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Research Article

Patterns of Prostate-Specific Antigen Testing and Prostate Biopsies during the COVID-19 Pandemic, in the United States

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Abstract

Purpose: This study examined changes in prostate disease screening (Prostatic-Specific Antigen [PSA] testing), prostate biopsy testing, and prostate cancer diagnoses during the COVID-19 pandemic, in the United States.

Materials and Methods: This analysis included de-identified patient test data from men ≥40 years, without prior International Classification of Diseases-10 record of prostate cancer since January 2016, who received PSA or prostate biopsy testing at Quest Diagnostics January 2018-April 2022. Monthly trends were evaluated for four periods prepandemic (January 2018-February 2020) and pandemic phases 1-3 (March-May 2020, (June 2020-May 2021, and (June 2021-April 2022).

Results: Meeting inclusion criteria were 24,638,829 PSA and 70,983 prostate biopsy results. Overall, 12,543,973 PSA tests were performed in pandemic phases 1-3, 4.3% above what would be expected based on prepandemic testing volume. The average monthly number of PSA tests decreased from 465,187 prepandemic to 295,786 in phase 1 of the pandemic (-36.4% vs prepandemic) before increasing to 490,081 (+5.4% vs prepandemic) in phase 2 and 525,058 (+12.9% vs prepandemic) in phase 3. Overall, 33,207 prostate biopsy specimens were analyzed during phase 1-3 of the pandemic, 12.1% fewer than expected based on prepandemic volumes. The average monthly number of prostate biopsy results decreased from 1453 prepandemic to 903 (-37.8% vs prepandemic) in phase 1 of the pandemic, 1268 (-12.7% vs prepandemic) in phase 2, and 1389 in phase 3 (-4.4% vs prepandemic).

Conclusion: PSA testing has exceeded prepandemic levels in pandemic phases 2-3, while a gap in prostate biopsies remains. These findings suggest that many prostate screening opportunities and cancer diagnoses have been missed. Efforts are needed to bring patients back for screening and diagnostic testing and to restore appropriate care for non–COVID-19–related medical conditions.

Introduction

Guidelines from the American Cancer Society (ACS) [1], the American Urological Association (AUA) [2], and the United States Preventive Services Task Force (USPSTF) [3] support shared, informed decision making for prostate cancer screening. During the early months of the COVID-19 pandemic, deferral of routine screening and other healthcare services was associated with marked decreases in new cancer diagnoses [4]. Resulting treatment delays could lead to more patients having advanced disease at diagnosis, requiring aggressive therapy, and succumbing to cancer [5-7]. Understanding trends in screening and diagnostic testing for prostate cancer may help identify gaps in patient care. We previously reported sharp declines in Prostate-Specific Antigen (PSA) screening and prostate biopsy testing in the early months of the pandemic, followed by rebounds through December 2020 [8]. With society having largely transitioned back to routine life and healthcare utilization, in the present study we examined whether patients who may have delayed care early during the pandemic are now returning for care, and whether these trends vary with age. To assess the impact of delays in care on PSA levels and,

potentially, stage migration, we also evaluated trends in PSA levels and prostate biopsy Gleason scores during the pandemic through April 2022.

Methods

The Quest Diagnostics database includes test data from patients residing in all US states and District of Columbia and is reflective of a diverse, heterogeneous population. The Quest Diagnostics market share has been consistent throughout the study period. For this study, we analyzed de-identified PSA test result data for men ages 40 years and older who had no record prostate cancer since January 2016, based on International Statistical Classification of Diseases and Related Health Problems, Tenth Revision codes. Each patient was counted no more than once within each month, using the most severe result of PSA or prostate biopsy testing. Total PSA testing was performed using the Siemens chemiluminescent method, and its result value (ng/mL) was standardized against the WHO international standard [9]. In this analysis, PSA level was categorized into three groups: <4.0 ng/mL, 4.0 ng/mL-49.9 ng/mL, and ≥50.0 ng/mL. PSA test results >4.0 ng/mL are considered elevated and results >50.0 ng/mL are considered highly elevated. Prostate biopsy results with cancer were reported with a Gleason score (6 to 10) on the basis of Gleason primary and secondary grades assigned to biopsy tissues. Gleason scores were grouped as <6, 6-7, or ≥8. Because prostate cancer risk increases substantially among men ≥60 years old [10], patients were segmented into age groups of 40-59 years and ≥60 years.

