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Our ref: JRS 21/12/2007

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Technology Appraisal Manager
NICE
[redacted]

Dear Chris

I am responding on behalf of [redacted] and the BTS, from the Oxford Sleep Unit, and also for the RCP who have said that they will be happy for the BTS to respond on their behalf.

We are most impressed with the thoroughness of the NICE process and overall the report is fair and exactly what we believe to be correct.

Using your headings:-

i) Do you consider that all of the relevant evidence has been taken into account?

Yes, mainly.

However, it is unfortunate that there is so little data on quality of life in patients with severe OSA which led to a meta analysis of this outcome not being possible in a severe subgroup. It also meant overall that many of the subscales just missed 'significance'. The mapping done by [redacted] group of ESS across to SF36 shows that the two are strongly correlated; thus one of the studies (86) that found a big difference in ESS, and no change in the vitality subscale of the SF36, is a clear outlier. The appraisal group is therefore right not to have made much of this apparent failure of CPAP to improve quality of life, it makes no sense.

We think that the cost efficacy data feel correct, although the inability to include the wider costs of vehicle accidents is disappointing. We would suggest that the inability/failure to do this is highlighted as a deficiency that, if taken into account, would further reduce the cost per QALY. There is only one brief reference to this in 4.3.2.

The section 4.3.11 specifically concludes that accident costs should be *excluded* because patients are stopped from driving when diagnosed, therefore treatment would make no further difference. However, this is a severely erroneous approach (as pointed out at the appraisals meeting). If there is no treatment available then there is no point in running a diagnostic service – thus the diagnosis is not made and patients remain on the roads, having accidents: diagnosis and treatment go hand in hand. There is no point in diagnosing just to take patients off the road and then not treating them.

ii) Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate?

Yes. Although some of the points above are pertinent.

Section 4.3.14 lumps different machine issues along with added humidification. Whereas it is correct to make no differentiation between fixed pressure and auto-CPAP machines (there is no evidence suggesting a significant difference in efficacy), there is data on humidification, as reviewed by the Cochrane group.

iii) Do you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS?

As regards the sections 1.1, yes.
In section 1.2 it might be wiser to say that *treatment is indicated in mild obstructive sleep apnoea with troublesome symptoms*. As it reads at present, it implies that CPAP is appropriate for mild symptoms, which most would not feel was the correct conclusion from the data.

As regards section 1.3, this is a potential problem. What is a specialist in sleep medicine? The SIGN OSA guidelines tried to define this and suggested that training as a respiratory registrar with a period on a sleep unit would be the minimum for a clinician. In fact on page 156 (8.4) there is already a definition of a specialist centre which we are surprised has not been used. The non-medical staff would have to have demonstrated an appropriate training on a suitable course or through an apprenticeship on an existing unit. It is important to point out that all the RCT data have come from such experienced units. There is no guarantee that similar results will accrue from inadequately trained staff/units.

A further problem is that 1.3 only refers to monitoring the initial response. Of course, if the patient is not supported thereafter with advice and replacement parts for the head gear and mask etc then he will stop using it and the whole process will have been a waste of time and money. Thus we think that a statement suggesting that continuing specialist support thereafter is required would be appropriate. Certainly these costs are in the economic model.

Therefore we would modify 1.3 to …. *and monitoring of the response should be carried out by a specialist service with appropriately trained medical and support staff.*

iv) Are there any equality related issues that may need special consideration?

Not that we can see.

