PSA Testing Use and Prostate Cancer Diagnostic Stage After the 2012 U.S. Preventive Services Task Force Guideline Changes

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ABSTRACT

Background: Most patients with prostate cancer are diagnosed with low-grade, localized disease and may not require definitive treatment. In 2012, the U.S. Preventive Services Task Force (USPSTF) recommended against prostate cancer screening to address overdetection and overtreatment. This study sought to determine the effect of guideline changes on prostate-specific antigen (PSA) screening and initial diagnostic stage for prostate cancer. **Patients and Methods:** A difference-in-differences analysis was conducted to compare changes in PSA screening (exposure) relative to cholesterol testing (control) after the 2012 USPSTF guideline changes, and chi-square test was used to determine whether there was a subsequent decrease in early-stage, low-risk prostate cancer diagnoses. Data were derived from a tertiary academic medical center's electronic health records, a national commercial insurance database (OptumLabs), and the SEER database for men aged ≥35 years before (2008–2011) and after (2013–2016) the guideline changes. **Results:** In both the academic center and insurance databases, PSA testing significantly decreased for all men compared with the control. The greatest decrease was among men aged 55 to 74 years at the academic center and among those aged ≥75 years in the commercial database. The proportion of early-stage prostate cancer diagnoses (<T2) decreased across age groups at the academic center and in the SEER database. **Conclusions:** In primary care, PSA testing decreased significantly and fewer prostate cancers were diagnosed at an early stage, suggesting provider adherence to the 2012 USPSTF guideline changes. Long-term follow-up is needed to understand the effect of decreased screening on prostate cancer survival.

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Background

Prostate cancer is the most common cancer in US men; in 2019, 174,700 new cases are estimated, accounting for 20% of all new cancers in men, with 31,700 deaths.[1] However, a lack of consensus remains regarding best practices for screening and treatment, partly because of the difficulty in distinguishing aggressive from indolent cancers.[2] Most prostate cancers are asymptomatic, are detected by primary care–directed screening, are slow-growing, and will not become clinically evident during the patient's lifetime. Autopsy studies detect prostate cancer in 30% of men by age 55 years and 60% of men by age 80 years.[3] Widespread implementation of prostate-specific antigen (PSA) screening has led to a significant increase in diagnosis and treatment of prostate cancer, including many inconsequential tumors,[4] with minimal or no effect on mortality rates.[5–9] Meanwhile, treatment of these cancers can lead to treatment-related adverse events, such as urinary incontinence or sexual dysfunction.[10,11]

The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) showed that systematic PSA testing resulted in higher prostate cancer diagnosis rates, particularly of early-stage disease, but without improvements in mortality.[7] In addition, the Prostate Cancer Intervention Versus Observation Trial (PIVOT) showed no survival advantage for surgery compared with no treatment in patients with localized prostate cancer.[12] Based on the results of these trials, the U.S. Preventive Services Task Force (USPSTF) published new guidelines in 2012 recommending against PSA screening in all men (D rating),[13] expanding on a 2008 recommendation against screening in men aged ≥75 years.[14] However, these recommendations were highly controversial because the death rate of prostate cancer had decreased 50% since the initiation of PSA testing in the United States, and


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randomized trials of PSA screening and surgical treatment of localized prostate cancer conducted in Europe showed significant survival benefits for both screening and treatment.[5,15,16] The controversy continued to increase based on criticisms of PLCO citing contamination of the control arm[17] and criticisms of PIVOT for selection of patients with comorbidities and indolent disease.[18] Finally, since 2012, the increased use of active surveillance for management of indolent disease in both the United States and Europe changed the risk/benefit ratio for prostate cancer screening by decoupling screening from treatment-related adverse events.[19] Because of this, in 2018, the USPSTF rolled back the 2012 recommendations and advised men aged 55 to 69 years to discuss the risks and benefits of screening with their healthcare providers (C rating).[20]

A better understanding of the effects of guideline changes, particularly regarding controversial topics such as cancer screening, may help inform future policy. Studies of Medicare beneficiaries have shown that the 2008 guideline changes were associated with a 2% decline in PSA screening for men aged ≥75 years and a decline in treatment by 42% at the population level but only by 8% among diagnosed men, suggesting that declines in screening and diagnosis were driving the decline rather than changes in treatment patterns.[21] Studies examining men of all ages have found conflicting results, observing significant declines[22,23] or no change[24] in PSA screening rates in the wake of the 2012 changes, and declines in testing have been suggested to underlie increases in late-stage disease burden from 2010 to 2014.[23] However, these studies did not control for secular trends, such as the Affordable Care Act (ACA), that might influence screening and diagnosis, and encompassed only 1 or 2 years of data after the guideline changes.

Given the controversy about this guideline change, clinician adherence and effects on prostate cancer diagnosis are poorly understood. Using multiple datasets from 2008 to 2016, this study sought to determine whether PSA testing rates changed in primary care after the 2012 USPSTF guideline changes and whether early-stage, low-risk prostate cancer diagnoses decreased after the downgrade in PSA screening recommendations. Our findings highlight the impact even controversial guideline changes can have on clinical practice.

