ARTICLE

Clinical Research

Trends in prostate cancer mortality in the United States of America, by state and race, from 1999 to 2019: estimates from the centers for disease control WONDER database

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BACKGROUND: In the United States of America (USA), prostate cancer (PC) is the most common cancer in men and the second cause of cancer mortality. Black men (BM) have a higher incidence and worse mortality when compared to white men (WM). We compared trends in PC mortality in the USA by race and state from 1999 to 2019.

METHODS: We extracted PC mortality data from the Centers for Disease Control (CDC) WONDER database using the International Classification of Diseases (ICD) 10 code C61. Age-Standardized Mortality Rates (ASMR) were divided into racial groups and reported by year and state. Due to the lack of available data in many states, analyses were conducted only for WM and BM using Joinpoint regression for trend comparisons.

RESULTS: Between 1999–2019, ASMR decreased at the national level in Black (−44.6%), Asian (−44.8%), White (−31.8%), and American Indian or Alaskan native men (−19.0%). ASMR decreased in all states for both races. The greatest drop in ASMR was in Kentucky (−47.0%) for WM and Delaware (−57.8%) for BM. In 2019, ASMRs in BM (13.4/100 000) were significantly higher than WM (7.3/100 000), American Indian or Alaskan Native (3.2/100 000), and Asian men (3.2/100 000) ($p < 0.001$). The highest ASMRs were in Nebraska (33.5/100 000) for BM and Alaska (11/100 000) for WM.

CONCLUSIONS: During the last 20 years, the PC mortality rate dropped in all states for all races, suggesting an advancement in management strategies. Although a higher decrease in ASMR was observed in BM, ASMR remain higher among BM. ASMRs were also found to be increasing in many states post USPSTF guideline change (2012), indicating a need for more education around optimized prostate cancer screening.

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INTRODUCTION

In the United States of America(USA), prostate cancer(PC) is the most frequently diagnosed non-skin cancer and the second leading cause of cancer mortality [1]. Black men (BM) have a 1.7-fold greater risk of diagnosis and a 2.3-fold increased death risk from PC compared to White men(WM) [2]. Indeed, BM have the highest PC incidence worldwide, with an earlier onset and a more aggressive clinical phenotype at presentation than other racial groups [3, 4]. PC incidence in the USA has been fluctuating throughout the past decades. A sharp rise was noted in the 1990s, coinciding with the widespread adoption of prostate-specific antigen(PSA) screening [5]. With the publication of US Preventive Services Task Force(USPSTF) guidelines against PC screening in 2012, the incidence of PC has declined concomitantly with decreased PSA screening [6–8]. Steady declines in PC mortality, although faster in BM than WM, were observed especially in Northern America from 2001–2015. The stabilization of mortality rates since 2012 is probably due to PSA screening and treatment advancements [9]. We hypothesized that PC mortality is decreasing in the USA; however, BM might have higher mortality rates than WM. To understand the dynamic changes, especially post-USPSTF guidelines, our principal aim was to compare PC mortality trends across states of the USA over recent decades, using the Centers for Disease Control and Prevention Wide-ranging ONline Data for Epidemiologic Research(CDC WONDER). Our secondary aim was to compare the differential trends amongst BM and WM within each state to identify any racial disparity in PC mortality.

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METHODS

PC mortality data(ICD 10 Code 61) in the USA were extracted from the CDC WONDER database, a comprehensive online public health information system, in collaboration with the National Center for Health Statistics and the Vital Statistics Cooperative Program 1999–2019 [10, 11]. It is updated annually from deaths registered by national civil registration systems and standardized for age. Dichotomized data by race is extracted from the online database and reported by year. According to the standard American population, ASMR was defined as mortality weighted to the distribution of mortality per 5-year age group [12]. Data from all 50 United States and the District of Colombia (DC) were analyzed. Most states started collecting data in 1999, whereas four states started collecting data in 2000, one from 2001, one from 2008, and one from 2009. Data were collected until 2019, except for three states until 2018 only. Data were missing for BM in 17 states. There were 107/1808(5.9%) missing data elements. Each data element includes ASMR in individual states and years. Institutional review board approval was not necessary as the collected data was publically available in a de-identified format.

Statistical analysis

To compare the mortality between two racial groups, the student *t*-test was performed using SPSS v 26. Joinpoint regression analysis with annualized data(from 1999–2019) was used to assess changes in linear slope for mortality trends over time. Joinpoint analysis assesses the overall trends in mortality, initially with no Joinpoints, and tests for changes in the model with the sequential addition of Joinpoints where there is a significant change in the slope of the line. Joinpoint software(Command Line Version 4.5.0.1) is provided by the USA National Cancer Institute Surveillance Research Program(Bethesda, MD) [13]. The model computes an estimated annual percentage change(EAPC) for each trend by fitting a regression line to the natural logarithm of the rates. Joinpoint software requires continuous data throughout the observation period to be suitable for analysis. Mortality data were missing in a small subset of states in the database for one or more calendar years. ASMR data from the year before were carried forward. However, states with five or more continuous missing elements were excluded. Changes in ASMR over the observation period are calculated as crude absolute differences between the first and last data points for the earliest and the most recent years available.

Sub-group analysis

To observe the trends before and after the newly published USPSTF guidelines in 2012 [6–8], we analyzed relative change for two groups: 1999–2012 and 2012–2019. We used 2013 for Delaware and 2014 for Minnesota as data for 2012 was unavailable. We carried out a joinpoint analysis from 2012–2019 to evaluate each state's AAPC(average annual percentage change).

Post-hoc analysis

We performed an interrupted time series(ITS) analysis for the states that showed increases in ASMR after guideline implementation [14, 15]. ITS is a quasi-experimental design that evaluates the effects of the pragmatic trial in a real-world setting when a randomized control trial is not feasible. We used SAS Macro developed by Caswell to perform ITS analysis for single outcomes series implementation [16], which has been used and validated [17, 18]. The Single-ITS analysis model included the baseline ASMR trend before USPSTF guideline implementation and change in level and trend afterward. For time-interruption, we considered a lag of 5 years and created models with a time-interruption point in 2017. Autocorrelation up to one order was assessed and accounted for in the model by using Newey-West autocorrelation adjusted standard errors [16].

RESULTS

Current PC mortality

Recent PC ASMR in the USA by race are shown in Fig. 1 and Supplementary Tables 1–3, reported per 100,000 individuals. Data were available for 34 states for BM. In 2019, BM had the highest ASMR(13.4), followed by WM(7.3), American Indian or Alaskan Native men(3.2), and Asian men(3.2) ($p < 0.001$). In 2019, Nebraska had the highest ASMR for BM(33.5) and Alaska (11) for WM. The ASMR for BM were above 11 in all states except New Jersey(10.9), Connecticut(10.8), and New York(10.3). For WM, the two states with the lowest ASMR were New York(6.0) and Kentucky(6.1). New York and New Jersey had some of the lowest ASMR for both WM and BM.

