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Sex and Race Disparities in Diverticulosis Prevalence

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Abstract

Background & Aims—The prevalence of diverticulosis differs with demographic features of patients, but evidence is limited. Well-defined demographic studies are necessary to understand diverticulosis biology. We estimated the prevalence of diverticulosis among patients of different ages, sexes, and races and ethnicities and calculated odds ratios.

Design—Using data from an endoscopic database, we identified 271,181 colonoscopy procedures performed from 2000 through 2012 at 107 sites in the United States. Our analysis included individuals 40 years and older who underwent colonoscopy examination for average-risk screening. The outcome was any reported diverticulosis on colonoscopy. Multivariate analyses were performed using logistic regression to estimate odds ratios (ORs) and 95% CI values, adjusting for confounding variables.

Results—The prevalence of diverticulosis increased with age in men and women of all races and ethnicities. Women 40–49 years old had significantly lower odds of any diverticulosis (OR, 0.71; 95% CI, 0.63–0.80) compared with men 40–49 years old, after adjustment. The strength of this association decreased with age. Compared with non-Hispanic white individuals, non-Hispanic black individuals (OR, 0.80; 95% CI, 0.77–0.83) and Asian/Pacific Islanders (OR, 0.38; 95% CI, 0.35–0.41) had lower odds of any diverticulosis. However, non-Hispanic black individuals (OR, 1.53, 95% CI, 1.44–1.62) had increased odds of any proximal diverticulosis, whereas Asian/Pacific Islanders (OR, 3.12; 95% CI, 2.67–3.66) had increased odds of only proximal diverticulosis.

Conclusions—In an analysis of data from 271,181 colonoscopy procedures, diverticulosis was less prevalent in women compared with men in the same age groups, indicating that sex hormones might affect pathogenesis. Differences in the odds of diverticulosis by race and ethnicity indicate a genetic contribution to risk.

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Keywords

diverticular disease; diverticulitis; diverticular hemorrhage

Introduction

Colonic diverticulosis is a common incidental finding on colonoscopy.¹ These defects form when colonic mucosa and submucosa herniate through the muscularis propria. Diverticula can hemorrhage, develop inflammation, and perforate.² These complications are unpredictable, have limited treatment options, and cause substantial patient suffering.^{3, 4} Diverticular disease is one of the most common digestive diseases in the United States and is the indication for numerous ambulatory visits, hospital admissions, and surgical procedures.^{5, 6} Health care expenditures total \$5.5 billion dollars annually.⁵

Developing diverticulosis is the first step in the diverticular disease cascade. While the etiopathogenesis of diverticulosis is poorly understood, there is emerging but limited evidence for endogenous sex hormones and genes in the biology of diverticulosis.^{7–11} We have reported that premenopausal age women are less likely to have diverticulosis than similar-age men, while postmenopausal age women and similar-age men appear to have the same risk.¹⁰ This single-center observation needs to be validated in a larger cohort. Moreover, there are unexplained disparities in the risk of diverticulitis¹² and diverticular hemorrhage¹³ by age, sex, race, and ethnicity. Whether these differences are attributable to variation in the prevalence of diverticulosis has not been well studied.

Characterizing the demographics of individuals who develop colonic diverticulosis has the potential to improve understanding of diverticulosis biology and is important to interpreting disparities in diverticular disease risk. In the present study, we used a large national endoscopic database to determine the prevalence of diverticulosis by age, sex, race, and ethnicity in individuals undergoing an average-risk screening colonoscopy. We also determined whether diverticulosis odds differed by individual characteristics.

Methods

The Clinical Outcome Research Initiative (CORI) was established in 1995 to study outcomes of endoscopic gastrointestinal procedures in diverse practice settings across the United States. Physicians participating in the CORI consortium generated gastrointestinal endoscopy reports using a structured computer program developed specifically for the initiative. Data were de-identified prior to transmission to a central data repository, where they were assessed for completeness and accuracy. Practice sites included hospitals, ambulatory care centers, private practices, universities, and Veteran's hospitals. Data from all participating practices were merged and stored in the National Endoscopic Database (NED). Data from the NED has been used previously to examine endoscopic findings.^{14–16}

