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Posttraumatic stress disorder and new-onset diabetes among adult survivors of the World Trade Center disaster

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ABSTRACT

Objective. To explore the temporal relationship between 9/11-related posttraumatic stress disorder (PTSD) and new-onset diabetes in World Trade Center (WTC) survivors up to 11 years after the attack in 2001.

Methods. Three waves of surveys (conducted from 2003 to 2012) from the WTC Health Registry cohort collected data on physical and mental health status, sociodemographic characteristics, and 9/11-related exposures. Diabetes was defined as self-reported, physician-diagnosed diabetes reported after enrollment. After excluding prevalent cases, there were 36,899 eligible adult enrollees. Logistic regression and generalized multilevel growth models were used to assess the association between PTSD measured at enrollment and subsequent diabetes.

Results. We identified 2143 cases of diabetes. After adjustment, we observed a significant association between PTSD and diabetes in the logistic model [adjusted odds ratio (AOR) 1.28, 95% confidence interval (CI) 1.14–1.44]. Results from the growth model were similar (AOR 1.37, 95% CI 1.23–1.52).

Conclusion. This exploratory study found that PTSD, a common 9/11-related health outcome, was a risk factor for self-reported diabetes. Clinicians treating survivors of both the WTC attacks and other disasters should be aware that diabetes may be a long-term consequence.

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Introduction

Type 2 diabetes mellitus (diabetes) is a nationwide epidemic, affecting more than 8% of the adult United States population (Li et al., 2012). Diabetes can lead to a host of serious health complications, including heart disease, blindness, and kidney disease (Centers for Disease Control and Prevention, 2011b). It is estimated to have cost the United States health care system \$245 billion in 2012 (American Diabetes Association, 2013a). The primary risk factors for type 2 diabetes include overweight/obesity, older age, family history, physical inactivity and black, Hispanic, and Asian race/ethnicity (American Diabetes Association, 2013b).

In addition to these well-established risk factors, psychological stress may lead to an increased susceptibility to diabetes. Numerous studies of trauma-exposed populations have found an association between PTSD and diabetes (Agyemang et al., 2012; Armenian et al., 1998; Boyko et al., 2010; Dedert et al., 2010; Goodwin and Davidson, 2005; Pietrzak et al., 2011; Trief et al., 2006). A study of asylum seekers

in the Netherlands found that those with PTSD were more likely to have been diagnosed with type 2 diabetes (Agyemang et al., 2012). The National Epidemiologic Survey on Alcohol and Related Conditions observed an increased risk of diabetes in those with PTSD, although this relationship was attenuated when adjusting for number of lifetime traumatic events (Pietrzak et al., 2011). Most of these studies have been cross-sectional, and thus have not firmly established a temporal relationship between PTSD and diabetes. However, the Millennium Cohort Study of US military service members, one of the few longitudinal analyses of this relationship, found twofold increased odds of incident diabetes among those with PTSD after 3 years of follow-up of its military population (Boyko et al., 2010).

The World Trade Center (WTC) Health Registry, established in 2003, collects longitudinal information on individuals exposed to the WTC attack in 2001, providing an opportunity to examine the temporal relationship between PTSD and subsequent diabetes. As PTSD is one of the most common mental health outcomes observed in WTC-affected populations (Brackbill et al., 2009; Farfel et al., 2008), Registry enrollees may have an increased risk of diabetes. To our knowledge, however, no studies have examined diabetes in WTC-affected populations. In the current study, we examined the relationship between 9/11-related PTSD and new-onset diabetes in the WTC Health Registry's adult population up to 11 years after the disaster.

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Research design and methods

Registry population

From September 2003 to November 2004, the WTC Health Registry (Registry) enrolled 71,434 persons who were exposed to the September 11, 2001, disaster in New York City or who subsequently assisted in the rescue, recovery and cleanup effort. In addition to rescue/recovery workers, the Registry includes Lower Manhattan residents, area workers, school staff and students, and commuters and passersby on 9/11. The Registry's recruitment methods have been described previously (Brackbill et al., 2009; Farfel et al., 2008). At the time of enrollment, registrants completed a Wave 1 (W1) baseline computer-assisted telephone (95%) or in-person (5%) interview about their 9/11-related exposures and health following the disaster (Farfel et al., 2008). Two subsequent surveys have been conducted to obtain updated information on enrollees' health status, healthcare utilization, and well-being. Both employed mail, web and telephone survey modes. The Wave 2 (W2) survey was conducted from November 2006 through December 2007 with a response rate of 68% (Brackbill et al., 2009). Wave 3 (W3) was conducted from July 2011 through March 2012, with a response rate of 63%. The Registry protocol was approved by the Centers for Disease Control and Prevention (CDC) and New York City Department of Health and Mental Hygiene institutional review boards. Enrollees provided verbal informed consent to participate in the Registry.