Changes in PC mortality between 1999 and 2019

ASMR at the study period's beginning and end are shown in Supplementary Tables 1–3. The overall trend for ASMR decreased over time across the USA for all racial groups. The widest drop was in Asian men(−44.82%). BM had a −44.6% change between 1999 and 2019, while WM and American Indian or Alaskan native men had a −31.8% and −19.0% change, respectively. ASMR decreased for BM in every state, mostly in Delaware(−57.8%) and Nevada(−55.3%). Similarly, ASMR for WM decreased in every state, especially in Kentucky(−47.0%) and South Dakota(−45.9%). Kentucky and Wisconsin had the smallest decrease in ASMR for BM(−14.9% and −20.3%, respectively), while New Hampshire and Alaska had the smallest measured declines in ASMR for WM(−11.5% and −16.0%, respectively).

Joinpoint regression for different races from 1999–2019

Overall, PC mortality decreased rapidly from 1999 to 2013(EAPC −2.78%), followed by a slow decrease(−0.08%) (Fig. 2). American Indian or Alaskan Native(−1.90%) and Asian or pacific islanders(−2.36%) showed a steady decline in mortality from 1999–2019. For BM, there was a rapid decline in mortality from 1999–2014(−3.68%), followed by a slow decline(−0.83%). However, WM showed discordant trends with a rapid decline from 1999–2013(−2.60%) followed by an increase from 2013–2019(+0.20%).

Joinpoint regression for changes in PC mortality for BM from 1999 to 2019

Significant trend changes are shown in Table 1 and Supplementary Fig. 1. Every state with reported data demonstrated an improving trend for most years between 1999–2019, except Kentucky, which showed a worsening trend in most years. The most rapid decreases in ASMR were in North Carolina(EAPC-4.6%) between 1999–2014 and Delaware(EAPC−4.3%) between 1999–2019. California and Oklahoma demonstrated slower decreases between 1999-2019 of EAPCs −2.0% and −2.3%, respectively. ASMR for BM declined consistently across the study period, with only 1 Joinpoint trend in all states except for Georgia, Kentucky, North Carolina, and Texas. Georgia, North Carolina, and Texas transitioned from improving to worsening trends, as demonstrated by 2 Joinpoint values. Georgia changed from EAPC−3.6% between 1999–2015 to a smaller worsening change of +0.9% between 2015–2019. In North Carolina, the EAPC was initially −4.6% between 1999–2014, then increased to +0.2% between 2014–2019. Similarly, the EAPC for Texas between 1999–2014 was −4.2% but increased to +1.1% between 2014–2019. Kentucky is the only state notable for 3 Joinpoints; there was a worsening trend initially between 1999–2004(EAPC + 2.4%), which then became improved from 2004–2015(EAPC−6.2%) to worsen again up to +8.7% between 2015–2019.

Joinpoint regression for changes in PC mortality for WM from 1999 to 2019

The results are shown in Table 1 and Supplementary Fig. 1. Every state began the period with an improving trend. Half of the states(25/50) demonstrated 2 Joinpoint values, of which 14 (Arkansas, California, Connecticut, Florida, Iowa, Maryland, Minnesota, Mississippi, Missouri, Ohio, Tennessee, Texas, Virginia, and Wisconsin) demonstrated a worsening second trend. Washington is the only state with 3 Joinpoint values: EAPC −1.3% between 1999–2009, −6.1% between 2009–2012, increasing to +1.2% between 2012–2019. The most negative EAPC was −6.1% measured in Washington between 2009–2012, followed by

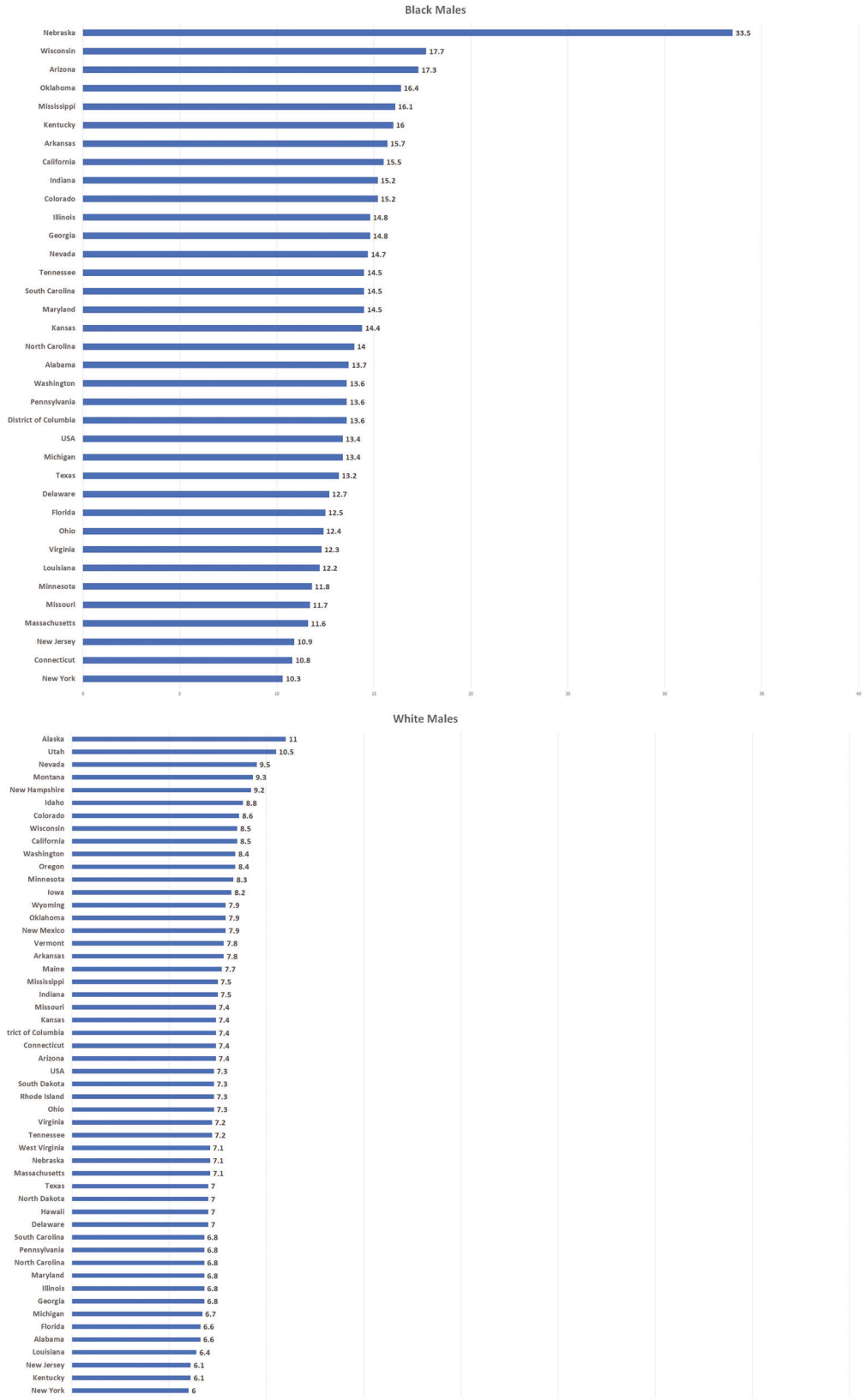

Fig. 1 Age-standardized mortality rates (ASMR) for Black and White males for prostate cancer (PC) in different states of the USA in 2019. All induced are per 100,000 individuals.

