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## Missed opportunities for HPV immunization among young adult women

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### Abstract

**BACKGROUND**—Despite the availability of a safe and efficacious vaccine against human papillomavirus, uptake of the vaccine in the United States is low. Missed clinical opportunities to recommend and to administer human papillomavirus vaccine are considered one of the most important reasons for its low uptake in adolescents; however, little is known about the frequency or characteristics of missed opportunities in the young adult (18–26 years of age) population.

**OBJECTIVE**—The objective of the study was to assess both the rates of and the factors associated with missed opportunities for human papillomavirus immunization among young adult women who attended an urban obstetrics and gynecology clinic.

**STUDY DESIGN**—In this cross-sectional study, medical records were reviewed for all women 18–26 years of age who were underimmunized (<3 doses) and who sought care from Feb. 1, 2013, to January 31, 2014, at an urban, hospital-based obstetrics and gynecology clinic. A missed opportunity for human papillomavirus immunization was defined as a clinic visit at which the patient was eligible to receive the vaccine and a dose was due but not administered. Multivariable logistic regression was used to test associations between sociodemographic variables and missed opportunities.

**RESULTS**—There were 1670 vaccine-eligible visits by 1241 underimmunized women, with a mean of 1.3 missed opportunities/person. During the study period, 833 of the vaccine eligible women (67.1%) had at least 1 missed opportunity. Overall, the most common types of visits during which a missed opportunity occurred were postpartum visits (17%) or visits for either sexually transmitted disease screening (21%) or contraception (33%). Of the patients with a missed opportunity, 26.5% had a visit at which an injectable medication or a different vaccine was administered. Women who identified their race as black had higher adjusted odds of having a

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missed opportunity compared with white women (adjusted odds ratio, 1.61 [95% confidence interval, 1.08–2.41],  $P < .02$ ). Women who reported a non-English- or non-Spanish-preferred language had lower adjusted odds of having a missed opportunity (adjusted odds ratio, 0.25 [95% confidence interval, 0.07–0.87],  $P = .03$ ). No other patient characteristics assessed in this study were significantly associated with having a missed opportunity.

**CONCLUSION**—A majority of young-adult women in this study had missed opportunities for human papillomavirus immunization, and significant racial disparity was observed. The greatest frequency of missed opportunities occurred with visits for either contraception or for sexually transmitted disease screening.

### Keywords

cervical cancer prevention; human papillomavirus; preventative medicine; vaccination

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Human papillomavirus (HPV) causes the majority of cervical, oropharyngeal, and anogenital cancers.<sup>1,2</sup> The Centers for Disease Control and Prevention (CDC) estimates that every year there are 330,000 new cases of precancerous cervical lesions and 30,000 new cases of HPV-attributable cancers in the United States.<sup>3</sup>

The total economic burden of preventing and treating HPV-related disease is estimated to be about \$8 billion per year.<sup>4</sup> Immunization against HPV has been shown to be safe and effective at preventing HPV-attributable precancerous lesions,<sup>5</sup> which has led the CDC Advisory Committee on Immunization Practices to recommend that HPV immunization be administered routinely to females at 11–12 years of age with a catch-up immunization through 26 years of age.<sup>6</sup>

Despite these recommendations, HPV immunization rates remain low. In 2016, the CDC reported that the 3-dose HPV vaccine completion rate among adolescent girls 13–17 years of age in the state of Connecticut was 55.2%. This is in contrast to the 93.5% vaccine uptake for the quadrivalent meningococcal conjugate vaccine and 93.7% for the tetanus, diphtheria, and acellular pertussis vaccine in both male and female adolescents of the same age group.<sup>7</sup>

Several studies in the United States have demonstrated that most young adult women 19–26 years of age do not have antibodies to the high-risk HPV types most commonly associated with cancer and included in the vaccines and therefore will also benefit from immunization.<sup>8–10</sup> Moreover, in one report, the HPV vaccine was at least 30% efficacious at preventing HPV 16/18–positive precancerous cervical lesions of moderate grade or worse in women 15–26 years of age, irrespective of their HPV infection status prior to immunization.<sup>11</sup> However, the uptake of the HPV vaccine is even lower among young adult women compared with adolescents,<sup>12</sup> and the CDC estimated that only 36% of women 19–26 years of age received 1 or more doses in 2013.<sup>13</sup>