Using data from the NED, we included in our analysis all individuals 40 years and older who had a colonoscopy with an indication for average-risk screening performed between January 1, 2000 and December 31, 2012. Although average risk screening routinely begins

at age 50, we included adults ages 40–49 to determine diverticulosis prevalence before the average age of menopause. We only included procedures with at least an adequate preparation. Adequate preparation included those judged by the endoscopist to be excellent, good, or fair but adequate. Use of the Boston Bowel Preparation Scale was recommended. We excluded any patient with an indication other than average risk screening. We extracted age at time of endoscopy, sex, race/ethnicity, endoscopy site and type for our analysis. Each endoscopist reported patient race/ethnicity. The primary outcome was the reporting of any colonic diverticulosis on colonoscopy. Among those with diverticulosis, 98.7% had a location documented. The category proximal diverticula included any diverticula reported in the cecum, ascending, hepatic, and/or transverse colon. The category distal diverticula included any diverticula reported in the splenic flexure, descending and/or sigmoid colon.

Statistical analysis

Proportions were calculated for categorical data. Age groups were created (40–49 years, 50–59 years, 60–69 years, 70–79 years, and over the age of 79 years). We calculated the prevalence of diverticulosis among average risk persons having a screening colonoscopy for each age category by demographics. Multivariate analyses were performed using logistic regression to estimate odds ratios and 95% confidence intervals while adjusting for confounding variables (age, sex, race/ethnicity, endoscopy site). Odds of diverticulosis by sex were modeled within age groups. Analyses were conducted using SAS version 9.4 (Cary, NC).

We followed the strengthening the reporting of observational studies in epidemiology (STROBE) guidelines for reporting observational studies.¹⁷ The University of North Carolina School of Medicine Institutional Review Board determined this study to be exempt from review.

Results

We identified 271,181 colonoscopy procedures with an indication for average-risk screening performed between 2000 and 2012 at 107 practice sites across the United States. These procedures represent 268,414 unique individuals. Among individuals who had an average-risk screening exam, 46% were women and 95% were between 50 and 79 years old (Table 1). The distribution of race/ethnicity in the cohort was 86% non-Hispanic white, 5% non-Hispanic black, 6% Hispanic and 2% Asian/pacific islander. Most (76%) of the procedures were performed in the community setting.

Diverticulosis was less prevalent in women compared with similar-age men until age 80 (Figure 1 and Table 2). Women 40–49 years old had a significantly reduced odds of any diverticulosis (OR 0.71, 95% CI 0.63 – 0.80) compared to men in the same age group after adjustment for race/ethnicity and endoscopy site (Table 2). Likewise, women 50–59 years old (OR 0.79, 95% CI 0.77 – 0.81), women 60–69 years old (OR 0.81, 95% CI 0.79 – 0.83) and women 70–79 years old (OR 0.91, 95% CI 0.87–0.95) had reduced odds of any diverticulosis compared to men. By the age of 80, there was no difference in the odds (OR 0.99, 95% CI 0.88 – 1.11) of diverticulosis.

The prevalence of diverticulosis differed by age and race/ethnicity (Figure 2 and Table 3). There was a progressive increase in diverticulosis prevalence by age group (Table 3). Compared with non-Hispanic whites, Asian/pacific islanders (OR 0.38, 95% CI 0.35 – 0.41), non-Hispanic blacks (OR 0.80, 95% CI 0.77 – 0.83), and Hispanic individuals (OR 0.93, 95% CI 0.89 – 0.96) had lower odds of diverticulosis after adjustment for age, sex, and endoscopy site (Table 3). Asian/pacific islanders had the highest prevalence of proximal colon only diverticulosis (5%), while Non-Hispanic black individuals had the highest prevalence of any proximal diverticulosis (12%) (Table 4).

Among average-risk individuals having a colonoscopy for a screening indication, the prevalence of any diverticulosis increased with age in men and women of all races and ethnicities (Figure 2). The prevalence of distal diverticulosis increased with age, as did any proximal diverticulosis (Table 4). The prevalence of proximal only diverticulosis did not consistently increase with age (Table 4).

Discussion

Using 271,181 colonoscopy procedures with an indication for average-risk screening performed at sites across the United States, we found that diverticulosis was less prevalent in women compared with similar-age men. This difference was greatest before the average age of menopause and decreased with increasing age. Non-Hispanic black and Asian/Pacific Islander individuals were less likely to have diverticulosis, but more likely to have proximal diverticula. Asian/Pacific Islander individuals were most likely to have only proximal diverticula, while Non-Hispanic black had any proximal diverticula. Diverticulosis was common even before the age of 50 and the prevalence increased with age in men and women of all races and ethnicities.