Patients and Methods

Study Design

A quasiexperimental, difference-in-differences (DID) design[25] was used to compare PSA versus cholesterol testing rates among men aged ≥35 years before (2008–2011; "prepolicy") and after (2013–2016; "postpolicy") the 2012 changes to the USPSTF prostate cancer screening guidelines. We focused on primary care providers because they are tasked with disease screening, whereas subspecialists likely use PSA testing to monitor disease after treatment. Cholesterol testing, like PSA testing, addresses conditions that are asymptomatic at onset, targets similar risk populations, is administered as a blood test, is widely accessible across care settings, and is mainly used by primary care physicians. The DID design allows the control to serve as the counterfactual, thereby accounting for secular trends such as increased access to care after the ACA. We adjusted for potential time-varying confounders that could bias estimates and tested for parallelism in prepolicy trends between the study and control populations before the guideline changes, adhering to published best practices to assess validity of the control as a suitable counterfactual.[25,26] We further compared rates of prostate and colorectal cancers (CRCs) diagnosed at an early stage both prepolicy and postpolicy. CRC has a patient population and clinically silent period similar to prostate cancer, yet screening guidelines were stable during the study period.

Data Sources

Primary data were derived from the electronic health records (EHRs) of a tertiary academic medical center containing encounter-level data from 2008 to 2016, including demographics, laboratory orders, insurance payer, clinical features, and provider specialty. The clinical data warehouse is described elsewhere.[27]

OptumLabs, co-founded by Mayo Clinic and Optum in late 2012, is a commercial data, infrastructure services, and care organization that is part of UnitedHealth Group. OptumLabs now has 30 partners and a HIPAA-compliant deidentified database of >200 million people. Records include inpatient, outpatient, pharmacy, and laboratory claims. Socioeconomic status (SES) was established using net worth as coded by the OptumLabs database. We used a 1% sample of the population from 2008 to 2016.[28]

The SEER Program is a national cancer database encompassing approximately one-third of the US population. We used 2008 to 2015 data for both prostate cancer and CRC diagnoses, including demographics and diagnostic stage. SEER data were available up to 2015 and lacked comorbidity scores.[29] Insurance was categorized as insured (Medicare or private), any Medicaid, or other/unknown/uninsured.

Study Participants

The screening population consisted of undiagnosed men aged ≥35 years seen by a primary care provider. Primary care was defined in EHR data by provider specialty (family medicine, family practice, geriatric medicine, or nurse practitioner–family), whereas the OptumLabs database already included a variable for provider type

that identified records from primary care providers. Charlson comorbidity scores were assigned at the start of each year, and ages were calculated between birth and encounter dates. Race was classified as white, Asian, black, Hispanic, and other/unknown. Insurance payer was categorized as Medicare, Medicaid, private, and other/unknown/uninsured. Annual testing rates were assessed independently: patients could be counted as receiving screening or not only once per annual eligibility period. Diagnosed patients were excluded after their diagnosis date.

Diagnostic stage was assessed in all first-time cancer diagnoses by calendar year. "Low-grade" was defined based on AJCC prognostic stage groups[30]; "early-stage" was defined as localized cancer (summary stage ≤2) at initial diagnosis. Cancers with unrecorded initial stage were excluded.

Statistical Analysis

Linear regression DID models compared changes in PSA screening relative to cholesterol testing after the 2012 USPSTF recommendation. The models account for secular changes, which include factors such as expanded access to care after the ACA, by assuming the control is a counterfactual for the exposure group had the policy not existed. We adhered to published best practices in assessing this assumption by testing for parallelism in the preintervention period (see supplemental eAppendices 1 and 2, available with this article at JNCCN.org).[25,26] Linear probability models were a function of separate binary indicator variables for exposure status, postpolicy status (2013–2016), and their product yielding their interaction (supplemental eAppendix 1). The DID estimate is represented by the interaction term, which describes the differential change between exposure and control after policy implementation. Charlson comorbidity score, age, race, and insurance or SES (net worth) were included in the models. The prepolicy period was defined as January 1, 2008, through December 31, 2011, and the postpolicy period as January 1, 2013, through December 31, 2016 (2015 for SEER). The implementation year, 2012, was excluded as a "washout" period.[13] Screening trends compared PSA (exposure) and cholesterol (control) testing. Diagnostic stage was separately examined for prostate cancer and CRC using chi-square test. We stratified analyses by age group. Statistical significance was defined by a 2-sided P value $<.05$. All analyses were performed with R 3.4.1 (The R Foundation) and RStudio 1.0.153 (RStudio).

Results

In the academic center's database, we identified 18,559 prepolicy and 78,281 postpolicy patients; 256 (1.4%) prepolicy and 874 (1.1%) postpolicy patients were excluded for prostate cancer diagnosis before annual PSA screening was tabulated. Before the 2012 USPSTF recommendation, 3,252 received any PSA tests (3,456 tests ordered) and 5,686 received any cholesterol tests (6,410 tests ordered); after the 2012 USPSTF recommendation, 8,306 patients received any PSA tests (8,914 total tests ordered) and 24,491 received any cholesterol tests (28,161 total tests ordered). Patients in the postpolicy group were slightly older, had more men aged 55 to 74 years, included slightly fewer on Medicare, and had slightly more black and Hispanic patients, but fewer Asian patients compared with the prepolicy group (Table 1).

