

Dear All

This review of the evidence for CPAP efficacy and cost effectiveness is extremely comprehensive and authoritative. There are aspects of the York economic model that I am not qualified to comment on, due to its specialist nature. My comments are relatively minimal. Because I have read it carefully, any simple errors spotted I mention in case no one else does.

General

- 1) It is disappointing that the wider costs of road traffic accidents cannot be included. I appreciate that NICE'S remit is health costs, however I do believe it would be appropriate in a document such as this to at least mention that there are other cost savings to make from reducing accident rates that further increase the value for money from treating OSA with CPAP. There are several other areas mentioned in the report but saying they are outside the area to be considered.
- 2) Efficacy is taken compared to placebo rather than baseline. I appreciate this choice is debatable. To use placebo as the comparator is scientifically correct to prove efficacy, but using baseline as the comparator provides the true increase in health status. Placebo CPAP comes with all the peripheral components of CPAP provision, the enthusiasm of finally having one's diagnosis made, the attention given, the prediction of improvement etc. It is likely that the placebo effect would wear off. Whilst I am not suggesting baseline as a comparator for this analysis, again I am suggesting that this point be included in the discussion: the possibility that the treatment effect may be larger than incorporated in the model, and that this is one of its limitations.

Specific

- 1) 3.1.3, page 22. It is a little misleading to say treatment is targeted at the symptom of sleepiness rather than correcting the breathing disturbance – if this were true then amphetamines would be a suitable treatment. It would be more correct to say that treatment is targeted at sleepiness through correction of the breathing disturbance.
- 2) Page 26 and others (e.g. 132). Adherence rates less than 100% are not solely due to treatment failures. Some stop using CPAP because their OSA gets better. This is achieved sometimes through weight loss, tonsillectomy, dental devices etc. It is therefore worth pointing this out and that not all treatment discontinuers return to baseline levels of health status. Again, I appreciate the very limited data on this issue, but a recognition of the limitation of the 'return to baseline' assumption should be acknowledged.
- 3) Page 27 – top paragraph. Not entirely clear to what population size the final cost figures apply.
- 4) Page 78. I think one of the references is wrong. You quote 77 as one of the driving simulator studies – I think you mean 118. This error recurs in several other places including pages 236, 221 where you quote Jenkinson et al [77] rather than Hack et al [118].
- 5) Page 127 and others (e.g. 150, 156). You assume the only vascular benefit from CPAP derives from a reduction in BP. There are two studies on cholesterol reduction following CPAP, and there is the completely uncontrolled data from Partinen et al and Marin et al suggesting a much larger effect. On the other hand, the BP reduction from CPAP in OSA might not be as effective at reducing stroke etc as found in drug trials for example. Thus there is considerable uncertainty, and taking a prediction from Framingham type models is a pragmatic solution. The uncertainties that this might be an over estimate are discussed, but not that it might be an underestimate – which is biologically plausible given the pulsatile nature of the BP rises at night, the cholesterol changes, and several other as yet completely unproven hypotheses based on intermittent hypoxia and vascular inflammation.
- 6) Page 143 and others. You correctly (in my view) point out that these trial results have been delivered in the context of a proper diagnosis by experts. Thus they are not 'extrapolatable' to other less rigorous environments. However it is not just proper diagnosis that is important, it is also the environment in which CPAP is delivered. All RCTs have been from units that provide a good CPAP induction program for patients. RCTs have shown that more effort from trained staff produce better adherence rates,

for example. So I would include proper CPAP provision by trained staff in these sections as well as proper diagnosis.

- 7) Page 143 and 153. The issue over dental devices is difficult since most areas do not provide or have the expertise to provide such devices on the NHS. I think the NHS prices you quote are way below what a hospital dental service would try and charge! There is no way around this other than to increase the assumed tariff to something a little more realistic.
- 8) Page 150. I think it would be worth pointing out how sensitive the York model is to the time horizon used. For example, if CPAP is only used for a year then it is very cost ineffective (e.g. as per the Chilcott model). This does feed through to clinical practice. For example, some areas have stopped following patients up after a year. The experience of our sleep nurses is that patients may stop using CPAP because of a problem which without expert help they don't immediately sort out, become sleepy, and then don't bother. Whereas with some input they can be re-established. Again this is soft, but the model informs clinical practice that by not ensuring continued use you are potentially wasting resources. In practice this follow up can be done anywhere and will eventually have to occur in general practice due to the numbers of patients involved.
- 9) Page 201, table 11.1. I do not understand why this table is a reduced version of the earlier one (5.2) on page 48. I have perhaps missed the explanation somewhere.
- 10) Page 201, table 11.2. 'Mild' rows. Surely removing the Robinson study (the positive one) should leave 0, -2.3 to 2.3, - I think the numbers are opposite the wrong authors.
- 11) It is extraordinary that the Monserrat 2001 study found no change in E&V in the SF36, but found such a big improvement in ESS, when they are measuring something so similar. I suspect they made an error we nearly made, that of mis-scoring the SF36 because of the change in direction of some of the numberings. I discussed this with Montserrat at a recent meeting and he agreed to go back and look if possible, as he too felt there was something extremely odd about the result.
- 12) Table on page 210, Summary component scores. There is probably an obvious reason but I am not sure why the Summary component scores from the Jenkinson paper are not included.

Prof J Stradling
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