Similar to a recent colonoscopy-based study,¹⁰ women were less likely to have colonic diverticulosis compared with similar age men. In contrast with the prior study, the large number of procedures in this analysis allowed us to look at the association with greater confidence across multiple age categories. Our results suggest that endogenous ovarian steroid hormones may reduce the risk of developing diverticulosis. Given the time it takes for diverticulosis to develop, there may even be a carryover of the protective effect after the age of menopause.

Mechanistically, steroid hormones may have a protective effect on connective tissues. Dysfunctional connective tissues and associated genes have been implicated in diverticulosis biology.^{7–9, 18–23} Despite finding a lower prevalence of diverticulosis in women overall, there is evidence that women over the age of 60 have a significantly increased risk of incident diverticulitis compared with men.¹² This sex-specific difference in diverticulitis risk cannot be explained by an increased prevalence of diverticulosis. Instead, there must be a sex-specific factor that disproportionally drives diverticulitis risk in women over the age of 60. This disparity may be due to environmental factors. Obesity and nonsteroidal anti-inflammatory drug use increase diverticulitis risk²⁴, while vigorous physical activity²⁵ reduces the risk. Menopause is associated with an increased risk of visceral fat accumulation. Furthermore, women are more likely than men to be obese (women 40%

versus men 35%) and are almost twice as likely to have the most severe class of obesity (women 10% versus men 6%).²⁶ Women are also less likely to be physically active and more likely to use nonsteroidal anti-inflammatory drugs compared to men.^{27, 28}

There are also unexplained racial disparities in the risk of diverticulitis¹² and diverticular hemorrhage.¹³ In the U.S., white individuals experienced the highest prevalence of hospital admissions for diverticulitis compared with black and Hispanic individuals. Asian/Pacific Islander individuals experience a much lower prevalence compared with all other races. Some of these disparities may be attributable to underlying variation in the prevalence of diverticulosis. Diverticulitis is most common in the distal colon. This study shows that non Hispanic whites have a higher prevalence of distal diverticulosis compared with non Hispanic black and Asian/Pacific Islanders, which could explain a higher incidence of diverticulitis in white individuals.

Diverticular hemorrhage is an arterial bleed that more commonly occurs in proximal diverticula compared to distal diverticula. Proximal diverticula are either congenital or acquired. Congenital diverticula are usually true diverticula that involve all three layers of the bowel wall. True diverticula may be less likely to hemorrhage compared to acquired diverticula. Acquired diverticula are mechanically vulnerable and form when the colonic mucosa and submucosa herniate through vascular portals in the muscularis propria. Similar to prior work^{29, 30} non Hispanic black individuals have the highest prevalence of any proximal diverticula, the majority of which are likely acquired diverticula and at risk of hemorrhage. This disparity in diverticulosis prevalence may explain why black individuals experience the highest prevalence of diverticular hemorrhage compared to other races. In contrast, Asian/Pacific Islanders have the highest prevalence of proximal only diverticulosis but are less likely to experience diverticular hemorrhage. Because the prevalence of proximal only diverticulosis did not increase with age, these diverticula are likely congenital, involve all three layers of the bowel wall, and are less likely to hemorrhage.

This work has limitations. Colonic diverticulosis is a common incidental finding on screening colonoscopy and reporting is optional. While diverticulosis was likely underreported, this reporting is unlikely to vary by age, sex and/or race/ethnicity. This type of non-differential misclassification would bias our results towards the null. Because there was significant variation in reporting diverticulosis, we included endoscopy site in our models, with no change in our results. The burden of colonic diverticulosis was not reported in this database. Therefore, we could not determine associations between demographics and number of diverticula. The burden of diverticula may drive some of the risk of complications. The accuracy of reporting diverticulosis location in the colon is unknown; as such, we categorized location into the two broad and clinically significant categories of proximal and distal. Each endoscopist reported patient race/ethnicity, which may result in misclassification of this variable. Additionally, the sites participating in CORI are not necessarily representative of all endoscopy practices in the United States. VA facilities and academic medical centers are likely over-represented. Because we included data from VA facilities, men make up more than half (54%) of our cohort. Furthermore, the majority (86%) of patients included in this study are non-Hispanic white, a proportion that differs from the U.S. population (60.4% 2010 U.S. Census). Individuals who participate in

colorectal screening are generally healthier than those who do not participate in screening. Differential screening rates may contribute to differences in diverticulosis, as those who are more or less likely to get screening may also be more or less likely to get diverticulosis. Because obesity increases the risk of diverticulosis in women¹⁰, the prevalence of diverticulosis in women may be higher in the general population.