In the OptumLabs 1% sample, we identified 93,334 prepolicy and 110,067 postpolicy patients. Patient counts for the control and exposure groups were equivalent for the OptumLabs analysis because patient records after the date of prostate cancer diagnosis were pre-excluded during the initial data extraction. Postpolicy patients (Table 1) were older, had more men aged 55 to 74 years and fewer aged 35 to 54 years, included fewer white patients but more with other/unknown race, and had more with unknown SES (net worth) compared with prepolicy patients. The number of patients in the academic center's population increased during the course of the study, due to an expanded primary care initiative, which is controlled for along with other background temporal trends through the DID model via the cholesterol control.

Unadjusted trends in annual PSA (exposure) and cholesterol (control) testing in the primary care setting, including composite rates and rates stratified by age group, are shown in Figure 1 for the tertiary academic center and OptumLabs. PSA testing declined in both sites, with the greatest decreases in PSA testing observed in men aged 55 to 74 years and ≥75 years, respectively. Modeled estimates accounting for background temporal trends (Table 2) show significant decreases in PSA testing both overall and by age group (all $P<.001$). PSA testing declined across all age groups by 8.0% (95% CI, −8.9% to −7.1%) in the academic center and by 3.6% (95% CI, −4.1% to −3.2%) in the OptumLabs population. The academic center had the largest changes in men aged 55 to 74 years (−13.0%) and smaller declines in men aged 35 to 54 (−4.8%) and ≥75 years (−8.5%). OptumLabs had its largest decrease in men aged ≥75 years (−8.2%), with smaller declines in men aged 55 to 74 (−2.8%) and 35 to 54 years (−4.1%).

In the academic center database, we identified 2,572 prostate and 413 CRC prepolicy diagnoses after excluding 288 (10.1%) and 204 (33.1%) without stage, respectively, and 1,397 prostate and 521 CRC postpolicy diagnoses after excluding 593 (29.8%) and 176 (25.3%) without stage, respectively. Postpolicy patients with prostate cancer had similar age, slightly higher comorbidity scores, more white and Asian patients, and more

Table 1. Characteristics of Patients Eligible for Screening

Characteristic	Academic Center			OptumLabs 1% Sample		
	Prepolicy	Postpolicy	Unadjusted Difference	Prepolicy	Postpolicy	Unadjusted Difference
Patients, n	18,559	78,281		93,334	110,067	
Mean age (95% CI), y	56.2 (56.0–56.4)	56.9 (56.8–57.0)	0.7 (0.5–1.0)	54.9 (54.8–55.0)	58.4 (58.4–58.5)	3.5 (3.4–3.7)
Mean Charlson comorbidity score (95% CI)	1.1 (1.1–1.2)	1.0 (1.0–1.1)	–0.1 (–0.1 to 0.0)			
Eligible patients by age, % (95% CI)						
35–54 y	51.6 (50.9–52.3)	46.6 (46.3–47.0)	–5.0 (–5.8 to –4.2)	53.1 (52.8–53.4)	42.1 (41.8–42.4)	–11.0 (–11.4 to –10.6)
55–74 y	35.3 (34.6–36.0)	41.8 (41.5–42.2)	6.5 (5.7–7.3)	37.7 (37.3–38.0)	43.8 (43.5–44.1)	6.1 (5.7–6.5)
≥75 y	13.1 (12.6–13.6)	11.5 (11.3–11.7)	–1.6 (–2.1 to –1.0)	9.2 (9.0–9.4)	14.1 (13.9–14.3)	4.9 (4.6–5.2)
Race, % (95% CI)						
White	54.1 (53.3–54.8)	53.4 (53.0–53.7)	–0.7 (–1.5 to 0.1)[a]	68.8 (68.5–69.1)	60.3 (60.1–60.6)	–8.5 (–8.9 to –8.1)
Asian	16.4 (15.8–16.9)	15.5 (15.2–15.8)	–0.9 (–1.5 to –0.3)[b]	3.0 (2.9–3.2)	3.3 (3.2–3.4)	0.3 (0.1–0.5)
Black	3.3 (3.1–3.6)	5.6 (5.5–5.8)	2.3 (2.0–2.6)	8.2 (8.0–8.4)	7.0 (6.8–7.1)	–1.2 (–1.4 to –1.0)
Hispanic	7.8 (7.4–8.2)	9.0 (8.8–9.2)	1.2 (0.8–1.6)	7.6 (7.4–7.8)	8.2 (8.0–8.4)	0.6 (0.4–0.8)
Other/Unknown	18.4 (17.9–19.0)	16.5 (16.2–16.7)	–1.9 (–2.5 to –1.3)	12.4 (12.2–12.6)	21.2 (20.9–21.4)	8.8 (8.5–9.1)
Insurance, % (95% CI)						
Medicare	32.0 (31.3–32.7)	25.0 (24.7–25.3)	–7.0 (–7.7 to –6.3)	N/A	N/A	N/A
Medicaid	3.1 (2.9–3.4)	2.0 (1.9–2.1)	–1.1 (–1.4 to –0.8)	N/A	N/A	N/A
Private	54.6 (53.9–55.3)	53.5 (53.1–53.8)	–1.1 (–1.9 to –0.3)[b]	N/A	N/A	N/A
Other/Unknown	10.3 (9.8–10.7)	19.5 (19.2–19.7)	9.2 (8.7–9.7)	N/A	N/A	N/A
Socioeconomic status/net worth, % (95% CI)						
≥$500k	N/A	N/A	N/A	21.0 (20.8–21.3)	18.1 (17.9–18.3)	–2.9 (–3.2 to –2.6)
$250k–$499k	N/A	N/A	N/A	23.7 (23.4–23.9)	20.4 (20.2–20.6)	–3.3 (–3.7 to –2.9)
$150k–$249k	N/A	N/A	N/A	13.7 (13.5–14.0)	11.9 (11.7–12.1)	–1.8 (–2.1 to –1.5)
$25k–$149k	N/A	N/A	N/A	16.9 (16.6–17.1)	15.6 (15.4–15.9)	–1.3 (–1.6 to –1.0)
<$25k	N/A	N/A	N/A	7.0 (6.9–7.2)	7.3 (7.1–7.4)	0.3 (0.0–0.5)[c]
Unknown	N/A	N/A	N/A	17.7 (17.4–17.9)	26.7 (26.4–27.0)	9.0 (8.6–9.4)