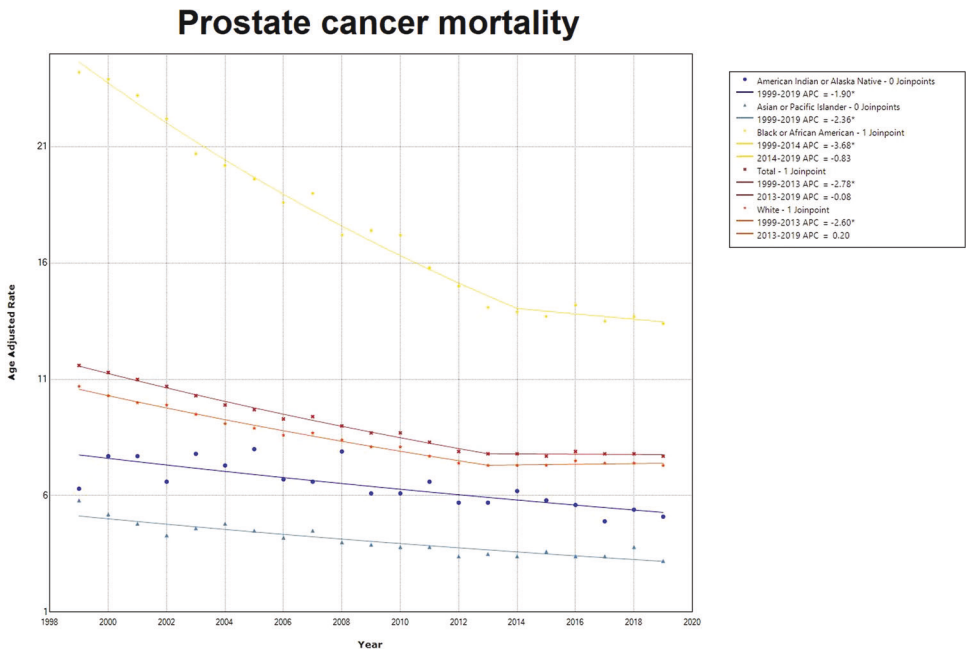

Fig. 2 Trends in ASMR per 100,000 individuals for PC in different races.

−4.9% in Michigan between 1999–2006. Arkansas demonstrated the largest increase in ASMR from 2017–2019(EAPC + 7.8%).

Sub-group analysis: changes in PC mortality pre and post-2012

Overall, for the entire country, for WM, ASMR decreased from 1999–2012 with a relative change of −30.84, which was reduced to −1.35 from 2012–2019. Similarly, for BM, ASMR decreased from 1999–2012 with a relative change of −38.02, which was reduced to −12.67 from 2012–2019. For WM, ASMR decreased in all 50 states and DC from 1999–2012, then increased in 22/50 states(44.0%) post-2012. Similarly, for BM, ASMR decreased in all 50 states and DC from 1990–2012, then increased in 7/34 states(20.6%) post-2012. Similar trends were observed when calculating AAPC using joinpoint analysis. For WM, AAPC decreased until 2012 in all states and increased post-2012 in 11/50(22.0%) states. For BM, similarly, AAPC was found to be decreasing in all states till 2012 and was found to be increasing in one state. The sub-group analysis is shown in Table 2.

Post-hoc analysis: ITS analysis

Based on subgroup analysis, 22 states were included for WM and 7 states for BM. For WM, while 11/22(50%) states showed a significant increase post interruption, 7/22(31.8%) had a significant increasing trend in ASMR post-2012, with the highest increasing trend in Alaska(1.70/year). For BM, all 7 states showed an increase in ASMR post-2012, with the highest increasing trend in Wisconsin(3.45/year). ITS results are shown in Fig. 3 and Supplementary Table 4.

DISCUSSION

We analyzed the trends in PC mortality in the USA by state and race from 1999–2019. ASMR decreased in all included states for both races, with a more pronounced drop in BM at the national level, in line with previous studies [1, 18]. Improvements in screening, diagnosing, and therapeutic modalities, especially for metastatic and castration-resistant disease, have contributed to the decline in mortality [9]. Furthermore, changes in the attribution of cause of death and possibly increased risk of cardiovascular disease leading to the death of patients under hormonal therapies could also explain this drop in mortality [1].

The highest ASMR was in Nebraska for BM. According to the Nebraska cancer registry, PC was the most diagnosed cancer in men accounting for 29% of new cancer diagnoses in recent years, with a median age of 65 years at diagnosis, and BM were significantly more likely to be diagnosed with PC than WM. The counties that had a significantly higher incidence of PC than the state were Boone, Burt, Cuming, Greeley, and Madison, as opposed to Dakota, Dawes, Dawson, Hall, Phelps, and Red Willow, which had a significantly lower incidence of PC compared to the state. Mortality from PC is declining in the state, which is in line with the national decline [19].

In 1999 and 2019, ASMRs in BM were significantly higher than in WM, concordantly with previous studies, probably due to an increased PC incidence and risk of developing aggressive forms in BM [9, 20–23]. Also, studies mentioned that BM had lower rates of PSA screening, guideline-compliant radiation therapy, and surgery despite having similar baseline characteristics as WM [24–26]. Another study conducted on high-risk PC patients concluded that BM, especially those of lower socioeconomic status, had a decreased number of bone scans, a lower likelihood of intent to treat, and a lower likelihood of undergoing radical prostatectomy than WM [27].

Indeed, among the most influential factors contributing to racial disparities between BM and WM were the social determinants of health(SDH), such as poverty and lack of education [28]. The adjustment for SDH reduced the differences in outcomes of PC between WM and BM [29, 30]. Interestingly, when adjusting for access to care, treatment, and cancer characteristics in advanced PC, the Black race was associated with better overall survival [31]. Similarly, other studies analyzing data from several clinical trials concluded non-different overall survival and better progression-free survival rates in BM than WM when adequate treatment for advanced PC was offered [32, 33]. A study conducted in a relatively equal-access setting such as the Veterans Affairs healthcare system also showed that among treated patients with PC, BM had a statistically significant lower risk (11%) of developing metastasis than WM [34]. An improvement in healthcare access was noted, reflecting on the PC mortality trends. PC ASMR in BM dropped by approximately 50%, from 24.2 in 1999 to 13.4 in 2019, at a higher rate than WM,

Table 1. Joinpoint analysis for PC ASMR in different states of the USA from 1990–2019 in (a) White males and (b) Black males.

