UNIVERSITY OF BIRMINGHAM

Literature search on the incidence of "shock" treatments from Implantable Cardioverter Defibrillators (ICDs) at 1, 3 and 6 months post first ICD implantation

Aggressive Research Intelligence Facility
West Midlands Health Technology Assessment Collaboration

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For the Drivers Medical Group
DVLA
Swansea

ARIF

WMHTAC
West Midlands HTA Collaboration

About ARIF and the West Midlands Health Technology Assessment Collaboration

The West Midlands Health Technology Assessment Collaboration (WMHTAC) is an organisation involving several universities and academic groups who collaboratively produce health technology assessments and systematic reviews. The majority of staff are based in the Department of Public Health and Epidemiology at the University of Birmingham. Other collaborators are drawn from a wide field of expertise including economists and mathematical modellers from the Health Economics Facility at the University of Birmingham, pharmacists and methodologists from the Department of Medicines Management at Keele University and clinicians from hospitals and general practices across the West Midlands and wider.

WMHTAC produces systematic reviews, technology assessment reports and economic evaluations for the UK National Health Service's Health Technology Assessment (HTA) programme, the National Institute for Health and Clinical Excellence (NICE). Regional customers include Strategic Health Authorities, Primary Care Trusts and regional specialist units. WMHTAC also undertakes methodological research on evidence synthesis and provides training in systematic reviewing and health technology assessment.

The two core teams within WMHTAC are the Aggressive Research Intelligence Facility (ARIF) and the Birmingham Technology Assessment Group (BTAG)

ARIF provides a rapid on-demand evidence identification and appraisal service primarily to commissioners of health care. Its mission is to advance the use of evidence on the effects of health care and so improve public health. The rapid response is achieved by primarily relying on existing systematic reviews of research, such as those produced by the Cochrane Collaboration, the National Institute for Health and Clinical Excellence (NICE), the NHS Centre for Reviews and Dissemination, and the NHS Health Technology Assessment (HTA) programme. In some instances, longer answers to questions are required in which case mini rapid reviews of existing systematic reviews and key primary studies are compiled, typically taking 1-2 months to complete.

Occasionally a full systematic review is required and then topics are referred to BTAG who coordinate the production of systematic reviews for several customers under a number of contracts. ARIF is intrinsically involved in the production of these systematic reviews.

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1 Aims

The aims of this report were to address the following questions submitted by the Drivers Medical Group:

1.1 Primary Questions

- What is the incidence of “shock” treatments from an Implantable Cardioverter Defibrillator (ICD) at 1, 3 and 6 months post first ICD implantation?
- What proportion of shock treatments are incapacitating?

1.2 Secondary Questions

- What is the incidence of further shocks following an initial incapacitating shock in these individuals in the following 2 years assuming that:

a) No new medication has been put into place or

b) Anti-arrhythmic medication or an interventional procedure has been introduced.

Further details are given in the request submitted by the Drivers Medical Group (Appendix 1 – Details of Request)

2 Background

Background information is given in the documentation supplied by the Drivers Medical Group contained in Appendix 1 – Details of Request.

Sudden cardiac death can occur as the result of ventricular arrhythmias associated with ventricular fibrillation (VF) or ventricular tachycardia (VT). In patients at risk of cardiac death a preventative measure is to implant a cardioverter defibrillator device (ICD), which consists of a pulse generator, sensing/pacing electrodes and defibrillation coils. Single chamber, dual chamber and biventricular pacemakers are available that differ in the number and positioning of electrodes. Potentially life-threatening ventricular arrhythmias are corrected by the ICD device by pacing or delivery of a shock, which may be of either low energy or high energy. ICD devices provide ‘appropriate’ shocks for VF, monomorphic or polymorphic VT and conditions associated with irregular heart rhythms such as Torsade de pointes. Occasionally ‘inappropriate’ shocks are delivered by the ICD due to misinterpretation of arrhythmia type. This is associated with atrial fibrillation, flutter and tachycardia, supraventricular, junctional and sinus tachycardia, premature ventricular contractions, over sensing and technical problems with the device (such as lead failure or electromagnetic interference).[1] For the purposes of this report the above definitions for appropriate and inappropriate shocks will be used, unless detailed otherwise.

2.1 ICD and driving

In the UK, individuals who have received an ICD device for secondary prevention of sudden cardiac death are precluded from holding a type 1 driving licence for 6 months and type 2 licenses are revoked.

It is currently unclear as to the exact timeframe in which the majority of arrhythmias requiring shock treatment actually occur. It is also unclear as to the severity of shocks and the proportion of shocks that may incapacitate individuals, hence causing danger. Finally, if an incapacitating shock has occurred, the likelihood of subsequent shocks occurring in relation to treatment options is also an area of uncertainty.

This report highlights the evidence surrounding the incidence of shocks in patients with an ICD and the severity and recurrence of shocks in these patients.

3 Methods

Outline methods were submitted to the Drivers Medical Group by email and acceptance subsequently confirmed (Appendix 2 – Outline methods).

Briefly these were:

- To undertake a search for studies looking at the incidence and severity of shocks in patients with ICD devices.
- To initially search for existing systematic reviews.
- To start by searching for articles published from 1990 onwards.
- To concentrate on prospective studies.
- To comment on Methodological quality of studies where possible.
- Where appropriate and possible data on relevant outcomes is to be extracted and tabulated.
- Data analysis will depend on information identified.

3.1 Searches

3.1.1 Existing Reviews

Searches to identify existing systematic reviews on this topic were performed utilising the well-established ARIF search protocol (Appendix 3 – Search strategies).

3.1.2 Primary Studies

Searches were undertaken for primary studies in MEDLINE, EMBASE, the Cochrane Library and CINAHL. The search strategy employed index terms and text terms for 'ICD,' 'arrhythmia' and 'shocks'. The strategy was developed iteratively and modified accordingly. The detailed search strategies can be found in Appendix 3 – Search strategies.