All comparisons are between the prepolicy (2008–2011) and postpolicy (2013–2016) periods in primary care. Time intervals were defined as calendar years and evaluated independently for patient-level eligibility. All *P* values are <.001 except where indicated.
Abbreviation: N/A, not available.
[a]*P*=.094.
[b]*P*<.01.
[c]*P*=.063.

patients with Medicaid and private insurance compared with prepolicy patients (supplemental eAppendix 3). Compared to prepolicy patients, postpolicy patients with CRC included fewer white and more Asian men, but there was no statistically significant difference in age, comorbidity, or insurance. In both the prepolicy and postpolicy periods, the prostate cancer group was generally older compared with the CRC group and had fewer Asian patients.

In the SEER sample, we identified 75,641 prostate and 20,250 CRC prepolicy diagnoses after excluding 1,945 (2.5%) and 821 (3.9%) without stage, respectively, and 44,904 prostate and 15,077 CRC postpolicy diagnoses after excluding 1,477 (3.2%) and 681 (4.3%) without stage, respectively. After the 2012 USPSTF recommendation (postpolicy), age slightly increased for patients with prostate cancer and decreased for those with CRC (supplemental eAppendix 3); both had fewer white individuals and a larger Medicaid proportion postpolicy. Patients with prostate cancer were slightly older than those with CRC in both the prepolicy and postpolicy periods.

Decreases in the unadjusted proportion of early-stage diagnoses (Table 3) were seen in both the academic center and SEER databases. The academic center had nearly uniform decreases across age groups, with an overall decline from 79.0% to 63.4% (−15.6%). In comparison, CRC diagnoses did not display significant changes, except for an increase from 46.3% to 58.6%

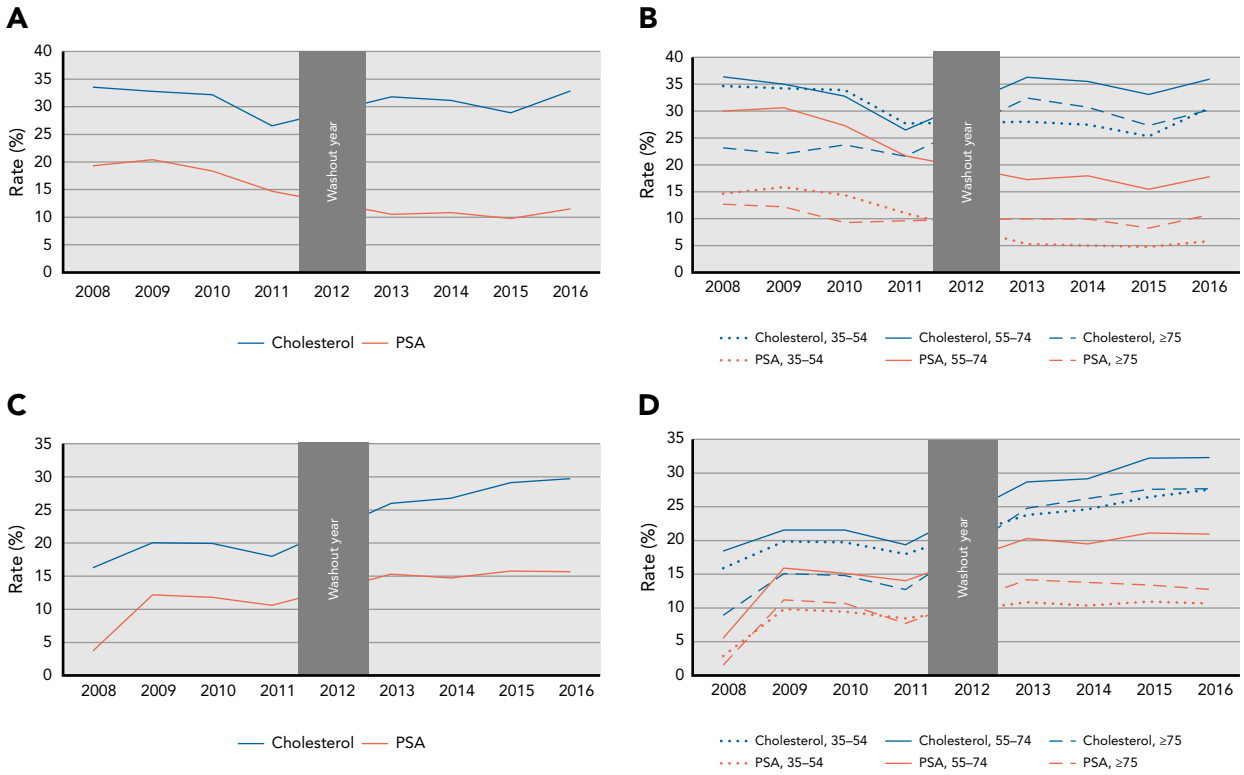

Figure 1. Unadjusted trends in PSA (exposure) and cholesterol (control) testing in (A) academic center, all ages, (B) academic center, by age group, (C) OptumLabs, all ages, and (D) OptumLabs, by age group.
Abbreviation: PSA, prostate-specific antigen.

