Use of The Implantable Cardiac Defibrillator (ICD) at The McGill University Health Centre (MUHC)

A Technology Assessment

By

The Technology Assessment Unit of the McGill University Health Centre

This analysis was prepared for the Technology Assessment Unit (TAU) of the McGill University Health Centre (MUHC).

by
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Invitation. This document was designed to assist decision-making in the McGill University Health Centre. Others are welcome to make use of it, preferably with acknowledgment. More important, to assist us in making our own evaluation, it would be deeply appreciated if potential users could inform us whether it has influenced policy decisions in any way, and even if it has not, whether it has been helpful in informing decision makers.

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Executive Summary

Background

Sudden Death. More than half of all cardiovascular deaths occur suddenly, mostly due to ventricular fibrillation. Many occur in apparently stable subjects who have survived a previous myocardial infarction but have impaired ventricular function. Ventricular fibrillation can usually be arrested by an electric shock applied to the heart using a defibrillator. This terminates the chaotic electrical activity, and allows a regular organized beat to resume.

The implantable cardiac defibrillator (ICD). This is a miniaturized pacemaker/ defibrillator that is implanted subcutaneously below the clavicle. In its simplest form an electrode passes intravenously from the defibrillator to the right ventricle. When it senses electrical abnormalities such as ventricular tachycardia or ventricular fibrillation it is programmed to initiate rapid pacing or to discharge a shock, as appropriate. Current versions cost approximately $23,000 and have a functional life of approximately 5-6 years. A simplified version, is likely to be available by September 2003 at a price of approximately $12,000. Increased use and competition will probably reduce the price of all these devices in the future.

Secondary Prevention. Implantation of an ICD in a patient who has survived ventricular fibrillation or symptomatic ventricular tachycardia, so-called "secondary prevention", is an effective means of prolonging life. Guidelines have been agreed on for the selection of suitable patients for ICD use as secondary prevention. The application of these guidelines at the MUHC has until recently resulted in a fairly constant implantation rate of a little less than 50 per year over the last three years.

Primary Prevention. The MADIT II study published in March 2002 found that implanting an ICD in any individual who had survived a previous myocardial infarction and who had an ejection fraction ≤ 30%, was associated with longer survival than medical therapy. Since this population had had no previous episode of ventricular fibrillation or a positive electrophysiologic study, this approach has become known as primary prevention. These case selection criteria have now been added to the already

accepted secondary prevention criteria, and incorporated into the updated American College of Cardiology/American Heart Association/NASPE Guidelines. They have been approved by the U.S Food and Drug Administration, and have with modification, been adopted by Medicare. The extent of the health benefit to be expected from primary prevention using these guidelines is uncertain due to the short follow-up of the relevant studies. A recent meta-analysis of primary prevention trials, including MADIT II, gives a weighted average reduction in overall mortality of 2.9 % per year over an average 26 month follow up.

Impact of MADIT II guidelines

Demand. The extent of the demand for ICD's that would result from application of MADIT II guidelines is unknown, and forecasts are speculative. The implant rate in the MUHC in the first six months of 2003 was slightly more than double the average rate in 2002. In the absence of any decision to restrict use, an increase of 100 implants over and above the 50 already chosen on MADIT II criteria seems likely, and an eventual increase of a further 100 per year quite possible (i.e. 50 on secondary and 200 on primary intervention criteria).

Impact. The long-term benefit of ICD implantation is unknown, but assuming a reduction in mortality of 2.9% per year, it is estimated that a policy of implanting 100 additional ICD's each year on the basis of MADIT II guidelines would result in an increasing number of life years saved for about 15 years at which time it would stabilize at approximately 110 life years saved each year (74 to 154 on sensitivity analysis). At this time, based on the cost of presently available equipment (approximately $22,000) it would be costing approximately $4,3 million per year.

Cost-effectiveness. Similarly, based on the cost of presently available equipment, the incremental cost-effectiveness compared to medical therapy from the point of view of the Québec health care system, would be approximately $42,000 per year of life saved, undiscounted, or $47,000 and $51,000 discounted at 3% and 5% respectively. Sensitivity analysis indicates a range from $31,000 to $62,000, undiscounted. Published estimates vary widely. We believe that until more confident follow-up data are

reported, estimates of cost-effectiveness of ICD therapy should not play a major role in policy decisions.

Potential effects of new low cost device. As noted above, a new simplified single-chamber ICD will probably soon become available at a price of approximately $12,000, including electrodes. Instruments of this type are designed only to treat ventricular fibrillation and lack the potential to manage rapid nonfatal arrhythmias. However, in primary prevention, the most commonly encountered malignant arrhythmia will be ventricular fibrillation which would be successfully managed with the simplified device. Exceptions, when a shock is not the appropriate therapy, would then have to be treated by replacing the simpler ICD by a more sophisticated model.

If it were assumed that for all the additional cases resulting from application of MADIT II guidelines the new simplified devices would be appropriate, and that the price would be approximately $12,000, the economic impact on the MUHC of installing 100 additional ICDs would be approximately $2,3 million per year after 15 years, and the cost-effectiveness of this intervention, from the point of view of the health-care system would be approximately $24,000 undiscounted, per year of life saved, (or $27,000 or $29,000 discounted at 3% and 5%, respectively).

Future MUHC policy

In the absence of any new funds identified for this purpose, any increased funding for ICD's would have to be obtained from within the present hospital budget. To give some sense of the extent to which hospital services might be affected, it is estimated that using the presently available sophisticated devices, the sum necessary to finance a program of 100 new implants per year, (approximately $4.3 million), would be the equivalent of closing approximately 31 acute care medical beds. If the simplified lower cost device could be used, 100 additional implants ($2.3 million), would be cost equivalent to the closure of 17 acute medical beds.

In view of these considerations, the committee recommends at this time:

1. That the MUHC, if possible with other institutions, urgently present this problem to government with a request that they consider the provision of special funds to finance ICD acquisition. The ministry should be urged to take part in a decision that will, in the absence of special funding, necessitate either a significant reduction in hospital services or a refusal to provide patients with effective therapy.

2*. Until special funding becomes available, the committee feels that ICD use at the MUHC should not be unlimited.* Accordingly, for the immediate future the MUHC should limit the use of ICDs along the following lines:

In the current year funding should be increased from the 2002 level (which allowed for approximately 50 implants), by approximately 50 %. This would allow for a total of 75 implants per year using the more sophisticated device (approx $22,000), or for a larger number using the simplified single chamber devices (approximately $12,000), the choice to be made at the discretion of the cardiologist concerned.

Acceptance of this recommendation will result in an increase in expenditure on ICD therapy from the present $1.2 million in 2002, to $1.8 million in 2003. Thereafter, assuming the same implant rate with constant prices and device longevity, expenditure on ICD therapy would increase from $1.8 million in 2003 to $3.2 million within 15 years. (However, further reduction in price is probable in the coming years).

3*. Patients should not be permitted to purchase their ICD or to pay for an upgrade of their ICD through use of private resources*. It is recognized that the principle of not allowing patients to upgrade the health services they receive by use of their own funds has been breached in the case of optical lenses and special splinting materials. Nevertheless, the committee believes the principle of refusing to provide two level health-care is accepted MUHC policy at this time. The fact that it has been breached does not mean that it has to be abandoned.

4. ICD policy must be formally adopted by the MUHC. The decision to restrict the use of ICD's would be taken for budgetary, not clinical, reasons. The responsibility for such a policy must therefore be clearly accepted by the institution.