(a) White males												
State	**Trend 1**			**Trend 2**			**Trend 3**			**AAPC**		
	Years	**EAPC (95% CI)**	**"P-Value"**	**Years**	**EAPC (95% CI)**	**"P-Value"**	**Years**	**EAPC (95% CI)**	**"P-Value"**	**Years**	**AAPC (95% CI)**	**"P-Value"**
Alabama	1999–2019	−2.4 (−2.9 to −1.8)	<0.001							1999–2019	−2.4 (−2.9 to −1.8)	<0.001
Alaska	2000–2019	−2.3 (−4 to −0.5)	0.014							2000–2019	−2.3 (−4 to −0.5)	0.014
Arizona	1999–2019	−2.1 (−2.4 to −1.7)	<0.001							1999–2019	−2.1 (−2.4 to −1.7)	<0.001
Arkansas	1999–2017	−2.7 (−3.1 to −2.2)	<0.001	2017–2019	7.8 (−6.9–24.8)	0.296				1999–2019	−1.7 (−3 to −0.3)	0.02
California	1999–2013	−1.8 (−2.2 to −1.5)	<0.001	2013–2019	0.7 (−0.5–2)	0.218				1999–2019	−1.1 (−1.5 to −0.7)	<0.001
Colorado	1999–2006	−3 (−4.6 to −1.5)	0.001	2006–2019	−0.5 (−1.1–0.1)	0.101				1999–2019	−1.4 (−2 to −0.8)	<0.001
Connecticut	1999–2014	−3 (−3.7 to −2.3)	<0.001	2014–2019	1.3 (−2.6–5.3)	0.497				1999–2019	−2 (−3 to −1)	<0.001
Delaware	1999–2019	−2.6 (−3.8 to −1.4)	<0.001							1999–2019	−2.6 (−3.8 to −1.4)	<0.001
District of Columbia	1999–2018	−2.9 (−3.9 to −1.8)	0.002							1999–2018	−2.9 (−3.9 to −1.8)	0.002
Florida	1999–2014	−2.5 (−2.8 to −2.3)	<0.001	2014–2019	0.3 (−1–1.7)	0.607				1999–2019	−1.8 (−2.2 to −1.5)	<0.001
Georgia	1999–2009	−3 (−3.8 to −2.2)	<0.001	2009–2019	−0.6 (−1.4 to −0.2)	0.154				1999–2019	−1.8 (−2.3 to −1.3)	<0.001
Hawaii	1999–2019	−2.1 (−3.5 to −0.6)	0.007							1999–2019	−2.1 (−3.5 to −0.6)	0.007
Idaho	1999–2019	−1.8 (−2.3 to −1.2)	<0.001							1999–2019	−1.8 (−2.3 to −1.2)	<0.001
Illinois	1999–2010	−3 (−3.7 to −2.3)	<0.001	2010–2019	−1 (−2 to −0.1)	0.036				1999–2019	−2.1 (−2.7 to −1.6)	<0.001
Indiana	1999–2005	−4.3 (−6.7 to −1.9)	0.002	2005–2019	−1.3 (−2 to −0.6)	0.001				1999-2019	−2.2 (−3 to −1.4)	<0.001
Iowa	1999–2013	−3 (−3.8 to −2.3)	<0.001	2013–2019	2.2 (−0.6–5.1)	0.12				1999-2019	−1.5 (−2.4 to −0.6)	0.001
Kansas	1999–2009	−3.1 (−4.5 to −1.7)	<0.001	2009–2019	0 (−1.4–1.5)	0.972				1999–2019	−1.6 (−2.5 to −0.6)	0.001
Kentucky	1999–2019	−2.3 (−2.8 to −1.8)	<0.001							1999–2019	−2.3 (−2.8 to −1.8)	<0.001
Louisiana	1999–2019	−2.2 (−2.7 to −1.6)	<0.001							1999–2019	−2.2 (−2.7 to −1.6)	<0.001
Maine	1999–2019	−1.8 (−2.4 to −1.1)	<0.001							1999–2019	−1.8 (−2.4 to −1.1)	<0.001
Maryland	1999–2013	−3.2 (−3.7 to −2.6)	<0.001	2013–2019	0.5 (−1.4–2.5)	0.572				1999–2019	−2.1 (−2.7 to −1.4)	<0.001
Massachusetts	1999–2011	−3.3 (−3.8 to −2.8)	<0.001	2011–2019	−0.7 (−1.7–0.3)	0.18				1999–2019	−2.3 (−2.7 to −1.8)	<0.001
Michigan	1999–2006	−4.9 (−6.1 to −3.7)	<0.001	2006–2019	−1.1 (−1.6 to −0.6)	<0.001				1999–2019	−2.4 (−2.9 to −1.9)	<0.001
Minnesota	1999–2014	−2.9 (−3.6 to −2.1)	<0.001	2014–2019	1.6 (−2.3–5.7)	0.396				1999–2019	−1.8 (−2.8 to −0.7)	0.001
Mississippi	1999–2013	−3 (−3.9 to −2)	<0.001	2013–2019	2.1 (−1.4–5.7)	0.232				1999–2019	−1.5 (−2.6 to −0.3)	0.011
Missouri	1999–2017	−2.2 (−2.7 to −1.7)	<0.001	2017–2019	7.7 (−7.3–25.2)	0.311				1999–2019	−1.3 (−2.7–0.2)	0.086
Montana	1999–2019	−1.5 (−2.3 to −0.7)	0.001							1999–2019	−1.5 (−2.3 to −0.7)	0.001
Nebraska	1999–2019	−1.9 (−2.5 to −1.4)	<0.001							1999–2019	−1.9 (−2.5 to −1.4)	<0.001
Nevada	1999–2019	−2 (−2.6 to −1.4)	<0.001							1999–2019	−2 (−2.6 to −1.4)	<0.001
New Hampshire	1999–2019	−2 (−2.7 to −1.3)	<0.001							1999–2019	−2 (−2.7 to −1.3)	<0.001
New Jersey	1999–2019	−2.6 (−3 to −2.2)	<0.001							1999–2019	−2.6 (−3 to −2.2)	<0.001
New Mexico	1999–2019	−2.2 (−2.7 to −1.7)	<0.001							1999–2019	−2.2 (−2.7 to −1.7)	<0.001

