

## CORRESPONDENCE



## Long-Term Effects of Finasteride on Prostate Cancer Mortality

**TO THE EDITOR:** One man in nine will receive a diagnosis of prostate cancer during his lifetime. We previously reported the results of the Prostate Cancer Prevention Trial, in which 18,882 men were randomly assigned to receive finasteride or placebo for 7 years. The study's primary end point — the prevalence of prostate cancer during the 7 years of the trial — was met: the risk of prostate cancer with finasteride was 24.8% lower than the risk with placebo.<sup>1</sup> Paradoxically, the risk of high-grade cancer (Gleason score of 7 to 10) was higher with finasteride, a finding that led to recommendations against the use of finasteride for the prevention of prostate cancer. Subsequent trials showed that finasteride improved detection of prostate cancer and high-grade prostate cancer by improving the performance characteristics of the prostate-specific antigen (PSA) test, digital rectal examination, and the prostate biopsy. These biases could explain the paradox, but the questions of whether the greater number of high-grade prostate cancers could have led to diminished survival or to an increase in prostate cancer mortality persisted.<sup>2</sup> In 2013, we addressed the first of these questions, finding similar survival rates in the two treatment groups of the Prostate Cancer Prevention Trial.<sup>3</sup>

To address the second question, participants with a potentially valid Social Security number, whether last known to be alive or previously deceased, were submitted to the National Death Index in December 2014. Deaths from prostate cancer were reviewed by an end-point review committee. The cumulative incidence of death from prostate cancer was calculated, including all participants who underwent randomization, with deaths due to a cause other than prostate cancer classified as a competing risk. (For details, see the Supplementary Appendix, available with the full text of this letter at NEJM.org.)

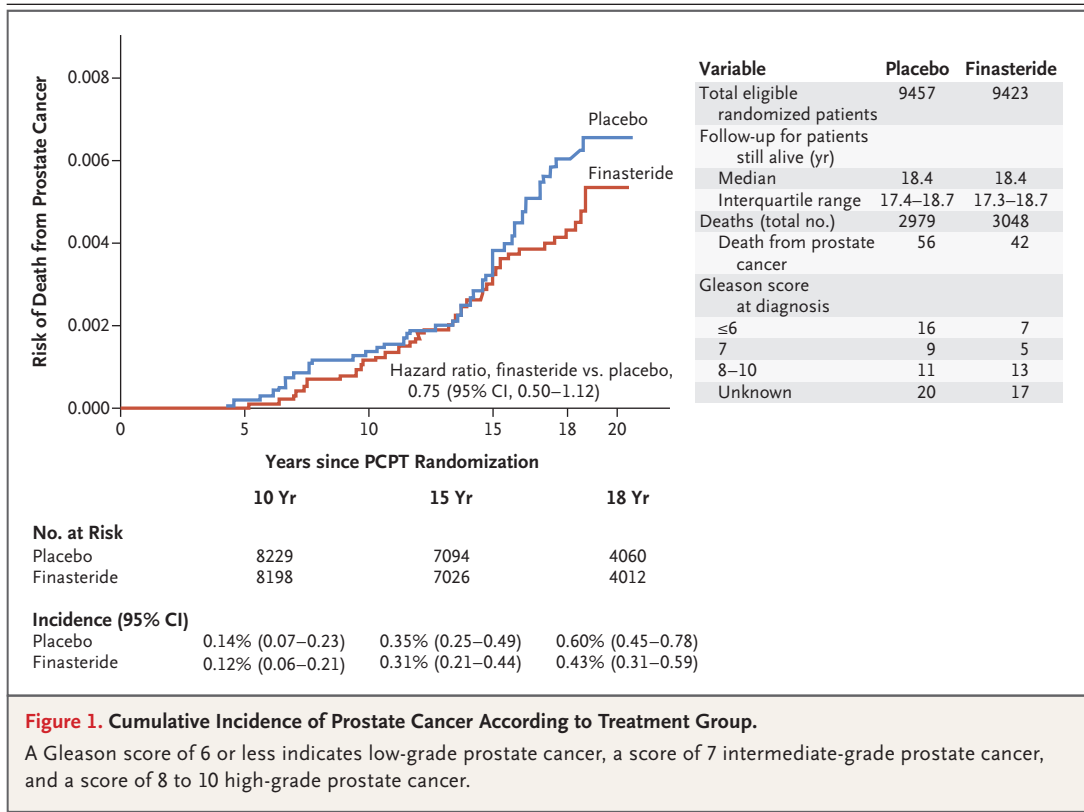
Figure 1 shows the results. With 296,842

