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Years of Life Lost From Metastatic Prostate Cancer According to Treatment Era and Race/Ethnicity

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ABSTRACT

Introduction: Randomized trials demonstrated improved survival in metastatic prostate cancer (mPCa) with the adoption of several systemic therapies. However, real-world data validating this effect and quantifying its magnitude in years of life lost (YLL) according to race/ethnicity are unavailable.

Methods: In surveillance, epidemiology, and end results (SEER) database (2004–2021), Caucasian, African American, Hispanic, and Asian/Pacific Islander mPCa patients aged 40–80 years treated in androgen deprivation therapy (ADT, 2004–2012), docetaxel (2013–2016), abiraterone (2017–2018), and androgen receptor pathway inhibitor (ARPI, 2019–2021) eras were identified. Age- and sex-matched controls were generated (Social Security Administration life tables and Monte Carlo simulation). YLL were quantified for mPCa patients and controls.

Results: Overall, 36,658 mPCa patients were identified: 22,725 (62.0%) Caucasians, 6956 (19.0%) African Americans, 4785 (13.0%) Hispanics, and 2192 (6.0%) Asians/Pacific Islanders. In the ADT era, YLL values were 10.7 in African Americans, 9.0 in Hispanics, 8.4 in Caucasians, and 6.5 in Asians/Pacific Islanders. In the docetaxel era, YLL values were 9.4 in African Americans, 8.4 in Hispanics, 7.3 in Caucasians, and 6.2 in Asians/Pacific Islanders. In the abiraterone era, YLL values were 8.4 in African Americans, 6.3 in Hispanics, 5.4 in Caucasians, and 4.4 in Asians/Pacific Islanders. In the ARPI era, YLL values were 4.3 in African Americans, 3.6 in Hispanics, 2.7 in Caucasians, and 1.7 in Asians/Pacific Islanders.

Conclusion: YLL values decreased with each novel treatment era, in all race/ethnicity groups. The most pronounced decrease in YLL values occurred with the introduction of ARPIs, in all race/ethnicity groups. Despite those survival advances, African Americans were invariably disadvantaged as evidenced by the highest YLL values.

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1 | Introduction

Randomized trials [1–7] demonstrated improved survival in metastatic prostate cancer (mPCa) with the introduction of several novel systemic therapies. However, real-world data validating this effect and quantifying its magnitude in years of life lost (YLL) [8–12] according to race/ethnicity (Caucasian, African American, Hispanic, and Asian/Pacific Islander) are unavailable.

We addressed this knowledge gap and tested the differences in YLL values associated with the introduction of each novel therapy era, using the androgen deprivation therapy (ADT) era (2004–2012) as reference. Novel therapy eras consisted of docetaxel era (2013–2016), abiraterone era (2017–2018), and androgen receptor pathway inhibitor (ARPI, 2019–2021) era. Within each of the four examined treatment eras, we tested for YLL differences according to race/ethnicity: Caucasian versus African American versus Hispanic versus Asian/Pacific Islander. Here, YLL values were computed for mPCa patients relative to simulated population controls according to Social Security Administration (SSA) life tables [13] and subsequent Markov modeling. We hypothesized that an important decrease in YLL values may occur with the introduction of each novel therapy. We also posited that no differences in YLL values distinguished each of the four examined race/ethnicity groups regardless of treatment era. We tested these hypotheses in the current study.

2 | Materials and Methods

2.1 | Study Population

Within the surveillance, epidemiology, and end results (SEER) database (2004–2021), we identified Caucasian, African American, Hispanic, and Asian/Pacific Islander patients aged 40–80 years, with histologically confirmed mPCa [14, 15]. Patients were stratified according to race/ethnicity (Caucasian, African American, Hispanic, and Asian/Pacific Islander) and treatment era: ADT (2004–2012), docetaxel (2013–2016), abiraterone (2017–2018), and ARPI (2019–2021) eras. Patients with unknown race/ethnicity, age at diagnosis, year of diagnosis, metastatic substage, and vital status were excluded. The SEER database contains de-identified, publicly available data, ensuring full anonymity of patient information.

