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## Re: Vasectomy and Prostate Cancer Incidence and Mortality in a Large US Cohort

Pratik Kanabur<sup>1</sup>, Jason M. Scovell<sup>2</sup>, and Ranjith Ramasamy<sup>1</sup>

<sup>1</sup>Department of Urology, University of Miami Miller School of Medicine, Miami, FL, USA.

<sup>2</sup>Department of Urology, Baylor College of Medicine, Houston, TX, USA.

### Experts' summary

In the September issue of the *Journal of Clinical Oncology*, Jacobs and colleagues [1] report on the association between vasectomy and prostate cancer incidence and mortality. Data from the Cancer Prevention Study Cohort II (1982–2012) was retrospectively analyzed. In this cohort, men aged between 40 yr and 90 yr of age without a previous history of prostate cancer were included. A total of 66 542 men were included to determine the association between vasectomy and prostate cancer incidence, and 363 726 men were included for prostate cancer mortality. Vasectomy status was determined primarily by matched questionnaires from participants' wives. Prostate cancer was identified by biennial follow-up questionnaires and was verified using both medical records and state cancer registries. Association between vasectomy and prostate cancer incidence and mortality was controlled for by age, race, education, body mass index, smoking, and history of prostate-specific antigen testing.

There was no difference in the incidence of prostate cancer in men who had undergone a vasectomy compared with those who did not have a vasectomy (hazard ratio [HR]: 1.02, confidence interval [CI]: 0.96–1.08). In this cohort, there was no association between vasectomy and risk of developing aggressive (HR: 0.95, CI: 0.84–1.08) prostate cancer. Men who had undergone a vasectomy were at an increased risk for nonaggressive prostate cancer (HR: 1.08, CI 1.01–1.15). This study did not find an increased risk between having a vasectomy and dying from prostate cancer (HR: 1.01, CI: 0.93–1.10).

### Experts' comments

Whether vasectomy is a risk factor for prostate cancer has been questioned with mixed findings in the literature [2–4]. Giovannucci and colleagues [3] published the first major evidence suggesting an increased risk of prostate cancer following vasectomy in an analysis of the Health Professionals Follow-up Study (HPFS). A recent updated analysis from the HPFS found a 10% greater risk of overall prostate cancer (risk ratio [RR]: 1.10, CI: 1.04–

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Corresponding Author: Ranjith Ramasamy, MD, University of Miami Miller School of Medicine, 1150 North West 14th Street, Miami, FL 33136.

Conflicts of interest

The authors have nothing to disclose.

1.17) and approximately 20% greater risk of high-grade prostate cancer (RR: 1.22, CI: 1.03–1.45) in men who had vasectomy [4]. In contrast, a meta-analysis of retrospective cohort studies by Liu and colleagues [5] found no risk between a vasectomy and prostate cancer (RR: 1.08, CI: 0.87–1.35). It is important to understand that association does not imply causation. Further, there is lack of a proven biological link or a plausible molecular mechanism with in vitro or animal studies for the association between vasectomy and prostate cancer [6].

Jacobs and colleagues [1] add compelling data by determining that there is no association between vasectomy and prostate cancer incidence and mortality in the large Cancer Prevention Study Cohort II. The evidence supports vasectomy to be a safe procedure and one that does not increase the risk of clinically significant prostate cancer. Interestingly, the study by Jacobs et al [1] found that men who had a vasectomy were at an increased risk of developing less aggressive prostate cancer, which is in direct contrast with the HPFS data suggesting an increased risk for more aggressive prostate cancer. Although these associations may be real and meaningful, the data is difficult to interpret given the conflicting findings.

When large data sets for hypothesis testing, such as those that are used in this study, there is a chance of finding statistically significant associations that may not be clinically or biologically relevant [7]. Until additional studies are performed that support an increased risk between vasectomy and prostate cancer, clinicians and patients should be reassured that vasectomy is a safe procedure and likely adds no long-term risk of developing life-threatening prostate cancer. Unfortunately, until such studies are performed, practitioners are required to discuss the potential risk of prostate cancer when counseling men undergoing vasectomy.

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