PREVENTION OF SUDDEN DEATH WITH DRUGS AND DEVICES

KEY POINTS:

1. Many patients who die of sudden cardiac death have no warning symptoms.
2. Many others patients have had previous heart attacks, or have commonly complained of other cardiac symptoms.
3. Between 75,000 and 100,000 patients suffer a sudden cardiac arrest in the UK each year, many of these deaths are premature tragic deaths, and many have had a previous heart attack.
4. Measures to reduce the risk of recurrent of sudden cardiac death in patients with structural heart disease include stopping smoking and drug therapy with b-blockers, ACE-inhibitors, anti-platelet agents and lipid-lowering therapy, and all patients should receive such treatment in primary or secondary care.
5. Patients admitted to hospital after resuscitation from sustained ventricular tachycardia or fibrillation should be appropriately investigated as in-patients, with a view to implantation of an ICD if appropriate, during that admission.
6. Patients who satisfy the 2000 NICE criteria for ICD implantation should have urgent investigations to confirm or exclude structural heart disease, including documentation of left ventricular ejection fraction, and electrical or mechanical evidence of left ventricular dyssynchrony, as well as assessment of symptoms of heart failure
7. Patients with a familial condition with a high risk of sudden death, including long QT syndrome, hypertrophic cardiomyopathy, Brugada syndrome, arrhythmogenic right ventricular dysplasia (ARVD), and following repair of tetralogy of Fallot, should be evaluated by an electrophysiologist, and if risk-assessment suggests it, they should receive and ICD.
8. Over 400 children and young adults suffer a tragic sudden unexplained death each year.
9. Sudden unexplained death in young people occurs approximately 15x more frequently when there is a diagnosis of epilepsy, with recurrent seizures.
10. A major challenge exists to; to identify patients at increased risk of SCD, to rescue more patients who suffer SCD, to prevent them having a further SCD and save these lives with ICDs.
11. Certain patients with symptomatic heart failure have now been shown to benefit from cardiac re-synchronisation therapy with biventricular pacing, and further benefit if the device can also defibrillate the heart from a life-threatening arrhythmia. These patients are identified in newer randomised-controlled trials, and the full implications of providing treatment have still to be evaluated and recommendations made.
12. Up to 800/million patients have been estimated to be possible candidates for ICD therapy to reduce the risk of sudden cardiac death. Even with large amounts of money, these numbers cannot possibly be treated currently in the UK due to workforce constraints.
13. If all these patients were identified for ICD therapy, there would be waiting lists many years long, because of lack of staff and catheter laboratory time for implantation, and lack of space for effective follow-up.
14. Because of these constraints, patients should currently be treated according to greatest need, and a 10-year plan to expand services to meet demand devised and implemented.
15. ICD therapy has an off-putting high up-front cost, but is cost-effective compared to many treatments, eg chronic haemodialysis for renal failure, drug treatment for mild

Dr Derek T. Connelly, Cardiothoracic Centre, Liverpool

hypertension, and CABG for patients without LMS or 3-vessel coronary artery disease, all of which are far more expensive per quality-of-life year (QALY) gained.

16. Currently in the UK, ICD tariffs are very high, but ICD hardware costs have fallen significantly over 5 years. Realistic costing is needed. National tariffs and "Payment by Results" should help.
17. A measure of the comparative costs of ICD therapy can be judged by realising that:

    - The USA now spends $2billion/year on ICDs, achieving implant rates of 300/million, compared to less than 40/million in the UK.
    - The USA spends $100billion/year on *inappropriate* prescribing of antibiotics therapy.
    - The USA spends $30billion/year on treatments that have no evidence-base.

INTRODUCTION

The national service framework (NSF) for heart disease will now include clear standards for prevention and treatment of cardiac arrhythmia and their consequences that will lead to improvement in the quality and access.

This document sets out standards for the prevention of sudden cardiac death, and for the assessment and treatment of patients who have survived a life-threatening arrhythmia, as set out under the following headings:

- the aim
- the standards
- the rationale
- effective interventions
- service models
- immediate priorities
- milestones and goals
- holding the NHS to account – performance indicators

AIMS OF THIS CHAPTER

To indicate how the NHS can reduce patients' risk of sudden cardiac death, eliminate their symptoms and return to as full and active a life as possible if they have suffered a life-threatening arrhythmia

By showing:

- why sudden cardiac death is an important health problem
- the evidence-based interventions that will reduce risk of sudden cardiac death
- the service models that the NHS must put in place to reduce inequalities and inappropriately low rates of effective interventions
- milestones marking progress in NSF goals
- measures that will be used to mark progress

STANDARDS

The following standards should be achieved by the NHS.