5.*These recommendations should be considered temporary and should be subject to review and amendment when necessary*. It is very likely that further reduction in the costs of the device or improvement in the hospital's budgetary situation could render these recommendations obsolete. Similarly, new research that will allow better identification of ICD candidates and give us more precise and extended information on the benefits that these devices provide will require revision of these recommendations. Significant changes in any of these factors will necessitate revision of these recommendations.

Use of The Implantable Cardiac Defibrillator (ICD)
at
The McGill University Health Centre (MUHC)

On Feb. 6, 2003 Mr. Victor Simon requested the Technology Assessment Unit to review the use of ICDs at the MUHC. The request is the result of the following situation. The effectiveness of ICDs in the secondary prevention of sudden death in certain defined patient groups has been well demonstrated. However, in March, 2002 the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II) published the results of a study which indicated that the ICD could effectively prevent sudden death in a much larger group of patients than those previously identified. These instruments are relatively expensive and the economic impact of accepting the expanded indications for ICD use would be considerable. The following report will address three issues:

1) The strength of the evidence extending the indications for ICD use reported in the MADIT II study.
2) The potential health and economic impact of adopting the extended (MADIT II) indications in the MUHC.
3) The most appropriate policy for the MUHC in light of the above information.

Method

This report is based on a review of recent (post-1998) published research studies, meta analyses, and guidelines, accessed through Medline, the bibliographies of published articles, and data supplied by the Cardiology Divisions of the two adult hospitals of the MUHC. The generous help of the consultants and others listed on the title page is gratefully acknowledged.

Background

In the general adult population the incidence of sudden death has been estimated to be 0.1% to 0.2% per year [1]. Sixty three percent of all cardiovascular deaths are sudden [2]. Sudden death claims 460,000 Americans [2] and 35-40,000 Canadians each year [3]. Most sudden deaths are cardiac and almost all of these are electrical (ventricular tachycardia (VT), ventricular fibrillation (VF), and asystole. Although *acute* myocardial infarction is the cause of approximately 20% of sudden cardiac deaths [3], these are not the subject of concern here. The focus of the present report is on the prevention of those sudden cardiac deaths that are *not* associated with a recent acute myocardial infarction. These deaths occur predominantly in those survivors of myocardial infarction who have associated ventricular dysfunction.

It has been estimated that 40% to 60% of post-infarction patients with moderate to severe left ventricular dysfunction will experience ventricular tachycardia or ventricular fibrillation [4]. Use of amiodarone [5] or the ICD [6] in such patients, before these malignant arrhythmias become manifest, is referred to as "primary prevention". The problem with such interventions is to identify who in this large population of susceptible individuals should become the object of interventions.

Until recently ICD trials have been confined to individuals who have experienced an episode of ventricular fibrillation or symptomatic ventricular tachycardia, or those who are presumed to have done so on grounds of clinical history and provocative electrophysiologic testing. Such interventions are referred to as "secondary prevention" and the benefit of ICD therapy under such circumstances has been well demonstrated. In 1998 the American College of Cardiology (ACC), the American Heart Association (AHA), and the North American Society for Pacing and Electrophysiology (NASPE) jointly recognized four Class I indications for implantable cardioverter-defibrillator therapy [7]:

1. Cardiac arrest due to ventricular fibrillation (VF) or ventricular tachycardia (VT), not due to transient or reversible causes. (Level A).

2. Spontaneous sustained VT. (Level B).
3. Syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiological study when drug therapy is ineffective or not tolerated. (Level B).
4. Nonsustained VT with coronary disease, prior MI, LV dysfunction, and inducible VF or sustained VT at electrophysiological study that is not suppressible by Class 1 antiarrhythmic drug. (Level B).

(B= Evidence less well established).

ICD use based on these guidelines can be considered *secondary* prevention, and until the publication of the MADIT II study in March 2002, use of the ICD at the MUHC was consistent with these guidelines. The question presently under consideration is whether the MUHC should now extend these criteria to include virtually all individuals who have both suffered a myocardial infarction and have impaired ventricular function (ejection fraction ≤ 30%), as suggested by the results of the MADIT II study?

The MADIT II Study

The MADIT-II study, published in March 2002 [6], was focused on patients with coronary artery disease who had survived a previous myocardial infarction, and had impaired ventricular function with an ejection fraction (EF) of 30% or less. Thus the patients in this study were drawn from a broad population. They were 85% male, average age 65 years, and 70 % were New York Heart Association (NYHA) class 1 or 2. None had had their myocardial infarction less than one month previously and 88% had suffered their infarction more than six months previously. Most had previously had coronary artery surgery (57%) or angioplasty (44%). Exclusion criteria were; previous cardiac arrest, or ventricular tachycardia causing syncope, that was not associated with an acute myocardial infarction; symptomatic hypotension while in stable rhythm; myocardial infarction within the previous three weeks; coronary surgery or angioplasty within the previous three months; advanced cerebrovascular disease; or any non- cardiac

condition making survival for the duration of the trial unlikely. Patients were randomized to receive an ICD (742) or to continue "conventional medical therapy" (490). While conventional medical therapy included ACE inhibitors (approximately 70 %), beta blockers (70%), and statins (approximately 65%), the use of amiodarone was low (approximately 12%).

Follow-up averaged 20 months (range, 6 days to 53 months). During this time there were 54 crossovers or 4.4% (22 control patients received an ICD during the trial, 21 designated ICD patients did not have a defibrillator implanted and 11 had a defibrillator removed) The overall annualized mortality rates were 11.88% in the conventional therapy group and 8.42% in the defibrillator group, giving an absolute annual reduction in mortality of 3.46% (HR 0.69, 95%CI, 0.51-0.93; P= 0.016). The rates of sudden death were 10% and 3.8% in the control and ICD groups respectively [W.Zareba. Personal communication]. Thus the reduction in overall deaths was attributable to a reduction in the rate of sudden death.

Comment. This appears to have been a well conducted trial. The two groups were almost identical in all important characteristics. It is unfortunate that the randomization technique was not described. The trial was unblinded, but this is unlikely to have caused bias in the counting of *all* deaths. The authors acknowledge support from the Guidant Corporation, a major manufacturer of ICDs.

The mortality reduction in MADIT II, a *primary* prevention trial, was of the same magnitude as has been observed in *secondary* prevention trials. A meta-analysis of three randomized controlled trials in which the ICD was used as a secondary prevention intervention was reported by Connolly and colleagues in 2000 [9]. This analysis was based on the pooled data of the AVID [10], CASH[11], and CIDS[12] trials, comparing ICD in 934 patients, with amiodarone therapy in 932 patients. These were patients presenting with ventricular fibrillation (51%), ventricular tachycardia (44%), or syncope (5%), on average 63 years of age, 81% male, with an average ejection fraction of 34 %, and 69%, and a history of myocardial infarction. After an average follow-up of 2.33

years the annual death rate in medically treated subjects was 12.3%, and in the ICD subjects 8%, giving an absolute reduction of 3.5% per year (HR 0.72, 95%CI 0.60-0.87. P=0.006).

Differences in the admission criteria may explain why MADIT II achieved as great a reduction in mortality as secondary intervention trials. Another difference, however, is that in contrast with MADIT II, the control subjects in the Connolly meta-analysis [9] were receiving amiodarone, a medication that has been shown in a substantial meta-analysis of 13 randomized controlled trials [5] to be associated with a 1.4% reduction in absolute mortality compared to other medical therapy. Thus the possibility must be considered that the benefit from ICD use in the MADIT II trial might have been not 3.5% but 2.1%(3.46-1.4) if control patients (not receiving ICD) had been treated with amiodarone. This issue requires clarification with further evidence. (For this reason we will use 2 .0% as the lower bound of probability in sensitivity analysis).