Searches were predominantly undertaken by an information specialist with additional searches by a research reviewer. Both interacted to ensure they were conducted appropriately. An information specialist and a research reviewer scanned the search results for relevance based on information in the title and abstract. Articles that adhered to the following broad criteria were obtained in full for further scrutiny:

Design: Prospective studies or retrospective cohort studies
Population: Patients with an ICD device
Outcome: Incidence and times of shocks. Severity of shocks
Exclusion: Case series, case reports and studies published pre-1990 (due to volume of results)

Full copy articles were assessed for their match to the questions being addressed (external validity) and the most informative articles subjected to further scrutiny and reporting. The reference lists of the most relevant articles were also checked in order to identify further relevant studies.

4 Results

The searches identified 704 articles after duplicate articles were removed. The titles and abstracts were scanned and 64 studies were initially selected and screened for relevance. No systematic reviews were identified. 36 primary studies were thought to contain relevant information and full copies were obtained. 11 articles were subsequently excluded as they did not contain the information required and the remaining 25 articles have formed the basis of this report. The information from these articles has been extracted and placed in two tables (Appendix 4 –section 7.4). The table in section 7.4.1 contains full information (where available) on the study design, type of patients included, the duration of follow-up and information on the type of device used. The table in section 7.4.2 contains a summary of the results in relation to total number of shocks, type of shocks and other information relevant to this request. The key findings are reported and commented upon in sections 4.1, 4.2 and 4.3 below. Most studies identified do not address the questions raised in this request directly so this report has included information from any appropriate study that may inform on the question. Most studies are prospective studies that have followed up a group of patients receiving an ICD device over time. There are some retrospective cohort studies and information was also available from some clinical trials (details of study designs are in the table in section 7.4.1). Any specific quality issues surrounding the studies are highlighted in the table in section 7.4.2.

The searches also retrieved 9 narrative reviews and 1 book chapter that have specifically looked at issues surrounding driving in ICD patients.[2-11] These articles are not commented on specifically in this report but are mentioned here for reference.

4.1 *What is the incidence of "shock" treatments from the ICD at 1,3 and 6 months post first ICD implantation*?

To address the question the evidence for total shock rates at the defined time points in the relevant studies and the types of shocks (appropriate or inappropriate) were examined. Further, some information was available on the time to first shock event. One study was also identified that detailed the timing of shock delivery over a 24 hour period and has been commented upon as this information maybe useful in predicting incidence of shocks at particular times of the day.[12]

Table 1 shows the results from studies that have recorded the number of patients who received at least one shock up to time points of 12 months. Therefore the number of patients and shocks are the same unit. The results are reported in the table as the number of patients receiving at least one shock (of any kind) per 100 patients.

Table 1 Studies reporting total shock incidence at 1, 3, 6 and 12 months.

Study	Sample size	1 month (at least one shock/100 patients)	3 month (at least one shock/100 patients)	6 month (at least one shock/100 patients)	12 month (at least one shock/100 patients)
Carroll & Hamilton 2005[13]	59	-	-	-	37
Kamphuis et al 2003[14]	132	-	-	6	26
Schron et al 2002[15]	373	-	-	-	39
Namerow et al 1999[16]	259 with ICD from 490	-	-	35.8	-
Grimm & Marchlinski 1995[17]	49	-	-	-	59
Grimm et al 1993[18]	241	-	-	8	15

None of the studies report number of shocks at 1 and 3 months after ICD implantation. Three studies report values at 6 months and these vary from 6 - 35.8 shocks per 100 patients. The incidence rates given in all of these studies are for shocks occurring within the time frame, and it is therefore not clear what the distribution of shocks up to that time point is. At 6 months the studies by Kamphuis *et al* [14] and Grimm *et al* [18] have similar incidence rates of 6 and 8 shocks per 100 patients. However, the patients in the study by Namerow *et al* [16] had an incidence rate of 35.8 per 100 patients at 6 months. The sample size was similar to the Grimm *et al* [18] study but the patients are a clinical trial population (see table in section 7.4.1) which may not be representative of the total patient population.

We identified an equation proposed by the Canadian Cardiovascular Society[7,19] to calculate the risk of harm to other road users or innocent bystanders caused by a patient who develops compromising ventricular arrhythmia whilst driving.

Risk of harm (RH) = (TD) (V) (SCI) (Ac)

TD is the time the patient spends driving during the year, V is a constant based on the type of vehicle driven (1.0 for commercial vehicles and 0.28 for a standard-sized passenger car), SCI is the risk of sudden death or incapacity during the year and Ac is the probability that sudden death or incapacity while driving will result in death or injury to others. The equation has been used to estimate risk in drivers[7] and assumes figures for the basis of the equation that non-commercial drivers spend 4% of their time driving and the risk of shock is 50% in patients in the first year after implant. The equation uses a base rate of 2% for Ac, (as this is the rate of

deaths at the wheel in non ICD individuals which result in death or injury to other road users). This equates to an annual yearly risk of harm to others of 0.0000224 or 1 in 45,000. [7]

This equation uses a 12 month incidence of 50% for shocks. Five of the studies in Table 1 give the number of patients receiving shocks up to 12 months and ranged from 15 – 59 per 100 patients (15 - 59%), suggesting the figure used in the equation is at the higher end of the evidence identified.

Table 2 presents the results of studies investigating appropriate and inappropriate shock rates. The sample size and time frame of the study have been indicated, as have the number of appropriate or inappropriate shocks per 100 patients. The method of assessing whether the shock is appropriate or inappropriate was not often reported in the studies but when it was it was often determined by assessment of records contained from the ICD (details where available are in the table in section 7.4.1).