Study outcome

Diabetes was defined as self-reported diabetes diagnosed after Registry enrollment, reported at either W2 or W3, by answering "yes" to the question, "Have you ever been told by a doctor or other health professionals that you had diabetes or sugar diabetes?" Additionally, the year of diagnosis had to have been \geq the year of W1 completion. For those who reported diabetes at both W2 and W3, the year reported at W2 was used. The surveys did not specify type 1 or type 2 diabetes; however, as the study sample only included adults, and type 2 accounts for 90% to 95% of adulthood diabetes diagnoses (Centers for Disease Control and Prevention, 2011b), we assumed the vast majority of reported cases were type 2.

Study variables

The main predictor of interest for this study was PTSD at W1. We used a 9/11-specific PTSD Checklist (PCL), a validated, 17-item, event-specific scale, to assess symptoms of PTSD in the 30 days preceding the interview, with some questions specifically referencing the events of 9/11. The PCL has been reported to have a sensitivity of 94% and specificity of 86% (Blanchard et al., 1996; Weathers et al., 1993). PTSD was also measured at W2 and W3. Individual items were scored from 1 (not at all) to 5 (extremely), with total scores ranging from 17 to 85. PTSD was defined as a score of 44 or greater, with no items missing.

Additional covariates included sociodemographic variables and 9/11-related exposures. Data on sex, age, race/ethnicity, education, and smoking status were obtained at W1. Enrollees were categorized into one of the following mutually-exclusive, hierarchical eligibility groups based on the likelihood and intensity of exposure: rescue/recovery workers; lower Manhattan residents; lower Manhattan area workers; passersby; and school students and staff.

Weight and height were ascertained at W3, and BMI was calculated as: $[\text{weight (pounds)} / \text{height (inches)}^2] \times 703$, rounded to the nearest tenth. The CDC's BMI guidelines for ages ≥ 15 years were used to exclude persons with biologically implausible values (Centers for Disease Control and Prevention, 2011a). Overweight was defined as a BMI between 25 and 29.9, and obese was a BMI of 30 or greater. We also

considered respondent history of hypertension, which was queried at all three waves, and history of high cholesterol, assessed at W3 only.

To define 9/11-related exposure, we used a 12-item index, based on a tool created by Adams et al. (2006) and later modified based on Registry data by Brackbill et al. (2013). This scale included information on an enrollee's exposures on 9/11 and during the subsequent recovery and cleanup effort, loss of loved ones or coworkers, job loss due to 9/11, and damage to or loss of property or a home. The number of disaster-related events or conditions experienced was summed, and enrollees were categorized as having had none/low (0–1 experiences), medium (2–3), high (4–5), or very high (6 or more) exposure.

Study population

Of 71,434 Registry enrollees, we included participants who completed the W3 follow-up survey ($n = 43,134$). We excluded enrollees who were < 18 years of age at 9/11 ($n = 739$), enrollees who reported having been diagnosed with diabetes before Registry enrollment (i.e., prevalent cases; $n = 2479$), and those missing a history of diabetes ($n = 456$). After removing those who were missing demographic or exposure data, 36,899 participants were included in this analysis.

Statistical analyses

The frequencies of sociodemographic and 9/11-exposure characteristics of persons with diabetes were compared with those of persons without diabetes in bivariate analyses. We also compared characteristics of the study population to W1-only participants who were not included in this analysis to assess possible bias from loss to follow-up. Logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CI) for the association between PTSD at W1 and new-onset diabetes. Multiple logistic regression models were adjusted for covariates that were significant in the bivariate analysis and that are commonly associated with diabetes, including age, sex, race/ethnicity, educational status at W1, hypertension, high cholesterol, and BMI at W3. Models that included smoking status at W1 and eligibility group were evaluated, but as the adjusted ORs (AORs) did not change substantially, these variables were not included in the final model. The 9/11 exposure index was no longer significant in the multivariable model and thus was not included in the final model. We tested for interactions between PTSD and other variables and found none. Model fit was assessed with the Hosmer–Lemeshow goodness of fit χ^2 test. Analyses used SAS version 9.2 (SAS Institute Inc., Cary, North Carolina).

We also conducted a three-wave, two-level hierarchical growth model, where PTSD was treated as a time-varying predictor. Measurements were nested within subjects. Due to the multilevel framework using repeated measurement occasions, missing data for PTSD did not result in pairwise deletion. This yielded a slightly larger study sample size compared with the single-level analysis, containing 37,856 subjects (level-2 units) and 113,568 measurement occasions. The same variables used in the single-level logistic regression were included, with the addition of a time factor. Age, race/ethnicity, sex, education, BMI, high cholesterol, and hypertension were all included as time-invariant predictors. Once an enrollee reported a diagnosis of diabetes, his or her PTSD status at subsequent waves was not included so as to not bias the temporal association between PTSD and new-onset diabetes. Data were prepared in SAS version 9.2 and multilevel analysis was conducted using HLM 7 (SSI International, Skokie, Illinois).