Table 1. continued

(a) White males												
State	**Trend 1**			**Trend 2**			**Trend 3**			**AAPC**		
	Years	**EAPC (95% CI)**	**"P-Value"**	**Years**	**EAPC (95% CI)**	**"P-Value"**	**Years**	**EAPC (95% CI)**	**"P-Value"**	**Years**	**AAPC (95% CI)**	**"P-Value"**
New York	1999–2006	−3.5 (−5 to −2)	<0.001	2006–2019	−1.7 (−2.3 to −1.1)	<0.001				1999–2019	−2.3 (−2.9 to −1.7)	<0.001
North Carolina	1999–2011	−2.8 (−3.4 to −2.3)	<0.001	2011–2019	−0.8 (−1.9–0.2)	0.113				1999–2019	−2 (−2.5 to −1.5)	<0.001
North Dakota	1999–2019	−2.8 (−3.9 to −1.8)	<0.001							1999–2019	−2.8 (−3.9 to −1.8)	<0.001
Ohio	1999–2014	−2.6 (−3.1 to −2.2)	<0.001	2014–2019	1.5 (−1–4.1)	0.227				1999–2019	−1.6 (−2.3to −1)	<0.001
Oklahoma	1999–2019	−1.3 (−1.6 to −0.9)	<0.001							1999–2019	−1.3 (−1.6 to −0.9)	<0.001
Oregon	1999–2019	−1.9 (−2.3 to −1.6)	<0.001							1999–2019	−1.9 (−2.3 to −1.6)	<0.001
Pennsylvania	1999–2012	−3.1 (−3.5 to −2.7)	<0.001	2012–2019	−0.1 (−1.2–1)	0.795				1999–2019	−2.1 (−2.5 to −1.6)	<0.001
Rhode Island	1999–2019	−1.9 (−2.8 to −1.1)	<0.001							1999–2019	−1.9 (−2.8 to −1.1)	<0.001
South Carolina	1999–2019	−2 (−2.5 to −1.5)	<0.001							1999–2019	−2 (−2.5 to −1.5)	<0.001
South Dakota	1999–2019	−3.1 (−3.8 to −2.3)	<0.001							1999–2019	−3.1 (−3.8 to −2.3)	<0.001
Tennessee	1999–2013	−3 (−3.5 to −2.4)	<0.001	2013–2019	0.7 (−1.4–2.8)	0.504				1999–2019	−1.9 (−2.6 to −1.2)	<0.001
Texas	1999–2012	−2.9 (−3.3 to −2.6)	<0.001	2012–2019	0.1 (−0.8–1)	0.851				1999–2019	−1.9 (−2.2to −1.5)	<0.001
Utah	1999–2019	−1.5 (−2.2 to −0.7)	0.001							1999–2019	−1.5 (−2.2 to −0.7)	0.001
Vermont	1999–2019	−1.8 (−2.8 to −0.7)	0.003							1999–2019	−1.8 (−2.8 to −0.7)	0.003
Virginia	1999–2014	−2.7 (−3.4 to −2)	<0.001	2014–2019	1.5 (−2.1–5.3)	0.401				1999–2019	−1.7 (−2.6 to −0.7)	0.001
Washington	1999–2009	−1.3 (−2 to −0.5)	0.003	2009–2012	−6.1 (−14.9–3.5)	0.185	2012-2019	1.2 (−0.2–2.5)	0.079	1999–2019	−1.2 (−2.6–0.3)	0.109
West Virginia	1999–2019	−2.3 (−3.1 to −1.6)	<0.001							1999–2019	−2.3 (−3.1 to −1.6)	<0.001
Wisconsin	1999–2014	−2.5 (−3 to −1.9)	<0.001	2014–2019	1.1 (−1.8–4)	0.445				1999–2019	−1.6 (−2.4 to −0.8)	<0.001
Wyoming	1999–2019	−2.9 (−4.3 to −1.5)	<0.001							1999–2019	−2.9 (−4.3 to −1.5)	<0.001
(b) Black Males												
Alabama	1999–2019	−3.7 (−4.4 to −3.1)	<0.001							1999–2019	−3.7 (−4.4 to −3.1)	<0.001
Arizona	2000–2019	−3.8 (−7.2 to −0.3)	0.036							2000–2019	−3.8 (−7.2 to −0.3)	0.036
Arkansas	1999–2019	−3.7 (−4.4 to −3)	<0.001							1999–2019	−3.7 (−4.4 to −3)	<0.001
California	1999–2019	−2 (−2.5 to−1.5)	<0.001							1999–2019	−2 (−2.5 to −1.5)	<0.001
Colorado	2000–2019	−3.1 (−5 to −1.2)	0.005							2000–2019	−3.1 (−5 to −1.2)	0.005
Connecticut	1999–2019	−3.1 (−4.4 to −1.7)	<0.001							1999–2019	−3.1 (−4.4 to −1.7)	<0.001
Delaware	1999–2019	−4.3 (−5.3 to −3.3)	<0.001							1999–2019	−4.3 (−5.3 to −3.3)	<0.001
District of Columbia	1999–2019	−2.7 (−3.6to −1.7)	<0.001							1999–2019	−2.7 (−3.6 to −1.7)	<0.001
Florida	1999–2019	−3.6 (−3.9to −3.3)	<0.001							1999–2019	−3.6 (−3.9 to −3.3)	<0.001
Georgia	1999–2015	−3.6 (−4.1 to −3.1)	<0.001	2015–2019	0.9 (−3.3–5.4)	0.653				1999–2019	−2.7 (−3.6 to −1.9)	<0.001
Illinois	1999–2019	−2.6 (−3.2 to −2)	<0.001							1999–2019	−2.6 (−3.2 to −2)	<0.001
Indiana	1999–2019	−3.6 (−4.7 to −2.4)	<0.001							1999–2019	−3.6 (-4.7 to −2.4)	<0.001
Kansas	1999–2019	−3.5 (−4.4 to −2.5)	<0.001							1999–2019	−3.5 (−4.4 to −2.5)	<0.001
Kentucky	1999–2004	2.4 (−6.4–11.9)	0.582	2004–2015	−6.2 (−9.1 to −3.3)	0.001	2015–2019	8.7 (−4.2–23.4)	0.175	1999–2019	−1.3 (−4.6–2.2)	0.462

Table 1. continued

(a) White males												
State	**Trend 1**			**Trend 2**			**Trend 3**			**AAPC**		
	Years	**EAPC (95% CI)**	**"P-Value"**	**Years**	**EAPC (95% CI)**	**"P-Value"**	**Years**	**EAPC (95% CI)**	**"P-Value"**	**Years**	**AAPC (95% CI)**	**"P-Value"**
Louisiana	1999–2019	−3.6 (−4.1 to −3.1)	<0.001							1999–2019	−3.6 (−4.1to −3.1)	<0.001
Maryland	1999–2019	−3.2 (−4 to −2.5)	<0.001							1999–2019	−3.2 (−4 to −2.5)	<0.001
Massachusetts	1999–2019	−2.4 (−3.7 to −1)	0.001							1999–2019	−2.4 (−3.7 to −1)	0.001
Michigan	1999–2019	−2.9 (−3.6 to −2.2)	<0.001							1999–2019	−2.9 (−3.6 to −2.2)	<0.001
Minnesota	2009–2018	−4.2 (−16.3 –9.8)	0.311							2009–2018	−4.2 (−16.3–9.8)	0.311
Mississippi	1999–2019	−3.3 (−3.7 to −2.8)	<0.001							1999–2019	−3.3 (−3.7 to −2.8)	<0.001
Missouri	1999–2019	−2.7 (−3.5 to −1.9)	<0.001							1999–2019	−2.7 (−3.5 to −1.9)	<0.001
Nevada	2001–2019	−3.2 (−5.9 to −0.4)	0.03							2001–2019	−3.2 (−5.9 to −0.4)	0.03
New Jersey	1999–2019	−3 (−3.7 to −2.4)	<0.001							1999-2019	−3 (−3.7 to −2.4)	<0.001
New York	1999–2019	−3.2 (−3.6 to −2.9)	<0.001							1999–2019	−3.2 (−3.6 to −2.9)	<0.001
North Carolina	1999–2014	−4.6 (−5.6 to −3.5)	<0.001	2014–2019	0.2 (−5.5–6.2)	0.944				1999–2019	−3.4 (−4.9 to −1.9)	<0.001
Ohio	1999–2019	−3.4 (−4 to −2.9)	<0.001							1999–2019	−3.4 (−4 to −2.9)	<0.001
Oklahoma	1999–2019	−2.3 (−3.8 to −0.9)	0.003							1999–2019	−2.3 (−3.8 to −0.9)	0.003
Pennsylvania	1999–2019	−2.8 (−3.5 to −2.2)	<0.001							1999–2019	−2.8 (−3.5 to −2.2)	<0.001
South Carolina	1999–2019	−3.4 (−3.8 to −3)	<0.001							1999–2019	−3.4 (−3.8 to −3)	<0.001
Tennessee	1999–2019	−3.4 (−4.1to −2.7)	<0.001							1999–2019	−3.4 (−4.1 to −2.7)	<0.001
Texas	1999–2014	-4.2 (−5 to −3.4)	<0.001	2014–2019	1.1 (−3.3–5.8)	0.606				1999–2019	−2.9 (−4.1 to −1.7)	<0.001
Virginia	1999–2019	−3.8 (−4.3 to −3.2)	<0.001							1999–2019	−3.8 (−4.3 to −3.2)	<0.001
Washington	1999–2019	−3.9 (−5.6 to −2.1)	<0.001							1999–2019	−3.9 (−5.6 to −2.1)	<0.001
Wisconsin	2000–2019	−2.6 (-4.1 to −1)	0.003							2000–2019	−2.6 (−4.1 to −1)	0.003