Standard
People admitted to hospital after resuscitation from sustained ventricular tachycardia or fibrillation should be appropriately investigated as in-patients, with a view to urgent implantation of an Implantable cardioverter-defibrillator (ICD) if appropriate

Standard
Patients who satisfy the NICE criteria for ICD implantation should have urgent investigations to confirm or exclude structural heart disease, including documentation of left ventricular ejection fraction, and electrical or mechanical evidence of
left ventricular dyssynchrony, as well as assessment of symptoms of heart failure

RATIONALE

Why set these standards for the NHS?

Sudden cardiac death (SCD) is defined as death due to a cardiac cause within 1 hour of onset of symptoms, or unwitnessed death due to a cardiac cause. In practice most sudden deaths occur very quickly after symptoms commence.

Sudden cardiac death is not the same as a heart attack, or myocardial infarction. A cardiac arrest and sudden cardiac death may be associated with early phases of a myocardial infarction. Many sudden deaths occur when there is not an acute myocardial infarction [1]. Cardiac arrest may occur as a consequence of electrical abnormalities of heart muscle cells, and some such conditions may be congenital or inherited. Sometimes a cardiac arrest may occur in patients who have not been known to have any pre-existing structural or electrical heart abnormality, and cardiac arrest may even be the first manifestation of certain heart diseases.

Most cardiac arrests are caused by ventricular fibrillation (VF) or fast ventricular tachycardia (VT). VF is almost always fatal unless treated urgently (within a few minutes). Some patients with badly damaged hearts, who may be at risk of cardiac arrest, may have short-lasting episodes of ventricular rhythm disturbances [2,3] (non-sustained ventricular tachycardia), which may or may not cause symptoms.

Sudden cardiac death is a major public health problem, claiming 75,000 to 100,000 lives each year on the UK [4]. Despite improvements in training of paramedics and ambulance personnel, and despite increased provision of automatic external defibrillators, survival rates for cardiac arrest in the community remain low at less than 5%. Furthermore, unless a cardiac arrest can be shown to be due to a transient or reversible cause, the risk of recurrence is high [1], especially in those patients with poor left ventricular function (low LVEF).

EFFECTIVE INTERVENTIONS

What can be done by the NHS?

In certain patient groups, particularly those with heart failure due to damage to the pumping mechanism of the left ventricle, the risk of sudden death can be reduced by medication. The most effective drugs for this are the beta-blockers, (see other cardiac drugs) which block the effects of adrenaline on the heart. Several beta-blockers exist, but only a small number (including bisoprolol, carvedilol and metoprolol) [5-7] are proven to be effective in reducing sudden death (and improving overall survival) in patients with heart failure. Beta-blockers need to be used very cautiously in patients with heart failure, starting at a very low dose, with very gradual increases in dosage. If used at too high a dose too quickly they may do more harm than good, and cause a deterioration in the patient's condition.

Antiarrhythmic drugs have been used for several decades to treat patients with abnormal ventricular rhythms, but there remains little evidence for their effectiveness [8,9]. In fact, for patients with poor left ventricular function, most of the older (Class 1) antiarrhythmic drugs can in fact increase the risk of recurrent arrhythmias and sudden death [10]. These drugs are best avoided in high-risk patients with ventricular arrhythmias, although some of them may still have a role in selected patients with other arrhythmias such as atrial fibrillation.

Some of the newer (Class 3) antiarrhythmic drugs may have a neutral or even a beneficial effect on the risk of sudden death [11,12], although even some class 3 drugs have been shown to be harmful [13]. They may be useful in symptomatic treatment in patients who have multiple episodes of ventricular arrhythmias, and may be useful in reducing the amount of therapy patient receive from their ICDs [14], but their effectiveness in preventing sudden death appears to be weak at best.