Table 2 Studies reporting on the number of appropriate and inappropriate shocks experienced by patients with an ICD device

Study	**Sample size**	**Follow-up time (average ± SD)**	**Appropriate shocks (at least one shock /100 patients)**	**Inappropriate shocks (at least one shock /100 patients)**
Alter et al 2005[20]	440	46 ± 37 months	-	12
Backenköhler et al 2004[21]	205	12 months	43	-
Rinaldi et al 2003[22]	171	841 ± 928 days	34	-
Theuns et al 2001[23]	26	8 ± 5 months	-	19
Sticherling et al 1999[24]	52	12 months	-	8
Rosenqvist et al 1998[25]	778	4 months	-	14.3
Schaumann et al 1996[26]	124	11 months	27	12.1
Villacastín et al 1996[27]	80	21 ± 19 months	20	10
Grimm & Marchlinski 1995[17]	49	12 months 24 months	16 49	
Grimm & Marchlinski 1994[28]	26	51 ± 16 months	35	-
Bremner et al 1993[29]	381	0-9 years	35	3
Grimm et al 1993[18]	241	6 months 12 months	7 13	

There is some difficulty in interpreting the information in Table 2 as the studies have different time frames associated with measuring the shocks. Some studies have reported incidence of shocks over the duration of the follow-up period whilst others have set a 12 month rate. The studies quoting rates over the follow-up period have a wide range of follow-up times (e.g. from 0-9 years in the study by Bremner *et al* [29]). Only 2 studies have information relevant to the time points in this request.[18,25] The study by Grimm *et al*[18] contains information at 6 months for appropriate shocks only and reports 7 shocks per 100 patients in this time frame. The study by Rosenqvist *et al*[25] contains information on inappropriate shocks at 4 months and reports 14.3 shocks per 100 patients in this time frame. Four studies have reported rates at 12 months, 3 give details of appropriate shocks and 1 of inappropriate shocks. For appropriate shocks the 12 month rates range from 13 - 43 (average 24) shocks per 100 patients and the study addressing inappropriate shocks found 8 shocks per 100 patients at 12 months.[24]

The time to event data is presented in Table 3. It is included as it offers some indication of the time at which shocks occurred relative to the entire time frame.

Table 3 Studies reporting the time to first shock event in patients with an ICD

Study	Sample size	Time to first shock	Range	Type of shock
Backenköhler et al 2004[21]	205	Median time 164.5 days	10.5 – 1727.5 days	Appropriate only
Rinaldi et al 2003[22]	171	Mean 290 days	1-1000 days	Appropriate only
Bremner et al 1993[29]	381	Mean 8.5 months Mean 10 months	$\pm$ 13 months $\pm$ 14 months	Any shock Appropriate only

The information identified in this area is difficult to interpret due to the wide ranges seen in studies. The first two studies detailed only investigated the time to first appropriate shock and both found a very wide range in number of days to the first shock event. The study by Bremner *et al* [29] reports time to first shock for any shock type, with a mean of 8.5 months in a population size of 381 patients, but again this was associated with a large range of 13 months.

4.1.1 Timing of shock delivery

One study was identified that reported on the time at which shocks occurred over a 24 hour period.[12] In this study patients who were implanted with a device that is capable of recording the time of shock delivery were investigated retrospectively to assess circadian variation in shock time delivery. The results are included here as it may be useful to assess the timing of shock delivery in relation to time of the day. The study showed that the majority of shocks were delivered between 6.00am and 12.00pm (42%) with 25% between 12pm-6pm and 20.5% between 6pm -12am. The lowest numbers of shocks were found between 12am-6am (12.5%).[12]

4.2 *What proportion of shock treatments are incapacitating?*

We were able to identify few studies that directly address this question. Information was available from 4 studies that have data related to this issue and these have been used to give an indication of the severity or effects of receiving a shock from the ICD device.[22,25,30,31] The results of these studies have not been tabulated as they have different outcomes. For details on the study characteristics see table 7.4.1 in Appendix 4.

From these studies, the best available evidence is from the study by Kou *et al* [30] as it gives some indication of unconsciousness associated with shocks. In this study it is reported that 9% of patients receiving an ICD device (n=180) had unconsciousness associated with an ICD shock. The study also includes information on time to the unconscious event with an average of 8 $\pm$ 8 months to the event occurring. [30]

Two studies by Pacifico *et al* [31] and Rinaldi *et al* [22] have included information on side effects associated with shock (all types). Pacifico *et al* [31] report dizziness in 25% of patients receiving a shock, fatigue in 19%, chest pain in 11% and dyspnea in 14%. Similarly Rinaldi *et al* [22] reported on symptoms before or just after shock delivery with 24% of patients experiencing dizziness and 4% chest pain.

The study by Rosenqvist *et al* [25] has classified adverse events related to the ICD device as severe or moderate according to the International Standards Organization (ISO) 14155 guidelines.[25] The ISO 14155 guidelines deal with the reporting of adverse events in clinical trials related to the use of medical devices. In this study events were classified as 'severe' if they caused 'hospitalisation or undue prolongation of hospitalisation because of potential disability or danger to life, necessitate intervention, or cause death'. All other events were regarded as mild. From the total population studied, which was very large (n=778), there were severe device-related events leading to death in 0.7%, non-lethal but severe events in 8% and mild device-related events in 3.8%.[25]

4.3 *What is the incidence of further shocks following an initial incapacitating shock in the following 2 years assuming a) no new medication/interventions have been put into place b) anti-arrhythmic medication or an interventional procedure has been introduced?*

There is no evidence available to address the effectiveness of treatment following an initial incapacitating shock and then recurrence of shocks in the following 2 years. One study was identified that looked at a group of patients who had experienced one shock in the previous 2 months and followed them up to investigate subsequent shock rates.[32] There are no details in this study about the incapacitating nature of the first shock or subsequent shocks. There was also no information regarding patient's treatment after the initial shock. This information is included as it is the only available evidence to address recurrence of shocks. After receiving the first shock, 60% of patients had received a second shock at 4 months.[32]

Table 4 gives details of studies that reported patients receiving more than one shock during follow-up. These studies are looking at the number of shocks in patients during the time frame of the study; however, it is not clear from this information as to the time gap between shocks.