EAPC indicates estimated annual percentage change, with 95% confidence intervals in brackets. *Significantly different from 0 ($P < 0.05$). AAPC (Average annual percentage change) indicates a summary trend measure over 1990–2019.

Table 2. Sub-group analysis of relative differences pre and post-2012.

State	White				Blacks			
	Pre- 2012 AAPC	Pre- 2012 Reative change	Post-2012 AAPC	Post-2012 Relative change	Pre- 2012 AAPC	Pre- 2012 Reative change	Post-2012 AAPC	Post-2012 Relative change
Alabama	−2.4 (−2.9 to -1.8)	−35.85	−2.4 (−2.9 to −1.8)	−2.94	−3.7 (−4.4 to −3.1)	−41.18	−3.7 (−4.4 to −3.1)	−14.38
Alaska	N/A	−38.17	-2.3 (-4 - -0.5)	35.80	N/A	N/A	N/A	N/A
Arizona	−2.1 (−2.4 to −1.7)	−20.79	−2.1 (−2.4 to −1.7)	−7.50	N/A	−65.10	N/A	66.35
Arkansas	−2.7 (−3.1 to −2.2)	−31.53	0.2 (−3.6 to 4.2)	2.63	−3.7 (−4.4 to −3)	−37.04	−3.7 (−4.4 to −3)	−16.04
California	−1.8 (−2.2 to −1.5)	−26.36	0.4 (−0.6 to 1.3)	4.94	−2 (−2.5 to −1.5)	−28.02	−2 (−2.5 to −1.5)	−7.19
Colorado	−1.9 (−2.7 to −1)	−23.68	−0.5 (−1.1 to 0.1)	−1.15	N/A	−34.05	−3.1 (−5 to −1.2)	−29.30
Connecticut	−3 (−3.7 to −2.3)	−37.86	0 (−2.5 to 2.6)	15.63	−3.1 (−4.4 to −1.7)	−31.00	−3.1 (−4.4 to −1.7)	−21.74
Delaware	−2.6 (−3.8 to −1.4)	−23.53	-2.6 (−3.8 to −1.4)	−10.26	−4.3 (−5.3 to −3.3)	−55.48	N/A	−5.22
District of Columbia	−2.9 (−3.9 to −1.8)	−26.72	N/A	−22.92	−2.7 (−3.6 to −1.7)	−37.13	−2.7 (−3.6 to −1.7)	−8.72
Florida	−2.5 (−2.8 to −2.3)	−30.21	−0.5 (−1.4 to 0.4)	−1.49	−3.6 (−3.9 to −3.3)	−35.15	−3.6 (−3.9 to −3.3)	−19.35
Georgia	−2.5 (−3.1 to −1.9)	−29.70	−0.6 (−1.4 to 0.2)	−4.23	−3.6 (−4.1 to −3.1)	−44.07	−1.1 (−3.3 −1.2)	−1.99
Hawaii	−2.1 (−3.5 to −0.6)	−31.09	−2.1 (−3.5 to −0.6)	−14.63	N/A	N/A	N/A	N/A
Idaho	−1.8 (−2.3 to −1.2)	−32.86	−1.8 (−2.3 to −1.2)	−6.38	N/A	N/A	N/A	N/A
Illinois	−2.7 (−3.3 to −2.2)	−30.56	−1 (−2 to −0.1)	−9.33	−2.6 (−3.2 to −2)	−30.47	−2.6 (−3.2 to −2)	−8.64
Indiana	−2.7 (−3.8 to −1.6)	−31.62	−1.3 (−2 to −0.6)	−6.25	−3.6 (−4.7 to −2.4)	−48.11	−3.6 (−4.7 to −2.4)	0.66
Iowa	−3 (−3.8 to −2.3)	−28.95	1.4 (−0.8 to 3.7)	1.23	N/A	N/A	N/A	N/A
Kansas	−2.4 (−3.5 to −1.3)	−34.95	0 (−1.4 to 1.5)	10.45	−3.5 (−4.4 to −2.5)	−31.03	N/A	−10.00
Kentucky	−2.3 (−2.8 to −1.8)	−31.30	−2.3 (−2.8 to −1.8)	−22.78	−3 (−6.4 to 0.5)	−34.04	2 (−4.5 to 9.1)	29.03
Louisiana	−2.2 (−2.7 to −1.6)	−32.38	−2.2 (−2.7 to −1.6)	−9.86	−3.6 (−4.1 to −3.1)	−38.67	−3.6 (−4.1 to −3.1)	−22.29
Maine	−1.8 (−2.4 to −1.1)	−30.39	−1.8 (−2.4 to −1.1)	8.45	N/A	N/A	N/A	N/A
Maryland	−3.2 (−3.7 to −2.6)	−33.65	0 (−1.5 to 1.5)	−1.45	−3.2 (−4 to −2.5)	−43.72	−3.2 (−4 to −2.5)	11.54
Massachusetts	−3.1 (−3.6 to −2.6)	−35.96	−0.7 (−1.7 to 0.3)	−2.74	−2.4 (−3.7 to −1)	−8.48	−2.4 (−3.7 to −1)	−23.18
Michigan	−3.2 (−3.8 to −2.5)	−34.26	−1.1 (−1.6 to −0.6)	−5.63	−2.9 (−3.6 to −2.2)	−44.49	−2.9 (−3.6 to −2.2)	2.29
Minnesota	−2.9 (−3.6 to −2.1)	−34.19	0.3 (−2.3 to 3)	7.79	N/A	−2.69	N/A	−34.81
Mississippi	−3 (−3.9 to −2)	−31.48	1.3 (−1.4 to 4.2)	1.35	−3.3 (−3.7 to −2.8)	−34.65	−3.3 (−3.7 to −2.8)	−18.69
Missouri	−2.2 (−2.7 to −1.7)	−32.67	0.5 (−3.4 to 4.6)	8.82	−2.7 (−3.5 to −1.9)	−40.85	−2.7 (−3.5 to −1.9)	−15.83
Montana	−1.5 (−2.3 to −0.7)	−41.91	−1.5 (−2.3 to −0.7)	17.72	N/A	N/A	N/A	N/A
Nebraska	−1.9 (−2.5 to −1.4)	−13.13	−1.9 (−2.5 to −1.4)	−17.44	N/A	N/A	N/A	N/A
Nevada	−2 (−2.6 to −1.4)	−33.59	−2 (−2.6 to −1.4)	11.76	N/A	−52.58	N/A	−5.77
New Hampshire	−2 (−2.7 to −1.3)	−13.46	−2 (−2.7 to −1.3)	2.22	N/A	N/A	N/A	N/A
New Jersey	−2.6 (−3 to −2.2)	−36.89	−2.6 (−3 to −2.2)	−6.15	−3 (−3.7 to −2.4)	−19.61	−3 (−3.7 to −2.4)	−33.54
New Mexico	−2.2 (−2.7 to −1.7)	−34.88	−2.2 (−2.7 to −1.7)	−5.95	N/A	N/A	N/A	N/A
New York	−2.7 (−3.5 to −1.9)	−30.61	−1.7 (−2.3 to −1.1)	−11.76	−3.2 (−3.6 to −2.9)	−33.67	−3.2 (−3.6 to −2.9)	−20.77
North Carolina	−2.7 (−3.1 to −2.2)	−30.00	−0.8 (−1.9 to 0.2)	−2.86	−4.6 (−5.6 to −3.5)	−41.87	−1.2 (−4.9 to 2.7)	−2.10
North Dakota	−2.8 (−3.9 to −1.8)	−26.09	−2.8 (−3.9 to −1.8)	−17.65	N/A	N/A	N/A	N/A
Ohio	−2.6 (−3.1 to −2.2)	−32.69	0.3 (−1.4 to 2)	4.29	−3.4 (−4 to −2.9)	−41.49	−3.4 (−4 to −2.9)	−12.06
Oklahoma	−1.3 (−1.6 to −0.9)	−23.81	−1.3 (−1.6 to −0.9)	−1.25	N/A	−36.55	−2.3 (−3.8 to −0.9)	−10.87
Oregon	−1.9 (−2.3 to −1.6)	−30.47	−1.9 (−2.3 to −1.6)	−5.62	−2.3 (−3.8 to −0.9)	N/A	N/A	N/A

