological) age, co-morbidities, patients' personal preferences and values, societal priorities, ...

9.1 UNCERTAINTIES IN THE EFFECTIVENESS OF THE ICD

There remains considerable uncertainty as to which patients benefit most from an ICD. This is illustrated by the fact that in only three of eight primary prevention trials, ICD therapy gave rise to a statistically significant reduction in all-cause mortality. If the results of *all eight* primary prevention ICD trials are pooled, absolute risk reduction of all-cause death by ICD therapy is estimated to be 4.8% (over a period of 2 to 4 years) with a relative risk of 0.75 (95% CI 0.59-0.96). If however, the results of the *four* trials in patients with *ischaemic heart disease* are pooled separately in a meta-analysis, a statistically significant benefit in terms of all-cause mortality can no longer be demonstrated (cf chapter 3). The same holds true for a meta-analysis of trials in which only patients with *nonischaemic disease* were included.[17]

The evidence in favour of ICD is most robust for patients with a severely reduced left ventricular function and clinical heart failure (no worse than NYHA class III). The trial that best represents current clinical practice is SCD-HeFT in which an absolute overall survival benefit of 1.8% per year in ICD-treated patients was obtained. From this trial it can be estimated that one has to implant an ICD in between 13 and 128 patients to save one life after three years (NNT 22, 95%CI 13-128).

Inserting ICDs in all patients that meet current guideline recommendations leads to implantation of devices in many that will never need them. From the results of SCD-HeFT, we can estimate that during 5 years of follow-up, 80 out of every 100 implanted patients will not benefit from their ICD.[11] Consequently, there is an urgent need to better identify subgroups of patients in whom a better prediction of benefit of the ICD is possible, in order to avoid imposing a needless burden on the patients' shoulders and preventing the waste of public resources. At present, there is no single test that has been prospectively evaluated that provides a high predictive value in identifying the patients at highest or lowest risk.

Uncertainties also stem from methodological difficulties encountered in RCTs that assess the effectiveness of ICDs. As discussed earlier, randomly assigning patients to devices is more difficult than assigning them to drugs and blinding patients and physicians is practically impossible when studying the effectiveness of a device, i.c. an ICD. Moreover, recruitment of patients for clinical trials started in a era when the treatment of AMI was different from nowadays practice. It is remarkable that no benefit at all in all-cause mortality could be identified in MADIT II in patients in whom the most recent AMI took place less than 18 months before randomisation.[35] Furthermore, DINAMIT showed that patients that are traditionally considered at very high risk for SCD, i.e. those who had a recent AMI, do not benefit from ICD.[41]

As can be inferred from Table 14, the age of patients enrolled in RCTs is well below 65 years. In SCD-HeFT, the largest of these trials, median age is 60 years which means that the majority of patients were less than 65 years old. In a post hoc subgroup analysis of the SCD-HeFT data, in patients older than 65 year, ICD was not better than placebo in reducing mortality during the trial. Because of the increasing rate of coexisting conditions associated with aging, the major portion of the clinical benefit noted for ICD implantation may occur in patients younger than 65 and extrapolating the overall SCD-HeFT results to all patients at risk for SCD may not be valid.

For some specific subgroups of patients with IHD we can reliably state that ICD is useless in preventing death. This is best documented in the early period following an AMI in patients with reduced EF and impaired cardiac autonomic function[41] and in combination with coronary artery bypass grafting.[36] Patients with NYHA class IV heart failure were excluded from most RCTs and probably do not benefit from an ICD due to their poor survival, death mostly being due to progressive heart failure. In SCD-HeFT, in a prespecified subgroup analysis, also patients in NYHA class III had no apparent reduction in risk of death as compared with placebo.

There is evidence from clinical trials that early reperfusion, ß-blockers, statins and ACE-inhibitors reduce the risk of SCD in selected AMI patients. Registry data indicate that a widespread use of evidence based therapy of AMI patients may lead to a reduction of the incidence of SCD in these patients.[27] Therefore, implementation of well-documented and proven therapeutic strategies in the acute phase of an AMI and later on is crucial. This would lead to a decrease in the absolute number of SCAs in post infarction patients, and hence the absolute benefit of ICD therapy will decrease as well, leading – all other factors remaining equal - to a less favourable cost-effectiveness. If however, the total number of patients at risk of SCD decreases and better stratification methods become available, fewer ICD implants would be needed and the budget impact of the therapy may become lower.

9.2 PATIENT VALUES AND SOCIETAL PRIORITIES

One can question the desirability of implanting an ICD in a patient with a poor quality of life and/or a poor life expectancy because of the additional burden of surgery and follow-up procedures and the very limited expected benefit these patients derive from the intervention. Patients with advanced HF may find a death due to a ventricular arrhythmia more appealing than that due to recurrent pulmonary edema or low output failure. Similarly, an elderly patient may not wish to have life prolonged and may find a lethal ventricular arrhythmia preferable to other possible causes of death.[133]

On the other end of the spectrum, it can be questioned whether patients who had a myocardial infarction many years ago and are feeling well, should be alarmed with the information that their inevitable death might be postponed, and replaced by another mode of death. In these patients there is a trade-off between blessed ignorance and running scared. A yearly risk of SCD of 2% can at best be annihilated by means of an ICD, at a non-monetary cost for the individual of an increased medicalisation of life, the need for a surgical procedure, repeat interventions every five years, a need for a lifelong follow-up 2 to 4 times a year, driving and leisure restrictions, and the risk of complications. For some patients, the security of having an ICD to terminate a lethal arrhythmia provides personal comfort for themselves and their families.

In others, the physical presence of a device and the stress associated with its firing, both appropriately and inappropriately, significantly impairs QoL. However, the scientific literature on the subject is scarce and does not demonstrate any clear impact of ICD on patients' quality of life.

In ICD therapy as in the whole of medicine, informed consent is a precondition for good clinical practice and an informed patient may reasonably decide not to undergo a prophylactic ICD implantation.

9.3 THE COST-EFFECTIVENESS ISSUE

Patients in whom an ICD is implanted have high early costs due to the cost of the device and the surgical procedure. Later on, the costs diminish but remain substantial due to the need for monitoring the ICD, for treating device complications and for adequately responding to appropriate and inappropriate shocks. In contrast to many other medical interventions, ICDs do not prevent complications that are costly to treat since they are only intended to prevent SCD, a complication that costs little or nothing to treat.[149]

There is conflicting evidence from the literature about the cost-effectiveness of ICD therapy in primary prevention, and depending on baseline characteristics of patients, time horizon, and the type of hospital, ICER values range between €47 256 and €572 056 per QALY. From the health economic model presented earlier, combining data from the SCD-HeFT trial and the Belgian Registry, we were able to predict a discounted incremental gain in life years due to ICD therapy of 1.20 years, or 1.02 QALYs. From the perspective of the Belgian Health Insurance System, and extrapolating the observed data to a patient's lifetime an ICER of €72 000 (95% CI €40 600 - €135 900) was calculated (base-case scenario).

Longevity of the device is a major determinant of the cost-effectiveness of ICD therapy (cf chapter 5) but remarkably, device longevity seems to be poorly documented in clinical literature.[150] Hauser reports an average service life of 814 single-chamber ICDs of 4.7±1 year compared with 4.0±1 year for 293 dual-chamber ICDs, indicating that the shift to (newer) dual-chamber models has significantly shortened battery life.[151] According to the Belgian data discussed earlier, longevity of ICDs implanted in 2001 was 4.56 years. In the base-case scenario, discussed in a previous chapter, when battery replacement frequency was established at 5 years, an ICER of €72 000 was obtained. Extending battery longevity from 5 to 7 years would result in a considerable improvement in efficiency with an ICER of €57 800 (Table 29).

In 2001, Zipes argued that manufacturers should create a selection of ICDs from which physicians can choose, ranging from sophisticated ICDs that could be used to treat HF and monitor a variety of physiological functions (the Rolls Royce type of ICD), to inexpensive ICDs with restricted detection and storage capabilities and a limited battery capacity to deliver only a few shocks (the Volkswagen type). If the patient used up that number of shocks, the device could be replaced with a more advanced unit.[152] The SCD-HeFT trial, the largest ICD trial ever done, did make use of a "cheap" single-lead device which did result in a significant reduction in all-cause mortality in patients with HF and an LVEF<36%. It remains to be demonstrated if more sophisticated ICDs result in a similar outcome. Very recently, this item is taken up again by Hlatky and Mark.[149] They argue that "although it might be possible to save money by using simpler, less fully featured ICDs, as were tested in SCD-HeFT, electrophysiologists currently prefer to use newer, more complex and more expensive devices". According to these authors, this behaviour can be explained by the fact that the training of electrophysiologists (and other physicians) emphasizes pathophysiological reasoning over empirical testing in clinical trials and hence, when manufacturers add new features to their devices that make pathophysiological sense, physicians may adopt them without demanding empirical proof of improved outcomes.

A convenient way of reducing the cost of the device and yet preserve the alleged benefits of sophisticated electronics, would be an increase of the battery capacity and hence augment longevity of the device. In one multicenter study[151], the effect of different battery capacities on ICD service life was evaluated. Large capacity batteries increased average service life by 2.3 years.

9.4 CONCLUSION

The clinical evidence for implanting an ICD in the primary prevention of sudden cardiac death is robust in only a small proportion of high-risk patients, i.e. in patients with ischemic heart disease and severely depressed left ventricular function with symptomatic heart failure, not worse than NYHA class III.

Most patients in whom an ICD is currently implanted, never receive an appropriate shock from the device, stressing the need for a better pre-implant risk stratification.

Our economic study, based on the Belgian registry and on SCD-HeFT data, provides a 95% CI for the base-case ICER of €40,600 to €136,000 per QALY and indicates that ICD use in primary prevention of sudden cardiac death is an inefficient therapy. From our model and a predicted yearly 2000 new ICD patients, we conclude that after a stabilisation period of 15 years after the extension of ICD reimbursement in primary prevention (SCD-HeFT patient profile), the projected net cost to the Health Authorities is huge and is estimated to amount to €154,000,000 per year.

An extension of the use of ICDs in clinical practice demands for a debate with all parties involved and should include a discussion on uncertainties in the effectiveness of ICDs, the repercussions of an implant on the patient's daily life and the enormous cost and budget impact of the device:

- Firstly, physicians should be encouraged to medically treat all myocardial infarction and heart failure patients according to evidence based best practice and to restrict implantation of ICDs in patients belonging to subgroups in which their benefit is best demonstrated.
- Secondly, patients have to be fully involved in the decision making process and thoroughly informed about the potential benefits, risks and associated discomforts and the subsequent need for a lifelong requirement for maintenance and follow-up of the device.
- Thirdly, there should be a debate on a society level related to the willingness to pay for expensive devices that only very modestly prolong longevity.
- Finally, industry should improve the performance of ICDs, e.g. by prolonging battery life.

The results of these discussions may lead to a more efficient reimbursement policy.

10 RECOMMENDATIONS

1. A further extension of the reimbursement of ICDs in the primary prevention of sudden cardiac death would result in an expansion of a technology towards an indication with an average ICER of €72 000 per QALY. An unrestricted ICD reimbursement for all patients meeting the criteria that have been used in pivotal clinical trials such as MADIT II and SCD-HeFT would result in inefficient use of resources. Long term annual budget impact would be enormous and is estimated at €154 million per year if 2000 new implants per year are considered from now on.
2. There is no evidence that ICDs incur more benefit than harm in the high elderly. It is unclear how this can be implemented into reimbursement criteria and whether the use of an age criterium would be acceptable from a societal point of view.
3. Longevity of the ICD is a major determinant of the cost-effectiveness of ICD therapy and increasing battery capacity would result in an improvement in efficiency. In a perfect world, longevity of an ICD should exceed a patient's life, obviating device replacement. Manufacturers should be encouraged to increase device longevity by imposing a longer device warranty period (five or more years or even lifetime).
4. The current Belgian reimbursement procedure (the so-called "convention") and the limitation of the number of implant centres has been responsible for preventing an unrestrained growth in the number in ICD implants. This procedure should be continued and the number of implant centres should remain limited in future years, leading to an optimal concentration of expertise and preventing an inappropriate increase in ICD implants consequent to a supply induced demand mechanism.
5. Investigating the RIZIV/INAMI application forms revealed some shortcomings. For later study and peer review of ICD practice in Belgium, a better application and registration procedure should be realized. Reporting baseline characteristics of patients, drug use, ejection fraction, NYHA class, co-morbid conditions, … should be mandatory. Application forms should be supplemented with a written informed consent of the patient.
6. Given the increasing use of device therapy in patients with heart failure, there is need to critically evaluate the clinical effectiveness and efficiency of cardiac resynchronisation therapy (CRT) in these patients as well as the incremental benefit of combined CRT plus ICD devices (CRT-D).

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12 APPENDICES

APPENDIXES TO CHAPTER 3

LITERATURE SEARCH ON CLINICAL EFFECTIVENESS

Electronic databases were searched for randomized controlled trials, systematic reviews and HTAs with the following general limits: English language, time period: 1 July 2003 – 8 January 2007, humans.

We searched Medline (Pubmed), Embase, Cochrane Library, NHS CRD Database (DARE, NHS EED, HTA). Reference lists of retrieved papers were hand searched. Expert slide presentations were consulted on line from tctmd.com. ICD manufacturers were contacted via Unamec, an organisation representing Belgian manufacturers, importers and distributors of medical devices.[153]

MEDLINE was searched via PubMed. Search terms were as follows: "defibrillators, implantable"[MeSH] OR (implantable OR internal) AND (defibrillator OR defibrillation OR defib* OR cardioversion OR cardioverter OR cardiover*), limited to clinical trial, meta-analysis and RCT. 251 references were identified of which, after reading the abstracts, 6 clinical papers were retrieved: 4 RCTs and 2 SRs.

EMBASE was searched using the following search string: ('defibrillator'/exp OR 'defibrillator') AND ([meta analysis]/lim OR [randomized controlled trial]/lim OR [systematic review]/lim) AND [article]/lim AND [english]/lim AND [humans]/lim AND [embase]/lim AND [2003-2006]/py. Papers referenced in Medline were automatically denied by the search engine. We identified 79 references of which we retrieved 3 after reading the abstracts. All three were SRs, published in 2006. One SR focussed on the use of β -blockers and the benefit from ICD[27] and another was limited to the impact of gender on survival in patients with an ICD. [58]

Handsearching resulted in one extra SR in which however, no meta-analysis was provided. [25] In the Cochrane Database of Systematic reviews, one protocol (2002) but no reports were available.

The CRD database was searched voor HTAs (2003 – 2007) using the lemma "MeSH defibrillator, implantable Explode". This resulted in 17 papers. Based on title, language, full-text availability and "record type", five HTA reports were retrieved. The HTA by Buxton published in August 2006[63] was not retained in the clinical effectiveness part of the current HTA because it focuses primarily on cost-effectiveness. Moreover, it searched clinical literature only until March 2003 and hence, from this point of view, the HTA by Bryant published in September 2005 was more up-to-date. [1]

The quality of the trials is generally low owing to the nature of comparing a device with drug therapy and the impossibility of double-blinding. [1]

Tables x displays the result of our literature search that resulted in four RCTs, four SRs and five HTAs. The shaded area refers to papers published before the predefined time window and are added for the sake of completeness. The asterisks indicate whether a certain paper is included in the corresponding review.

Overview of retrieved papers.

	RCTs			SRs				HTAs				
	SEC PREV	PRIMARY PREV	CLINICAL CONTEXT	NANTHAKUMAR	DESAI	GOLDBERGER	ABDULLA	ONTARIO	ICSI	BLUE CROSS	NHS	MSAC
YEAR				2004	2004	2006	2006	2003	2005	2005	2005	2006
1996		MADIT I	ischaemic	*		*	*	*	*	*	*	*
1997		CABG-PATCH	ischaemic	*		*	*	*	*	*	*	*
1997	AVID				*	*					*	
2000	CASH				*	*					*	
2000	CIDS				*	*					*	
2002		MADIT II	ischaemic	*		*	*	*	*	*	*	*
2002		CAT	nonischaemic	*	*	*	*			*	*	*
2003		AMIOVIRT	nonischaemic	*	*	*	*			*		
2004		DEFINITE	nonischaemic	*	*	*	*		*	*		*
2004		DINAMIT	ischaemic	*		*	*		*	*		*
2005		SCD-HeFT	ischaemic + nonischaemic	*	*	*	*		*	*		*

REIMBURSEMENT OF ICDS IN BELGIUM

Belgian coverage for ICD in 2001 (Dutch)

Deze overeenkomst is toepasselijk op rechthebbenden zoals bedoeld in de gecoördineerde wet die:

1. lijdt aan een van de volgende hartritmestoornissen :

   a. Een meer episodes van spontane langdurige ventrikeltachycardie (VT) of spontane ventrikelfibrillatie (VF) bij een patiënt bij wie een electrofysiologisch onderzoek en/of de spontane ventriculaire arythmieën niet toelaten om accuraat de doeltreffendheid van andere therapieën dan de defibrillator te voorzien of bij wie een behandeling met antiaritmica om ernstige medische redenen een contra-indicatie is.

   b. Recurrente episodes van spontane langdurige VT of VF ondanks behandeling met antiaritmica, behandeling gecontroleerd door elektrofysiologisch onderzoek of door niet invasieve methodes.

   c. Spontane langdurige VT of VF bij een patiënt bij wie, na en ondanks een behandeling met antiaritmica, heelkunde of ablatie, bij fysiologisch onderzoek klinisch significante VT of VF kunnen worden verwekt.

De onder de punten 1 tot 3 vermelde VT of VF moeten al naar het geval, een hemodynamische collaps of een hartstilstand hebben veroorzaakt. Bedoelde ritmestoorniseen zijn niet van metabolische noch toxische oorsprong. De VT of VF in de acute fase van een infarct of post-infarct op basis van een acute ischemie of van een nieuw infarct zijn als indicatie uitgesloten.

2. met het oog op de indicatiestelling en/of de inplanting, een volledig hemodynamisch, angiografisch (inclusief een coronarografie) en elektrofysiologisch onderzoek (obligaat verricht in de inrichting) hebben ondergaan.

Belgian coverage for ICD in 2001 (French)

La présente convention est applicable à des bénéficiaires, tels que visés dans la loi coordonnée, qui :

1. Souffrent d'un des troubles du rythme cardiaque suivants :
    a. Un ou plusieurs épisodes de tachycardie ventriculaire spontanée de longue durée (TV) ou de fibrillation ventriculaire spontanée (FV) chez un patient dont l'examen électrophysiologique et/ou les arythmies ventriculaires spontanées ne permettent pas de prévoir une efficacité précise d'autres thérapies que le défibrillateur, ou chez qui un traitement par antiarythmiques est contre-indiqué pour des raisons médicales majeures.
    b. Episodes récurrents de TV de longue durée ou de FV, spontanées malgré un traitement antiarythmique, contrôlés par examen électrophysiologique ou par des méthodes non invasives.
    c. TV de longue durée ou FV, spontanées chez un patient chez qui, après et malgré un traitement par antiarythmiques, chirurgie ou ablation, des TV ou FV cliniquement significatives à l'examen physiologique, et de longue durée peuvent être induites.

Les TV ou les FV mentionnées sous les points 1 à 3, doivent avoir causé respectivement un collapsus hémodynamique ou un arrêt cardiaque. Les troubles du rythme visés ne sont pas d'origine métabolique ou toxique. Les TV ou les FV en phase aiguë d'un infarctus ou post-infarctus sur la base d'une ischémie aiguë, ou d'un nouvel infarctus sont exclues des indications.

2. Le patient doit, en vue de l'indication et/ou de l'implantation, subir un examen hémodynamique, angiographique (y compris une coronarographie) et électrophysiologique complet.

Belgian coverage for ICD in 2005 (Dutch)

1. Hartstilstand (datum te vermelden op de klinische samenvatting alsook of er sprake is van "out of hospital") tengevolge van:
    - ventrikelfibrillatie of –tachycardie, niet te wijten aan een voorbijgaande of reversiebele oorzaak (acuut myocardinfarct, elektrolietenstoornis, geneesmiddelen, trauma);

    of tengevolge van vermoedelijke ventrikelfibrillatie:
    - wanneer de klinische toestand een contra-indicatie vormt voor elektrofysiologisch onderzoek;
    - wanneer het onderzoek geen majeure ventriculaire aritmieën kan uitlokken.
2. Spontaan opgetreden sustained ventrikeltachycardie, gepaard gaande met hypotensie:
    - geen elektrofysiologisch onderzoek om reden van:
    - niet opwekbaar bij een elektrofysiologisch onderzoek;
    - wel opwekbaar bij een elektrofysiologisch onderzoek;
    - spontaan opgetreden ondanks behandeling met klasse 3 antiaritmica (Sotalol of Amiodarone).

3. Nonsustained ventrikeltachycardie na een vroeger doorgemaakt myocardinfarct, zonder reversibele ischemie, met een ejectiefractie kleiner dan 40% met induceerbare sustained ventriculaire aritmie tijdens elektrofysiologisch onderzoek, ten vroegste 7 dagen na het acuut infarct, niet onderdrukbaar door anti-aritmica: expliciet te vermelden in de klinische samenvatting.
4.
    a. Symptomatische nonsustained ventrikeltachycardie bij patiënten die op een harttransplantatie wachten, en niet permanent in het ziekenhuis verblijven;
    b. Symptomatische sustained ventrikeltachycardie bij patiënten die op een harttransplantatie wachten, en niet permanent in het ziekenhuis verblijven. (Vermeld de te verwachten tijd voor eventuele harttransplantatie, bv.: reeds op de actieve wachtlijst vs. kandidaat transplantatie in de toekomst).
5. Syncope tengevolge van een tachy-aritmie:
    - induceerbare sustained ventriculaire aritmie tijdens elektrofysiologisch onderzoek;
    - langdurige en hemodynamisch compromitterende nonsustained ventrikeltachycardie tijdens elektrofysiologisch onderzoek;
    - etiologie te weerhouden op andere gronden (te motiveren):
6. Familiale of genetische aandoeningen met een gekend geassocieerd risico op ventriculaire aritmieën, en met een hoog risico op plotse dood voor de patiënt in kwestie op basis van spontane of induceerbare ventriculaire aritmieën, of van een bezwarende familiale voorgeschiedenis:
    - lang QT syndroom; Brugada syndroom; hypertrofische cardiomyopathie;
    - aritmogene rechter ventrikeldysplasie.

De overeenkomst maakt ook melding van een aantal contra-indicaties:

1. Aanhoudende of zeer frequent recidiverende ventrikeltachycardie of –fibrillatie die een rationeel gebruik van een defibrillator onmogelijk maken.
2. Ventriculaire aritmieën behandelbaar door radiofrequente catheterablatie, zoals snel voortgeleide voorkamerfibrillatie in het kader van een Wolff-Parkinson-White syndroom, rechter ventrikel uitstroombaan VT, idiopatische linker ventrikel VT, bundeltak reentry VT, ...
3. Significante psychiatrische aandoeningen die kunnen verergeren door het inplanten van een toestel of die een systematische follow-up in de weg zouden kunnen staan.
4. Terminale rechthebbenden met een levensverwachting van minder dan 6 maanden.

Belgian coverage for ICD in 2005 (English)

1. Cardiac arrest (date to mention on the clinical summary as well if "out of hospital")

Caused by:

a. Ventricular fibrillation or -tachycardia, not linked to a temporary or reversible cause (acute myocardial infarct, electrolyte imbalance, medicines, traumatism)

Or due to supposed ventricular fibrillation:

b. When the clinical condition is a contraindication for electrophysiological testing

c. When during electrophysiological testing no major ventricular arrhythmia can be provoked

2. Spontaneous sustained ventricular tachycardia with hypotension
    a. No electrophysiology has been performed
    b. Not inducible during electrophysiological testing
    c. Inducible during electrophysiological testing
    d. Spontaneously occurring despite treatment with class 3 arrhythmic (Sotalol or Amiodarone)
3. Non sustained ventricular tachycardia following a previous myocardial infarct, without reversible ischemia, with a ejection fraction below 40% , with inducible sustained ventricular arrhythmia during electrophysiology , at earliest 7 days after the acute infarction , not suppressed b y arrhythmia. (To be mentioned explicitly)
4.
    a. Symptomatic non-sustained ventricular tachycardia in patients waiting for heart transplantation, and who don't stay permanently in the hospital
    b. Symptomatic sustained ventricular tachycardia in patients waiting for heart transplant and who don't stay permanently in the hospital (mention the delay for possible heart transplantation (e.g.: already on the active waiting list vs. candidate transplantation for the future)
5. Syncope due to tachy-arrhythmia:
    a. Inducible sustained ventricular arrhythmia during EPS
    b. Prolonged and hemodynamic compromising non-sustained ventricular tachycardia during electrophysiological testing
    c. Aetiology otherwise specified
6. Familial or genetic disorders with a known associated risk for ventricular arrhythmias, and with a elaborated motivated high risk for sudden cardiac death of the patient based on spontaneous or inducible ventricular arrhythmia, or suspected familiar causes:
    a. Long QT syndrome;
    b. Brugada syndrome;
    c. Cardiomyopathia with hypertrophy;
    d. Arrhythmogenic right ventricular dysplasia;

SHORTHAND DESCRIPTION OF BELGIAN COVERAGE CRITERIA FROM 2002 ON.

Indication category #	Considered as …	Shorthand description
1	secondary prevention	Cardiac arrest, VF
2	secondary prevention	Symptomatic sustained VT
3	primary prevention	IHD + nonsustained VT + EPS
4	secondary prevention	Symptomatic VT + bridge to transplant
5	secondary prevention	Syncope, attributed to tachyarrhythmia
6	primary prevention	(Asymptomatic) genetic disorders

Comprehensive description of indications available in appendix.

MEDICARE COVERAGE FOR ICD (JANUARY 27, 2005)

A. CMS has determined that the evidence is adequate to conclude that an implantable cardioverterdefibrillator (ICD) is reasonable and necessary for the following:

- Patients with ischaemic dilated cardiomyopathy (IDCM), documented prior myocardial infarction (MI), New York Heart Association (NYHA) Class II and III heart failure, and measured left ventricular ejection fraction (LVEF) < 35%;
- Patients with nonischaemic dilated cardiomyopathy (NIDCM) > 9 months, NYHA Class II and III heart failure, and measured LVEF < 35%;
- Patients who meet all current CMS coverage requirements for a cardiac resynchronization therapy (CRT) device and have NYHA Class IV heart failure;

For each of these groups, the following additional criteria must also be met:

- 1. Patients must be able to give informed consent;
- 2. Patients must not have:
    - Cardiogenic shock or symptomatic hypotension while in a stable baseline rhythm;
    - Had a coronary artery bypass graft (CABG) or percutaneous transluminal coronary angioplasty (PTCA) within the past 3 months;
    - Had an acute MI within the past 40 days;
    - Clinical symptoms or findings that would make them a candidate for coronary revascularization;
    - Irreversible brain damage from preexisting cerebral disease;
    - Any disease, other than cardiac disease (e.g. cancer, uremia, liver failure), associated with a likelihood of survival less than one year;
- 3. Ejection fractions must be measured by angiography, radionuclide scanning, or echocardiography;
- 4. Myocardial infarctions must be documented and defined according to the consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the Redefinition of Myocardial Infarction;

- 5. The beneficiary receiving the ICD implantation for primary prevention is enrolled in either an FDAapproved category B IDE clinical trial (42 CFR §405.201), a trial under the CMS Clinical Trial Policy (NCD Manual §310.1) or a qualifying data collection system including approved clinical trials and registries.

B. CMS has determined that the evidence, though less compelling at this time, is adequate to conclude that an ICD is reasonable and necessary for patients with NIDCM > 3 months, NYHA Class II or III heart failure, and measured LVEF < 35%, only if the following additional criteria are also met:

- Patients must be able to give informed consent;
- Patients must not have:
    - Cardiogenic shock or symptomatic hypotension while in a stable baseline rhythm;
    - Had a CABG or PTCA within the past 3 months;
    - Had an acute MI within the past 40 days;
    - Clinical symptoms or findings that would make them a candidate for coronary revascularization;
    - Irreversible brain damage from preexisting cerebral disease;
    - Any disease, other than cardiac disease (e.g. cancer, uremia, liver failure), associated with a likelihood of survival less than one year;
- Ejection fractions must be measured by angiography, radionuclide scanning, or echocardiography;
- Myocardial infarctions must be documented and defined according to the consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the Redefinition of Myocardial Infarction;
- The beneficiary receiving the ICD implantation for this indication is enrolled in either an FDAapproved category B IDE clinical trial (42 CFR §405.201), a trial under the CMS Clinical Trial Policy (NCD Manual §310.1) or a prospective data collection system.[57]

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ACC/AHA/ESC 2006 GUIDELINES FOR MANAGEMENT OF PATIENTS WITH VENTRICULAR ARRHYTHMIAS AND THE PREVENTION OF SUDDEN CARDIAC DEATH.

