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Article type : Original Article

Abrogation of survival disparity between blacks and whites following the USPSTF's 2012 prostate specific antigen-based prostate cancer screening recommendation*

Running title: USPSTF's 2012 recommendation and disparity

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/CNCR.33179

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# of Text Pages: 19
# of Tables: 3
# of Figures: 4

*This work was supported by the cancer center grant from the National Cancer Institute (Grant P30CA072720) and generous support from the Marion and Norman Tanzman Charitable Foundation and Mr. Malcolm Wernik.

Disclosure: All authors have no significant conflict of interest with the content of this study.
Precis: Following the USPSTF's 2012 recommendation against PSA-based prostate cancer screening, survival disparity between white and black men vanished. This observation was largely due to a decrease in survival among white men while survival in black men largely remained steady.

Author Contributions:
Isaac E. Kim, Jr: conception of study, data analysis, drafting and editing manuscript.
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Total word count: 4867

ABSTRACT

Background: In May 2012, the U.S. Preventive Services Task Force (USPSTF) recommended against prostate-specific antigen (PSA)-based screening for prostate cancer (PCa), assigning it a grade D. This decision was then modified to a grade C for men between ages 55 and 69 in 2018. We hypothesized that changes in screening practices would reduce survival outcomes for both black and white men but maintain racial discrepancies in outcomes.

***Methods*:** Using the Surveillance, Epidemiology, and End Results (SEER) database, we examined PCa-specific survival based on race and year of diagnosis. January 2010 to December 2012 was categorized as the pre-USPSTF era, while January 2014 to December 2016 was classified as the post-USPSTF era. Year 2013 was considered the transition year and excluded from the analysis.

***Results*:** We identified 49,388 men in the pre-USPSTF era who were diagnosed with PCa, of which 83.7% were white and 16.3% were black. In the post-USPSTF era, 41,829 were diagnosed with PCa, of which 82.7% were white and 17.3% were black. Men diagnosed in the post-USPSTF era, when compared to the pre-USPSTF era, were found to have more adverse clinical features. In the pre-USPSTF era, whites were less likely to die from PCa than blacks. This survival disparity between whites and blacks was no longer observed in the post-USPSTF era.

***Conclusions*:** In men diagnosed with PCa from 2014 to 2016, survival disparity between whites and blacks was not observed due to a decrease in survival among white men, while the survival of black men remained steady.

Key words: prostate cancer, racial disparity, screening, prostate-specific antigen, SEER

INTRODUCTION

There is a wide disparity in prostate cancer (PCa) outcomes between white and black men. In 2019, it has been reported that black men when compared to white men have a 1.75 fold higher incidence and 2.20 fold higher mortality [1]. Proposed explanations for such differences include both biology and socioeconomics. For example, divergent androgen signaling involving 5α-reductase (SRD5A2), TA repeat alleles, androgen synthesis, CYP17, androgen deactivation, CYP3A4, AR, and CAG repeats have all been proposed as contributing factors, as higher levels of free testosterone have been reported in black compared to white men [2]. Similarly, based on a limited sample size, various growth factors and apoptosis-related proteins such as IGF-1, EGFR, EphB2, BCL-2, MDM2, inflammation, and various cytokines have also been implicated in PCa

racial disparity [3-7]. In contrast, some have pointed to socioeconomic factors such as unequal access and differences in attitude toward screening [8-10]. Indeed, it has been recently reported that when various socioeconomic factors are adjusted, disparities in PCa outcomes between whites and blacks no longer exist [11,12]. Accordingly, it is likely that the impact of any significant changes in PCa screening policies may vary based on race.

Since its introduction as a screening test for PCa in 1987, the effectiveness of prostate-specific antigen (PSA) has drawn considerable controversy, largely due to the possibility of overdiagnosis and overtreatment of PCa [13]. Studies from The European Randomized Study of Screening for Prostate Cancer (ERSPC) and the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) found overdiagnosis rates ranging from 17 to 50% of PCa cases detected by the PSA screening test [14]. Furthermore, Lu-Yao and colleagues reported that most deaths among men with PCa are due to non-PCa causes [15]. Treatments for PCa also carry the risk for death, cardiovascular events, urinary incontinence, erectile dysfunction, and bowel dysfunction [14]. For example, while radical prostatectomy is considered a definitive procedure for treating PCa, approximately 7% of patients who undergo the procedure experienced major medical or surgical complications with 0.29% dying within 30 days of surgery based on data from trials and cohort studies [16].

Regardless, the adoption of PSA screening has coincided with considerable improvements in mortality rates and features of PCa at presentation with U.S. PCa mortality rates declining by almost 30% in the 1990s. Etzioni and colleagues found that the stage shift induced by PSA screening was responsible for 45 to 70% of this decline [17]. The ERSPC study reported that PSA screening was responsible for a reduction in PCa mortality of 27% [18]. Likewise, van Leeuwen and colleagues found that PSA screening led to reductions in PCa metastasis of 53% after 8.5 years of observation [19].

In May 2012, the U.S. Preventive Services Task Force (USPSTF) recommended against prostate-specific antigen (PSA)-based screening for PCa, assigning it a grade D [14]. This guideline was partly based on the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO), which was conducted in the U.S. and reported no evidence of a mortality benefit with PSA testing [20]. After accounting for differential screening intensity between the control and intervention groups, however, Tsodikov and colleagues found that the PLCO trial actually demonstrated a 27 to 32% lower risk of PCa mortality with PSA screening [21].

Thus, in May 2018, the USPSTF upgraded its recommendation for PSA-based screening for men age 55 to 69 years to a grade C [22]. Nevertheless, the USPSTF's guidelines discouraging PCa screening have had lasting effects on screening rates and features of PCa at presentation. Studies showed that between 2010 and 2013, screening rates for men age 50 to 59 years, 60 to 74 years, and 75 years and older decreased from 33.2% to 24.8%, 51.2% to 43.6%, and 43.9% to 37.1%, respectively [23]. Similarly, Ahlering and colleagues reported a 22.6% reduction in surgical volume, increases in median PSA from 5.1 to 5.8 ng/mL, and increases in mean age from 60.8 to 62.0 years [24]. They found that the proportion of low-grade Gleason score (GS) 3+3 cancers decreased from 30.2 to 17.1%, while that of the high-grade GS ≥ 8 cancers increased from 8.4 to 13.5%.

While several studies have shown increases in more aggressive features of PCa at presentation [25,26], to our knowledge, there have been no studies examining the effect of the USPSTF's 2012 PCa screening recommendation on racial disparities, specifically survival differences between white and black men. We hypothesized that survival outcomes for both black and white men would decrease due to changes in screening practices, but that the racial discrepancies in outcomes would persist. Therefore, we investigated how the USPSTF's recommendations may have affected survival differences between blacks and whites diagnosed with PCa.