Table 4 Studies detailing repeated shocks in patients with an ICD device

Study	Sample size	Time frame	Patients experiencing >1 shock
Kolb et al 2006[33]	100	Mean follow-up 52 months	Single chamber average no of shocks 1.5 ± 2.7 Dual chamber average no of shocks 14 ± 19
Carroll & Hamilton 2005[13]	59	12 months	8% >1 shock
Kamphuis et al 2003[14]	132	12 months	6% >3 shocks
Bänsch et al 1998[34]	421	26 ± 18 months	6.5% >1 shock
Grimm et al 1993[18]	241	12 months	6 ± 9 per patient
Kou et al 1991[30]	180	16 ± 12 months	Average 11 ± 17 shocks/person

A range of 6.5% to 8% of patients receiving >1 shock is reported in 2 studies, with follow-up times of 26 ±18 months and 12 months. One study reports 6% of patients experiencing >3 shocks.[14] Three studies report the average number of shocks per patient with a range between 1.5 – 11 shocks per person.[18,30,33] One study reports higher rates with dual chamber devices.[33]

5 Conclusion

It has not been possible to directly answer the questions posed in this request. The studies identified that include information on the incidence of shocks were primarily addressing other questions. Furthermore it was difficult to collate this information in the form of simple incidence rates at 1,3 and 6 months as population groups, follow-up times etc differed between studies. Studies often report the total number of episodes corrected by the device in a patient population (which may include other therapies delivered by the device) rather than the actual number of shocks per patient. Three studies contained information on the incidence of shocks at 6 months, which ranged from 6 - 35.5 shocks per 100 patients. With regard to severity of shock, there is very little data available related to this and severity is difficult to measure in this context as symptoms are likely to be very diverse. No evidence was identified to address specifically the issue surrounding recurrence of shocks post first incapacitating shock in patients who remain on medication, switch medication or have a procedure. Recurrence rates of shocks are measured in some studies in relation to the number of shocks experienced, but this information is of limited use to this request without information on the time

between shocks. In order to fully address the questions posed in this request a prospective study would need to be designed and carried out that specifically sought to investigate these issues.

5.1 Limitations of this report

This is not a systematic review but a rapid assessment for relevant literature. Although the search strategies were broad and comprehensive for both systematic reviews and primary studies, the searches for the latter were restricted to prospective studies and studies that measured the incidence of shock in patients with ICD devices. To aid comprehensiveness the reference lists of relevant articles were scanned for further studies. The results discussed in this report are from relevant articles from 704 identified articles. The information presented in this report could be further scrutinised to investigate the sources of variation in the results presented, however, a more in-depth analysis of the included results would need to be undertaken and is unlikely to add much additional information. Due to a lack of evidence directly addressing the questions raised in this request, the information contained has been taken from studies that are primarily addressing other questions. It is therefore likely that there are other studies that also have information nested within them that may be relevant to the questions posed in this request. It was not possible within the limitations of this report to identify all such studies that may have information of this nature.

6 References

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7 Appendices

7.1 Appendix 1 – Details of Request

1 ARIF REQUEST FORM

Date of request: 6/12/2006

Lead Medical Adviser issuing request: Name – Dr Jonathan Hanley, Secretary to the Cardiac Panel

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1. Without worrying about the structure of the question, state in full the nature and context of the problem.

1. We need to know the incidence of “shock” treatments from the ICD at 1, 3, and 6 months post first ICD implantation.

2. What proportion of shock treatment is incapacitating i.e. sufficiently sudden and intrusive to conclude that driving would be sufficiently compromised to make the affected individual a source of danger to themselves or other road users?

3. If an initial shock is incapacitating in an individual, what is the incidence of further incapacitating shocks in the same person over the proceeding 2 years if:-

   (a) No new medication/interventions have been put into place
   (b) Anti-arrhythmic medication } has been introduced
   Interventional procedure eg ablation

2. Please give a background to the question. Why has DMG raised this problem?

1. Currently an ICD implanted for secondary prevention (i.e. has been implanted after a putative arrhythmic event e.g. failed sudden cardiac death) precludes the holding of an ordinary driving licence for 6 months.
   This is based on the premise that the vast majority of recurrent arrhythmias requiring therapy occur during the first 6 months after implantation. What is not clear is whether there is evidence available that can confirm that the majority of such arrhythmias occur within a smaller window of time. e.g. the first 3 months post implantation for instance. Is there literature within the last 5 years than can clarify this?

2. ICD therapy in the form of "shock" (²_30j) treatment for ventricular arrhythmias has variable physical and neurological manifestations to include violent bodily movement(the man who throws the contents of his drink into the air!) or impairment of consciousness. The arrhythmia immediately preceding the shock may also impair alertness/awareness. The problem is that not all shock of similar strength affect different individuals in a uniform way. I.e. some may experience minor symptoms or just be aware of the device going off, others may be incapacitated. Also, curiously and anecdotally, in the same individual a shock may not produce the same physical or neurological expression. i. e. that person may on one occasion be incapacitated yet on another occasion not be so.

3. If an ICD "shock" causes incapacity then unless measures have been put into place to prevent recurrence (e.g. anti-arrthymic medication or radiofrequency ablation procedure to irritant focus) then a driving licence is withheld for 2 years.

3. Giving references where appropriate, briefly detail the sources you have used to obtain background information on the *options* and *issues,* which might be important for the problems, you describe.