Table 2. continued

State	White				Blacks			
	Pre- 2012 AAPC	Pre- 2012 Reative change	Post-2012 AAPC	Post-2012 Relative change	Pre- 2012 AAPC	Pre- 2012 Reative change	Post-2012 AAPC	Post-2012 Relative change
Pennsylvania	−3.1 (−3.5 to −2.7)	−34.91	−0.1 (−1.2 to 1)	−1.45	−2.8 (−3.5 to −2.2)	−29.17	−2.8 (−3.5 to −2.2)	−20.00
Rhode Island	−1.9 (−2.8 to −1.1)	−42.31	−1.9 (−2.8 to −1.1)	21.67	N/A	N/A	N/A	N/A
South Carolina	−2 (−2.5 to −1.5)	−29.81	−2 (−2.5 to −1.5)	−6.85	−3.4 (−3.8 to −3)	−40.61	−3.4 (−3.8 to −3)	−16.67
South Dakota	−3.1 (−3.8 to −2.3)	−43.70	−3.1 (−3.8 to −2.3)	−3.95	N/A	N/A	N/A	N/A
Tennessee	−3 (−3.5 to −2.4)	−33.65	0.1 (−1.5 to 1.8)	4.35	−3.4 (−4.1 to −2.7)	−42.91	−3.4 (−4.1 to −2.7)	−7.64
Texas	−2.9 (−3.3 to −2.6)	−31.37	0.1 (−0.8 to 1)	0.00	−4.2 (−5 to −3.4)	−50.64	−0.4 (−3.4 – 2.6)	13.79
Utah	−1.5 (−2.2 to −0.7)	−25.00	−1.5 (−2.2 to −0.7)	9.38	N/A	N/A	N/A	N/A
Vermont	−1.8 (−2.8 to −0.7)	−33.85	−1.8 (−2.8 to −0.7)	−9.30	N/A	N/A	N/A	N/A
Virginia	−2.7 (−3.4 to −2)	−35.24	0.3 (−2.1 to 2.7)	5.88	−3.8 (−4.3 to −3.2)	−44.98	−3.8 (−4.3 to −3.2)	−16.89
Washington	−2.4 (−4.5 to −0.3)	−31.86	1.2 (−0.2 to 2.5)	9.09	−3.9 (−5.6 to −2.1)	−22.58	N/A	−29.17
West Virginia	−2.3 (−3.1 to −1.6)	−42.20	−2.3 (−3.1 to −1.6)	12.70	N/A	N/A	N/A	N/A
Wisconsin	−2.5 (−3 to −1.9)	−32.50	0 (−1.8 to 2)	4.94	N/A	−36.04	−2.6 (−4.1 to −1)	24.65
Wyoming	−2.9 (−4.3 to −1.5)	−39.84	−2.9 (−4.3 to −1.5)	6.76	N/A	N/A	N/A	N/A

concordantly with other studies [9, 35]. This is a good indicator of a narrowing racial disparity in access to high-standard healthcare [1]. However, for further PC risk reduction, promotion of healthier diets, screening, diagnosis, and access to treatment is still needed, particularly in rural areas.

It is unclear in the literature if rurality is a contributor to PC mortality. Some studies suggest that rural patients did not have higher mortality from PC as they still have access to quality care even if longer driving is needed [36]. On the other hand, studies present evidence that rural men are less likely to be screened, diagnosed, and treated for PC; therefore, mortality from PC is increased in rural areas [37, 38]. In our study, the smallest decreases in ASMR during the last decades were in Kentucky and Wisconsin for BM, and New Hampshire and Alaska for WM. These states are indeed considered among the most rural states [39]. Also, some states with a high percentage of rurality, such as Maine, Vermont, Mississippi, and Montana [40], had higher ASMRs for WM than the national level in our study. Similarly, some states with a low percentage of rurality, such as New York and New Jersey [40], had the lowest ASMRs for WM. However, Nevada had one of the highest ASMR for WM while being one of the states with the least percentage of rurality(6%) [40]. Also, Kentucky had one of the lowest ASMR for WM, although having a high percentage of rurality(42%) [40]. Therefore, we could not make strong conclusions concerning the contribution of rurality to PC mortality due to the limitation of the database. Indeed, further studies are needed to assess the effect of rurality on PC mortality through analyzing the mortality at the county level of each state.

In American Indians or Alaskan Natives, mortality from PC decreased during the studied period, however, at a smaller rate. Indeed, previous studies concluded that trends of mortality from PC in American Indian or Alaskan Native men did not significantly decrease from 1999-2009, probably due to the low socioeconomic level being a barrier to access to appropriate care [41, 42]. A lower rate of PSA screening was seen in American Indians or Alaskan Natives, which had a lower incidence of and higher mortality from PC than WM [43].

