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Platinum Priority

Reply from Authors re: Robert J. Hamilton, Gerald L. Andriole, Stephen J. Freedland. 5 α -Reductase Inhibitors: Preventing the Treatable. *Eur Urol* 2012;62:242–4

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We appreciate the opportunity to respond to the comments of Hamilton and colleagues [1]. While we are pleased that our paper has initiated this dialogue, we note that these authors have overlooked the primary focus of the manuscript and articulated several flawed assertions.

First, we do *not* conclude that finasteride should be widely administered to prevent benign prostatic hyperplasia (BPH). Rather, we contend that the prophylactic benefit of finasteride for incident BPH merits recognition as an additional favorable outcome when weighing a chemoprevention strategy for prostate cancer [2]. In this sense, we propose that scientific and health policy debate over 5 α -reductase inhibitor (5-ARI) prevention of prostate cancer should acknowledge the substantive, clinically significant benefits of concomitant BPH prophylaxis in asymptomatic older men.

Second, contrary to these authors' assertion, the medical community has not pronounced 5-ARIs "unsuitable" for prostate cancer prevention. Both the American Urological Association and the American Society of Clinical Oncology have concluded that asymptomatic men may benefit from a discussion about 5-ARIs for prostate cancer prevention [3]. While analyses of both the Prostate Cancer Prevention Trial (PCPT) and the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial have suggested statistically significant increases in the incidence of high-grade (Gleason sum ≥ 7) disease [4,5], the clinical significance of these observations remains unclear, and the issue of detection bias, a potential *benefit* of 5-ARI therapy, has not been resolved [6].

Third, to reject 5-ARI chemoprevention simply out of concern that providers and patients will be unable to grasp the concept of prostate-specific antigen adjustment profoundly underestimates the health care community's ability to apply innovative practices and undermines core principles of translational medicine. Every important public health endeavor must overcome practical and cultural

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challenges in its application. As surgeon-scientists, it is our obligation to identify these translational challenges and actively pursue solutions rather than rejecting a potentially promising therapy out of hand as presenting insurmountable barriers to implementation.

Fourth, although 49% of the BPH events were attributable to increased urinary symptoms in this study, the authors fail to note that participants were censored at time of symptom onset. Hence it is likely that many symptomatic men subsequently initiated medication, underwent surgery, and/or developed urinary retention after developing symptoms.

Finally, although BPH may be treatable, dismissing the concept of preventing a condition that affects three of four men by age 70 diminishes both the public health burden of prostate disease and the suffering of individual patients. The incidence and prevalence of prostate cancer and BPH increase sharply with age, and the global population is growing older: By 2030, approximately 20% of the US population will be 65 yr of age and older, including >20 million men [7]. These observations portend substantial and sustained increases in the number of prostate cancer and BPH cases with attendant strains on finite health care resources. At a population level, finasteride prophylaxis might offer significant cost savings, precluding the need for relatively expensive α -blocker, anticholinergic, phosphodiesterase type 5 inhibitor, or surgical therapy while simultaneously reducing the burden of prostate cancer diagnosis, treatment, and follow-up. Recent data also suggest that the medical morbidity of symptomatic BPH is substantially underappreciated. Older men with lower urinary tract symptoms, *many of whom do not actively seek treatment*, are up to 63% more likely to suffer recurrent falls, which can lead to fractures [8]. In addition, Foley catheter

insertion is a considerable source of urinary tract trauma, affecting an estimated tens of thousands of US men annually [9,10].

Conflicts of interest: The authors have nothing to disclose.

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