Author's response to reviews

Title: Finasteride in the treatment of clinical benign prostatic hyperplasia: A systematic review of randomised trials

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PDF covering letter
Response to Dr Wilt

Some general points

We are grateful for the detailed comments, though we were a bit taken aback to see that the comments were taken to be “compulsory” revisions. It is true that some recommendations can be compulsory, especially when they refer to matters of fact, or from an editorial decision. However, the process of peer review should perhaps better be regarded as interesting and informative, a learning process whichever side of the process one stands.

Many of the comments made are subjective, and we would not regard them as compulsory. For instance, there is a recommendation to omit the description on NNT. The original draft did not have a description, but one was inserted at the behest of our advisory panel of urologists and GPs. We acceded to this because it made the paper more accessible to those unfamiliar with NNT (which is extensively used in the UK, though not in other parts of the world), at the risk of boring some who are familiar with it.

Another general point worth making at the beginning is that a number of the comments made refer to comparisons of finasteride with other potential treatments, both conventional and alternative. At the time we wrote, we felt that the evidence base for alpha blockers and alternative therapies was limited. For the latter we have some good reviews, but of limited data. For the former, Dr Wilt’s review of Terazosin was not then available. So we stick to our original aim, clearly stated in the introduction: “Our aim in this systematic review and meta-analysis was to examine results for the standard dose of 5 mg finasteride according to duration of treatment so that men and their professional advisers would know what to expect, and when, both with and without treatment.” That seems a fair aspiration for a systematic review. Use of that information by professionals and patients to make choices about the relative merits of the benefits and harms of treatments is another matter. Evidence is a tool, not a rule.

More specific points:

1 We were again taken aback at the repeated reference to figures being misleading. The dictionary definition is to give false or confusing information. All we have done is to follow the widely used convention in urology reports of truncating scales for items like urinary flow rate and symptom scores. This is a common practice in urology and science and medicine generally, and though we understand Dr Wilt’s argument, we do
not consider this misleading. Presumably neither does BioMed, nor any other science or medical journal we know of, as none has a rule to prohibit the use of graphical representations with truncated scales.

2 We disagree with the argument that primary care treatment of symptoms of lower urinary tract obstruction is only to do with symptoms. Professionals and patients are aware that acute retention and surgery are possible outcomes, and many would regard avoiding surgery or hospital admission as a much more useful outcome. We have to avoid making ex cathedra assumptions about what motivates professionals and patients, and rather give them good quality evidence on which to base their decisions. It’s what Dave Sackett and friends were talking about in their 1996 BMJ editorial on EBM. The more one searches the more one finds that patients are rarely asked about outcomes important to them. In our limited experience talking with patients about outcomes, different patients make different judgements about the benefits and potential for harm of treatment. Having the best information available on what outcomes have been measured may be second best, but it is a start, and while providing it we can avoid biasing it with our own judgements.

For symptom scores we do not state that there is a statistically significant difference. Indeed, we found that statistical tests on pooled data were not possible because no dispersion information was given in the original studies. Statistical tests could possibly be done, but only by making more assumptions than we felt justified. We say this in the early paragraphs of the Results section. For this reason an analysis that compared symptoms scores between finasteride and placebo at (say) one or two years, was not possible. We do point out that most of the individual trials found statistical significance, and we show that at the 5% and 1% levels in Table 1.

3 Whether the change in symptom score from baseline is, or is not, appropriate is a matter of opinion. It is used by Dr Wilt in his recent meta-analysis of terazosin in much the same way as we do here for finasteride. In clinical trials in BPH a placebo is appropriate because in some men spontaneous improvement occurs, whether through some regression to the mean or because of physiological changes being uncertain. In practice placebo is not used, so philosophically professionals and patients want two pieces of information. They want to know that doing something is better than doing nothing, and if something is done, what happens. Table 1 demonstrates that statistical significance of a high order was reached in almost all studies (and hardly likely to be less significant in a meta-analysis, if that were possible). This paper provides the answer to the second part.
Because the PLESS study was large and could dominate, we performed a sensitivity analysis with and without the PLESS trial. It made no difference to results.

We do not think that a comparison with alpha blockers is necessary here. PREDICT is published in abstract form only, a little while ago. If we do not include abstracts in systematic reviews because of concerns about quality or accuracy of data, it is logically inconsistent to use them for discussion points. Again, the Boyle systematic review of permixon showed that the studies were all shorter than three months, and most considerably so. This is hardly the basis for useful comparison, and is why we avoided comparing across treatments.

Again, a discussion about the relative costs of benefits of different treatments is another discussion, and could take up more space than this paper.

Now that there are more, and good, systematic reviews available, the appropriate way forward would be a thoughtful review drawing on the systematic reviews and other evidence. This could include the best information on cost, patient views and so on. The discussion of this paper is not the appropriate place, nor do we wish to do it here.

The paper has been changed, to shorten the abstract, and particularly to enhance the conflict of interest section for the absence of any doubt over our independence from sponsors.