A more recent and more comprehensive meta-analysis by Lee and colleagues included over 5,000 patients extracted from nine studies [13]. Five of these [6,14-17] were *primary* prevention trials (including MADIT II) in which 1494 individuals were treated by ICD therapy and 1636 by conventional medical therapy, and followed-up for an average of 26 months. Applying corrections for the average length of follow-up of each to derive annual mortality rates, gives a weighted average reduction in overall mortality of 2.9% per year, a value we will use as “ best estimate”.

There is, therefore, abundant evidence that ICD therapy is capable of lowering overall mortality in patients with substantial post-ischemic left ventricular dysfunction, and good evidence to support extension of the indications for ICD therapy from secondary to primary prevention. The MADIT II criteria, myocardial infarction survivors with impaired ventricular function (EF≤ 30%), have now been incorporated into the updated ACC/ AHA/ NASPE Guidelines [7], and approved by the US Food and Drug Administration [8]. They have not yet been approved in full by the US Medicare authority [http://www.cms.hhs.gov/ncdr/memo.asp?id=39].

However, because of the paucity of data, particularly on follow up from the end of the second year onwards, the actual extent of the reduction in absolute mortality to be anticipated from the use of the ICD in primary prevention is far less certain. We will base estimates on the value of 2.9% [13], with +/- 0.9% in sensitivity analysis to allow for the possibility that even the MADIT II estimate of 3.5% might underestimate the benefit of ICD therapy

The consequences of basing ICD policy on the MADIT II study .

Over the last four years, during most of which time patient selection has been consistent with the ACC 1998 secondary prevention guidelines, the number of patients receiving ICD's at the MUHC has been fairly stable, ranging between 44 and 50 per year (Appendix 1,Table 1). (The number of ICDs used is higher than the number of patients implanted, the difference being due to battery replacements and a small amount of wastage). However, the cardiologists responsible for ICD therapy at the MUHC have already started to accept patients referred on the basis of the new (primary prevention) MADIT II, criteria, and the implant rate in the first six months of 2003 is already almost twice the average rate in 2002.

Patient Demand.

There are no data available on which to base estimates of what the demand for the ICD would be if MADIT II indications were used. However, to get some feel for the health consequences and budgetary impact of adopting MADIT II criteria at the MUHC we will estimate the effects of increasing the implant rate by 100, and 200 cases per year chosen on MADIT II criteria, over and above the 50 carried out on secondary prevention criteria.

Health impact.

We will consider a hypothetical post MI, ICD implanted population, 80% male, with an ejection fraction of 30% or less, of average age 65 years (present average age of

implanted patients at MUHC is 67 years). We will assume that in the first post-implant year the mortality rate is 12% per year (it was 11.88% in MADIT II [6]). However, in MADIT II there was only 20 months of follow up and the outcome over a longer period is unknown. To estimate the full health effects of ICD therapy two assumptions are necessary.

First, it is necessary to assume by how much the *overall* mortality rate of such patients increases each year, due to all factors including co-morbidities and increasing age. We have assumed that the mortality rate of such patients will increase exponentially, in the same proportion as the increase in mortality rate in the Québec population of comparable age (60-64 yrs, 0.97%: 65-69 yrs, 1.61%, 70-74 yrs, 2.56 etc.[Institute of Statistics, Québec, 2003]).

We also do not know whether the reduction in overall mortality of 2.9% observed in implanted patients in the first two years would continue in subsequent years. A possible clue is that projection of the Kaplan-Meier curves to three years (admittedly with a much reduced number and consequently large confidence intervals) suggests an increasing benefit of ICD over this time [6,fig 2]. We have therefore based estimates on the assumption of a constant mortality rate *ratio*. That is to say the ratio of the mortality rate in ICD and control patients observed in the first year (9.1%/12%) remains constant in subsequent years (see Appendix 2, Table 1). In sensitivity analysis we also consider a model based on a constant mortality *rate difference* such that the initial mortality rate with ICD less the mortality rate without ICD remains constant from year to year. (See Appendix 2, Table 2). Another possibility, namely that patients who are susceptible to ventricular fibrillation become manifest in the first few years, the benefits of ICD therapy thus being confined to this period, is not considered. In confining our study to the former two models that both assume continuing benefit, we are using hypotheses that favour ICD use.

With the above assumptions, a policy of implanting an *additional* 100 ICD's each year would, by the end of the 15th year be causing an additional 110 life years saved each

year as long as the programme was continued (Appendix 2). Accordingly, to implant 200 additional patients each year would result after 15 years in an additional 220 life years saved each year.

Sensitivity analysis. The influence of varying the input variables on the number of life years saved is shown in Appendix 3, Table 1. The health benefits are, as might be expected, sensitive to changes in the percentage lives saved by ICD therapy. If we assume an absolute mortality rate reduction due to ICD use of 2% instead of 2.9%, 100 additional implants per year would result in only 72 life years saved each year after 15 years, instead of 110. The equivalent figure for a mortality rate reduction of 3.8 % would be 154 life years saved annually. Estimates based on the second scenario, a constant mortality rate *difference* result in somewhat fewer life years saved than estimates based on a constant mortality rate *ratio*. With the former assumption, and a mortality rate reduction of 2.9%, a policy of implanting 100 ICD's per year would result in 74 rather than 110 additional life years saved each year (Appendix 2,Table 2). The effect of changing the input variables under the assumptions of this scenario are shown in Appendix 3, Table 2.

Economic Impact.

Estimates of the direct costs of ICD therapy to the MUHC are shown in Appendix 4. Professional charges are not included. On the basis of the constant mortality rate ratio model , and use of the currently available equipment, a policy of implanting 100 additional ICDs per year would, by the end of the 15th year be costing the MUHC an additional $4,283,904 each year (Appendix 4, Table 1). The effect on costs of using the constant mortality rate difference model are shown in Appendix 4, Table 2.

However, it is probable that within the next few months a new simplified single-chamber ICD will become available at a price of approximately $12,000, including electrodes. Such instruments will be designed only to treat ventricular fibrillation and will lack the potential to manage rapid nonfatal arrhythmias. They can be expected to save the lives of those patients chosen by MADIT II criteria who develop ventricular fibrillation, but for

those who present with other malignant arrhythmias, they will have to be replaced by a more sophisticated device.

If it were assumed that for all the additional cases resulting from application of MADIT II guidelines, the less sophisticated devices would be appropriate, the economic impact on the MUHC of installing 100 additional ICD's would be approximately $2.3 million a year after 15 years.

Cost-effectiveness.

The above cost estimates were calculated from the point of view of the MUHC and thus do not consider professional charges. An estimate of the incremental cost-effectiveness, from the point of view of the Québec health-care system, can be derived by adding the professional fees to the MUHC costs already estimated. (Appendix 1a). It is assumed that the frequency of physician and hospital visits, would be approximately the same for ICD patients as for patients maintained on usual drug medication. These are estimated in Appendix 1 b.

Based on the constant mortality rate ratio model with these assumptions, and the use of currently available devices, it is estimated that to carry out an additional 100 ICD implants would by the 15 th year, have saved 110 years of life, and with professional costs included, would have cost the health care system approximately $4,627,703. Thus, based on the costs of currently available equipment, the resulting incremental cost-effectiveness ratio would be $42,070 (undiscounted) per year of life saved (Appendix 5.Table 1), or $47,458 or $50,949, discounted at 3% and 5% per year, respectively over 15 years.