MATERIALS AND METHODS

Data Sources

The study cohort consisted of patients from the Surveillance, Epidemiology, and End Results (SEER) Program, which collects cancer incidence data from population-based cancer registries across the U.S. using the SEER*Stat database. SEER registries record data on patient demographics, primary tumor site, tumor morphology, stage at diagnosis, first course of treatment, and follow up. Information on incident cancer cases was available from the Incidence - SEER 9 Regs Research Data, Nov 2018 Sub (1975 - 2016), which covers approximately 9.4% of the U.S. population. The following geographic areas were covered: San Francisco-Oakland SMSA, Connecticut, Detroit (Metropolitan), Hawaii, Iowa, New Mexico, Seattle (Puget Sound), Utah, and Atlanta.

Study Variables

Information on the following study variables were extracted for each population subset: age, PSA, clinical Gleason Score, pathologic Gleason Score, and Summary Stage. Summary Stage incorporates the most precise clinical and pathologic documentation of the extent of PCa.

Statistical Analysis

The primary study outcome was PCa-specific survival based on race and diagnostic time period. Secondary study outcomes examined changes in the distribution of age, PSA, clinical Gleason Score, pathologic Gleason Score, and Summary Stage over time. PCa-specific survival for each diagnostic time period was measured using the Kaplan-Meier method. Disparities between the races within each time period were analyzed using the log rank test and Cox proportional hazards model. Given that the maximum follow-up time for patients diagnosed in 2016 was 36 months, the temporal endpoints for both survival curves were capped at 36 months. Differences in the distribution of patients over time by PSA, clinical Gleason Score, pathologic Gleason Score, and Summary Stage were analyzed using Pearson's chi-square test.

January 2010 to December 2012 was designated as the pre-USPSTF era, while January 2014 to December 2016 was designated as the post-USPSTF era. A one-year buffer in 2013 between the two eras accounted for the time it would take for the recommendations to take effect. All analyses were conducted with Stata/SE 15.0. A *p*-value of less than or equal to 0.05 was considered significant for all analyses.

RESULTS

Significant decrease in survival correlates with grade and stage migration in the post-USPSTF era

The study population was composed of 91,217 patients diagnosed with prostate cancer from January 2010 to December 2012 and January 2014 to December 2016 based on the SEER cause-specific death classification for PCa. As PCa screening was discouraged in 2012, the total number of new PCa diagnosed decreased from the pre- to post-USPSTF era (49,388 to 41,829) (Table 1). PSA on diagnosis tended to be higher following the recommendation against PSA-based PCa screening, as the median level in the pre- and post-USPSTF era were 6.3 and 7.3 ng/ml, respectively ($p < 0.001$). The lower incidence in PCa in the post-USPSTF era was

accompanied by a decrease and increase in the proportion of low-risk and more aggressive PCa, respectively. Specifically, between the two eras, men with clinical Gleason Score 6 (3+3) decreased from 19,505 (42.5%) to 12,819 (33.2%), while those with 8 or higher increased from 7788 (17%) to 8882 (23%) ($p < 0.001$). Likewise, in men who chose radical prostatectomy over the same time periods, pathologic Gleason Score of 6 decreased from 4384 (26.4%) to 1812 (14.1%), while Gleason score of 8 increased from 1709 (10.3%) to 2042 (15.9%) ($p < 0.001$). Finally, the number of localized disease on diagnosis decreased from 39,625 (81.5%) to 31,065 (75.9%), while that of distant disease increased from 2497 (5.1%) to 3278 (8%) ($p < 0.001$). When cause-specific survival was analyzed between the two eras, a significantly shorter survival was detected in the post-USPSTF era ($p < 0.0001$, log-rank test) (Fig 1).

When factors associated with cause-specific survival were analyzed using the Cox proportional hazards model, era of diagnosis, age, PSA, clinical Gleason Score, and stage on presentation were found to be significant. However, race was not associated with death from PCa ($p = 0.0624$) (Table 2).

Prostate cancer disparity in survival between blacks and whites are no longer present in the post-USPSTF era

In the pre-USPSTF era, there were 41,378 whites and 8010 blacks diagnosed with PCa. The numbers during the post-USPSTF era were 34,607 and 7222 for whites and blacks, respectively (Table 3). As expected, median PSA for both whites and blacks increased from the pre to post-USPSTF era (6.2 to 7.2 ng/ml, whites; 6.9 to 8.0 ng/ml, blacks). Distribution of PSA on presentation for whites and blacks demonstrated a significant change from the pre- to post-USPSTF era ($p < 0.0001$ for both eras). When compared between the two races, PSA distribution remained significantly different in both eras ($p < 0.0001$ for both eras). However, the magnitude of change in PSA for white and blacks from pre- to post-USPSTF era was not significantly different ($p = 0.1007$, multinomial logistic regression with generalized logit function). The percentage of whites with PSA ≤ 10 ng/ml on diagnosis decreased from 75.6% in the pre-USPSTF era to 68.1% in the post-USPSTF era. For blacks, the change of percentage with PSA ≤ 10 ng/ml during the same time periods was from 68.4% to 61.1%. On the other hand, percentages of whites and blacks with PSA greater than 20 ng/ml increased in the post-USPSTF era from 11 to 15.2% and 15.9 to 21.5%, respectively.

With respect to clinical Gleason Score distribution, both whites and blacks demonstrated a significant difference between the pre- and post-USPSTF era ($p < 0.0001$ for both eras). For example, whites with low-risk (Gleason Score 6) disease decreased from 43.4% to 34%. Concerning blacks, the percentage of Gleason Score 6 PCa during the same periods decreased from 37.4% to 28.8%. In contrast, whites and blacks with high-risk disease (Gleason Score 8 or higher) increased from 16.9 to 22.9% and 17.3 to 23.4% when the two eras were analyzed. However, when the change in distribution of clinical Gleason score between pre- and post-USPSTF era was compared between the two races, the difference was not significant (p = 0.2844, multinomial logistic regression with generalized logit function).

As for pathologic Gleason Score distribution, a significant difference between the two eras was observed for both races ($p < 0.0001$ for both eras). Between the pre- and post-USPSTF era, whites with pathologic Gleason Score 6 decreased from 26.5 to 14.2%, while for blacks, the change was from 25.3 to 13.5%. The percentage of whites with pathologic Gleason score ≥ 8 increased from 10.6 (pre-USPSTF) to 16.3% (post-USPSTF). For blacks, the change in numbers with high-risk PCa pathologically also increased between the two eras (8.3 to 13.6%). Again, the change in the distribution of pathologic Gleason Score from pre- to post-USPSTF era between the two races was not significant (p = 0.9631, multinomial logistic regression with generalized logit function).

Concerning clinical stage on presentation, both whites and blacks showed a significant change from pre- to post-USPSTF era ($p < 0.0001$ for both eras). In the pre-USPSTF era, whites and blacks who present with a regional and distant disease were 18.7 and 17.6%, respectively (p = 0.024). In comparison, in the post-USPSTF era, the respective percentages for whites and blacks were 24.6 and 21.6% ($p < 0.0001$). When the change in the distribution of clinical stage between pre-and post-USPSTF era was compared between the blacks and whites, the difference was significant ($p < 0.0001$, multinomial logistic regression with generalized logit function).