Results

Of 36,899 study participants, 2143 (5.8%) reported having been diagnosed with diabetes between Registry enrollment (2003–2004) and March 2012. Table 1 shows the sociodemographic characteristics and 9/11-related exposures of the study population. Persons with diabetes were more likely to be male, older, a race/ethnicity other than non-

Table 1

Characteristics of adult World Trade Center Health Registry enrollees with and without new-onset diabetes, 2003–2011.^a

| Characteristic | Diabetes N = 2134 (%) | No diabetes N = 34,765 (%) |
|----------------------------------|--------------------------|-------------------------------|
| Sex | | |
| Male | 65.4 | 61.6 |
| Female | 34.6 | 38.4 |
| Age at 9/11 (years) | | |
| 18–24 | 1.7 | 5.8 |
| 25–44 | 42.8 | 55.7 |
| 45–64 | 52.0 | 36.2 |
| ≥65 | 3.5 | 2.3 |
| Race/ethnicity | | |
| Non-Hispanic white | 57.8 | 72.4 |
| Non-Hispanic black | 15.4 | 9.2 |
| Hispanic | 15.8 | 10.9 |
| Asian | 7.6 | 4.8 |
| Other | 3.4 | 2.8 |
| Hypertension | | |
| Yes | 71.5 | 36.3 |
| No | 28.5 | 63.7 |
| High cholesterol ^b | | |
| Yes | 63.3 | 37.4 |
| No | 36.7 | 62.6 |
| BMI, kg/m ^{2b} | | |
| Obese (≥30) | 58.3 | 29.5 |
| Overweight (25–29.9) | 30.7 | 39.9 |
| Normal/low (<25) | 11.0 | 30.6 |
| Education | | |
| Less than high school | 4.1 | 2.8 |
| High school graduate | 23.2 | 17.2 |
| Some college | 30.6 | 24.2 |
| College graduate | 42.1 | 55.8 |
| Eligibility group | | |
| Rescue/recovery workers | 50.6 | 47.7 |
| Lower Manhattan area residents | 8.8 | 13.5 |
| Lower Manhattan area workers | 36.2 | 34.2 |
| Passersby/commuters on 9/11 | 4.3 | 4.4 |
| School staff and students | 0.1 | 0.1 |
| Smoking status at enrollment | | |
| Current | 17.4 | 14.3 |
| Former | 32.9 | 27.7 |
| Never | 49.6 | 57.9 |
| 9/11 exposure index ^c | | |
| Very high | 8.9 | 8.0 |
| High | 21.4 | 20.1 |
| Medium | 39.7 | 39.5 |
| Low/none | 30.0 | 32.4 |
| PTSD at enrollment | | |
| Yes | 21.8 | 13.8 |
| No | 78.2 | 86.2 |

BMI, body mass index. PTSD, post-traumatic stress disorder.

^a Diabetes defined as self-reported, physician-diagnosed diabetes first reported on a follow-up survey (2007–2008 or 2011–2012). Excludes Registry enrollees <18 years at 9/11, those diagnosed with diabetes pre-W1, and those missing a year of diagnosis or diagnosis history.

^b Measured at W3.

^c 9/11 exposure index created defined as the sum of the following exposures: having been in the towers on 9/11, having witnessed traumatic events on 9/11, injury on 9/11, belief that he or she would be injured or killed on 9/11, relatives or friends who were injured or killed on 9/11, dust cloud, and lost a home or job due to 9/11.

Hispanic white, have reported high cholesterol or hypertension, and be overweight or obese. College graduates, never smokers, and Lower Manhattan residents on 9/11 were less likely to report new-onset diabetes. Those with PTSD at W1 were more likely to report new-onset diabetes (8.9%) compared to those who did not have PTSD (5.3%) (χ^2 statistic = 104.07, $P < 0.0001$).

