Impact of Ethnicity on Primary Treatment Choice and Mortality in Men With Prostate Cancer: Data From CaPSURE

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A B S T R A C T

Purpose

Men diagnosed with prostate cancer have multiple options available for treatment. Previous reports have indicated a trend of differing modalities of treatment chosen by African American and white men. We investigated the role of ethnicity in primary treatment choice and how this affected overall and cancer-specific mortality.

Methods

By utilizing data abstracted from Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE), patients were compared by ethnicity, primary treatment, number of comorbidities, risk level according to modified D'Amico criteria, age, highest educational level attained, type of insurance, treatment facility, and perception of general health. Multinomial logistic regression analysis was performed to determine the effect of the tested variables on primary treatment and mortality.

Results

African American men were more likely to receive nonsurgical therapy than white men with equivalent disease characteristics. Whites were 48% less likely than African Americans to receive androgen deprivation therapy (ADT) compared with surgery ($P = .02$) and were 25% less likely than African Americans to receive radiation therapy compared with surgery ($P = .08$). Whites with low-risk disease were 71% less likely to receive ADT than African American men with similar disease ($P = .01$). Adjusted overall and prostate cancer–specific mortality were not significantly different between whites and African Americans (hazard ratios, 0.73 and 0.37, respectively). Risk level, type of treatment, and type of insurance had the strongest effects on risk of mortality.

Conclusion

There is a statistically significant difference in primary treatment for prostate cancer between African American and white men with similar risk profiles. Additional research on the influence of patient/physician education and perception and the role that socioeconomic factors play in mortality from prostate cancer may be areas of focus for public health initiatives.

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INTRODUCTION

Prostate cancer represents a significant public healthcare burden because of the frequency of diagnosis and the long natural history of the disease.¹ Although there is no consensus as to what constitutes optimal treatment for the various stages of prostate cancer, several reports have focused on how treatment affects health-related outcomes.²⁻⁵ Factors that may play a role in treatment choice after prostate cancer diagnosis include pretreatment risk classification, overall health status, the patient's health perception and understanding of the treatment options, and the treating physician's preferences and skill set. A recent review of the factors considered by

patients when making treatment choices identified cancer eradication and treatment effectiveness as the most important and identified a surprisingly low consideration of treatment adverse effects and family influence.⁵ The myriad treatment choices reflect the ability of the patient and physician to best choose the appropriate management. However, there is a significant amount of treatment regret, particularly among African American and low-income men.^{2,5}

Another area of intense discussion is the disparity in prostate cancer outcomes between African American and white men. An analysis of data from the National Center for Health Statistics from 1975 to 2004 has shown that African American men have greater than twice the prostate cancer mortality of

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white men.⁶ Recent data have suggested that treatment variance between ethnic groups may provide an explanation for the disparity in survival with prostate cancer.^{7,8} Others have investigated the role of factors such as biologic differences, socioeconomic status, and overall health in survival among African American men diagnosed with prostate cancer.⁹⁻¹⁶ Because of conflicting data in the literature regarding the role of various factors in treatment choice, we investigated the association of pretreatment clinical factors with treatment choice by ethnicity. We hypothesized that these factors could predict variation in treatment between ethnic groups and, additionally, that this variation may explain the difference in prostate cancer-specific mortality. To test our hypothesis, we utilized the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) database, a primarily community-based data set of more than 13,000 men with biopsy-proven prostate cancer.

METHODS

Data

CaPSURE is a registry of men with biopsy-proven prostate cancer. Started in 1995, there have been 13,805 enrollees through July 2008. Tests, treatments, and disease characteristics were reported at 40 participating sites around the country. The majority of sites were community urologic clinics, three were academic practices, and three were Veterans Affairs (VA) urologic clinics. Health-related quality of life, resource use, and satisfaction with care were reported by participants twice each year for most years of the study. There were 4,284 participants who reported a health-related quality of life questionnaire within 12 months before selecting primary treatment by 2007, with follow-up beyond treatment. Ethnicity was primarily reported by the participant and was reported by the physician when the participant did not report ethnicity. Risk was categorized by using a modification of the D'Amico definition, in which stage T2c is considered intermediate in CaPSURE. Comorbidities were enumerated by using participant reports of a condition in these 17 categories: arthritis, hypertension, heart disease, stroke, diabetes, lung disease, cancer, kidney, blood disease, stomach, urinary, eyes, ears/nose/throat (ENT), liver, infection, mental, and endocrine. Insurance was categorized one of four ways: Medicare (either in addition to another insurance or Medicare only), any private insurance, VA, other (ie, Medicaid, self pay, charity), or unknown insurance. Education was categorized as the highest level started: high school (or less), college, and graduate or professional school.