To determine the impact of above changes on survival disparity between whites and blacks, we assessed cause-specific survival in the pre- and post-USPSTF era. During the pre-USPSTF era, blacks had a significantly worse survival ($p < 0.0001$, log-rank test) (Fig 2). However, the disparity in survival between whites and blacks was no longer observed in the post-USPSTF era (p = 0.4804, log-rank test). Comparing the same data within each race demonstrated that whites experienced a significant decrease in survival while blacks did not (p <

0.0001 for whites and p = 0.3960 for blacks, log-rank test) (Fig 3). A multivariate analysis was carried out to determine which factors were associated with cause-specific survival in both eras (Tables 4 and 5). The results demonstrated that age, serum PSA level, clinical Gleason Score, and stage on presentation correlated with survival in both eras. However, race was associated with survival only in the pre-USPSTF era (p = 0.4781).

Survival disparity between blacks and whites are not present in men older than age 75 in the pre-USPSTF era

The absence of a survival disparity between whites and blacks in the post-USPSTF era was surprising and suggested that the superior survival seen in whites with PCa in the pre-USPSTF era may be due to a difference in PCa screening intensity. To assess this possibility, we examined the outcomes between whites and blacks in men older than or equal to age 75 in the pre-USPSTF era (years 2010-2012), because the recommendation against PSA-based PCa screening in this age group was made in 2008. The total number of men in this category was 7234 and 855 for whites and blacks, respectively (Table 6). PSA distribution between the two races older than age 75 was significantly different (p = 0.002). Percentages of whites and blacks with PSA ≤ 10 ng/ml were 53.1 and 46.6%, respectively. The difference in clinical Gleason Score distribution between whites and blacks, however, was not statistically significant (p = 0.143). Due to a low sample size in men older than or equal to age 75 who opted for radical prostatectomy (only 22 blacks), pathologic Gleason Score was not analyzed. Stage on presentation was also similar between the two races if the age was older than or equal to 75 in the pre-USPSTF era (p = 0.070). Finally, cause-specific survival between whites and blacks older than or equal to age 75 were not significantly different in the pre-USPSTF era (p = 0.2293, log-rank test) (Fig 4).

DISCUSSION

The present study found multiple significant changes in the epidemiology of PCa between the pre- and post-USPSTF eras. As expected, there was a significant shift toward a more aggressive PCa following the USPSTF recommendation against PSA-based PCa screening in 2012. However, this shift toward a higher risk disease coincided with a decreased cause-specific

survival for whites but not blacks. Collectively, our findings pose significant questions for PCa screening and PCa disparity between whites and blacks.

The observation that there was a migration toward higher grade and stage disease following the USPSTF's grade D recommendation for PSA-based PCa screening has been proposed by multiple investigators [24-26]. In the present study, the percentage of men with low-risk disease (Gleason Score 6) and localized disease decreased dramatically from the pre- to post-USPSTF era. Simultaneously, a significant decrease in cause-specific survival for men with a newly diagnosed with PCa was found in the years following the USPSTF's recommendation against using PSA in 2012. Such temporal change in the PCa survival following diagnosis was confirmed to be independent of age, PSA, clinical Gleason Score, and stage on presentation. Since the temporal trend of decreasing PCa mortality over the last decade has stopped recently, it is reasonable to conclude that the USPSTF's 2012 recommendation has had an adverse effect on PCa outcomes.

The most important observation of the present study is that the task force's recommendation against PSA-based PCa screening in 2012 may have had an unintended effect on PCa survival disparities between whites and blacks. Specifically, the disparity in cause-specific survival between whites and blacks present in the pre-USPSTF era was not observed in the post-USPSTF era. However, the abrogation of this disparity was not due to an increase in survival for black men with PCa but rather was the result of decreased survival for the white cohort. A detailed analysis of changes in the racial difference of serum PSA, clinical Gleason Score, pathologic Gleason Score, and stage on presentation distribution between the two eras using the multinomial logistic regression with generalized logit function demonstrated that only change in stage was significantly different ($p<0.0001$) (Table 3). Specifically, the percentage of whites with regional and distant disease on diagnosis increased from 18.7 to 24.6 % between the pre- and post-USPSTF era. In comparison, the change in blacks was from 17.6 to 21.6%. Moreover, as shown in Tables 4 and 5, the hazard ratios for regional and distant stages were 2.264 and 76.350 in the pre-USPSTF era and 2.182 and 66.759 in the post-USPSTF era, all with p-values of <0.0001. Taken together, the decreased survival in whites in the post-USPSTF era is explained, at least in part, by the increased percentage of regional/distant disease.

The precise explanation for the decreased survival in whites in the post-USPSTF era is not clear. However, because race was independent of standard clinical variables (serum PSA,

clinical Gleason Score, and stage) in predicting survival only in the pre-USPSTF era, it is likely that there is a non-biologic factor that disappeared following the USPSTF's 2012 recommendation. In this regard, a provocative hypothesis is that the screening intensity for whites in the pre-USPSTF era was higher than that of blacks. As a result, more whites may have benefitted from an early definitive intervention. Indeed, this proposed difference in screening intensity between whites and blacks may be a surrogate of access to care and healthcare insurance status. Such a concept is supported by the observation that following the USPSTF's 2008 recommendation against PCa screening in men ≥ 75 years old, the odds ratio of having PCa screening decreased in white but not in black men[23]. Notwithstanding, the abrogation of disparity in survival outcome in the post-USPSTF era suggests that PSA-based PCa screening may have benefitted whites more than blacks. This concept is consistent with the observation that the PCa survival disparity between whites and blacks older than or equal to age 75 was not present in the pre-USPSTF era examined in this study (2010-2012); in this age group, PSA-based PCa screening was discouraged in 2008. Regardless of the underlying explanation, our current observation raises a serious concern in that the disparity in outcome between whites and blacks resolved in the post-USPSTF era by downward leveling of the outcome in whites rather than an improvement in the outcome in blacks.

The abrogation of survival disparity following the recommendation against PSA-based PCa screening also shed additional light on potential reasons for racial disparity in PCa. Specifically, understanding the extent to which socioeconomic factors and biology each play in mortality among black men is critical to understanding the worse PCa outcome in blacks. Herein, our observation suggests that racial disparities in PCa-specific survival are significantly affected by socioeconomics, as a change in PCa screening policy was associated with a significant impact in PCa outcome between whites and blacks. This concept is consistent with the recent report in which the PCa outcome was similar between whites and blacks when adjusted for socioeconomic factors in an equal access setting [11,12]. Therefore, as it has been reported that the outcomes of radical prostatectomy have wide variations across high volume tertiary centers [27], we contend that the optimal approach to addressing PCa disparity in blacks is through community education and identifying and addressing critical socioeconomic disadvantages of blacks.

The distribution of clinical Gleason Score in our study suggests the possibility that the window for making a difference in PCa outcome may lie with the low- and intermediate-risk and

not high-risk disease. Indeed, due to near negligible metastatic rate of Gleason Score 6 PCa, active surveillance is now the recommended treatment in men with a low-risk PCa. According to this concept, a meaningful impact on outcome is made when the disease is detected in high-risk disease with screening. Our data revealed, however, that the percentage of men who present with Gleason Score 8 or higher high-risk PCa was essentially the same between whites and blacks in both the pre- and post-USPSTF era (16.9 vs 17.2% in the pre-USPSTF era and 22.9 vs 23.4% in the post-USPSTF era). Thus, it is likely that there are low-risk patients who may benefit from a definitive therapy and that identifying these men early may be an effective strategy to improve PCa outcome.

