Costs and Quality-of-Life Effects of Implantable Cardioverter-Defibrillators

Running title: Systematic Review of ICD Costs and Outcomes

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ABSTRACT
While the clinical efficacy of implantable cardioverter-defibrillators (ICDs) has been convincingly demonstrated in clinical trials, the impact of ICDs on health care costs and recipients’ quality of life (QOL) is less certain. We reviewed and summarized the existing medical literature on health care costs and QOL effects of ICDs. MEDLINE and the Institute for Scientific Information Web of Knowledge were searched for publications reporting costs of care and QOL assessments of ICD recipients. Unpublished and non-peer reviewed “gray” publications were excluded. We included articles if they reported primary, original patient data that were collected after 1993, when non-thoracotomy defibrillators entered clinical practice. Two reviewers independently evaluated publications for relevance and quality, abstracted study data, and summarized the findings. Excessive heterogeneity among studies prevented formal meta-analysis, thus a narrative synthesis was performed and key themes were identified from the literature. There were limited published data on the costs of ICD care, especially for primary prevention of sudden cardiac death. The literature on ICD QOL lacked large, multi-center, longitudinal studies. Many ICD QOL studies were performed among small numbers of patients at single centers. Initial ICD implantation costs ranged (2006 $U.S.) from $28,500 to $55,200, with annual follow-up costs ranging from $4,800 to $17,000. QOL was higher for ICD recipients than for patients treated with antiarrhythmic drugs, but there was a substantial prevalence of anxiety, depression, and “loss of control” among ICD recipients, particularly among those who had received ICD shocks. In conclusion, ICD implantation remains costly but may be becoming less expensive over time, and ICD recipients’ QOL is significantly impacted by their devices.
The purpose of this systematic review was to summarize and assess the current knowledge base of quality of life (QOL) and health care costs for patients with implantable cardioverter-defibrillators (ICDs), and to identify gaps in the ICD QOL and cost literature that would be appropriate targets for future research.

**Methods**

We searched English language publications in MEDLINE, the Institute for Scientific Information Web of Knowledge, and the Cochrane Library of Systematic Reviews from 1994-2006. Searches were restricted to articles that referenced an electronically-available abstract. The keyword search strategy was: implantable AND (defibrillator OR defibrillators) AND (quality of life OR adaptation, psychological OR attitude to health OR health status OR cost-benefit OR health care costs OR life change events). Reference lists of all articles eventually reviewed in full-length format were hand searched to find additional potential candidate articles.

Studies were deemed eligible if they reported primary, original health care costs or QOL assessments of implantable cardioverter-defibrillator patients. Studies were excluded if they reported patient data from earlier than 1994, as non-thoracotomy ICDs (i.e., the modern version of the ICD that does not require cardiac surgery for implantation) did not enter clinical practice in the United States until late in 1993. Following recently published guidelines of systematic reviews of medical devices, we excluded “gray” publications and other non-peer-reviewed reports due to concerns about such data being biased.\(^1\) We also excluded abstracts presented at national meetings that were not subsequently published in full manuscript form.\(^1\)

Two reviewers independently reviewed the abstracts and titles for likelihood of meeting inclusion criteria, and the full text of articles identified as a potentially qualifying by either reviewer was obtained and studied by both reviewers in detail. Data extracted from each article
included the date, location, setting of the study, details about the patient population, whether any intervention was used, the methods of QOL or cost measurement, the main results, and statistical measures of significance. For comparison purposes, costs were converted to 2006 U.S. dollars using the consumer price index for health care. Non-U.S. currencies were converted to U.S. dollars using the appropriate foreign exchange rate on the date of publication.

Methodological quality scores ranging from 1 (very low) to 5 (very high) were independently assigned by each reviewer based on the study’s strength of design, appropriateness of execution, internal validity, statistical quality, and generalizability. The reviewers then conferred, compared the results of all abstracted elements, and attempted to reconcile any widely divergent abstracted data or quality scores. The final quality score was computed for each article by averaging the final quality scores of both reviewers.

**Results**

We initially identified 259 potential ICD studies of cost or QOL using the broad search strategy outlined above. After applying exclusion criteria, 7 cost studies and 27 QOL studies were retained, with 1 study qualifying as both a cost and QOL investigation (Figure 1).