OTHER SPECIFIC POINTS

2.2 in the preliminary appraisal consultation document says that *OSAHS is usually diagnosed by a sleep medicine specialist by overnight oximetry in the persons home, or occasionally by an overnight polysomnography in the sleep medicine centre*. It then defines the condition on the basis of AHI – only derivable from a respiratory polysomnography type study, not oximetry! The evidence for any of this has not really been reviewed but is important. OSAHS includes the word [redacted] at the end and is not just a sleep study but includes clinical assessment, mainly the history. We would say that:-
OSAH[redacted] is usually diagnosed from a suggestive history and a positive sleep study. In most cases limited studies of oxygenation and/or respiration ('respiratory polysomnography' or 'limited studies') are enough to provide a diagnosis and assess severity (this is the case in moderate to severe disease and when no other diagnosis such as heart failure is likely). In a minority, further studies using more extensive multi-channel equipment (full polysomnography) may be required, especially when alternative diagnoses are being considered. (Indeed this is what page 156 (8.4) of the main document actually says too.) *The [redacted] of OSAH[redacted] is usually assessed on both symptoms (often the degree of sleepiness) [redacted] the sleep study, either by using the apnoea hypopnoea index (AHI) or oxygen desaturation index, which are roughly equivalent. Mild OSAH (*no S*),when using sleep study alone, is often defined as AHI 5-14, moderate 15-30, and severe >30: the cut off between mild and moderate when using desaturation index is sometimes set at 10 rather than 15.*

In 2.3, *abnormalities* should read *characteristics*, as the retrognathia (and other subtle differences) that can contribute to OSA can be within the normal range rather than abnormal.

In 2.4, we would add *witnessed apnoeas* and *otherwise unexplained nocturia* to the list of OSA symptoms. We would also stress the value of recognizing and treating OSA by adding *Thus referral to a specialist sleep service is recommended when OSAS is suspected.*

In 4.1.11 the text says that *no study found a statistically significant difference in any of the sub scales* etc. This is [redacted] correct, the Lancet 1999 study from our group (Jenkinson, 77) did find a significant difference as shown on your pages 208 (Emotional role, Mental health), 209 (Physical role), 210 (Vitality). For some reason (previously pointed out), the summary component scores (Mental and Physical) from the Jenkinson study (table 3, paper page 2102) have been accidentally left out of the tables on page 210. This should be corrected as the mental component

summary score was significantly different between real and placebo (P = 0.002). In addition the study from Engleman (78) also showed a significant difference in the vitality subscore (your page 210). Thus the statement in 4.3.5 is unduly pessimistic in my view.
In the blood pressure assessment, it is unclear why the Faccenda data (94) are not included, other than in the table of studies considered.

In 4.1.13. There is an error in reporting the minimal likely compliance (23-82%), i.e. the 23%. This probably comes from the same error on page 10 of the overview, there is an entry in table 3 under Stradling et al 1997 suggesting a compliance of 0.64 and 0.23 at 6 weeks. We assume this is the Thorax 1997:51;72 paper and these data have been quoted incorrectly. The minimal compliance figures were 0.64 and 0.73 with a further 0.23 and 0.25 undecided at 6 weeks whether to continue or not. These numbers should be corrected in the table and in section 4.1.13.

Section 4.1.14 is in our view not quite correct and would suggest ……*...that there are enough trained medical staff in secondary care to investigate the necessary numbers of patients with likely OSA, but further training of support staff for CPAP provision will be necessary over the coming years. There are currently insufficient resources and training in primary care for the continued supervision of patients with OSAHS on CPAP*.

Section 4.3.11 We did not understand this section. Some of the so called driving simulators do not really simulate driving at all (e.g. 'Steer Clear'). When the more sophisticated simulators were used, then the RCTs were positive. Therefore we think that this section is too 'pessimistic' on this issue and should imply that the data are mixed but the more sophisticated simulations suggest a significant improvement on CPAP. This is also the section containing the rather odd decision to exclude the costs of road traffic accidents as discussed above.

Section 4.3.13 suggests that OSAHS is very rare among young people. In children of the age where enlarged tonsils are often found (usually 2 to 8yrs or so), OSAHS is relatively common, in adolescents the prevalence is probably lower but, in the USA, studies have suggested that the increasing levels of obesity are generating significant numbers of cases. We would suggest simply changing *very rare even* to *less common*.

There is a statement on page 4 of the overview that compliance is a problem with CPAP. This implies that it is a *particular* problem, whereas in fact (as pointed out at the appraisal meeting) the compliance is better than with anti-hypertensives and anti-asthma therapy. We think the statement should simply read that compliance can be improved with the methods detailed, rather than starting with the statement that there is a problem.

We hope these comments are useful and that the committee will consider incorporating them into the final appraisal.

One again, congratulations on a very professional effort.

[redacted]For the BTS, RCP and Oxford Sleep Unit.