The strength of our study is that a population-based database was used. Therefore, the results represent a real-world practice patterns, trends, and outcomes that cannot be ascertained from a randomized controlled trial. Yet, in interpreting our data, the following limitations should be considered. First, the SEER database is an observational cohort. As such, potential biases such as differing preferences in treatment choice cannot be removed. Second, the main endpoint was the cause-specific survival over a three-year period. In assessing PCa outcomes, this is a very short follow-up. Nevertheless, the observation that the disparity existed in one period but not the other supports the validity of our analysis. Lastly, because SEER does not contain PCa screening data, the magnitude of the impact of USPSTF's 2012 recommendation on PCa screening rate between whites and blacks is not clear at the present time. Indeed, not having actual screening data to show a direct cause and effect relationship is a main limitation of our study. Accordingly, our study should be considered a hypothesis-generating investigation and additional studies utilizing different population-based databases should be carried out to confirm the current results.

CONCLUSIONS

Racial disparities in PCa-specific survival remain a challenging problem. The current study suggests that a carefully developed and disseminated PCa screening strategy may be the optimal approach to improving PCa outcomes in both whites and blacks.

ACKNOWLEDGEMENT

We thank Ms. Juliana Kim for her assistance with formatting the figures.

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Figure Legends

Figure 1. Prostate cancer-specific survival in pre- (2010-2012) and post-USPSTF (2014-2016) eras. Following the USPSTF's recommendation against PSA-based prostate cancer in 2012, prostate cancer-specific survival decreased significantly.

Figure 2. Prostate cancer-specific survival between blacks and whites in pre- (left panel) and post-USPSTF (right panel) eras. Blacks, when compared to whites, had a poorer survival in the pre- but not in the post-USPSTF era.

Figure 3. Prostate cancer-specific survival in pre- and post-USPSTF eras between whites (right panel) and blacks (left panel). Whites showed a decrease in survival in the post-USPSTF era when compared to the pre-USPSTF era. In contrast, blacks showed no change in survival between the pre- and post-USPSTF eras.

Figure 4. Prostate cancer-specific survival in pre-USPSTF era between whites and blacks older than or equal to age 75. Survival was not significantly different between the two races.

Table 1. Patient characteristics in pre- vs post-USPSTF era.

	n (%), pre-USPSTF era (2010-2012)	***n (%), post-USPSTF era (2014-2016)***	***p-value***
Sample size	49388	41829	
Whites	41378	34607	
Blacks	8010	7222	
PCa-specific Mortality	1895 (3.83%)	1173 (2.8%)	
Median age (years)	65	66	<0.001*
PSA (ng/ml)			<0.001**
Median	6.3	7.3	
≤ 10	31636 (74.4)	24675 (66.9)	
10 < PSA ≤ 20	5867 (13.8)	6195 (16.8)	
> 20	5020 (11.8)	6005 (16.3)	

Total	42523	36875	
Clinical Gleason Score			<0.001**
≤ 3 + 3	19505 (42.5)	12819 (33.2)	
3 + 4	12943 (28.2)	11245 (29.1)	
4 + 3	5695 (12.4)	5687 (14.7)	
≥ 8	7788 (17.0)	8882 (23.0)	
Total	45931	38633	
Pathologic Gleason Score			<0.001**
≤ 3 + 3	4384 (26.4)	1812 (14.1)	
3 + 4	7778 (46.8)	6218 (48.4)	
4 + 3	2765 (16.6)	2771 (21.6)	
≥ 8	1709 (10.3)	2042 (15.9)	
Total	16636	12843	
Stage			<0.001**
Localized	39625 (81.5)	31065 (75.9)	
Regional	6492 (13.4)	6576 (16.1)	
Distant	2497 (5.1)	3278 (8.0)	
Total	48614	40919	

*Wilcoxon Rank Sum; **Pearson Chi Squared Correlation

PCa = prostate cancer

Table 2. Cox proportional hazards analysis of factors associated with prostate cancer cause-specific survival.

	Sample size (%)	**HR (95% CI)**	**p-value**
Era			
2010-2012 (Pre-USPSTF)	49,388	1 (Referent)	

2014-2016 (Post-USPSTF)	41,829	1.312 (1.216-1.414)	<0.0001
Age (years)			
<55	9,455 (10.37%)	1 (Referent)	
55-70	55,831 (61.21%)	1.177 (0.989-1.400)	0.061
>70	25,931 (28.43%)	5.419 (4.580-6.411)	<0.0001
Race			
White	75,985 (83.30%)	1 (Referent)	
Black	15,232 (16.70%)	1.093 (0.996-1.199)	0.0624
PSA			
≤10	56,311 (70.92%)	1 (Referent)	
10 < PSA ≤ 20	12,062 (15.19%)	3.090 (2.604-3.666)	<0.0001
> 20	11,025 (13.89%)	34.548 (30.798-38.754)	<0.0001
Clinical Gleason Score			
≤3+3	32,324 (38.22%)	1 (Referent)	
3+4	24,188 (28.60%)	2.190 (1.717-2.793)	<0.0001
4+3	11,382 (13.46%)	6.629 (5.262-8.352)	<0.0001
≥8	16,671 (19.71%)	41.804 (34.418-50.775)	<0.0001
Stage			
Localized	70,690 (78.95%)	1 (Referent)	
Regional	13,068 (14.60%)	2.248 (1.919-2.632)	<0.0001
Distant	5,775 (6.45%)	72.677 (66.080-79.932)	<0.0001

Table 3. Characteristics of whites and blacks diagnosed with prostate cancer in pre- and post-USPSTF era.

	Whites		**Blacks**		**p-value***
	n (%), pre-USPSTF (2010-2012)	**n (%), post-USPSTF (2014-2016)**	**n (%), pre-USPSTF (2010-2012)**	**n (%), post-USPSTF (2014-2016)**	

Sample size	41378	34607	8010	7222	
PCa-specific Mortality	1524 (3.68%)	985 (2.85%)	353 (4.4%)	188 (2.6%)	
Median age (years)	66	66	63	63	
PSA (ng/ml)					0.1423
Median	6.2	7.2	6.9	8.0	
≤ 10	26760 (75.7)	20767 (68.1)	4876 (68.4)	3908 (61.2)	
10 < PSA ≤ 20	4747 (13.4)	5079 (16.7)	1120 (15.7)	1116 (17.4)	
> 20	3884 (11.0)	4633 (15.2)	1136 (15.9)	1372 (21.4)	
Total	35391	30479	7132	6396	
Clinical Gleason Score					0.2844
≤ 3 + 3	16739 (43.4)	10902 (34.1)	2766 (37.4)	1917 (28.8)	
3 + 4	10582 (27.5)	9164 (28.7)	2361 (31.9)	2081 (31.3)	
4 + 3	4705 (12.2)	4589 (14.4)	990 (13.4)	1098 (16.5)	
≥ 8	6511 (16.9)	7329 (22.9)	1277 (17.3)	1554 (23.4)	
Total	38537	31984	7394	6650	
Pathologic Gleason Score					0.9631
≤ 3 + 3	3844 (26.5)	1557 (14.2)	540 (25.3)	255 (13.5)	
3 + 4	6712 (46.3)	5237 (47.8)	1066 (50.0)	981 (51.8)	
4 + 3	2415 (16.6)	2372 (21.7)	350 (16.4)	399 (21.1)	
≥ 8	1531 (10.6)	1785 (16.3)	178 (8.3)	257 (13.6)	
Total	14502	10951	2134	1892	
Stage					<0.0001
Localized	33134 (81.3)	25530 (75.4)	6491 (82.4)	5535 (78.4)	