By far the most effective therapy at reducing sudden cardiac death in high-risk individuals is the ICD [15]. Its use has already been approved by the National Institute for Clinical Excellence (NICE) in September 2000 [4], and the NICE recommendations are due to be reviewed in the near future, with consideration given to patient groups included in recently-published clinical trials. The recommendations given below may therefore need to be updated when the new NICE guidance becomes available. Currently the following indications are approved in England and Wales:

'Secondary prevention' [16-19] i.e. for patients who present, in the absence of a treatable cause*, with:

- Cardiac arrest due to either VT or VF.
- Spontaneous sustained VT causing syncope or significant haemodynamic compromise.
- Sustained VT without syncope / cardiac arrest, with left ventricular ejection fraction < 35%, in the absence of New York Heart Association (NYHA) Class 4 heart failure symptoms.

* (footnote) It has traditionally been assumed that cardiac arrest occurring in the acute phase of myocardial infarction does not constitute a long-term risk of recurrent cardiac arrest, and is not an indication for ICD implantation. The data supporting this approach were obtained long before the implementation of sensitive troponin assays, and there is now a risk that many patients with ventricular arrhythmias and a mildly raised troponin will be inappropriately labelled as having "VT / VF secondary to acute MI". It should therefore be made clear that ventricular arrhythmias *per se* may cause a rise in troponin T or troponin I, especially if resuscitation has been required.

'Primary prevention' [2,3] for patients with:

- a history of previous myocardial infarction and all of the following:
  (1) non-sustained VT on 24 hour ambulatory ECG monitoring
  (2) inducible VT on electrophysiological testing
  (3) left ventricular dysfunction with LVEF < 35%, in the absence of New York Heart Association (NYHA) Class 4 heart failure symptoms
- a familial condition with a high risk of sudden death, including long QT syndrome, hypertrophic cardiomyopathy, Brugada syndrome, arrhythmogenic right ventricular dysplasia (ARVD), and following repair of tetralogy of Fallot

Risk stratification for these conditions is dealt with elsewhere (ref McKenna and Griffiths chapters). Furthermore, the possible expanded indications for ICD implantation will be added to this section depending on the outcome of the new NICE guidance later this year.

The ICD as part of hybrid therapy for patients with life-threatening arrhythmias and a risk of sudden cardiac death

An ICD is not a cure. Its purpose is to treat ventricular arrhythmias after they occur, but it is not designed to prevent the arrhythmias actually occurring. Many patients with ICDs often need several medications for heart failure / poor left ventricular function, and some will require antiarrhythmic drugs [14]. Many will have required revascularisation, either by coronary artery bypass grafting or by percutaneous coronary angioplasty, and some will require revascularisation at some stage after ICD implantation. Those patients with coronary artery disease (whether revascularised or not) will require antiplatelet therapy and lipid-lowering therapy. Over and above all these considerations, these patients may need support in the day-to-day activities of living with an ICD. Patients having ICDs for 'primary prevention' indications will have to stop driving a car for at least one month, and those with 'secondary prevention' indications are banned from driving for at least six months [20]. Patients who subsequently get shocks from their ICDs are likely to be banned from driving for even longer. Vocational drivers (LGV and PCV licence holders) will lose their vocational licences and probably their livelihoods. Some patients are comforted by the thought of having their own implantable "life-saver" within their chests, but many are worried by the ever-present reminder of their cardiac risk and their mortality. A shock from the device is invariably painful, even although it may be life-saving, and some patients live in fear of shocks (appropriate or inappropriate) from the device. Some patients suffer increased anxiety as a result of having a defibrillator, and a small minority have severe psychological problems in adapting to life with a defibrillator implant [21].

The NICE guidance recognised these problems and recommended that protocols for the implantation of ICDs should be developed [4], to include:

- early referral of appropriate patients
- rapid decision making and implantation
- conscious sedation [22] rather than general anaesthesia
- a rehabilitative approach to after-care which includes psychological preparation for living with an ICD
- early discharge
- efficient and comprehensive follow-up

Preparing patients for life with an ICD

Paradoxically, "early referral" and "rapid decision making and implantation" leaves little time for "psychological preparation for living with an ICD". Often psychological problems are dealt with after the implant, not before. At the present time there is limited evidence for the efficacy of specific psychological therapies or rehabilitative strategies targeted at ICD patients. Electrophysiology nurse specialists are essential to support patients before and after ICD implantation, and crucial to achieving a good result in living with an ICD, (see Chapter 30).

