Effectiveness of implantable defibrillators for preventing arrhythmic events and death: a meta-analysis

CRD summary
This review compared implantable cardioverter defibrillators (ICDs) with medical therapy. The authors concluded that ICDs are highly effective in both primary and secondary prevention. No information was given about study selection (possible source of bias) and information about participants was limited (possibly limiting generalisability). Overall, however, the results appear to support the authors' conclusions.

Authors' objectives
To compare the effectiveness of implantable cardioverter defibrillators (ICDs) with medical strategies for the prevention of arrhythmic events and death.

Searching
MEDLINE (from 1966 to April 2002), EMBASE (from 1980 to April 2002) and the Cochrane Library (2002) were searched; the search terms were detailed in the paper. No language restrictions were applied. The reference lists of relevant papers were also checked.

Study selection
Study designs of evaluations included in the review
Only randomised controlled trials (RCTs) were sought.

Specific interventions included in the review
Studies that compared ICD devices with medical therapy were sought. ICD devices were implanted transvenously or by thoracotomy. The comparators in the included studies were anti-arrhythmic drugs (amiodarone, sotalol, metoprolol), 'conventional therapy', or usual care. Studies that evaluated defibrillator thresholds or mechanisms of drug or device action were excluded. The average duration of follow-up ranged from 18 to 66 months.

Participants included in the review
The inclusion criteria for the participants specified adults (aged 18 years or older) who had been resuscitated from 'sudden death' (the authors call this 'secondary prevention'), or who had a low left ventricular ejection fraction (LVEF less than or equal to 0.40) and were thought to be at risk of lethal cardiac arrhythmia (called 'primary prevention'). The participants in the included studies were those resuscitated from near death because of ventricular fibrillation or ventricular tachycardia, some of whom had suffered a prior myocardial infarction. Others had sustained ventricular tachycardia; were undergoing coronary artery bypass graft (CABG) with LVEF less than or equal to 0.35 and abnormal electrocardiogram; had dilated cardiomyopathy and LVEF less than or equal to 0.30; or were post myocardial infarction with ventricular tachycardia or low LVEF.

Outcomes assessed in the review
The primary outcomes of interest were mortality all-cause mortality, cardiac death, arrhythmic mortality and cardiac arrest. In the 'Results' section, the outcomes were grouped as all-cause mortality, arrhythmic death and nonarrhythmic death. In the included studies, death was classified by internal criteria in the individual studies and/or the Hinkle and Thaler method. Treatment-related complications were also reported.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.
Assessment of study quality
The criteria for assessing quality included blinding of randomisation, the numbers followed up, and blinding or objectivity of the outcome measures. Four reviewers independently assessed the studies for quality. Any disagreements were resolved by discussion with two other reviewers.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The extracted data included study design, the participants' diagnostic criteria, details of the interventions and outcomes, and details of any industrial support (e.g. from the device manufacturers).

Methods of synthesis
How were the studies combined?
The studies were combined using the Mantel-Haenszel method. The relative risk (RR) and risk difference, along with 95% confidence intervals (CIs), were calculated for the primary and secondary prevention trials separately and overall. A fixed-effect analysis was used unless heterogeneity was significant (P<0.10), and then a random-effects analysis was performed. Where a significant reduction in the risk difference was found, the numbers-needed-to-treat were calculated. Subgroup analyses were performed to see the relative effects in differing clinical subgroups (ischaemic heart disease, absence of ischaemia, revascularisation) and of industry-sponsored studies. Adverse events were reported as weighted percentages.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared statistic, where a P-value of less than or equal to 0.10 was considered statistically significant. Clinical heterogeneity was taken into account by analysing the primary and secondary studies separately. Sensitivity analyses were used to assess the effects of individual studies on the overall results.

Results of the review
Nine RCTs (5,314 participants) were included. Five of these were on primary prevention (3,291 participants) and four were on secondary prevention (2,023 participants).

Overall, less than 1.5% of the participants were lost to follow-up. There were 1,292 deaths.

Pooling all studies showed a 30% reduction in all-cause mortality (P<0.001); the RR was 0.66 (95% CI: 0.46, 0.96, P=0.03) for primary prevention and 0.75 (95% CI: 0.64, 0.87, P=0.0002) for secondary prevention.

Compared with the anti-arrhythmic drugs group, there was a 57% reduction in arrhythmic death in the ICD treatment group; the RR was 0.34 (95% CI: 0.23, 0.50, P<0.00001) for primary prevention and 0.50 (95% CI: 0.38, 0.66, P<0.00001) for secondary prevention.

Overall, there was no excess of nonarrhythmic deaths in the ICD treated group; the RR was 0.95 (95% CI: 0.74, 1.21) for primary prevention and 0.95 (95% CI: 0.71, 1.27) for secondary prevention.

Subgroup analyses: studies with industrial sponsorship showed significantly greater benefit of ICDS than those without such sponsorship. Results also differed between groups of studies defined by differing clinical conditions (further details were provided in the paper).

Treatment-related complications: peri-operative death with ICD implantation occurred in 1.2% of the participants without concomitant thoracotomy and CABG versus, for example, 5.5% of the participants in one large CABG trial. Other commonly reported adverse events in the ICD-treated group were infection (3.7%), pericardial effusion and tamponade (0.6%), pneumothorax (1.4%), lead dislodgement or fracture (2.3%) and device malfunction (2.0%). In the anti-arrhythmic agents-treated group, amiodarone pulmonary toxicity was the most common reported adverse event (weighted mean 4.8%, range: 3.0 to 5.7).
Authors' conclusions
ICDs are highly effective in reducing the risk of arrhythmic death in either primary or secondary prevention. The impact on all-cause mortality is related to the underlying risk of arrhythmia-related death relative to other causes.

CRD commentary
The aims of this review were clear, and the search strategy and quality assessment appear to have been good. There was no information on how the authors went about selecting studies for the review. If the selection procedure was inappropriate it is possible that the review could be biased. Information about the participants in the included studies (e.g. ages, concomitant disease) was limited; this could affect the generalisability of the review. There were some discrepancies in the numbers of studies and of participants in the tables and text. Using a meta-analysis to combine the studies was appropriate, and the authors considered the possible effects of statistical and clinical heterogeneity. The results would appear to support the authors' conclusions.

Implications of the review for practice and research
Practice: The authors do not appear to be generally recommending this treatment in practice. They suggested that the effectiveness (both cost and therapeutic) would be maximised by using ICDs in those people at highest risk of life-threatening arrhythmias.

Research: The authors stated that the impact of ICD usage on health policies, including cost-effectiveness and access to this therapy, should be further assessed.

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