Regional	5605 (13.8)	5683 (16.8)	887 (11.3)	893 (12.6)	
Distant	1999 (4.9)	2642 (7.8)	498 (6.3)	636 (9.0)	
Total	40738	33855	7876	7064	

*Multinomial Logistic Regression with Generalized Logit Function

PCa = prostate cancer

Table 4. Cox proportional hazards analysis of factors associated with prostate cancer cause-specific survival in the pre-USPSFT era (2010-2012).

	Sample size (%)	**HR (95% CI)**	**p-value**
Age (years)			
<55	5,508 (11.15%)	1 (Referent)	
55-70	30,151 (61.05%)	1.0166 (0.832-1.242)	0.8715
>70	13,729 (27.80%)	4.470 (3.685-5.421)	<0.0001
Race			
White	41,378 (83.78%)	1 (Referent)	
Black	8,010 (16.22%)	1.185 (1.056-1.330)	0.0045
PSA (ng/ml)			
≤10	31,636 (74.40%)	1 (Referent)	
10 < PSA ≤ 20	5,867 (13.80%)	3.395 (2.754-4.185)	<0.0001
> 20	5,020 (11.81%)	37.558 (32.598-43.272)	<0.0001
Clinical Gleason Score			
≤3+3	19,505 (42.47%)	1 (Referent)	
3+4	12,943 (28.18%)	2.131 (1.635-2.777)	<0.0001
4+3	5,695 (12.40%)	2.595 (2.291-2.940)	<0.0001
≥8	7,788 (16.96%)	41.033 (33.288-50.580)	<0.0001
Stage			
Localized	39,625 (81.51%)	1 (Referent)	
Regional	6,492 (13.35%)	2.264 (1.871-2.740)	<0.0001
Distant	2,497 (5.14%)	76.350 (68.096-85.603)	<0.0001

Table 5. Cox proportional hazards analysis of factors associated with prostate cancer cause-specific survival in the post-USPSTF era (2014-2016).

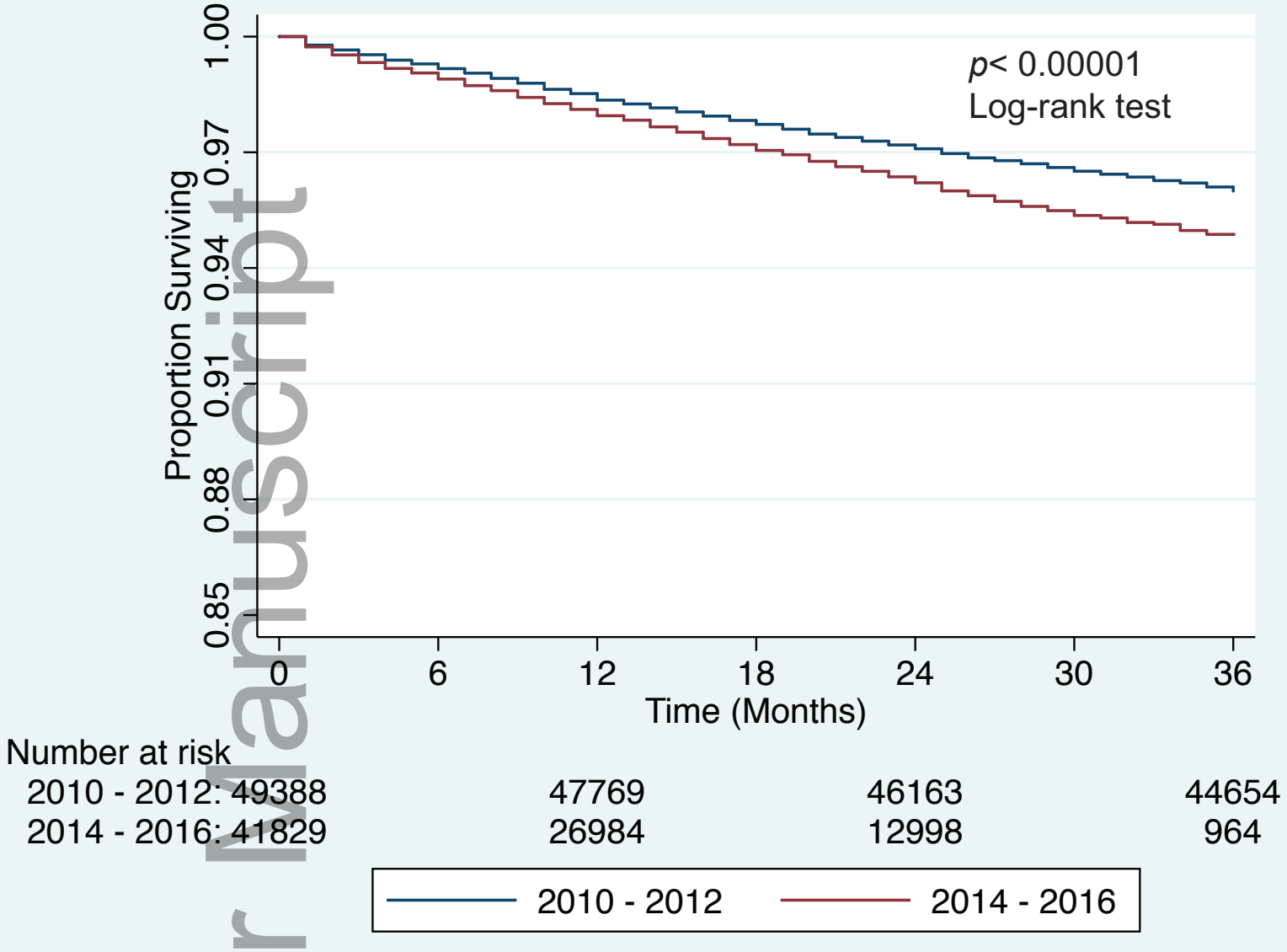
	Sample size (%)	HR (95% CI)	p-value
Age (years)			
<55	3,947 (9.44%)	1 (Referent)	
55-70	25,680 (61.39%)	1.687 (1.180-2.410)	0.0020
>70	12,202 (29.17%)	8.4367 (5.955-11.950)	<0.0001
Race			
White	34,607 (82.73%)	1 (Referent)	
Black	7,222 (17.27%)	0.9454353 (0.809-1.105)	0.4781
PSA (ng/ml)			
≤ 10	24,675 (66.92%)	1 (Referent)	
10 < PSA ≤ 20	6,195 (16.80%)	2.494 (1.854-3.355)	<0.0001
> 20	6,005 (16.28%)	29.074 (23.894-35.378)	<0.0001
Clinical Gleason Score			
≤ 3+3	12,819 (33.18%)	1 (Referent)	
3+4	11,245 (29.11%)	2.645 (1.411-4.956)	0.0015
4+3	5,687 (14.72%)	6.430 (3.484-11.868)	<0.0001
≥ 8	8,883 (22.99%)	49.255 (28.929-83.863)	<0.0001
Stage			
Localized	31,065 (75.92%)	1 (Referent)	
Regional	6,576 (16.07%)	2.182 (1.646-2.894)	<0.0001
Distant	3,278 (8.01%)	66.759 (56.207-79.292)	<0.0001