Authors: Douglas P. Zipes (Co-Chair) , A. John Camm (Co-Chair) , Martin Borggrefe, Alfred E. Buxton, Bernard Chaitman, Martin Fromer, Gabriel Gregoratos, George Klein, Arthur J. Moss, Robert J. Myerburg, Silvia G. Priori, Miguel A. Quinones, Dan M. Roden, Michael J. Silka, Cynthia Tracy

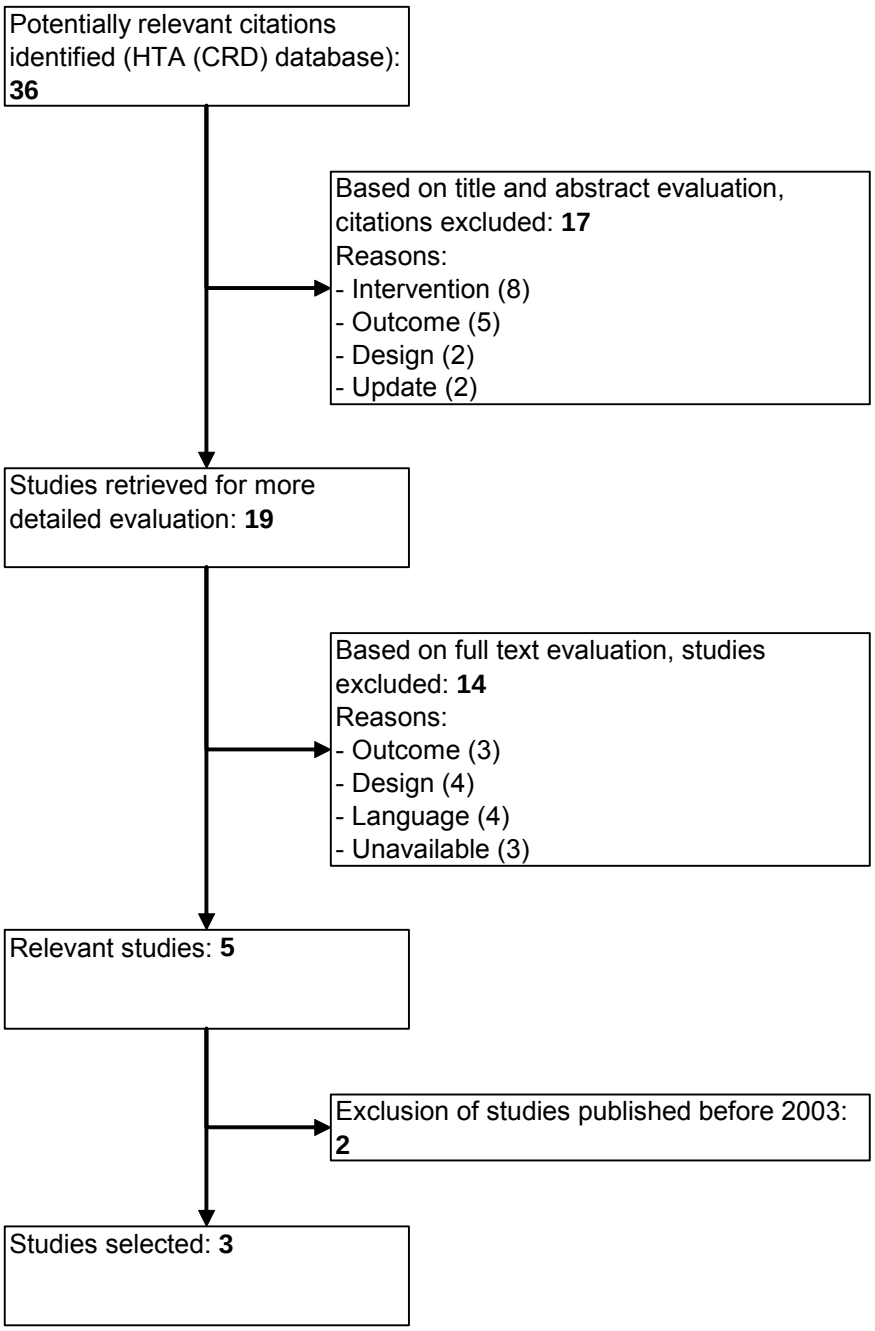
Table 3 Inconsistencies between ACC/AHA/ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of SCD and other published ACC/AHA and ESC guidelines with respect to ICD therapy for primary prevention to reduce total mortality by a reduction in SCD

Group addressed in recommendation	Guideline and class of recommendation with level of evidence[a] for each group				
	2005 ACC/AHA HF	2005 ESC HF	2004 ACC/AHA STEMI	2002 ACC/AHA/NASPE PM and ICD	Comment from the ACC/AHA/ESC VA and SCD guidelines
LVD d/t MI, LVEF 30% or less, NYHA II, III	*Class I; LOE: B*	*Class I; LOE: A*	*Class IIa; LOE: B*	*Class IIa; LOE: B*	VA and SCD has combined all trials that enrolled patients with LVD d/t MI into one recommendation, *Class I; LOE: A*
LVD d/t MI, LVEF 30% to 35%, NYHA II, III	*Class IIa; LOE: B*	*Class I; LOE: A*	N/A	N/A	
LVD d/t MI, LVEF 30% to 40%, NSVT, positive EP study	N/A	N/A	*Class I; LOE: B*	*Class IIb; LOE: B*	
LVD d/t MI, LVEF 30% or less, NYHA I	*Class IIa; LOE: B*	N/A	N/A	N/A	VA and SCD has expanded the range of LVEF to 30% to 35% or less for patients with LVD d/t MI and NYHA functional class I into one recommendation, *Class IIa; LOE: B*
LVD d/t MI, LVEF 31% to 35% or less, NYHA I	N/A	N/A	N/A	N/A	
NICM, LVEF 30% or less, NYHA II, III	*Class I; LOE: B*	*Class I; LOE: A*	N/A	N/A	VA and SCD has combined all trials of NICM, NYHA II, III into one recommendation, *Class I; LOE: B*
NICM, LVEF 30% to 35%, NYHA II, III	*Class IIa; LOE: B*	*Class I; LOE: A*	N/A	N/A	
NICM, LVEF 30% or less, NYHA I	*Class IIb; LOE: C*	N/A	N/A	N/A	VA and SCD has expanded the range of LVEF to 30% to 35% or less for patients with NICM and NYHA functional class I into one recommendation, *Class IIb; LOE: B.*
NICM, LVEF 31% to 35% or less, NYHA I	N/A	N/A	N/A	N/A	

ACC/AHA HF, ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult;[6] ACC/AHA/NASPE PM and ICD, ACC/AHA/NASPE 2002 Guidelines Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices;[1] ACC/AHA STEMI, ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction;[2] EP, electrophysiological; ESC HF, ESC 2005 Guidelines for the Diagnosis and Treatment of Chronic Heart Failure;[5] LOE, level of evidence; LVD d/t MI, left ventricular dysfunction due to prior myocardial infarction; LVEF, left ventricular ejection fraction; N/A, populations not addressed; NICM, nonischemic cardiomyopathy; NSVT, nonsustained ventricular tachycardia; NYHA, New York Heart Association functional class; SCD, sudden cardiac death; VA, ventricular arrhythmias.
[a]For an explanation of Class Recommendation and Level of Evidence, see *Table 2*. For further discussion, please see the Introduction.

APPENDIXES TO CHAPTER 4

APPENDIX 1: FLOW DIAGRAM OF HTA'S SELECTION PROCESS.



APPENDIX 2: ASSESSMENT OF THE SELECTED HTA REPORTS (INAHTA CHECKLIST).

Buxton M, Caine N, Chase D, Connelly D, Grace A, Jackson C, et al. A review of the evidence on the effects and costs of implantable cardioverter defibrillator therapy in different patient groups, and modelling of cost-effectiveness and cost-utility for these groups in a UK context. Health Technology Assessment. 2006; 10(27): 1-180.

Item	Yes	Partly	No
Preliminary			
1. Appropriate contact details for further information?	X		
2. Authors identified?	X		
3. Statement regarding conflict of interest?	X		
4. Statement on whether report externally reviewed?	X		
5. Short summary in non-technical language?	X		
Why?			
6. Reference to the question that is addressed and context of the assessment?	X		
7. Scope of the assessment specified?	X		
8. Description of the health technology?	X		
How?			
9. Details on sources of information?	X		
10. Information on selection of material for assessment?	X		
11. Information on basis for interpretation of selected data?	X		
What?			
12. Results of assessment clearly presented?	X		
13. Interpretation of the assessment results included?	X		
What then?			
14. Findings of the assessment discussed?	X		
15. Medico-legal implications considered?	X		
16. Conclusions from assessment clearly stated?	X		
17. Suggestions for further action?	X		

Note: 1) Aspects of HTA dealt with: safety, efficacy, efficiency, quality of life; 2) Both primary and secondary prevention; 3) Literature search from Nov 1999 up to March 2003 for efficacy assessment and from 1996 to July 2003 for efficiency assessment (9 economic studies selected); 4) Inclusion of a primary economic evaluation.

Bryant J, Brodin H, Loveman E, Payne E, Clegg A. The clinical and cost-effectiveness of implantable cardioverter defibrillators: a systematic review. Health Technology Assessment. 2005; 9(36): 1-150.			
Item	**Yes**	**Partly**	**No**
Preliminary			
1. Appropriate contact details for further information?	X		
2. Authors identified?	X		
3. Statement regarding conflict of interest?	X		
4. Statement on whether report externally reviewed?	X		
5. Short summary in non-technical language?	X		
Why?			
6. Reference to the question that is addressed and context of the assessment?	X		
7. Scope of the assessment specified?	X		
8. Description of the health technology?	X		
How?			
9. Details on sources of information?	X		
10. Information on selection of material for assessment?	X		
11. Information on basis for interpretation of selected data?	X		
What?			
12. Results of assessment clearly presented?	X		
13. Interpretation of the assessment results included?	X		
What then?			
14. Findings of the assessment discussed?	X		
15. Medico-legal implications considered?	X		
16. Conclusions from assessment clearly stated?	X		
17. Suggestions for further action?	X		
Note: 1) Aspects of HTA dealt with: safety, efficacy, efficiency, quality of life; 2) Both primary and secondary prevention; 3) Literature search up to November 2003 for efficacy assessment and October 2003 for efficiency assessment (12 economic studies selected).			

Ontario Ministry of Health and Long-Term Care. Implantable cardioverter defibrillator – prophylactic use. Report. Toronto: Medical Advisory Secretariat - Ontario Ministry of Health and Long-Term Care (MAS); 2003.			
Item	**Yes**	**Partly**	**No**
Preliminary			
1. Appropriate contact details for further information?	X		
2. Authors identified?			X
3. Statement regarding conflict of interest?			X
4. Statement on whether report externally reviewed?			X
5. Short summary in non-technical language?	X		
Why?			
6. Reference to the question that is addressed and context of the assessment?	X		
7. Scope of the assessment specified?	X		
8. Description of the health technology?	X		
How?			
9. Details on sources of information?	X		
10. Information on selection of material for assessment?		X	
11. Information on basis for interpretation of selected data?		X	
What?			
12. Results of assessment clearly presented?		X	
13. Interpretation of the assessment results included?		X	
What then?			
14. Findings of the assessment discussed?	X		
15. Medico-legal implications considered?			X
16. Conclusions from assessment clearly stated?	X		
17. Suggestions for further action?	X		
Note: 1) Aspects of HTA dealt with: safety, efficacy, efficiency, risk stratification; 2) Focus on primary prevention (mainly Madit II inclusion criteria); 3) Literature search from January 1996 to January 2003.			

Haute Autorite de sante / French National Authority for Health. Implantable cardioverter defibrillators: update. Report. Paris: Haute Autorite de sante/French National Authority for Health (HAS); 2001.			
Item	**Yes**	**Partly**	**No**
Preliminary			
1. Appropriate contact details for further information?	X		
2. Authors identified?	X		
3. Statement regarding conflict of interest?	X		
4. Statement on whether report externally reviewed?		X	
5. Short summary in non-technical language?	X		
Why?			
6. Reference to the question that is addressed and context of the assessment?	X		
7. Scope of the assessment specified?	X		
8. Description of the health technology?	X		
How?			
9. Details on sources of information?	X		
10. Information on selection of material for assessment?	X		
11. Information on basis for interpretation of selected data?	X		
What?			
12. Results of assessment clearly presented?	X		
13. Interpretation of the assessment results included?	X		
What then?			
14. Findings of the assessment discussed?	X		
15. Medico-legal implications considered?		X	
16. Conclusions from assessment clearly stated?	X		
17. Suggestions for further action?	X		
Note: 1) Aspects of HTA dealt with: safety, efficacy, efficiency, risk stratification, quality of life; 2) Both primary and secondary prevention; 3) Literature search up to 2000 (7 economic studies selected).			

Hider P. Outcomes from the use of the implantable cardiac defibrillator: a critical appraisal of the literature. Report. Christchurch: New Zealand Health Technology Assessment (NZHTA); 1997.			
Item	**Yes**	**Partly**	**No**
Preliminary			
1. Appropriate contact details for further information?	X		
2. Authors identified?	X		
3. Statement regarding conflict of interest?			X
4. Statement on whether report externally reviewed?			X
5. Short summary in non-technical language?	X		
Why?			
6. Reference to the question that is addressed and context of the assessment?	X		
7. Scope of the assessment specified?	X		
8. Description of the health technology?	X		
How?			
9. Details on sources of information?		X	
10. Information on selection of material for assessment?	X		
11. Information on basis for interpretation of selected data?	X		
What?			
12. Results of assessment clearly presented?	X		
13. Interpretation of the assessment results included?	X		
What then?			
14. Findings of the assessment discussed?	X		
15. Medico-legal implications considered?		X	
16. Conclusions from assessment clearly stated?	X		
17. Suggestions for further action?	X		
Note: 1) Aspects of HTA dealt with: safety, efficacy, efficiency, quality of life, risk stratification; 2) Both primary and secondary prevention; 3) Literature search up to 1997 (7 economic studies selected); 4) Statement that the report has not been peer reviewed.			

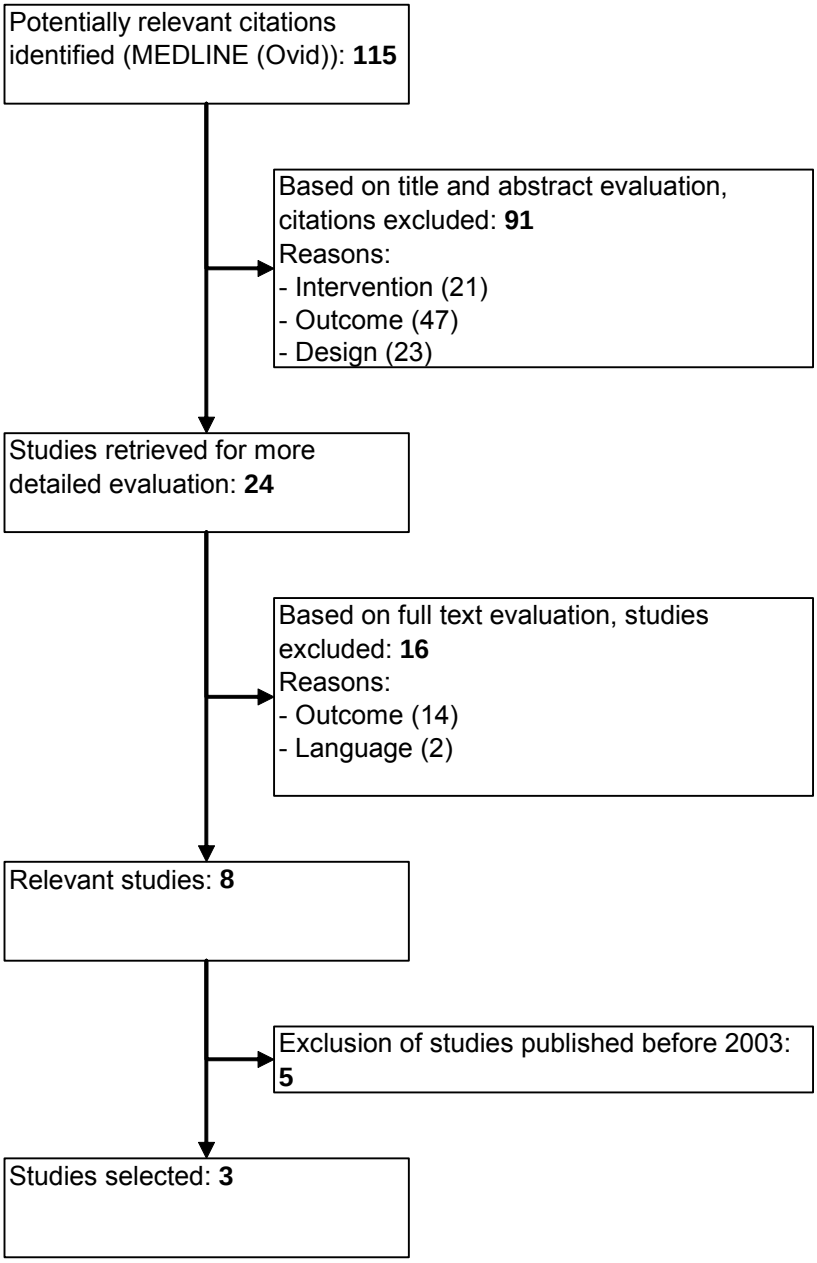
APPENDIX 3: SEARCH STRATEGY OF THE REVIEWS ASSESSING THE EFFICIENCY OF ICD

Date	26-10-2006		
Database	MEDLINE (Ovid)		
Date covered	1966 to present		
Search Strategy	**#**	***Search History***	***Results***
	1	"costs and cost analysis"/ or cost-benefit analysis/ or "cost of illness"/ or health care costs/ or drug costs/	93420
	2	Cost effectiveness analysis.mp.	2643
	3	Cost minimization analysis.mp.	184
	4	Cost utility analysis.mp.	458
	5	economics/ or resource allocation/ or health care rationing/	34950
	6	exp economics, hospital/ or economics, medical/ or fees, medical/ or exp "fees and charges"/ or health care sector/	41911
	7	Health economics.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	929
	8	Economic evaluation.mp.	2259
	9	Economics, Pharmaceutical/	1638
	10	Pharmacoeconomic$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	1643
	11	Budgets/	7062
	12	Budget impact analysis.mp.	8
	13	pric$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	22852
	14	Health Expenditures/	8959
	15	Health Expenditure?.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	9334
	16	Financ$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	68734
	17	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	237469
	18	from 17 keep 1-10	10
	19	Defibrillators, Implantable/	5197
	20	Defibrillators, Implantable/ec	230
	21	limit 20 to "review articles"	59
	22	Implant$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	199529
	23	Defibrillat$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	10900
	24	Cardiover$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	6942
	25	Intern$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]	397091
	26	22 or 25	588541
	27	23 and 26	7194
	28	24 and 26	4309
	29	27 or 28	7485
	30	19 or 29	7485
	31	30 and 17	261
	32	31 or 20	315
	33	limit 32 to "reviews (sensitivity)"	115

Date	04-01-2007		
Database	EMBASE		
Date covered	All publication years		
Search Strategy	**#**	***Search History***	***Results***
	#1	'socioeconomics'/de	78027
	#2	'cost benefit analysis'/de	42815
	#3	'cost effectiveness analysis'/de	47697
	#4	'cost of illness'/de	7004
	#5	'cost control'/de	30338
	#6	'economic aspect'/de	85498
	#7	'financial management'/de	75529
	#8	'health care cost'/de	68087
	#9	'health care financing'/de	8566
	#10	'health economics'/de	24676
	#11	'hospital cost'/de	7952
	#12	(fiscal OR financial OR ('finance'/exp OR 'finance') OR ('funding'/exp OR 'funding'))	126304
	#13	'cost minimization analysis'/de	1085
	#14	estimate*:ti,ab,de,cl	312380
	#15	cost:ti,ab,de,cl	304321
	#16	'#15 *4 #14'	39062
	#17	variable*:ti,ab,de,cl	310996
	#18	'#17 *4 #15'	50422
	#19	cost*:ti,ab,de,cl	356485
	#20	unit:ti,ab,de,cl	211909
	#21	'#20 *4 #19'	22181
	#22	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #16 OR #18 OR #21	539352
	#23	'defibrillator'/de	8816
	#24	#22 AND #23	666
	#25	'cardiac resynchronization therapy'/de	1042
	#26	#24 NOT #25	609
	#27	#26 AND [embase]/lim	527
	#28	#1 AND [review]/lim	89
Note: Of the 89 citations returned, 6 were excluded because they were duplicates of already identified OVID MEDLINE citations. This leaves **83** unique EMBASE citations.			

Date	04-01-2007		
Database	DARE (CRD)		
Date covered	All publication years		
Search Strategy	#	Search History	Results
	1	MeSH Defibrillators, Implantable	14
Note: Of the 44 citations returned, 1 was excluded because it was a duplicate of an already identified OVID MEDLINE citation. This leaves **13** unique DARE citations.			

APPENDIX 4: FLOW DIAGRAM OF (SYSTEMATIC) REVIEWS' SELECTION PROCESS.



APPENDIX 5: SEARCH STRATEGY OF THE PRIMARY ECONOMIC EVALUATIONS OF ICD

Date	29-11-2006		
Database	MEDLINE (Ovid)		
Date covered	1966 to present		
Search Strategy	**#**	***Search History***	***Results***
	1	"costs and cost analysis"/ or cost-benefit analysis/ or "cost of illness"/ or health care costs/ or drug costs/	98381
	2	Cost effectiveness analysis.mp.	2986
	3	Cost minimization analysis.mp.	210
	4	Cost utility analysis.mp.	539
	5	economics/ or resource allocation/ or health care rationing/	35960
	6	exp economics, hospital/ or economics, medical/ or fees, medical/ or exp "fees and charges"/ or health care sector/	43289
	7	Health economics.mp. [mp=ti, ot, ab, nm, hw]	1019
	8	Economic evaluation.mp.	2600
	9	Economics, Pharmaceutical/	1729
	10	Pharmacoeconomic$.mp. [mp=ti, ot, ab, nm, hw]	1841
	11	Budgets/	7273
	12	Budget impact analysis.mp.	11
	13	pric$.mp. [mp=ti, ot, ab, nm, hw]	24978
	14	Health Expenditures/	9387
	15	Health Expenditure?.mp. [mp=ti, ot, ab, nm, hw]	9813
	16	Financ$.mp. [mp=ti, ot, ab, nm, hw]	73079
	17	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	250595
	18	from 17 keep 1-10	10
	19	Defibrillators, Implantable/	5722
	20	Defibrillators, Implantable/ec	255
	21	limit 20 to "review articles"	60
	22	Implant$.mp. [mp=ti, ot, ab, nm, hw]	218447
	23	Defibrillat$.mp. [mp=ti, ot, ab, nm, hw]	12201
	24	Cardiover$.mp. [mp=ti, ot, ab, nm, hw]	7871
	25	Intern$.mp. [mp=ti, ot, ab, nm, hw]	437522
	26	22 or 25	646894
	27	23 and 26	8124
	28	24 and 26	4944
	29	27 or 28	8455
	30	19 or 29	8455
	31	30 and 17	293
	32	31 or 20	350
Note; of the 350 citations returned, 26 were duplicates. This leaves 324 unique MEDLINE citations.			

Date	04-01-2007		
Database	EMBASE		
Date covered	All publication years		
Search Strategy	**#**	***Search History***	***Results***
	#1	'socioeconomics'/de	78027
	#2	'cost benefit analysis'/de	42815
	#3	'cost effectiveness analysis'/de	47697
	#4	'cost of illness'/de	7004
	#5	'cost control'/de	30338
	#6	'economic aspect'/de	85498
	#7	'financial management'/de	75529
	#8	'health care cost'/de	68087
	#9	'health care financing'/de	8566
	#10	'health economics'/de	24676
	#11	'hospital cost'/de	7952
	#12	(fiscal OR financial OR ('finance'/exp OR 'finance') OR ('funding'/exp OR 'funding'))	126304
	#13	'cost minimization analysis'/de	1085
	#14	estimate* :ti,ab,de,cl	312380
	#15	cost:ti,ab,de,cl	304321
	#16	'#15 *4 #14'	39062
	#17	variable* :ti,ab,de,cl	310996
	#18	'#17 *4 #15'	50422
	#19	cost*:ti,ab,de,cl	356485
	#20	unit :ti,ab,de,cl	211909
	#21	'#20 *4 #19'	22181
	#22	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #16 OR #18 OR #21	539352
	#23	'defibrillator'/de	8816
	#24	#22 AND #23	666
	#25	'cardiac resynchronization therapy'/de	1042
	#26	#24 NOT #25	609
	#27	#26 AND [embase]/lim	527
Note: Of the 527 citations returned, 138 were excluded because they were duplicates of already identified OVID MEDLINE citations. This leaves 389 unique EMBASE citations.			

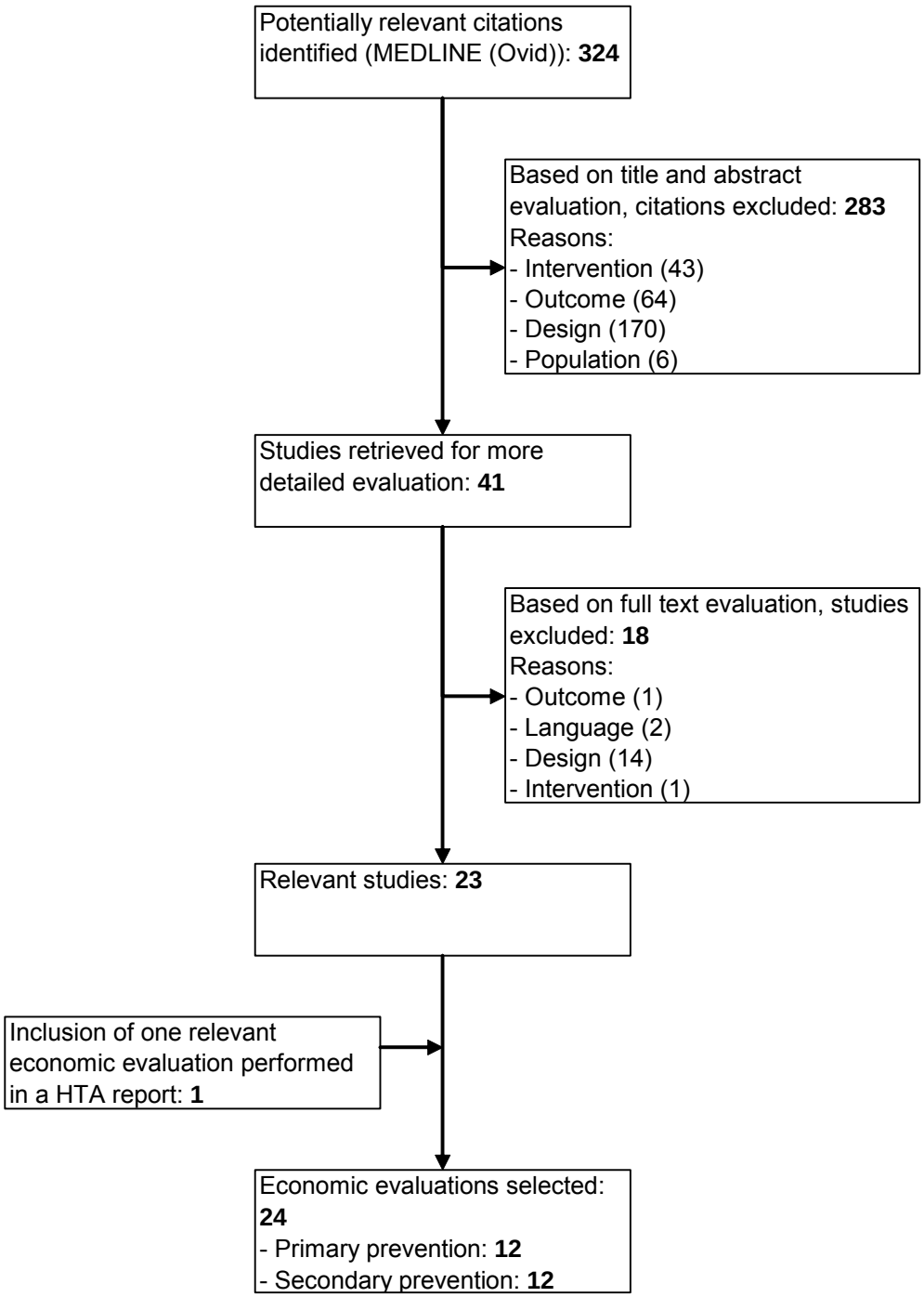
Date	04-01-2007		
Database	ECONLIT (Ovid)		
Date covered	1969 to December 2006		
Search Strategy	**#**	***Search History***	***Results***
	1	implantable defibrillator$.mp. [mp=heading words, abstract, title, country as subject]	1
	2	implantable cardioverter defibrillator$.mp.	0
	3	defibrillator$.mp.	3
	4	icd.mp.	10
	5	or/1-4	13
Note: Of the 13 citations returned, 1 was excluded because it was a duplicate of an already identified OVID MEDLINE citation. This leaves 12 unique ECONLIT citations.			
Date	04-01-2007		
Database	NHS EED (CRD)		
Date covered	All publication years		
Search Strategy	**#**	***Search History***	***Results***
	1	MeSH Defibrillators, Implantable	64
Note: Of the 64 citations returned, 61 were excluded because they were duplicates of already identified OVID MEDLINE citations. This leaves 3 unique NHS EED citations.			