In addition, there are substantial racial and socioeconomic disparities in the uptake of the HPV vaccine. Previous research has found that women of lower socioeconomic status or of racial/ethnic minority backgrounds were less likely to complete the immunization series than either higher-income women or women identifying as white.<sup>14</sup> These disparities in the

uptake of the HPV vaccine are of particular concern, given both the higher incidence and the poorer outcomes of cervical cancer among women who are of either racial or ethnic minorities or from lower-income groups.<sup>15,16</sup>

Missed clinical opportunities to recommend and to administer the HPV vaccine are considered one of the most important reasons for its low uptake in the United States.<sup>17</sup> A study of more than 400,000 women demonstrated that >96% of unvaccinated adolescent girls had at least 1 missed opportunity for immunization over a 6 year period.<sup>18</sup> Studies from pediatric practices have shown that clinic-specific strategies that identify and decrease missed opportunities can substantially increase the uptake of the HPV vaccine.<sup>19</sup> However, most of the efforts to increase vaccine uptake have been focused on adolescents and pediatric practices. There is little information about such efforts in young adult populations that are eligible for immunization or with obstetrics-gynecology practices.<sup>20</sup> Continued efforts are needed to improve coverage and understand missed opportunities among young adults.

This study aims to assess both the rates of and the factors associated with missed opportunities for HPV immunization among young adult women (18–26 years old) who attended an urban obstetrics and gynecology clinic in New Haven, CT, that cares for a large proportion of women from racial/ethnic minority and low-income backgrounds.<sup>21,22</sup> Understanding the frequency of, and risk factors for, missed opportunities in this high-risk population may be integral to guiding interventions aimed at increasing the uptake of the HPV vaccine.

## Materials and Methods

In this cross-sectional study, electronic medical records were reviewed for all women 18–26 years of age who were underimmunized (had received 0, 1, or 2 doses of the HPV vaccine), who were vaccine eligible and who were seen at the Yale New Haven Hospital Women's Center, a hospital-based obstetrics and gynecology clinic that serves primarily low-income patients of racial and ethnic minority backgrounds, from February 1, 2013, to January 31, 2014.

Using a standardized form, data were collected regarding the number of visits, sociodemographic variables (age, race, ethnicity, preferred language, insurance), pregnancy status, and receipt of HPV vaccine. Additional data were collected for the subset of women considered to have missed opportunities (see the following text), which included reasons for visits as documented in the clinic note as well as documentation of administration of other immunizations and injectable medications.

HPV immunization status was determined by evaluating the immunization history section of the electronic medical record in which the dates of vaccine administration are documented and reviewing all Women's Center clinic notes and scanned records from the study period for the mention of receipt or offer of the HPV vaccine by a provider.

The Institutional Review Board at Yale University approved this project.

## Measures

A vaccine-eligible visit was defined as a visit at which the patient was between 18 and 26 years of age, was not pregnant, and was underimmunized or had never been immunized. A missed opportunity was defined as a vaccine-eligible visit at which the patient was due for either the first, second, or third dose of the HPV vaccine but it was not administered.

The recommendations from the CDC's Advisory Committee on Immunization Practices are that any available HPV vaccine product (bivalent, quadrivalent, or nonavalent) be used to continue or complete the series for protection against HPV 16 and 18.<sup>6</sup> Accordingly, we considered the use of any HPV vaccine as a capitalized opportunity. If the patient had received a dose of the vaccine before the visit, the patient was not defined as eligible for another dose until at least 8 weeks after a first dose or 16 weeks after the second dose (and 24 weeks between the first and third dose).

Insurance was classified as public, private, uninsured, and other. Public insurance included Medicaid, Medicare, Indian Health Service, and military insurance. Self-reported race and ethnicity were classified as non-Hispanic white, non-Hispanic black (subsequently referred to as white and black, respectively), His-panic, and non-Hispanic other.

## Statistical analysis

Logistic regression models were estimated to identify patient characteristics associated with at least 1 missed opportunity for HPV immunization during the 1 year study period. All patient characteristics were first evaluated individually for association with missed opportunities using simple regression models (ie, including 1 patient characteristic at a time).

For the multivariable logistic regression model, backward stepwise selection was used to select the final group of variables, in which variables with the highest p-values were removed in sequence until all variables in the final model had a value of  $P \geq .1$ . A value of  $P < .05$  was considered to be statistically significant.

This is a descriptive and exploratory study utilizing a convenience sample consisting of the number of women who attended the clinic during a 12 month period. Data were analyzed using Stata statistical software 12.0 (StataCorp, College Station, TX).