Table 6. Characteristics of whites and blacks older than or equal to age 75 diagnosed with prostate cancer in pre-USPSTF era.

	n (%), Whites	n (%), Blacks	p-value
Sample size	7234	855	
PCa-specific Mortality	849 (11.7%)	114 (13.3%)	
Median age (years)	79	78	<0.001*
PSA (ng/ml)			0.002**
Median	9.5	11	
4 < PSA ≤ 10	2886 (53.1)	319 (46.6)	
10 < PSA ≤ 20	1144 (20.3)	144 (21.1)	
> 20	1494 (26.6)	221 (32.3)	
Total	5624	684	
Clinical Gleason Score			0.143**
≤ 3 + 3	1606 (26.6)	184 (26.2)	
3 + 4	1433 (23.6)	192 (27.4)	
4 + 3	982 (16.2)	104 (14.8)	
≥ 8	2052 (33.8)	221 (31.5)	
Total	6073	701	
Stage			0.070**
Localized	5594 (80.9)	652 (81.3)	
Regional	420 (6.1)	34 (4.2)	
Distant	898 (13.0)	116 (14.5)	
Total	6912	802	

*Wilcoxon Rank Sum; **Pearson Chi Squared Correlation

PCa = prostate cancer



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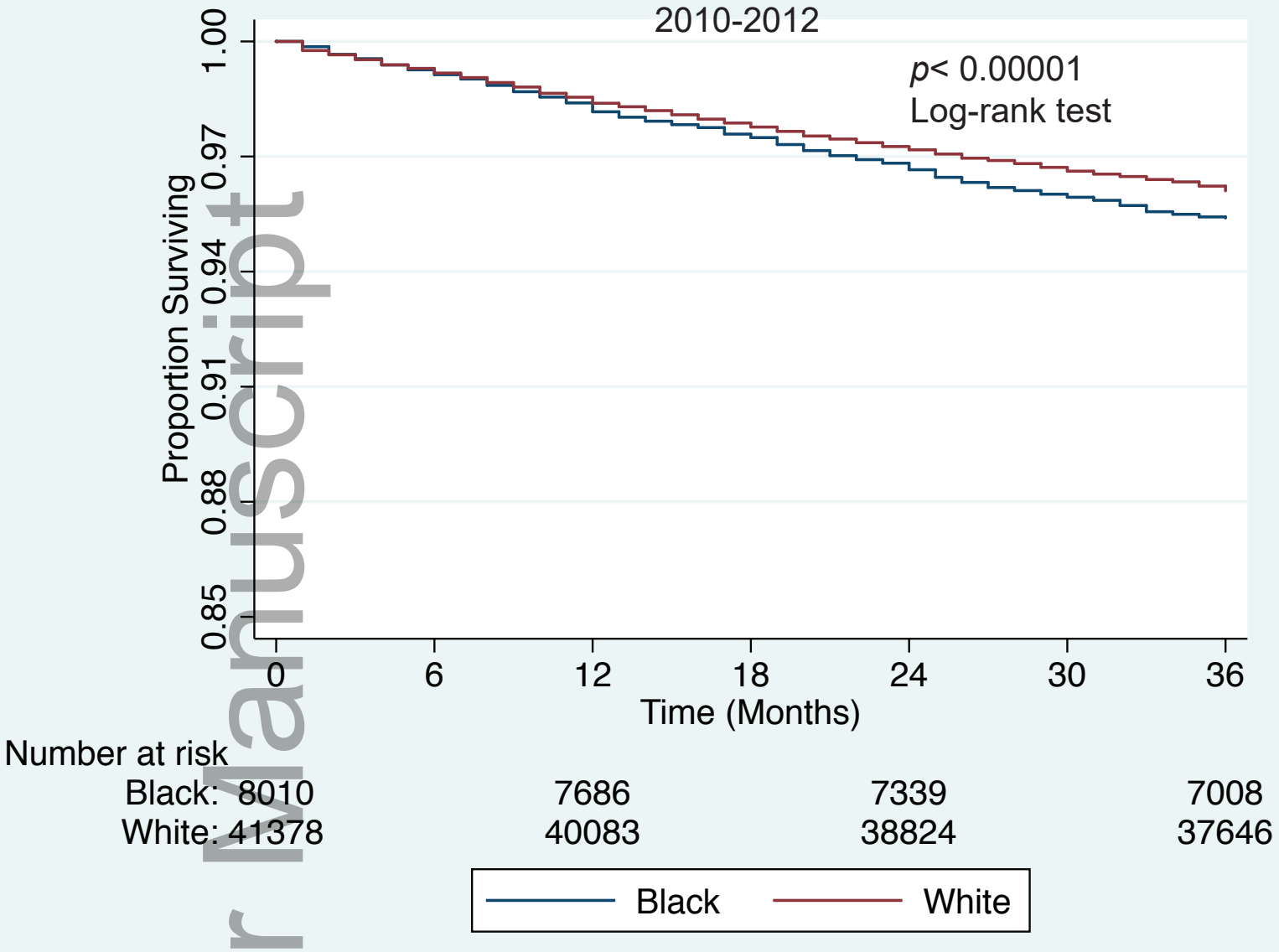