2.2 | Statistical Analyses

Statistical analyses consisted of two steps. In the first part of the analyses, Caucasian, African American, Hispanic, and Asian/Pacific Islander mPCa patients' characteristics were tabulated according to treatment era: ADT, docetaxel, abiraterone, and ARPI eras.

In the second part of the analyses, we addressed YLL. For each mPCa patient, a simulated control was generated using SSA lifetables (2004–2021) [13], and survival was modeled using Markov chain methodology. Follow-up duration of simulated population controls reflected the actual follow-up of SEER cases. Based on observed overall survival (OS) in mPCa patients and in simulated population controls, YLL values were computed for mPCa patients relative to controls. Kaplan–Meier (KM) plots

were used to graphically depict survival in mPCa patients and simulated controls. The log-rank tested for statistically significant differences. YLL values computation was applied until the age of 80 years. This approach was applied separately to each of the four examined treatment eras: ADT, docetaxel, abiraterone, and ARPI eras. Additionally, within each treatment era, a further stratification according to race/ethnicity (Caucasian, African American, Hispanic, and Asian/Pacific Islander) was applied.

R software environment for statistical computing and graphics (R version 4.4.2, R Foundation for Statistical Computing, Vienna, Austria) was used for all analyses. All tests were two-sided, with a significance level of $p < 0.05$.

3 | Results

3.1 | Descriptive Characteristics of the Study Population

Overall, 36,658 mPCa patients were identified: 22,725 (62.0%) Caucasians, 6956 (19.0%) African Americans, 4785 (13.0%) Hispanics, and 2192 (6.0%) Asians/Pacific Islanders. Relative to more historical treatment eras, mPCa patients in more contemporary treatment eras were older and less frequently harbored M1c stage (Table 1).

3.2 | ADT Era: Race/Ethnicity-Specific YLL in mPCa Patients vs. Age- and Sex-Matched Simulated Population Controls

In the ADT era, 12,769 mPCa patients were identified, with 7975 (62.5%) Caucasians, 2510 (19.7%) African Americans, 1552 (12.2%) Hispanics, and 732 (5.6%) Asians/Pacific Islanders. For each patient, one simulated population control was generated. In Caucasian mPCa patients, survival at 80 years was 41% (95% CI: 40–42) versus 94% (95% CI: 93–94) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 8.4 years, when Caucasian mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

In African American mPCa patients, survival at 80 years was 30% (95% CI: 28–31) versus 92% (95% CI: 90–94) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 10.7 years, when African American mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

In Hispanic mPCa patients, survival at 80 years was 40% (95% CI: 37–42) versus 92% (95% CI: 90–94) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 9.0 years, when Hispanic mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

In Asian/Pacific Islander mPCa patients, survival at 80 years was 51% (95% CI: 47–55) versus 92% (95% CI: 89–95) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an

TABLE 1 | Descriptive characteristics of Caucasian, African American, Hispanic, and Asian/Pacific Islander metastatic prostate cancer patients, aged 40–80 years, in androgen deprivation therapy era (ADT, 2004–2012), docetaxel era (2013–2016), abiraterone era (2017–2018), and androgen receptor pathway inhibitor (ARPI) era (2019–2021), within the Surveillance, Epidemiology, and End Results database (SEER 2004–2021).