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4. Please give name and contact details of any expert or clinical contact e.g. relevant Panel Chairman/expert Panel member.

Dr Mark Anderson
BSc MD MRCP
Consultant Cardiologist
Cardiac Centre
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Morriston
Swansea
SA6 6NL
[redacted]

Dr Mike Griffiths
Ma MD FRCP
Consultant Cardiologist
The Queen Elizabeth Hospital
Edgbaston
Birmingham
B15 2 TH

[redacted]

[redacted]

5. What is the nature of the target population of the issue detailed above? Eg. age profile, vocational drivers, young drivers, other co-morbid features.

Group 1 drivers of all ages.

6. What are the outcomes you consider particularly important in relation to the question posed? What decisions rest on these outcomes?

1. The results of the literature search could possibly allow relicencing to occur earlier than 6 months post ICD implant. 2. If the vast majority of shocks were not incapacitating again this might allow earlier licensing. 3. The results may allow us to consider our current licensing standards. (Section 1 Item 3.)

7. What is the latest date that an ARIF response would be of value | 29 / 2 |

Please either:: 0121 414 7878 marking FAO ARIF

E-mail as a word document or pdf attachment to: [redacted]

Post to: - Dr David Moore
Senior Research Reviewer and Analyst
Aggressive Research Intelligence Facility
West Midlands Health Technology Assessment Collaboration
Department of Public Health
University of Birmingham
Edgbaston
Birmingham
B15 2TT

Please ring 0121 414 3166 or 6769 if you have any queries, or you want to check the progress with your request.

7.2 Appendix 2 – Outline methods

To determine:

1. The risk and/or incidence of shocks associated with first implantation of an ICD device at 1,3 and 6 months

2. The proportion of shocks that are incapacitating causing danger to a potential driver or other road user

3. Incidence of further shocks over a two year period in these individuals assuming that a) no new medication has been put into place or b) Anti-arrhythmic medication or an interventional procedure has been introduced

The questions will be best addressed by cohort or large prospective studies that have followed-up patients with an ICD over time and assessed the incidence of adverse events such as shocks. This information will give an estimation of the incidence of shocks in patients with an ICD device over a period of time Preliminary searches suggest such evidence is available.

Information will be sought from these studies on the severity of shocks using adverse event data. Ideally we would hope to identify such data reported using the International Standards Organisation (ISO) standards for reporting adverse events associated with medical devices.

In order to answer question 3, studies that have followed-up patients who have already had one incapacitating shock and are either on anti-arrhythmic drugs or who have undergone an interventional procedure will be sought. We will use any studies containing relevant data to address this question. From our initial searches, we believe it is likely there will be insufficient published evidence to adequately answer this question.

Method:

- MEDLINE (1995-2007)*, EMBASE (1995-2007)* and the Cochrane Library (Issue 4 2006) and other relevant databases will be searched using a comprehensive search strategy for background information and studies. With changes in device type, information will be most relevant from the last 5 years
- The identified articles will be screened by an analyst for relevance
- Systematic reviews and primary studies following a cohort of patients with an ICD that report the frequency and severity of shocks will be selected and the studies with the largest sample size and/or most robust with regard to study design will be commented upon.
- The methodological quality of these studies will be discussed.
- Data on relevant outcomes will be extracted and reported.

*Searches were expanded subsequently but only studies published pre-1990 were included in this report

7.3 Appendix 3 – Search strategies

7.3.1 ARIF Reviews Protocol

SEARCH PROTOCOL FOR ARIF ENQUIRIES

(Oct 2006)

In the first instance the focus of ARIF's response to requests is to identify systematic reviews of research. The following will generally be searched, with the addition of any specialist sources as appropriate to the request.

1. Cochrane Library

- Cochrane Reviews
- Database of Abstracts of Reviews of Effects (DARE)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Health Technology Assessment (HTA) database

2. ARIF Database

An in-house database of reviews compiled by scanning current journals and appropriate WWW sites. Many reviews produced by the organisations listed below are included.

3. NHS CRD

- DARE
- Health Technology Assessment Database
- Completed and ongoing CRD reviews

4. Health Technology Assessments and Evidence Based guidelines

- NICE appraisals and work plans for TARs, Interventional Procedures and Guidelines programmes, Public Health excellence
- SBU – Swedish Council on Technology Assessment in Health Care
- NHS Coordinating Centre for Health Technology Assessments
- Canadian Agency for Drugs and Technologies in Health
- New Zealand Health Technology Assessment
- STEER Reports (no longer published)
- Agency for Healthcare Research and Quality (AHRQ)
- Alberta Heritage Foundation
- McGill Medicine Technology Assessment Unit of MUHC (McGill University Health Centre)
- Monash reports – Centre for Clinical Effectiveness, Monash University
- US Department of Veterans Affairs
- NHS QIS (Quality Improvement Scotland)
- SIGN (Scottish Intercollegiate Guidelines Network)

5. Clinical Evidence

6. Bandolier

7. National Horizon Scanning Centre

8. TRIP Database

9. Bibliographic Databases

- Medline – systematic reviews
- Embase – systematic reviews
- Other specialist databases

10. Contacts

- Cochrane Collaboration (via Cochrane Library)
- Regional experts, especially Pharmacy Prescribing Unit, Keele University (& MTRAC) and West Midlands Drug Information Service for any enquiry involving drug products.