Testing trends were evaluated for four periods: prepandemic baseline (January 2018 -February 2020), pandemic phase 1 (March 2020- May 2020), pandemic phase 2 (June 2020- May 2021), and pandemic phase 3 (June 2021-April 2022). The "Expected" number of cases is the prepandemic monthly mean multiplied by the number of months in each pandemic phase. Note that the time frame for the prepandemic period was equal to the sum of the 3 pandemic phases (26 months). The Wilcoxon rank-sum test was used to compare the average monthly numbers between the prepandemic baseline period and pandemic phases 1, 2, and 3, both separately and combined. Chi-square analysis was done to compare the proportion of Gleason score groups between the prepandemic phase and pandemic phases 1, 2, and 3. Data analyses were performed using SAS Studio 3.81 on SAS version 9.4 (SAS Institute). This study was deemed exempt by the WCG Institutional Review Board (Puyallup, WA).

Results

A total of 24,638,829 PSA tests were included in the analysis, with a mean (Standard Deviation) patient age of 62.4 (10.4) years. Overall, 12,094,856 PSA tests were performed prepandemic and 12,543,973 PSA tests were performed in the collective pandemic phases 1-3, 4.3% above what would be expected based on prepandemic testing volume (P<0.01) (Table 1). The average monthly number of PSA tests decreased from 465,187 prepandemic to 295,786 in pandemic phase 1 (-36.4% vs prepandemic, P<0.01) before increasing to 490,081 (+5.4% vs prepandemic, P=0.07) in pandemic phase 2 and 525,058 (+12.9% vs prepandemic, P<0.01) in pandemic phase 3 (Figure 1).Highly elevated PSA (≥50 ng/mL) results represented 0.15% (36,105/23,751,470) of all PSA results. Overall, highly elevated PSA test results were detected in 17,121/12,094,856 patients prepandemic and 18,984/11,656,614 patients during pandemic phases 1-3 (a 10.9% increase; P<0.01). The monthly average number of PSA results ≥50 ng/mL decreased from 659 prepandemic to 506 (-23.2% vs prepandemic, P=0.02) in pandemic phase 1 before increasing to 707 (+7.4% vs prepandemic, P=0.08) in pandemic phase 2 and 816 (+24.0% vs prepandemic, P<0.01) in pandemic phase 3. A total of 70,983 prostate biopsy analyses were included, with a mean (standard deviation) patient age of 66.6 (8.2) years. Overall, 12.1% fewer prostate biopsy specimens were analyzed during pandemic phases 1-3 than during the prepandemic period (33,207 vs 37,776; P<0.01; Table 1). The average monthly number of prostate biopsy results decreased from 1453 prepandemic to 903 (-37.8% vs prepandemic) in pandemic phase 1, 1268 (-12.7% vs prepandemic) in pandemic phase 2, and 1389 in pandemic phase 3 (-4.4% vs prepandemic) (Figure 2). A total of 4,572 biopsy specimens with high grade (Gleason score >8) were identified during phases 1-3 of the pandemic, 3.4% (P<0.01) below the 4,771 cases observed during the prepandemic period. Gleason scores ≥8 were identified in 13.1% (4,721/37,776) of biopsy specimens analyzed prepandemic and 13.8% (4572/33,207) of those analyzed during pandemic phases 1-3. The monthly average number of specimens with Gleason scores ≥8 decreased from 182 prepandemic to 130 during pandemic phase 1 (-28.2% vs prepandemic; P=0.02) and 172 during pandemic phase 2 (-5.3% vs prepandemic; P=0.18) before rebounding to 193 in pandemic phase 3 (+6.0% vs prepandemic; P=0.17).