	Caucasian <i>n</i> = 22,725 (62.0%)			African American <i>n</i> = 6956 (19.0%)			Hispanic <i>n</i> = 4785 (13.0%)			Asian/Pacific Islander <i>n</i> = 2192 (6.0%)		
	ADT era <i>n</i> = 7975 (35.0%)	Docetaxel era <i>n</i> = 5267 (23.0%)	Abiraterone era <i>n</i> = 3490 (15.0%)	ADT era <i>n</i> = 5993 (27.0%)	Docetaxel era <i>n</i> = 1567 (23.0%)	Abiraterone era <i>n</i> = 1019 (15.0%)	ADT era <i>n</i> = 1552 (32.0%)	Docetaxel era <i>n</i> = 1086 (23.0%)	Abiraterone era <i>n</i> = 720 (15.0%)	ADT era <i>n</i> = 1427 (30.0%)	Docetaxel era <i>n</i> = 506 (23.0%)	Abiraterone era <i>n</i> = 347 (16.0%)
Age, years, median (IQR)	68 (61, 74)	68 (62, 74)	68 (63, 74)	69 (63, 75)	65 (59, 71)	65 (60, 71)	66 (59, 72)	66 (59, 72)	67 (60, 73)	67 (61, 73)	68 (62, 73)	68 (63, 74)
Metastatic substage, <i>n</i> (%)												
M1a	686 (8.0%)	419 (8.0%)	274 (8.0%)	498 (8.0%)	190 (8.0%)	80 (8.0%)	112 (7.0%)	87 (8.0%)	51 (7.0%)	96 (6.0%)	34 (7.0%)	18 (6.0%)
M1b	5544 (70.0%)	3898 (74.0%)	2524 (72.0%)	4368 (73.0%)	1707 (68.0%)	700 (69.0%)	1037 (67.0%)	776 (71.0%)	475 (66.0%)	979 (69.0%)	374 (74.0%)	255 (73.0%)
M1c	1745 (22.0%)	950 (18.0%)	692 (20.0%)	1127 (19.0%)	613 (24.0%)	239 (23.0%)	403 (26.0%)	223 (21.0%)	194 (27.0%)	352 (25.0%)	98 (19.0%)	74 (21.0%)

Abbreviation: IQR = interquartile range.

average YLL value of 6.5 years, when Asian/Pacific Islander mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

3.3 | Docetaxel Era: Race/Ethnicity-Specific YLL in mPCa Patients vs. Age- and Sex-Matched Simulated Population Controls

In the docetaxel era, 8426 mPCa patients were identified, with 5267 (62.5%) Caucasians, 1567 (18.6%) African Americans, 1086 (12.9%) Hispanics, and 506 (6.0%) Asians/Pacific Islanders. For each patient, one simulated population control was generated. In Caucasian mPCa patients, survival at 80 years was 45% (95% CI: 44–47) versus 92% (95% CI: 91–93) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 7.3 years, when Caucasian mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

In African American mPCa patients, survival at 80 years was 33% (95% CI: 30–36) versus 91% (95% CI: 89–93) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 9.4 years, when African American mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

In Hispanic mPCa patients, survival at 80 years was 42% (95% CI: 38–45) versus 93% (95% CI: 90–95) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 8.4 years, when Hispanic mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

In Asian/Pacific Islander mPCa patients, survival at 80 years was 51% (95% CI: 47–56) versus 91% (95% CI: 88–94) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 6.2 years, when Asian/Pacific Islander mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

3.4 | Abiraterone Era: Race/Ethnicity-Specific YLL in mPCa Patients vs. Age- and Sex-Matched Simulated Population Controls

In the abiraterone era, 5576 mPCa patients were identified, with 3490 (62.6%) Caucasians, 1019 (18.3%) African Americans, 720 (12.9%) Hispanics, and 347 (6.2%) Asians/Pacific Islanders. For each patient, one simulated population control was generated. In Caucasian mPCa patients, survival at 80 years was 56% (95% CI: 54–58) versus 92% (95% CI: 91–93) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 5.4 years, when Caucasian mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

In African American mPCa patients, survival at 80 years was 38% (95% CI: 35–42) versus 93% (95% CI: 90–95) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$).