APPENDIX 6: CLASSIFICATION OF ECONOMIC STUDIES

<table>
<tr><td></td><td></td><td colspan="3">Are both costs (inputs) and consequences (outputs) of the alternatives examined?</td></tr>
<tr><td></td><td></td><td colspan="2">No</td><td rowspan="2">Yes</td></tr>
<tr><td></td><td></td><td>Examines consequences only</td><td>Examines costs only</td></tr>
<tr><td rowspan="4">Is there a comparison of at least two alternatives?</td><td rowspan="2">No</td><td colspan="2">Partial evaluation</td><td>Partial evaluation</td></tr>
<tr><td>Outcome description</td><td>Cost description</td><td>Cost-outcome description</td></tr>
<tr><td rowspan="2">Yes</td><td colspan="2">Partial evaluation</td><td>Full economic evaluation</td></tr>
<tr><td>Efficacy or effectiveness evaluation</td><td>Cost comparison</td><td>Cost-minimisation analysis (CMA)
Cost-effectiveness analysis (CEA)
Cost-utility analysis (CUA)
Cost-benefit analysis (CBA)</td></tr>
</table>

Adapted from Drummond et al., 1997

APPENDIX 7: FLOW DIAGRAM OF THE ECONOMIC EVALUATIONS' SELECTION PROCESS.



APPENDIX 8: DATA EXTRACTION OF ECONOMIC EVALUATIONS

Author	**Mark et al., 2006**		
Country	USA (90%), Canada (9%), New Zealand (1%)		
Design	Cost-effectiveness analysis Cost-utility analysis RCT-based economic evaluation (SCD-HeFT, n = 2,521)		
Perspective	Reported: societal Own assessment: health care payers		
Time window	Trial dates: 1997 – 2001 (Mean trial follow-up: 45.5 months) Empirical trial follow-up: 5 years Modelling: extrapolation to lifetime costs and outcomes		
Interventions	Single chamber ICD versus conventional medical therapy (since survival in the "conventional medical therapy + placebo" and the "conventional medical therapy + Amiodarone" groups was equivalent)		
Population	NYHA class II or III symptoms LVEF ≤ 35%		
Assumptions	- Efficacy of ICD: SCD-HeFT hazard ratio (all-cause mortality) = 1 (year 0 to 1.5 of the trial) then = 0.66 (years 1.5 to 5) (i.e. an average hazard ratio of 0.77 for the 5 years) - Extrapolation to lifetime: hazard ratio (total mortality) remains constant (i.e. survival benefit equivalent), i.e. at the ratio of 0.66 - Generator replacement: every 5 years		
Data source for costs	Setting: inpatient and outpatient costs Costs in 2003 US $ Within-trial resource consumption data Hospital billing and Medicare Fee Schedule cost data		
Cost items included	Hospital costs (including ICD and leads), physician fees, outpatient costs, medication costs		
Data source for outcomes	Within-trial life expectancy and utilities (TTO)		
Discounting	Costs: 3% Outcome: 3%		
Costs	*Undiscounted values*	ICD	Placebo
	Empirical 5-years	$61,938	$42,971
	Lifetime	$158,840	$79,028
Outcomes	*Undiscounted values*	ICD	Placebo
	Life expectancy (lifetime)	10.87	8.41
	QALY weights	0.85	0.85
Cost-effectiveness	Base-case results (lifetime, discounted at 3%): Incremental costs: $62,420 Incremental life expectancy: 1.63 ICER: $38,389 / LYG ICUR: $41,530 / QALY		
Sensitivity analysis	Time horizon: ICER at 5 years: $127,503 / LYG ICER at 8 years: $88,657 / LYG ICER at 12 years: $58,510 / LYG Lifetime extrapolation assumptions: Benefit of ICD stops after 5 years (i.e. hazard ratio = 1): $98,771 / LYG Constant hazard ratio of 0.77 after 5 years: $57,696 / LYG ICD and lead costs (50% increase): $45,239 / LYG Generator replacement every 7 year= $32,525 / LYG Risk stratification: NYHA class II only: $29,872 / LYG NYHA class III only: ICD dominated (ICD has equivalent clinical outcome to medical therapy and is more expensive) Ischemic: $38,630 / LYG Non ischemic: $38,557 / LYG LVEF ≤ 30%: $39,080 / LYG LVEF > 30%: $35,692 / LYG Age ≥ 65 years: $43,943 / LYG		

	Age < 65 years: $35,488 / LYG QRS ≥ 120: $40,140 / LYG QRS < 120: $37,264 / LYG
Conclusions	"Prophylactic implantation of ICD in patients with stable, moderately symptomatic heart failure with an ejection fraction ≤ 35% is an economically efficient way to increase health benefits in this population assuming that the observed benefits of ICD therapy in SCD-HeFT persist for at least 8 years."
Remarks	

Author	**Al-Khatib et al., 2005**		
Country	USA		
Design	Cost-effectiveness analysis Cost-utility analysis in the sensitivity analysis Model-based analysis		
Perspective	Reported: societal Own assessment: health care payers		
Time window	Lifetime Modelling: extrapolation to lifetime costs and outcomes		
Interventions	ICD versus conventional medical therapy (no further specification of this alternative in the text)		
Population	*Medical therapy group:* Duke university medical centre patients meeting the MADIT II eligibility criteria (n = 1,285, follow-up: 15 years): - History of MI - LVEF ≤ 30% Exclusion criteria: - NYHA class IV symptoms *ICD group:* hypothetical cohort		
Assumptions	- Extrapolation to lifetime: Benefit of ICD remains constant after 3 years, i.e. at the MADIT II hazard ratio (all-cause mortality) of 0.69 (i.e. survival benefit constant) - Identical (non-device) health care costs in both medical therapy and ICD groups - Generator replacement: every 5 years		
Data source for costs	Setting: inpatient costs Costs in 2002 US$ Resource consumption data from Duke cardiovascular database Cost data from published studies and DRGs		
Cost items included	In-hospital costs, ICD related costs (ICD placements, follow-up visits, battery replacement, ICD complications)		
Data source for outcomes	Duke cardiovascular database National death index MADIT II trial (3 years follow-up)		
Discounting	Costs: 3% Outcome: 3%		
Costs	*Undiscounted values*	ICD	Medical therapy
	Lifetime	$152,893	$47,721
	Empirical 3 years	$73,882	$20,463
Outcomes	*Undiscounted values*	ICD	Medical therapy
	Life expectancy (lifetime)	10.88	8.26
	Life expectancy (Empirical 3 years)	2.61	2.46
Cost-effectiveness	Base-case results (lifetime, discounted at 3%): Incremental costs: $90,829 Incremental life expectancy: 1.81 ICER: $50,500 / LYG		
Sensitivity analysis	Survival benefit decreases, i.e. hazard ratio of 0.69 (relative risk reduction in mortality 31%) for 3 years, then 1 (relative risk reduction in mortality 0%) : $123,400 / LYG CUA (utility weight: 0.88 in both treatment arms): $57,300 / QALY gained Time horizon: 3 years: $367,200 / LYG 6 years: $167,900 / LYG 12 years: $79,900 / LYG 15 years: $67,800 / LYG ICD and lead costs (50% decrease): $45,200 / LYG Generator replacement every 10 years: $42,200 / LYG Other influential parameters: mortality hazard ratio for ICD versus conventional medical therapy.		
Conclusions	"The ICER associated with that (constant) survival benefit is reasonably favourable." "ICD therapy in MADIT II patients is economically attractive…, this therapy would even be more attractive if its costs is reduces and its longevity extended"		
Remarks			

Author	**Zwanziger et al., 2006**		
Country	USA		
Design	Cost-effectiveness analysis RCT-based economic evaluation (MADIT II) (n = 1,095)		
Perspective	Reported: societal Own assessment: health care payers		
Time window	Trial dates: 1997 – 2002 (mean trial follow-up: 22 months) Empirical trial follow-up: 3.5 years Modelling: extrapolation to 12-year costs and outcomes (in sensitivity analysis)		
Interventions	ICD versus conventional medical therapy (ACE inhibitors, □-blockers, lipid lowering drugs)		
Population	Previous MI LVEF ≤ 30%		
Assumptions	- Hazard ratio over 3.5 years (all-cause mortality) = 0.677 - Generator replacement: every 5 years		
Data source for costs	Setting: inpatient and outpatient costs Costs in 2001 US $ Within-trial resource consumption data Medicare cost data		
Cost items included	Hospitalisations, visits (physicians, ER), outpatient procedures (diagnostic tests, procedures and ambulatory surgeries), medications, other health care services (nursing home stay, home health care…), ICD		
Data source for outcomes	Within-trial life expectancy		
Discounting	Costs: 3% Outcome: 3%		
Costs	*Discounted values*	ICD	Medical therapy
	Empirical 3.5 years	$84,100	$44,900
Outcomes	*Discounted values*	ICD	Medical therapy
	Life expectancy (empirical 3.5 years)	2.892	2.725
Cost-effectiveness	Base-case results (3.5 years, discounted at 3%): Incremental costs: $39,200 Incremental life expectancy: 0.167 ICER: $235,000 / LYG		
Sensitivity analysis	Extrapolation to 12-year time horizon: - Benefit of ICD remains constant (i.e. hazard rate same as in trial) "optimistic": $78,600 / LYG - Benefit of ICD gradually declines (i.e. hazard rate increases linearly after 3.5 years): $91,300 / LYG - Greater mortality risk in ICD than in medical therapy after 7.1 years (i.e. hazard rate increases faster after 3.5 years) "pessimistic": $114,000 / LYG Risk stratification: Age ≥ 65 years: $133,000 / LYG Age < 65 years: $870,000 / LYG NYHA ≥ II: $164,000 / LYG NYHA I: $366,000 / LYG QRS ≥ 120: $196,000 / LYG QRS < 120: $334,000 / LYG BUN > 25 mg / dl: $113,000 / LYG BUN ≤ 25 mg / dl: $353,000 / LYG LVEF ≤ 25%: $274,000 / LYG LVEF > 25%: $147,000 / LYG ICD device costs (50% decrease): $166,000 / LYG		
Conclusions	"The within-trial ICER is a poor estimate of the lifetime value". "Although the study is not designed for this purpose, the analyses suggest that the ICER is more favourable in higher-risk subgroups". "The estimated ICER is relatively high at 3.5 years but is projected to be substantially lower over the course of longer time horizons."		
Remarks			

Author	**Sanders et al., 2004**		
Country	USA		
Design	Cost-effectiveness analysis Cost-utility analysis Model-based analysis (Markov model, 1 month cycle period)		
Perspective	Reported: societal		
Time window	Lifetime		
Interventions	ICD versus conventional therapy (MADIT II does not include a comparison with the anti-arrhythmic drug Amiodarone)		
Population	Patients meeting MADIT II criteria: - History of MI (one month or more before entry) - LVEF ≤ 30% Exclusion criteria: - NYHA class IV symptoms		
Assumptions	- Mortality modelled to match that observed in MADIT II. Total mortality assumed to be composed of: sudden cardiac, non-sudden cardiac and non-cardiac mortality. - Hazard ratio over 3 years (all-cause mortality) = 0.69 (MADIT II) - Efficacy of ICD in reducing SCD = 67% - Extrapolation to lifetime: benefit of ICD continues throughout the patient lifetime - Generator replacement: every 7 years		
Data source for costs	Setting: inpatient and outpatient costs Costs in 2003 US $ Patient registry, hospital charges, literature		
Cost items included	Direct medical costs: Hospitalisations, visits, procedures, ICD Direct non-medical costs: travel and inconvenience (no details)		
Data source for outcomes	Literature for QALY weights MADIT II trial for life expectancy		
Discounting	Costs: 3% Outcome: 3%		
Costs	*Undiscounted values*	ICD	Conventional therapy
	Lifetime	$166,800	$85,900
Outcomes	*Undiscounted values*	ICD	Conventional therapy
	Life expectancy (lifetime)	9.60	7.01
	QALY weights	0.88	0.88
Cost-effectiveness	Base-case results (lifetime, discounted at 3%): Incremental costs: $67,900 Incremental life expectancy: 1.85 Incremental QALYs: 1.33 ICER: $36,700 / LYG ICUR: $50,900 / QALY gained		
Sensitivity analysis	Influential parameters: efficacy in preventing SCD, QALY weight, total cardiac mortality. Proportion of sudden versus non-sudden death (total mortality 12%): SCD / NSCD = 4; $37,900 / QALY SCD / NSCD = 0.25; $132,500 / QALY ICD costs (60% decrease): $33,500 / QALY gained Generator replacement every 5 years: $58,100 / QALY Generator replacement every 11 years: $44,300 / QALY Lifetime extrapolation assumption (i.e. benefit of ICD stops after 3 years): $112,600 / QALY		
Conclusions	"The ICER is more favourable in patient populations with high rates of cardiac mortality and of sudden cardiac death."		
Remarks			

Author	**Sanders et al., 2005**			
Country	USA			
Design	Cost-effectiveness analysis Cost-utility analysis Model-based analysis (Markov model, 1 month cycle period)			
Perspective	Reported: societal			
Time window	Lifetime			
Interventions	ICD versus conventional (control) therapy			
Population	RCT	Inclusion criteria		
	MADIT I	Myocardial infarction three weeks or more before study; non-sustained VT; LVEF ≤35%		
	CABG Patch	Scheduled for CABG, LVEF ≤35%, abnormalities on ECG		
	MUSTT	CAD, LVEF ≤ 40%, asymptomatic non-sustained VT within 6 months and not within 4 days after an MI or CABG		
	MADIT II	MI one month or more before study; LVEF ≤ 30%		
	DEFINITE	LVEF ≤35%, ambient arrhythmias, symptomatic heart failure, presence of non-ischemic cardiomyopathy		
	DINAMIT	Within 4 to 40 days of an MI, EF ≤ 35%, impaired autonomic tone by heart rate variability		
	COMPANION	NYHA III or IV, EF ≤ 35%, QRS = 120 ms, PR > 150 ms, sinus rhythm, and a hospitalization for the treatment of CHF in the preceding 12 months		
	SCD-HeFT	NYHA class II or III symptoms, EF ≤ 35% and on optimal medical therapy		
Assumptions	- ICD efficacy: all cause mortality RRR based on the hazard ratios reported by each RCT. Total mortality assumed to be composed of: sudden cardiac, non-sudden cardiac and non-cardiac mortality. - Extrapolation to lifetime: benefit of ICD continues throughout the patient lifetime - Generator replacement: every 5 year			
	RCT	Hazard ratios (all-cause mortality)	RCT	Hazard ratios (all-cause mortality)
	MADIT I	0.46	DEFINITE	0.65
	CABG Patch	1.07	DINAMIT	1.08
	MUSTT	0.45	COMPANION	0.64
	MADIT II	0.69	SCD-HeFT	0.77
Data source for costs	Setting: inpatient and outpatient treatment costs Costs in US $ 2005 Hospital charges, patient registries			
Cost items included	Direct medical costs: ICD, hospitalisations, procedures, visits			
Data source for outcomes	Literature for QALY weights Primary prevention trials for life expectancy (reported hazard ratios)			
Discounting	Costs: 3% Outcome: 3%			
Costs	*Discounted values*		ICD	Conventional therapy
	MADIT I		$130,400	$38,300
	CABG Patch		$134,400	$78,600
	MUSTT		$145,800	$44,300
	MADIT II		$136,900	$57,500
	DEFINITE		$184,900	$84,400
	DINAMIT		$147,200	$88,300
	COMPANION		$106,100	$37,800
	SCD-HeFT		$128,800	$57,800
Outcomes	*Discounted values*		ICD	Conventional therapy
	QALY weights (undiscounted)		0.88	0.88
	MADIT I		7.70	4.06
	CABG Patch		8.01	8.41
	MUSTT		8.86	4.72
	MADIT II		8.20	6.16
	DEFINITE		11.75	9.03
	DINAMIT		8.96	9.44
	COMPANION		5.88	4.01
	SCD-HeFT		7.59	6.19

Cost-effectiveness	*Base-case results*	☐ costs	☐ life expectancy	☐ QALY	ICER	ICUR
	MADIT I	$92,100	3.64	2.64	$25,300	$34,900
	CABG Patch	$55,700	- 0.40	- 0.29	Dominated	Dominated
	MUSTT	$101,500	4.14	2.99	$24,500	$34,000
	MADIT II	$79,400	2.03	1.47	$39,000	$54,100
	DEFINITE	$100,500	2.73	1.96	$36,800	$51,300
	DINAMIT	$58,800	- 0.48	- 0.34	Dominated	Dominated
	COMPANION	$68,300	1.87	1.36	$36,500	$50,300
	SCD-HeFT	$71,000	1.40	1.01	$50,700	$70,200
Sensitivity analysis	Influential parameters: ICD efficacy in reducing mortality, ICD cost, frequency generator replacement, QALY weight, time horizon. ICD costs (from $27,975 to $10,000, i.e. a 64% decrease): MUSTT: $27,900 / QALY SCD-HeFT: $52,400 / QALY Generator replacement every 7 year: MUSTT: $30,800 / QALY SCD-HeFT: $62,300 / QALY Lifetime extrapolation assumption (i.e. benefit of ICD stops after 3 years): MUSTT: $70,200 / QALY SCD-HeFT: $171,800 / QALY Time horizon: "cost-effectiveness became more favourable as time horizon increased". Estimates at 3, 5, 12 years (on a graph).					
Conclusions	"Great variations in the health and economic outcomes among trial populations" "Significant degree of heterogeneity among the trials in the effectiveness of the ICD in reducing the rate of death from any cause" "the prophylactic implantation of an ICD has a CER below $100,000 per QALY gained in populations in which a significant device associated reduction in mortality has been demonstrated"					
Remarks						

Author	**Chan et al. 2006**			
Country	USA			
Design	Cost-utility analysis Model-based analysis (Markov model, 3 months cycle period)			
Perspective	Societal			
Time window	Lifetime			
Interventions	- Conventional medical therapy (as in MADIT II RCT) ("Medical therapy") - ICD for all ("ICD") - Risk stratification with Microvolt T-wave alternans ("MTWA"): ICD for MTWA positive and indeterminate (i.e. non-negative), medical therapy for negative MTWA.			
Population	Hypothetical cohort of patients meeting MADIT II criteria: - Ischemic hart disease - LVEF ≤ 30%			
Assumptions	- ICD all cause mortality risk reduction compared to medical therapy: 31.6% (31% in MADIT II) - All-cause mortality hazard ratio: 2.35 for MADIT II non-negative MTWA patients compared to negative MTWA patients. - Extrapolation to lifetime: benefit of ICD is constant throughout the patient lifetime - Baseline probability of testing MTWA negative: 33% - Generator replacement: every 6 years			
	Annual all-cause mortality rates for:	%		
	Medical therapy	10.1		
	ICD	6.9		
	MTWA non-negatives	12.5		
	MTWA negatives	5.3		
Data source for costs	Costs in 2004 US $ Medicare reimbursement rates, hospital costs, literature, Duke database			
Cost items included	Direct medical costs: ICD, hospitalisation, Indirect costs: lost productivity due to morbidity			
Data source for outcomes	Literature			
Discounting	Costs: 3% Outcome: 3%			
Costs	*Discounted values*	ICD	MTWA	Medical therapy
	Lifetime	$158,000	$136,500	$80,800
Outcomes	*Discounted values*	ICD	MTWA	Medical therapy
	QALY weights	0.88	0.88	0.88
	QALYs (lifetime)	7.25	7.00	5.86
	Life-expectancy (lifetime)	8.2	8.0	6.7
Cost-effectiveness	Base-case results (lifetime, discounted at 3%): ICD versus Medical therapy: Incremental cost: $77,200 Incremental QALY: 1.38 ICUR: $55,800 / QALY MTWA versus Medical therapy: ICUR: $48,800 / QALY ICD versus MTWA: ICUR: $88,700 / QALY			
Sensitivity analysis	Influential parameters ICD versus medical therapy: annual mortality rates, ICD cost, QALY weights.			
Conclusions	"ICD strategy compared to MTWA risk-stratification strategy is unlikely to be cost-effective" "MTWA risk-stratification is more cost-effective than ICD for all in MADIT II population" 'Implanting ICDs in all MADIT II eligible patients is not cost-effective"			
Remarks				

Author	**Sanders et al., 2001**			
Country	USA			
Design	Cost-utility analysis Cost-effectiveness analysis Model-based analysis (Markov model, 1 month cycle) (Use of observational database: MITI patient registry, n = 3,000)			
Perspective	Reported: societal			
Time window	Lifetime			
Interventions	- ICD (transvenous) - Amiodarone therapy - No antiarrhythmic drug (AAD) treatment			
Population	Patients admitted to a cardiac care unit between 1988 – 1994 (MITI patient registry) with: - Past MI - Non-symptomatic arrhythmia - Non-sustained ventricular arrhythmia Patients stratified according to LVEF (n = 3,000) : ≤ 30%, 31-40%, > 40%			
Assumptions	- Total mortality is composed of: sudden cardiac death, non-sudden cardiac death, non-cardiac death - Extrapolation to lifetime based on the cardiac mortality rates observed in the MITI patient registry follow-up. Non-cardiac mortality assumed to be equal to that of the general US population. - Generator replacement: every 7 years			
	Efficacy assumptions (%)	ICD (efficacy in reducing SCD mortality – opinion based)	Amiodarone (efficacy in reducing total mortality)	
	Low efficacy	40%	4%	
	Moderate efficacy	60%	11%	
	High efficacy	80%	19%	
Data source for costs	Setting: inpatient and outpatient costs Costs in 1999 US $ Resource consumption data from the MITI patient registry Costs data from MITI registry and literature.			
Cost items included	Direct medical costs: hospitalisations, visits, procedures, medications, ICD Direct non-medical costs: travel and inconvenience (no details)			
Data source for outcomes	MITI patient registry for mortality (life expectancy) Literature for QALY weights			
Discounting	Costs: 3% Outcome: 3%			
Costs	*Discounted values*	ICD	Amiodarone	No AAD treatment
	LVEF ≤ 30%			
	- Low efficacy	$119,600	$82,700	$70,100
	- Moderate efficacy	$123,700	$86,200	$70,100
	- High efficacy	$128,100	$90,100	$70,100
	LVEF 31 - 40%			
	- Low efficacy	$129,500	$94,100	$78,300
	- Moderate efficacy	$131,400	$96,800	$78,300
	- High efficacy	$133,400	$99,700	$78,300
	LVEF > 40%			
	- Low efficacy	$150,300	$111,100	$91,700
	- Moderate efficacy	$151,500	$113,200	$91,700
	- High efficacy	$152,600	$115,100	$91,700
Outcomes	*Discounted values*	ICD	Amiodarone	No AAD treatment
	QALY weights	0.88	0.88	0.88
	LVEF ≤ 30%			
	- Low efficacy	6.7	6.13	6.07
	- Moderate efficacy	7.08	6.49	6.07
	- High efficacy	7.50	6.90	6.07
	LVEF 31 - 40%			
	- Low efficacy	8.74	8.43	8.43
	- Moderate efficacy	8.94	8.74	8.43
	- High efficacy	9.15	9.08	8.43
	LVEF > 40%			

	- Low efficacy	11.58	11.36	11.44	
	- Moderate efficacy	11.70	11.62	11.44	
	- High efficacy	11.82	11.85	11.44	
Cost-effectiveness	*Base case results (lifetime, discounted)*	ICD versus no AAD treatment		ICD versus Amiodarone	
		ICER	ICUR	ICER	ICUR
	LVEF ≤ 30%				
	- Low efficacy	$78,000	$88,600	$64,900	$73,700
	- Moderate efficacy	$52,700	$59,800	*$63,300*	*$71,800*
	- High efficacy	$40,600	$46,100	$63,300	$71,700
	LVEF 31 - 40%				
	- Low efficacy	$164,000	$186,300	$113,200	$128,100
	- Moderate efficacy	$102,800	$116,800	$173,400	$195,700
	- High efficacy	$75,600	$85,900	$463,800	$517,100
	LVEF > 40%				
	- Low efficacy	$421,700	$479,200	$183,000	$206,400
	- Moderate efficacy	$227,800	$258,800	*$501,500*	*$557,900*
	- High efficacy	$157,200	$178,600	Dominated	Dominated
Sensitivity analysis	Includes probabilistic sensitivity analysis Most influential parameters: LVEF, efficacy of ICD, rate of SCD mortality, ICD cost, QALY weight.				
Conclusions	"Use of ICD in patients with past MI and severely depressed left ventricular function may provide substantial clinical benefit at an acceptable cost"				
Remarks					

Author	**McGregor et al., 2004**
Country	Canada
Design	Cost-effectiveness analysis Mode-based analysis (no details of the model)
Perspective	Health care system
Time window	15 years
Interventions	ICD versus conventional medical therapy (i.e. ACE inhibitors, beta blockers, statins – use of Amiodarone is low (12%))
Population	Hypothetical cohort of 100 patients meeting the MADIT II criteria: - History of MI (one month or more before entry) - LVEF ≤ 30%
Assumptions	- Overall mortality rate in the first follow-up year: 12% - Absolute reduction in all-cause mortality with ICD versus conventional medical therapy in the first year: 2.9% (Meta analysis of 5 primary prevention trials - Lee et al.) - Extrapolation to 15 years: the ratio of the mortality rates of ICD and control patients observed in the first year remains constant in subsequent years.
Data source for costs	Local hospital costs and professional fees Costs in CAN $ 2002/3 (?)
Cost items included	Direct medical costs
Data source for outcomes	Life expectancy based on literature and assumptions
Discounting	3% (no information whether for cost alone or cost and outcome)
Costs	
Outcomes	
Cost-effectiveness	Base-case results (15 years): Incremental life expectancy: 1.1 (undiscounted) Incremental costs: $46,277 (undiscounted) ICER: $42,000 / LYG (undiscounted) ICER: $47,460 / LYG (discounted)
Sensitivity analysis	Influential parameters: ICD cost, ICD efficacy (absolute mortality reduction) ICD cost (40% reduction)): ICER $27,000 / LYG (discounted) Time horizon (6-year ICER): $98,200 / LYG (undiscounted)
Conclusions	"ICD gives only marginally competitive value for money". "The CER indicates that this is a relatively costly technology"
Remarks	Rather poor quality of reporting. A more conservative absolute reduction in all-cause mortality (2.9% vs 3.46% in MADIT II trial) was assumed to account for the lack of use of Amiodarone in the control group

Author	**Mushlin et al., 1998**		
Country	USA		
Design	Cost-effectiveness analysis RCT-based economic evaluation (MADIT I) (n = 181)		
Perspective	Health care payers		
Time window	Trial dates: 1990 – 1996 (mean trial follow-up: 27 months) Empirical trial follow-up: 4 years		
Interventions	ICD versus conventional medical therapy (mainly Amiodarone) (ICD transthoracic and transvenous)		
Population	Patients meeting MADIT I criteria: - Past MI (3 weeks or more before entry) - LVEF ≤ 35% - Asymptomatic non-sustained VT - Inducible VT at electrophysiological testing not suppressed by procainamide		
Assumptions	Reduction in total mortality: 54% (Hazard ratio of 0.46)		
Data source for costs	Setting: inpatient and outpatient costs Costs in 1995 US $ Within-trial resource consumption data Hospital billing costs, Medicare costs and payment rates, Drug Topics Red Book wholesale prices		
Cost items included	Hospitalisations, visits (ER, physicians), procedures & tests, medications, community services (ambulance service, nursing home care, physical therapy)		
Data source for outcomes	Within-trial life expectancy		
Discounting	Costs: 3% Outcome: 3%		
Costs	*Discounted values*	ICD	Medical therapy
	Empirical 4 years	$97,560	$75,980
Outcomes	*Undiscounted values*	ICD	Medical therapy
	Life expectancy (empirical 4 years)	3.66	2.80
Cost-effectiveness	Base-case results (4 years, discounted at 3%) Incremental life expectancy: 0.80 Incremental costs: $21,580 ICER: $27,000 / LYG		
Sensitivity analysis	ICD implanted transvenously only: ICER $22,800 / LYG ICD device costs: 25% decrease: $13,100 / LYG 50% decrease: $3,300 / LYG Time horizon (8 years): $16,900 / LYG		
Conclusions	"ICD is cost-effective" "Despite its high initial costs, ICD therapy in selected individuals appears to be cost-effective"		
Remarks			