(+12.3%; $P<.01$) in men aged 55 to 74. SEER showed smaller decreases in early-stage prostate cancer, decreasing overall from 82.6% to 77.7% (−4.9%), with the largest decline in men aged ≥75 years (−10.1%), followed by 55 to 74 years (−4.1%) and 35 to 54 years (−2.6%). CRC diagnoses also decreased, but to a lesser degree, from 44.0% to 41.7% overall (−2.3%), with men aged ≥75 years showing the largest decrease (−4.0%), followed by those aged 55 to 74 years (−2.3%; $P<.01$), whereas men aged 35 to 54 years had no significant change. All results were significant at $P<.001$ unless noted otherwise.

Discussion

This large, retrospective, observational study found that PSA testing rates in the primary care setting decreased relative to cholesterol screening across age groups in both an academic medical center and a large commercial claims database after the controversial 2012 USPSTF recommendation against PSA screening in men of all ages. The academic center saw the largest decreases among men aged 55 to 74 years—the population that many clinicians view as the target prostate cancer screening population. Although the USPSTF has never endorsed PSA screening, their updated 2018 guidelines upgraded its recommendation from a grade D to a C rating for men aged 55 to 69 years, softening an explicit recommendation against screening to one that assigns the decision to patients and their doctors after discussing the risks and benefits.[20] In the commercial database, the greatest decrease in PSA testing was seen in men aged ≥75 years, reflecting continued improvement in adherence to 2008 USPSTF guidelines. Coinciding with these declines in PSA testing was a decrease in the proportion of patients diagnosed with early-stage prostate cancer, as would be expected based on results of randomized PSA screening trials showing fewer diagnoses in the nonscreened control arm.[6,7,30] It is notable that the decline in diagnoses was confined to early-stage cancers, potentially decreasing the number of cancers identified when curable, but also reducing rates of overdiagnosis (and subsequent overtreatment).[16]

These findings show that the guideline changes had durable effects on practice patterns through 2016, in line with previous work showing declines of 3% to 10% in PSA screening across age groups with data through 2013.[31] A recent survey study showed that men aged 55 to 59 years, 60 to 74 years, and ≥75 years had similar decreases in screening after the 2012 guidelines,[32] whereas another

Table 2. Changes in PSA and Cholesterol Testing

Age Group	Eligible, n[a]		PSA Screening (Exposure)			Cholesterol Screening (Control)			
	Prepolicy (Control/Exposed)	Postpolicy (Control/Exposed)	Prepolicy, %	Postpolicy, %	Unadjusted Difference, Percentage Points (95% CI)	Prepolicy, %	Postpolicy, %	Unadjusted Difference, Percentage Points (95% CI)	Adjusted DID Estimate, Percentage Points (95% CI)
Academic center									
All men	18,559/18,303	78,281/77,407	17.8	10.7	–7.1 (–7.7 to –6.5)	30.6	31.3	0.7 (0.0–1.4)	–8.0 (–8.9 to –7.1)
35–54 y	9,574/9,566	36,517/36,484	13.6	5.3	–8.3 (–9.0 to –7.6)	32.0	28.1	–3.9 (–4.9 to –2.9)	–4.8 (–6.0 to –3.7)
55–74 y	6,556/6,389	32,756/32,256	26.5	17.1	–9.4 (–10.6 to –8.2)	31.6	35.2	3.6 (2.4–4.8)	–13.0 (–14.7 to –11.4)
≥75 y	2,429/2,348	9,008/8,667	10.8	9.8	–1.0 (–2.4 to 0.4)	22.6	29.9	7.3 (5.4–9.2)	–8.5 (–11.0 to –6.1)
OptumLabs 1% sample									
All men	93,334	110,067	9.6	15.4	5.8 (5.5–6.1)	18.6	28.0	9.4 (9.0–9.8)	–3.6 (–4.1 to –3.2)
35–54 y	49,571	46,359	7.6	10.7	3.1 (2.7–3.5)	18.3	25.6	7.3 (6.8–7.8)	–4.1 (–4.8 to –3.5)
55–74 y	35,148	48,215	12.9	20.5	7.6 (7.1–8.1)	20.2	30.7	10.5 (9.9–11.1)	–2.8 (–3.6 to –2.0)
≥75 y	8,615	15,493	8.2	13.5	5.3 (4.5–6.1)	13.1	26.7	13.6 (12.6–14.6)	–8.2 (–9.6 to –6.9)

All comparisons are between the prepolicy (2008–2011) and postpolicy (2013–2016) periods in primary care. Time intervals were defined as calendar years and evaluated independently for patient-level eligibility. Adjusted DID estimates are corrected for age, Charlson comorbidity score, race, and insurance provider type for the academic center, whereas the OptumLabs sample is corrected for age, race, and socioeconomic status (net worth). Charlson comorbidity score and age were derived on an annual basis. All *P* values are <.001.