**ICD Costs.** The 7 cost analyses (Table 1) were either economic analyses of clinical trials, cost-effectiveness analyses using primary, unpublished data, or observational studies for which patient-level cost data were available. Cost results were reported in 2 general categories: the cost of initial ICD implantation and the follow-up cost of ongoing ICD therapy.

**Initial ICD Implantation Costs.** Three randomized clinical trials of ICDs included economic sub-studies. O’Brien et al.\(^2\) measured implant costs among patients in the Canadian Implantable Defibrillator Study (CIDS), Mushlin et al.\(^3\) evaluated the initial cost of ICD implantation in the Multicenter Automatic Defibrillator Trial, and Larsen et al.\(^4\) studied the
initial ICD implantation cost among Amiodarone Versus Implantable Defibrillator (AVID) trial enrollees. Mean implantation costs in these studies ranged from approximately $36,000 to $54,000 (2006 $U.S.). Substantially higher initial costs were found in the 2 U.S. clinical trials.

Other studies of ICD costs relied on observational data collected outside of clinical trial settings. Owens, Sanders, et al. estimated ICD implantation cost from Medicare and health maintenance organization administrative records. More recently, the same investigators again estimated the cost of ICD implantation using similar primary sources along with the Myocardial Infarction Triage and Intervention trial registry. Weiss et al. used propensity score matching to assess outcomes and costs of care for Medicare beneficiaries. Hsu et al. assessed costs among patients receiving ICDs in the Kaiser Permanente Health Care System. Reports from these four studies suggested that average implantation costs have substantially declined from over $50,000 in the mid-1990s to nearly $30,000 currently.

**Annual ICD Costs after Implantation.** In follow-up studies of clinical trial enrollees, O’Brien et al. determined that the average annual health care costs attributable to the ICD were approximately $5,000. Much higher annual costs ($16,000-$17,000) were found in the 2 U.S. clinical trials of ICDs. Using unpublished data from Medicare and Kaiser Permanente, Owens et al., Hsu et al., and Weiss et al. found average annual costs ranged from $10,000 to $17,000 among ICD recipients in the 1990s. In more recent work, Sanders et al. estimated the annual cost of care for patients with ICDs has fallen to less than $7,000 per year.

**ICD Quality of Life.** Published assessments of QOL among ICD recipients included a wide variety of survey instruments to assess beliefs, attitudes, and behaviors associated with ICD receipt. Although several of these studies reported Medical Outcomes Study/Short Form-36 (SF-36) scores, tests for heterogeneity indicated insufficient homogeneity to permit formal meta-
analysis of the data, and no other QOL instrument was used with sufficient frequency to permit statistical combination of the results. We therefore summarized these 27 studies (Table 2) in terms of common content domains.

**ICD Quality of Life compared with Antiarrhythmic Drug Therapy.** Several articles compared QOL among ICD recipients to QOL of patients receiving pharmacologic therapy. Bainger and Fernsler\(^9\) measured QOL immediately before and 3 months after ICD implantation and found no significant QOL differences except for a slight decrease in the psychological/spiritual domain of the Quality of Life Index (pre-implant: 25, post-implant: 24, p<.05.) Irvine et al.\(^10\) compared QOL outcomes between treatment groups in the CIDS trial and found that ICD patients had more energy, more physical mobility, less sleep disturbance, and less lifestyle impairment than anti-arrhythmic drug patients (p<.05 for all comparisons). Schron et al.\(^11\) compared the QOL outcomes of ICD versus anti-arrhythmic drug therapy in the AVID trial and found that both treatment groups underwent comparable QOL decrements. A more significant decline in QOL was reported both by ICD patients who had received shocks and by anti-arrhythmic drug patients who had adverse side effects. Herbst et al.\(^12\) compared QOL in non-randomized samples of ICD and anti-arrhythmic patients and found that ICD patients had significantly less impairment in physical functioning, emotional functioning, vitality, and sleep.