7.3.2 Search Strategies

Database: Ovid MEDLINE(R) 1950 to January Week 3 2007
Search Strategy:

1 exp Defibrillators, Implantable/ or Defibrillators/
2 icd.mp.
3 (implantable adj (defibrillator$ or cardioverter$)).mp.
4 or/1-3
5 shock$.mp. or exp Shock/
6 countershock$.mp.
7 or/5-6
8 incidence.mp. or exp Incidence/
9 frequency.mp.
10 occurrence.mp.
11 or/8-10
12 4 and 7 and 11
13 (drive or driver$ or driving).mp
14 4 and 7 and 13
15 12 or 14

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1950 to Present
Search Strategy:

1 icd.mp.
2 implantable defibrillator$.mp.
3 implantable cardioverter$.mp.
4 or/1-3
5 shock$.mp.
6 countershock$.mp.
7 or/5-6
8 4 and 7
9 limit 8 to yr="2005 - 2007"
10 limit 9 to yr="2006 - 2007"

Database: EMBASE 1980 to 2007 Week 03
Search Strategy:

1 icd.mp.

2 implantable defibrillator$.mp. or exp Defibrillator/
3 implantable cardioverter$.mp.
4 or/1-3
5 exp SHOCK/ or shock$.mp.
6 countershock$.mp.
7 or/5-6
8 incidence.mp. or exp INCIDENCE/
9 frequency.mp.
10 occurrence.mp.
11 or/8-10
12 4 and 7 and 11

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature 1982 to December Week 2 2006
Search Strategy:

1 icd.mp.
2 exp Defibrillators, Implantable/ or implantable cardioverter$.mp.
3 implantable defibrillator$.mp.
4 or/1-3
5 exp SHOCK/ or shock$.mp.
6 countershock$.mp.
7 or/5-6
8 incidence.mp. or exp INCIDENCE/
9 frequency.mp.
10 occurrence.mp.
11 or/8-10
12 4 and 7 and 11
13 4 and 7

Database: Cochrane Library (Wiley internet version) 2006 Issue 4
Search strategy

#1 icd
#2 implantable next cardioverter*
#3 MeSH descriptor Defibrillators, Implantable explode all trees
#4 defibrillator*
#5 (#1 OR #2 OR #3 OR #4)
#6 adverse next effect*
#7 "quality of life"
#8 shock*
#9 driving
#10 side next effect*
#11 (#6 OR #7 OR #8 OR #9 OR #10)
#12 (#5 AND #11)

Trials Registers searched:

National Research Register
ClinicalTrials.gov

Other sites searched:

NCCHTA NHS Coordinating Centre for Health Technology Assessments
NICE, Interventional Procedures
AHRQ Agency for Healthcare Research and Quality
CADTH Canadian Agency for Drugs and Technologies in Health
MSAC Medical Services Advisory Committee
NIH National Institute of Health (US)
NZHTA New Zealand Health Technology Assessment
SBU Swedish Council on Technology Assessment in Health Care
NHS QIS (Quality Improvement Scotland)
Scottish Medicines Consortium
Clinical Evidence

Centre for Reviews and Dissemination
eMedicine
GP Notebook
Merck Manual

TRIS Online (National Transportation Library)
TRL (Tranportation Research Laboratory)
UNESCO
Highways Agency
CARE Europe
US Driving Assessment Symposia
Monash University Accident Research Centre
NHTSA (National Highway Traffic Safety Association)
National Centre for Statistics and Analysis (NHTSA)
NZ Fitness to Drive
Driving Assessment 2001, 2003 and 2005 International Driving Symposia on Human Factors in Driver Assessment, Training and Vehicle Design Various locations

Search terms used: icd, implantable next cardioverter*, defibrillator*, cardiac

7.4 Appendix 4 - details of included studies

7.4.1 Details of study, populations, follow-up and devices

Study	Year of study and place	Number of patients	Type of study	Patients details	Duration of follow up	Type of device and shock measurement
Chen et al 2006[35]	2000-2006 China	50	Prospective follow-up of consecutive patients	Ave age 56.8 ± 12.6 (84% male) with life threatening VT	3-67 months (mean 26.7)	Non-thoracotomy system single and dual chamber
Kolb et al 2006[33]	2000-2003 Germany	100	Randomised patients to single or dual chamber ICD (93% follow up – intention to treat used)	Ave age 60 ± 12 (89% male)	1,3,6,9 and 12 months (mean follow-up time was longer 52 months)	Information taken at clinic follow up visits range of devices used
Alter et al 2005[20]	1994-2005 Germany	440	Prospective - Cohort of patients having an ICD over 10 year period	Ave age 56 ± 14 years (82% male) mixed population of coronary diseases	46 ± 37 months	Pectoral non-thoractomy ICD lead Device recorded events
Carroll & Hamilton 2005[13]	Unclear USA	59	Prospective study	Ave age 63 (71% male) mixed population	12 months	No information
Backenköhler et al 2004[21]	Unclear Germany	205	Clinical trial population	Patients split into two populations (a) 202 survivors of cardiac arrest ave age 63 ± 11 (78% male) (b) 43 previously asymptomatic patients ave age 62 ± 10 (91% male)	(a) 3.8 ± 2.4 years (b) 4.2 ± 2 years	Single and dual chamber devices in both groups 161:84
Rinaldi et al 2003[22]	1984-2001 UK	171	Retrospective analysis of patient's records and ECG results	Ave age 62 mixed population	841 ± 928 days	Medtronic devices Single and dual chamber
Kamphuis et al 2003[36]	1998-1999 Netherlands	132	Longitudinal study - patient reported QoL using questionnaires but includes information on shocks	Mean age 55.2 years (73.5% Male)	1, 6 and 12 months	No details of devices
Schron et al 2002[15]	1993-1997 North America	373	Follow-up of patients in the AVID trial	Ave age 65 (81% male) patients with VT	3, 6 and 12 months	Shocks categorised by cardiac electro physiologist
Theuns et al 2001[23]	1998-2000 Netherlands	26	Prospective - Follow-up of patients with a new device detection system	Ave age 59 ± 15 (77% male)	Mean follow-up 8 ± 5 months	Phylax AV (Biotronik) with SMART detection™ system
Sticherling et al 1999[24]	Unclear Germany	52	Prospective - follow-up study	Ave age 62 ± 12 (88.5% male)	1, 3 month follow up	CPI Ventak AV II DR
Grimm et al 1999[37]	1992-1998 USA	144	Prospective – follow-up study	Ave age 54 ± 15 (82% male) mixed population	21 ± 15 months	Range of devices including Medtronic Jewel and CRI Ventak