Abbreviations: Difference-in-differences, DID; PSA, prostate-specific antigen.

[a]Eligible patients are listed for both the prepolicy and postpolicy periods. For the academic center, the first number is the initial number identified and used for the cholesterol control group, and the second number represents the PSA-exposed group which has excluded records after prostate cancer diagnoses. For the OptumLabs sample, these are equivalent as initial data extraction pre-excluded records after prostate cancer diagnosis date.

Table 3. Changes in Early-Stage Diagnoses for Prostate Versus Colorectal Cancer

Age Group	Prostate Cancer					Colorectal Cancer				
	Prepolicy		Postpolicy			Prepolicy		Postpolicy		
	Total Diagnosed, n	Early-Stage, n (%)	Total Diagnosed, n	Early-Stage, n (%)	Difference, Percentage Points (95% CI)	Total Diagnosed, n	Early-Stage, n (%)	Total Diagnosed, n	Early-Stage, n (%)	Difference, Percentage Points (95% CI)
Academic center										
All	2,572	2,032 (79.0)	1,397	885 (63.4)	−15.6 (−18.6 to −12.6)	413	198 (47.9)	521	279 (53.6)	5.7[a] (−0.7 to 12.1)
35–54 y	332	267 (80.4)	143	93 (65.0)	−15.4 (−24.3 to −6.5)	122	48 (39.3)	168	73 (43.5)	4.2[a] (−7.3 to 15.7)
55–74 y	1,895	1,488 (78.5)	1,095	691 (63.1)	−15.4 (−18.8 to −12.0)	203	94 (46.3)	266	156 (58.6)	12.3[b] (3.2–21.4)
≥75 y	345	277 (80.3)	159	101 (63.5)	−16.8 (−25.4 to −8.2)	88	56 (63.6)	87	50 (57.5)	−6.1[a] (−20.6 to 8.4)
SEER										
All	75,641	62,469 (82.6)	44,904	34,875 (77.7)	−4.9 (−5.4 to −4.4)	20,250	8,915 (44.0)	15,077	6,286 (41.7)	−2.3 (−3.3 to −1.3)
35–54 y	8,587	6,901 (80.4)	4,476	3,481 (77.8)	−2.6 (−4.1 to −1.1)	4,841	2,062 (42.6)	3,802	1,576 (41.5)	−1.1[a] (−3.2 to 1.0)
55–74 y	53,875	44,525 (82.6)	33,256	26,110 (78.5)	−4.1 (−4.6 to −3.6)	10,437	4,661 (44.7)	8,067	3,423 (42.4)	−2.3[b] (−3.7 to −0.9)
≥75 y	13,179	11,043 (83.8)	7,172	5,284 (73.7)	−10.1 (−11.3 to −8.9)	4,972	2,192 (44.1)	3,208	1,287 (40.1)	−4.0 (−6.2 to −1.8)

All comparisons are between the prepolicy (2008–2011) and postpolicy (2013–2016) periods. Time intervals were defined as calendar years and evaluated independently for patient-level eligibility. Differences are unadjusted and evaluated by chi-square test. All *P* values are <.001 except where indicated.

[a]*P*>.05.

[b]*P*<.01.

found significant declines of 5% to 10% in men aged <75 years.[33] These studies only included data through 2013—1 year after the recommendation changes; therefore, our findings show that the guideline changes had durable effects on practice patterns through 2016. An analysis of OptumLab's privately insured patients showed a 38.4% decline in PSA testing that was restricted to men aged ≥75 years, whereas no significant changes were seen in younger men. Again, this study was limited to data through 2013 and calculated raw rates of PSA testing that did not account for secular trends.[34] By including data through 2016 and accounting for secular trends through the DID method, we found declines in PSA testing across ages, demonstrating that the declines were generalized and not restricted to an academic practice. It is of interest that the academic center showed greater declines in PSA testing, suggesting a closer adherence to the guidelines. Whether this is true generally or is caused by other factors, such as regional difference in practice patterns, should be tested by analyzing EHR-extracted data in academic and non-academic settings.

We observed reductions in unadjusted proportions of prostate cancers diagnosed at an early stage, particularly compared with CRCs, showing that the number and proportion of low-risk prostate cancer diagnoses decreased after the guideline changes, consistent with ongoing attempts to reduce overtreatment.[11,19,35,36] Data from SEER have shown that prostate cancer incidence as a whole has declined substantially in recent years,[31] including early-stage cancers, although the decrease in early-stage cancers has attenuated since 2013.[37] Our study included more years after the guideline changes, and our results suggest continued but modest declines in the proportion of early-stage cancers. Future work will need to evaluate whether the 2018 upgrade of the recommendations to a C rating[20] will affect PSA testing rates.