	Prepandemic baseline (January 2018- February 2020)		Pandemic Phase 1 (March 2020- May 2020)		Pandemic Phase 2 (June 2020- May 2021)		Pandemic Phase 3 (June 2021- April 2022)	
	Number	Monthly average	Number	Monthly average; Change percent; P value	Number	Monthly average; Change percent; P value	Number	Monthly average; Change percent; P value
Total Prostate Specific Antigen (PSA) Tests	1,20,94,856	4,65,187	8,87,359	2,95,786 -36.4 0.01	58,80,971	4,90,081 5.4 0.07	57,75,643	5,25,058 12.9 <0.01
PSA ≤4.0 ng/mL	1,07,70,980	4,14,268	7,84,303	2,61,434 -36.9 <0.01	52,56,113	4,38,009 5.7 0.04	51,63,787	4,69,435 13.3 <0.01
PSA 4.0-49.9 ng/mL	13,06,755	50,260	1,01,538	33,846 -32.7 0.01	6,16,371	51,364 2.2 0.5	6,02,877	54,807 9 0.01
PSA ≥50.0 ng/mL	17,121	659	1,518	506 -23.2 0.02	8,487	707 7.4 0.08	8,979	816 24 <0.01
Age 40-59 years	51,35,197	1,97,508	3,59,245	1,19,748 -39.4 0.01	24,47,276	203940 3.3 0.39	23,91,036	2,17,367 10.1 <0.01
Age ≥60 years	69,59,659	2,67,679	5,28,114	1,76,038 -34.2 0.01	34,33,695	286141 6.9 0.02	33,84,607	3,07,692 14.9 <0.01
Prostate Biopsies	37,776	1,453	2,710	903 -37.8 0.01	15,220	1268 -12.7 <0.01	15,277	1389 -4.4 0.09
Gleason score <6	18,513	712	1,258	419 -41.2 0.01	7,175	597 -16.2 <0.01	6,985	635 -10.8 <0.01
Gleason score 6-7	14,542	559	1,061	354 -36.8 0.01	5,982	499 -10.9 <0.01	6,174	561 0.4 0.97
Gleason score >8	4,721	182	391	130 -28.2 0.02	2,063	172 -5.3 0.18	2,118	193 6 0.17
Age 40-59 years	8,565	329	581	194 -41.2 0.02	3,029	252 -23.4 <0.01	2953	268 -18.5 <0.01
Age ≥60 years	29,211	1,124	2,129	710 -36.8 0.01	12,191	1016 -9.6 0.01	12324	1120 -0.3 0.92

Table 1: Prostate-specific antigen (PSA) and prostate biopsy testing, January 2018 through April 2022.

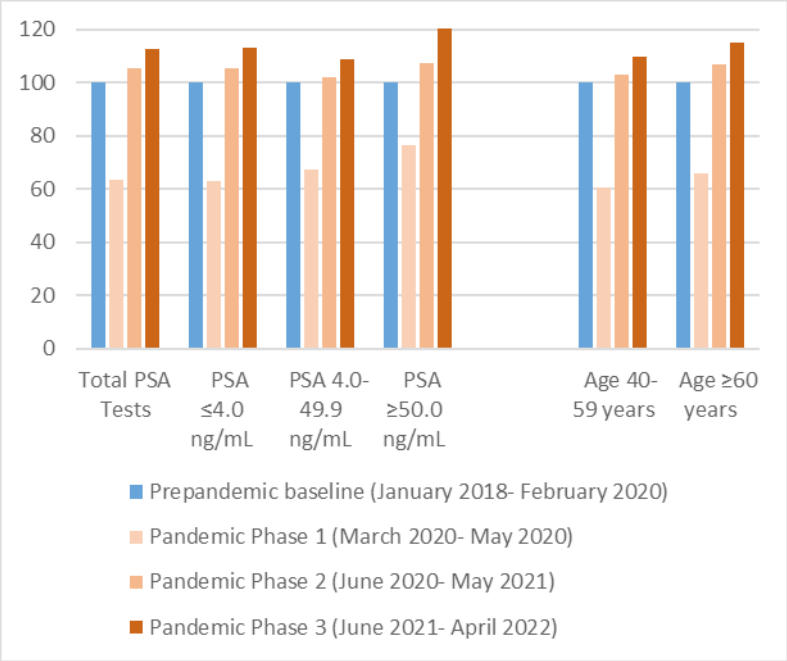

Figure 1: Relative prostate-specific antigen (PSA) monthly mean testing prepandemic (scale 100) and pandemic periods1-3 overall and by PSA level and patient age groups.