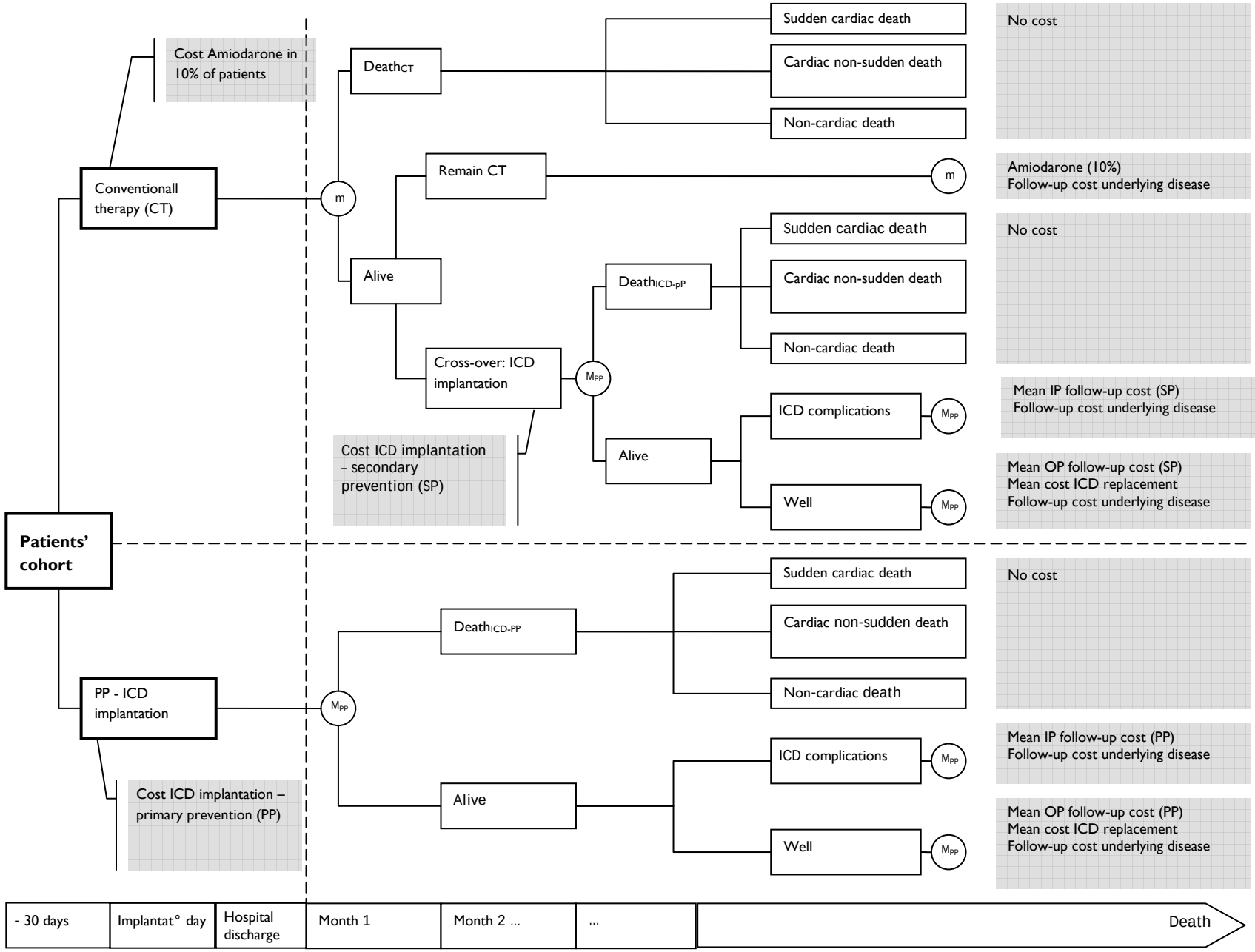
Author	**Hancock et al., 2006**		
Country	Australia		
Design	Cost-effectiveness analysis Model-based analysis (decision tree)		
Perspective	Health care payers		
Time window	Lifetime		
Interventions	ICD versus optimal pharmacologic treatment (no Amiodarone – see description of this treatment in table 38 of report)		
Population	SCD-HeFT population		
Assumptions	- Mortality data derived from the SCD-HeFT trial (empirical trial follow-up 5 years) - Extrapolation to lifetime: mortality rates observed during the first 5 years of the SCD-HeFT trial will continue in the future - Generator replacement: every 7 years		
Data source for costs	Setting: inpatient costs Costs in OZ $ 2005 DRG, Medicare benefit schedule		
Cost items included	ICD, hospitalisation, medications		
Data source for outcomes	Life expectancy based on SCD-HeFT trial		
Discounting	Costs: 5% Outcome: 5%		
Costs	*Discounted (20 months time span)*	ICD	Optimal therapy
	Public hospital	$24,780	$2,470
	Private hospital	$53,940	$2,430
Outcomes	*Undiscounted values*	LYG	
	Empirical 5 years	0.21	
	10 years	0.64	
	Lifetime	2.63	
Cost-effectiveness	Base-case (lifetime, discounted at 5%): Incremental life expectancy: 1.23 Incremental costs (20 months time span): $22,300 (public hospital) ; $51,500 (private hospital) ICER: $39,900 / LYG (public hospital) ; $95,000 / LYG (private hospital)		
Sensitivity analysis	Time span: 5 years: $127,700 / LYG (public hospital) ; $293,100 / LYG (private hospital) 10 years: $78,400 / LYG (public hospital) ; $154,300 / LYG (private hospital) Lifetime extrapolation assumption (i.e. benefit of ICD versus optimal therapy in terms of mortality rates stops after 5 years): $83,300 / LYG (public hospital) ; $200,900 / LYG (private hospital) Variations in costs ICD and generator life had little effect on ICER.		
Conclusions	ICD is recommended in SCD-HeFT eligible patients		
Remarks			

Author	**Chen et al., 2004**		
Country	USA		
Design	Cost-utility analysis Model-based analysis (decision-tree)		
Perspective	Societal		
Time window	9-year time span		
Interventions	ICD versus standard congestive heart failure (CHF) drug therapy (i.e. diuretics, ACE inhibitors, beta-blockers, digitalis, Amiodarone)		
Population	Hypothetical cohort of patients with: - Diagnosis of CHF - NYHA class II or III symptoms		
Assumptions	- Total mortality annual hazard rate is constant. - Total all-cause mortality is 20% (total mortality includes pump failure, sudden cardiac and other cause mortality) - ICD fully prevents SCD (i.e. 100% efficacy), so that total mortality under ICD is reduced to 12% annually. - Generator replacement: every 5 years		
Data source for costs	Setting: inpatient and outpatient costs Costs in US $ 2002 Red book 2002, DRGs, Bureau Labour statistics		
Cost items included	Direct medical costs: medications, visits, procedures, hospitalisations, ICD Indirect costs: time lost due to hospitalisations and visits (at the hourly wage of $23)		
Data source for outcomes	Literature		
Discounting	Costs: 3% Outcome: 3%		
Costs	*Discounted values*	ICD	Drug therapy
	Total costs (9-year)	$122,950	$15,220
Outcomes	*Undiscounted values*	ICD	Drug therapy
	QALY weight (first years post-implant)	0.64	0.71
	QALY weight (subsequent years)	0.71	0.71
	Total QALYs (9-year, discounted)	2.90	1.90
Cost-effectiveness	Base-case results (9-years, discounted at 3%, direct and indirect costs): QALY gained: 0.9986 Incremental costs: $97,725 ICUR: $97,865 / QALY		
Sensitivity analysis	Influential parameters: QALY weights, % SCD in total mortality, ICD cost ICD cost (20% decrease): $86,370 / QALY Generator replacement (every 7 years): $95,954 / QALY		
Conclusions	"Despite the favourable assumption of ICD in preventing 100% of CHF sudden deaths, we were unable to show that ICD is cost-effective for CHF patients"		
Remarks			

Author	**Goldenberg et al., 2005**		
Country	USA		
Design	Cost-effectiveness analysis Model-based analysis (no details on the model)		
Perspective	Societal		
Time window	Lifetime		
Interventions	ICD versus non-ICD therapy (surgery or drug therapy - no Amiodarone)		
Population	Young subjects with inherited life-threatening cardiac arrhythmia (genetic cardiac disorder): - Long QT syndrome (LQTS) - Hypertrophic cardiomyopathy (HCM)		
Assumptions	- Total mortality = SCD, non-SCD, non-cardiac death - Annual risk of SCD (high-risk patients): 1% (LQTS), 2% (HCM) - Efficacy of ICD in preventing SCD: 95% - Generator replacement: every 5-year		
Data source for costs	Costs in $ 2001 Bureau of Labor Statistics, Medical Expenditure Panel Survey, Medicare costs		
Cost items included	Direct medical costs: ICD, hospitalisations, procedures, medication Indirect costs: mortality time costs		
Data source for outcomes	Literature		
Discounting	Costs: 3% Outcome: 3%		
Costs	*Discounted values (Direct medical costs)*	ICD	No-ICD
	High-risk LQTS patients – Males	$144,670	$13,260
	High-risk LQTS patients – Females	$148,140	$12,930
	High-risk HCM patients – Males	$142,675	$12,960
	High-risk HCM patients – Females	$145,330	$13,055
Outcomes	*Undiscounted values Life expectancy (Lifetime)*	ICD	No-ICD
	High-risk LQTS patients – Males	58.8	48.7
	High-risk LQTS patients – Females	61.0	45.7
	High-risk HCM patients – Males	57.4	33.6
	High-risk HCM patients – Females	34.6	59.8
Cost-effectiveness	Base-case (societal, lifetime, discounted): *Incremental life expectancy:* High-risk LQTS patients – Males: 3.7 High-risk LQTS patients – Females: 5.2 High-risk HCM patients – Males: 8.5 High-risk HCM patients – Females: 8.8 *ICER:* High-risk LQTS patients – Males : $3,330 / LYG High-risk LQTS patients – Females : cost-saving High-risk HCM patients – Males: cost-saving High-risk HCM patients – Females: cost-saving		
Sensitivity analysis	Robust findings under all change parameters.		
Conclusions	"In patients with LQTS and HCM, early intervention with ICD therapy is cost-effective and results in cost savings due to gains in productivity"		
Remarks	Including mortality time costs in the cost side of an ICER (expressed in LYG) may not be appropriate since the denominator already captures mortality effects[95]. For information, using only direct medical costs, the ICER are (our computations): High-risk LQTS patients – Males: $37,856 / LYG High-risk LQTS patients – Females: $29,082 / LYG High-risk HCM patients – Males: $17,758 / LYG High-risk HCM patients – Females: $18,356 / LYG		

APPENDIXES TO CHAPTER 5

APPENDIX 1: MODEL STRUCTURE (SEE PAGE AFTER)


Patients' cohort
Conventionall therapy (CT)
Cost Amiodarone in 10% of patients
m
Death CT
Sudden cardiac death
Cardiac non-sudden death
Non-cardiac death
No cost
Remain CT
m
Amiodarone (10%)
Follow-up cost underlying disease
Alive
Cross-over: ICD implantation
Cost ICD implantation – secondary prevention (SP)
Death ICD-pP
Sudden cardiac death
Cardiac non-sudden death
Non-cardiac death
No cost
MPP
Alive
ICD complications
MPP
Well
MPP
Mean IP follow-up cost (SP)
Follow-up cost underlying disease
Mean OP follow-up cost (SP)
Mean cost ICD replacement
Follow-up cost underlying disease
PP - ICD implantation
Cost ICD implantation – primary prevention (PP)
MPP
Death ICD-PP
Sudden cardiac death
Cardiac non-sudden death
Non-cardiac death
No cost
Alive
ICD complications
MPP
Well
MPP
Mean IP follow-up cost (PP)
Follow-up cost underlying disease
Mean OP follow-up cost (PP)
Mean cost ICD replacement
Follow-up cost underlying disease
- 30 days
Implantat° day
Hospital discharge
Month 1
Month 2 ...
...
Death

APPENDIX 2: PROTOCOL FOR THE ANALYSIS OF THE DATABASE

Data available

2001: Patients implanted with an ICD between 1.1.2001 and 31.12.2001

- Codes convention: 772380
- Follow-up: 1.1.2001 – 31.12.2005
- Data available:
  - Données soins de santé, Pharmanet, population
  - Clinical data first implant: etiology, LVEF, indication
  - Clinical data replacement implant: etiology, LVEF, date previous ICD, reason for ICD change, number of shocks delivered

2005: Patients implanted with an ICD between 1.1.2005 – 31.12.2005

- Codes convention: 686302 (first ICD); 687971-687982 (replacement ICD)
- Follow-up : 1.1.2005 – 31.12.2005
- Data available :
  - Données soins de santé, Pharmanet, population
  - Clinical data first implant: etiology, LVEF, indication, cause of death
  - Clinical data replacement implant: etiology, LVEF, indication, date previous ICD, reason for ICD change, number of shocks delivered

ICD costs in primary prevention

ICD implantation costs

PATIENTS' SELECTION

Number ($N_{ICD\text{-}PP\text{-}2005}$) of patients who underwent first ICD implantation for primary prevention in 2005

Code convention first ICD in 2005: 686302

Code primary prevention (PP): 3 (INAMI DB – indication)

PRE-ICD IMPLANTATION (TABLE PROTOCOL 1)

Definition of the period: 30 days before ICD implantation day

1. Number ($N_{pre\text{-}ICD\text{-}PP\text{-}2005}$) of patients that meet the period definition
2. Pre-ICD implantation **diagnostic procedures** performed up to **30** days before ICD implantation day. Per item (i.e. group of procedure – see appendix 1) and for $N_{pre\text{-}ICD\text{-}PP\text{-}2005}$: number of patients, number of item, mean number of item per patient
3. Pre-ICD implantation **pre-operative procedures** performed up to **3** days before ICD implantation. Per item and for $N_{pre\text{-}ICD\text{-}PP\text{-}2005}$: number of patients, number of item, mean number of item per patient

4. **Hospital charges for 2 days in a cardiac ward =** (2 * (« prix moyen de journée » – patient share)) + (2 * « forfait par journée d'hospitalisation pour prestations de biologie clinique ») + (1 * « forfait par admission pour la permanence médicale intra hospitalière»).
5. Total **costs** pre-ICD implantation period: per category (b, c, d) and for the total (b + c + d): total costs and mean cost per patient (min, max, 95% CI)

Notes and assumptions:

- Diagnostic and pre-operative procedures can be performed either in hospital or ambulatory.
- We assume there is no additional fee for physician visits related to those procedures.
- We ignore all drugs consumed before ICD implantation (not relevant for our analysis).
- If we restrict the resources consumed to the ICD hospitalization period, we miss an important bulk of diagnostic procedures for ICD that have been done during a previous hospitalization (e.g. for MI). Therefore, it is assumed that some relevant diagnostic procedures leading to ICD implantation in PP patients may be performed up to 30 days before ICD implantation.
- For all non-cardiologic diagnostic procedures and some cardiologic procedures (point c above), the period considered is limited to a few days before ICD implantation. This temporal link with ICD implantation is required in order to be sure that the procedures are associated with ICD. Temporal link: 3, 4, 5 or 6 days before ICD implantation? Perform the analysis separately for all those periods. We will then have to choose what period is the most clinically relevant. Given the results, we choose to use 3 days pre-ICD implantation. This is the most clinically relevant time period. Furthermore, the variation in costs between the different days is rather limited.
- Hospital length of stay (LoS) before ICD implantation: for many patients, hospitalization stay before ICD implantation can be rather long and not fully attributable to ICD implantation. This is because many patients in PP will be first hospitalized for a given cardiac condition (e.g. MI), then stay in the hospital up to the decision for their ICD implantation. It is therefore hard to determine an average pre-ICD hospital stay based on our data. Based on expert opinion, we impute the cost of 2 days in an accredited cardiac unit per patient.
- Hospital stay costs (« verpleegdagprijs) : An average cost per day (per hospital) is provided by the SPF Santé Publique (this includes the 12è and « partie variable du BMF »). From this average cost, the patients' share has to be subtracted. The perspective of the model is indeed "health care payer" . Average cost per day in accredited cardiac ward = €359.314. Patient share: €40.59 on the first day; €13.32 from day 2 on.

ICD IMPLANTATION (TABLE PROTOCOL 2)

Definition of the period: ICD implantation day

1. **Material.** For $N_{ICD\text{-}PP\text{-}2005}$: proportion of patients per ICD/lead type.
2. **"Prestations techniques"** associated with ICD implantation. Per item and for $N_{ICD\text{-}PP\text{-}2005}$: number of item, mean number of item per patient
3. Total **costs** ICD implantation day. Per category (a, b) and for the total (a + b): total costs and mean cost per patient (min, max, 95% CI)

POST-ICD IMPLANTATION (TABLE PROTOCOL 3)

Definition of the period: from ICD implantation day to hospital discharge

1. Post-ICD implantation **procedures**. Per item and for $N_{ICD\text{-}PP\text{-}2005}$: number of patients, number of item, mean number of item per patient
2. Post ICD implantation **complications**. Per item and for $N_{ICD\text{-}PP\text{-}2005}$: number of patients, number of item, mean number of item per patient
3. **Hospital charges.** For $N_{ICD\text{-}PP\text{-}2005}$: mean length of stay (LoS) post-ICD implantation per patient, mean number of forfaits "clinical biology" per patient, mean number of forfaits "produits pharmaceutiques" per patient, mean number of forfaits "imagerie médicale" per patient.
4. **Anti-arrhythmic drugs** taken during the post-ICD implantation period (if outside the forfaits in c) and relevant to ICD. For $N_{ICD\text{-}PP\text{-}2005}$: number (and %) of patients on Amiodarone, on Sotalol and on Anti-arrhythmic class I
5. **Other resources used.** For $N_{ICD\text{-}PP\text{-}2005}$: number (and %) of patients who used other resources.
6. Total **costs** post-ICD implantation. Per category (a, b, c, d, e) and for the total (a + b + c + d + e): total costs and mean cost per patient (min, max, 95% CI)
7. **Total costs ICD implantation** (Pre-ICD implantation + ICD implantation day + post-ICD implantation): mean total cost per patient (min, max, 95% CI).

Notes and assumptions:

1. ICD related resource consumption occurring in hospital only
2. Other resources used: this comprises the remaining resources used (i.e. other than those listed in the appendix) during the post-ICD implantation hospitalization. Other (i.e. non-ICD related) resource consumptions occurring during the post-ICD implantation hospitalization are assumed to be related indirectly to ICD: this would not have occurred, had the patient not been hospitalized for ICD
3. We assume that PM controls will never be performed without ICD control concomitantly.
4. Hospital charges: forfait per admission for "permanence médicale" has already been accounted for in the pre-ICD implantation period
5. Anti-arrhythmics taken during the hospitalization post-ICD implantation: are those drugs included in the listed forfaits? The link between the commercial name of the drugs and ATC codes can be performed by the IMA. However, what is the correspondence between ATC codes and INAMI drugs codes in hospital?

ICD costs in secondary prevention

ICD implantation costs

PATIENTS' SELECTION

Number ($N_{ICD\text{-}SP\text{-}2005}$) of patients who underwent first ICD implantation for secondary prevention in 2005

Code convention first ICD: 686302

Code secondary prevention (SP): 1.1 + 1.2 + 1.3 + 2.1 + 2.2 + 2.3 + 2.4 (INAMI DB - indication)

PRE-ICD IMPLANTATION

Same computations as for ICD primary prevention costs

ICD IMPLANTATION

Same computations as for ICD primary prevention costs

POST-ICD IMPLANTATION

Same computations as for ICD primary prevention costs

ICD follow-up costs

PATIENTS' SELECTION:

Definition of the period: from (first ICD implantation) hospital discharge day up to death or up to 31.12.2005

Monthly number ($N_{FU\text{-}SP\text{-}2001}$) of patients who underwent first ICD implantation for secondary prevention in and who meet the period definition

Code convention ICD in 2001: 772380

Code first ICD: INAMI DB

Code secondary prevention: 1.1 + 1.2 + 1.3 + 2.1 + 2.2 + 2.3 + 2.4 (INAMI DB - indication)

Notes:

- For the selected patient group to be analyzed, provide a table with the monthly number of patients alive.

OUTPATIENT FOLLOW-UP (TABLE PROTOCOL 4)

1. Ambulatory **ICD controls** during the follow-up. Per month: number of patients with ICD controls, number of controls, mean number of controls per patient
2. **Other procedures** (ECG, PM control) associated with ICD control. Per item and per month: number of patients, number of items, mean number of item per patient
3. **Physician fees** associated with ICD control. Per month and per physician: number of patients, number of consultations, mean number of consultations per patient.
4. **Drug** consumption. Per month: number (and %) of patients on Amiodarone, on Sotalol and on Anti-arrhythmic class I
5. **Total costs OP follow-up**. Per category (a, b, c, d) and for the total (a + b + c + d): total costs and mean cost per patient per year (min, max, 95% CI).

Notes and assumptions:

- Procedures and physician fees are only accounted for if in association with a code for ICD control, i.e. if performed on the same day.

INPATIENT FOLLOW-UP (TABLE PROTOCOL 5)

1. ICD-related **re-hospitalizations**. Per month: number of patients alive, number of patients hospitalized, number of hospitalizations, mean number of hospitalizations per patient alive, mean number of hospitalizations per hospitalized patient.
2. ICD-related **procedures** performed during the hospital stay. Per item: mean number of item per hospitalisation
3. **Material used**: Per item: mean number of item per hopitalisation

4. **"Prestations techniques".** associated with ICD re-hospitalization. Per item: mean number of item per hospitalization
5. **Hospital charges.** Per hospitalization: mean length of stay (LoS), mean number of forfaits "clinical biology", mean number of forfaits "produits pharmaceutiques", mean number of forfaits "permanence médicale", mean number of forfait "imagerie médicale".
6. **Drugs** taken during the hospitalisation (if outside the forfait) and relevant to ICD. Per hospitalization: number (and %) of patients on Amiodarone, on Sotalol and on Anti-arrhythmic class I
7. **Other resources used** during the hospital stay. Per hospitalisation: number (and %) of patients who used other resources
8. **Total costs IP follow-up. Per category (b, c, d, e, f, g) and for the total (b + c + d + e + f + g):** mean cost per hospitalization (min, max, 95% CI). Per year and for the total: total costs and mean cost per patient alive (min, max, 95% CI).

Notes and assumptions:

- There may be one-day hospitalizations (687971)
- Re-hospitalization LoS: from hospital admission up to hospital discharge around each re-hospitalization code identified.
- Other resources used: all resources used during the hospitalization are accounted for, even the non-ICD related (e.g. a patient develops pneumonia during the hospital stay). These are assumed to be related to ICD indirectly (i.e. this would have not occurred, had the patient not been hospitalized for its ICD)
- Ok with hospitalization causes? Other hospitalization linked with ICD identifiable?
- Hospitalization charges: exclude INAMI codes for "partie variable du BMF" and work with the SPF costs.

ICD replacement costs (due to battery end of life): re-implantation

Patients' selection:

1. Number ($N_{REP\text{-}PP\text{-}2005}$) of patients who underwent ICD replacement in 2005 due to battery end of life and who had a PP indication for their initial ICD implantation
   - Code ICD Replacement: 687971-687982
   - Code primary prevention: 3 (INAMI DB - indication)
   - Code EOL: "Batterij uitputting" (INAMI DB - vervanging reden)
2. Number ($N_{REP\text{-}SP\text{-}2005}$) of patients who underwent ICD replacement in 2005 and who had an SP indication for their initial ICD implantation (about 275 patients)
   - Code ICD Replacement: 687971-687982
   - Code secondary prevention: 1.1 + 1.2 + 1.3 + 2.1 + 2.2 + 2.3 + 2.4 (INAMI DB - indication)
   - Code EOL: "Batterij uitputting" (INAMI DB - vervanging reden)

Pre-ICD re-implantation (Table protocol 6)

Definition of the period: From hospital admission to re-implantation day

1. Pre-ICD replacement **pre-operative procedures**. Per item and for N_{REP}: number of patients, number of items, mean number of item per patient.
2. **Hospital charges.** For N_{PRE}: mean length of stay (LoS) pre-ICD replacement per patient, mean number of forfaits "clinical biology" per patient, mean number of forfaits "produits pharmaceutiques" per patient, mean number of forfaits "permanence médicale", mean number of forfait "imagerie médicale".
3. **Drugs** taken during the period (if outside the forfait) and relevant to ICD. Per hospitalization: number (and %) of patients on Amiodarone, on Sotalol and on Anti-arrhythmic class I
4. **Other resources used** during the hospital stay. Per hospitalisation: number (and %) of patients who used other resources
5. Total **costs** pre-ICD replacement. Per category (a, b, c, d) and for the total (a+b+c+d): total costs and mean cost per patient (min, max, 95% CI)

Notes and assumptions:

- Per default all diagnostic procedures identified before first ICD implantation have been retained for ICD replacement.
- Other non-ICD related resource consumptions occurring pre-ICD replacement are assumed to be related indirectly to ICD: this would have not occurred, had the patient not been hospitalized for its ICD

ICD re-implantation (Table protocol 7)

Definition of the period: ICD re-implantation day

1. **Material.** For N_{REP}: proportion of patients per ICD/lead type
2. **"Prestations techniques"** associated with ICD implantation. Per item and for N_{REP}: number of patients, number of item, mean number of item per patient
3. Total **costs** ICD replacement day. Per category (a, b) and for the total (a + b): total costs and mean cost per patient (min, max, 95% CI)

Post-ICD re-implantation (Table protocol 8)

Definition of the period: From ICD replacement day up to hospital discharge

1. Post-ICD replacement **procedures**. Per item and for N_{REP}: number of patients, number of item, mean number of item per patient
2. Post ICD replacement **complications**. Per item and for N_{REP}: number of patients, number of item, mean number of item per patient
3. **Hospital charges.** For N_{REP}: mean length of stay (LoS) post-ICD implantation per patient, mean number of forfaits "clinical biology" per patient, mean number of forfaits "produits pharmaceutiques" per patient.
4. **Anti-arrhythmic drugs** taken during the period (outside the forfaits in c) and relevant to ICD. For N_{REO}: number (and %) of patients on Amiodarone, on Sotalol and on Anti-arrhythmic class I
5. **Other resources used.** For N_{REP}: number (and %) of patients who used other resources.
6. Total **costs** post-ICD replacement. Per category (a, b, c, d, e) and for the total (a + b + c + d + e): total costs and mean cost per patient (min, max, 95% CI)

7. **Total costs ICD replacement** (Pre-ICD replacement + ICD replacement day + post-ICD replacement): mean total cost per patient (min, max, 95% CI).

Notes and assumptions:

- Resource consumption occurring in hospital only
- Other non-ICD related resource consumptions occurring post-ICD replacement are assumed to be related indirectly to ICD: this would have not occurred, had the patient not been hospitalized for its ICD
- PM control if linked with ICD control
- Cost of replacement due to EOL only. Replacements due to other reason are accounted for in the follow-up costs of ICD implanted patients (i.e. replacement for complication, recall…). This assumes that no replacement for EOL occurred during the follow-up period of ICD implanted patients.

Non-ICD follow-up costs

= FU cost of the underlying disease (incurred both by the Control Therapy (CT) and the ICD branches of the model)

- Assumption: both ICD and CT patients undergo the same treatment costs for their underlying disease
- Patient selection: same as point 3.2 (2001 SP) above
- Computations: Aggregate all costs and subtract all identified ICD-related costs (point 3). Compute an aggregated average yearly follow-up costs for patients.