In conclusion, we found that diverticulosis was less prevalent in women compared with similar-age men in a large national endoscopic database, supporting a role for sex hormones in diverticulosis pathogenesis. Asian/Pacific Islander individuals were most likely to have proximal only diverticula, while Non-Hispanic black individuals had both distal and proximal diverticula. Differences in the risk of diverticulosis by race/ethnicity are congruent with genetic contribution to risk and account for some proportion of variation in diverticular disease risk. However, it remains unclear why women 60 years or older have a greater burden of diverticulitis than men of the same age.

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Need to Know

Background

We estimated the prevalence of diverticulosis among patients of different ages, sexes, and races and ethnicities and calculated odds ratios.

Findings

In an analysis of data from 271,181 colonoscopy procedures, the prevalence of diverticulosis increased with age in men and women of all races and ethnicities. Diverticulosis was less prevalent in women compared with similar-age men. There were also differences in the prevalence and distribution of diverticulosis by race/ethnicity.

Implications for Patient Care

Differences in diverticulosis prevalence by age and race account for some proportion of variation in diverticular disease risk. However, it not clear why women 60 years or older have a greater burden of diverticulitis than men of the same age.

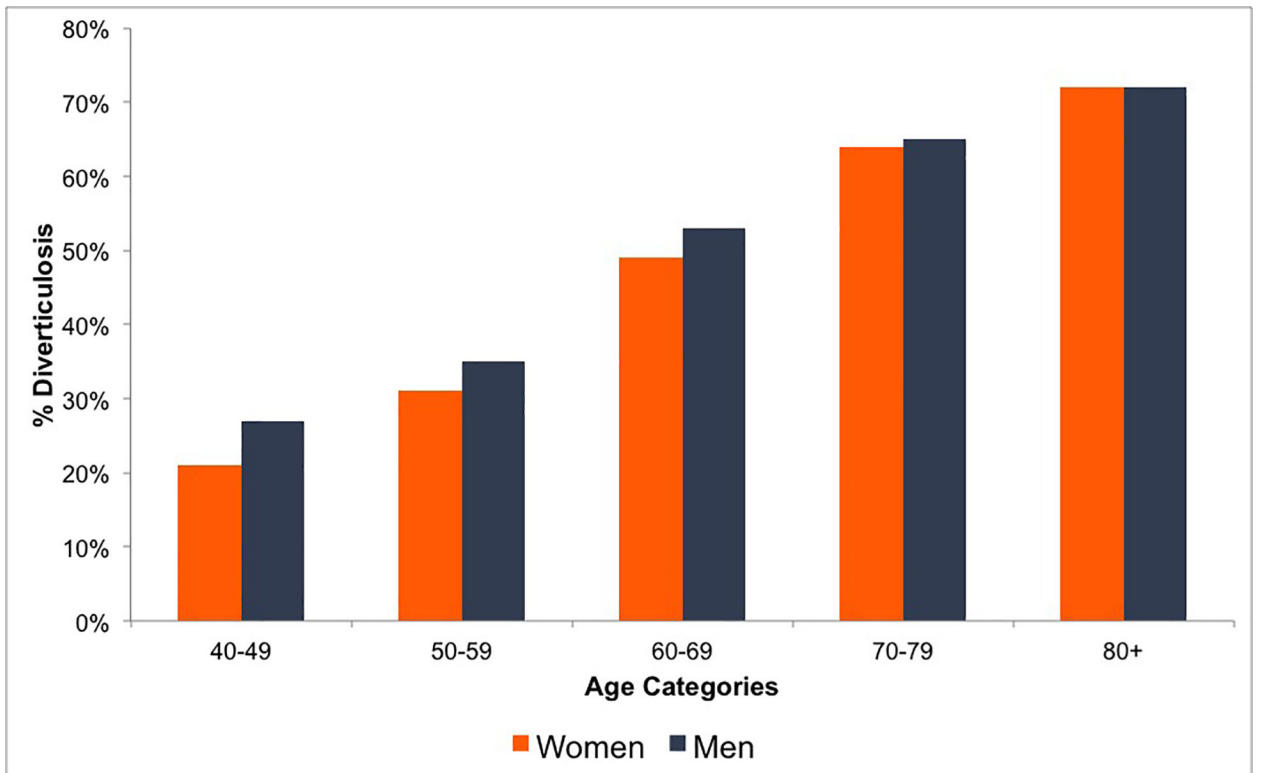


Figure 1. Diverticulosis on screening colonoscopy in average risk persons by age and sex. Women are in orange bars and men in navy blue.

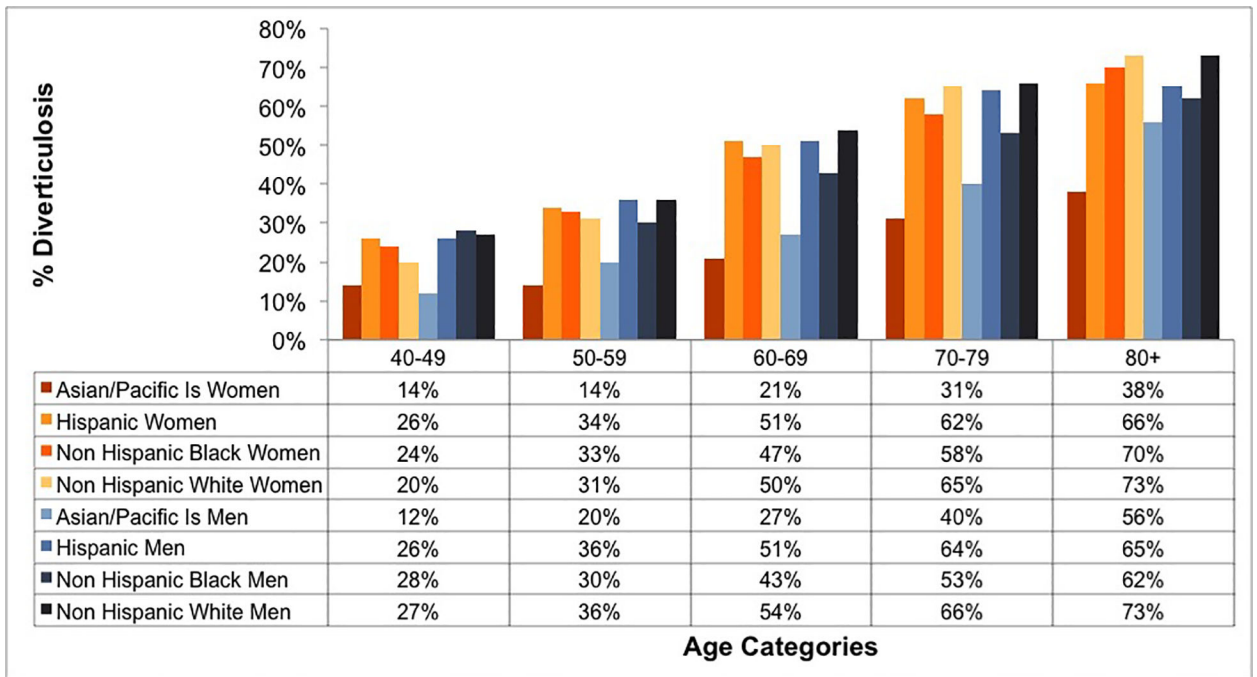


Figure 2. Diverticulosis on screening colonoscopy in average risk persons by age, sex and race/ethnicity.

Table 1.

Characteristics

	Average-Risk Screening Colonoscopy
	N= 271,181
Age, years (%)	
40–49	2%
50–59	49%
60–69	32%
70–79	14%
80+	2%
Sex (%)	
Women	46%
Men	54%
Race/Ethnicity (%)	
Non Hispanic White	86%
Non Hispanic Black	5%
Hispanic	6%
Asian/Pacific Islander	2%
Other/Unknown	1%
Site type (%)	
Community	76%
Health Maintenance Organization	3%
Military	2%
University	9%
Veterans Affairs	11%
Region of United States (%)	
North Central	8%
North East	15%
North West	11%
South Central	11%
South East	17%
South West	38%

Table 2.