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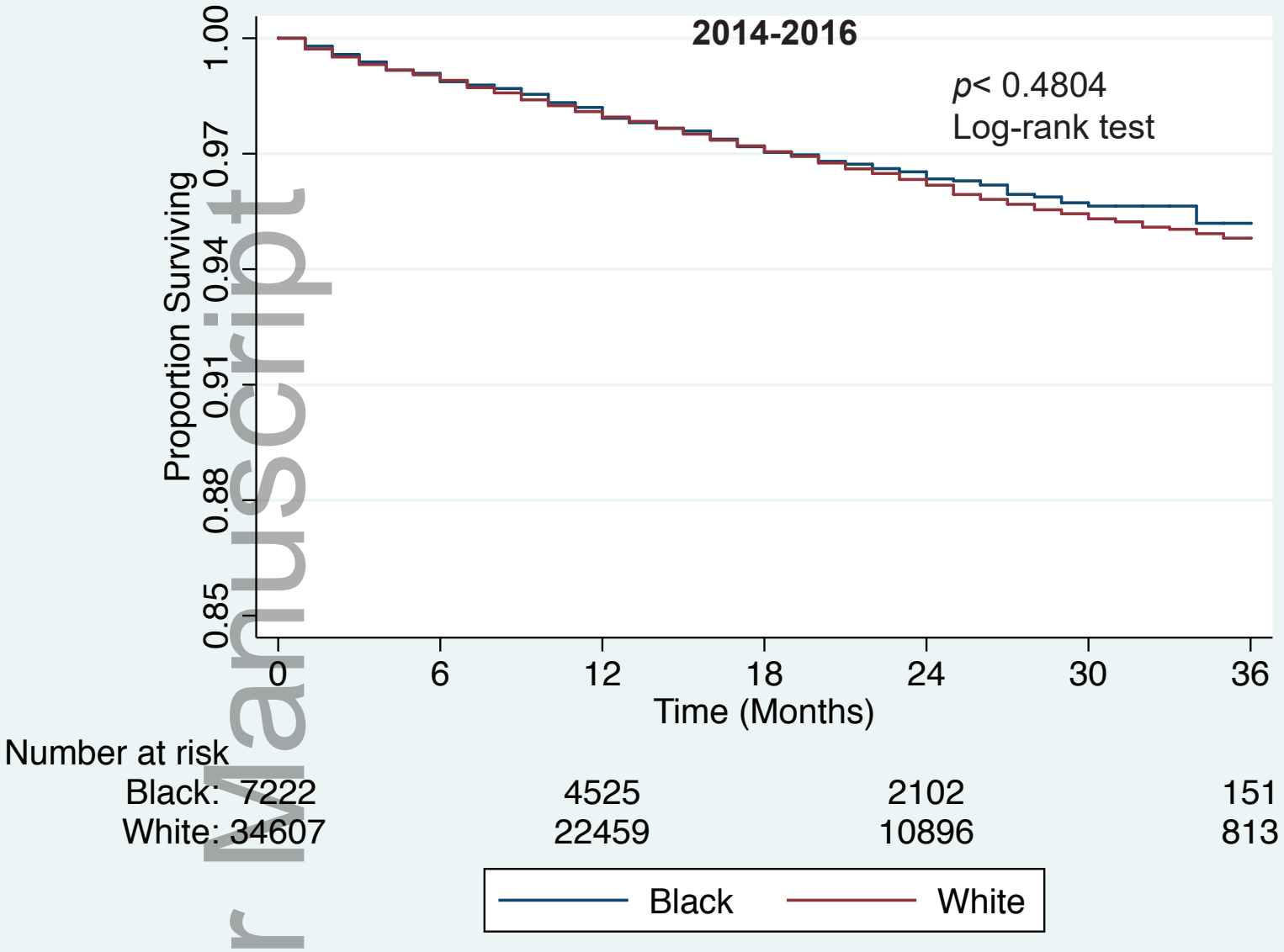

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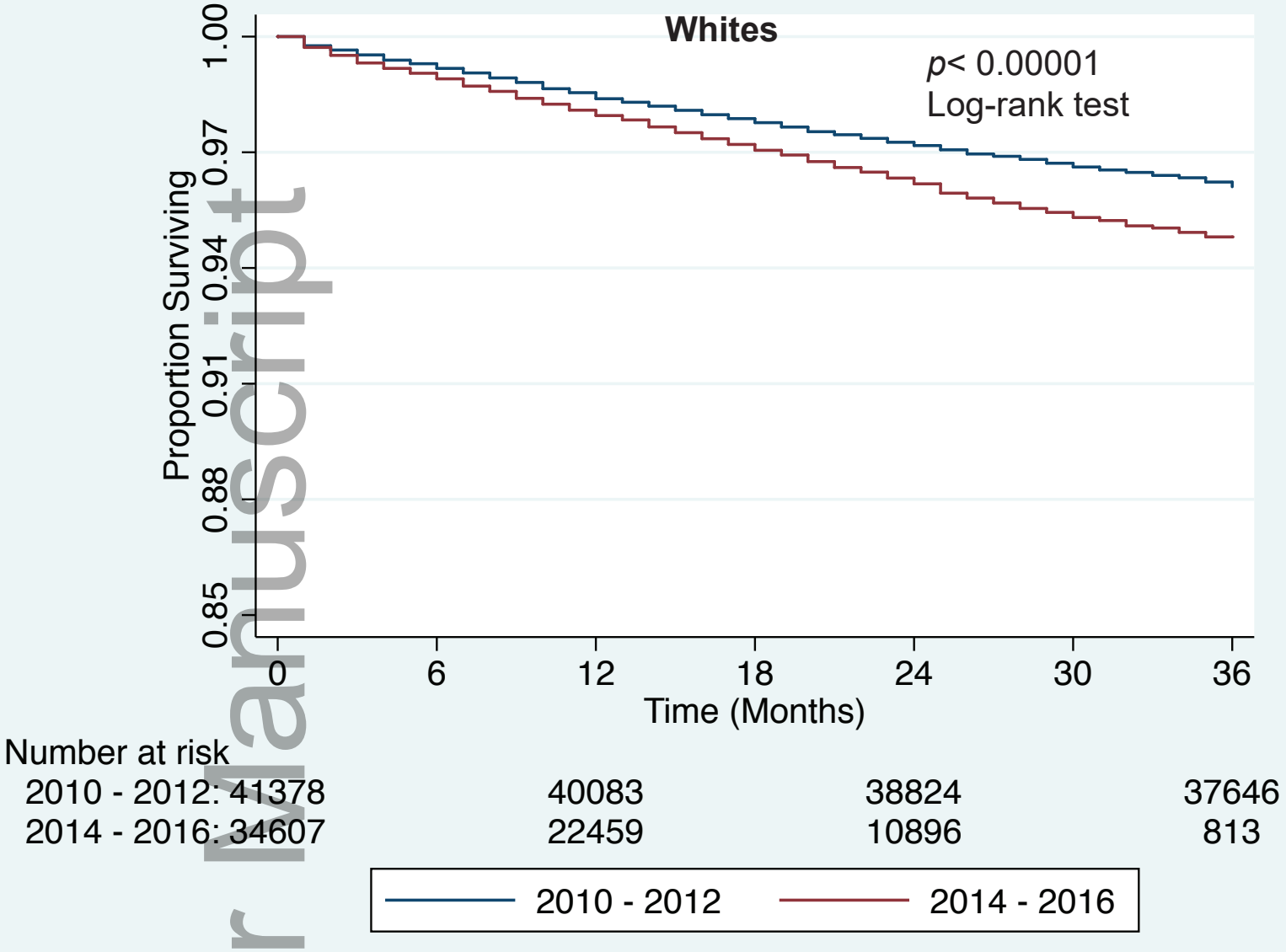