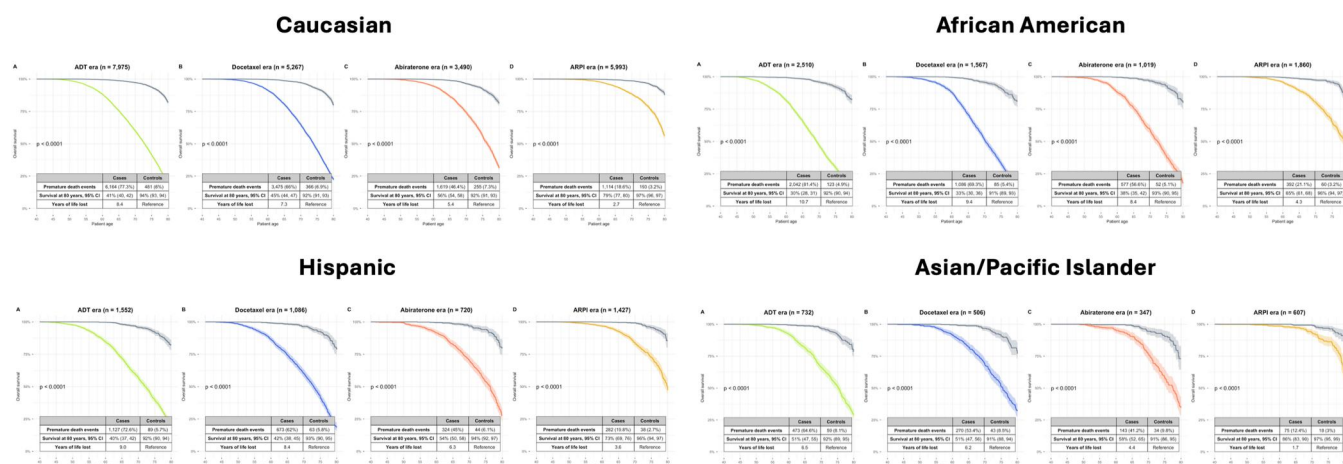


FIGURE 1 | Kaplan-Meier plots depicting observed and predicted (simulated population controls) survival for Caucasian, African American, Hispanic, and Asian/Pacific Islander metastatic prostate cancer patients aged 40–80 years, within the Surveillance, Epidemiology, and End Results database (SEER, 2004–2021), in androgen deprivation therapy era (ADT, 2004–2012), docetaxel era (2013–2016), abiraterone era (2017–2018), and androgen receptor pathway inhibitor (ARPI, 2019–2021) era. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1002/pros.70211)]