Study	Year of study and place	Number of patients	Type of study	Patients details	Duration of follow up	Type of device and shock measurement
Namerow et al 1999[16]	1990-1996 USA + Germany	490 (53% randomised to ICD)	Follow-up of patients in CABG patch trial for QoL life study that also included incidence of shocks		6 months post ICD	Details of device type in original trial but not included in this study
Pacifico et al 1999[31]	Unclear USA + Europe	151	Clinical trail patients in the placebo arm of a clinical trial	Ave age 61 ± 11 years (82% male) with life threatening VT	12 months follow-up at 1,3,6,9 and 12 monthly intervals	No details of device type
Bänsch et al 1998[34]	1988-1995 Germany	421	Prospective - Consecutive patients	Ave age 58 ± 13 years (76.7% male) mixed population VT/VF patients and syncope	26 ± 18 months	Specific devices not detailed, range of devices used
Rosenqvist et al 1998[25]	1993-1994 European	778	Prospective – follow-up study	Ave age 58 ± 13 mixed population (82% male)	1, 3 and 12 months – average follow up was 4 months.	Medtronic 7219 jewel ICD
Schaumann et al 1996[26]	1995 Germany	124	Prospective study looking at efficacy of detection in ICD devices	Mean age 64 ± 10 years (88% male)	Patients visiting an outpatient clinic in 11 months period	
Villacastín et al 1996[27]	1986-1994 Spain	80	Prospective study of 38 patients and retrospective analysis of 42 patients.	Ave age 60 (71% male) survivors of a cardiac arrest and recurrent VT.	2-3 month intervals for up to 82 months (mean 21 ± 19 months)	
D'Avila et al 1995[12]	From1991 Belgium	46	Retrospective analysis - patients with a device that records time of shock included	Patients with ICD devices which were able to record shock time. Ave age 58.7 ± 11.9 years	9.4 ± 5.6 months	Ventax PRx/1700/1705 Device recorded time of shock
Grimm & Marchlinski 1995[17]	1982-1991 USA	49	Prospective study	Ave age 56 ± 14 years patients with cardiomyopathy (59% male)	25 ± 25 months	CPI 1400/10/20 CPI 1500/10/20 CPI 1550/55/1600 CPI PRx Medtronic PCD Ventak Cadence Device recorded events
Hamer et al 1994[32]	1988-1992 USA	29	Prospective - Patients who experienced a shock in previous 2 months included in study	Ave age 63 years mixed population	4 months follow up	Ventak 1550,1600, PRx, 1700, 1510 Patients wore an ECG device during study
Grimm & Marchlinski 1994[28]	Unclear USA	26	Prospective - Possibly a sub-group of previous study used to evaluate shocks in patients without previous shock on receiving a new device	Patients receiving a new device – no shocks were received with previous device in previous 3-5 years Ave age 56 ± 15 (73% male)	51 ± 16 months	CPI 1400/10/20 CPI 1500/10/20 CPI 1550/55/1600 CPI PRx Medtronic PCD Ventak Cadence

Study	Year of study and place	Number of patients	Type of study	Patients details	Duration of follow up	Type of device and shock measurement
				mixed population		Device documented and symptom assessment
Bremner et al 1993[29]	1983-1992 USA	381	Prospective - Consecutive patients	Ave age 62 years (80% male) cardiac arrest patients	0-9 years	Appropriate shocks classified by symptoms before the shock
Grimm et al 1993[18]	1982-1991 USA	241	Prospective - Consecutive patients	Ave age 60 ± 11 (80% male) mixed population	26 ± 22 months	CPI 1400/10/20 CPI 1500/10/20 CPI 1550/55/1600 CPI PRx Medtronic PCD Ventak Cadence Device documented shocks
Fogoros et al 1991[38]	1982-1991 USA	209	Prospective - Consecutive patients	Ave age 62 ± 10 (78% male) Mixed population	23 ± 21 months follow up	No details of device type. Appropriate shocks assessed by preceding symptoms
Kou et al 1991[30]	1986-1990 USA	180	Prospective - Cohort study from 2 centres	Ave age 60 ± 11 years (81% male)	16 ± 12 months	Ventak 1520, 1510, 1500 Symptoms and device recorded
Zilo et al 1991[39]	1982-1990 USA	53	Prospective - Consecutive patients followed-up	Ave age 58 (78% male) VF patients	31.5 ± 25 months	Device recorded events and symptom assessment

7.4.2 Results from included studies

Study	Comments and result findings	Time frame of measuring shock	Total who experience shocks per 100 patients	Appropriate shocks per 100 patients	Inappropriate shocks per 100 patients
Chen et al 2006[35]	Study in Chinese population 265 shocks of any type recorded in 38 patients	As study follow-up	78		22 (not clear if shocks only or if includes other therapies)
Kolb et al 2006[33]	Long-term follow-up study comparing single chamber with dual chamber ICD devices. Study contains survival free of shock curve. Average number of shocks in the single chamber patients was 1.5 $\pm$ 2.7 (range 0-10) and 14 $\pm$ 19 (range 0-305) in the dual chamber group. This was not statistically significant and the range of shocks in dual chamber group is very wide,	As study follow-up		No information on shock type	
Alter et al 2005[20]	This study was specifically looking at complications associated with devices, not appropriate therapies Overall 31% incidence of complications, unclear if only shocks	As study follow-up			12
Carroll & Hamilton 2005[13]	37% had shock in first 12 months (any reason) 8% had more than one shock QoL study that had some information on number of shocks received	12 months	37	No information on shock type	
Backenköhler et al 2004[21]	Only appropriate shocks investigated At least one shock in 42% group (a) and 51% group (b) Time to event data showed median time to first shock 151 days (a) range 10-1,624 and 178 days (b) range 11-1,831	12 months		43	
Rinaldi et al 2003[22]	Dizziness was reported by 24% of patients and chest pain in 4% Time to first appropriate shock was 290 + 272 days (range 1-1000) mean number of appropriate shocks 7.4 $\pm$ 11			34	
Kamphuis et al 2003[36]	26% of patients received an ICD shock Shocks in first 6 months 6% Shocks in second 6 months 15% Shocks in both 4% 6% had more than 3 shocks No shocks in 12 months 75%	6 months 12 months	6 26	No information on shock type	