Our subgroup and post-hoc analysis also showed that ASMR has increased post-2012 changes in USPSTF guidelines in a few states, especially for WM. Even if ASMR for BM remained stable in most states, there were indications of an increase in a few states. Similar trends were observed in a SEER database analysis. Post-USPSTF era, men diagnosed with PC had more adverse clinical features as compared to pre-USPSTF era, with a decrease in survival rate among WM and a steady survival rate among BM [44]. USPSTF recommendation relied on the results of two trials [45, 46], which provided compatible evidence that screening reduced PC mortality after accounting for differences in implementation and settings, although traditional analysis showed different results [47]. Studies also showed a shift towards higher grade and stage upon diagnosis with an increase in metastatic PC [48]. Overall, these observations can be influencing two different trends; an increase in ASMR of PC in recent years and decreasing the racial gap with an increase in mortality in WM. A better innovative approach is needed for PSA screening and further management of PC patients. Recent studies have also shown favorable harm-benefit tradeoffs than were implied a decade ago, indicating a need to reconsider PSA-based screening, particularly for BM [49].

This study's strengths include using annual mortality data from national surveillance statistics, assessing population-level trends over an extended period, and allowing comparisons in trends rather than absolute annual mortality rates. Regarding limitations, CDC WONDER database lacked ASMR data for BM in 17 states(Alaska, Hawaii, Idaho, Iowa, Maine, Montana, Nebraska, New Hampshire, New Mexico, North Dakota, Oregon, Rhode Island, South Dakota, Utah, Vermont, West Virginia, and Wyoming). Although Alaska had a relatively high percentage of BM(33.6%), BM percentage was<10% in 12 other states and <20% in 4 others, thus engendering no bias. The prevalence of morbidity associated with PC was not assessed.

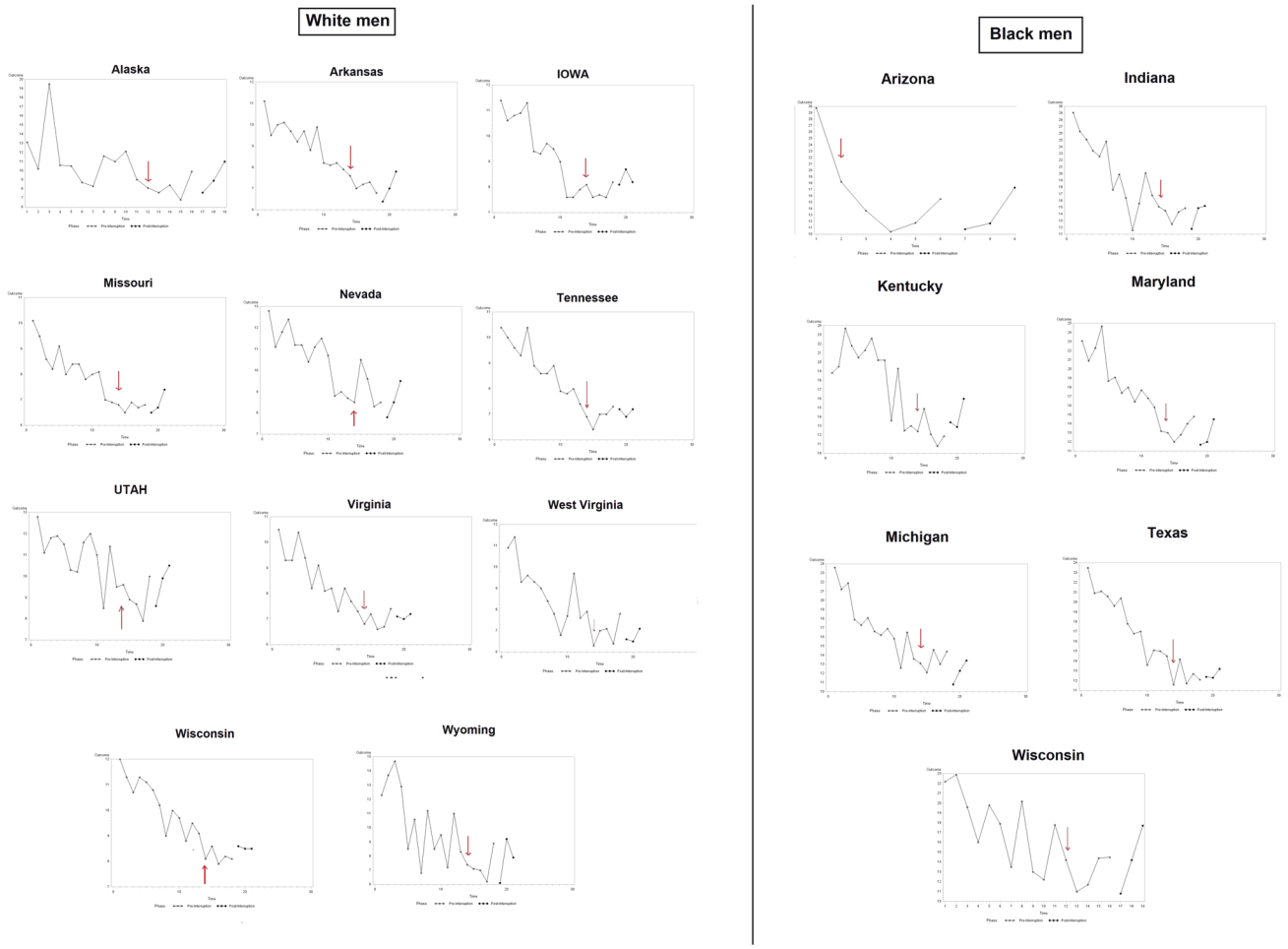

Fig. 3 Interrupted time-series analysis showing changes in ASMR trends. (Post hoc analysis). Red arrow indicates the year 2012.

Our primary aim was to understand changes in mortality trends; there may be substantial differences in PC prevalence between states that we cannot elucidate in this report. Also, we combined PC subtypes and different staging, as mortality data is not recorded separately for each pathological subtype. We could not evaluate the contribution of rurality to the mortality trends of PC as our objective was only to evaluate these trends at the state level. We will consider further evaluating mortality at the county level to assess the effect of ruralism/urbanism on PC mortality. Finally, as with any observational study, causal statements regarding the observed trends cannot be made. The discussion may assist future researchers and policymakers in focusing on equal access to care and special consideration for specific populations.

CONCLUSION

During the last 20 years, PC mortality rate has consistently dropped for all races across the USA, marking an advancement in management strategies. Even though a higher decrease in ASMR was observed in the Black and Asian racial groups, ASMR is still high in BM compared to WM. ASMR is also found to be increasing in many states following the USPSTF guideline changes regarding PSA screening(2012), indicating a need for more education around optimized PC screening.

DATA AVAILABILITY

The datasets generated during and/or analyzed during the current study are available in the WONDER database, https://wonder.cdc.gov/

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AUTHOR CONTRIBUTIONS

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COMPETING INTERESTS

The authors declare no competing interests.

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