Cost-effectiveness of ICD therapy

ICDs are expensive, and in the UK the expense of the device and the implant procedure has hindered development and led to an implantation rate significantly behind that of other comparable Western European countries. Cost analyses have been performed in several randomised controlled trials, but many of these are limited by the short duration of the studies [23]: if a study is terminated after three years or less (because of a dramatic reduction in mortality in patients treated with the device) and the device could last for up to six years, the apparent cost efficacy (in cost per life year saved) may be reduced not by 50%, but by up to 75%, and the device appears to be up to four times more expensive (in terms of "buying" additional years of life) than it ought to be. In economic terms, therefore, ICDs appear to be victims of their own success – they are highly efficacious in improving survival, they are proven in studies of short duration, and short duration studies exaggerate the expense of the devices. This is borne out by published data: cost analysis of studies lasting 5 years or more (such as MADIT) [24] have shown that the cost per year of life saved is around US$ 23,000 – 27,000; for shorter-duration studies such as AVID [25] and CIDS [26], the cost per year of life saved is calculated at over US$60,000.

A formal cost analysis, based on patient data from two large implanting centres in the UK (Liverpool and Papworth), has recently been completed as part of a Health Technology Assessment program. The cost-effectiveness conclusions in this analysis have however been criticised, both by other centres in the UK and by the report's own authors, as

- it is not based on randomised controlled trials but on observational data,
- many of the procedures for patient assessment and treatment have been "streamlined" in the past few years, and
- device costs have come down in recent years with bulk purchasing and competitive tendering.

Furthermore, the "quality of life" data in this study takes no account of the recent increase in usage of ICDs which incorporate biventricular pacing, (see left ventricular dyssynchrony) (see below) [27,28]. These devices have been proven to improve symptoms of heart failure, reduce the need for hospitalisation for heart failure, and improve quality of life in selected patients. In many large centres in the UK, biventricular ICDs now constitute up to 40% of ICD implants.

One consistent finding from all ICD trials is that the patients who are most likely to benefit from ICDs are those with poor left ventricular systolic function (LVEF less than or equal to 35%). In the meta-analysis of the major "secondary prevention" studies [19], almost all the benefit from ICD therapy was seen in this group of patients. The more recent studies (which will be considered by NICE in its deliberations) have targeted various groups of patients with poor LVEF, either patients post myocardial infarction [29] or patients with

heart failure [28,30]. Some evidence from subgroups of these trials suggests that patients with evidence of slow electrical conduction within the ventricles of the heart (manifest on the ECG by a wide QRS complex of more that 120 ms) may be at higher risk of sudden death, and that risk can be significantly reduced by ICD therapy. Coincidentally, this patient group may also be likely to benefit from biventricular pacing if they have symptomatic heart failure, and we can therefore identify a group of patients who might have improved quality of life (responding to biventricular pacing for heart failure) as well as living longer (consequent upon a reduction in sudden death from the defibrillator) if a defibrillator with biventricular pacing capabilities is implanted [28]. Such devices have been available in the UK since January 2000, and the implant rate continues to increase (figs from industry) as implant success rates improve and procedure times shorten. They are certainly more complex to implant than a single-chamber or dual-chamber ICD, but with experience a successful implant of a biventricular device can be obtained in more that 90% of appropriate cases. There is now strong evidence from randomised clinical trial data that ICDs with biventricular pacing, in patients with symptomatic heart failure associated with poor LVEF and wide QRS complexes, can reduce mortality and improve symptoms of heart failure, exercise capacity, NYHA class and quality of life [28].

SERVICE MODELS

Implantation of ICDs

Until recently, nearly all ICDs were implanted in tertiary cardiac centres by fully trained cardiac electrophysiologists or by pacemaker specialists. However, the implant technique is relatively straightforward, and there is no requirement for on-site cardiac surgical facilities. In recent years therefore there has been a certain amount of devolution of ICD services to district general hospitals (DGHs). In some parts of the UK this has been achieved by the appointment of fully-trained electrophysiologists to district general hospital posts; in others, a “hub and spoke” model has been implemented whereby one or more cardiologists from a regional centre have worked with colleagues in their local DGHs to set up local services and assist with initial implants and with “trouble-shooting” during follow-up.

In the future, whether most implants will be performed in regional cardiac centres or whether many will be devolved to DGHs with pacing and catheter laboratory facilities remains to be seen. It is important that centres where ICDs are implanted are able to adhere to the guidelines produced by the European Society of Cardiology [31], as mandated by the NICE guidance (Sep 2000) [4]. Different solutions may be reached in different regions [32], depending on local service provision, enthusiasm, expertise and competing local priorities.