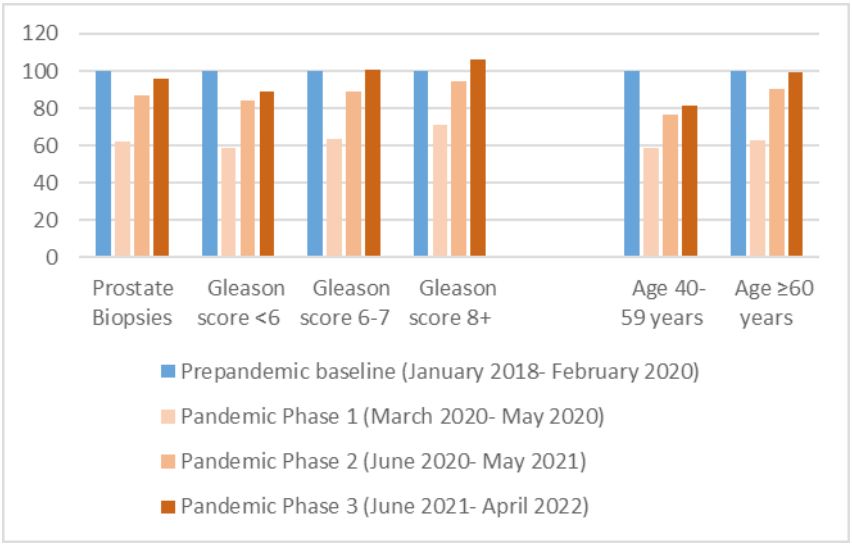

Figure 2: Relative prostate biopsy monthly mean testing prepandemic (scale 100) and pandemic periods1-3 overall and by Gleason score and patient age groups.

The total number of PSA tests performed increased from the prepandemic period to phases 1-3 of the pandemic, overall (3.7% increase) and in both the 40- to 59-year-old age group (1.2% increase) and the ≥60-year-old age group (5.6% increase) (Table 2). The biggest increase was seen for highly elevated PSA results ≥50 ng/mL (10.8% increase, P <0.01) and the smallest for PSA results of 4.0-49.9 ng/mL (1.1%, P<0.01). The overall number of prostate biopsy evaluations dropped by 12.1% (P <0.01) from prepandemic levels, with the largest declines in the 40- to 59-year–old age group (-23.3%) and those for with prostate biopsy Gleason scores <6 (-16.7%). (Figure 3) shows how the proportion of Gleason score groups has shifted, especially from prepandemic and pandemic phase

1 to pandemic phases 2-3. This shift in proportion of Gleason score groups was significant (P<0.01) for all pandemic phases compared to the prepandemic phase.

	Prepandemic Baseline (January 2018- February 2020) Number	Pandemic Phases 1-3 (May 2020- April 2022) Number	Difference	Percent difference	P value
Prostate Specific Antigen (PSA)	1,20,94,862	1,25,43,973	4,49,111	3.7	0.02
PSA <4.0 ng/mL	1,07,70,968	1,12,04,203	4,33,235	4	0.01
PSA 4.0-49.9 ng/mL	13,06,760	13,20,786	14,026	1.1	0.24
PSA ≥50.0 ng/mL	17,134	18,984	1,850	10.9	0.01
Age 40-59 years	51,35,208	51,97,557	62,349	1.2	0.12
Age ≥60 years	69,59,654	73,46,416	3,86,762	5.6	<0.01
Prostate biopsies	37,778	33,207	-4,571	-12.1	<0.01
Gleason score <6	18,512	15,418	-3,094	-16.7	<0.01
Gleason score 6-7	14,534	13,217	-1,317	-9.1	0.03
Gleason score ≥8	4,732	4,572	-160	-3.4	0.52
Age 40-59 years	8,554	6,563	-1,991	-23.3	<0.01
Age ≥60 years	29,224	26,644	-2,580	-8.8	0.03

Table 2: Impact of COVID-19 pandemic on prostate-specific antigen (PSA) testing and prostate biopsies, through April 2022.