Tables for the protocol

Table protocol 1: ICD implantation costs - Pre-ICD implantation

b. Diagnostic procedures 30 days before ICD implantation			
Diagnostic Ischemia			
Item	*INAMI code*		*INAMI label*
Coronary angiography	453110	453121	Coronarografie, één of twee kransslagaders, één invalshoek, minimum zes clichés
	453132	453143	Coronarografie, één of twee kransslagaders, maximum voor het geheel van twee of meer invalshoeken (minimum zes clichés per invalshoek)
	464111	464122	Coronarografie, één of twee kransslagaders, één invalshoek, minimum 6 clichés
	464133	464144	Coronarografie, één of twee kransslagaders, maximum voor het geheel van twee of meer invalshoeken (minimum 6 clichés per invalshoek)
Exercise testing	475812	475823	Inspannings- of hypoxieproef, met continue monitoring van minstens één afleiding vóór elke belastingsverandering, op het einde van de proef en gedurende minstens drie minuten na het beëindigen van de proef, meerdere elektrocardiografische registraties op verschillende afleidingen en bloeddrukmetingen, met uittreksels en gestandaardiseerd protocol
Cardiac radionuclide imaging	442411	442422	Scintigrafie van een orgaan, van een stelsel of van een deel van het lichaal buiten die genoemd onder de nrs. 442433 - 442444 of 442470 - 442481
	442396	442400	Scientigrafieën en tomografische onderzoeken Tomografisch onderzoek tijdens een scintigrafie, met verwerking op computer die ten minste twee niet-parallelle reconstructievlakken omvat, met protocol en iconografische documenten, niet cumuleerbaar met de verstrekkingen 442411-442422, 442455-442466, 442610-442621 en 442632-442643 voor het onderzoek van een zelfde orgaan of stelsel van organen dat met een zelfde gemerkt produkt wordt verricht
	442595	442606	Functionele scintigrafische test die twee opeenvolgende tomografische onderzoeken omvat, met verwerking op computer, die ten minste twee niet-parallelle reconstructievlakken omvat, met protocol en iconografische documenten, niet cumuleerbaar met de verstrekkingen 442411-442422, 442455-442466, 442610-442621 en 442632-442643 voor het onderzoek van een zelfde functie dat met een zelfde gemerkt produkt wordt verricht
	442610	442621	Functionele scintigrafie van een orgaan of stelsel van organen,met test sequentele inzameling van de gegevens, kwantitatieve analyse met telsysteem (computer) die activiteitscurven in de tijd en/of tabellen met cijfergegevens en/of parametrische beelden omvat, met protocol en iconografische documenten
Diagnostic LVEF			
Item	*INAMI code*		*INAMI label*
Angio-cardiography	453073	453084	Angiocardiopneumografie, één invalshoek, minimum zes clichés
	453095	453106	Angiocardiopneumografie, maximum voor het ganse onderzoek, twee of meer invalshoeken (minimum zes clichés per invalshoek)
	464074	464085	Angiocardiopneumografie, één invalshoek, minimum zes clichés
	464096	464100	Angiocardiopneumografie, maximum voor het ganse onderzoek, twee of meer invalshoeken (minimum zes clichés per invalshoek)
	476173	476184	Kwantitatieve analyse met computer van het ventriculogram met op zijn minst het berekenen van het systolisch eindvolume, het diastolisch eindvolume en de uitstotingsfractie, minimum twee metingen, met protocol
Echo-cardiography	460412	460423	Cardiovasculaire echografieen : Transthoracale mono- en bidimensionele echografie (met respectievelijk ten minste 3 en 2 coupes en registratie op papier en/of magneetband)
	460456	460460	Volledig transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen en in spectraal mode ter hoogte van minstens drie klepopeningen. De opname en archivering van het onderzoek op

			magneetband of digitale drager is vereist evenals een gedetailleerd protocol
	460574	460585	Volledig transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen ter hoogte van minstens 3 klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
	461215	461226	Herhaling binnen het kalenderjaar van de verstrekking 460456 - 460460 of 469814 - 469825 voor één van de volgende indicaties. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol en het bijhouden van een register van de herhalingsonderzoeken
	461230	461241	Beperkt transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	461252	461263	Beperkt transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en kleuren-Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	469652	469663	Beperkt transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	469674	469685	Beperkt transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en kleuren-Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	469814	469825	Volledig transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen en in spectraal mode ter hoogte van minstens drie klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
	469836	469840	Volledig transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen ter hoogte van minstens 3 klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
Cathe-terization	476011	476022	Hartcatheterismen buiten het continu toezicht op de hartfunctie - Hartcatheterismen met grafisch registreren van de drukcurven op verschillende niveaus, inclusief eventueel de afnamen van bloedmonsters voor doseren, de radioscopische controles met televisie, de elektrocardiografische controles, de denudatie en de inspuiting van contrastmiddelen met of zonder krachtsinspanningsproef of farmacodynamische proef, met protocol en tracés (mogen niet worden gecumuleerd met de raadplegingen) : Langs de aders
	476033	476044	Hartcatheterismen buiten het continu toezicht op de hartfunctie - Hartcatheterismen met grafisch registreren van de drukcurven op verschillende niveaus, inclusief eventueel de afnamen van bloedmonsters voor doseren, de radioscopische controles met televisie, de elektrocardiografische controles, de denudatie en de inspuiting van contrastmiddelen met of zonder krachtsinspanningsproef of farmacodynamische proef, met protocol en tracés (mogen niet worden gecumuleerd met de raadplegingen) : Langs de aders met transseptale punctie
	476055	476066	Hartcatheterismen buiten het continu toezicht op de hartfunctie - Hartcatheterismen met grafisch registreren van de drukcurven op verschillende niveaus, inclusief eventueel de afnamen van bloedmonsters voor doseren, de radioscopische controles met televisie, de elektrocardiografische controles, de denudatie en de inspuiting van contrastmiddelen met of zonder krachtsinspanningsproef of farmacodynamische proef, met protocol en tracés (mogen niet worden gecumuleerd met de raadplegingen) : Langs de slagaders
	476070	476081	Hartcatheterismen buiten het continu toezicht op de hartfunctie - Hartcatheterismen met grafisch registreren van de drukcurven op verschillende niveaus, inclusief eventueel de afnamen van bloedmonsters voor doseren, de radioscopische controles met televisie, de elektrocardiografische controles, de denudatie en de inspuiting van contrastmiddelen met of zonder krachtsinspanningsproef of farmacodynamische proef, met protocol en tracés (mogen niet worden gecumuleerd met de raadplegingen) : Langs de aders en de slagaders, gecombineerd
	476195	476206	Hartcatheterismen met het oog op angiocardiografieën en/of angiopneumografieën, inclusief de eventuele denudatie, radioscopische controles met televisie, elektrocardiografische controles (mogen niet worden gecumuleerd met de raadpleging)
Diagnostic Arrhythmia			

Item	*INAMI code*		*INAMI label*
24h-ECG	476210	476221	Monitoring Holter : continu elektrocardiografisch registreren gedurende ten minste 24 uur,door middel van een draagbaar toestel met magneetband of met ingebouwd geheugen, inclusief de raadpleging bij het plaatsen en het wegnemen van het toestel, met protocol en mogelijkheid tot reproduceren van de volledige tracés
	476232	476243	Herhaling binnen een jaar van verstrekking nr 476210 - 476221
	476254	476265	Monitoring Holter : continue electrocardiografische analyse gedurende ten minste 24 uur, door middel van draagbaar toestel, inclusief de raadpleging bij het plaatsen en het wegnemen van het toestel met protocol en mogelijkheid tot reproduceren van een deel van de tracés
EPS	476276	476280	Uitgebreid electrofysiologisch onderzoek voor het opwekken en beëindigen van tachycardieën met behulp van drie of meer catheters,inclusief afname van bloedstalen, radioscopische en electrocardiografische controles, toediening van farmaca en contraststoffen, met protocol en tracés
	476291	476302	Beperkt elektrofysiologisch onderzoek tot studie van de sinusknoopfunctie en van de atrioventriculaire geleiding met behulp van een of meerdere catheters met inbegrip van de electrocardiografische opnamen
	476313	476324	Diagnose en/of behandeling van tachycardieën door middel van electrische prikkels via één of meerdere endocavitair geplaatste catheters met inbegrip van de electrocardiografische opnamen
Tilt-test	476335	476346	Tilt-test op 60° met minimumduur van 45' of tot optreden van syncope, onder continue electrocardiografische controle en niet-invasieve bloeddrukmonitoring, al dan niet met toediening van farmaca, met protocol
Signal averaged electro-cardiogram	475834	475845	Registratie met kwalitatieve en kwantitatieve analyse van een elektrocardiografie met hoge amplitudo via orthogonale afleidingen ter opsporing van abnormale potentialen, bij gedokumenteerd kamerarythmia-risico, met protocol
c. Pre-operative procedures: 3,4,5 or 6 days before implantation			
Cardiologic procedures			
Item	*INAMI code*		*INAMI label*
ECG	475075	475086	Elektrocardiografische onderzoekingen, met protocol, ten minste 12 verschillende derivaties
ECG + monitoring	214034	214045	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat, benevens het elektrocardiogram, op zijn minst bestendig een van de volgende parameters volgt : de arteriële druk door middel van een intraarteriële catheter, de intracavitaire of pulmonale druk door middel van een intracardiale catheter, de intracraniële druk door middel van een intracraniële catheter (buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests), inclusief de eventuele registraties : De tweede, derde, vierde en vijfde dag, per dag
	214012	214023	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat, benevens het elektrocardiogram, op zijn minst bestendig een van de volgende parameters volgt : de arteriële druk door middel van een intraarteriële catheter, de intracavitaire of pulmonale druk door middel van een intracardiale catheter, de intracraniële druk door middel van een intracraniële catheter (buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests), inclusief de eventuele registraties : De eerste dag
	212030	212041	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat op zijn minst bestendig het elektrocardiogram volgt, inclusief de eventuele registraties, buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests : De tweede en derde dag, per dag 212030-212041 mogen niet worden samengevoegd met 475031475042, 475075-475086 en 475451-475462 (1.8.1988)
Other procedures			
Item	*INAMI code*		*INAMI label*
Pulmonary function	471251	471262	Volledige spirografie met bepalen van maximum adem minuten volume
	471273	471284	Spirografie met bronchodilatatieproef

	471295	471306	Spirografie met pharmacodynamische provocatieproef al dan niet gevolgd van bronchodilatatie
	471310	471321	Bepalen van het residuair volume
	471354	471365	Meten van diffusiecapaciteit
	471376	471380	Studie van de ventilatiemechaniek
X-ray	452712	452723	Radiografie van de thorax en de inhoud ervan, minimum twee clichés
	452690	452701	Radiografie van de thorax en de inhoud ervan, één cliché
d. Hospital charges (for 2 days)			
Item	*INAMI code*		*INAMI label*
"Verpleegdagprijs" - after 01/07/2002			
"prix moyen de journée"	NA	NA	Du SPF santé publique, on dispose du prix de journée (12è + partie variable) par hospital. 2 * the average cost per day for the 17 accredited cardiac centers.
Patients' share	?	?	Can we derive an average patient'share per day (?) This has to be subtracted from the "prix moyen de journée" provided by the SPF
Forfaits per day:			
Clinical biology	-	592001	Forfaitair honorarium dat per verpleegdag wordt betaald voor de verstrekkingen inzake klinische biologie van de in een ziekenhuis opgenomen rechthebbenden
Forfaits per admission:			
"Permanence médicale"	-	590225	Forfaitair honorarium voor de intramuraal aanwezige medische permanentie in het ziekenhuis, per opneming in een acute dienst A, C, D, E, G, (i), K, L, M of NIC van een algemeen ziekenhuis dat beschikt over een erkende functie voor gespecialiseerde spoedgevallen

Table protocol 2: ICD implantation costs - ICD implantation

a. Material			
Item	*INAMI code*		*INAMI label*
ICD + leads	-	686302	Overeenkomsten, implanteerbare hartdefibrillatoren + toebehoren
- KI2			Info in the INAMI DB
- KI3-2el			Info in the INAMI DB
- KI3-3el			Info in the INAMI DB
b. "Prestations techniques" for ICD implantation			
Item	*INAMI code*		*INAMI label*
Aesthesia	200012	200023	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een hogere categorie dan K 600 of N 1000 of I 1500
	200034	200045	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 600 of N 1000 of I 1500 en hoger dan K 510 of N 850 of I 1000
	200056	200060	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 510 of N 850 of I 1000 en hoger dan K 450 of N 750 of I 850
	200071	200082	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 450 of N 750 of I 850 en hoger dan K 390 of N 650 of I 750
	200093	200104	Anesthese verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 390 of N 650 of I 750 en hoger dan K 300 of N 500 of I 600
	200130	200141	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 300 of N 500 of I 600 en hoger dan K 270 of N 450 of I 550
	200152	200163	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 270 of N 450 of I 550 en hoger dan K 240 of N 400 of I 450
	200196	200200	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 240 of N 400 of I 450 en hoger dan K 180 of N 300 of I 350
	200211	200222	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 180 of N 300 of I 350 en hoger dan K 120 of N 200 of I 250
	200255	200266	Anesthesie verricht tijdens een verstrekking : Gerangschikt in categorie K 120 of N 200
	201073	201084	Algemene, rachi- of epidurale anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie lager dan K 120 of N 200 of I 200 en hoger dan K 75 of N 125 of I 125
	201110	201121	Algemene, rachi- of epidurale anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 75 of N 125 of I 125 en hoger dan K 24 of N 40 of I 40
	201132	201143	Algemene, rachi- of epidurale anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 24 of N 40 of I 40
	201154	201165	Anesthesie verricht tijdens een verstrekking : Bijkomend honorarium voor de heelkundige bewerking onder diepe hypothermie (centrale temperatuur onder 33°)
	201176	201180	Anesthesie verricht tijdens een verstrekking : Bijkomend honorarium voor de ingrepen op het hart of op de grote intrathoracale bloedvaten, met extracorporale circulatie of voor de verstrekkingen nrs. 318010 - 318021, 318054 - 318065 en 318076 - 318080
	201353	201364	Anesthesie verricht tijdens een verstrekking : Bijkomende honoraria voor ingrepen op het hart of de grote intrathoracale bloedvaten, op kloppend hart, zonder extracorporele circulatie

	201294	201305	Anesthesie verricht tijdens een verstrekking : Bijkomend honorarium voor een anesthesie, verricht bij een heelkundige verstrekking waarvan de waarde meer bedraagt dan K750 of N 1250, met uitsluiting van de heelkundige verstrekkingen die overeenstemmen met de nrs.201154-201165 en 201176-201180
Surgery	229132	229143	Inplanten van elektroden in de hartholte langs intraveneuze weg en onderhuids plaatsen van de hartprikkelaar
	229154	229165	Inplanten van elektroden in de hartholte langs intraveneuze weg en van een auriculaire elektrode door mediastinoscopie en onderhuids plaatsen van de hartprikkelaar
	229110	229121	Inplanten van elektroden in het myocardium door thoracotomie en onderhuids plaatsen van de hartprikkelaar

Table protocol 3 : ICD implantation costs – Post-ICD implantation

a. Post-operative procedures			
Item	*INAMI code*		*INAMI label*
Echo-cardiography	-	460423	Cardiovasculaire echografieen : Transthoracale mono- en bidimensionele echografie (met respectievelijk ten minste 3 en 2 coupes en registratie op papier en/of magneetband)
	-	460460	Volledig transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen en in spectraal mode ter hoogte van minstens drie klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist evenals een gedetailleerd protocol
	-	460585	Volledig transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen ter hoogte van minstens 3 klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
	-	461226	Herhaling binnen het kalenderjaar van de verstrekking 460456 - 460460 of 469814 - 469825 voor één van de volgende indicaties. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol en het bijhouden van een register van de herhalingsonderzoeken
	-	461241	Beperkt transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	-	461263	Beperkt transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en kleuren-Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	-	469663	Beperkt transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	-	469685	Beperkt transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en kleuren-Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	-	469825	Volledig transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen en in spectraal mode ter hoogte van minstens drie klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
	-	469840	Volledig transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen ter hoogte van minstens 3 klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
24h-ECG	-	476221	Monitoring Holter : continu elektrocardiografisch registreren gedurende ten minste 24 uur,door middel van een draagbaar toestel met magneetband of met ingebouwd geheugen, inclusief de raadpleging bij het platsen en het wegnemen van het toestel, met protocol en mogelijkheid tot reproduceren van de volledige tracés
	-	476243	Herhaling binnen een jaar van verstrekking nr 476210 - 476221
	-	476265	Monitoring Holter : continue electrocardiografische analyse gedurende ten minste 24 uur, door middel van draagbaar toestel, inclusief de raadpleging bij het plaatsen en het wegnemen van het toestel met protocol en mogelijkheid tot reproduceren van een deel van de tracés
ECG	-	475086	Elektrocardiografische onderzoekingen, met protocol, ten minste 12 verschillende derivaties
ECG + monitoring	-	214045	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat, benevens het elektrocardiogram, op zijn minst bestendig een van de volgende parameters volgt : de arteriële druk door middel van een intraarteriële catheter, de intracavitaire of pulmonale druk door middel van een intracardiale catheter, de intracraniële druk door middel van een intracraniële catheter (buiten de narcoses, de

			heelkundige en verloskundige bewerkingen en buiten de functionele harttests), inclusief de eventuele registraties : De tweede, derde, vierde en vijfde dag, per dag
	-	214023	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat, benevens het elektrocardiogram, op zijn minst bestendig een van de volgende parameters volgt : de arteriële druk door middel van een intraarteriële catheter, de intracavitaire of pulmonale druk door middel van een intracardiale catheter, de intracraniële druk door middel van een intracraniële catheter (buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests), inclusief de eventuele registraties : De eerste dag
	-	212041	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat op zijn minst bestendig het elektrocardiogram volgt, inclusief de eventuele registraties, buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests : De tweede en derde dag, per dag 212030-212041 mogen niet worden samengevoegd met 475031475042, 475075-475086 en 475451-475462 (1.8.1988)
X-ray	-	452723	Radiografie van de thorax en de inhoud ervan, minimum twee clichés
	-	452701	Radiografie van de thorax en de inhoud ervan, één cliché
ICD or PM control	-	475904	Controle van de deugdelijkheid of herprogrammatie van een anti-tachycardiepacemaker of A.I.C.D., met meting van de stimulatie- en gevoeligheidsdrempel, met protocol en tracés
	-	475860	Controle van de deugdelijkheid of herprogrammatie van een pacemaker, single chamber, met meting van de stimulatie - en gevoeligheidsdrempel, met protocol en tracés
	-	475882	Controle van de deugdelijkheid of herprogrammatie van een pacemaker (D.D.D.) double chamber, met meting van de stimulatie- en gevoeligheidsdrempel, met protocol en tracés
b. Post-operative complications			
Item	*INAMI code*		*INAMI label*
Proxy "cardiac problem"	-	229084	Heelkundige behandeling van hartwonden
	-	229261	Pericardotomie
	-	149144	Hartmassage door uitwendige handelingen
	-	212122	Elektrische defibrillatie van het hart in geval van circulatiestilstand en/of elektrostimulatie van het hart door uitwendige hartprikkelaar, inclusief de elektrocardiografische controle, buiten de ingrepen met open thorax en de verstrekkingen 229110 - 229121, 229132 - 229143, 229154 - 229165, 229176 – 229180
	-	229202	Thoracotomie met rechtstreekse massage van het hart
Proxy "lead or device problem"	-	229180	Vervangen van een onderhuidse hartprikkelaar of van een blijvende intracavitaire elektrode
	-	589444	Percutane extractie van een elektrode bij een patiënt met een ingeplante hartstimulator of een ingeplante hartdefibrillator of percutaan verwijderen van een intracardiaal vrijzittend vreemd lichaam, met uitsluiting van de farmaceutische produkten, de contrastmiddelen en het wegwerpmateriaal
	-	684622	Implanteerbare defibrillator
	-	684644	Bijkomende tussenkomst voor de elektroden en geïmplanteerd toebehoren voor de defibrillator
	-	687982	Vervangingsdefibrillator en toebehoren
Proxy "pneumothorax"	-	471564	Exsufflatie van spontane pneumothorax door voortdurende aspiratie, inclusief radioscopisch onderzoek bij het plaatsen van de drain
	-	687584	Disposable drainagesysteem van de thorax (pericard, pleura, mediastinum) met minstens drie kamers per stuk
	-	227500	Pleurotomie (één of meer drains)
c. Hospital charges			
Item	*INAMI code*		*INAMI label*
"Verpleegdagprijs" - after 01/07/2002			

"prix moyen de journée" SPF Santé publique	NA	NA	2 * the average cost per day for the 17 accredited cardiac centers. Take the average cost per hospital from SPF santé publique. Exclude INAMI codes for "partie variable du BMF"
Patients' share	?	?	This has to be subtracted from the "prix de journée" (perspective of the health care payers)
Forfaits per day:			
Clinical biology	-	592001	Forfaitair honorarium dat per verpleegdag wordt betaald voor de verstrekkingen inzake klinische biologie van de in een ziekenhuis opgenomen rechthebbenden
Forfaits per admission:			
"Imagerie médicale"	-	460784	Medische beeldvorming - Radiologie, artikel 17, forfaitair honorarium inzake medische beeldvorming per opneming
"produits pharmaceutiques"	-	751004	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait antibiotica Z
	-	751026	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A1
	-	751041	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 2
	-	751063	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 3
	-	751085	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 4
	-	751100	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 6
	-	751122	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 7
	-	751144	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait B 3
	-	751166	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait B 4
	-	751181	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait : C 3
	-	751542	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep (vergoeding aan 25%) met complement forfaitaire vergoeding : categorie B
	-	751564	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep (vergoeding aan 25%) met complementaire forfaitaire vergoeding - categorie B : generieken of kopieën afgeleverd
	-	751586	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep (vergoeding aan 25%) met complementaire forfaitaire vergoeding - categorie B : referentiespecialiteiten afgele
	-	751645	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding : categorie B
	-	751660	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	751682	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	751741	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : antibiotica toegediend buiten de peri-operatieve periode van heelkundige ingreep : categorie B
	-	751763	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	751785	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	752124	Vol bloed en labiele bloedprodukten - menselijk vol bloed
	-	752146	Vol bloed en labiele bloedprodukten - Erytrocytenconcentraat - eenheid type "volwassene" : per eenheid erytrocytenconcentraat "volwassene"

	-	752220	Vol bloed en labiele bloedprodukten - CMV negatief erytrocytenconcentraat : per eenheid CMV negatief erytrocytenconcentraat
	-	752404	Vol bloed en labiele bloedprodukten - leucocytenconcentraat : per eenheid leucocytenconcentraat
	-	752426	Vol bloed en labiele bloedprodukten - Bevroren vers menselijk plasma bestemd om te worden gebruikt voor geprogrammeerde autologe transfusies : per eenheid
	-	752441	Vol bloed en labiele bloedprodukten - Vers ingevroren menselijk plasma virus geïnactiveerd : per eenheid vers ingevroren virus geïnactiveerd menselijk plasma
	-	752463	Vol bloed en labiele bloedprodukten - Gedeleucocyteerd erytrocytenconcentraat : eenheid "volwassene" : per eenheid "volwassene" gedeleucocyteerd erytrocytenconcentraat, filter inbegrepen
	-	752500	Vol bloed en labiele bloedprodukten : Gedeleucocyteerd bloedplaatjesconcentraat : per geheel veelvoud van de eenheid die minstens 0,5 x 10(11) bloedplaatjes bevat en waarvan het aantal leucocyten niet hoger ligt dan 1 x 10(6) in het eindproduct, filter i
	-	752522	Vol bloed en labiele bloedprodukten : Gedeleucocyteerd één donor bloedplaatjesconcentraat : per concentraat dat minstens 4x10(11) bloedvaatjes bevat voor ucocytering en maximum 1x10(6) leucocyten na deleucocytering, filter inbegrepen
	-	752544	Vol bloed en labiele bloedprodukten - Erytrocytenconcentraat autoloog
	-	755720	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie A
	-	755742	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie B
	-	755764	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie C
	-	755786	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie Cs
	-	755963	Honoraria en forfaits zuurstof in de ziekenhuisofficina's
	-	750746	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden in psychiatrische ziekenhuizen en chronische ziekenhuizen (geïsoleerde Sp- en G-diensten) : andere toedieningen : categorie B
	-	750864	Generieken of kopieën afgeleverd aan gehospitaliseerde rechthebbenden in psychiatrische ziekenhuizen en chronische ziekenhuizen (geïsoleerde Sp- en G-diensten) - categorie Bg
	-	753745	Referentiespecialiteiten afgeleverd aan gehospitaliseerde rechthebbenden in psychiatrische ziekenhuizen en chronische ziekenhuizen (geïsoleerde Sp- en G-diensten) - categorie Br

d. Pharmaceuticals outside forfait

Item	*ATC codes*		
Anti-arrhythmic Class III			
Amiodarone	C01BD01		
Sotalol	C07AA07		
Anti-arrhythmic Class I			
Procainamide	C01BA02		
Quinidine	C01BA51	C01BA71	Note: there are 2 different ATC codes for Quinidine
Lidocaine	C01BB01		
Mexiletine	C01BB02		
Tocainide	C01BB03		
Flecainide	C01BC04		
Propafenone	C01BC03		
Encainide	C01BC08		

e. Other resources used during hospital stay for post-ICD implantation

Item	*INAMI code*	*INAMI label*
Sum of all other INAMI codes not listed in the above tables		

Table protocol 4: ICD follow-up costs – Outpatient (OP)

a. & b. Outpatient follow-up procedures			
Item	*INAMI code*		*INAMI label*
ICD control	475893	-	Controle van de deugdelijkheid of herprogrammatie van een anti-tachycardiepacemaker of A.I.C.D., met meting van de stimulatie- en gevoeligheidsdrempel, met protocol en tracés
If on the same day as ICD control, compute also the following procedures:			
ECG	475075	-	Elektrocardiografische onderzoekingen, met protocol, ten minste 12 verschillende derivaties
	475090	-	Elektrocardiografische onderzoekingen thuis, met protocol
PM control	475856	-	Controle van de deugdelijkheid of herprogrammatie van een pacemaker, single chamber, met meting van de stimulatie - en gevoeligheidsdrempel, met protocol en tracés
	475871	-	Controle van de deugdelijkheid of herprogrammatie van een pacemaker (D.D.D.) double chamber, met meting van de stimulatie- en gevoeligheidsdrempel, met protocol en tracés
c. Physician fees for consultation – if on the same day as ICD control procedure			
Item	*INAMI code*		*INAMI label*
Cardiologist	102093	-	Raadpleging, in de spreekkamer, van de geneesheer, specialist voor cardiologie, inclusief eventueel schriftelijk verslag
	102594	-	Raadpleging in de spreekkamer van de geaccrediteerde geneesheer, specialist voor cardiologie, inclusief een eventueel schriftelijk verslag
Internist	102034	-	Raadpleging, in zijn spreekkamer, van de geneesheer, specialist voor inwendige geneeskunde, inclusief een eventueel schriftelijk verslag
	102550	-	Raadpleging in de spreekkamer, van de geaccrediteerde geneesheer, specialist voor inwendige geneeskunde, inclusief eventueel schriftelijk verslag

d. Drugs (OP)			
Item	*ATC code*		
Anti-arrhythmic Class III			
Amiodarone	C01BD01		
Sotalol	C07AA07		
Anti-arrhythmic Class I			
Procainamide	C01BA02		
Quinidine	C01BA51	C01BA71	Note: there are 2 different ATC codes for Quinidine
Lidocaine	C01BB01		
Mexiletine	C01BB02		
Tocainide	C01BB03		
Flecainide	C01BC04		
Propafenone	C01BC03		
Encainide	C01BC08		

Table protocol 5: ICD follow-up costs – Inpatient (IP)

a. Re-hospitalizations – IP follow-up			
Item	*INAMI code*		*INAMI label*
"Accessoire-related"	-	229180	Vervangen van een onderhuidse hartprikkelaar of van een blijvende intracavitaire elektrode
	-	589444	Percutane extractie van een elektrode bij een patiënt met een ingeplante hartstimulator of een ingeplante hartdefibrillator of percutaan verwijderen van een intracardiaal vrijzittend vreemd lichaam, met uitsluiting van de farmaceutische produkten, de contrastmiddelen en het wegwerpmateriaal
	-	684644	Bijkomende tussenkomst voor de elektroden en geïmplanteerd toebehoren voor de defibrillator
"Device-related"	-	684622	Implanteerbare defibrillator
	-	772380	Overeenkomsten revalidatie : implanteerbare hartdefibrillatoren
	687971	687982	Vervangingsdefibrillator en toebehoren
b. ICD-related procedures – IP follow-up			
Item	*INAMI code*		*INAMI label*
Pulmonary function	-	471262	Volledige spirografie met bepalen van maximum adem minuten volume
	-	471284	Spirografie met bronchodilatatieproef
	-	471306	Spirografie met pharmacodynamische provocatieproef al dan niet gevolgd van bronchodilatatie
	-	471321	Bepalen van het residuair volume
	-	471365	Meten van diffusiecapaciteit
	-	471380	Studie van de ventilatiemechaniek
X-ray	-	452723	Radiografie van de thorax en de inhoud ervan, minimum twee clichés
	-	452701	Radiografie van de thorax en de inhoud ervan, één cliché
Echo-cardiography	-	460423	Cardiovasculaire echografieen : Transthoracale mono- en bidimensionele echografie (met respectievelijk ten minste 3 en 2 coupes en registratie op papier en/of magneetband)
	-	460460	Volledig transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen en in spectraal mode ter hoogte van minstens drie klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist evenals een gedetailleerd protocol
	-	460585	Volledig transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen ter hoogte van minstens 3 klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
	-	461226	Herhaling binnen het kalenderjaar van de verstrekking 460456 - 460460 of 469814 - 469825 voor één van de volgende indicaties. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol en het bijhouden van een register van de herhalingsonderzoeken
	-	461241	Beperkt transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	-	461263	Beperkt transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en kleuren-Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	-	469663	Beperkt transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem

	-	469685	Beperkt transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en kleuren-Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	-	469825	Volledig transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen en in spectraal mode ter hoogte van minstens drie klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
	-	469840	Volledig transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen ter hoogte van minstens 3 klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
24h-ECG	476210	476221	Monitoring Holter : continu elektrocardiografisch registreren gedurende ten minste 24 uur,door middel van een draagbaar toestel met magneetband of met ingebouwd geheugen, inclusief de raadpleging bij het plaatsen en het wegnemen van het toestel, met protocol en mogelijkheid tot reproduceren van de volledige tracés
	476232	476243	Herhaling binnen een jaar van verstrekking nr 476210 - 476221
	476254	476265	Monitoring Holter : continue electrocardiografische analyse gedurende ten minste 24 uur, door middel van draagbaar toestel, inclusief de raadpleging bij het plaatsen en het wegnemen van het toestel met protocol en mogelijkheid tot reproduceren van een deel van de tracés
ECG	475075	475086	Elektrocardiografische onderzoekingen, met protocol, ten minste 12 verschillende derivaties
ECG + monitoring	214034	214045	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat, benevens het elektrocardiogram, op zijn minst bestendig een van de volgende parameters volgt : de arteriële druk door middel van een intraarteriële catheter, de intracavitaire of pulmonale druk door middel van een intracardiale catheter, de intracraniële druk door middel van een intracraniële catheter (buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests), inclusief de eventuele registraties : De tweede, derde, vierde en vijfde dag, per dag
	214012	214023	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat, benevens het elektrocardiogram, op zijn minst bestendig een van de volgende parameters volgt : de arteriële druk door middel van een intraarteriële catheter, de intracavitaire of pulmonale druk door middel van een intracardiale catheter, de intracraniële druk door middel van een intracraniële catheter (buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests), inclusief de eventuele registraties : De eerste dag
	212030	212041	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat op zijn minst bestendig het elektrocardiogram volgt, inclusief de eventuele registraties, buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests : De tweede en derde dag, per dag 212030-212041 mogen niet worden samengevoegd met 475031475042, 475075-475086 en 475451-475462 (1.8.1988)
ICD or PM control	475893	475904	Controle van de deugdelijkheid of herprogrammatie van een anti-tachycardiepacemaker of A.I.C.D., met meting van de stimulatie- en gevoeligheidsdrempel, met protocol en tracés
	475856	475860	Controle van de deugdelijkheid of herprogrammatie van een pacemaker, single chamber, met meting van de stimulatie - en gevoeligheidsdrempel, met protocol en tracés
	475871	475882	Controle van de deugdelijkheid of herprogrammatie van een pacemaker (D.D.D.) double chamber, met meting van de stimulatie- en gevoeligheidsdrempel, met protocol en tracés
c. Material used – IP follow-up			
Item	*INAMI code*		*INAMI label*
"Accessoire-related"	-	229180	Vervangen van een onderhuidse hartprikkelaar of van een blijvende intracavitaire elektrode
	-	589444	Percutane extractie van een elektrode bij een patiënt met een ingeplante hartstimulator of een ingeplante hartdefibrillator of percutaan verwijderen van een intracardiaal vrijzittend vreemd lichaam, met uitsluiting van de farmaceutische produkten, de contrastmiddelen en het

			wegwerpmateriaal
	-	684644	Bijkomende tussenkomst voor de elektroden en geïmplanteerd toebehoren voor de defibrillator
"Device-related"	-	684622	Implanteerbare defibrillator
	-	772380	Overeenkomsten revalidatie : implanteerbare hartdefibrillatoren
	-	687982	Vervangingsdefibrillator en toebehoren

d. "Prestations techniques"