## Results

During the 1 year study period, a total of 1410 women, 18–26 years of age, had a total of 6988 visits, with a mean of 4.9 visits per person. Of these women, 169 (11.9%) had received 3 doses of the HPV vaccine prior to the study period and were excluded from the analyses (Figure 1). The final group included 1241 age-eligible women who were underimmunized (had received <3 doses of the HPV vaccine) and had at least 1 visit during the study period.

Of the underimmunized women, 833 (67.1%) had at least 1 missed opportunity for immunization, 362 (29.2%) had noneligible pregnancy visits, 39 (3.1%) received a dose during the study period and did not have any further eligible visits, and 7 (0.6%) were

offered the vaccine and declined it. Of the 833 underimmunized women, there was a mean of 1.3 (range 0–9) missed opportunities per person. Women eligible to receive their first dose were equally likely to have a missed opportunity compared with those who were eligible to receive their second or third dose (odds ratio, 0.72 [95% confidence interval (CI), 0.48–1.08];  $P = .11$ ). Characteristics of the underimmunized women and women with at least 1 missed opportunity are shown in Table 1.

The types of visits that were associated with missed opportunities are shown in Figure 2. The most common types were visits for contraception (33%; for medroxyprogesterone acetate [58%] and other types of contraception [42%]), visits for sexually transmitted disease (STD) screening (21%), and postpartum visits (17%). Of the patients with a missed opportunity, 221 (26.5%) had at least 1 vaccine-eligible visit at which an injectable medication (medroxyprogesterone acetate) or a different vaccine was administered.

Results from simple and multivariable logistic regression are detailed in Table 2. The independent variables included in the final model were race, preferred language, and insurance. Women who identified their race as black had 61% higher adjusted odds of having a missed opportunity compared with white women (adjusted odds ratio [aOR], 1.61 [95% CI, 1.08–2.41];  $P = .02$ ). Women who identified their preferred language as other than English or Spanish were less likely to have a missed opportunity compared with preferred English speakers (aOR, 0.25 [95% CI, 0.07–0.87];  $P = .03$ ). Associations between missed opportunities and age, Hispanic ethnicity, Spanish language, or parity were not statistically significant.

## Comment

Despite the availability of a safe and cost-effective vaccine against HPV,<sup>23</sup> the uptake of the vaccine in the United States is low. The consequences of maintaining the low HPV immunization rates are not insignificant. In 2017, immunization experts estimated that if the HPV immunization rate could be raised to 80%, an additional 53,000 cases of cervical cancer could be prevented during the lifetime of those younger than 12 years; this is equivalent to 4400 new cases of cervical cancer for every year that the immunization rate does not increase.<sup>24</sup>

Missed opportunities for administering the HPV vaccine are a major barrier to achieving high rates of immunization. Several studies in adolescents have identified factors associated with the low uptake of the HPV vaccine, such as a lack of knowledge about it, cost, or reluctance of providers to recommend the vaccine<sup>25,26</sup>; however, less is known about the frequency or characteristics of missed opportunities to administer the vaccine in the young adult population (18–26 years of age).<sup>27,28</sup>

One qualitative study reported that gaps in knowledge about cervical cancer, HPV, and the HPV vaccine as well as other barriers, such as poor access to transportation and prioritizing other responsibilities over health, were important obstacles to immunization in these women.<sup>29</sup> Our study contributes to the literature by specifically examining patient characteristics and providing detailed descriptive analysis of clinical factors such as the reason for the visit

or concomitant care received during a visit. Such information may provide a greater context for missed opportunities for immunization when a woman engages in a clinical visit in a women's health setting and insight into strategies for addressing these missed opportunities.

Our study found that women who self-identify as black were more likely to have had a missed opportunity compared with white women. The racial disparities observed in our study are consistent with previous research reporting that racial minorities, specifically non-Hispanic blacks, are less likely to receive a recommendation to vaccinate from health care providers and are less likely to complete the HPV vaccine series.<sup>30,31</sup> Although studies have shown there has been progress in closing the gap in uptake among minorities (particularly among Hispanics and women living below the poverty level),<sup>7</sup> our study suggests there is still disparity among women of the black race.