Our findings suggest that guideline changes affect physician behavior, at least in terms of the controversial recommendations regarding prostate cancer screening. In addition, the decrease in diagnosis of early-stage prostate cancer shows that the guidelines affect important disease characteristics in patients. Fewer early-stage cancers will decrease the number of men overtreated for prostate cancer and thereby diminish the burden of adverse effects associated with treatment, such as incontinence and erectile dysfunction.[10,11,38,39] However, some randomized trials of screening and treatment have shown mortality reductions in screened populations and among men treated, as opposed to observed, for early-stage prostate cancer.[5,15] Because prostate cancer has a long natural history, changes in mortality rates in the population might not be seen for several years after guideline changes.

Our study has limitations that should be mentioned. First, we used a nonrandomized design and thus could not prove that the 2012 USPSTF recommendations caused any of the observed changes in PSA testing; however, studying changes over time, using multiple datasets, and controlling for patient demographics reduced the chance that the results were confounded by variations in unobserved patient characteristics. Our analysis assumed that cholesterol testing patterns serve as a counterfactual that reflects secular changes in practice patterns, because cholesterol testing is widely practiced, administered via blood test, and applied in men across a spectrum of ages, and guidelines regarding its use did not change during the study period. We followed published best practices in assessing this assumption by testing for parallelism in the prepolicy period.[25,26] If this assumption was inaccurate, the results of our analysis could be biased.

Conclusions

After the USPSTF's 2012 grade D recommendation against PSA screening, we observed declines in primary care PSA testing rates relative to cholesterol testing patterns and a decrease in the proportion of prostate cancers diagnosed at an early stage. Our study shows that primary care physicians respond to guideline changes by changing their practice patterns. Guideline adherence was not absolute, evidenced by the continued use of PSA testing, and likely reflects controversies surrounding PSA testing. Our findings show that as the healthcare system moves to a more efficient, patient-centered focus and guidelines and quality metrics become widespread, providers are rapidly responding to guideline recommendations. However, advances in screening technologies are likely to beget clinical scenarios that parallel the controversies surrounding PSA testing. It is important to consider how best to meet needs for disease screening in adults and the efficient use of health services. Further research is needed to understand the effects of the USPSTF's guideline changes on cancer survival.

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Supplemental online content for:

PSA Testing Use and Prostate Cancer Diagnostic Stage After the 2012 U.S. Preventive Services Task Force Guideline Changes

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eAppendix 1. Supplemental Methods: Regression Equations

Difference-in-Differences Analysis

$$Outcome_{itk} = \beta_o + \beta_1 Postpolicy_t + \beta_2 Exposed_k + \beta_3 Postpolicy_t Exposed_k + \gamma_1 Race_i + \gamma_2 Age_i + \gamma_3 Insurance_i + \gamma_4 CharlsonComorbidity_i + \varepsilon_{ict} \quad \textbf{(1)}$$

Indexed patient, time period (eligibility interval), and cohort (exposed = prostate) are represented by *i*, *t*, and *k*, respectively. *Postpolicy* was an indicator for the time period after implementation of the U.S. Preventive Services Task Force guideline changes (2013–2016). *Exposed* was an indicator for the cohort eligible for prostate-specific antigen (exposure) or cholesterol (control) testing. Potential confounders were *race* (white, Asian, black, Hispanic, other), *age*, *insurance* (Medicare, Medicaid, private, other), and *Charlson comorbidity score*. β_3 is the difference-in-differences estimate, which provides the differential change between the exposure and control groups after policy implementation.

Parallel Trends Assumption: Testing for Prepolicy (2008–2011) Trend Divergence of Exposure and Control

$$Outcome_{itk} = \beta_o + \beta_1 TimeTrend_t + \beta_2 Exposed_k + \beta_3 TimeTrend_t Exposed_k + \gamma_1 Race_i + \gamma_2 Age_i + \gamma_3 Insurance_i + \gamma_4 CharlsonComorbidity_i + \varepsilon_{ict} \quad \textbf{(2)}$$

Difference-in-differences analysis allows for a natural retrospective experiment while accounting for secular changes by assuming that the control is a valid counterfactual for the exposed group had the policy not been implemented. By showing that prepolicy trends are similar between exposure and control groups, it is reasonable to then consider the control as the counterfactual, as established by published best practices. The parallelism of prepolicy trends can be performed either by graphical inspection or by the following statistical method. Data are restricted to the prepolicy period (before 2012), and a linear *TimeTrend* variable is used to denote the time interval since the beginning of the study period. Otherwise, the terms are equivalent to those in Equation 1. The difference-in-differences estimator, β_3, is the interaction of the linear time trend and exposure to the policy, measuring any prepolicy divergence between the exposure and control groups. If this term is statistically insignificant, then no prepolicy difference is observed, supporting the control as a valid counterfactual. The prepolicy trends analysis comparing prostate-specific antigen (exposure) versus cholesterol (control) testing in primary care screening is presented in supplemental eAppendix 2.

eAppendix 2. Prepolicy Trends in Prostate-Specific Antigen and Cholesterol Testing in the Primary Care Setting

Age Group	Trend Difference, Percentage Points (95% CI)	*P* Value
All	0.6 (−0.2 to 1.4)	.13
35–54 y	0.8 (−0.2 to 1.8)	.13
55–74 y	0.4 (−1.0 to 1.8)	.60
≥75 y	−0.4 (−2.2 to 1.5)	.70