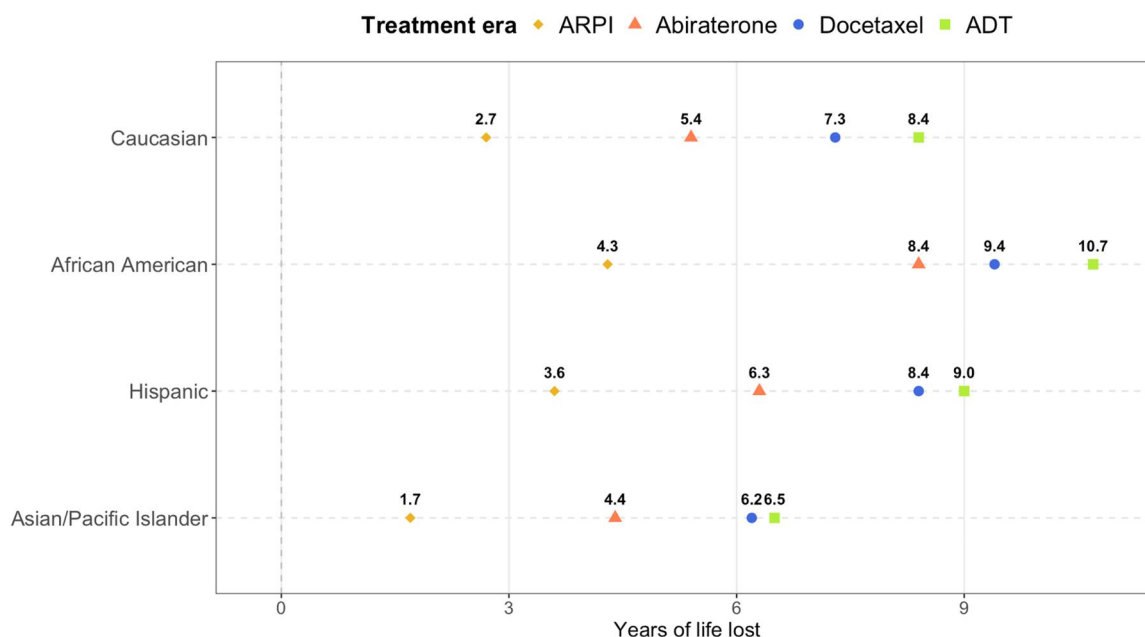


FIGURE 2 | Forrest plot depicting years of life lost in Caucasian, African American, Hispanic, and Asian/Pacific Islander metastatic prostate cancer patients within the Surveillance, Epidemiology, and End Results database (SEER, 2004–2021), according to treatment era: androgen deprivation therapy (ADT, 2004–2012) era, docetaxel era (2013–2016), abiraterone era (2017–2018), and androgen receptor pathway inhibitor (ARPI, 2019–2021) era. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1002/pros.70211)]

These survival rates resulted in an average YLL value of 8.4 years, when African American mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

In Hispanic mPCa patients, survival at 80 years was 54% (95% CI: 50–58) versus 94% (95% CI: 92–97) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 6.3 years, when Hispanic mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

In Asian/Pacific Islander mPCa patients, survival at 80 years was 58% (95% CI: 52–65) versus 91% (95% CI: 86–95) in

simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 4.4 years, when Asian/Pacific Islander mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

3.5 | ARPI Era: Race/Ethnicity-Specific YLL in mPCa Patients vs. Age- and Sex-Matched Simulated Population Controls

In the ARPI era, 9887 mPCa patients were identified, with 5993 (60.6%) Caucasians, 1860 (18.8%) African Americans, 1427

(14.4%) Hispanics, and 607 (6.2%) Asians/Pacific Islanders. For each patient, one simulated population control was generated. In Caucasian mPCa patients, survival at 80 years was 79% (95% CI: 77–80) versus 97% (95% CI: 96–97) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 2.7 years, when Caucasian mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

In African American mPCa patients, survival at 80 years was 65% (95% CI: 61–68) versus 96% (95% CI: 94–97) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 4.3 years, when African American mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

In Hispanic mPCa patients, survival at 80 years was 73% (95% CI: 69–76) versus 96% (95% CI: 94–97) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 3.6 years, when Hispanic mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

In Asian/Pacific Islander mPCa patients, survival at 80 years was 86% (95% CI: 83–90) versus 97% (95% CI: 95–99) in simulated population controls of the same age, sex, and year of inclusion ($p < 0.0001$). These survival rates resulted in an average YLL value of 1.7 years, when Asian/Pacific Islander mPCa patients were contrasted to simulated population controls ($p < 0.0001$, Figures 1 and 2).

4 | Discussion

Despite well-established survival benefits from most recent treatment eras in mPCa patients, real-world data validating and quantifying improved survival in a race/ethnicity-specific fashion are unavailable. We tested the concept of YLL [8–12] in mPCa patients relative to simulated population controls according to treatment era and race/ethnicity and made several noteworthy observations.

First, the current study is the first population-based evaluation of mPCa patients, where survival across different treatment eras according to race/ethnicity is examined. Moreover, it represented the first assessment of YLL values based on simulated population controls according to treatment era and race/ethnicity. Previous population-based studies [16, 17] have not relied on the YLL concept. They have validated a survival benefit and an increasingly larger survival benefit over time, but not according to specific treatment era and specific race/ethnicity. This was done in the current study.