Use of the simplified, lower cost ICD would result in a cost-effectiveness ratio of approximately $24,000 (undiscounted), per year of life saved ($27,000 or $29,000 discounted at 3% and 5% respectively).

Sensitivity analysis**.** The effect of changing the anticipated annual reduction in mortality on the estimated cost-effectiveness is shown in Appendix 5, Table 1. Values based on presently available equipment, range from $31,256 to $61,931 undiscounted, or $35,357 to $70,101 discounted at 3%.. Estimates of costs are fairly precise being based on studies carried out at the MUHC. The only area of uncertainty relates to the costs of treating complications of ICD therapy (Appendix 1, Table 1b and 2). However, the sum of these costs ($509) constitutes so small a fraction of the total ($24,170) i.e. 2.1%, that major variations would have little effect on the overall estimate.

Since the costs of ICD therapy occur early while the benefits are accumulated more slowly, estimates of cost-effectiveness will also vary greatly according to the time horizon under consideration. Because of the lack of outcome data for longer than two to three years, most estimates of the cost-effectiveness of ICD therapy in the literature have been calculated over a fairly short time horizon which will result in underestimation of the benefits in relation to the costs. On the other hand, the longer the time horizon, the greater the assumptions that must be made. This is one reason why results of estimates reported in the literature vary widely.

O'Brien and colleagues in a study based in Canada, collected prospectively the health resources used on the first 450 randomized patients enrolled in the CIDS trial [12], (ICD 212, amiodarone 218). They found that over 6.3 years the average cost per patient was $87,715 (ICD) vs. $38,600 (amiodarone). Discounting both at 3% gave an incremental cost-effectiveness of ICD therapy of $213,543 per life-year gained [18]. One reason for this estimate being so much higher than ours is their limitation of the time horizon to 6.3 years. If in our estimates we had limited the time horizon to 6 years we would have arrived at an undiscounted cost-effectiveness ratio of $98,176 per year of life instead of $42,070. A second reason is that they based their estimates on an absolute reduction in mortality produced by the ICD of 1.9%, the finding in the CIDS study [12], compared to the reduction of 2.9% used here. If in addition to a six-year time horizon we had assumed an absolute reduction in mortality due to ICD of 2%, the resultant

undiscounted cost-effectiveness ratio would have been approximately $140,891 per life year.

Larson and colleagues abstracted data from three combined secondary prevention trials, AVID [10], CASH [11], and CIDS [12] to obtain empirical estimates of survival differences[19]. With 3% discounting of costs and benefits, and assuming a six-year time horizon they arrived at a cost-effectiveness ratio of US $79,291.

Mushlin and colleagues studied 181 patients randomized in the MADIT (1996) secondary prevention study to receive ICD therapy or conventional medical therapy for an average period of 27 months. To judge by the large number who developed pulmonary reactions, probably most or all controls were receiving amiodarone. The incremental discounted cost-effectiveness ratio was estimated to be US $27,000 per life year over four years and US $16,900 per life year over eight years [20].

Thus, cost-effectiveness estimates that are carried out in the absence of robust follow-up data inevitably vary over a wide range. Our estimate of approximately $47, 458 is based on the possibly optimistic prediction that health benefits will continue indefinitely.

Future ICD policy at the MUHC?

Present Programme. Present policy at the MUHC is that all ICD implants must be authorized by an EP qualified cardiologist by consultation. Over the past 3 years there have been slightly less than 50 new implants per year, and the annual ICD outlay is approximately $1.2 million per year. Because of the costs of continuing care and battery replacement of successive cohorts, this number will increase each year that the program continues. If maintained at 50 per year, using the same assumptions, it will, by 15 years, be costing approximately $2.1 million and saving approximately 55 life years each year.

It is clear however, that the rate of 50 implants per year at the MUHC will not continue. The present policy of the cardiologists concerned is now to apply MADIT II indications when requested by colleagues at the time of referral, and the implant rate in the first six months of 2003 is already slightly more than twice the rate in 2002.

Future Policy. The first question to decide is whether this trend should be controlled or left to find its own level. Second, if control is decided on, at what level should ICD use be set? In considering these questions the following issues must be considered:

- the possibility of selecting a subgroup at particularly high risk, to receive ICD therapy and identifying patients who are unlikely to benefit.
- the efficacy and cost of alternative therapy if the ICD is not used,
- the quality of life of implanted patients,
- the ethical considerations and legal constraints on these decisions,
- the cost-effectiveness of ICD therapy ,
- the opportunity costs.

Selection of high-risk subgroups. The high cost of ICD therapy makes it very desirable to identify factors by which to predict which of the post myocardial infarction patients with low ejection fractions are at greatest risk so that ICD use might be confined to such patients. In addition to the criteria presently used to identify patients for secondary prevention (presentation with ventricular fibrillation or symptomatic ventricular tachycardia), there are several other interesting potential criteria for the selection of high-risk cases.

La Rovere and colleagues were recently able to identify in a population of patients with " dilated cardiomyopathy", a group at high risk of sudden death by the presence of reduced power in the low-frequency heart rate variability spectrum and the frequency of ventricular premature beats on a 24-hour Holter recording. In a validation sample of 242 patients, the 3 year sudden death rate was 23% compared with 3% in individuals without these risk factors [21].

In July, 2003, Hohnloser and colleagues reported on a study of 129 patients with MADIT II criteria in whom microvolt T-wave alternans testing had been prospectively assessed [22]. At 24 months of follow-up, there had been no sudden cardiac deaths among patients who had no T-wave alternans, compared with a rate of 15.6% among the remaining patients.

Zareba, at the 23rd Annual Scientific Meeting of NASPE, reported that a study of a MADIT II sub-population showed on multivariate analysis that both atrial fibrillation (P= 0.021) and QRS duration greater than 0.12 msec (P = 0.013) were significant predictors of overall death in the control group [23]. However, QRS duration was only marginally significant as a predictor of outcome in implanted patients [Zareba W. personal communication].

Several other authors have reported that QRS prolongation is an independent, but not very strong predictor of mortality [24-28], and the Center for Medicare and Medicaid Services (CMS), has announced its intention to expand coverage to "patients with prior myocardial infarction and left ventricular ejection fraction less than or equal to 0.30 and an electrical conduction abnormality in the heart (QRS) duration of greater than 120 msec". [//www.cms.hhs.gov/ncdr/memo.asp?id=39]. In response to this NASPE has expressed concern that these criteria are not based on published observations or peer review [http://www.naspe.org/naspe_in_action/Washington/advocacy/view/?id=8746]. Their point seems valid, and we believe that although the possibility of prediction of high-risk cases in the future is very promising, we do not yet have the evidence by which to select a subgroup to receive ICD therapy.

Finally, the results of the CABG Patch trial [15] raise the possibility that ischemia may be an important factor that has so far been underestimated. In this trial which found no difference in mortality between implanted and control subjects, randomization and ICD implantation were carried out *at the time* of coronary bypass surgery. A possible

explanation for the negative result is that the surgery successfully eliminated ischemia, and that ischemia may therefore be an important component of the substrate that favours ventricular fibrillation. More thorough correction of ischemia might in the future allow us to avoid the necessity of using ICD's in some otherwise eligible patients.