Of note, the cost of the HPV vaccine is covered under most Medicaid plans for women up through 26 years of age. Likewise, most private insurance covers the cost of the vaccine for women up until their 27th birthday. Uninsured women can have the cost of the vaccine covered by the Connecticut Vaccine Program until they turn 19 years of age.<sup>32</sup> Women who are 19 years of age or older and uninsured would need to pay out of pocket for the vaccine, which can range between \$150 and \$200 per dose.

Our study population consisted of women who had access to care and who were predominantly insured through Medicaid. Therefore, the disparity in missed opportunities for HPV immunization among racial and ethnic minorities after controlling for insurance status is especially concerning and warrants further investigation. The disparity may be driven by a multitude of factors including possible provider biases and assumptions, sociocultural beliefs about vaccines and cervical cancer, or perceived quality of patient-provider interactions.

Understanding the nature of this disparity can facilitate development of strategies to eliminate missed opportunities for immunization with the HPV vaccine and potentially reduce disparities in cervical dysplasia and cancer.

There was no statistically significant association between missed opportunities and preferring either the Spanish or the English language. However, women whose preferred language was one other than Spanish or English were less likely to have a missed opportunity.

While our study was not designed to explore this association in greater depth, based on our extensive experience with this diverse patient population, representing 12 different languages, we believe this association could be related to several potential factors. It is possible that many of these women come from cultures where it is improper to question recommendations from an authority figure, and hence, these women are more likely to be agreeable to the vaccine. The combination of this increased willingness to trust in the clinicians with a significant language barrier (eg, women not fully understanding what they are agreeing to) may have contributed to the lower rate of missed opportunities in this population group.

Of the missed opportunity visits, 26.5% occurred when another vaccine or injectable medication was administered. These visits are excellent opportunities for providers to encourage patients to receive the HPV immunization because studies have shown that patients are more willing to accept the HPV vaccine when it is viewed as routine or when given with other injections.<sup>33</sup>

Although some data suggest that providers are less likely to recommend the HPV vaccine to avoid giving multiple injections in 1 visit, Wallace et al<sup>34</sup> found that providers overestimate concerns of patients about multiple immunizations, and education and reassurance from providers often address these concerns. This suggests that interventions that bundle administration of the HPV vaccine with other vaccines or injectable medications might help avoid missed opportunities in clinics that cater to young adults.

In obstetrics and gynecology clinics, many injectable medications (such as medroxyprogesterone acetate) are given during nurse-only visits. In our study, the large number of missed opportunities that occurred when other injectable medications were administered highlights the potential role of nurses in promoting uptake of HPV vaccine and the potential value in developing protocols for the nurse-initiated recommendation of the HPV vaccine.

The 2 most common missed opportunity visit types were for contraception and STD screening visits. As Dilley et al<sup>35</sup> recently advocated, these visits could be prime opportunities for women's health providers to improve the rates of HPV immunization because most of these patients are planning to become or already are sexually active, and a recommendation for HPV vaccine could easily be integrated into a broader discussion of reproductive health and family planning.

A common context for missed opportunities among young adult women during our study period were postpartum visits. In contrast to other vaccines such as Tdap (tetanus, diphtheria, and pertussis), influenza, and MMR (measles, mumps, and rubella), the HPV vaccine is not routinely available in the immediate inpatient postpartum period and may not be a priority for patients or providers in follow-up visits in the outpatient setting.<sup>36</sup>

One study of more than 48,000 age-eligible, unvaccinated pregnant women found that only 1.8% of the women had received a dose of HPV vaccine during the first postpartum year.<sup>37</sup> Interventions focused on implementing routine HPV immunization during the inpatient postpartum admission and system-generated reminders to complete the immunization series in postpartum follow-up appointments are likely to improve the uptake in this age group.<sup>35,38,39</sup>

Our study has several limitations. This was a single-center study from a clinic that provides care to a predominantly low-income, minority population. Therefore, our findings may not be generalizable to other settings. Future research is needed in different clinical settings to validate our findings and inform the generalizability of our results.

Our data also relied on electronic medical records from a single health care system; immunizations administered by providers not affiliated with our system may not have been



completely captured. This may result in a potential overestimation of missed opportunities. However, in our study population, this is unlikely to have been a major issue. In a different study from our institution, a sample of adult women who sought care at our clinic were interviewed to assess all prior sources of care since 2006, when the HPV vaccine was introduced. We found that an accurate HPV vaccine history could be ascertained in 82% of these women by reviewing electronic medical records because the majority of these adult women received care either exclusively at our clinic or at one of the other sites within the Yale–New Haven Hospital System (unpublished data).

