Is varenicline cost-effective enough to be funded by the NHS now?

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These are promising times for those treating smokers in the UK services with the launch of an effective new smoking cessation medication after many years when there has been little new to offer those unable to quit with existing treatments. ASH have issued a preliminary guide to varenicline (1) and The Cochrane Collaboration have completed a comprehensive efficacy review to be published early in the 2007 (Cochrane Library 2007, Issue 1) (2). This note is intended to supplement these by providing an estimate of the cost effectiveness of varenicline in the NHS.

Background

In September varenicline (Champix, Pfizer) was given a marketing license to aid smoking cessation by the European Medicines Agency (3). Following the launch of varenicline in the UK on December 5th PCTs and others will need to decide if they fund varenicline. Whether varenicline is viewed as sufficiently effective and safe for the NHS need not be in doubt, given the extensive license review undertaken by the EMEA and the FDA in the US. As a new drug it will be subject to post-marketing surveillance and will be part of the MHRA "yellow card" safety reporting scheme (4). No unexpected side effects have come to light after several months of use in the USA.

On the important issue of cost-effectiveness to the NHS, NICE guidance on varenicline will probably not be issued until the late Spring of 2007 (5). However, unless their previous very positive recommendations on existing smoking cessation treatments are completely reversed, they are likely to conclude that varenicline is also highly cost-effective and will recommend it to the NHS.

How cost-effective is varenicline?

Cost-effectiveness models for smoking cessation treatments are quite complicated, involving lifetime effectiveness projections, lifetime health gains, economic discounting, and costs in practice (6). In the 2002 NICE assessment of the cost-effectiveness of NRT and bupropion (Zyban, GSK) all these elements were considered. Fortunately, a cost-effectiveness estimate for varenicline sufficiently accurate for NHS funding decisions need not involve detailed statistics and economics. One need only use an established NHS cost-effectiveness figure for bupropion and modify it for differences in cost and efficacy between varenicline and bupropion. Below are the simple calculations.

(1) The NICE upper limit is about £20-30K to gain a life year in the NHS

Although NICE do not publish the figure, it is accepted that they typically recommend a treatment to the NHS if the cost is less than about £20 - £30K for each life year gained (LYG).

(2) Bupropion gains a life year for about £1100.
In 2002 NICE recommended bupropion and NRT to the NHS and cited them as, "among the most cost effective of all healthcare interventions" (7). Quoting several alternative figures they concluded with a general LYG figure at UK discount rates of "below £2,000 per life year gained". This figure being at least 10 – 15 times below the NICE "bar" they probably did not need to be more precise. The average for NHS treatments is about £15k to gain a life year. More precise details were given in the parallel NHS Health Technology Assessment (8). It gave the following LYG estimates:

Bupropion SR	£1100	(range £640 - £1500)
NRT	£1700	(range £1000 - £2400)

(3) In practice varenicline will cost about 60% more than bupropion
A12-week course of varenicline will cost £164, compared to about £120 - £150 for NRT and £80 for the full 8 week course of bupropion. In practice, many smokers starting treatment will not return to take the full course and this changes the actual cost to the NHS. The packaging of varenicline (2-week or 4-week packs) allows it to be prescribed according to the same regime that NICE recommended for NRT: 2 weeks, 2 weeks, 4 weeks, 4 weeks. Bupropion is prescribed in 4 week packs. Assuming that 70%, 50% and 40% of patients return for additional medication after 2, 4, and 8 weeks respectively, gives an average cost to treat a smoker with varenicline of about £96. For bupropion the average cost would be about £60, and for NRT about £79. In practice varenicline will therefore cost about 60% more than bupropion and 20% more than NRT.

(4) Varenicline is about twice as effective as bupropion
The efficacy of varenicline and bupropion have been directly compared in two large well-designed multicentre trials, and one less well designed trial where previous users of bupropion were allowed to take part (2). In the two better designed trials bupropion increased the 12 month continuous success rate by 6% above that for counseling alone and varenicline increased it by 13%. The specific efficacy of varenicline was therefore about twice that of bupropion.

[This figure from direct comparisons of the two treatments in the same trial can be almost exactly replicated by comparing how much more effective than placebo each treatment is across all the placebo controlled trials that have only included one or other treatment. Cochrane (9) calculate an odds ratio of 2.00 for bupropion and 3.22 from the four varenicline trials (2) (note: the ASH document omits two trials and therefore cites a slightly lower figure of 2.85). The increases in 12 month continuous abstinence rates were about 8% and 14% for bupropion and varenicline, respectively. The numbers needed to treat were 13 and 7 for bupropion and varenicline, respectively. Hence, to achieve each long term

success attributable to bupropion one might need to treat almost twice as many smokers as with varenicline].

(5) Varenicline cost-effective estimate
Combining figures from (2), (3) and (4) gives a cost-effectiveness estimate for varenicline, based on the NHS estimate for bupropion:

Varenicline cost per life year gained = (£1,100 x 1.6)/2.0 ~ £900.

In the above, the NHS cost per LYG figure of £1,100 for bupropion is multiplied by 1.6 because varenicline costs about 60% more and is divided by 2 because on current evidence it is about twice as effective. The difference between the LYG figures for bupropion and varenicline is within the margin of error of these calculations and too small to be of any practical significance.

Conclusion
The figure above shows that varenicline is about 20 - 30 times more cost effective than the NICE upper limit for the NHS. Therefore, if PCTs are currently funding bupropion and NRT prescriptions they should also fund varenicline prescriptions on at least an equal basis. Even if NICE produces a different figure, based possibly on a different discount rate than used in 2002 for bupropion and NRT they will still give positive guidance on varenicline. If they do use a different model then their previous estimates for bupropion and NRT will also need to change, leaving the relative cost effectiveness of the 3 treatments the same.

Varenicline for 24 weeks?
For the calculation above, the assumption has been that varenicline is prescribed for 12 weeks. As mentioned in the ASH document, the license allows it to be prescribed for an additional 12 weeks for those not smoking at 12 weeks. There is only one published trial testing the efficacy of the additional 12 weeks of treatment. One trial is usually not enough to form a good evidence base, even when it is a large multinational trial. Hence, it is far more difficult to anticipate NICE guidance on the additional 12 weeks.

Although the effect of the extra 12 weeks treatment was shown to be statistically significant in the trial, the additional clinical benefit was about half that achieved by the initial course of 12 weeks in the four 12-week treatment trials (6.7% vs 14% additional 1 year quitters). The trial did not identify a sub-group of smokers for whom the additional 12 weeks treatment was more beneficial. The estimate of cost per life year gained will therefore be about twice the figure for the initial 12 weeks, in the region of £2,000. This is still well below the NICE limit for the NHS and should therefore receive a positive recommendation. However, if smoking cessation medication budgets are restricted and demand for varenicline is high, there will be a health benefit from treating 2 smokers for 12 weeks, rather than 1 smoker for 24 weeks at the same cost.

Potential conflict of Interest
JS has acted on an ad-hoc basis as an adviser/consultant to several organisations with an interest in smoking cessation, including NICE, DH, MRC and several manufacturers and developers of smoking cessation products and technologies. The current note was undertaken as an independent piece of work and was not supported or prompted by any organisation.

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