Statistical Analysis

The initial analysis utilized generalized logit regression to test effects of ethnicity and other participant characteristics on primary treatment decision. First, a test was performed for a difference between the ethnicities in each of the other characteristics that we hypothesized might affect treatment decision. The list of potentials included education, site type, insurance, age, risk, count of comorbidities, response to the question of general health (ie, In general, would you say your health is excellent; very good; good; fair; or poor?), and ethnicity. Main effects and interactions between pairs of variables were tested for two-way significance at the 5% level. Odds ratios (ORs) were reported for the most parsimonious model, which best described the effects of ethnicity and the other included characteristics on treatment decision. We additionally tested the best parsimonious model on subsets of high, intermediate, or low risk. We also tested whether effects of ethnicity on treatment were the same over time by using the Cochran-Mantel-Haenszel χ^2 test of homogenous ethnicity-treatment associations across the time periods of 1995 to 1999, 2000 to 2003, and 2004 to 2007.

The second analysis tested the effects of ethnicity, risk, age at diagnosis, primary treatment type, comorbidities, education, site, insurance, and health perception on prostate cancer-specific mortality or all-cause mortality with Cox proportional hazards regressions by using time from diagnosis to death or last contact with participant. Informed by our analyses of effects on treatment

Table 1. Patient Demographics

Characteristic	Patients by Ethnicity						P*
	African American		White		Other		
	No.	%	No.	%	No.	%	
Overall	304	7	3,841	90	139	3	
Mean time to follow-up, months	42		41		38		
Age at diagnosis, years							< .01
39-59	92	30	991	26	41	29	
60-69	144	47	1,603	42	60	43	
70-92	68	22	1,247	32	38	27	
Site of treatment							< .01
Academic	6	2	311	8	18	13	
VA	12	4	82	2	12	9	
Community	286	94	3,448	90	109	78	
Type of insurance							< .01
Medicare	99	33	1,758	46	47	34	
Private	141	46	1,868	49	62	45	
VA	12	4	87	2	10	7	
Other	52	17	128	3	20	14	
Educational level							< .01
High school	186	64	1,400	37	72	52	
College	78	27	1,466	39	40	29	
Graduate	26	9	911	24	26	19	
Missing	14		64		1		

Abbreviation: VA, Veterans Affairs.

*Pearson χ^2 test, does not include missing values.

decision, we included in our analysis of mortality those characteristics that first were independently associated with treatment. Ethnicity was forced into the model first, and the other covariates were added one at a time in order of strongest association with mortality. The hazard ratio (an estimate of risk of mortality) for each ethnicity category was tested for two-way statistical significance at the 5% level. All data were analyzed by using SAS (SAS Institute, Cary, NC).

RESULTS

The demographic and clinical characteristics of 4,284 men who met criteria for inclusion are summarized in Tables 1 and 2. Overall, 90% of the study population were white, 7% were African American, and 3% were represented in other ethnic groups (eg, Hispanic, Asian, Native American, or mixed). There was a significant association of age at diagnosis and ethnicity. Seventy-seven percent of African American men were diagnosed at younger than age 70 years compared with 68% of whites and 72% of men of other ethnicities. There were also significant differences in the type of site at which men received their treatment. Although the majority of patients in each group were treated in community-based practices, African Americans and men of other ethnicities were more likely to be treated at a VA facility. A higher percentage of whites and others received treatment at an academic institution than did African Americans (8% and 13% v 2%, respectively). A significant association was noted in the type of insurance reported by the various groups. A higher percentage of whites had Medicare than did African Americans and others (46% v 33% and 34%, respectively), likely because of the older age observed in the white cohort. There were significant differences in the highest level