In the self-report designations of race and ethnicity, the majority of women who designated themselves as being of Hispanic ethnicity did not provide a particular race, which is why we used a combined race/ethnicity variable.

Lastly, the data collection focused on detailed information about the missed opportunity visits. Similar information was not obtained about opportunities at which patients were immunized. Because only 3.1% of women appropriately received a dose of the HPV vaccine during the study period without any missed opportunity, the validity of comparisons of those visits would be impaired by poor statistical power.

## Conclusions

This study, conducted in a diverse urban population, found that a majority of underimmunized vaccine-eligible young-adult women (18–26 years of age) had at least 1 missed opportunity in their interaction with an obstetrics and gynecology clinic over a 1 year study period, most of which were related to postpartum visits or to visits for either contraception or STD screening. Interventions that aim to eliminate these missed opportunities are likely to improve the uptake of the HPV vaccine in this population of young adult women.

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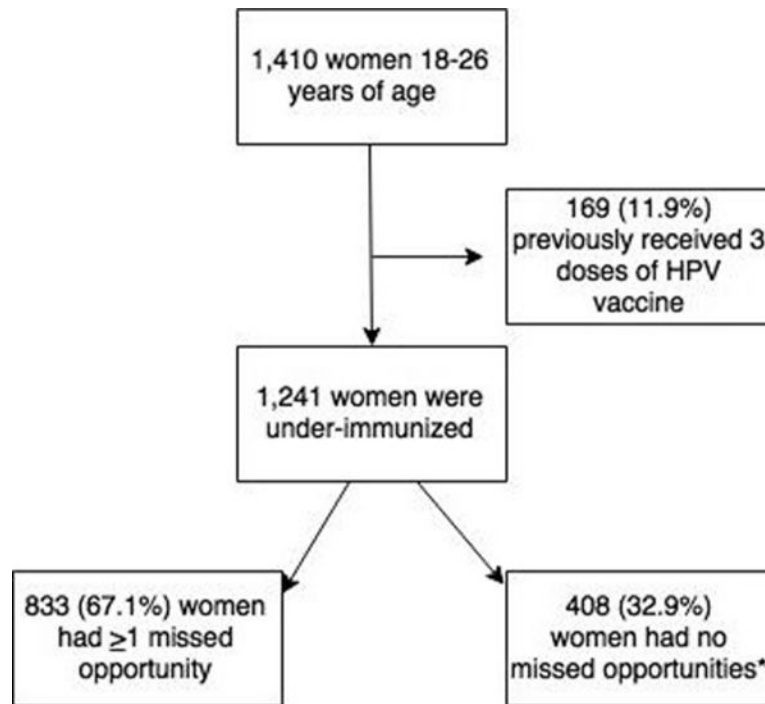
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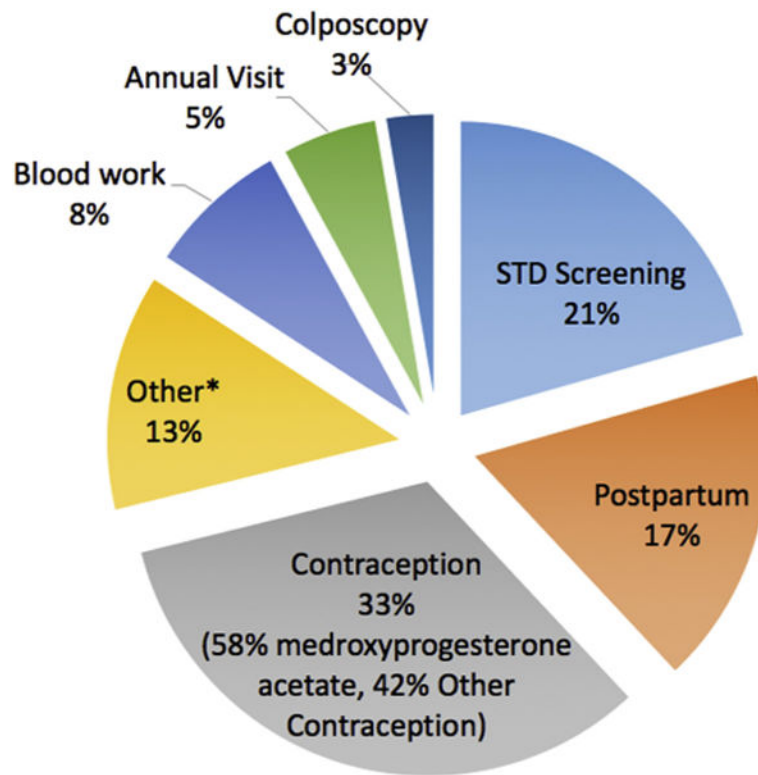
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**FIGURE 1. Classification of women seen for obstetrics-gynecology care, February 1, 2013 to January 31, 2014**

Flowchart showing classification of women seen for obstetrics-gynecology care at The Women's Center, Feb. 1, 2013, and Jan. 31, 2014. Asterisk indicates that these women had only vaccine-ineligible encounters.