Study	Comments and result findings	Time frame of measuring shock	Total who experience shocks per 100 patients	Appropriate shocks per 100 patients	Inappropriate shocks per 100 patients
Schron et al 2002[15]	Follow-up of AVID trial patients	12 months	39	94% of all shocks	6% of all shocks
Theuns et al 2001[23]	Results are reported as number of episodes treated by shock not number of patients. E.g 20 episodes of VT occurred in 4 patients, 10 were treated with shock therapy. This trial was evaluating a tachycardia discrimination algorithm designed to distinguish supraventricular from ventricular tachycardia	As study follow-up		No information	19
Sticherling et al 1999[24]	Inappropriate shocks measured by patient - 12 patients (23%) of total patients had appropriate therapy for VT but number of shocks detailed by episodes not patients. Evaluation of dual chamber ICD devices	As study follow-up		No information	8
Grimm et al 1999[37]	Inappropriate shocks only investigated This study was looking at complications associated with third generation ICD devices	As study follow-up		No information	16
Namerow et al 1999[16]	35.8% of patients received a shock in the first 6 months. 6-month QoL follow-up study of CABG Patch trial patients Paper presents a cumulative frequency plot of incidence of ICD discharges.	6 months	35.8	No information on type of shock	
Pacifico et al 1999[31]	48% had shock for any reason 25% associated with Dizziness 19% Fatigue 11% chest pain 14% dyspnea Information of side effects associated with shock	As study follow-up	48	No information on shock type	
Bänsch et al 1998[34]	54.8% of patients had at least one shock with 6.5% having more than one. Investigation into syncope in ICD patients with some information on shocks	As study follow-up	54.8	No information on shock type	
Rosenqvist et al 1998[25]	Severe device related adverse events and mild adverse events reported. Paper contains some information on inappropriate delivery of treatment from ICD. Severe device –related events were 0.7% for death and 8% for non-lethal but severe For mild adverse events 3.8% were due to ICD procedure 9 patients required hospitalisation (1.2% of total)	As study follow-up		No information	14.3

Study	Comments and result findings	Time frame of measuring shock	Total who experience shocks per 100 patients	Appropriate shocks per 100 patients	Inappropriate shocks per 100 patients
	It is not clear if these events are shocks or other device related events				
Schaumann et al 1996[26]	Overall incidence of shocks 39.1% follow-up times ranged from 6-49 months (average 20 months).	As study follow-up	39.1	27	12.1
Villacastín et al 1996[27]	30% of patients had a shock of any cause. Univariate analysis found significant correlation between LVEF% and incidence of shocks	As study follow-up	30	20	10
D'Avila et al 1995[12]	Shocks were assessed over a 24 hour period. 12am-6am – 11.4% 6am-12pm – 42% 12pm-6pm – 25% 6pm-12am – 20.5% Time between shocks 1-17 months average 4.3 ± 4 months Study investigating time to delivery of shock over an average 24 hour period to investigate circadian variation in shock delivery time	24 hours		No information on shock type	
Grimm & Marchlinski 1995[17]	59% had at least one shock . 20% had at least one shock of any type in the first year and 58% in the second year. Low patient numbers.	12 months	59	16 at one year 49 at two years	No information
Hamer et al 1994[32]	30 days – 31% ± 9% (standard error) 60 days – 41% ± 9% 90 days – 52% ± 9% 120 days – 60% ± 9% Subsequent shocks are being measured in patients who have had a shock in the previous 2 months	4 months post first shock	60	No information on shock type	
Grimm & Marchlinski 1994[28]	50% of patients had at least one shock. Brief report	As study follow-up	50	35	No information
Bremner et al 1993[29]	Time to first shock of any cause 8.5 ± 13 months Time to first appropriate shock 10 ±14 months range 0-5.5 years. Undetermined shocks in 46% of patients	As study follow-up		35	3
Grimm et al 1993[18]	76% had more than one shock. Any shock rates were 8% at 6 months and 15% at 12 months. Average of 6 ± 9 per patient of any shock (range 1-61)	6 month 12 month	8 15	7 13	No information
Fogoros et al 1991[38]	Risk of appropriate shock investigated 1 year risk 34% ± 3% 2 year risk 49% ± 5%	12 month		42.5	No information

Study	Comments and result findings	Time frame of measuring shock	Total who experience shocks per 100 patients	Appropriate shocks per 100 patients	Inappropriate shocks per 100 patients
Kou et al 1991[30]	59% of patients experienced at least one shock (average 11 ± 17 shocks/person) 9% of total population had unconsciousness associated with shock. Ave time to unconscious event was 8 ± 8 months (range 0.6-33 months) Study investigating severity of shocks related to unconsciousness. Description of cases also included	As study follow-up	59	No information on shock type	
Zilo et al 1991[39]	60% of patients experienced at least one shock of any kind. No data on appropriate or inappropriate rates	As study follow-up	60	No information on shock type	