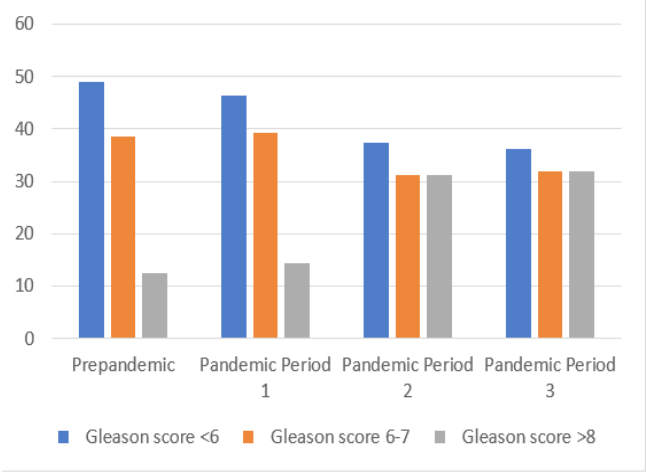

Figure 3: Proportion of prostate biopsies by Gleason score group during prepandemic and pandemic periods 1-3.

Discussion

The monthly trends in test volumes over the 52-month period reflected in the study demonstrate the validity of the observed dramatic changes during the early months of the pandemic. Specifically, we saw sharp declines in PSA testing and prostate biopsy analyses during pandemic phase 1. When we combined observations from the 3 pandemic phases, PSA testing exceeded prepandemic levels (+3.7% overall)-most notably for results >50 ng/mL (10.9%). This suggests more men likely presented with advanced prostate cancer than would be expected, particularly in pandemic phases 2-3, potentially because of delayed or missed PSA testing in pandemic phase 1. The increased observed PSA testing in pandemic phases 2 and 3 was stronger for men >60 years of age than for men 40-59 years of age. This is encouraging if it reflects a tendency of older men to utilize healthcare resources, given the increasing risk of cancer

with advancing age. In contrast, prostate biopsy testing volumes declined during the pandemic (-12.1%). The decline was seen for all 3 Gleason score categories, with progressively less-sharp declines with increasing Gleason score group. This finding suggests that the least aggressive prostate cancers are more commonly not being identified during the pandemic. When analyzed by age, the gap in prostate biopsies was far more pronounced for younger men (ages 40-59 years; -23.3%) than for older men (ages >60 years; -8.8%).

Most striking is the somewhat paradoxical increase in volume of PSA testing and concurrent volume decline in prostate biopsies, including among those with Gleason scores consistent with high-grade cancer. One explanation is that PSA testing is most commonly ordered by primary care physicians, whereas urologists generally obtain prostate biopsies and order tissue analysis; obtaining appointments with urologists may be more challenging [11,12], particularly during the pandemic. This situation may worsen with increasing demand of urologists who may be currently performing more vasectomies [13]. Second, the decline in reliance on Digital Rectal Examination (DRE), again most commonly performed by primary care physicians, may contribute to fewer prostate biopsies and detection of prostate cancers. The DRE as performed in primary care settings has been shown to have limited clinical utility based on an extensive meta-analysis [14]. As early as 2014, the Canadian Task Force on Preventive Health Care no longer recommended screening with DRE in the general population [15]. Regardless of the cause or combination of factors, the rise in the number of men with very high PSA values suggests that more men are presenting with advanced prostate disease. The decline in prostate biopsies results, especially those indicating cancer, suggests that we are continuing to not identify many men with prostate cancer of all Gleason scores. The long-term consequence of short delays may be minimal [5,16,17] However, as we are now into the third year of the pandemic, we are navigating uncharted territory regarding understanding the clinical impact of extended delays in healthcare. Delays in prostate cancer diagnoses can lead to worse outcomes, including stage migration toward more advanced disease. Delays for some men likely greatly exceed 6 months, a time when biochemical disease progression may occur [17-19]. limitation of the study is that patients might have obtained testing from different laboratories during the pandemic, and we did not adjust trends in PSA and biopsy test volumes for changes in overall testing volume or market share at our laboratory. In addition, we could not assess reasons for care deferral of care or how these reasons varied across phases of the pandemic.

In conclusion, these findings suggest that PSA testing has rebounded to exceed prepandemic numbers. However, diagnosis of prostate cancer is likely still being delayed for a substantial number of men, especially for younger men and those with low Gleason scores of 6 or 7, whose symptoms may not prompt urologic evaluation. These men may benefit from multidisciplinary management to avoid further diagnostic and therapeutic delays if they choose so. Efforts are needed to bring such patients back for diagnostic testing and, in general, to restore appropriate care for non–COVID-19-related medical conditions. This pandemic is not over, nor is this the final pandemic. Understanding the changed dynamics in healthcare services and gaps in care allows policy makers to understand and attempt to address potential critical gaps in future healthcare services.

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