Second, the current results regarding YLL values according to treatment era and race/ethnicity revealed important differences. First, relative to the ADT era, the introduction of each novel treatment paradigm resulted in lower YLL values. Specifically, absolute YLL values were lowest in the ARPI era (1.7–4.3), followed by the abiraterone era (4.4–8.4), followed by the docetaxel era (6.2–9.4), followed by the ADT era (6.5–10.7). These observations provided a population-based validation of improved

survival reported within prospective randomized trials [1–7], where most contemporary treatment paradigms resulted in the highest survival benefits.

Third, despite the highly encouraging decrease in YLL values that was recorded with the advent of each novel treatment era, important differences in YLL values within each of the four examined treatment eras were recorded between the four examined race/ethnicity groups. For example, in the ARPI era, the YLL value of 4.3 recorded in African Americans greatly exceeded the YLL value of 2.7 recorded in Caucasians. Similarly, in the abiraterone era, the YLL value of 8.4 recorded in African Americans greatly exceeded the YLL value of 5.4 recorded in Caucasians. These differences indicated that African American mPCa patients exhibit a survival disadvantage relative to their Caucasian counterparts in all four examined treatment eras. However, the magnitude of this disadvantage has decreased over time. Additionally, a less pronounced survival disadvantage was recorded in Hispanics relative to their Caucasian counterparts. For example, in the ARPI era, the YLL value of 3.6 recorded in Hispanics greatly exceeded the YLL value of 2.7 recorded in Caucasians. Similarly, in the abiraterone era, the YLL value of 6.3 recorded in Hispanics greatly exceeded the YLL value of 5.4 recorded in Caucasians. However, the magnitude of this disadvantage has decreased over time. Conversely, the lowest YLL values were recorded in Asians/Pacific Islanders. For example, in the ARPI era, the YLL value of 1.7 was recorded in Asians/Pacific Islanders relative to the YLL value of 2.7 recorded in Caucasians. Similarly, in the abiraterone era, the YLL value of 4.4 was recorded in Asians/Pacific Islanders relative to the YLL value of 5.4 recorded in Caucasians. Similarly, the magnitude of this disadvantage decreased in the same structure. These differences suggest that African American and Hispanic races/ethnicities are indicators of less favorable survival or less favorable response to systemic therapy relative to Caucasians. Conversely, the most favorable phenotype and/or treatment efficacy appear to be operational in Asians/Pacific Islanders. In consequence, efforts should be made to identify modifiable patient and/or treatment characteristics that could be targeted to obliterate or at least decrease this survival disadvantage in African Americans and Hispanics. Conversely, studies should also focus on Asians/Pacific Islanders to identify potential patient and/or treatment characteristics that result in better survival than that observed in Caucasians.

Despite the valuable insights and the use of novel metrics such as YLL that this study relied on, several limitations must be acknowledged. First, its design is retrospective. Second, the identification of cases was made within the SEER database, which does not provide granular clinical detail, such as the extent of metastatic disease, and, moreover, PSA values at diagnosis are also not universally available. Additionally, comorbidities and subsequent sequential treatments are unknown, which could have influenced survival outcomes. Third, data on patient comorbidities were unavailable, potentially impacting both treatment decisions and life expectancy. In consequence, the current observations should be validated in independent large-scale databases. For example, the National Cancer Database (NCDB) offers OS data on mPCa patients that could be used for YLL analyses.

5 | Conclusions

YLL values decreased with each novel treatment era, in all race/ethnicity groups. The most pronounced decrease in YLL values occurred with the introduction of ARPIs, in all race/ethnicity groups. Despite those survival advances, African Americans were invariably disadvantaged as evidenced by the highest YLL values.

Funding

The authors have nothing to report.

Ethics Statement

The institutional review board waived study-specific ethics approval owing to the anonymous design of the SEER database.

Consent

Not applicable. This study used a population-based dataset (SEER database).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data used in the present study were extracted from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute. SEER data are available to researchers upon request and approval from the SEER program (<https://seer.cancer.gov/>). Restrictions apply to the availability of these data, which were used under license for the current study. Interested researchers may obtain access to SEER data by completing the data-use agreement process outlined on the SEER website.

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