Table 2. Patient Clinical Characteristics and Primary Treatment Type

Variable	Patients by Ethnicity						<i>P</i> *
	African American		White		Other		
	No.	%	No.	%	No.	%	
Risk level							< .01
Low	110	38	1,686	46	54	42	
Intermediate	87	30	1,227	34	37	29	
High	92	32	733	20	37	29	
Missing values	15		195		11		
No. of comorbidities							.58
0	36	12	537	14	22	16	
1	81	28	1,053	28	32	23	
2	88	30	1,018	27	35	25	
≥ 3	86	30	1,160	31	50	36	
Missing values	13		73		0		
Health perception							< .01
Excellent	35	12	811	21	27	19	
Very good	84	28	1,585	41	41	29	
Good	100	33	980	26	35	25	
Fair	74	24	393	10	30	22	
Poor	11	4	72	2	6	4	
Primary treatment							< .01
RP	150	49	2,136	56	65	47	
RT	103	34	1,223	32	51	37	
ADT	33	11	194	5	15	11	
AS	8	3	78	2	3	2	
Other†	10	3	210	5	5	4	

Abbreviations: RP, radical prostatectomy; RT, radiation therapy; ADT, androgen deprivation therapy; AS, active surveillance.

*Pearson χ^2 test, does not include missing values.

†Other includes cryotherapy and TUMT.

Table 3. ORs of Primary Treatment Type Versus RP

Treatment Variable	Analysis		
	OR	95% CI	<i>P</i>
White v African American			
RP	1.0		—
RT	0.75	0.54 to 1.03	.08
ADT	0.52	0.31 to 0.89	.02
AS	0.52	0.22 to 1.25	.15
Other	1.99	0.89 to 4.47	.09
Other v African American			
RP	1.0		—
RT	0.95	0.56 to 1.63	.86
ADT	1.01	0.44 to 2.29	.99
AS	0.69	0.16 to 2.97	.62
Other	1.41	0.38 to 5.18	.60
Other v white			
RP	1.0		—
RT	1.27	0.81 to 2.01	.30
ADT	1.93	0.95 to 3.90	.07
AS	1.32	0.37 to 4.64	.67
Other	0.71	0.25 to 2.04	.52

NOTE. Analysis was adjusted for risk, age, health perception, number of comorbidities, educational level, and type of insurance.

Abbreviations: RP, radical prostatectomy; OR, odds ratio; RT, radiation therapy; ADT, androgen deprivation therapy; AS, active surveillance.

of education attained between the three ethnic groups. Thirty-six percent of African Americans and 48% of other men completed some education beyond high school level compared with 63% of white men.

There were significant differences in risk classification between the ethnic groups. A lower percentage of African American men presented with low risk disease compared with white men (38% v 46%; $P < .01$), whereas a higher percentage of African American men presented with high-risk disease compared with white men (32% v 20%; $P < .01$). There were no significant differences between African Americans and the other ethnic groups. Although there was not a significant difference in the number of comorbidities reported between the ethnic groups, there was a statistically significant difference in health perception. Fewer African American men than white men rated their health as excellent (12% v 21%) or very good (28% v 41%). However, the majority of men in all groups rated their health as excellent, very good, or good.

There was a significant correlation between ethnicity and type of treatment, as African American and other ethnic groups were less likely to have radical prostatectomy (RP) than radiation therapy (RT; $P = .03$ and $.04$, respectively) or androgen deprivation therapy (ADT; $P < .01$ for both groups) compared with whites. Similar percentages of patients underwent active surveillance and other treatments.

We examined the effect of age, prognostic risk, comorbidities, health perception, insurance, education, and type of treatment facility on treatment and mortality. The variables that were associated with

treatment in a univariate test—and also that, subsequently, in a multivariate model were independently associated with treatment or changed the effect of ethnicity on treatment—were included. Thus, a multinomial logistic regression model was designed that controlled for D'Amico risk level, age, health perception, number of comorbidities, education level, and insurance status. Treatment facility was not included, as it did not have a significant effect. The results are listed in Table 3. White men were 48% less likely to receive ADT than RP compared with African American men (OR, 0.52; 95% CI, 0.31 to 0.89; $P = .02$). White men also were less likely to receive RT than RP and were more likely to choose other treatment modalities instead of RP compared with African American men; however, this trend did not quite reach the level of statistical significance ($P = .08$ and $.09$, respectively). Men of other ethnicities also were more likely to receive ADT than RP compared with white men ($P = .07$). There were no significant differences in primary treatment between African American men and men of other ethnic groups.