Prevalence and Adjusted Odds of Any Diverticulosis by Sex Within Age Groups

Age, years	Sex	n	Prevalence Diverticulosis %	Odds Ratio (95% Confidence Interval) ^I
40–49	Men	971	27%	Reference
	Women	617	21%	0.71 (0.63, 0.80)
50–59	Men	24,841	35%	Reference
	Women	19,169	31%	0.79 (0.77, 0.81)
60–69	Men	25,230	53%	Reference
	Women	18,796	49%	0.81 (0.79, 0.83)
70–79	Men	13,059	65%	Reference
	Women	11,808	64%	0.91 (0.87, 0.95)
80+	Men	2,256	72%	Reference
	Women	2,536	72%	0.99 (0.88, 1.11)

^IAdjusted for race/ethnicity and site

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Table 3.

Prevalence and Adjusted Odds of Any Diverticulosis by Age Group, Race, and Ethnicity

	n	Prevalence Diverticulosis %	Odds Ratio (95% Confidence Interval)
Age group¹			
40–49	1,588	24%	Reference
50–59	44,010	33%	1.58 (1.50, 1.67)
60–69	44,026	51%	3.28 (3.11, 3.46)
70–79	24,867	64%	5.61 (5.31, 5.93)
80+	4,792	72%	7.97 (7.42, 8.56)
Race and Ethnicity²			
Non Hispanic White	104,222	45%	Reference
Non Hispanic Black	5,498	38%	0.80 (0.77, 0.83)
Hispanic	7,271	44%	0.93 (0.89, 0.96)
Asian/Pacific Islander	969	22%	0.38 (0.35, 0.41)

¹Adjusted for sex, race/ethnicity, and site²Adjusted for age, sex, and site

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Table 4. Prevalence and Adjusted Odds of Diverticulosis Location by Sex, Age Group, Race and Ethnicity

	Any Proximal	OR (95%CI)	Only Proximal	OR (95%CI)	Any Distal	OR (95%CI)	Only Distal	OR (95%CI)
Sex¹								
Men	9%	Reference	1%	Reference	44%	Reference	37%	Reference
Women	7%	0.80 (0.78, 0.83)	1%	0.87 (0.81, 0.94)	41%	0.82 (0.81, 0.84)	34%	0.87 (0.86, 0.89)
Age group²								
40–49	5%	Reference	1%	Reference	23%	Reference	19%	Reference
50–59	6%	1.32 (1.17, 1.48)	1%	1.38 (1.08, 1.77)	32%	1.55 (1.46, 1.64)	27%	1.54 (1.44, 1.64)
60–69	10%	2.26 (2.02, 2.54)	1%	1.41 (1.10, 1.82)	50%	3.26 (3.06, 3.46)	41%	2.86 (2.69, 3.05)
70–79	13%	3.29 (2.93, 3.70)	1%	1.42 (1.09, 1.84)	63%	5.58 (5.25, 5.94)	51%	4.20 (3.93, 4.48)
80+	16%	4.34 (3.80, 4.95)	1%	1.38 (0.99, 1.94)	71%	7.79 (7.19, 8.43)	56%	4.93 (4.55, 5.34)
Race and Ethnicity³								
Non Hispanic White	8%	Reference	1%	Reference	44%	Reference	37%	Reference
Non Hispanic Black	12%	1.53 (1.44, 1.62)	3%	2.47 (2.19, 2.78)	35%	0.73 (0.70, 0.76)	25%	0.64 (0.61, 0.67)
Hispanic	9%	1.04 (0.97, 1.11)	2%	1.35 (1.16, 1.58)	42%	0.89 (0.86, 0.93)	34%	0.90 (0.86, 0.94)
Asian/Pacific Islander	11%	1.15 (1.03, 1.27)	5%	3.12 (2.67, 3.66)	16%	0.29 (0.27, 0.32)	11%	0.26 (0.24, 0.29)

¹Odds ratio adjusted for age, race/ethnicity, and site

²Odds ratio adjusted for sex, race/ethnicity, and site

³Odds ratio adjusted for age, sex, and site