**ICD Quality of Life Compared to Other Patient Groups.** Quality-of-life comparisons between ICD patients and similar patient groups appeared frequently in the literature. Namerow et al.\(^13\) compared QOL 6 months after revascularization between ICD recipients and non-recipients in the Coronary Artery Bypass Grafting-Patch trial. ICD patients had less improvement in health (p=.03), particularly among the 101 of 206 ICD recipients whose device had fired. Herrmann et al.\(^14\) discovered no significant difference in QOL between convenience
samples of ICD recipients and coronary artery disease patients, although increased shocks produced a modest decrease in QOL (p<.05). Burns et al.\textsuperscript{15} compared ICD patients’ acceptance of device therapy to that of pacemaker recipients and found ICD patients had significantly lower Florida Patient Acceptance Survey scores for overall device acceptability (76 versus 85, p<.001) and lower functional capacity scores (55 versus 72, p<.001). Godemann et al.\textsuperscript{16} compared SF-36 scores between 93 ICD recipients and scores derived from the general German adult population; ICD patients had significantly lower mean general health perception (54 versus 68), lower mean emotional role function (77 versus 90), lower mean physical role function (57 versus 84), and lower mean physical functional ability (68 versus 86).

**Negative Effects of ICD Shocks on Quality of Life.** In addition to the findings above, several additional studies suggested ICD patients receiving shocks had lower QOL. Carroll and Hamilton\textsuperscript{17} found that shocked patients had more anxiety (p<0.015), lower mental health (p<0.04), lower vitality scores (p<0.03), and more fatigue (p<0.005). Hegel et al.\textsuperscript{18} found that 7 of 21 ICD patients reported increasing levels of anxiety, depressed mood, and fear of shocks that persisted over 2 years (p<0.05). Schuster et al.\textsuperscript{19} determined that fear of shock or device malfunction strongly correlated with increased anxiety (r=0.52 and 0.47 respectively, p<.001) among 39 ICD recipients. Heller et al.\textsuperscript{20} found that 34 of 58 ICD patients had health anxiety, and the experience of shocks was associated with increased anxiety, thoughts of dying, dependence on others, and fatigue. Pauli et al.\textsuperscript{21} determined that ICD patients experiencing shocks had State-Trait Anxiety Scores similar to those of panic disorder patients (means: ICD= 48±12, panic disorder= 50±13, no reported p-values). Ahmad et al.\textsuperscript{22} found that among 86 ICD patients who had been shocked, 79% reported the shock severity to be “moderate to severe,” yet 75% also reported the ICD to be a "tolerable, lifesaving device," and 26% were "not bothered much by
shocks.” Pelletier et al.\textsuperscript{23} discovered that among 74 ICD recipients, 82% were concerned about the unpredictability of ICD shocks.

**Non-Effect of ICD Shocks on Quality of Life.** In contrast to the majority of studies showing a decline in QOL associated with ICD shocks, 4 studies indicated little relationship between ICD shocks and QOL. In a second study by Pelletier et al.,\textsuperscript{24} only 7.5% of ICD patients who had received a shock reported that their devices had affected their lives negatively, and 48% indicated their ICDs were an important source of security. In a study by Chevalier et al.,\textsuperscript{25} no difference was found between shocked and non-shocked ICD patients on the Beck Depression Inventory, the Hamilton Anxiety Scale, and the Minnesota Multiphasic Personality Inventory. Hsu et al.\textsuperscript{8} observed no differences between ICD patients’ recalled pre-implant SF-36 or Duke Activity Status Index scores and reported post-implant scores. Similarly, Duru et al.\textsuperscript{20} examined the SF-36 scores among 76 pacemaker recipients, 45 shocked ICD patients, and 31 non-shocked ICD patients, and found no significant QOL differences.

**Mediating Factors in the Shock-QOL Relation.** Sears et al.\textsuperscript{26} used multivariate regression analyses to identify independent predictors of QOL in ICD recipients. Pre-existing clinical depression, anxiety, optimism, and social support accounted for 40% of the variance in observed mental health QOL, but ICD shock history only accounted for a further 3.5% of the variance, suggesting little independent effect of ICD shocks on QOL. In the only published therapeutic intervention study for ICD-related anxiety, Kohn et al.\textsuperscript{27} performed a randomized controlled trial of cognitive behavioral therapy versus usual care and found that therapy significantly decreased depression and anxiety among patients who had experienced ICD shocks.

