Response to: Implantable cardioverter defibrillators for the treatment of arrhythmias and cardiac resynchronisation therapy for the treatment of heart failure (review of TA95 and TA120)

1. The general standard of writing in the document is not high. For example, the word “parameter” is used frequently, and incorrectly. Little things, such as switching back and forth between UK and US spellings (“ischemic” and “ischaemic”) are just irritating.

   There is frequent use of the construction “… with both conditions” – which is unhelpful. There’s a section entitled “People with both conditions” in the executive summary, but there is no effort to define what these conditions might be. The definition appears later in the main text, but is a very unhelpful and ambiguous separation of patients. Sliding between “people with both conditions” and “population 3”, for example, reads poorly. Subsequently throughout the text the phrase “patients with both conditions” appears – and given that the division of patients into these conditions is wholly artificial and with limited clinical relevance, confusing every time it appears.

   Sentences such as “No significant difference was found in QoL” appear very frequently, but are very ambiguous – no difference between groups? Or between baseline and treatment? Similarly “Up to 30% of the ICDs groups” reported adverse effects: well, is that 30% of the groups had at least one patient with an adverse effect, or 30% of the patients randomised to ICD?

   These are just some sentences picked out more or less at random, but such imprecision is rife throughout the document, and lessens one’s confidence in it. Some of the prose is simply impenetrable.

   I have no doubt that the economic analysis has been conducted thoroughly and rigorously, but the overall document reads as if there has been minimal input from actual clinicians.

2. The figures did not survive to reach my desk, so I am unable to comment further about any of them.

3. One of the premises in the executive summary is incorrect: “[…] ICDs in addition to optimal pharmacological therapy (OPT) for the treatment of people who are at increased risk of SCD as a result of ventricular arrhythmias despite receiving OPT” – around half of sudden death is due to bradycardia. ICDs have a pacing function and thus prevent death from bradycardia, too.

4. Surely one of the objectives should have been to attempt to assess the clinical- and cost- effectiveness of CRT-D versus CRT-P using the

existing data.

5. One of the reasons I think there must have been little clinical input into the writing of the document is the categorisation of the patient populations. The division of patients into different populations is not especially helpful, and the definitions of the different populations suggest that there is a deal of misunderstanding in thinking about the patients.
    a. The first population, those at risk of sudden death: either this should consider all people at risk of sudden death (including congenital heart disease, hypertrophic cardiomyopathy, chanelopathies and so forth); or should acknowledge that the defining feature of the group actually being considered in the manuscript is those with left ventricular systolic dysfunction. It's important, too, to recognise that sudden cardiac death can be due to bradycardias, not just ventricular tachyarrhythmias.

    b. For the second population, statements suggesting that the trials examined were conducted in patients "at risk of heart failure due to LVSD and cardiac dyssynchrony" are profoundly incorrect and suggest a fundamental misunderstanding of the patient group studied. In the key studies of CRT, the patients were recruited on the basis of having left bundle branch block, and absolutely NOT on the basis of any measure of "dyssynchrony".

       The only exception was CARE-HF in which a small sub-set of patients were included on the basis of left bundle branch block, a QRS duration between 120 and 150 ms, and some echocardiographic evidence of dyssynchrony.

       Sections headed "*People with heart failure as a result of LVSD and cardiac dyssynchrony*" are just simply wrong from the outset. (The phrasing in fact suggests that the "cardiac dyssynchrony", whatever that is, is the cause of the heart failure.) I suspect what the authors actually mean is "People with heart failure caused by left ventricular systolic dysfunction who have left bundle branch block".

       The call for a trial in patients with "non-ischaemic cardiomyopathy in the absence of dyssynchrony" is similarly flawed. Perhaps the authors mean "People with heart failure caused by left ventricular systolic dysfunction in the presence of normal coronary arteries who do not have left bundle branch block".

6. Although some mention is made of men *v* women in the CRT section, none seems to be made in the ICD section. Meta-analysis suggests that there is no benefit from ICDs in women (*Arch Intern Med* 2009;**169:**1500)

7. The section on heart failure physiology reads like an undergraduate text from 20 years and is wrong in several regards. The section on medical therapy is similarly poor.

8. Definitions of cardioversion *v* defibrillation are wrong.

9. The section defining what CRT does is simply woeful.

10. “modern ICDs provide the functionality of a standard pacemaker” – no: are there any ICDs that do not?

11. There appears to have been no effort at all made to address important issues in trying to determine clinical- and cost- effectiveness of these devices. Concerns include, for example:
    a. For CRT
        i. Whether there is any virtue in offering CRT to people with atrial fibrillation
        ii. Whether there is any virtue at all in measuring “dyssynchrony”
        iii. Whether there is any virtue in offering CRT to people without left bundle branch block
        iv. Whether clinical “response” relates to survival benefits or not.
    b. For ICDs
        i. What features should help guide selection of patients for ICD?
        ii. what are the consequences of using published risk scores to guide selection in terms of clinical- and cost-effectiveness?