Follow-up of ICDs

More important than implantation is the long-term monitoring, follow-up and support of these patients. Traditionally, ICD clinics have been run on the format of pacemaker clinics, usually coordinated by clinical cardiac scientific officers (physiological measurement cardiac technicians). However, ICDs are a lot more complex to follow up than pacemakers, and the patients tend to have significantly more ongoing problems. Ideally, an ICD follow-up clinic should be run not only by one or more cardiac technician, but in conjunction with an electrophysiology nurse practitioner or nurse specialist, trained in management of arrhythmias and heart failure and able to identify situations where each patient’s medical therapy may need to be adjusted. Medical input to the follow-up clinic should be routinely available, as a high proportion of patients are likely to need adjustment in their other heart medication as well as adjustments in device programming,

particularly as the proportion of biventricular ICDs increases, and the follow-up clinic therefore takes on the management of patients with severe heart failure. Some centres have already linked ICD follow-up clinics to established heart failure clinics, and this is to be commended.

Training and Workforce for ICDs

An increasing number of DGHs are performing ICD follow-up clinics. Crucial to the success of these ventures are the training of cardiac technicians to a high level, an appropriate level of medical and/or specialist nursing input to the clinics, and the forging of links with the tertiary centre for assessment of the many complex arrhythmia problems which may occur during follow-up. In particular, physicians and technicians following up ICD patients in DGHs should be aware of the drug therapy options, programming options, and ablation options which may be necessary for treatment of both atrial and ventricular arrhythmias in their patients. Courses are run both by industry and by professional bodies such as BPEG and UKICES, and in future it is intended that all physicians and clinical cardiac scientific officers treating patients with implantable devices should have a professional qualification approved by one of these bodies.

IMMEDIATE PRIORITY

The immediate priorities for implementing this area of the NSF are:

- delivering the early milestones

This will be monitored through performance management processes

MILESTONES AND GOALS

The milestones and goals set out below refer principally to secondary and tertiary care and *current* NICE Guidelines.

Milestones for hospitals admitting patients with ventricular arrhythmias

Milestone 1

By April 2006, every hospital should ensure that all people admitted with a diagnosis of ventricular tachycardia or ventricular fibrillation undergo echocardiography to determine the type and severity of structural heart disease (including LVEF).

By April 2006, every hospital should ensure that patients with sustained ventricular arrhythmias (VT or VF) not due to a transient or reversible cause and no contraindication to ICD implant, should be referred urgently for consideration of ICD implant during that hospitalisation.

Milestone 2

By April 2007, every hospital should have:

Clinical audit data no more than 12 months old that describe the delivery of the investigations and treatments listed above

Milestones for hospitals performing ICD implantation and follow-up

Milestone 1

By April 2006, every hospital performing ICD implantation should have:

- Two experienced ICD implanters.
- Clinical audit data for each implant, documenting reasons for implant, diagnosis, presenting arrhythmia (if any), LVEF, QRS width, and adherence to NICE guidance (or, if outside NICE guidance, additional reason or evidence for implant).

By April 2006, every hospital performing ICD follow-up should have:

- A computerised database of their patients.
- A multidisciplinary ICD follow-up clinic, with at least two experienced cardiac technicians and a suitably experienced cardiologist or a specialist electrophysiology nurse.
- An agreed protocol for access to rehabilitation and psychological support for patients.

Milestone 2

By April 2007, every hospital performing ICD implantation should have:

- Clinical audit data on follow-up of their implants, including complication rates such as re-operation and infection.
- Clinical audit data on ICD prescription, particularly with reference to biventricular pacing in those likely to benefit from this.

By April 2007, every hospital performing ICD follow-up should have:

- Clinical audit data on heart drugs and monitoring of their patients, with particular reference to medication for heart failure, secondary prevention of coronary heart disease, and monitoring for side-effects of antiarrhythmic drugs.
- Clinical audit data on rehabilitation and support for their patients, including referral rates to cardiac rehabilitation programs and psychological support programs.

HOLDING THE NHS TO ACCOUNT

The Commission for Health Improvement and Regional Offices of the NHS Executive will use both local and national indicators to judge the performance of individual organisations.