Parallel trends are assessed only in the prepolicy period (2008–2011). Time intervals were defined as calendar years and were evaluated independently for patient-level eligibility. The trend difference is obtained as the difference-in-differences estimator (β_3 in Equation 2 in eAppendix 1) for the interaction of the linear time trend and exposure to the policy. When this term is statistically insignificant, there is no observable prepolicy difference. A negative trend difference indicates a decline in the exposure group relative to the control. Adjusted difference-in-differences estimates are corrected for age, Charlson comorbidity score, race, and insurance provider type. Charlson comorbidity score and age were derived on an annual basis.

eAppendix 3. Characteristics of Diagnosed Patient Population

Characteristic	Prostate Cancer				Colorectal Cancer			
	Prepolicy	Postpolicy	Unadjusted Difference, Percentage Points (95% CI)	*P* Value	Prepolicy	Postpolicy	Unadjusted Difference, Percentage Points (95% CI)	*P* Value
Academic center								
Patients, n	2,572	1,397			413	521		
Mean age, y	64.8	65.0	0.2 (–0.4 to 0.7)	.51	62.6	61.7	–0.9 (–2.6 to 0.8)	.28
Charlson comorbidity score (mean, median)	0.5, 0	0.9, 0	0.4 (0.3–0.5)	<.001	0.5, 0	0.9, 0	0.0 (–0.3 to 0.3)	.96
Eligible patients by age, %								
35–54 y	12.9	10.2	–2.7 (–4.7 to –0.7)	.013	29.5	32.2	2.7 (–3.3 to 8.7)	.37
55–74 y	73.7	78.4	4.7 (2.0–7.4)	.001	49.2	51.1	1.9 (–4.6 to 8.4)	.56
≥75 y	13.4	11.4	–2.0 (–4.1 to 0.1)	.066	21.3	16.7	–4.6 (–9.7 to 0.5)	.073
Race, %								
White	56.1	64.4	8.3 (5.1–11.5)	<.001	62.7	52.2	–10.5 (–16.8 to –4.2)	<.01
Asian	7.0	9.6	2.6 (0.8–4.4)	<.01	14.3	20.5	6.2 (1.4–11.0)	.013
Black	3.1	4.2	1.1 (–0.1 to 2.3)	.075	3.1	3.1	0.0 (–2.2 to 2.2)	.95
Hispanic	8.5	7.6	–0.9 (–2.7 to 0.9)	.33	9.4	13.4	4.0 (–0.1 to 8.1)	.059
Other/Unknown	25.3	14.3	–11.0 (–13.5 to –8.5)	<.001	10.4	10.7	0.3 (–3.7 to 4.3)	.87
Insurance, %								
Medicare	52.8	46.7	–6.1 (–9.4 to –2.8)	<.001	45.0	43.6	–1.4 (–7.8 to 5.0)	.65
Medicaid	2.2	4.4	2.2 (1.0–3.4)	<.001	7.7	7.9	0.2 (–3.3 to 3.7)	.95
Private	37.4	43.2	5.8 (2.6–9.0)	<.001	39.5	43.2	3.7 (–2.6 to 10.0)	.25
Other/Unknown	7.6	5.6	–2.0 (–3.6 to –0.4)	.016	7.7	5.4	–2.3 (–5.5 to 0.9)	.14
SEER								
Patients, n	75,641	44,904			20,250	15,077		
Mean age (95% CI), y	65.6	65.8	0.2 (0.1–0.3)	<.001	64.7	63.8	–0.9 (–1.1 to –0.6)	<.001
Eligible patients by age, %								
35–54 y	11.4	10.0	–1.4 (–1.8 to –1.0)	<.001	23.9	25.2	1.3 (0.4–2.2)	<.01
55–74 y	71.2	74.1	2.9 (2.4–3.4)	<.001	51.5	53.5	2.0 (0.9–3.1)	<.001
≥75 y	17.4	16.0	–1.4 (–1.8 to –1.0)	<.001	24.6	21.3	–3.3 (–4.2 to –2.4)	<.001
Race, %								
White	73.4	71.3	–2.1 (–2.6 to –1.6)	<.001	70.9	68.4	–2.5 (–3.5 to –1.5)	<.001
Asian	4.9	5.2	0.3 (0.0–0.6)	.036	9.5	10.4	0.9 (0.3–1.5)	<.01
Black	14.3	15.5	1.2 (0.8–1.6)	<.001	10.7	11.4	0.7 (0.0–1.4)	.039
Hispanic	4.4	4.4	0.0 (–0.2 to 0.2)	.53	6.1	6.5	0.4 (–0.1 to 0.9)	.10
Other/Unknown	3.0	3.6	0.6 (0.4–0.8)	<.001	2.8	3.3	0.5 (0.1–0.9)	.025
Insurance, %								
Insured	84.6	81.6	–3.0 (–3.4 to –2.6)	<.001	84.3	82.0	–2.3 (–3.1 to –1.5)	<.001
Medicaid	3.2	5.0	1.8 (1.6–2.0)	<.001	8.3	11.3	3.0 (2.4–3.6)	<.001
Other/Unknown	12.2	13.5	1.3 (0.9–1.7)	<.001	7.4	6.7	–0.7 (–1.2 to –0.2)	<.01

All comparisons are between the prepolicy (2008–2011) and postpolicy (2013–2016) periods. Time intervals were defined as calendar years and evaluated independently for patient-level eligibility.