**Loss of Control and Psychological Adjustment.** The need for psychological adjustment to the “loss of control” relating to the ICD was the focus of other QOL studies.
Dickerson et al.\textsuperscript{28} performed qualitative content analyses of interview transcripts or essays by 62 ICD patients, and found patients struggled to regain control of their lives by “making a truce with the device” and “forming a new vision for living.” Similarly, a qualitative study by Eckert and Jones\textsuperscript{29} also reported lack of control as a central theme. Conversely, Flemme et al.\textsuperscript{30} determined that patients’ “social ability” and “the ability to act,” as measured by the Brodsky ICD questionnaire, increased significantly after implantation (p<.05), while “fear of life situation” decreased significantly (p<.05).

\textbf{Driving and Social Relations.} Particular attention was devoted in the literature to the effect of restrictions on ICD patients’ driving and their interpersonal relationships. Schuster et al.\textsuperscript{19} found that driving restrictions strongly correlated with decreased self-efficacy. Pelletier et al.\textsuperscript{23} found that ICD patients frequently resumed driving despite physicians’ warnings: 51% were driving at 3 months and 69% were driving at 6 months. In a qualitative analysis of 21 ICD patients by Kamphuis et al.,\textsuperscript{31} many patients reported the excessive concern of family members as “constraining.” Eckert and Jones\textsuperscript{29} found that ICD recipients had to make lifestyle changes (e.g. not carrying children, avoiding crowds) due to concerns that the device could fire and the recipient would inadvertently injure someone else. In a QOL study of 20 juvenile ICD recipients and their parents by DeMaso et al.\textsuperscript{32}, parents reported a significant negative impact of the ICD on their child’s interpersonal relationships (p<.001).

\textbf{Sexuality.} The literature indicated that ICDs also have important effects on patients’ sexuality. Hegel et al.\textsuperscript{18} found that sexual interest decreased at 1 year post-implant and significantly increased again at 2 years (scores: 2.4 at baseline, 1.7 at 1 year, 2.2 at 2 years, p<.01), suggesting the possibility of a coping phenomenon. Heller et al.\textsuperscript{33} observed a positive correlation between ICD patients who resumed working and their sexual interest and frequency.
Kohn et al., in their study of cognitive behavioral therapy and ICD QOL, found that sexual difficulties were more frequently reported by the control group (65% versus 22%, p< .01), suggesting that therapy was beneficial in addressing issues of ICD-related sexual dysfunction.

**Work and Leisure Activities.** ICDs substantially influenced patients’ work and leisure activities. Duru et al. determined that ICD patients reported more limitations in leisure activity than pacemaker patients. Chevalier et al. found that only 19% of ICD patients returned to work after receiving their device. Heller et al. observed that only 34% of ICD recipients who had been employed at the time of device implantation resumed working after receiving their device. Namerow et al. found that ICD patients reported more physical limitations than coronary artery disease patients. Hamilton and Carroll, noted that older patients with ICDs had significantly decrements in physical health in the year after implantation. Interpretation of these studies was complicated by the fact that many ICD recipients also had significant heart disease, which may have been the predominant cause of patients’ physical limitations.

**Discussion**

The best published estimates indicate ICD implantation costs approximately $28,500-$55,200, and subsequent annual ICD-related follow-up costs range from $4,800-$17,000. While insufficient data exist to confirm a time trend in ICD costs, it is plausible that current costs are in the lower half of these ranges. The literature also suggests that QOL for ICD recipients is better than the QOL of patients taking anti-arrhythmic drugs, but ICD recipient QOL is not as high as that of the general public or among recipients of more “benign” cardiac devices such as pacemakers. Concerns about ICD shocks and the negative effect of ICDs on patients’ sense of control, social interactions, driving, sexuality, capacity to work, and ability to engage in leisure activities appear to adversely influence ICD recipients’ perceptions of health and well-being.


**Figure Legend**

Implantable Cardioverter-Defibrillator Systematic Review Article Inclusion/Exclusion Pathway. The leftmost box indicates the number of electronic abstracts identified using a broad electronic search combined with hand searches of reference lists. The block arrows indicate progression to the next level of review. The line arrows indicate the numbers of articles that were excluded and the reasons for exclusion. Abbreviations: ICD = implantable cardioverter-defibrillator. QOL = quality of life. * One retained study qualified as both a quality-of-life and a cost article.