HPV, human papillomavirus.



**FIGURE 2. Types of visits for women with missed opportunities**

Asterisk indicates the category of other: the most common were visits for menstrual problems, preoperation screening, postoperation follow-up, nutrition counseling, hospitalization follow-up, anemia, urinary tract infections, and endometriosis. STD, sexually transmitted disease.

TABLE 1

## Characteristics of underimmunized women

Characteristics	1 Missed opportunities (n = 833)	No missed opportunities (n = 408)	All women (n = 1241)
Age, y, median (range)	23 (18–26)	22 (18–26)	23 (18–26)
Race/ethnicity, n, %			
Non-Hispanic white	80 (9.6)	52 (12.8)	132 (10.6)
Hispanic	329 (39.5)	164 (40.2)	493 (39.7)
Non-Hispanic black	367 (44.1)	147 (33.0)	514 (41.4)
Non-Hispanic other <sup>a</sup>	10 (1.2)	6 (1.5)	16 (1.3)
Not identified	47 (5.6)	39 (9.6)	86 (6.9)
Insurance type, n, %			
Private/commercial	55 (6.6)	20 (4.9)	75 (6.0)
Public	642 (77.1)	311 (76.2)	953 (76.8)
Uninsured	120 (14.4)	67 (16.4)	187 (15.1)
Other	16 (1.9)	10 (2.5)	26 (2.1)
Preferred language, n, %			
English	689 (82.7)	322 (78.9)	1011 (81.5)
Spanish	133 (16.0)	62 (15.2)	195 (15.7)
Other <sup>b</sup>	11 (1.3)	24 (5.9)	35 (2.8)
Previously pregnant, n, %	648 (77.8)	311 (76.2)	959 (77.3)

<sup>a</sup>Other race: American Indian, Asian, and Native Hawaiian;

<sup>b</sup>Other languages: Arabic, Turkish, Chinese, Farsi, French, Pashto, Serbian, Sign, Swahili, Tigrinya, Vietnamese, and Hindi.

**TABLE 2**

Association between patient characteristics and missed opportunities

Characteristics	OR <sup>d</sup>	95% CI	P value	aOR <sup>b</sup>	95% CI	P value
Age	1.02	0.97–1.07	.39	c	c	c
Race/ethnicity						
Non-Hispanic white	Reference			Reference		
Hispanic	1.31	0.88–1.94	.19	1.23	0.81–1.90	.33
Non-Hispanic black	1.62	1.09–2.42	.01	1.61	1.08–2.41	.02
Non-Hispanic other <sup>d</sup>	1.08	0.37–3.16	.88	1.45	0.47–4.48	.52
Not identified	c	c	c	c	c	c
Insurance type						
Private	Reference			Reference		
Public	0.75	0.44–1.27	.29	0.65	0.36–1.16	.15
Uninsured	0.65	0.36–1.18	.16	0.55	0.28–1.08	.08
Other	0.58	0.22–1.49	.26	0.51	0.18–1.44	.21
Preferred language						
English	Reference			Reference		
Spanish	1.01	0.72–1.39	.98	1.23	0.81–1.88	.33
Other <sup>e</sup>	0.21	0.13–0.44	.01	0.25	0.07–0.87	.03
Previously pregnant	1.09	0.83–1.45	.54	c	c	c

aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.

<sup>a</sup>Odds ratios were calculated with simple logistic regression;

<sup>b</sup>Adjusted odds ratios were calculated with multivariable logistic regression adjusting for race, preferred language, and insurance;

<sup>c</sup>Omitted from analysis;

<sup>d</sup>Other races: American Indian, Asian, and Native Hawaiian;

<sup>e</sup>Other languages: Arabic, Turkish, Chinese, Farsi, French, Pashto, Serbian, Sign, Swahili, Tigrinya, Vietnamese, and Hindi.