Because ADT typically is administered in patients with advanced age or higher-risk disease, we examined the association of ethnicity with type of treatment within risk subgroups. After analysis was adjusted for demographic characteristics, whites were 71% less likely to receive ADT than RP compared with African Americans for low-risk disease (OR, 0.29; 95% CI, 0.11 to 0.73; $P = .009$; Table 4). Whites also were less likely to receive RT than RP for low-risk disease compared with African Americans, but this did not reach statistical significance (OR, 0.67; 95% CI, 0.41 to 1.09; $P = .11$). For high-risk disease, a similar association with ADT was seen, as whites were less likely to receive ADT than RP compared with African Americans (OR, 0.52; 95% CI, 0.23 to 1.15; $P = .10$). There were no significant differences between the other ethnic groups and African Americans or whites.

To determine if the differences in treatment had an effect on prostate cancer–specific mortality, we performed a proportional

Table 4. ORs of Primary Treatment Type Versus RP by Risk Level

Treatment Variable	Analysis by Treatment Type							
	RT		ADT		AS		Other	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
White v African American								
Low	0.67	0.41 to 1.09	0.29	0.11 to 0.73	0.44	0.15 to 1.31	1.41	0.32 to 6.15
Intermediate	0.87	0.4 to 1.58	1.44	0.35 to 5.94	0.78	0.08 to 7.50	1.77	0.38 to 8.12
High	0.90	0.48 to 1.71	0.52	0.23 to 1.15	0.71	0.07 to 6.92	2.95	0.82 to 10.5
Other v white								
Low	1.26	0.63 to 2.51	1.28	0.27 to 6.00	1.15	0.23 to 5.87	1.19	0.26 to 5.38
Intermediate	1.47	0.65 to 3.33	2.16	0.42 to 11.2	4.41	0.42 to 46.7	0.74	0.09 to 6.02
High	0.92	0.34 to 2.48	2.35	0.77 to 7.2	NA†		0.37	0.04 to 3.26

NOTE. Low-risk group, n = 1,850; intermediate-risk group, n = 1,351; high-risk group, n = 862; unknown risk, n = 221.

Abbreviations: RP, radical prostatectomy; RT, radiation therapy; ADT, androgen deprivation therapy; AS, active surveillance; OR, odds ratio.

*Adjusted for age, health perception, number of comorbidities, educational level, & type of insurance

†The model for the high-risk subgroup in the other ethnicity group does not have enough data for AS.

hazards regression analysis on the ethnic groups for overall or prostate cancer–specific mortality (Table 5). Crude hazard ratio values demonstrated a nonsignificant tendency for worse overall and prostate cancer–specific mortality rates for African American men compared with white men (OR, 1.18; 95% CI, 0.82 to 1.70; $P = .37$; and OR, 1.81; 95% CI, 0.85 to 3.85; $P = .12$, respectively). However, when analysis was adjusted for risk classification, primary treatment, age, health perception, number of comorbidities, educational level, and type of insurance, the higher risk of overall and prostate cancer–specific mortality in African Americans disappeared (OR, 0.73; 95% CI, 0.47 to 1.14; $P = .16$; and OR, 0.37; 95% CI, 0.11 to 1.20; $P = .10$, respectively). No differences were detected between the other ethnic groups and whites or African Americans.

To determine which factor or factors had the strongest effect on the risk of mortality in African Americans, a stepwise model was constructed in which each variable was added and the individual hazard ratios were compared (Table 6). Starting with the crude model testing only for ethnicity, there was a reduction in risk of mortality for ethnicity with the addition of each variable, except with the addition of the number of comorbidities, to the model. The final model, which included all variables, is what was used to determine the adjusted prostate cancer–specific mortality, as seen in Table 5. The variables with the strongest associations with mortality in the models were risk classification and type of treatment ($P < .01$ in all models). The type of insurance also had a significant effect until construc-

tion of the final model, for which it demonstrated a suggestion of correlation ($P = .07$).