Item	*INAMI code*		*INAMI label*
Aesthesia	200012	200023	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een hogere categorie dan K 600 of N 1000 of I 1500
	200034	200045	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 600 of N 1000 of I 1500 en hoger dan K 510 of N 850 of I 1000
	200056	200060	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 510 of N 850 of I 1000 en hoger dan K 450 of N 750 of I 850
	200071	200082	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 450 of N 750 of I 850 en hoger dan K 390 of N 650 of I 750
	200093	200104	Anesthese verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 390 of N 650 of I 750 en hoger dan K 300 of N 500 of I 600
	200130	200141	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 300 of N 500 of I 600 en hoger dan K 270 of N 450 of I 550
	200152	200163	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 270 of N 450 of I 550 en hoger dan K 240 of N 400 of I 450
	200196	200200	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 240 of N 400 of I 450 en hoger dan K 180 of N 300 of I 350
	200211	200222	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 180 of N 300 of I 350 en hoger dan K 120 of N 200 of I 250
	200255	200266	Anesthesie verricht tijdens een verstrekking : Gerangschikt in categorie K 120 of N 200
	201073	201084	Algemene, rachi- of epidurale anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie lager dan K 120 of N 200 of I 200 en hoger dan K 75 of N 125 of I 125
	201110	201121	Algemene, rachi- of epidurale anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 75 of N 125 of I 125 en hoger dan K 24 of N 40 of I 40
	201132	201143	Algemene, rachi- of epidurale anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 24 of N 40 of I 40
	201154	201165	Anesthesie verricht tijdens een verstrekking : Bijkomend honorarium voor de heelkundige bewerking onder diepe hypothermie (centrale temperatuur onder 33°)
	201176	201180	Anesthesie verricht tijdens een verstrekking : Bijkomend honorarium voor de ingrepen op het hart of op de grote intrathoracale bloedvaten, met extracorporale circulatie of voor de verstrekkingen nrs. 318010 - 318021, 318054 - 318065 en 318076 - 318080
	201353	201364	Anesthesie verricht tijdens een verstrekking : Bijkomende honoraria voor ingrepen op het hart of de grote intrathoracale bloedvaten, op kloppend hart, zonder extracorporele circulatie
	201294	201305	Anesthesie verricht tijdens een verstrekking : Bijkomend honorarium voor een anesthesie, verricht bij een heelkundige verstrekking waarvan de waarde meer bedraagt dan K750 of N 1250, met uitsluiting van de heelkundige verstrekkingen die overeenstemmen met de nrs.201154-201165 en 201176-201180

Surgery	229132	229143	Inplanten van elektroden in de hartholte langs intraveneuze weg en onderhuids plaatsen van de hartprikkelaar
	229154	229165	Inplanten van elektroden in de hartholte langs intraveneuze weg en van een auriculaire elektrode door mediastinoscopie en onderhuids plaatsen van de hartprikkelaar
	229110	229121	Inplanten van elektroden in het myocardium door thoracotomie en onderhuids plaatsen van de hartprikkelaar

e. Hospital charges

Item	*INAMI code*		*INAMI label*
"Verpleegdagprijs" - before 01/07/2002			
Prix de journée	?	?	We need the net cost per day of hospitalization (perspective of the health care payers), excluding the patient's share
"Verpleegdagprijs" - after 01/07/2002			
"prix moyen de journée" SPF Santé publique	NA	NA	LoS * the average cost per day for the 17 accredited cardiac centers. Take the average cost per hospital from SPF santé publique. Exclude INAMI codes for "partie variable du BMF"
Patients' share	?	?	Can we derive an average patient' share per day (?) This has to be subtracted from the "prix de journée" (perspective of the health care payers)
Forfaits per day:			
Clinical biology	-	592001	Forfaitair honorarium dat per verpleegdag wordt betaald voor de verstrekkingen inzake klinische biologie van de in een ziekenhuis opgenomen rechthebbenden
Forfaits per admission:			
"Imagerie médicale"	-	460784	Medische beeldvorming - Radiologie, artikel 17, forfaitair honorarium inzake medische beeldvorming per opneming
"Permanence médicale"	-	590166	Forfaitair honorarium voor de intramuraal aanwezige medische permanentie in het ziekenhuis, per opneming in een acute dienst A, C, D, E, G, (i), K, L, M of NIC van een algemeen ziekenhuis dat beschikt over een erkende functie eerste opvang van spoedgevallen
	-	590181	Forfaitair honorarium voor de intramuraal aanwezige medische permanentie in het ziekenhuis per opneming in een acute dienst A, C, D, E, G, (i), K, L, M of NIC van een algemeen ziekenhuis dat beschikt over een erkende functie voor gespecialiseerde spoedgevallen
	-	590203	Forfaitair honorarium voor de intramuraal aanwezige medische permanentie in het ziekenhuis, per opneming in een acute dient A, C, D, E, G, (i), K, L, M of NIC van een algemeen ziekenhuis dat beschikt over een erkende functie voor intensieve zorg
	-	590225	Forfaitair honorarium voor de intramuraal aanwezige medische permanentie in het ziekenhuis, per opneming in een acute dienst A, C, D, E, G, (i), K, L, M of NIC van een algemeen ziekenhuis dat beschikt over een erkende functie voor gespecialiseerde spoedgevallen
"produits pharmaceutiques"	-	751004	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait antibiotica Z
	-	751026	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A1
	-	751041	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 2
	-	751063	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 3
	-	751085	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 4
	-	751100	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 6
	-	751122	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 7
	-	751144	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait B 3
	-	751166	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait B 4
	-	751181	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait : C 3
	-	751542	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep

			(vergoeding aan 25%) met complement forfaitaire vergoeding : categorie B
	-	751564	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep (vergoeding aan 25%) met complementaire forfaitaire vergoeding - categorie B : generieken of kopieën afgeleverd
	-	751586	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep (vergoeding aan 25%) met complementaire forfaitaire vergoeding - categorie B : referentiespecialiteiten afgele
	-	751645	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding : categorie B
	-	751660	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	751682	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	751741	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : antibiotica toegediend buiten de peri-operatieve periode van heelkundige ingreep : categorie B
	-	751763	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	751785	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	752124	Vol bloed en labiele bloedprodukten - menselijk vol bloed
	-	752146	Vol bloed en labiele bloedprodukten - Erytrocytenconcentraat - eenheid type "volwassene" : per eenheid erytrocytenconcentraat "volwassene"
	-	752220	Vol bloed en labiele bloedprodukten - CMV negatief erytrocytenconcentraat : per eenheid CMV negatief erytrocytenconcentraat
	-	752404	Vol bloed en labiele bloedprodukten - leucocytenconcentraat : per eenheid leucocytenconcentraat
	-	752426	Vol bloed en labiele bloedprodukten - Bevroren vers menselijk plasma bestemd om te worden gebruikt voor geprogrammeerde autologe transfusies : per eenheid
	-	752441	Vol bloed en labiele bloedprodukten - Vers ingevroren menselijk plasma virus geïnactiveerd : per eenheid vers ingevroren virus geïnactiveerd menselijk plasma
	-	752463	Vol bloed en labiele bloedprodukten - Gedeleucocyteerd erytrocytenconcentraat : eenheid "volwassene" : per eenheid "volwassene" gedeleucocyteerd erytrocytenconcentraat, filter inbegrepen
	-	752500	Vol bloed en labiele bloedprodukten : Gedeleucocyteerd bloedplaatjesconcentraat : per geheel veelvoud van de eenheid die minstens 0,5 x 10(11) bloedplaatjes bevat en waarvan het aantal leucocyten niet hoger ligt dan 1 x 10(6) in het eindproduct, filter i
	-	752522	Vol bloed en labiele bloedprodukten : Gedeleucocyteerd één donor bloedplaatjesconcentraat : per concentraat dat minstens 4x10(11) bloedvaatjes bevat voor ucocytering en maximum 1x10(6) leucocyten na deleucocytering, filter inbegrepen
	-	752544	Vol bloed en labiele bloedprodukten - Erytrocytenconcentraat autoloog
	-	755720	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie A
	-	755742	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie B
	-	755764	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie C
	-	755786	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie Cs

	-	755963	Honoraria en forfaits zuurstof in de ziekenhuisofficina's
	-	750746	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden in psychiatrische ziekenhuizen en chronische ziekenhuizen (geïsoleerde Sp- en G-diensten) : andere toedieningen : categorie B
	-	750864	Generieken of kopieën afgeleverd aan gehospitaliseerde rechthebbenden in psychiatrische ziekenhuizen en chronische ziekenhuizen (geïsoleerde Sp- en G-diensten) - categorie Bg
	-	753745	Referentiespecialiteiten afgeleverd aan gehospitaliseerde rechthebbenden in psychiatrische ziekenhuizen en chronische ziekenhuizen (geïsoleerde Sp- en G-diensten) - categorie Br

f. Drugs outside forfait

Item	*ATC code*		
Anti-arrhythmic Class III			
Amiodarone	C01BD01		
Sotalol	C07AA07		
Anti-arrhythmic Class I			
Procainamide	C01BA02		
Quinidine	C01BA51	C01BA71	Note: there are 2 different ATC codes for Quinidine
Lidocaine	C01BB01		
Mexiletine	C01BB02		
Tocainide	C01BB03		
Flecainide	C01BC04		
Propafenone	C01BC03		
Encainide	C01BC08		

g. Other resources used during hospital stay – IP follow-up

Item	*INAMI code*	*INAMI label*
Sum of all other INAMI codes not listed in the above tables		

Table protocol 6 - ICD re-implantation – Pre-ICD re-implantation

a. Pre-operative procedures – Pre-ICD replacement			
Cardiologic procedures			
Item	*INAMI code*		*INAMI label*
ECG	-	475086	Elektrocardiografische onderzoekingen, met protocol, ten minste 12 verschillende derivaties
ECG + monitoring	-	214045	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat, benevens het elektrocardiogram, op zijn minst bestendig een van de volgende parameters volgt : de arteriële druk door middel van een intraarteriële catheter, de intracavitaire of pulmonale druk door middel van een intracardiale catheter, de intracraniële druk door middel van een intracraniële catheter (buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests), inclusief de eventuele registraties : De tweede, derde, vierde en vijfde dag, per dag
	-	214023	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat, benevens het elektrocardiogram, op zijn minst bestendig een van de volgende parameters volgt : de arteriële druk door middel van een intraarteriële catheter, de intracavitaire of pulmonale druk door middel van een intracardiale catheter, de intracraniële druk door middel van een intracraniële catheter (buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests), inclusief de eventuele registraties : De eerste dag
	-	212041	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat op zijn minst bestendig het elektrocardiogram volgt, inclusief de eventuele registraties, buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests : De tweede en derde dag, per dag 212030-212041 mogen niet worden samengevoegd met 475031475042, 475075-475086 en 475451-475462 (1.8.1988)
Other procedures			
Item	*INAMI code*		*INAMI label*
Pulmonary function	-	471262	Volledige spirografie met bepalen van maximum adem minuten volume
	-	471284	Spirografie met bronchodilatatieproef
	-	471306	Spirografie met pharmacodynamische provocatieproef al dan niet gevolgd van bronchodilatatie
	-	471321	Bepalen van het residuair volume
	-	471365	Meten van diffusiecapaciteit
	-	471380	Studie van de ventilatiemechaniek
X-ray	-	452723	Radiografie van de thorax en de inhoud ervan, minimum twee clichés
	-	452701	Radiografie van de thorax en de inhoud ervan, één cliché
b. Hospital charges			
Item	*INAMI code*		*INAMI label*
"Verpleegdagprijs" - after 01/07/2002			
"prix moyen de journée" SPF Santé publique	NA	NA	LoS * the average cost per day for the 17 accredited cardiac centers. Take the average cost per hospital from SPF santé publique. Exclude INAMI codes for "partie variable du BMF"
Patients' share	?	?	Can we derive an average patient' share per day (?) This has to be subtracted from the "prix de journée" (perspective of the health care payers)
Forfaits per day:			
Clinical biology	-	592001	Forfaitair honorarium dat per verpleegdag wordt betaald voor de verstrekkingen inzake klinische biologie van de in een ziekenhuis opgenomen

			rechthebbenden
Forfaits per admission:			
"Imagerie médicale"	-	460784	Medische beeldvorming - Radiologie, artikel 17, forfaitair honorarium inzake medische beeldvorming per opneming
"Permanence médicale"	-	590166	Forfaitair honorarium voor de intramuraal aanwezige medische permanentie in het ziekenhuis, per opneming in een acute dienst A, C, D, E, G, (i), K, L, M of NIC van een algemeen ziekenhuis dat beschikt over een erkende functie eerste opvang van spoedgevallen
	-	590181	Forfaitair honorarium voor de intramuraal aanwezige medische permanentie in het ziekenhuis per opneming in een acute dienst A, C, D, E, G, (i), K, L, M of NIC van een algemeen ziekenhuis dat beschikt over een erkende functie voor gespecialiseerde spoedgevallen
	-	590203	Forfaitair honorarium voor de intramuraal aanwezige medische permanentie in het ziekenhuis, per opneming in een acute dient A, C, D, E, G, (i), K, L, M of NIC van een algemeen ziekenhuis dat beschikt over een erkende functie voor intensieve zorg
	-	590225	Forfaitair honorarium voor de intramuraal aanwezige medische permanentie in het ziekenhuis, per opneming in een acute dienst A, C, D, E, G, (i), K, L, M of NIC van een algemeen ziekenhuis dat beschikt over een erkende functie voor gespecialiseerde spoedgevallen
"produits pharmaceutiques"	-	751004	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait antibiotica Z
	-	751026	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A1
	-	751041	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 2
	-	751063	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 3
	-	751085	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 4
	-	751100	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 6
	-	751122	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 7
	-	751144	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait B 3
	-	751166	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait B 4
	-	751181	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait : C 3
	-	751542	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep (vergoeding aan 25%) met complement forfaitaire vergoeding : categorie B
	-	751564	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep (vergoeding aan 25%) met complementaire forfaitaire vergoeding - categorie B : generieken of kopieën afgeleverd
	-	751586	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep (vergoeding aan 25%) met complementaire forfaitaire vergoeding - categorie B : referentiespecialiteiten afgele
	-	751645	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding : categorie B
	-	751660	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	751682	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	751741	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : antibiotica toegediend buiten de peri-operatieve periode van heelkundige ingreep : categorie B
	-	751763	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	751785	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat

	-	752124	Vol bloed en labiele bloedprodukten - menselijk vol bloed
	-	752146	Vol bloed en labiele bloedprodukten - Erytrocytenconcentraat - eenheid type "volwassene" : per eenheid erytrocytenconcentraat "volwassene"
	-	752220	Vol bloed en labiele bloedprodukten - CMV negatief erytrocytenconcentraat : per eenheid CMV negatief erytrocytenconcentraat
	-	752404	Vol bloed en labiele bloedprodukten - leucocytenconcentraat : per eenheid leucocytenconcentraat
	-	752426	Vol bloed en labiele bloedprodukten - Bevroren vers menselijk plasma bestemd om te worden gebruikt voor geprogrammeerde autologe transfusies : per eenheid
	-	752441	Vol bloed en labiele bloedprodukten - Vers ingevroren menselijk plasma virus geïnactiveerd : per eenheid vers ingevroren virus geïnactiveerd menselijk plasma
	-	752463	Vol bloed en labiele bloedprodukten - Gedeleucocyteerd erytrocytenconcentraat : eenheid "volwassene" : per eenheid "volwassene" gedeleucocyteerd erytrocytenconcentraat, filter inbegrepen
	-	752500	Vol bloed en labiele bloedprodukten : Gedeleucocyteerd bloedplaatjesconcentraat : per geheel veelvoud van de eenheid die minstens 0,5 x 10(11) bloedplaatjes bevat en waarvan het aantal leucocyten niet hoger ligt dan 1 x 10(6) in het eindproduct, filter i
	-	752522	Vol bloed en labiele bloedprodukten : Gedeleucocyteerd één donor bloedplaatjesconcentraat : per concentraat dat minstens 4x10(11) bloedvaatjes bevat voor ucocytering en maximum 1x10(6) leucocyten na deleucocytering, filter inbegrepen
	-	752544	Vol bloed en labiele bloedprodukten - Erytrocytenconcentraat autoloog
	-	755720	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie A
	-	755742	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie B
	-	755764	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie C
	-	755786	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie Cs
	-	755963	Honoraria en forfaits zuurstof in de ziekenhuisofficina's
	-	750746	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden in psychiatrische ziekenhuizen en chronische ziekenhuizen (geïsoleerde Sp- en G-diensten) : andere toedieningen : categorie B
	-	750864	Generieken of kopieën afgeleverd aan gehospitaliseerde rechthebbenden in psychiatrische ziekenhuizen en chronische ziekenhuizen (geïsoleerde Sp- en G-diensten) - categorie Bg
	-	753745	Referentiespecialiteiten afgeleverd aan gehospitaliseerde rechthebbenden in psychiatrische ziekenhuizen en chronische ziekenhuizen (geïsoleerde Sp- en G-diensten) - categorie Br

c. Drugs outside forfait

Item	*ATC code*		
Anti-arrhythmic Class III			
Amiodarone	C01BD01		
Sotalol	C07AA07		
Anti-arrhythmic Class I			
Procainamide	C01BA02		
Quinidine	C01BA51	C01BA71	Note: there are 2 different ATC codes for Quinidine
Lidocaine	C01BB01		
Mexiletine	C01BB02		

Tocainide	C01BB03		
Flecainide	C01BC04		
Propafenone	C01BC03		
Encainide	C01BC08		
d. Other resources used during hospital stay – IP follow-up			
Item	*INAMI code*	*INAMI label*	
Sum of all other INAMI codes not listed in the above tables			

Table protocol 7: ICD re-implantation – ICD re-implantation

a. Material			
Item	*INAMI code*		*INAMI label*
ICD + leads	687971	687982	Overeenkomsten, implanteerbare hartdefibrillatoren + toebehoren
- KI2			Info in the INAMI DB
- KI3-2el			Info in the INAMI DB
- KI3-3el			Info in the INAMI DB
b. "Prestations techniques" for ICD implantation			
Item	*INAMI code*		*INAMI label*
Aesthesia	200012	200023	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een hogere categorie dan K 600 of N 1000 of I 1500
	200034	200045	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 600 of N 1000 of I 1500 en hoger dan K 510 of N 850 of I 1000
	200056	200060	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 510 of N 850 of I 1000 en hoger dan K 450 of N 750 of I 850
	200071	200082	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 450 of N 750 of I 850 en hoger dan K 390 of N 650 of I 750
	200093	200104	Anesthese verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 390 of N 650 of I 750 en hoger dan K 300 of N 500 of I 600
	200130	200141	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 300 of N 500 of I 600 en hoger dan K 270 of N 450 of I 550
	200152	200163	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 270 of N 450 of I 550 en hoger dan K 240 of N 400 of I 450
	200196	200200	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 240 of N 400 of I 450 en hoger dan K 180 of N 300 of I 350
	200211	200222	Anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 180 of N 300 of I 350 en hoger dan K 120 of N 200 of I 250
	200255	200266	Anesthesie verricht tijdens een verstrekking : Gerangschikt in categorie K 120 of N 200
	201073	201084	Algemene, rachi- of epidurale anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie lager dan K 120 of N 200 of I 200 en hoger dan K 75 of N 125 of I 125
	201110	201121	Algemene, rachi- of epidurale anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 75 of N 125 of I 125 en hoger dan K 24 of N 40 of I 40
	201132	201143	Algemene, rachi- of epidurale anesthesie verricht tijdens een verstrekking : Gerangschikt in een categorie gelijk aan of lager dan K 24 of N 40 of I 40
	201154	201165	Anesthesie verricht tijdens een verstrekking : Bijkomend honorarium voor de heelkundige bewerking onder diepe hypothermie (centrale temperatuur onder 33°)
	201176	201180	Anesthesie verricht tijdens een verstrekking : Bijkomend honorarium voor de ingrepen op het hart of op de grote intrathoracale bloedvaten, met extracorporale circulatie of voor de verstrekkingen nrs. 318010 - 318021, 318054 - 318065 en 318076 - 318080
	201353	201364	Anesthesie verricht tijdens een verstrekking : Bijkomende honoraria voor ingrepen op het hart of de grote intrathoracale bloedvaten, op kloppend hart, zonder extracorporele circulatie

	201294	201305	Anesthesie verricht tijdens een verstrekking : Bijkomend honorarium voor een anesthesie, verricht bij een heelkundige verstrekking waarvan de waarde meer bedraagt dan K750 of N 1250, met uitsluiting van de heelkundige verstrekkingen die overeenstemmen met de nrs.201154-201165 en 201176-201180
Surgery	229132	229143	Inplanten van elektroden in de hartholte langs intraveneuze weg en onderhuids plaatsen van de hartprikkelaar
	229154	229165	Inplanten van elektroden in de hartholte langs intraveneuze weg en van een auriculaire elektrode door mediastinoscopie en onderhuids plaatsen van de hartprikkelaar
	229110	229121	Inplanten van elektroden in het myocardium door thoracotomie en onderhuids plaatsen van de hartprikkelaar
	229176	229180	Vervangen van een onderhuidse hartprikkelaar of van een blijvende intracavitaire elektrode

Table protocol 8 : ICD re-implantation – Post-ICD re-implantation

a. Post-ICD replacement procedures			
Item	*INAMI code*		*INAMI label*
Echo-cardiography	-	460423	Cardiovasculaire echografieen : Transthoracale mono- en bidimensionele echografie (met respectievelijk ten minste 3 en 2 coupes en registratie op papier en/of magneetband)
	-	460460	Volledig transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen en in spectraal mode ter hoogte van minstens drie klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist evenals een gedetailleerd protocol
	-	460585	Volledig transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen ter hoogte van minstens 3 klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
	-	461226	Herhaling binnen het kalenderjaar van de verstrekking 460456 - 460460 of 469814 - 469825 voor één van de volgende indicaties. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol en het bijhouden van een register van de herhalingsonderzoeken
	-	461241	Beperkt transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	-	461263	Beperkt transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en kleuren-Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	-	469663	Beperkt transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	-	469685	Beperkt transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en kleuren-Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
	-	469825	Volledig transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen en in spectraal mode ter hoogte van minstens drie klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
	-	469840	Volledig transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen ter hoogte van minstens 3 klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
24h-ECG	-	476221	Monitoring Holter : continu elektrocardiografisch registreren gedurende ten minste 24 uur,door middel van een draagbaar toestel met magneetband of met ingebouwd geheugen, inclusief de raadpleging bij het plaatsen en het wegnemen van het toestel, met protocol en mogelijkheid tot reproduceren van de volledige tracés
	-	476243	Herhaling binnen een jaar van verstrekking nr 476210 - 476221
	-	476265	Monitoring Holter : continue electrocardiografische analyse gedurende ten minste 24 uur, door middel van draagbaar toestel, inclusief de raadpleging bij het plaatsen en het wegnemen van het toestel met protocol en mogelijkheid tot reproduceren van een deel van de tracés
ECG	-	475086	Elektrocardiografische onderzoekingen, met protocol, ten minste 12 verschillende derivaties
ECG +	-	214045	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat, benevens het elektrocardiogram,

monitoring			op zijn minst bestendig een van de volgende parameters volgt : de arteriële druk door middel van een intraarteriële catheter, de intracavitaire of pulmonale druk door middel van een intracardiale catheter, de intracraniële druk door middel van een intracraniële catheter (buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests), inclusief de eventuele registraties : De tweede, derde, vierde en vijfde dag, per dag
	-	214023	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat, benevens het elektrocardiogram, op zijn minst bestendig een van de volgende parameters volgt : de arteriële druk door middel van een intraarteriële catheter, de intracavitaire of pulmonale druk door middel van een intracardiale catheter, de intracraniële druk door middel van een intracraniële catheter (buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests), inclusief de eventuele registraties : De eerste dag
	-	212041	Continu toezicht op de hartfunctie (met of zonder toezicht op andere vitale waarden) met een waaktoestel dat op zijn minst bestendig het elektrocardiogram volgt, inclusief de eventuele registraties, buiten de narcoses, de heelkundige en verloskundige bewerkingen en buiten de functionele harttests : De tweede en derde dag, per dag 212030-212041 mogen niet worden samengevoegd met 475031475042, 475075-475086 en 475451-475462 (1.8.1988)
X-ray	-	452723	Radiografie van de thorax en de inhoud ervan, minimum twee clichés
	-	452701	Radiografie van de thorax en de inhoud ervan, één cliché
ICD or PM control	-	475904	Controle van de deugdelijkheid of herprogrammatie van een anti-tachycardiepacemaker of A.I.C.D., met meting van de stimulatie- en gevoeligheidsdrempel, met protocol en tracés
	-	475860	Controle van de deugdelijkheid of herprogrammatie van een pacemaker, single chamber, met meting van de stimulatie - en gevoeligheidsdrempel, met protocol en tracés
	-	475882	Controle van de deugdelijkheid of herprogrammatie van een pacemaker (D.D.D.) double chamber, met meting van de stimulatie- en gevoeligheidsdrempel, met protocol en tracés
b. Post-ICD replacement complications			
Item	*INAMI code*		*INAMI label*
Proxy "cardiac problem"	-	229084	Heelkundige behandeling van hartwonden
	-	229261	Pericardotomie
	-	149144	Hartmassage door uitwendige handelingen
	-	212122	Elektrische defibrillatie van het hart in geval van circulatiestilstand en/of elektrostimulatie van het hart door uitwendige hartprikkelaar, inclusief de elektrocardiografische controle, buiten de ingrepen met open thorax en de verstrekkingen 229110 - 229121, 229132 - 229143, 229154 - 229165, 229176 – 229180
	-	229202	Thoracotomie met rechtstreekse massage van het hart
Proxy "lead or device problem"	-	229180	Vervangen van een onderhuidse hartprikkelaar of van een blijvende intracavitaire elektrode
	-	589444	Percutane extractie van een elektrode bij een patiënt met een ingeplante hartstimulator of een ingeplante hartdefibrillator of percutaan verwijderen van een intracardiaal vrijzittend vreemd lichaam, met uitsluiting van de farmaceutische produkten, de contrastmiddelen en het wegwerpmateriaal
	-	684622	Implanteerbare defibrillator
	-	684644	Bijkomende tussenkomst voor de elektroden en geïmplanteerd toebehoren voor de defibrillator
	-	687982	Vervangingsdefibrillator en toebehoren
Proxy "pneumothorax"	-	471564	Exsufflatie van spontane pneumothorax door voortdurende aspiratie, inclusief radioscopisch onderzoek bij het plaatsen van de drain
	-	687584	Disposable drainagesysteem van de thorax (pericard, pleura, mediastinum) met minstens drie kamers per stuk

	-	227500	Pleurotomie (één of meer drains)
c. Hospital charges			
Item	*INAMI code*		*INAMI label*
"Verpleegdagprijs" - after 01/07/2002			
"prix moyen de journée" SPF Santé publique	NA	NA	2 * the average cost per day for the 17 accredited cardiac centers. Take the average cost per hospital from SPF santé publique. Exclude INAMI codes for "partie variable du BMF"
Patients' share	?	?	This has to be subtracted from the "prix de journée" (perspective of the health care payers)
Forfaits per day:			
Clinical biology	-	592001	Forfaitair honorarium dat per verpleegdag wordt betaald voor de verstrekkingen inzake klinische biologie van de in een ziekenhuis opgenomen rechthebbenden
Forfaits per admission:			
"produits pharmaceutiques"	-	751004	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait antibiotica Z
	-	751026	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A1
	-	751041	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 2
	-	751063	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 3
	-	751085	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 4
	-	751100	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 6
	-	751122	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait A 7
	-	751144	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait B 3
	-	751166	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait B 4
	-	751181	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : Profylaxis-forfait : C 3
	-	751542	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep (vergoeding aan 25%) met complement forfaitaire vergoeding : categorie B
	-	751564	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep (vergoeding aan 25%) met complementaire forfaitaire vergoeding - categorie B : generieken of kopieën afgeleverd
	-	751586	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep (vergoeding aan 25%) met complementaire forfaitaire vergoeding - categorie B : referentiespecialiteiten afgele
	-	751645	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding : categorie B
	-	751660	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	751682	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	751741	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden : antibiotica toegediend buiten de peri-operatieve periode van heelkundige ingreep : categorie B
	-	751763	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat
	-	751785	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden - Categorie B, inclusief antibiotica toegediend tijdens peri-operatieve periode van heelkundige ingreep maar uitzondering op forfaitaire vergoeding en antibiotica toegediend buiten peri-operat