NHS organisations will be expected to demonstrate that, in implementing this NSF, they are making full use of the new mechanisms for improving the quality of care. This includes ensuring that local systems for clinical governance and life-long learning are used to promote the quality of services for the prevention and treatment of CHD.

NHS Performance Assessment Framework

Nationally the Performance Assessment Framework (PAF) and the associated High Level Performance Indicators (HLPIs) can be used to assess overall performance of the NHS. Equally the PAF can be used to assess performance of a specific aspect of the NHS, supported by suitable indicators. The CHD performance indicators, relevant to this chapter, fit within the areas of the Performance Assessment Framework as follows:

SUMMARY

This chapter has described

- why sudden death is an important problem
- the evidence-based interventions to reduce the likelihood of sudden death in high-risk patients
- service models to ensure equality and quality of care
- milestones to mark progress and the NSF goals
- measures that will be used to judge progress and performance

LAY SUMMARY

Patients who are saved from cardiac arrest and admitted to hospital are at high risk from the same thing happening to them again. This can be prevented by having a defibrillator fitted, provided this is appropriate and there is no other correctable cause from for the cardiac arrest.

Even if a patient has never had a cardiac arrest, there are now research studies that show that patients at high risk from a cardiac arrest can be distinguished from others by certain tests. Research shows that patients with abnormal or damaged hearts, usually after a heart attack may be at high-risk if the damage has been quite severe. These patients are likely to live longer if they receive an implanted defibrillator.

More recently, it has become clear that if patients have damaged hearts and have heart failure, an implanted defibrillator can allow them to live longer, and if this is fitted using special pacing techniques, there will also be a significant improvement in heart failure symptoms and quality of life.

Patients with deformed hearts at birth or rare inherited conditions may also be threatened by a cardiac arrest. These conditions cause overgrowth of heart muscle, weaken heart muscle, replace it with fatty tissue or affect the electrical currents in the heart, as in:

- Long QT syndrome.
- Hypertrophic cardiomyopathy.
- Brugada syndrome, arrhythmogenic.
- Right ventricular dysplasia (ARVD).
- Following repair of tetralogy of fallot.

Such patients should see an expert in arrhythmias, (cardiac electrophysiologist), and should also be considered for an implantable defibrillator.

Dr Derek T. Connelly, Cardiothoracic Centre, Liverpool

REFERENCES:

1. Cobb LA, Baum RS, Alvarez H III, Schaffer WA. Resuscitation from out-of-hospital ventricular fibrillation: 4 years follow-up. Circulation 1975; 52: Suppl III: 223-35.
2. Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. N Engl J Med 1996; 335: 2933-40.
3. Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G, for the MUSTT Investigators. A randomized study of the prevention of sudden death in patients with coronary artery disease. N Engl J Med 1999; 341: 1882-90.
4. National Institute for Clinical Excellence. Guidance on the use of implantable cardioverter defibrillators for arrhythmias, September 2000. http://www.nice.org.uk.
5. CIBIS-II investigators. The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II)): a randomised trial. Lancet 1999; 353: 9-13
6. Packer M, Bristow MR, Cohn JN et al. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. N Engl J Med 1996; 334: 1349-55.
7. MERIT-HF investigators. Effect of metoprolol CR-XL in chronic heart failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF). Lancet 1999; 353: 2001-7.
8. The CASCADE Investigators. Randomized antiarrhythmic drug therapy in survivors of cardiac arrest (the CASCADE Study). Am J Cardiol 1993; 72: 280-7.
9. Mason JW. A comparison of seven antiarrhythmic drugs in patients with ventricular tachyarrhythmias. N Engl J Med 1993; 329: 452-8.
10. The Cardiac Arrhythmia Suppression Trial (CAST) Investigators. Preliminary report: effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. N Engl J Med 1989; 321:406-12
11. Amiodarone Trials Meta-Analysis Investigators. Effect of prophylactic amiodarone on mortality after acute myocardial infarction and in congestive heart failure: meta-analysis of individual data from 6500 patients in randomised trials. Lancet 1997; 350: 1417-24.
12. Pedersen OD, Bagger H, Keller N, Marchant B, Kober L, Torp-Pedersen C. Efficacy of dofetilide in the treatment of atrial fibrillation-flutter in patients with reduced left ventricular function: a Danish investigations of arrhythmia and mortality on dofetilide (diamond) substudy. Circulation. 2001; 104: 292-6.
13. Waldo AL, Camm AJ, deRuyter H, et al. Effect of d-sotalol on mortality in patients with left ventricular dysfunction after recent and remote myocardial infarction. The SWORD Investigators. Survival With Oral d-Sotalol. Lancet. 1996; 348: 7-12.
14. Pacifico A, Hohnloser SH, Williams JH, Tao B, Saksena S, Henry PD, Prystowsky EN. Prevention of implantable-defibrillator shocks by treatment with sotalol. N Engl J Med 1999; 340: 1855-62.
15. Mirowski M, Reid PR, Mower MM, Watkins L, Gott VL, Schauble JF, et al. Termination of malignant ventricular arrhythmias with an implanted automatic defibrillator in human beings. N Engl J Med 1980; 303: 322-4.
16. The AVID Investigators. A comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. N Engl J Med 1997; 337: 1576-83.
17. Connolly SJ, Gent M, Roberts RS, Dorian P, Roy D, Sheldon RS et al. Canadian implantable defibrillator study (CIDS): a randomized trial of the implantable cardioverter defibrillator against amiodarone. Circulation. 2000;101:1297-302.
18. Kuck KH, Cappato R, Siebels J, Ruppel R. Randomized comparison of antiarrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest : the Cardiac Arrest Study Hamburg (CASH). Circulation 2000;102:748-54.

