Re: Timothy J. Wilt, Tien N. Vo, Lisa Langsetmo, et al. Radical Prostatectomy or Observation for Clinically Localized Prostate Cancer: Extended Follow-up of the Prostate Cancer Intervention Versus Observation Trial (PIVOT)

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External Validity of the Updated Prostate Cancer Intervention Versus Observation Trial (PIVOT)

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An update to the Prostate Cancer Intervention Versus Observation Trial (PIVOT) described the effect of radical prostatectomy (RP) versus observation on all-cause mortality for men with clinically localized prostate cancer (PCa), and showed that RP provides small, long-term reductions in death and increases in years of life gained [1]. Prior work showed that previous results from PIVOT lacked external validity for US patients [2]. In an attempt to assess the generalizability of the recent PIVOT follow-up, we evaluated the characteristics of PCa patients within the most up-to-date National Cancer Data Base (NCDB), a nationwide, hospital-based registry sponsored by the American College of Surgeons and American Cancer Society. Within the NCDB, we followed the PIVOT inclusion criteria and isolated patients who were ≤75 yr of age with localized PCa and had prostate-specific antigen (PSA) ≤50 ng/mL, life expectancy ≥10 yr, ≥1 yr of follow-up data, and RP or observation as their initial treatment. Subsequently, we compared age, Charlson-Deyo comorbidity index (CCI), race, PSA, clinical T stage, Gleason score, and D’Amico risk score for our NCDB cohort to the patient population in PIVOT.

From 2004 to 2014 we identified 354,717 patients treated with RP and 57,724 patients treated with observation. Compared to PIVOT, NCDB patients were younger (60.3 vs 67.0 yr) and had more patients with no CCI comorbidities (92.9% vs 56.1%). The relative youth of the NCDB cohort is further evidenced by the fact that 45.6% and 9.4% of patients were aged 60–69 yr and 70–75 yr, respectively, compared to 56.6% and 33.1% in PIVOT. Moreover, only 33.3% of NCDB patients had D’Amico low-risk PCa, compared to 40.5% in PIVOT.

The NCDB extracts more than 70% of incident cancer diagnoses in the USA from more than 1500 hospitals, theoretically providing an accurate representation of patients receiving cancer care in the USA. Our analysis showed that men in PIVOT were older with more comorbidities than their NCDB counterparts. It has been shown that older men with lower life expectancy are less likely to benefit from RP [3]. Thus, owing to their younger age and lower comorbidity, North-American patients with clinically localized PCa seen in practice are likely to obtain a greater survival benefit from RP than what was reported in PIVOT. In addition, a greater proportion of patients included in PIVOT had low-risk disease that is unlikely to benefit from active treatment [4,5]. These patients dilute the benefit of RP as the NCDB (ie, patients seen in clinical practice) had a lower proportion of such patients.

While our work defines differences within the two populations, we do not intend to remark that the authors’ findings are inaccurate or compare the outcomes of RP and observation in either cohort. We merely contend that the study population may have differed significantly from the
source population that the trial aimed to investigate. This indicates that findings from the PIVOT follow-up might lack external validity and generalizability to the contemporary patient population undergoing treatment for clinically localized PCa. The trial is different from the clinical population in ways that may affect the outcome examined and may artificially undermine the benefit that patients receive from RP.

Conflicts of interest: Firas Abdollah is a consultant for GenomeDx Biosciences. The remaining authors have nothing to disclose.

CRediT authorship contribution statement

Methodology, Formal analysis, Data curation. Firas Abdollah: Conceptualization, Formal analysis, Methodology, Investigation, Project administration, Writing - review & editing.

References