person-years of follow-up and a median follow-up of 18.4 years, of 9423 men randomized to finasteride, there were 3048 deaths of which 42 were due to prostate cancer; of 9457 randomized to placebo, there were 2979 deaths, 56 due to prostate cancer. With the small number of deaths due to prostate cancer, the 25% lower risk of death from prostate cancer with finasteride was not statistically significant.

PSA-detected prostate cancer will likely increase with recommendations to offer screening to men 55 to 65 years of age.<sup>4</sup> Screening may reduce the risk of death from prostate cancer but often leads to the detection of prostate cancer that will remain asymptomatic during a man's life. If indolent cancers are treated with surgery or radiation, complications, including impotence and incontinence, are common. If managed with active surveillance, up to 45% of men will ultimately receive treatment; they will also face frequent examination, repeated invasive biopsies, and anxiety.<sup>5</sup> Finasteride is a generic agent that is used to treat lower urinary tract symptoms, prevents complications from these symptoms, and prevents prostate cancer. The early concerns regarding an association between finasteride and an increased risk of high-grade prostate cancer have not been borne out.

### THIS WEEK'S LETTERS

- 393 Long-Term Effects of Finasteride on Prostate Cancer Mortality
- 394 Epinephrine in Out-of-Hospital Cardiac Arrest
- 398 Timing of Renal-Replacement Therapy in Acute Kidney Injury and Sepsis
- 399 A Man with a Self-Inflicted Gunshot Wound
- 401 The Next Phase of Human Gene-Therapy Oversight



Phyllis J. Goodman, M.S.  
 Catherine M. Tangen, Dr.P.H.

Fred Hutchinson Cancer Research Center  
 Seattle, WA

Amy K. Darke, M.S.  
 M. Scott Lucia, M.D.  
 Leslie G. Ford, M.D.  
 Lori M. Minasian, M.D.  
 Howard L. Parnes, M.D.  
 Michael L. LeBlanc, Ph.D.  
 Ian M. Thompson, Jr., M.D.

CHRISTUS Santa Rosa Hospital Medical Center  
 San Antonio, TX  
 thompsoni@uthscsa.edu

Supported by grants (UM1 CA182883 and U10 CA37429) from the National Cancer Institute.

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

1. 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.
2. Redman MW, Tangen CM, Goodman PJ, Lucia MS, Coltman CA Jr, Thompson IM. Finasteride does not increase the risk of high-grade prostate cancer: a bias-adjusted modeling approach. *Cancer Prev Res (Phila)* 2008;1:174-81.
3. Thompson IM Jr, Goodman PJ, Tangen CM, et al. Long-term survival of participants in the Prostate Cancer Prevention Trial. *N Engl J Med* 2013;369:603-10.
4. US Preventive Services Task Force. Screening for prostate cancer: US Preventive Services Task Force recommendation statement. *JAMA* 2018;319:1901-13.
5. Klotz L, Vesprini D, Sethukavalan P, et al. Long-term follow-up of a large active surveillance cohort of patients with prostate cancer. *J Clin Oncol* 2015;33:272-7.

DOI: 10.1056/NEJMc1809961

## Epinephrine in Out-of-Hospital Cardiac Arrest

**TO THE EDITOR:** In reporting the results of the PARAMEDIC2 (Prehospital Assessment of the Role of Adrenaline: Measuring the Effectiveness of Drug Administration in Cardiac Arrest) trial,

Perkins et al. (Aug. 23 issue)<sup>1</sup> note that during the initial prehospital resuscitation phase, the rate of return of spontaneous circulation was three times as high among patients who received epi-