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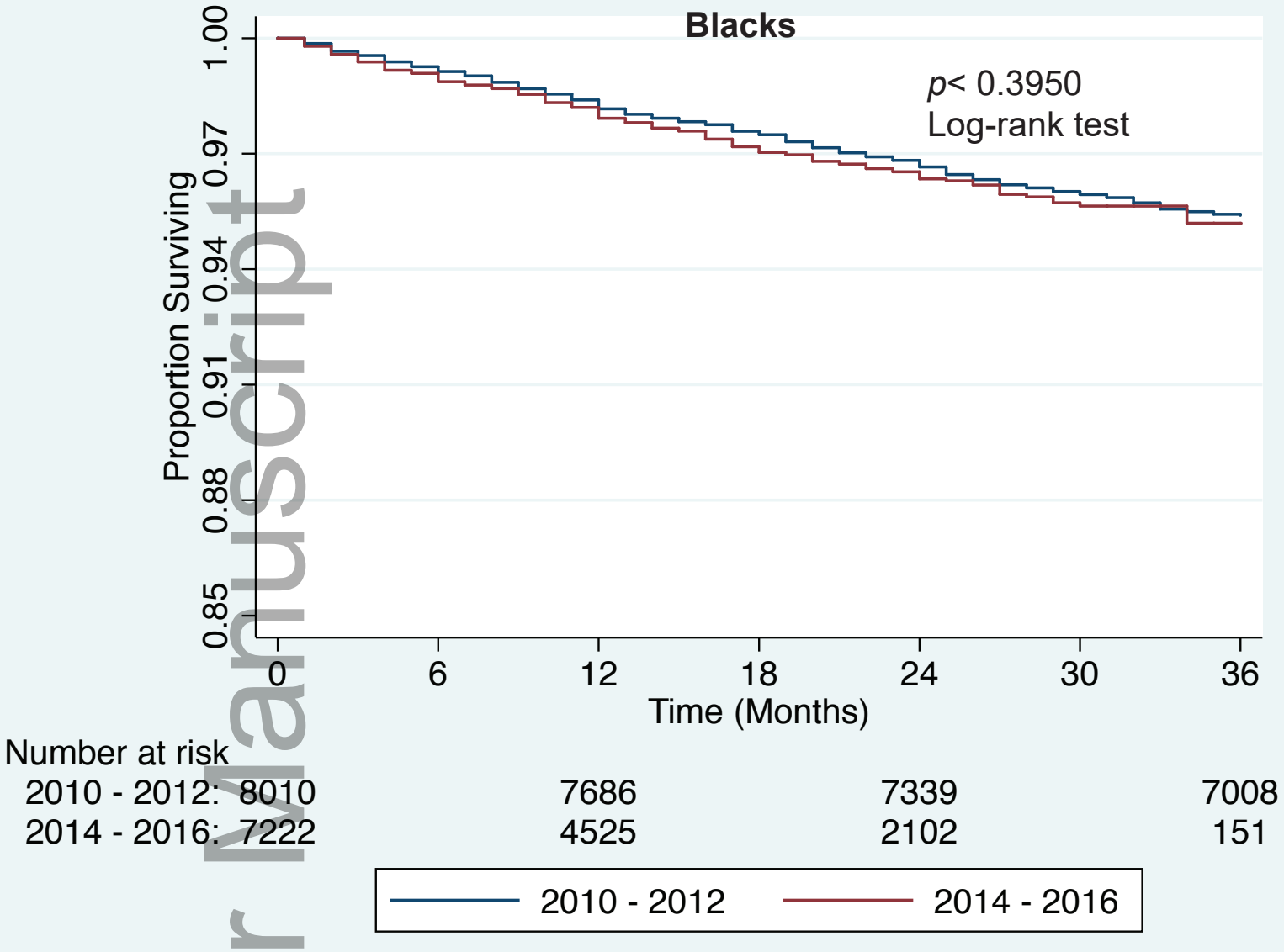

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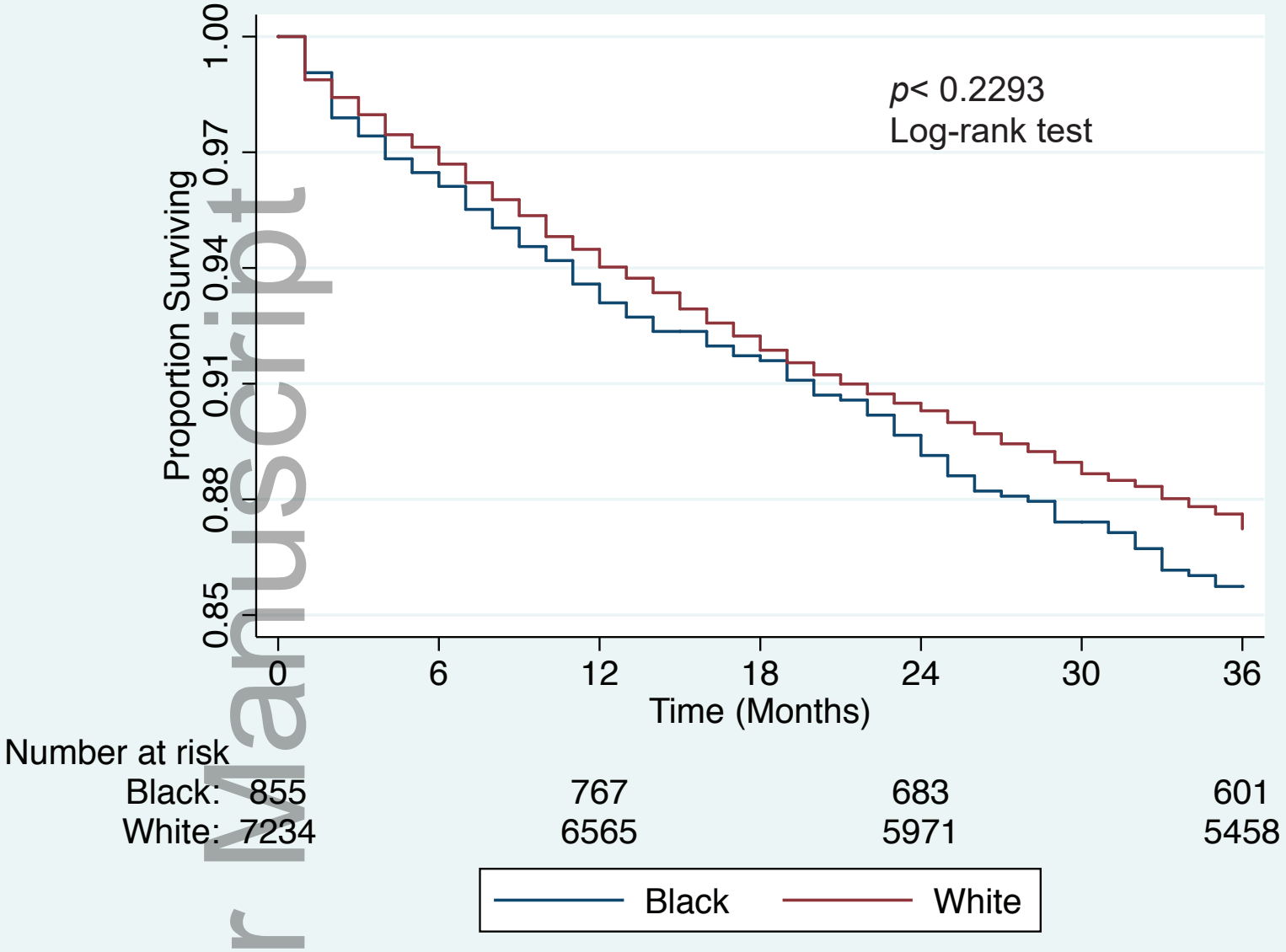

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