	-	752124	Vol bloed en labiele bloedprodukten - menselijk vol bloed
	-	752146	Vol bloed en labiele bloedprodukten - Erytrocytenconcentraat - eenheid type "volwassene" : per eenheid erytrocytenconcentraat "volwassene"
	-	752220	Vol bloed en labiele bloedprodukten - CMV negatief erytrocytenconcentraat : per eenheid CMV negatief erytrocytenconcentraat
	-	752404	Vol bloed en labiele bloedprodukten - leucocytenconcentraat : per eenheid leucocytenconcentraat
	-	752426	Vol bloed en labiele bloedprodukten - Bevroren vers menselijk plasma bestemd om te worden gebruikt voor geprogrammeerde autologe transfusies : per eenheid
	-	752441	Vol bloed en labiele bloedprodukten - Vers ingevroren menselijk plasma virus geïnactiveerd : per eenheid vers ingevroren virus geïnactiveerd menselijk plasma
	-	752463	Vol bloed en labiele bloedprodukten - Gedeleucocyteerd erytrocytenconcentraat : eenheid "volwassene" : per eenheid "volwassene" gedeleucocyteerd erytrocytenconcentraat, filter inbegrepen
	-	752500	Vol bloed en labiele bloedprodukten : Gedeleucocyteerd bloedplaatjesconcentraat : per geheel veelvoud van de eenheid die minstens 0,5 x 10(11) bloedplaatjes bevat en waarvan het aantal leucocyten niet hoger ligt dan 1 x 10(6) in het eindproduct, filter i
	-	752522	Vol bloed en labiele bloedprodukten : Gedeleucocyteerd één donor bloedplaatjesconcentraat : per concentraat dat minstens 4x10(11) bloedvaatjes bevat voor ucocytering en maximum 1x10(6) leucocyten na deleucocytering, filter inbegrepen
	-	752544	Vol bloed en labiele bloedprodukten - Erytrocytenconcentraat autoloog
	-	755720	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie A
	-	755742	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie B
	-	755764	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie C
	-	755786	Diagnostische middelen en verzorgingsmiddelen afkomstig van de ziekenhuisofficina en afgeleverd aan gehospitaliseerde rechthebbenden - categorie Cs
	-	755963	Honoraria en forfaits zuurstof in de ziekenhuisofficina's
	-	750746	Specialiteiten afgeleverd aan gehospitaliseerde rechthebbenden in psychiatrische ziekenhuizen en chronische ziekenhuizen (geïsoleerde Sp- en G-diensten) : andere toedieningen : categorie B
	-	750864	Generieken of kopieën afgeleverd aan gehospitaliseerde rechthebbenden in psychiatrische ziekenhuizen en chronische ziekenhuizen (geïsoleerde Sp- en G-diensten) - categorie Bg
	-	753745	Referentiespecialiteiten afgeleverd aan gehospitaliseerde rechthebbenden in psychiatrische ziekenhuizen en chronische ziekenhuizen (geïsoleerde Sp- en G-diensten) - categorie Br

f. Drugs outside forfait			
Item	*ATC code*		
Anti-arrhythmic Class III			
Amiodarone	C01BD01		
Sotalol	C07AA07		
Anti-arrhythmic Class I			
Procainamide	C01BA02		
Quinidine	C01BA51	C01BA71	Note: there are 2 different ATC codes for Quinidine
Lidocaine	C01BB01		
Mexiletine	C01BB02		
Tocainide	C01BB03		
Flecainide	C01BC04		
Propafenone	C01BC03		
Encainide	C01BC08		

e. Other resources used during hospital stay for post-ICD implantation		
Item	*INAMI code*	*INAMI label*
Sum of all other INAMI codes not listed in the above tables		

APPENDIX 3: RESOURCE CONSUMPTION AND COST OF ICD IMPLANTATION IN PRIMARY PREVENTION (ALL COSTS IN 2005 EUROS)

Cost of ICD implantation in primary prevention (Pre-ICD implantation period)

Resource	Total number of ICD patients	Resource consumption					RIZIV costs			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Diagnostic procedures 30 days before ICD implantation										
Coronary angiography	104	19	0.19231	0.00	2.00	20	51.59 €	0 €	540 €	5,366 €
Exercise testing	104	17	0.18269	0.00	2.00	19	5.32 €	0 €	61 €	554 €
Cardiac radionuclide imaging	104	28	0.40385	0.00	3.00	42	75.65 €	0 €	551 €	7,867 €
Angiocardiography	104	41	0.53846	0.00	2.00	56	65.86 €	0 €	319 €	6,849 €
Echocardiography	104	42	0.54808	0.00	5.00	57	35.07 €	0 €	301 €	3,647 €
Catheterization	104	34	0.42308	0.00	3.00	44	73.20 €	0 €	527 €	7,613 €
24-ECG	104	44	0.67308	0.00	4.00	70	32.85 €	0 €	203 €	3,417 €
EPS	104	93	1.05769	0.00	3.00	110	895.35 €	0 €	2,580 €	93,116 €
Tilt-test	104	0	0.00000	0.00	0.00	0	0.00 €	0 €	0 €	0 €
Signal averaged	104	6	0.05769	0.00	1.00	6	1.76 €	0 €	31 €	183 €
Total			*4.07693*				*1,236.65 €*			*128,612 €*
Pre-operative procedures 3 days before ICD implantation										
ECG	111	68	1.1261	0	5	125	17.41 €	0 €	77 €	1,933 €
ECG-monitoring	111	2	0.0180	0	1	2	2.20 €	0 €	122 €	245 €
Pulmonary function	111	1	0.0360	0	4	4	1.29 €	0 €	143 €	143 €
X-ray	111	56	0.7478	0	4	83	9.01 €	0 €	46 €	1,000 €
Total			*1.9279*				*29.91 €*			*3,320 €*
Hospital charges for 2 days										
Hospital stay in a cardiac unit	na	na	na	na	na	na	718.63 €	na	na	na
Patient share (% to subtract)	na	na	na	na	na	na	53.91 €	na	na	na
Clinical biology (forfait)	na	na	na	na	na	na	99.02	na	na	na
Medical permanency (forfait)	na	na	na	na	na	na	37.11 €	na	na	na
Total	na	na	na	na	na	na	*908.67 €*	na	na	na
Total							**2,175.23 €**			

Cost of ICD implantation in primary prevention (ICD implantation period)

Resource	Total number of ICD patients	Resource consumption				RIZIV costs					
		Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost	95% CI - Lower bound	95% CI - Upper bound
Material (ICD + electrodes) used for ICD implantation											
Total	112	1.0714	1	3	120	22,171.35 €	16,650 €	47,226 €	2,483,191 €	21416.44	22926.26
Procedures for ICD implantation											
Anaesthesia	112	0.7946	0	2	89	144.16 €	0 €	827 €	16,146 €	110.01	178.32
Surgery	112	1.0268	0	2	115	263.40 €	0 €	524 €	29,501 €	243.61	283.19
Total						*407.56 €*			*45,647 €*		
Total						**22,578.91 €**					

Cost of ICD implantation in primary prevention (Post-ICD implantation period)

Resource	Total number of ICD patients	Resource consumption					RIZIV costs			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Post-operative procedures										
Echocardiography	106	10	0.10377	0.00	2.00	11	5.87 €	0 €	105 €	623 €
24-ECG	106	19	0.18868	0.00	2.00	20	8.62 €	0 €	106 €	913 €
ECG	106	83	1.67925	0.00	22.00	178	25.99 €	0 €	341 €	2,755 €
ECG-monitoring	106	47	0.74528	0.00	2.00	79	32.18 €	0 €	229 €	3,411 €
X-ray	106	97	1.89623	0.00	20.00	201	22.86 €	0 €	228 €	2,423 €
ICD or PM control	106	98	1.92453	0.00	6.00	204	169.23 €	0 €	398 €	17,938 €
Total			*6.53774*				*264.75 €*			*28,063 €*
Post-operative complications										
Proxy "cardiac problem"	106	15	0.1604	0	3	17	9.81 €	0 €	184 €	1,040 €
Proxy "lead or device problem"	106	1	0.0094	0	1	1	1.72 €	0 €	182 €	182 €
Proxy "pneumothorax"	106	5	0.0472	0	1	5	2.96 €	0 €	72 €	313 €
Total			*0.2170*				*14.49 €*			*1,536 €*
Hospital charges										
Hospital stay in accredited cardiac unit	106		4.29245				1,461.79 €			
Clinical biology (forfait)	106	52	2.2170	0	22	235	48.12 €	0 €	460 €	5,101 €
Imagerie médicale (forfait)	106	38	0.4151	0	2	44	31.34 €	0 €	183 €	3,322 €
Pharmaceutical products (forfait)	106	62	18.4811	0	175	1959	24.69 €	0 €	631 €	2,617 €
Total							*1,565.94 €*			
Pharmaceuticals outside forfait										
Anti-arrhythmics class III	106	13	0.9340	0	19	99	0.08 €	0 €	2 €	9 €
Anti-arrhythmics class I	106	0	0.0000	0	0	0	0.00 €	0 €	0 €	0 €
Total			*0.9340*				*0.08 €*			*9 €*
Other resources consumed during hospital stay										
Other	106	106	42.8208	4	147	4539	517.02 €			54,804 €
Total			*42.8208*				*517.02 €*			*54,804 €*
Total							**2,362.28 €**			

APPENDIX 4: RESOURCE CONSUMPTION AND COST OF ICD IMPLANTATION IN SECONDARY PREVENTION (ALL COSTS IN 2005 EURO)

Cost of ICD implantation in secondary prevention (Pre-ICD implantation period)

Resource	Total number of ICD patients	Resource consumption					RIZIV costs			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Diagnostic procedures 30 days before ICD implantation										
Coronary angiography	370	89	0.24595	0	2	91	68.88	0	606.62	25486.41
Exercise testing	370	80	0.23784	0.00	2.00	88	7.03 €	0 €	61 €	2,599 €
Cardiac radionuclide imaging	370	80	0.33784	0.00	5.00	125	60.82 €	0 €	753 €	22,502 €
Angiocardiography	370	196	0.72703	0.00	4.00	269	83.56 €	0 €	816 €	30,917 €
Echocardiography	370	230	0.86757	0.00	5.00	321	56.04 €	0 €	308 €	20,735 €
Catheterization	370	210	0.65135	0.00	3.00	241	109.57 €	0 €	839 €	40,542 €
24-ECG	370	132	0.68378	0.00	10.00	253	33.18 €	0 €	432 €	12,277 €
EPS	370	261	0.85135	0.00	3.00	315	659.74 €	0 €	2,580 €	244,102 €
Tilt-test	370	1	0.00270	0.00	1.00	1	0.21 €	0 €	76 €	76 €
Signal averaged	370	38	0.10811	0.00	2.00	40	3.26 €	0 €	61 €	1,205 €
Total			*4.46757*				*1,082.29 €*			*400,443 €*
Pre-operative procedures 3 days before ICD implantation										
ECG	399	259	1.24561	0	8	497	19.26	0	123.84	7686.6
ECG-monitoring	399	58	0.1679	0	3	67	19.90 €	0 €	337 €	7,939 €
Pulmonary function	399	6	0.0501	0	4	20	1.63 €	0 €	143 €	651 €
X-ray	399	213	0.8872	0	6	354	10.43 €	0 €	66 €	4,163 €
Total			*2.3509*				*51.22 €*			*20,439 €*
Hospital charges for 2 days										
Hospital stay in a cardiac unit	na	na	na	na	na	na	718.628	na	na	na
Patient share (% to subtract)	na	na	na	na	na	na	53.91 €	na	na	na
Clinical biology (forfait)	na	na	na	na	na	na	99.02 €	na	na	na
Medical permanency (forfait)	na	na	na	na	na	na	37.11	na	na	na
Total	na	na	na	na	na	na	*908.67 €*	na	na	na
Total							**2,042.18 €**			

Cost of ICD implantation in secondary prevention (ICD implantation period)

Resource	Total number of ICD patients	Resource consumption				RIZIV costs			
		Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Material (ICD + electrodes) used for ICD implantation									
Total	401	1.1721	1	5	470	21,579.18 €	16,650 €	45,210 €	8,653,251 €
Procedures for ICD implantation									
Anaesthesia	401	0.8279	0	5	332	148.39 €	0 €	2,038 €	59,503 €
Surgery	401	0.8928	0	2	358	247.48 €	0 €	546 €	99,239 €
Total						*395.87 €*			*158,743 €*
Total						**21,975.05 €**			

Cost of ICD implantation in secondary prevention (Post-ICD implantation period)

Resource	Total number of ICD patients	Resource consumption					RIZIV costs			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Post-operative procedures										
Echocardiography	375	30	0.088	0.00	2.00	33	6.22 €	0 €	167 €	2,334 €
24-ECG	375	42	0.14933	0.00	5.00	56	6.65 €	0 €	204 €	2,495 €
ECG	375	256	1.592	0.00	11.00	597	24.65 €	0 €	170 €	9,242 €
ECG-monitoring	375	124	0.6	0.00	5.00	225	46.85 €	0 €	551 €	17,568 €
X-ray	375	342	1.71467	0.00	35.00	643	20.68 €	0 €	387 €	7,756 €
ICD or PM control	375	322	1.85867	0.00	12.00	697	161.17 €	0 €	713 €	60,439 €
Total			*6.00267*				*266.22 €*			*99,835 €*
Post-operative complications										
Proxy "cardiac problem"	375	60	0.1627	0	2	61	9.97 €	0 €	114 €	3,740 €
Proxy "lead or device problem"	375	31	0.0880	0	2	33	15.86 €	0 €	364 €	5,949 €
Proxy "pneumothorax"	375	7	0.0320	0	3	12	1.73 €	0 €	168 €	648 €
Total			*0.2827*				*27.56 €*			*10,337 €*
Hospital charges										
Hospital stay in accredited cardiac unit (Mean length of stay)			5.90133				2,014.55 €			
Clinical biology (forfait)	375	190	2.5067	0	47	940	50.44 €	0 €	770 €	18,916 €
Imagerie médicale (forfait)	375	102	0.3333	0	3	125	25.61 €	0 €	261 €	9,605 €
Pharmaceutical products (forfait)	375	201	27.9120	0	1255	10467	48.01 €	0 €	2,969 €	18,003 €
Total							*2,138.61 €*			
Pharmaceuticals outside forfait										
Anti-arrhythmics class III	375	35	2.1840	0	187	819	0.50 €	0 €	90 €	187 €
Anti-arrhythmics class I	375	2	0.0720	0	25	27	0.03 €	0 €	10 €	13 €
Total			*2.2560*				*0.53 €*			*200 €*
Other resources consumed during hospital stay										
Other resources	375	375	44.5867	3	166	16720	810.99 €			304,121 €
Total			*44.5867*				*810.99 €*			*304,121 €*
Total							**3,243.91 €**			

APPENDIX 5: RESOURCE CONSUMPTION AND COST OF ICD RE-IMPLANTATION (DUE TO BATTERY END OF LIFE) IN PRIMARY PREVENTION (ALL COSTS IN 2005 EURO)

ICD re-implantation in primary prevention (Pre-ICD re-implantation period)

Resource	Total number of ICD patients	Resource consumption					RIZIV costs			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Pre-operative procedures										
ECG	9	5	1.5556	0	4	14	24.08 €	0 €	62 €	217 €
ECG-monitoring	9	2	0.5556	0	3	5	45.89 €	0 €	337 €	413 €
Pulmonary function	9	0	0.0000	0	0	0	0.00 €	0 €	0 €	0 €
X-ray	9	4	1.2222	0	6	11	14.50 €	0 €	66 €	131 €
Total			*3.3333*				*84.47 €*			*760 €*
Hospital charges										
Hospital stay in cardiac unit			2.4444				818.49 €			
Clinical biology (forfait)	9	6	2.0000	0	10	18	49.51 €	0 €	253 €	446 €
Imagerie médicale (forfait)	9	9	1.4444	1	2	13	129.00 €	69 €	246 €	1,161 €
Permanence médicale (forfait)	9	9	1.4444	1	2	13	51.57 €	36 €	71 €	464 €
Pharmaceutical products (forfait)	9	9	46.7778	1	230	421	24.23 €	6 €	88 €	218 €
Total							*1,072.80 €*			
Pharmaceuticals outside forfait										
Anti-arrhythmics class III	9	1	0.2222	0	2	2	0.09 €	0 €	1 €	1 €
Anti-arrhythmics class I	9	0	0.0000	0	0	0	0.00 €	0 €	0 €	0 €
Total			*0.2222*				*0.09 €*			*1 €*
Other resources consumed during hospital stay										
Other resources	9	9	58.8889	33	126	530	1,994.65 €			261,635 €
Total			*58.8889*				*1,994.65 €*			*261,635 €*
Total							**3,152.01 €**			

ICD re-implantation in primary prevention (ICD re-implantation period)

Resource	Total number of ICD patients	Resource consumption				RIZIV costs			
		Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Material (ICD + electrodes) used for ICD implantation									
Total	10	1.1	0	3	11	26,701.23 €	17,915 €	42,142 €	267,012 €
Procedures for ICD implantation									
Anaesthesia	10	1.5	1	3	15	134.38 €	83 €	277 €	941 €
Surgery	10	4.2	2	10	42	280.63 €	182 €	622 €	2,806 €
Total						*415.01 €*			*3,747 €*
Total						**27,116.24 €**			

ICD re-implantation in primary prevention (Post-ICD re-implantation period)

Resource		Resource consumption					RIZIV costs			
	Total number of ICD patients	Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Post-operative procedures										
Echocardiography	9	0	0	0.00	0.00	0	0.00 €	0 €	0 €	0 €
24-ECG	9	1	0.22222	0.00	2.00	2	9.06 €	0 €	82 €	82 €
ECG	9	6	1.66667	0.00	5.00	15	25.80 €	0 €	77 €	232 €
ECG-monitoring	9	3	0.77778	0.00	4.00	7	37.39 €	0 €	153 €	337 €
X-ray	9	5	1.11111	0.00	3.00	10	13.76 €	0 €	38 €	124 €
ICD or PM control	9	8	2.55556	0.00	8.00	23	210.64 €	0 €	612 €	1,896 €
Total			*6.33334*				*296.65 €*			*2,670 €*
Post-operative complications										
Proxy "cardiac problem"	9	4	0.5556	0	2	5	33.99 €	0 €	122 €	306 €
Proxy "lead or device problem"	9	0	0.0000	0	0	0	0.00 €	0 €	0 €	0 €
Proxy "pneumothorax"	9	0	0.0000	0	0	0	0.00 €	0 €	0 €	0 €
Total			*0.5556*				*33.99 €*			*306 €*
Hospital charges										
Hospital stay in cardiac unit (Mean length of stay)			3.33333				1,126.04 €			
Clinical biology (forfait)	9	6	2.7778	0	10	25	69.52 €	0 €	253 €	626 €
Pharmaceutical products (forfait)	9	6	38.7778	0	158	349	13.29 €	0 €	39 €	120 €
Total							1,208.85 €			
Pharmaceuticals outside forfait										
Anti-arrhythmics class III	9	1	4	0	36	36	0.65	0	5.81	5.81
Anti-arrhythmics class I	9	0	0.0000	0	0	0	0.00 €	0 €	0 €	0 €
Total			4.0000				0.65 €			6 €
Other resources consumed during hospital stay										
Other	9	9	0.0000	0	0	0	855.35 €	140 €	2,596 €	7,698 €
Total			*0.0000*				*855.35 €*			*7,698 €*
Total							**2,395.49 €**			

APPENDIX 6: RESOURCE CONSUMPTION AND COST OF ICD RE-IMPLANTATION (DUE TO BATTERY END OF LIFE) IN SECONDARY PREVENTION (ALL COSTS IN 2005 EURO)

ICD re-implantation in secondary prevention (Pre-ICD re-implantation period)

Resource	Total number of ICD patients	Resource consumption					RIZIV costs			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Pre-operative procedures										
ECG	138	88	0.9275	0	10	128	14.36 €	0 €	155 €	1,981 €
ECG-monitoring	138	12	0.1884	0	5	26	12.64 €	0 €	551 €	1,744 €
Pulmonary function	138	0	0.0000	0	0	0	0.00 €	0 €	0 €	0 €
X-ray	138	104	1.1739	0	10	162	14.60 €	0 €	111 €	2,015 €
Total			*2.2899*				*41.60 €*			*5,740 €*
Hospital charges										
Hospital stay in cardiac unit	138		2.9565				995.67 €			
Clinical biology (forfait)	138	102	3.0797	0	78	425	60.19 €	0 €	1,367 €	8,307 €
Imagerie médicale (forfait)	138	138	1.1087	0	2	153	99.13 €	0 €	273 €	13,680 €
Permanence médicale (forfait)	138	134	1.0797	0	2	149	38.55 €	0 €	71 €	5,319 €
Pharmaceutical products (forfait)	138	133	18.4783	0	416	2550	20.62 €	0 €	520 €	2,846 €
Total							*1,214.16 €*			
Pharmaceuticals outside forfait										
Anti-arrhythmics class III	138	12	1.0725	0	48	148	0.08 €	0 €	3 €	11 €
Anti-arrhythmics class I	138	0	0.0000	0	0	0	0.00 €	0 €	0 €	0 €
Total			*1.0725*				*0.08 €*			*11 €*
Other resources consumed during hospital stay										
Other resources	138	138	54.1884	21	186	7478	1,199.68 €			165,556 €
Total			*54.1884*				*1,199.68 €*			*165,556 €*
Total							**2,455.52 €**			

ICD re-implantation in secondary prevention (ICD re-implantation period)

Resource	Total number of ICD patients	Resource consumption				RIZIV costs			
		Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Material (ICD + electrodes) used for ICD implantation									
Total	159	na	na	na	na	20,187.30 €	16,317 €	42,142 €	3,209,781 €
Procedures for ICD implantation									
Anaesthesia	159	na	na	na	na	140.06 €	40 €	1,050 €	19,468 €
Surgery	159	na	na	na	na	237.12 €	91 €	997 €	34,619 €
Total						*377.18 €*			*54,088 €*
Total						**20,564.48 €**			

ICD re-implantation in secondary prevention (Post-ICD re-implantation period)

Resource		Resource consumption					RIZIV costs			
	Total number of ICD patients	Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Post-operative procedures										
Echocardiography	138	6	0.050725	0.00	2.00	7	4.70 €	0 €	210 €	649 €
24-ECG	138	2	0.014493	0.00	1.00	2	0.77 €	0 €	65 €	106 €
ECG	138	76	0.75362	0.00	6.00	104	11.67 €	0 €	93 €	1,610 €
ECG-monitoring	138	28	0.34058	0.00	5.00	47	16.74 €	0 €	551 €	2,310 €
X-ray	138	76	0.82609	0.00	7.00	114	10.26 €	0 €	80 €	1,416 €
ICD or PM control	138	126	1.55072	0.00	8.00	214	142.17 €	0 €	530 €	19,620 €
Total			*3.53623*				*186.31 €*			*25,710 €*
Post-operative complications										
Proxy "cardiac problem"	138	37	0.3116	0	2	43	19.07 €	0 €	122 €	2,631 €
Proxy "lead or device problem"	138	136	0.0000	0	0	0	0.00 €	0 €	0 €	0 €
Proxy "pneumothorax"	138	1	0.0072	0	1	1	0.41 €	0 €	57 €	57 €
Total			*0.3188*				*19.48 €*			*2,688 €*
Hospital charges										
Hospital stay in cardiac unit (Mean length of stay)			2.97826				1,003.19 €			
Clinical biology (forfait)	138	71	1.4130	0	10	195	29.51 €	0 €	283 €	4,072 €
Pharmaceutical products (forfait)	138	83	10.8043	0	173	1491	11.77 €	0 €	195 €	1,624 €
Total							1,044.47 €			
Pharmaceuticals outside forfait										
Anti-arrhythmics class III	138	9	0.42754	0	15	59	0.04	0	1.54	4.92
Anti-arrhythmics class I	138	0	0.0000	0	0	0	0.00 €	0 €	0 €	0 €
Total			0.4275				0.04 €			5 €
Other resources consumed during hospital stay										
Other	138	138	35.0362	3	119	4835	1,735.11 €	16 €	35,577 €	239,445 €
Total			*35.0362*				*1,735.11 €*			*239,445 €*
Total							**2,985.41 €**			

APPENDIX 7: RESOURCE CONSUMPTION AND COST OF OUTPATIENT FOLLOW-UP IN SECONDARY PREVENTION

Outpatient follow-up costs - 1rst year post ICD - Secondary prevention

Resource	Total number of ICD patients	Resource consumption					Resource cost (INAMI / RIZIV)			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Medical procedures										
ICD control	134	129	5.186	2.00	18.00	669	286.24 €	0 €	943 €	38,357 €
ECG	134	107	1.946	0.00	8.00	251	26.35 €	0 €	82 €	3,530 €
PM control	134	16	0.256	0.00	4.00	33	8.73 €	0 €	173 €	1,170 €
Total			*7.388*				*321.32 €*			*43,058 €*
Physician visits										
Cardiologist	134	83	1.442	0	8	186	21.87 €	0 €	114 €	2,931 €
Internist	134	10	0.109	0	4	14	1.72 €	0 €	58 €	231 €
Total			*1.550*				*23.59 €*			*3,161 €*
Total per patient							**345 €**			

Outpatient follow-up costs - 2rst year post ICD - Secondary prevention

Resource	Total number of ICD patients	Resource consumption					Resource cost (INAMI / RIZIV)			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Medical procedures										
ICD control	121	113	5.062	1.00	93.00	572	234.89 €	0 €	587 €	28,422 €
ECG	121	95	1.637	0.00	7.00	185	21.29 €	0 €	91 €	2,576 €
PM control	121	14	0.221	0.00	2.00	25	7.53 €	0 €	98 €	911 €
Total			*6.920*				*263.71 €*			*31,909 €*
Physician visits										
Cardiologist	121	76	1.257	0	4	142	20.03 €	0 €	90 €	2,423 €
Internist	121	2	0.027	0	2	3	0.53 €	0 €	46 €	64 €
Total			*1.283*				*20.56 €*			*2,487 €*
Total per patient							**284 €**			

Outpatient follow-up costs - 3d year post ICD - Secondary prevention

Resource	Total number of ICD patients	Resource consumption					Resource cost (INAMI / RIZIV)			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Medical procedures										
ICD control	109	98	4.112	1.00	10.00	403	214.35 €	0 €	600 €	23,364 €
ECG	109	78	1.592	0.00	5.00	156	19.48 €	0 €	77 €	2,123 €
PM control	109	10	0.194	0.00	4.00	19	6.43 €	0 €	129 €	701 €
Total			*5.898*				*240.26 €*			*26,188 €*
Physician visits										
Cardiologist	109	59	1.235	0	7	121	19.14 €	0 €	111 €	2,086 €
Internist	109	5	0.051	0	1	5	0.94 €	0 €	26 €	103 €
Total			*1.286*				*20.08 €*			*2,189 €*
Total per patient							**260 €**			

Outpatient follow-up costs - 4st year post ICD - Secondary prevention

Resource	Total number of ICD patients	Resource consumption					Resource cost (INAMI / RIZIV)			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Medical procedures										
ICD control	99	94	4.160	1.00	10.00	391	232.96 €	0 €	641 €	23,063 €
ECG	99	83	1.713	0.00	6.00	161	21.86 €	0 €	93 €	2,164 €
PM control	99	6	0.074	0.00	2.00	7	2.19 €	0 €	52 €	217 €
Total			*5.947*				*257.01 €*			*25,444 €*
Physician visits										
Cardiologist	99	59	1.468	0	9	138	22.21 €	0 €	131 €	2,199 €
Internist	99	4	0.064	0	2	6	1.08 €	0 €	52 €	107 €
Total			*1.532*				*23.29 €*			*2,307 €*
Total per patient							**280 €**			

APPENDIX 8: RESOURCE CONSUMPTION AND COST OF INPATIENT FOLLOW-UP IN SECONDARY PREVENTION

Inpatient follow-up costs - 1rst year post ICD - Secondary prevention

Resource	Total number of ICD patients	Resource consumption					Resource cost (INAMI / RIZIV)			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Re-hospitalisation due to:										
"Accessoire problems"	134	3	1.000	0	2	4	5.28 €	0 €	364 €	708 €
"Device problem"	134	1	0.250	0	1	1	174.99 €	0 €	23,449 €	23,449 €
Total			*1.250*				*180.27 €*			*24,157 €*
Procedures during re-hospitalisation										
Pulmonary function	134	2	1.500	0.00	4.00	6	1.08 €	0 €	125 €	144 €
X-ray	134	4	12.500	2.00	29.00	50	4.13 €	0 €	312 €	554 €
Echocardiography	134	3	2.500	0.00	4.00	10	5.00 €	0 €	257 €	669 €
24h-ECG	134	1	7.750	0.00	31.00	31	11.21 €	0 €	1,503 €	1,503 €
ECG	134	3	9.000	0.00	28.00	36	3.99 €	0 €	407 €	535 €
ECG-monitoring	134	3	4.750	0.00	9.00	19	8.36 €	0 €	759 €	1,120 €
ICD or PM control	134	2	1.750	0.00	6.00	7	5.03 €	0 €	578 €	674 €
Total			*39.750*				*38.80 €*			*5,200 €*
Prestations techniques during re-hospitalisation										
Anaesthesia	134	4	2.250	1	3	9	11.39 €	0 €	927 €	1,527 €
Surgery	134	1	0.250	0	1	1	3.36 €	0 €	451 €	451 €
Total			*2.500*				*14.75 €*			*1,977 €*
Hospital charges										
Clinical biology (forfait)	134	4	28.250	4	52	113	12.64 €	0 €	721 €	1,693 €
Imagerie médicale (forfait)	134	4	3.500	2	5	14	6.08 €	0 €	254 €	814 €
Permanence médicale (forfait)	134	4	3.500	2	5	14	3.54 €	0 €	168 €	474 €
Pharmaceutical products (forfait)	134	4	45.750	1	177	183	0.79 €	0 €	46 €	106 €
Total			*81.000*				*23.05 €*			*3,088 €*
Other resources consumed during the hospital stay										
Other	134	4	134.000	36	258	536	273.05 €	0 €	15,636 €	36,589 €
Total			*134.000*				*273.05 €*			*36,589 €*
Total per patient							**529.92 €**			