DISCUSSION

The disparity in incidence and mortality between minority and white patients diagnosed with prostate cancer is a significant public health concern and is the subject of intense investigation. In this study, we have attempted to ascertain the association of ethnicity, age, risk level, comorbidities, health perception, educational level, and type of insurance with treatment choice and then correlate how these factors play a role in mortality between ethnic groups. Our data show that nonwhite men are less likely to undergo surgery for prostate cancer when analysis is controlled for multiple factors. African American men, in particular, are more likely to receive ADT for low-risk disease compared with their white counterparts. Most significantly, we have shown that adjustment for several factors, including risk and type of treatment, mitigates the high risk seen in African American men of overall and prostate cancer–specific mortality.

Differences in stage and grade at presentation in African American men have been postulated to play a role in adverse outcomes. Variations in expression of particular genes have been shown to increase the risk of aggressive cancers in African American men and may predict prostate cancer mortality.^{11,17,18} In a review by Powell,¹⁹ several studies were cited that identified the association of the high rate of

Table 5. Crude and Adjusted Hazard Ratio of All-Cause and Prostate Cancer–Specific Mortality

Ethnic Group	All-Cause Mortality						Prostate Cancer–Specific Mortality					
	Crude (No. of deaths = 350)			Adjusted (No. of deaths = 321)			Crude (No. of deaths = 57)			Adjusted (No. of deaths = 51)		
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
African American v white	1.18	0.82 to 1.70	.37	0.73	0.47 to 1.14	.16	1.81	0.85 to 3.85	.12	0.37	0.11 to 1.20	.10
African American v other	0.92	0.47 to 1.79	.81	0.69	0.35 to 1.38	.30	1.28	0.27 to 6.04	.76	0.84	0.15 to 4.69	.84
Other v white	1.28	0.72 to 2.28	.40	1.06	0.58 to 1.92	.86	1.42	0.34 to 5.85	.63	0.44	0.10 to 2.01	.29

NOTE. Analysis was adjusted for risk, primary treatment, age, health perception, number of comorbidities, educational level, and type of insurance.

Abbreviation: HR, hazard ratio.

Table 6. Risk of Prostate Cancer–Specific Mortality by Race With Stepwise Adjustment

Variable by Model	Analysis		
	HR	95% CI	P
Model 1			
Ethnicity: African American v white	1.81	0.85 to 3.85	.12
Model 2			
Ethnicity, risk*	1.58	0.74 to 3.38	.24
Model 3			
Ethnicity, risk,* treatment*	1.09	0.49 to 2.39	.84
Model 4			
Ethnicity, risk,* treatment,* type of insurance†	0.71	0.29 to 1.74	.45
Model 5			
Ethnicity, risk,* treatment,* type of insurance,† age	0.61	0.24 to 1.55	.30
Model 6			
Ethnicity, risk,* treatment,* type of insurance,† age, health perception	0.55	0.21 to 1.46	.23
Model 7			
Ethnicity, risk,* treatment,* type of insurance,† age, health perception, No. of comorbidities	0.59	0.22 to 1.57	.29
Model 8			
Type of insurance,‡ age, health perception, No. of comorbidities, educational level	0.37	0.11 to 1.20	.10

Abbreviation: HR, hazard ratio.

* $P < .01$ for overall effect of individual variable.† $P < .05$ for overall effect of individual variable.‡ $P = .07$ for overall effect of individual variable.

prostatic intraepithelial neoplasia in African American men with more aggressive cancers and that showed that socioeconomic status alone does not reduce the likelihood of presenting with later stage disease or of dying as a result of prostate cancer. Although there have not been extensive data to compare the outcomes of other minority groups with African Americans, a report by Latini et al¹⁵ showed that, although Latino men present with socioeconomic characteristics similar to African Americans, their clinical characteristics, primary treatment, and overall survival were more similar to non-Latino whites. Similarly, this study demonstrates that African American men were younger at the time of diagnosis and that a higher percentage presented with high-risk disease.