Alternative therapy. The only serious alternative to ICD therapy is amiodarone. This drug has been found to lower mortality [5]. It can be taken by mouth, and since it is an outpatient treatment, the cost to the MUHC is minimal. However, as demonstrated in the Conolly meta analysis [9] amiodarone does not give the same level of protection from sudden death as the ICD. Furthermore, it is associated with toxic reactions, some of them serious. These include liver toxicity, pulmonary toxicity, peripheral neuropathy, and hyperthyroidism. In the amiodarone meta-analysis referred to above [5], by the end of two years 41% of amiodarone assigned patients and 27% of control patients had permanently discontinued medication. The 14% difference was primarily related to adverse effects associated with amiodarone. Experience with this drug at the MUHC suggests that less than 50% of patients are likely to be on therapy after five years [M.Sami. Personal communication]. Thus, amiodarone is not the therapeutic equivalent of the ICD, and is at best a fallback therapy to consider when the ICD is not available or cannot be used.

Quality of life. To measure the quality of life attributable to ICD therapy is not easy since there is already an increased prevalence of major depressive disorder (15% to 18%) in post myocardial infarction patients [29,30]. However, in both the CIDS and AVID trials comparison of quality of life was made between patients randomized to ICD and to drug therapy [31,32]. Both found that psychological functioning was on the whole, better with than without ICD therapy. The factor that has been shown to influence the level of anxiety most is the frequency of shocks [33], and every effort must therefore be made to reduce their number.

Ethical Issues. A full discussion of the ethical issues surrounding the use of ICD's is not possible here. An excellent analysis is available in a paper by Hoffmaster [34]. “Should a

health care technology that has been demonstrated to be safe and effective in prolonging life be withheld from patients simply because it is too expensive?" he asks. This is a rationing decision and the responsibility for rationing, can no longer be shunted downwards from Government and upper levels of hospital administration to the bedside, since it imposes divided loyalties on physicians who must simultaneously act as patient advocates and gatekeepers. One important conclusion is that while the individual physician must retain decision-making power within the limits of what is available, the responsibility for defining these limits is societal or institutional.

Next, Hoffmaster concludes that "it does not make sense to ask whether a particular rationing decision is right". One must ask rather whether the decision was made ” in the right way". He concludes that the ethics of allocation and rationing is ultimately about matters of institutional design, the development of “morally defensible structures and procedures for making these decisions". We believe that the structure and functioning of TAU are consistent with the principles underlying his conclusions.

Another issue of concern is whether patients should be allowed to purchase their own ICD's, or, if only a simple less expensive device is available, whether they should be allowed to upgrade their device using their own funds. Dr Solly Benatar, Professor of Medicine and Director, Bioethics Centre, University of Cape Town consulted on this issue was of the opinion that patients *should* be permitted to purchase their own appliances. While concern about this from egalitarian and solidarity perspectives is understandable, he states, precedents have already been set for other appliances and patients already have to pay for their own medications in Canada. If the opposite decision is taken it should be justified in the face of the precedents that have been set.

Such justification can be found in arguments offered by Dr David Roy, Director of the Center for Bioethics of the Clinical Research Institute of Montréal. He believes that patients should *not* be permitted to obtain ICDs through use of private resources for three reasons: First, the fact that the principle of not allowing patients to upgrade devices through private resources has already been breached in the cases of optical

lenses and special splinting material should not be used to justify the use of private resources to obtain ICDs. "The three types of devices have a totally different relationship to human life". Lenses and splinting material relate to an increase in the quality of life. The ICD relates to life rather than death. The term "to upgrade devices" tends to mask of this important difference.

"Second, the continuing production of novel medical technologies combined with limited societal resources for healthcare inevitably means that any society has to accept that some inequities in access to these technologies will be unavoidable. However, it is essential to realize that while some inequities are unavoidable, other inequities are morally intolerable. The inequities of access to technologies and devices that mean the difference between dying or continuing to live are morally intolerable. Although such inequities will not be recognized as morally intolerable in all societies, they should be recognized as morally intolerable in Canadian societies that have set up a national health service precisely to prevent people with similar medical conditions needing similar medical services being divided into two classes, those who continue to live because they can pay for the care they need versus those who must die because they cannot pay for the care. Third, separation of Canadians into two such classes based on the possession or lack of sufficient wealth to pay for the same kind of care that each class needs is unjustly discriminating.…… it leads to an exclusion from life of those who are too poor to pay for an ICD". While Dr. Roy's arguments clearly apply to the issue of obtaining or not obtaining an ICD, the extent to which they apply to the upgrading of an ICD is open to discussion.

Legal Issues. Dickens [35] addresses the possibility of challenges to funding decisions that deny or ration patients' access to ICD's. Challenges of refusal to offer ICD therapy may be directed against physicians, hospitals, or provincial governments. If hospitals or provincial governments refuse to allow physicians to exercise their clinical judgment by refusing to make an ICD available, "the physicians legally cannot be faulted". A hospital that declines to make ICD therapy available should not be liable as such for an alleged Charter violation, but might be exposed to liability under the provincial human rights law

if there has been discrimination, for example on grounds of patients' physical or mental disability. On the other hand, "a uniform or overall long funding decision may also be shown to be purely administrative or policy based as opposed to operational, and so not amenable to judicial review".

There is a growing legal concern, he adds, that physicians may feel they should not recommend a therapy to which patients have limited access. On the contrary "they are obliged to disclose" treatments that they consider to be in their patients' best interest, and in the case of the ICD, if these are not available physicians must also inform patients whether their transfer to other facilities might hasten access to ICD therapy. This includes transfer to other provinces or to the USA when patients have adequate financial resources.

These brief extracts cannot do justice to Dicken's review of the legal issues relating to ICD use, nor can the outcome of future jurisprudence be foretold. However, two conclusions can be drawn. Physicians who, for reasons of lack of resources, deny their patients available treatment that they believe to be optimal could be challenged in law. On the other hand, a hospital could justifiably make a rationing decision and a physician who acted according to such a decision should not be held liable. The responsibility for such denial must not therefore be left to the physician. It must be based on formally adopted hospital policy.

Cost-effectiveness The estimated cost-effectiveness based on presently existing technology of $42,070 per life year ($47,458 and $50,949 discounted at 3% and 5% respectively), suggests that this technology gives only marginally competitive value for money. By comparison, the TAU recently recommended a program of antiviral treatment for patients with Chronic Hepatitis C with an estimated cost-effectiveness ratio of approximately $4,000 or $7,000 discounted at 3% and 5% respectively. Other more costly interventions have been accepted by the MUHC, such as renal haemodialysis (approximately $85,000 [36]), or Left Ventricular Assist Device as a permanent intervention (approximately $65,000 [37]). However, the former was accepted long

before the full extent and cost of this technology could be estimated, and in the latter case acceptance has been provisional, on the understanding that special funding will be provided. If the projected simpler, less costly new devices prove to be safe and effective their use will result in a more attractive cost-effectiveness ratio, namely $24,073 per life year, undiscounted ($27,154 and $29,149 discounted at 3% and 5%, respectively). There is also reason to hope that with increasing use and increasing competition the prices of all these devices may fall substantially.

As discussed above, estimates of cost-effectiveness made at a time when we have no information on the long-term effectiveness of ICD therapy depend on so many assumptions that they are basically unreliable and should not play a major role in policy formation. More important, policy can never be determined by cost-effectiveness alone. Of greater importance are issues such as affordability, and what must be "done without" in order to acquire a technology, and the values held by the decisionmakers.