Inpatient follow-up costs - 2d year post ICD - Secondary prevention

Resource	Total number of ICD patients	Resource consumption					Resource cost (INAMI / RIZIV)			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Re-hospitalisation due to:										
"Accessoire problems"	121	1	0.008	0	1	1	1.42 €	0 €	172 €	172 €
"Device problem"	121	0	0.000	0	0	0	0.00 €	0 €	0 €	0 €
Total			*0.008*				*1.42 €*			*172 €*
Procedures during re-hospitalisation										
Pulmonary function	121	0	0.000	0.00	0.00	0	0.00 €	0 €	0 €	0 €
X-ray	121	0	0.000	0.00	0.00	0	0.00 €	0 €	0 €	0 €
Echocardiography	121	0	0.000	0.00	0.00	0	0.00 €	0 €	0 €	0 €
24h-ECG	121	0	0.000	0.00	0.00	0	0.00 €	0 €	0 €	0 €
ECG	121	1	0.008	0.00	1.00	1	0.13 €	0 €	16 €	16 €
ECG-monitoring	121	0	0.000	0.00	0.00	0	0.00 €	0 €	0 €	0 €
ICD or PM control	121	0	0.000	0.00	0.00	0	0.00 €	0 €	0 €	0 €
Total			*0.008*				*0.13 €*			*16 €*
Prestations techniques during re-hospitalisation										
Anaesthesia	121	1	0.008	0	1	1	0.65 €	0 €	78 €	78 €
Surgery	121	0	0.000	0	0	0	0.00 €	0 €	0 €	0 €
Total							*0.65 €*			*78 €*
Hospital charges										
Clinical biology (forfait)	121	1	0.017	0	2	2	0.42 €	0 €	51 €	51 €
Imagerie médicale (forfait)	121	1	0.008	0	1	1	0.84 €	0 €	102 €	102 €
Permanence médicale (forfait)	121	1	0.008	0	1	1	0.28 €	0 €	34 €	34 €
Pharmaceutical products (forfait)	121	1	0.008	0	1	1	0.05 €	0 €	6 €	6 €
Total							*1.59 €*			
Other resources consumed during the hospital stay										
Other	121	1	0.372	0	45	45	32.07 €	0 €	3,881 €	3,881 €
Total			*0.372*				*32.07 €*			*3,881 €*
Total per patient							**35.86 €**			

Inpatient follow-up costs - 3d year post ICD - Secondary prevention

Resource	Total number of ICD patients	Resource consumption					Resource cost (INAMI / RIZIV)			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Re-hospitalisation due to:										
"Accessoire problems"	109	2	0.028	1	2	3	4.25 €	0 €	284 €	464 €
"Device problem"	109	0	0.000	0	0	0	0.00 €	0 €	0 €	0 €
Total			*0.028*				*4.25 €*			*464 €*
Procedures during re-hospitalisation										
Pulmonary function	109	0	0.000	0.00	0.00	0	0.00 €	0 €	0 €	0 €
X-ray	109	1	0.018	0.00	2.00	2	0.22 €	0 €	24 €	24 €
Echocardiography	109	1	0.009	0.00	1.00	1	0.57 €	0 €	62 €	62 €
24h-ECG	109	0	0.000	0.00	0.00	0	0.00 €	0 €	0 €	0 €
ECG	109	1	0.092	0.00	10.00	10	1.42 €	0 €	155 €	155 €
ECG-monitoring	109	2	0.046	1.00	4.00	5	1.75 €	0 €	153 €	191 €
ICD or PM control	109	2	0.028	1.00	2.00	3	2.13 €	0 €	131 €	233 €
Total			*0.193*				*6.09 €*			*665 €*
Prestations techniques during re-hospitalisation										
Anaesthesia	109	1	0.028	0	3	3	2.37 €	0 €	259 €	259 €
Surgery	109	1	0.009	0	1	1	2.50 €	0 €	273 €	273 €
Total							*4.87 €*			*532 €*
Hospital charges										
Clinical biology (forfait)	109	1	0.110	0	12	12	2.14 €	0 €	234 €	234 €
Imagerie médicale (forfait)	109	2	0.037	1	3	4	2.68 €	0 €	217 €	292 €
Permanence médicale (forfait)	109	2	0.037	1	3	4	1.30 €	0 €	107 €	142 €
Pharmaceutical products (forfait)	109	2	0.037	2	2	4	0.16 €	0 €	11 €	17 €
Total							*6.28 €*			
Other resources consumed during the hospital stay										
Other	109	2	1.046	20	94	114	19.03 €	0 €	1,728 €	2,074 €
Total			*1.046*				*19.03 €*			*2,074 €*
Total per patient							**40.52 €**			

Inpatient follow-up costs - 4st year post ICD - Secondary prevention

Resource	Total number of ICD patients	Resource consumption					Resource cost (INAMI / RIZIV)			
		Number of patients with the resource	Mean resource consumption per ICD patient	Min	Max	Total resource consumption	Mean cost per ICD patient	Min	Max	Total cost
Re-hospitalisation due to:										
"Accessoire problems"	99	2	0.020	1	1	2	3.68 €	0 €	182 €	364 €
"Device problem"	99	2	0.020	1	1	2	170.76 €	0 €	14,106 €	16,905 €
Total			*0.040*				*174.44 €*			*17,269 €*
Procedures during re-hospitalisation										
Pulmonary function	99	0	0.000	0.00	0.00	0	0.00 €	0 €	0 €	0 €
X-ray	99	1	0.020	0.00	2.00	2	0.27 €	0 €	27 €	27 €
Echocardiography	99	1	0.010	0.00	1.00	1	0.63 €	0 €	62 €	62 €
24h-ECG	99	1	0.010	0.00	1.00	1	0.66 €	0 €	65 €	65 €
ECG	99	2	0.040	1.00	3.00	4	0.63 €	0 €	46 €	62 €
ECG-monitoring	99	1	0.020	0.00	2.00	2	0.77 €	0 €	76 €	76 €
ICD or PM control	99	2	0.061	2.00	4.00	6	5.15 €	0 €	306 €	510 €
Total			*0.162*				*8.11 €*			*802 €*
Prestations techniques during re-hospitalisation										
Anaesthesia	99	2	0.020	1	1	2	1.68 €	0 €	83 €	166 €
Surgery	99	0	0.000	0	0	0	0.00 €	0 €	0 €	0 €
Total							*1.68 €*			*166 €*
Hospital charges										
Clinical biology (forfait)	99	2	0.081	3	5	8	1.74 €	0 €	108 €	172 €
Imagerie médicale (forfait)	99	2	0.020	1	1	2	1.47 €	0 €	73 €	146 €
Permanence médicale (forfait)	99	2	0.020	1	1	2	0.71 €	0 €	35 €	70 €
Pharmaceutical products (forfait)	99	2	0.020	1	1	2	0.11 €	0 €	6 €	11 €
Total							*4.03 €*			
Other resources consumed during the hospital stay										
Other	99	2	1.303	63	66	129	12.94 €	0 €	792 €	1,281 €
Total			*1.303*				*12.94 €*			*1,281 €*
Total per patient							**201.20 €**			

APPENDIXES TO CHAPTER 6

APPENDIX 1 : LITERATURE ON PATIENT ISSUES: SEARCH STRATEGIES

Recherches realisées le 6/2/2007

MEDLINE

Database: Ovid MEDLINE(R) <1996 to January Week 4 2007>

Search Strategy:----------

1. Defibrillators, Implantable/es [Ethics] (18)
2. from 1 keep 1-18 (18)

Database: Ovid MEDLINE(R) <1996 to January Week 4 2007>

Search Strategy:----------

1. Defibrillators, Implantable/es [Ethics] (18)
2. from 1 keep 1-18 (18)
3. Defibrillators, Implantable/ae, px, ct, es [Adverse Effects, Psychology, Contraindications, Ethics] (731)
4. Defibrillators, Implantable/ae, px, ct, es, ut [Adverse Effects, Psychology, Contraindications, Ethics, Utilization] (827)
5. Patients/px [Psychology] (1557)
6. limit 4 to (humans and "review articles" and (dutch or english or flemish or french or spanish)) (101)
7. from 6 keep 1-101 (101)

PSYCHINFO

Database: PsycINFO <2000 to January Week 5 2007>

Search Strategy:----------

1. defibrillator$.mp. (55)
2. implantable.mp. (75)
3. 1 and 2 (33)
4. from 3 keep 1-33 (33)

EMBASE

(implantable AND [1996-2006]/py) AND ('defibrillator'/exp AND [systematic review]/lim AND ([dutch]/lim OR [english]/lim OR [french]/lim OR [spanish]/lim) AND [humans]/lim AND [embase]/lim AND [1996-2006]/py)

CRD

defibrillator

+ hand searching

APPENDIX 2 : CLINICAL CASES FOR ETHICAL ROUND TABLE

Clinical Case 1: The issue of the patient that is unworried & well …

A 57 year old man had a heart attack 10 years ago. At the time of the first follow-up visit, his doctor explained that a quite large part of the heart muscle was lost, but that his body had adapted remarkably well to it. Since then, the patient is examined by his cardiologist once or twice a year. An exercise test has been performed a few times and no residual cardiac problems were detected.

Five years later the patient underwent hip surgery after which he kept some difficulties when walking.

We are January 2007. The patient is feeling happy and has had no major cardiac symptoms after his infarction, except for some shortness of breath on exertion. Last week, he was routinely examined for his yearly check-up. The doctor explains that everything is OK, his cardiac status has not changed compared to previous follow-up exams. But … the cardiologist now tells him (for the first time in ten years) that, as any post-infarction patient, he has an increased risk of dying suddenly due to a cardiac arrest but a new device has become reimbursed that could save him in case this would happen

- His risk of dying within the first three years is estimated to be 15% when he continues his actual standard therapy. This risk could be reduced to 11% when an ICD is being implanted.[k]
- This patient meets current criteria for reimbursement of an ICD. The absolute **benefit** in terms of 3-yr-mortality related to an implant in his particular case is 4% (15-11=4%). The **harms** which could be induced are, apart from the discomforts related to the surgical procedure, an increased medicalisation of the patient, regularly ambulatory follow-ups of the device, 5-yearly replacement of the device, the risk of inappropriate shocks, driving restrictions, …. On the other hand, dying suddenly is no longer an option and will be replaced by another mode of death (in this particular case most probably death due to heart failure).

- **Is it mandatory for the cardiologist to explain and discuss with every patient such as the one described here, the pros and cons of the ICD ?**

[k] Data extrapolated from MADIT II and SCD-HeFT trials.

Clinical Case 2: The issue of an upper age limit for primary prevention of sudden death

A 82-year old man had a heart attack 3 years ago. An angiography revealed a severely reduced cardiac pump function (ejection fraction of 30%). Bypass surgery was performed successfully and after that the patient did well. He resumed his previous (limited) daily activities: walking with his dog, minor activities in the garden and helping his wife in the kitchen.

We are now January 2007. The patient is feeling happy and has no symptoms. Last week, he was routinely examined by his cardiologist for his yearly check-up. The cardiologist explains that everything is OK, his cardiac status has not changed compared to previous follow-up exams. But … he is being told that, being a post-infarction patient with a depressed pump function, he has an increased risk of dying suddenly but a device has become reimbursed that could reduce his risk of sudden cardiac death ….

→ The patient's risk of dying within 3 years, when continuing standard care is estimated to be 40%. This risk could be reduced to 35% by implanting an ICD.

→ This patient meets the current criteria for reimbursement of an ICD. The **benefit** related to an implant in his particular case is low, given his limited life expectancy, due to the advanced age and the cardiac disease. **However**, this patient is very likely to die from progressive heart failure (instead of dying suddenly due to a cardiac arrest). Progressive heart failure means increasing problems of shortness of breath, repetitive hospital admissions, pulmonary oedema, …

- **Is there a patients' age limit for a cardiologist to propose a patient the implant of an ICD ?**
- **To what extent does the cost of the device play a role in the decision making process (the device itself costs 25.000 €, the surgical procedure, follow-up and complications costs not included).**

Clinical Case 3: The issue of co-morbidity

A 60-year old man had a quite large infarction last year. He did recover fairly well and has no cardiac symptoms. The man is severely limited in his daily activities because of a chronic lung disease (COPD). He has been a smoker since he was 16 years old and successfully stopped smoking after his infarction. Nevertheless, the problems of shortness of breath that had been prevalent since many years, persist. He is not able to walk outside his house but has organised his indoor life in an acceptable way: he is happy watching TV, reading books and playing cards with his wife and neighbours.

Last week, he was routinely examined by his cardiologist for a yearly check-up. The cardiologist explains that his heart is OK and his cardiac status has not changed compared to previous follow-up exams. But … as any patient that survived a heart attack, he is at increased risk of dying suddenly but a device has become reimbursed that could reduce this risk of sudden cardiac death.

→ His life expectancy[l] is limited due to the lung disease and is estimated to be 3 to 5 years. His underlying risk of sudden cardiac arrest is estimated to be 10% per year.

→ This patient meets the current criteria for reimbursement of an ICD. The benefit related to an implant in his particular case is low, given his limited life expectancy due to the lung disease.

- **How much does life expectancy interfere with the decision to whether or not discuss and decide to implant an ICD ?**

[l] Medicare exludes patients with "any disease, other than cardiac disease (e.g. cancer, uremia, liver failure) associated with a likelihood of survival of less than one year". Currently, in Belgium an ICD implant is not reimbursed in the following subjects: "Terminale rechthebbenden met een levensverwachting van minder dan 6 maanden".

APPENDIXES TO CHAPTER 7

ALGORITHM USED FOR TRANSLATION OF 2001 REPORTED INDICATIONS TO 2005 ACCEPTED INDICATIONS.

1. Er zijn symptomen (geef voorkeur aan het symptoom zoals het expliciet aangestipt wordt door de aanvrager op het blad "medische gegevens" – "données médicales"; de beschrijving vd symptomatologie in de platte tekst dient slechts ter verduidelijking)**.**

    - Gaat het om een reanimatie, ventrikelfibrillatie, hartstilstand, cardiac arrest, mort subite, plotse dood, ….
        - Indien geen EFO uitgevoerd of EFO positief: → #1.1
        - Indien EFO gecontraïndiceerd: → #1.2
        - Indien EFO negatief: → #1.3
    - Gaat het om een collaps, syncope, hypotensie, duizeligheid, syncopale neiging, shock, … of evt dyspnoe, angor, ongemak, lipothymie, … :
    - Is er gedocumenteerde sustVT op ekg, monitoring of holter (al dan niet terzelfdertijd met het event) en er is geen sprake van TXP:
        - geen EFO uitgevoerd: → #2.1
        - EFO negatief: → #2.2
        - EFO positief: → #2.3
    - #2.4 kan samen voorkomen met elke 2.x. Wordt daarom slechts gecodeeerd indien de index-aritmie zich voordeed onder amiodarone of sotalol en er in het dossier geen sprake is van EFO.
        - Er is voldaan aan criteria i. + daarenboven komt pt op wachtlijst TXP: → #4.2
        - Is er gedocumenteerde nonsustVT op ekg, monitoring of holter (al dan niet terzelfdertijd met het event):
            - ischemisch hartlijden en positieve EFO: → #3
            - niet ischemisch én TXP: → #4.1
    - Het symptoom is "syncope van ongekende oorsprong", dwz verdachte symptomen (omschreven als "syncope") maar geen gedocumenteerde aritmieën die een voldoende verklaring geven voor de syncope:
        - op EFO induceerbare sustVT: → #5.1
        - op EFO induceerbare nonsustVT: → #5.2
        - geen of negatieve EFO maar volgens cardioloog toch tachy-aritmie als oorzaak van syncope: → #5.3

2. Er zijn geen symptomen maar wel aritmieën.

    - Het gaat om ischemisch hartlijden (zeer ruim te beschouwen indien een van de volgende vermeldingen: *ooit*: infarct, angor, PCI, CABG al dan niet met klepchirurgie, stenting, ischemische cardiomyopathie …:
        - Asympt nonsustVT en EFO postitief: → #3
        - Asympt sustVT en EFO postitief: → #3
    - Geen ischemisch hartlijden en evenmin familiaal of genetisch syndroom, dwz het gaat om een andere onderliggende hartziekte zoals idiopatische cardiomyopathie, valvulaire cardiomyopathie, rechter ventrikel displasie, … → #9

3. Geen reanimatie EN familiaal of genetisch syndroom.

    - #6. Wordt gecodeerd als de implantatie gebeurt als primair preventieve maatregel, onafhankelijk of er al dan niet spontane of geïnduceerde aritmieën zijn. Keuze tss 6.1, 6.2, 6.3, 6.4.

HOSPITAL CHARACTERISTICS IN BELGIAN REGISTRY

The implanting ICD-centers were compared for different items. The data of the year 2001 and 2005 are combined. Hospitals with less than 30 ICD-patients during those selected two years are not included.

Sex distribution

	Men	%	Women	%	Total
1	125	84%	24	16%	149
2	73	84%	14	16%	87
3	110	78%	31	22%	141
4	27	82%	6	18%	33
5	36	84%	7	16%	43
6	127	81%	30	19%	157
7	96	86%	15	14%	111
9	169	83%	34	17%	203
10	54	87%	8	13%	62
11	70	88%	10	13%	80
13	49	88%	7	13%	56
15	30	86%	5	14%	35
16	28	90%	3	10%	31
17	42	91%	4	9%	46
18	32	84%	6	16%	38
Total	1068	84%	204	16%	1272

Age distribution

	0-65	%	66+	%	Total
1	74	50%	75	50%	149
2	37	43%	50	57%	87
3	80	57%	61	43%	141
4	20	61%	13	39%	33
5	22	51%	21	49%	43
6	74	47%	83	53%	157
7	55	50%	56	50%	111
9	95	47%	108	53%	203
10	21	34%	41	66%	62
11	26	33%	54	68%	80
13	28	50%	28	50%	56
15	14	40%	21	60%	35
16	17	55%	14	45%	31
17	21	46%	25	54%	46
18	15	39%	23	61%	38
Total	599	47%	673	53%	1272

Statute

	General	%	Independent	%	Total
1	122	82%	26	18%	148
2	82	94%	5	6%	87
3	122	88%	17	12%	139
4	32	97%	1	3%	33
5	41	95%	2	5%	43
6	147	94%	9	6%	156
7	99	89%	12	11%	111
9	175	87%	27	13%	202
10	53	85%	9	15%	62
11	77	96%	3	4%	80
13	48	87%	7	13%	55
15	31	89%	4	11%	35
16	26	84%	5	16%	31
17	42	91%	4	9%	46
18	35	92%	3	8%	38
Total	1132	89%	134	11%	1266

Preferential tariff

	No prefer. tariff	%	Preferential tariff	%	Total
1	108	72%	41	28%	149
2	71	82%	16	18%	87
3	114	81%	27	19%	141
4	22	67%	11	33%	33
5	24	56%	19	44%	43
6	118	75%	39	25%	157
7	86	77%	25	23%	111
9	148	73%	55	27%	203
10	49	79%	13	21%	62
11	69	86%	11	14%	80
13	42	75%	14	25%	56
15	21	60%	14	40%	35
16	22	71%	9	29%	31
17	39	85%	7	15%	46
18	29	76%	9	24%	38
Total	962	76%	310	24%	1272

Class

The non-protected and the widows, counting for too small numbers, are not included in the table.

	actif	%	disabled	%	retired	%	total
1	40	28%	23	16%	78	55%	141
2	24	28%	9	11%	52	61%	85
3	52	39%	23	17%	59	44%	134
4	12	39%	6	19%	13	42%	31
5	11	28%	8	20%	21	53%	40
6	41	28%	17	11%	91	61%	149
7	35	32%	15	14%	59	54%	109
9	55	29%	21	11%	114	60%	190
10	12	21%	6	10%	40	69%	58
11	20	26%	3	4%	55	71%	78
13	17	31%	10	18%	28	51%	55
15	5	16%	5	16%	22	69%	32
16	13	42%	5	16%	13	42%	31
17	14	31%	5	11%	26	58%	45
18	11	31%	4	11%	21	58%	36
Total	362	30%	160	13%	692	57%	1214

Criterion 120 days of hospitalization

	< 120 days hosp.	%	120 days or more hosp.	%	Total
1	142	95%	7	5%	149
2	81	93%	6	7%	87
3	132	94%	9	6%	141
4	32	97%	1	3%	33
5	41	95%	2	5%	43
6	148	94%	9	6%	157
7	107	96%	4	4%	111
9	197	97%	6	3%	203
10	61	98%	1	2%	62
11	77	96%	3	4%	80
13	52	93%	4	7%	56
15	35	100%	0	0%	35
16	30	97%	1	3%	31
17	46	100%	0	0%	46
18	38	100%	0	0%	38
Total	1219	96%	53	4%	1272

Criterion 6 or more hospital admissions

	< 6 hosp.	%	6 or more hosp.	%	Total
1	142	95%	7	5%	149
2	81	93%	6	7%	87
3	132	94%	9	6%	141
4	32	97%	1	3%	33
5	41	95%	2	5%	43
6	148	94%	9	6%	157
7	107	96%	4	4%	111
9	197	97%	6	3%	203
10	61	98%	1	2%	62
11	77	96%	3	4%	80
13	52	93%	4	7%	56
15	35	100%	0	0%	35
16	30	97%	1	3%	31
17	46	100%	0	0%	46
18	38	100%	0	0%	38
Total	1219		53		1272

Manufacturer

	Biotronik	%	Guidant	%	Medtronic	%	St.J. Med.	%	Total
1	10	9%	44	38%	55	47%	8	7%	117
2	3	3%	30	35%	45	52%	8	9%	86
3	1	1%	25	18%	113	80%	2	1%	141
4	0	0%	7	23%	20	65%	4	13%	31
5	1	2%	18	42%	17	40%	7	16%	43
6	10	7%	80	53%	34	23%	27	18%	151
7	3	3%	45	41%	39	36%	22	20%	109
9	17	9%	120	63%	41	21%	14	7%	192
10	0	0%	29	47%	24	39%	9	15%	62
11	19	24%	22	28%	12	15%	26	33%	79
13	3	6%	29	55%	16	30%	5	9%	53
15	0	0%	11	32%	12	35%	11	32%	34
16	3	10%	5	16%	17	55%	6	19%	31
17	3	7%	22	48%	13	28%	8	17%	46
18	0	0%	7	18%	8	21%	23	61%	38
Total	73	6%	494	41%	466	38%	180	15%	1213

Replacement

	Primo	%	Replace	%	
1	87	58%	62	42%	149
2	73	84%	14	16%	87
3	129	91%	12	9%	141
4	27	82%	6	18%	33
5	29	67%	14	33%	43
6	114	73%	43	27%	157
7	84	76%	27	24%	111
9	136	67%	66	33%	202
10	44	71%	18	29%	62
11	64	80%	16	20%	80
13	46	82%	10	18%	56
15	32	94%	2	6%	34
16	27	87%	4	13%	31
17	30	65%	16	35%	46
18	37	97%	1	3%	38
Total	959	76%	311	24%	1270

One should take into account that centers performing ICD-therapy since 1989 have more indication for device replacement than those centers that started later.

Device class

	KI2	%	KI3-2el	%	KI3-3el	%	Total
1	70	75%	18	19%	5	5%	93
2	40	60%	25	37%	2	3%	67
3	40	68%	9	15%	10	17%	59
4	21	72%	6	21%	2	7%	29
5	24	83%	3	10%	2	7%	29
6	63	51%	47	38%	13	11%	123
7	49	50%	34	35%	15	15%	98
9	86	57%	32	21%	33	22%	151
10	38	90%	2	5%	2	5%	42
11	40	54%	25	34%	9	12%	74
13	20	53%	9	24%	9	24%	38
15	21	62%	8	24%	5	15%	34
16	14	45%	10	32%	7	23%	31
17	41	89%	5	11%	0	0%	46
18	16	42%	18	47%	4	11%	38
Total	583	61%	251	26%	118	12%	952

UNDERLYING HEART DISEASE IN THE BELGIAN REGISTRY

The following tables compare the ICD-population according to the underlying heart disease (ischaemic, idiopathic and other).

Nomenclature

	Other	%	Idio	%	Isch	%
first implant 2005	135	19%	103	15%	471	66%
renewal ambulatory 2005	6	25%	1	4%	17	71%
renewal hospital 2005	33	19%	25	15%	113	66%
first implant 2001	56	20%	35	13%	188	67%
Total	230		164		789	

Hospital

	Other	%	Idio	%	Isch	%	Total
1	33	23%	21	14%	92	63%	146
2	9	14%	4	6%	53	80%	66
3	40	29%	18	13%	80	58%	138
4	1	25%	0	0%	3	75%	4
5	6	14%	5	12%	31	74%	42
6	33	24%	10	7%	96	69%	139
7	18	17%	17	16%	73	68%	108
9	32	17%	35	18%	125	65%	192
10	10	17%	6	10%	42	72%	58
11	7	9%	16	21%	53	70%	76
13	9	18%	8	16%	33	66%	50
14	0	0%	0	0%	7	100%	7
15	9	26%	1	3%	24	71%	34
16	8	26%	9	29%	14	45%	31
17	10	26%	3	8%	26	67%	39
18	4	11%	10	27%	23	62%	37
19	1	10%	1	10%	8	80%	10
20	0	0%	0	0%	6	100%	6
Total	230	19%	164	14%	789	67%	1183

Status

	Other	%	Idio	%	Isch	%
General	209	20%	136	13%	703	67%
Independent	21	16%	28	22%	81	62%
Total	230	20%	164	14%	784	67%

Preferential tariff

	Other	%	Idio	%	Isch	%
No preferential tariff	187	21%	123	14%	581	65%
Preferential tariff	43	15%	41	14%	208	71%
Total	230	19%	164	14%	789	67%

Class

	Other	%	Idio	%	Isch	%
Non protected	3	15%	2	10%	15	75%
Active	148	44%	41	12%	147	44%
Disabled	30	19%	35	23%	89	58%
Retired	41	6%	80	13%	518	81%
Widow	8	24%	6	18%	20	59%
Total	230	19%	164	14%	789	67%

Hospitalized more than 120 days

	Other	%	Idio	%	Isch	%
No 120 days hospitalized	218	19%	153	13%	763	67%
120 days or more hospitalized	12	24%	11	22%	26	53%
Total	230	19%	164	14%	789	67%

Hospitalized more than 6 times

	Other	%	Idio	%	Isch	%
No 6 hospitalizations	215	21%	146	14%	672	65%
6 or more hospitalizations	15	10%	18	12%	117	78%
Total	230	19%	164	14%	789	67%

Region

	Other	%	Idio	%	Isch	%
Flanders	161	20%	119	15%	520	65%
Brussels	12	18%	12	18%	42	64%
Walloon	56	18%	32	11%	215	71%
Total	229	20%	163	14%	777	66%

Renewal

	Other	%	Idio	%	Isch	%
No renewal	180	20%	130	14%	602	66%
Renewal	50	18%	34	13%	187	69%
Total	230	19%	164	14%	789	67%

Type of device

	Other	%	Idio	%	Isch	%
KI2	123	22%	60	11%	371	67%
KI3-2el	45	19%	38	16%	157	65%
KI3-3el	6	5%	31	28%	73	66%
Total	174	19%	129	14%	601	66%

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KCE reports

33 Effects and costs of pneumococcal conjugate vaccination of Belgian children. D/2006/10.273/54.
34 Trastuzumab in Early Stage Breast Cancer. D/2006/10.273/25.
36 Pharmacological and surgical treatment of obesity. Residential care for severely obese children in Belgium. D/2006/10.273/30.
37 Magnetic Resonance Imaging. D/2006/10.273/34.
40 Functional status of the patient: a potential tool for the reimbursement of physiotherapy in Belgium? D/2006/10.273/53.
47 Medication use in rest and nursing homes in Belgium. D/2006/10.273/70.
48 Chronic low back pain. D/2006/10.273.71
49 Antiviral agents in seasonal and pandemic influenza. Literature study and development of practice guidelines. D/2006/10.273/67.
50 Cost-effectiveness analysis of rotavirus vaccination of Belgian infants D/2007/10.273/11
58 The Implantable Cardioverter Defibrillator. D/2007/10.273/23

All KCE reports are available with a French or Dutch executive summary. The scientific summary is often in English.