Carter et al. (1) suggest that prostate-specific antigen velocity (PSAV, change in PSA over a defined interval) is a useful measure to detect life-threatening prostate cancer during a window of curability 10–15 years before diagnosis. They recommend that a PSAV greater than 0.35 ng/mL per year should be used to refer men with a PSA concentration less than 4.0 ng/mL for biopsy. This recommendation is based on two findings in their study: 1) a nearly fourfold increase in the hazard ratio for prostate cancer mortality associated with a unit increase in PSAV and 2) an area under the receiver operating characteristics curve for PSAV of 0.75 compared with 0.74 for PSA.

The recommendation that PSAV be used as a trigger for biopsy runs counter to the evidence from a variety of large prospective and retrospective studies, including our own (2). We found that after taking the level of PSA into account, the hazard ratio for PSAV either dropped to marginal or statistically nonsignificant (close to 1.0) or flips direction (<1.0), implying a decreased risk of prostate cancer for higher velocity.

PSAV, PSA density (PSA divided by volume of the prostate), and complexed PSA concentration are some of the PSA-related markers that have been proposed as providing more useful information than PSA concentration; however, all face the challenges that they correlate highly with PSA and are harder to measure. The correlation between PSA and PSAV was .70 in the Carter et al. study, so the incremental information provided by PSAV is questionable. Studies assessing independent prognostic information of markers should provide adjusted hazard ratios for both markers and should put both markers on the same scale (continuous or dichotomized at a cut point) for a fair and equally powerful comparison. Moreover, PSAV is both more subjective and difficult to standardize than PSA. To truly assess whether a change in PSA concentration of 0.35 ng/mL per year improves detection, even in men who have low (≤4 ng/mL) PSA concentrations, the sensitivity, specificity, and positive predictive value of the test at this threshold should be assessed and compared with tests using only PSA concentrations, which was not done in the study by Carter et al.

We have shown (3) that even among men who have PSA concentrations less than 4.0 ng/mL, risk of prostate cancer and of high-grade disease are on a continuum with PSA concentration; thus, no threshold exists that simultaneously achieves sufficiently high sensitivity and specificity for superior performance of this screening test. Without the sensitivity and specificity table for PSAV, and based on only 20 prostate cancer deaths, we cannot infer that any specific PSAV threshold provides incremental value in detection of disease, whether potentially fatal or otherwise.

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References
when we restricted our dataset to include only PSA levels less than 4.0 ng/mL at 10–15 years before diagnosis. Furthermore, using this restricted dataset at 10–15 years before diagnosis, PSA was not a statistically significant variable ($P = .29$) in a proportional hazards model that included age, date of diagnosis, and PSA as continuous variables. The addition of PSAV to this model statistically significantly improved the fit of the model based on the likelihood ratio test ($P = .03$). The area under the receiver operating characteristics curve for PSA and PSAV (after adjusting for age and date of diagnosis) at 10–15 years before diagnosis when PSA levels were less than 4.0 ng/mL was 0.467 (95% confidence interval [CI] = 0.219 to 0.714 and 0.649 (95% CI = 0.405 to 0.894). It is of no surprise to us that data from the Prostate Cancer Prevention Trial (5) show no strong correlation between PSAV and any prostate cancer because it is likely that many men in this trial were diagnosed with indolent disease.

In our opinion, the added value of PSAV derives from the fact that the window of opportunity for detection of curable disease is large—especially among men with PSA values in the range of 2.0–2.5 ng/mL (6)—and that PSAV may allow detection of life-threatening disease at a point when the PSA level is below most clinical decision thresholds. If an asymptomatic man with a normal digital rectal examination and a PSA level of 2.0 ng/mL has a persistent PSAV of 0.4 ng/mL per year, it is likely that he will have curable disease 3–4 years later if he underwent a biopsy at that point based on PSAV. Thus, all men who reach a PSA threshold of 2.0 ng/mL could be subjected to prostate biopsy to avoid exceeding a 20% likelihood that any prostate cancer exists, as suggested by Thompson et al. (5). Alternatively, changes in PSA levels could be monitored, biopsy and the high risk of serendipitous detection of a cancer for which treatment will confer no benefit avoid, and life-threatening disease could still be detected at a point when cure is likely among those men whose PSA levels do accelerate. In a randomized screening trial, 50% of men with PSA levels of 2.0–2.9 ng/mL will have PSA levels less than 3.0 ng/mL 4 years later (7).

Thus, tracking PSA history and performing a prostate biopsy on those men with a PSAV that suggests the presence of life-threatening disease seems to us to be a worthwhile trade-off to biopsy referral of all men based on a given PSA threshold.

### References


