Finasteride reduced prostate cancer but led to more high grade tumours and sexual side effects

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Thompson IM, Goodman PJ, Tangen CM, et al. ***The influence of finasteride on the development of prostate cancer.*** *N Engl J Med 2003;**349**:215–24.*

QUESTION: In healthy men, does finasteride prevent prostate cancer?

Design
Randomised {allocation concealed*}†, blinded {participants, healthcare providers, data collectors, outcome assessors, and data analysts}†,* controlled trial with ≥7 years of follow up.

Setting
USA.

Patients
16 295 men who were ≥55 years of age, had a normal digital rectal examination and an American Urological Association symptom score <20, and did not have clinically significant coexisting conditions. 61% of men either had a biopsy at the end of the study or their prostate cancer status was known.

Intervention
Men were allocated to finasteride, 5 mg/day (n=8137), or placebo (n=8158).

Main outcome measures
Prostate cancer rate and adverse events.

Main results
Analysis was by intention to treat. More men in the finasteride group than the placebo group refused an end of study biopsy {25% *v* 23%, p<0.001}‡. Fewer men in the finasteride group than the placebo group had prostate cancer; higher grade tumours were more frequent for finasteride than for placebo (table). More men in the finasteride group than the placebo group had erectile dysfunction, loss of libido (table), and reduced volume of ejaculate (60% *v* 47%), whereas more men in the placebo group had urinary urgency, urinary retention (table), benign prostatic hyperplasia (8.7% *v* 5.2%), and urinary tract infection (1.3% *v* 1.0%) (p<0.001 for all comparisons).

Conclusion
In healthy men, finasteride reduced prostate cancer, but high grade tumours and sexual side effects were more frequent for finasteride than for placebo.

*See glossary.
†Information provided by author.
‡p Value calculated from data in article.

Finasteride v placebo in healthy men at mean 7 years§

Outcomes	Finasteride	Placebo	RRR (95% CI)	NNT (CI)
Prostate cancer	18%	24%	25% (19 to 31)	17 (13 to 23)
Urinary urgency	13%	16%	17% (11 to 23)	37 (28 to 59)
Urinary retention	4.2%	6.3%	33% (24 to 41)	48 (37 to 69)
			RRI (CI)	**NNH (CI)**
High grade tumour (Gleason score ≥7)	6.4%	5.1%	27% (7.3 to 50)	74 (43 to 248)
Erectile dysfunction	67%	61%	9.6% (7.2 to 12)	18 (14 to 23)
Loss of libido	65%	60%	9.8% (7.4 to 12)	18 (14 to 23)

§Abbreviations defined in glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

COMMENTARY

Prostate cancer is the second most common cause of cancer death in American men and is the most frequent non-dermatological malignancy[1]. Sensitivity of prostate cancer to androgen deprivation has been well known since the 1940s, and hormonal manipulation has been a standard part of the management of advanced prostate cancer for several decades. The recent availability of anti-androgens, such as finasteride that inhibits conversion of testosterone to dihydrotestosterone and effectively blocks androgen effect on prostate tissue, has raised the possibility that androgen deprivation might be preventive for prostate cancer as well as therapeutic. It is also known, however, that patients as a rule do not die from androgen responsive prostate cancer, but rather from disease that has become hormone refractory despite the therapy.[2]

The trial by Thompson *et al* suggests that finasteride therapy indeed reduces the incidence of prostate cancer in prostate biopsies of men who had normal prostate specific antigen levels and normal prostate exams by ultrasound and digital rectal exam upon study entry. Unfortunately, the reduction in prostate cancers was accompanied by an absolute increase in higher Gleason grade (ie, more aggressive) cancers in the finasteride treated group as well as increased incidence of sexual side effects. For this reason, the question is whether finasteride is most effective in prevention of clinically insignificant cancers and ineffective in prevention of tumours that are more likely to lead to metastatic disease and death—or perhaps even increases the risk as suggested by the study results? Thus, the ability of this therapy to prevent death from prostate cancer is still very much in question. Clearly, prevention of prostate cancer with finasteride comes at a cost, and we do not yet know what those costs will be.

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1 Landis SH, Murray T, Bolden S, *et al.* Cancer statistics, 1999. *CA Cancer J Clin* 1999;**49**:8–31.
2 Maximum androgen blockade in advanced prostate cancer: an overview of 22 randomised trials with 3283 deaths in 5710 patients. *Lancet* 1995;**346**:265–9.