Opportunity costs. It is estimated that to implant an additional 100 of the presently available devices per year would, after 15 years add approximately $4.3 million to the annual costs of the institution. Could this sum be better spent for some other purpose? Unless new funds are forthcoming, any increase in costs will have to be financed from the existing hospital budget with a resultant reduction in hospital services. Which of the hospital's services would be reduced as a result of providing this sum is, of course, unknown. To give some sense of the size of the reduction of services involved, this sum could theoretically be found by closure of approximately 31 acute care medical beds. (Equivalent figures for the simpler device would be $2.3 million and 17 acute medical beds)

Conclusion

The TAU Committee notes that to take a policy decision that will significantly influence health outcomes and hospital budget should, whenever possible, be supported by more substantial evidence of outcome over a longer follow-up than is presently available.

Nevertheless, a decision must clearly be made in the absence of such evidence even if it is only to guide policy for the immediate future.

In view of the above considerations the committee recommends at this time:

1. ***That the MUHC, if possible with other institutions, urgently present this problem to government with a request that they consider the provision of special funds to finance ICD acquisition.*** The ministry should be urged to take part in a decision that will, in the absence of special funding, necessitate either a significant reduction in hospital services or a refusal to provide patients with effective life saving therapy**.**

2. ***Until special funding becomes available, the committee feels that ICD use at the MUHC should not be unlimited.*** Accordingly, the MUHC should restrict the use of ICDs along the following lines:

   In the current year funding should be increased from the 2002 level (which allowed for approximately 50 implants), by approximately 50 %. This would allow for 75 implants per year, using the more sophisticated device (costing approximately $22,000), or for a larger number, using the simplified single chamber devices (costing approximately $12,000), the choice to be made at the discretion of the cardiologists concerned.

   Acceptance of this recommendation will result in an increase in expenditure on ICD therapy from the present approximately $1.2 million in 2002, to $1.8 million in 2003. Thereafter, if the same implant rate with constant prices and device longevity were assumed, expenditure on ICD therapy would increase each year, from $1.8 million in 2003 to $3.2 million within 15 years. However, such a scenario is unlikely both because of the probability of further reduction in price in the coming years, and the likelihood that better selection of subjects will substantially reduce the demand for implants.

Patients should not be permitted to purchase their ICDs or to pay for an upgrade of their ICD through use of private resources. It is recognized that the principle of not allowing patients to upgrade the health services they receive by use of their own funds has been breached in the case of optical lenses and special splinting materials. Nevertheless, the committee believes the principle of refusing to provide two level health-care is accepted MUHC policy at this time. The fact that it has been breached does not mean that it has to be abandoned.

4. ***ICD policy must be formally adopted by the MUHC***. Any decision to restrict the use of ICDs would be taken for economic, not clinical, reasons. The responsibility for such a policy must therefore be clearly accepted by the institution.

5. ***These recommendations should be considered temporary and should be subject to review, with amendment, when necessary***. It is very likely that further reduction in the costs of the device or improvement in the hospital's budgetary situation could render these recommendations obsolete. Similarly, new research that will allow better identification of ICD candidates and give us more precise information on the extent of the benefits that these devices provide will require revision of these recommendations. Changes in any of these factors will necessitate review of these recommendations.

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Appendix 1

1a: Estimation of direct costs of ICD Implants to the MUHC

Costs for device and electrodes: $22,863

Table 1 lists the number and costs of ICDs for fiscal years 1999/00, to 2002/03 (April 1 to March 31) at the MUHC. Data was retrieved from the 4D Client V6.7 database at the MUHC. Cost information for devices and electrodes were provided by Ms Christiane Berubé (Manager,Cardiovascular Division, MUHC).

a) Assumed average unit cost of ICD device: $20,000
b) Assumed average unit cost of electrodes: $2,500/single chamber, $3,000/dual chamber.

Table 1: The implantation of ICDs at the MUHC, fiscal years 1999 to 2003.

Year	ICDs[1] Total	New patients	ICDs Replace/ wastage	Dual chamber[2]	Single chamber[2]	Costs of device[3]	Costs of electrodes[4]	Total costs electrodes + devices
1999-2000	47	44	3	25 (54%)	21 (46%)	940,000	127,500	1,067,500
2000-2001	59	48	11	27 (50%)	27 (50%)	1,180,000	148,500	1,328,500
2001-2002	60	50	10	48 (84%)	9 (16%)	1,200,000	166,500	1,366,500
2002-2003	51	44	7	37 (73%)	14 (27%)	1,020,000	146,000	1,166,000

[1]: Total number of ICDs = (new ICDs + wastage ICDs + replacement ICDs), at RVH and MGH.
[2]: Excluding wastage ICDs.
[3]: Costs of device = unit cost for ICD ($20,000) X ICDs total
[4]: Costs of electrodes = unit cost of single chamber ($2500) X the number of single chamber + unit cost of dual chamber ($3000) X the number of dual chamber.
Thus, costs for device and electrodes= $1,166,000/51 = $22,863

Costs without professional costs:

c) Implant procedure cost: **$112/patient**
The professional cost (surgeon, anesthetist, cardiologist) was excluded. One nurse and one technician at mean salary $28/hr , spending two hours each: (2+2) X $28 = $112/patient

d) Post implant procedure cost: **$92/patient**
= nursing cost + specialist technician cost + X-ray + ECG test = $49+$5+$$23+$15
On average, a 3-4 hours post implant hospital stay period would be required for patients receiving an ICD. One nurse (mean salary $28/hr), supervising approximately 2 patients in main-recovery room, would be involved. Meanwhile, one specialist technician, at a salary of $32/hr, also is involved in teaching the patient about the device, spending on average 10 minutes.
Nursing cost: 3.5 X $ 28 / 2 = $49/patient
Specialist technician cost: 10/60 X $32 = $5/patient
X-ray (excluding professional fee): $23/test
ECG test (excluding professional fee): $15/test.

e) Initial costs: $23,067/patient
= ICD device + electrodes + implant procedure + post implant procedure = $22863+$112+$92

f) Follow up costs: **$17/patient /visit**
Periodic clinic follow up starts one week after the implant, followed by one visit every three months per year. During periodic follow-up visit, one administrative person at a salary of $16/hr spending 5 minutes and one technician at a salary of $32/hr spending 30 minutes are normally required for each patient's visit. Cost per patient per visit is $17.33 (5/60 X 16 +30/60 X 32). In total, there are 5 visits during the first year of implantation, thereafter, 4 visits per year.

g) Estimated costs of treating complications of ICD: $435

Complication rates were derived from literature published after Jan. 1997. (N= the numbers of patients involved in each report, Reported rate = percent complications reported, Assumed rate = the percent assumed for current estimates, based on current experience at MUHC.

Table 2: ICD complications and costs for ICD associated complications

Complications (Reference)	Year	N	Reported rate (%)	Assumed Rate (%)	Unit cost ($)	Total Cost ($) Rate x Unit Cost
Lead displacement				7.0% (MUHC rate in 2002 =10.7%).	2,704[1]	189
MADIT II	2002	724	1.8			
AVID	1997	507	0.6			
Takahashi et al.	2002	174	1.7			
Kühlkamp et al.	2002	300	4.0			
Schoels et al.	2001	293	2.4			
Infection				1.0%).	23,271[2]	233
MADIT II	2002	724	0.7			
AVID	1997	507	2.0			
Takahashi et al.	2002	174	1.7			
Chua et al.	2000	36	1.0			
Kelly et al.	2001		<1.0			
Giamarellou et al.	2001		0.8-1.5			
Pneumothorax				1.0% (obs).	77[3]	0.77
AVID	1997	507	1.6	0.1% (drain)	3453[4]	3.54
Takahashi et al.	2002	174	0.6			
Kühlkamp et al.	2002	300	2.0			
Perforation				0.3% (obs)	135[5]	0.41
AVID	1997	507	0.2	0.1% (thora)	7,000[6]	7.0
Takahashi et al.	2002	174	0.6			
Bleeding				0.2% (transf)	112[7]	0.22
AVID	1997	507	1.2			
Haematoma				0.5% (surg)	56[8]	0.28
AVID	1997	507	2.6			
Takahashi et al.	2002	174	1.7			
Kühlkamp et al.	2002	300	3.0			
InapproppDisch				5.0%	17[9]	0.85
Kühlkamp et al.	2002	300	7.0			
TOTAL COST:						**$435.00**

[1]: Reposition, change lead: single chamber lead + implant procedure+ post implant procedure (items b, c, d in appendix 1).

