

# Results from the reduce trial on the effect of prostate size on incident lower urinary tract symptoms in men with mild to no current symptoms: do they justify prophylactic intervention?

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Lower urinary tract symptoms (LUTS) in men constitute a key aspect of urological service delivery. Fundamentally, guidelines focus on the severity of the symptoms, and prioritise management of symptoms according to the extent to which they bother the patient (1). A simple logical approach is to categorise what symptoms are present, whether they are storage (urgency, increased daytime frequency, nocturia), voiding (slow stream, hesitancy) or post voiding (post micturition dribble, sensation of incomplete emptying), and address the particular symptoms impacting on quality of life. In general, mere size of prostate does not suggest the need for intervention; if there are no current LUTS, it is impossible to improve quality of life, while serious adverse events (notably acute urinary retention) are sufficiently rare that a large number of men would have to be treated to prevent one adverse event.

The *post hoc* analysis of the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial reported by Simon and colleagues in *European Urology* (2) potentially provides evidence that could support a modification. Namely, might it be appropriate to consider preventive intervention in asymptomatic men found to have a large prostate? The REDUCE study (Clinical Trials.gov Identifier: NCT00056407) was a four year study comparing safety and effectiveness of dutasteride compared to placebo in preventing the development of prostate cancer in men that were defined as being at an increased risk for prostate cancer. Eligible men were aged 50–75 years, had prostate volume <80 mL, prostate-specific antigen (PSA) of >2.5 ng/mL (50–60 years) or 3.0 (60–75 years) but <10 ng/mL, and a negative prostate biopsy within 6 months of enrolment.

The analysis by Simon *et al.* aimed to determine the effect of prostate size on progression to incident LUTS among men with mild to no LUTS (IPSS <8). In effect, they were evaluating the influence of prostate size on the emergence of symptoms in the 4 years of the study. Overall, 193 out of 1,550 asymptomatic or mildly symptomatic men in the placebo group developed “incident LUTS”, of whom 69 had a prostate size below 40 mL, and 124 above. Incident LUTS was defined as “the first report of medical treatment, surgery, or sustained, clinically significant LUTS”. In itself, this provides useful information: firstly, that many men even with a comparatively large prostate have low severity of LUTS (in this study, 1,357 out of 1,550 men); secondly, that there is some link of prostate size to incident LUTS.

In addition, data was provided for the dutasteride treated men, for whom a difference in incident LUTS with prostate size was not evident. It was reported the reduction in the absolute risk of incident LUTS in men with a prostate volume of 40.1–80 mL treated with dutasteride was 11.7%. This was said to equate to a number needed to treat (NNT) to prevent emergence of incident LUTS of nine. However, the denominators used in calculating that figure did not appear to include the large number of asymptomatic men, which would have meant a larger NNT.

Accordingly, the question can be asked about the merit of preventive intervention using 5- $\alpha$  reductase inhibition to reduce medical treatment, surgery, or clinically significant LUTS (the basis of incident LUTS used in the trial). Of course, 5- $\alpha$  reductase inhibitors are a medical treatment, and we cannot argue logically in favour of using medical treatment in asymptomatic men to

prevent future medical treatment for the minority that might become symptomatic within 4 years. We could support such an approach to prevent surgery of severe LUTS, but the paper does not really describe the breakdown of the incident LUTS patients into component categories (medical *vs.* surgical *vs.* severe LUTS). In addition, since this was a clinical trial in which patients were closely followed up, there may have been a higher chance of proceeding to interventional therapy than in the less strict follow up regime typically used in real life practice. Furthermore, while the adverse effects of 5-alpha reductase inhibition are comparatively modest, they certainly exist. For example, erectile dysfunction and breast changes are well recognised, while a possible link to osteoporosis (3) or psychological effects (4) have been reported. Thus, we would really need to see a low NNT to justify such an intervention, but it does not seem to be particularly low, so far as we can tell.

Thus, it is valuable to learn that for men with mild to no current LUTS, prostate size was associated with a higher risk of developing incident LUTS, but only among men in the placebo group. This may help selection of men for closer follow-up, but it does not provide sufficient justification to advocate prophylactic use of 5-alpha reductase inhibition in asymptomatic men.

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### Footnote

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### References

1. Oelke M, Bachmann A, Descalcaud A, *et al.* EAU guidelines on the treatment and follow-up of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. *Eur Urol* 2013;64:118-40.
2. Simon RM, Howard LE, Moreira DM, *et al.* Does prostate size predict the development of incident lower urinary tract symptoms in men with mild to no current symptoms? Results from the REDUCE trial. *Eur Urol* 2016;69:885-91.
3. Lin WL, Hsieh YW, Lin CL, *et al.* A population-based nested case-control study: the use of 5-alpha-reductase inhibitors and the increased risk of osteoporosis diagnosis in patients with benign prostate hyperplasia. *Clin Endocrinol (Oxf)* 2015;82:503-8.
4. Ganzer CA, Jacobs AR. Emotional consequences of finasteride: fool's gold. *Am J Mens Health* 2016. [Epub ahead of print].

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