Dr Derek T. Connelly, Cardiothoracic Centre, Liverpool

19. Connolly SJ, Hallstrom AP, Cappato R, Schron EB, Kuck KH, Zipes DP, et al. Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials. Eur Heart J 2000;21:2071-8.
20. Driving and Vehicle Licensing Authority. At a glance guide to the current medical standards of fitness to drive – a guide for medical practitioners. http://www.dvla.gov.uk/at_a_glance/content.htm
21. Bourke JP, Turkington D, Thomas G, McComb JM, Tynan M. Florid psychopathology in patients receiving shocks from implanted cardioverter-defibrillators. Heart. 1997;78: 581-3.
22. Lipscomb KJ, Linker NJ, Fitzpatrick AP. Subpectoral implantation of a cardioverter defibrillator under local anaesthesia. Heart. 1998;79: 253-5.
23. Salukhe TV, Dimopoulos K, Sutton R, et al. Life-years gained from defibrillator implantation: markedly nonlinear increase during 3 years of follow-up and its implications. Circulation. 2004;109: 1848-53.
24. Mushlin AI, Hall WJ, Zwanziger J, Gajary E, Andrews M, Amrron R, Zou KH, Moss AJ. The cost-effectiveness of automatic implantable cardiac defibrillators: results from MADIT. Circulation 1998; 97: 2129-35.
25. Larsen G, Hallstrom A, McAnulty J, et al. Cost-effectiveness of the implantable cardioverter-defibrillator versus antiarrhythmic drugs in survivors of serious ventricular tachyarrhythmias: results of the Antiarrhythmics Versus Implantable Defibrillators (AVID) economic analysis substudy.Circulation 2002; 105: 2049-57
26. O'Brien BJ, Connolly SJ, Goeree R, Blackhouse G, Willan A, Yee R, Roberts RS, Gent M. Cost-effectiveness of the implantable cardioverter-defibrillator : results from the Canadian implantable defibrillator study (CIDS). Circulation 2001;103:1416-21.
27. Abraham WT, Fisher WG, Smith AL et al. Cardiac resynchronization in chronic heart failure. N Engl J Med 2002; 346: 1845-53.
28. Bristow MR, Saxon LA, Boehmer J et al, for the COMPANION investigators. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med 2004; 350: 2140-50.
29. Moss AJ, Zareba W, Hall WJ et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction N Engl J Med 2002; 346: 877-83.
30. Bardy GH, for the SCD-HeFT investigators. The Sudden Cardiac Death in Heart Failure Trial. http://www.sicr.org/scdheft/index.html , accessed March 2004.
31. Levy S, Hauer RN, Raviele A, Daubert JC, Campbell RW, Breithardt G. Recommendations for qualifications of centres implanting defibrillators Eur Heart J 1996; 17: 1796-99
32. Winters SL, Packer DL, Marchlinski FE, Lazzara R, Cannom DS, Breithardt GE, et al. Consensus statement on indications, guidelines for use, and recommendations for follow-up of implantable cardioverter defibrillators. PACE 2001; 24: 262-9.