[2]: Explant (see items c, d in appendix 1), plus re-implant (see item e in appendix 1).

[3]: Observation (see item d in appendix, excluding ECG test ($15).

[4]: Chest drainage in recovery room for 24 hrs ($28/hr/2X24 + X-ray), followed by observation in surgical ward for 7 days ($442/day X 7).

[5]: Observation in recovery room 8hrs ($28/hr/2X8+ X-ray).

[6]: Assumed equivalent to CABG of mild to moderate severity at MUHC = $7,000 (Dep. of Finance).

[7]: Requiring 2 units blood. Blood is at present supplied to MUHC without charge. Recovery room for 8 hrs ($28/hr/2X8).

[8]: Procedure room for 30 min (0.5X$28/hrX2), followed by observation in recovery room for 2hrs ($28/hr/2X2).

[9]: Adjustment at pacemaker clinic (see item f in appendix 1).

h) Total first year costs to MUHC for implanting 100 ICDs: $2,358,700

=initial costs (c) +follow-up cost (f)+treatment of complications (g) = ($23,067+$17x5 visits in year 1+$435)x100

1b: Estimation of costs to provincial health care system not charged to MUHC

i) Implant procedure:
Surgeon ($600/implant), anesthetist ($140/implant), and cardiologist ($375/implant) = $1115/implant.

j) Post implant procedure:
Radiologist: $5/ X-ray test

k) Clinic visit during follow up:
Cardiologist: $50/visit

l) Battery replacement :
Implant: $1150 [surgeon ($600/implant), anesthetist ($140/implant), and cardiologist ($375/implant)].
Follow-up: $50 (cardiologist)

m) Treatment of complications of ICD:

Table 3: Per patient costs to the provincial health care system not charged to MUHC. Treating complications of ICD (professional cost plus cost of blood).

Complications	Rate (%) (see Table2) (A)	Treatment	Professional fee per event ($) (B)	Professional cost per patient ($) (A) X (B)
Lead displacement	7	Replacement	Surgeon ($150) anesthetist ($140), cardiologist ($375), radiologist ($5) Total: $670	47
Infection	1	Explant and reimplant	[surgeon ($600), anesthetist ($140), cardiologist ($375), radiologist ($5)] X 2. Total: $2240	22
Pneumothorax (obs.) (drain)	1 0.1	Observation Drainage	Radiologist ($5) Surgeon ($75), anesthetist ($140), Total: $220	0.05 0.22
Perforation (obs.) (thora.)	0.3 0.1	Observation Thoracotomy	Radiologist ($5) Surgeon ($786) anesthetist($140) Total: $926	0.02 0.93
Bleeding (transf.)	0.2	Transfusion	Cost of two units = $700	1.4
Haematoma (surg.)	0.5	Observation	No professional cost	0
InapproppDisch	5	Readjustment	Cardiologist ($50)	2.5
Total				**$ 74.00**

Table 4: Estimation of the total cost of ICD therapy.

Items	Cost to MUHC ($) (A)	Cost to health care system [1] ($) (B)	Total cost ($) (A)+(B)
Initial cost	23067	1120	**24187**
Complication cost	435	74	**509**
Battery replacement cost			
Initial cost	22988	1115	**24103**
Follow-up	17	50	**67**

[1]: Includes professional fees plus cost of blood (not normally charged to MUHC).

Appendix 2

Estimation of the health impact of implanting 100 ICDs per year at the MUHC

We will consider implanting ICDs each year in a hypothetical population of 100 patients. Characteristics: EF≤30%, 80% male, of average age 65 with an average mortality rate without ICD in year one of 12% (MADIT II =11.88%) [6]. To estimate the mortality rates without ICD over the next15 years, we assume that after year one it will increase exponentially in the same proportion as the increase in mortality rate of the Quebec population of comparable age (60-64yrs: 0.97%; 65-69yrs:1.61%, etc. [Institute of Statistics, Quebec, 2003]). Eg, annual increase in mortality rate =EXP[(LN1.61/0.97)/5]. We then estimate the mortality rate with ICD according to two models, a constant mortality rate *ratio* and a constant mortality rate *difference.*

Table 1: Life years saved based on constant mortality rate *ratio* model. Assumed: *the ratio of mortality rates* in ICD and non-ICD groups in year one (12% - 2.9%/12%) *remains constant* each year thereafter.

	Year		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Total
Without ICD	**Mortality rate**		**0.12**	**0.13**	**0.15**	**0.16**	**0.18**	**0.20**	**0.22**	**0.24**	**0.26**	**0.29**	**0.31**	**0.34**	**0.38**	**0.42**	**0.46**	
	Alive year end	100	88	76	65	55	45	36	28	21	16	11	8	5	3	2	1	
	Alive mid-year		94	82	71	60	50	40	32	25	19	14	10	6	4	3	1	
With ICD	**Mortality rate**		0.09	0.10	0.11	0.12	0.14	0.15	0.16	0.18	0.20	0.22	0.24	0.26	0.29	0.32	0.35	
	Alive year end	100	91	82	73	64	55	47	39	32	26	20	15	11	8	6	4	
	Alive mid-year		95	86	77	68	59	51	43	36	29	23	18	13	10	7	5	
	Life yrs saved		1	4	6	8	10	11	11	11	10	9	8	7	6	4	3	110
				1	4	6	8	10	11	11	11	10	9	8	7	6	4	107
					1	4	6	8	10	11	11	11	10	9	8	7	6	103
						1	4	6	8	10	11	11	11	10	9	8	7	97
							1	4	6	8	10	11	11	11	10	9	8	90
								1	4	6	8	10	11	11	11	10	9	82
									1	4	6	8	10	11	11	11	10	73
										1	4	6	8	10	11	11	11	62
											1	4	6	8	10	11	11	52
												1	4	6	8	10	11	41
													1	4	6	8	10	30
														1	4	6	8	20
															1	4	6	12
																1	4	6
																	1	1
Annual total life years saved			1	6	12	20	30	41	52	62	73	82	90	97	103	107	110	
Cumulative total life years saved																		**887**

Table 2: Life years saved based on constant mortality rate *difference* model. Assumed: the mortality rate *difference* between ICD and non-ICD groups remains *constant* at 2.9% per year.