The increased rate of high-risk disease in African American men may play a role in the higher likelihood of this population receiving nondefinitive therapy. However, several studies have shown that men of different ethnicities with localized disease are not necessarily treated similarly.^{4,20} Underwood et al⁷ reported that African American and Hispanic men with well-differentiated disease were less likely to receive definitive therapy (ie, surgery or radiation) than white men with similar disease. This disparity widened in men with moderately or poorly differentiated disease, though this difference decreased with time. This study highlights the importance of the patient and treating physician to understand the role of biologic and sociologic factors when deciding therapy for prostate cancer. An important aspect of this understanding is to define the factors that drive patient decision of treatment. In a recent review by Zeliadt et al,⁵ men ultimately made the treatment decision on the basis of cancer eradication and treatment effectiveness. Though adverse effects, such as incontinence and erectile dysfunction, were considered, these were less likely to alter treatment choice. Importantly, African American and low-income men

have a higher level of treatment regret^{2,5}; fewer treatment options offered, less written information provided, and choice of less-aggressive therapy are identified as potential sources of this distress.

The issue of treatment choice in prostate cancer is particularly difficult, in that there is no one optimal treatment for a particular stage of disease. However, general consensus can be applied, particularly with the use of nomograms that are easily available to practitioners and patients. The fact that there is an ethnic disparity in the type of treatment received, regardless of stage, indicates that factors beyond the variety of treatments available exist. As in previous reports, our study shows that African American men are more likely to receive RT or ADT than surgery. White men are 25% less likely than African American men to receive RT and are 48% less likely to receive ADT. Despite the reservation of primary ADT monotherapy, usually, for patients with advanced disease, we also showed that whites were much less likely to receive ADT for low-risk disease (OR, 0.29) than were African Americans. This stands in distinction from the population, identified in previous reports, who typically receive ADT. Kawakami et al³ investigated the use of ADT as primary therapy by using the CaPSURE database. They showed that 14% of men were treated with ADT and that this cohort was older, had more advanced disease, had an increased number of comorbidities, and were of lower socioeconomic status than men who received other treatments or watchful waiting. The long-term use of primary ADT in clinically localized prostate cancer has not been borne out by clinical trials, especially in those with low-risk disease, and may lead to significant morbidity and mortality.^{21,22}

Our findings of a significant difference in the type of treatment received between ethnic groups led us to investigate if this had any bearing on mortality. Crude analysis suggested a worse overall and prostate cancer–specific mortality in African American men than in whites. Adjustment of sociodemographic factors, clinical presentation, and type of treatment completely obviated this increased risk. This is not unexpected in light of recent data that show that the mortality disparity in cancer can be mitigated by these factors. In a recent systematic meta-analysis, Bach et al¹⁰ showed that the 16% excess mortality experienced by African Americans with cancer can be reduced to 7% by administration of comparable treatment and by controlling for population mortality. Furthermore, Underwood et al²³ showed a similar cancer-free survival between African Americans and non-African Americans undergoing surgery after analysis was controlled for baseline measures of cancer severity. By using data from an equal access center, Tewari et al¹³ demonstrated that the increased overall and cancer-specific mortality experienced by African Americans can be reduced to nonsignificant levels when analysis is adjusted for insurance status and income. Our results prove the multifactorial etiology of the higher mortality seen in African American men and show that risk, type of treatment, and type of insurance have the strongest effects. The results presented highlight the importance of pretreatment characteristics and the type of treatment chosen for prostate cancer. In fact, our results may actually underestimate the magnitude of disparity in the type of treatment chosen. CaPSURE is a database compiled by physicians and clinics who volunteered to provide data. This potential selection bias suggests that the findings reflect the treatment disparity in better practices in the United States and not US practice in general.

Additional basic research to investigate the biologic factors that play a role in the early and aggressive appearance of prostate cancer in

African American men is needed to reduce the associated risk of mortality. Screening and educational programs have already shown an improvement in outcomes for men who usually present with high-risk features.²⁴ Additionally, practice patterns in the community may be improved by educating physicians who treat minorities with prostate cancer, specifically by discouraging the use of primary ADT monotherapy in men with low-risk characteristics.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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