	Year		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Total
Without ICD	**Mortality rate**		**0.12**	**0.13**	**0.15**	**0.16**	**0.18**	**0.20**	**0.22**	**0.24**	**0.26**	**0.29**	**0.31**	**0.34**	**0.38**	**0.42**	**0.46**	
	Alive year end	100	88	76	65	55	45	36	28	21	16	11	8	5	3	2	1	
	Alive mid-year		94	82	71	60	50	40	32	25	19	14	10	6	4	3	1	
With ICD	**Mortality rate**		0.09	0.10	0.12	0.13	0.15	0.17	0.19	0.21	0.23	0.26	0.29	0.32	0.35	0.39	0.43	
	Alive year end	100	91	81	72	62	53	44	36	28	22	16	12	8	5	3	2	
	Alive mid-year		95	86	77	67	58	48	40	32	25	19	14	10	7	4	2	
	Life yrs saved		1	4	6	7	8	8	8	7	6	5	4	3	2	2	1	74
				1	4	6	7	8	8	8	7	6	5	4	3	2	2	73
					1	4	6	7	8	8	8	7	6	5	4	3	2	71
						1	4	6	7	8	8	8	7	6	5	4	3	69
							1	4	6	7	8	8	8	7	6	5	4	66
								1	4	6	7	8	8	8	7	6	5	61
									1	4	6	7	8	8	8	7	6	56
										1	4	6	7	8	8	8	7	50
											1	4	6	7	8	8	8	43
												1	4	6	7	8	8	35
													1	4	6	7	8	27
														1	4	6	7	19
															1	4	6	11
																1	4	5
																	1	1
Annual total life years saved			1	5	11	19	27	35	43	50	56	61	66	69	71	73	74	
Cumulative total life years saved																		**662**

Appendix 3

Health impact. Sensitivity analysis of life years saved.

Estimates of the number of life years saved over 15 years following 100 implants, assuming the first year mortality rate *without ICD* 12% and three different reductions in mortality rate with ICD (2%. 2.9%, and 3.8%). Mortality rates without ICD increases in the same proportion as mortality rates increase with age in the Quebec general population (see second row of Appendix 2, Table 1). Mortality rates *with ICD* each year are based on two different models.

Table 1: ***Constant mortality rate ratio*.** The ratio of the mortality rate with ICD to the mortality rate without ICD in year one is maintained throughout subsequent years.

First year mortality rate without ICD (A%)	**Constant mortality rate ratio (rate with ICD/rate without ICD)**		
	(12% -2%) / 12%	**(12% –2.9%) / 12%**	**(12% -3.8%) /12%**
	Life years saved over next 15 years by doing 100 implants		
12%	72	110	154

Table 2: ***Constant mortality rate difference*.** Every year the difference between the rates with ICD and without ICD is the same as in year one.

First year mortality rate without ICD	**Constant mortality rate difference (rate without ICD - rate with ICD)**		
	12%-2%	**12%-2.9%**	**12%-3.8%**
	Life years saved over next 15 years by doing 100 implants		
12%	50	74	100

Appendix 4

Estimation of economic impact on the MUHC of implanting 100 ICDs per year (professional cost excluded).

Estimations of the economic impact of a policy of implanting 100 ICDs per year based on two different models: constant mortality *ratio* and constant mortality rate *difference* (see Appendix 2, Table 1& Table 2). Cost data showed in Appendix I, Table 4. First year cost = initial cost X100 + (follow-up cost+ complication treatment cost) x the number alive at mid-year. Assumed battery change required at the beginning of the 6th and 11th years.
In all other years, only follow-up cost taken into consideration.

Table 1: Estimated costs based on the constant mortality *ratio* model.

Year		1	2	3	4	5	6			9		11	12	1	4		1
Mortality without ICD		0.12	0.13	0.15	0.16	0.18	0.20	0.22	2		0.29	0.31	0.34	38	0.		
Mortality with ICD		0.09	0.10	0.11	0.12	0.14	0.15	0.16	18		0.22	0.24	0.26	29	0.		
Alive year end	100	91	82	73	64	55	47	39	2		20	15	11		6		
Alive mid-year	100	95	86	77	68	59	51	43	6		23	18	13		7		
Costs($)		2356411	5870	5249	4635	4035	1368390	2918	417		1558	528122	906	59	4		4283
			2356411	5870	5249	4635	4035	1368390	918		1962	1558	22	06	6		4283
				2356411	5870	5249	4635	4035	3	0	2417	1962	1558	2812	9		4283
					2356411	5870	5249	4	0	390	2918	2417	1962	558			4282
						2356411	5870		6		1368	2918	2417	962	1	2	4281
							2356411	5870	2		4035	1368390	2918	417	1	1558	3753444
								2356411	870		4635	4035	1368390	918	2	1962	3751887
									356411		5249	4635	4035	3683	2	2417	3749924
										411	5870	5249	4635	035		2918	3747507
											2356	5870	5249	635	4	13683	3744589
												2356411		249	4	4035	2376199
													2356411	870	5	4635	2372165
														3564	5	5249	2367530
																5870	2362281
																23564	2356411
Annually costs ($)		2356411	2362281	2367530	2372165	2376199	3744589	3747507	37	4	887	3753	4281567	4282472	42831	4283904	
Total cost ($)																	51996607

Table 2. **Estimated costs based on the constant mortality rate *difference* model.**

Year		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Total
Mort. without ICD		0.12	0.13	0.15	0.16	0.18	0.20	0.22	0.24	0.26	0.29	0.31	0.34	0.38	0.42	0.46	
Mort. with ICD		0.09	0.10	0.12	0.13	0.15	0.17	0.19	0.21	0.23	0.26	0.29	0.32	0.35	0.39	0.43	
Alive year end	100	91	81	72	62	53	44	36	28	22	16	12	8	5	3	2	
Alive mid-year	100	95	86	77	67	58	48	40	32	25	19	14	10	7	4	2	
Costs($)		2356411	5860	5213	4560	3914	1327304	2708	2174	1698	1286	435969	660	442	281	168	4148649
			2356411	5860	5213	4560	3914	1327304	2708	2174	1698	1286	435969	660	442	281	4148481
				2356411	5860	5213	4560	3914	1327304	2708	2174	1698	1286	435969	660	442	4148200
					2356411	5860	5213	4560	3914	1327304	2708	2174	1698	1286	435969	660	4147757
						2356411	5860	5213	4560	3914	1327304	2708	2174	1698	1286	435969	4147097
							2356411	5860	5213	4560	3914	1327304	2708	2174	1698	1286	3711129
								2356411	5860	5213	4560	3914	1327304	2708	2174	1698	3709843
									2356411	5860	5213	4560	3914	1327304	2708	2174	3708144
										2356411	5860	5213	4560	3914	1327304	2708	3705970
											2356411	5860	5213	4560	3914	1327304	3703262
												2356411	5860	5213	4560	3914	2375958
													2356411	5860	5213	4560	2372044
														2356411	5860	5213	2367485
															2356411	5860	2362272
																2356411	2356411
Annually costs ($)		2356411	2362272	2367485	2372044	2375958	3703262	3705970	3708144	3709843	3711129	4147097	4147757	4148200	4148481	4148649	
Total cost ($)																	**51112702**

Appendix 5

Cost-effectiveness. Sensitivity analysis.

Table 1: Undiscounted cost-effectiveness, based on constant mortality rate *ratio* model.

mortality ICD	Mortality rate ratio (rate with ICD / without ICD)	Costs of 100 implants followed for 15 yrs [1] ($)	Life years saved by 100 implants, over 15 years	Cost-effectiveness ($ / life year saved)
12%	(12% - 2%) / 12%	4459062	72	61931
12%	(12% - 2.9%) / 12%	4627703	110	42070
12%	(12% - 3.8%) / 12%	4813353	154	31256

[1]: Costs of doing 100 implants include professional cost. The cost of complications has not been included after the end of the first year, as the majority occur shortly after implantation of the ICD.