Table 2 shows crude and adjusted ORs for new-onset diabetes. Sex lost statistical significance in the multivariable model, as did having less than a high school degree. The odds of reporting diabetes increased with age. Race was a significant predictor, with Asian enrollees showing a more than threefold increased odds compared to non-Hispanic white enrollees (AOR = 3.27, 95% CI = 2.72–3.94). Black and Hispanic

Table 2

Crude and adjusted logistic regression models of the association between PTSD and new-onset diabetes among adult World Trade Center Health Registry enrollees, 2003–2011 (N = 36,899).^a

| | Unadjusted OR (95% CI) | Adjusted ^b OR (95% CI) |
|-------------------------------|------------------------|-----------------------------------|
| Sex | | |
| Male | 1.18 (1.07–1.29) | 1.06 (0.96–1.17) |
| Female | 1.00 | 1.00 |
| Age at 9/11 (years) | | |
| 18–24 | 1.00 | 1.00 |
| 25–44 | 2.67 (1.91–3.73) | 1.57 (1.12–2.22) |
| 45–64 | 4.98 (3.56–6.97) | 2.45 (1.74–3.46) |
| ≥65 | 5.32 (3.54–7.98) | 3.01 (1.98–4.59) |
| Race/ethnicity | | |
| Non-Hispanic white | 1.00 | 1.00 |
| Non-Hispanic black | 2.09 (1.84–2.37) | 1.65 (1.43–1.90) |
| Hispanic | 1.83 (1.61–2.07) | 1.68 (1.46–1.92) |
| Asian | 1.99 (1.68–2.36) | 3.27 (2.72–3.94) |
| Other | 1.52 (1.19–1.94) | 1.47 (1.14–1.90) |
| Hypertension | | |
| Yes | 4.40 (4.00–4.85) | 2.51 (2.26–2.78) |
| No | 1.00 | 1.00 |
| High cholesterol ^c | | |
| Yes | 2.89 (2.64–3.16) | 1.93 (1.75–2.12) |
| No | 1.00 | 1.00 |
| BMI, kg/m ^{2c} | | |
| Obese (≥30) | 5.52 (4.79–6.36) | 4.02 (3.44–4.68) |
| Overweight (25–29.9) | 2.15 (1.85–2.50) | 1.78 (1.52–2.09) |
| Normal/low (<25) | 1.00 | 1.00 |
| Education | | |
| Less than high school | 1.92 (1.53–2.42) | 0.99 (0.78–1.26) |
| High school graduate | 1.79 (1.60–2.01) | 1.24 (1.10–1.39) |
| Some college | 1.68 (1.52–1.87) | 1.30 (1.16–1.44) |
| College graduate | 1.00 | 1.00 |
| Eligibility group | | |
| Rescue/recovery workers | 1.00 | 1.00 |
| Residents | 0.61 (0.52–0.72) | 0.61 (0.52–0.72) |
| Area workers | 1.00 (0.91–1.10) | 1.00 (0.91–1.10) |
| Passersby | 0.93 (0.75–1.15) | 0.93 (0.75–1.15) |
| School staff and students | 0.61 (0.15–2.52) | 0.61 (0.15–2.52) |
| Smoking status at enrollment | | |
| Current | 1.42 (1.26–1.61) | 1.42 (1.26–1.61) |
| Former | 1.39 (1.26–1.53) | 1.39 (1.26–1.53) |
| Never | 1.00 | 1.00 |
| 9/11 exposure index | | |
| Very high | 1.21 (1.02–1.43) | 1.21 (1.02–1.43) |
| High | 1.15 (1.02–1.30) | 1.15 (1.02–1.30) |
| Medium | 1.09 (0.98–1.21) | 1.09 (0.98–1.21) |
| Low/none | 1.00 | 1.00 |
| PTSD at enrollment | | |
| Yes | 1.73 (1.56–1.93) | 1.28 (1.14–1.44) |
| No | 1.00 | 1.00 |

PTSD, posttraumatic stress disorder. BMI, body mass index.

^a Excludes those <18 years at 9/11, those diagnosed with diabetes pre-W1, and those missing a year of diagnosis or diagnosis history.

^b Hosmer–Lemeshow goodness of fit χ^2 test ($P = 0.23$).

^c Measured at W3.

enrollees were also more likely to develop new-onset diabetes. High cholesterol, hypertension, and overweight/obesity all remained strongly associated with diabetes after adjustment. The association between PTSD at W1 and new-onset diabetes also remained significant (AOR = 1.28, 95% CI = 1.14–1.44).

The results from the growth model, shown in Table 3, were similar to those of the single-level logistic regression. The growth parameter was statistically significant, showing that the odds of diabetes increased over time (AOR = 3.58, 95% CI = 3.39–3.79). Controlling for all other predictors (including time), PTSD was significantly associated with new-onset diabetes (AOR = 1.37, 95% CI = 1.23–1.52).

Discussion

We observed a significant association between 9/11-related PTSD at Registry enrollment and new-onset diabetes reported at follow-up.

Table 3

Multilevel growth model results of the association between PTSD and new-onset diabetes among adult World Trade Center Health Registry enrollees, 2003–2011 (N = 37,856).^a

| | Adjusted OR (95% CI) |
|-------------------------------|----------------------|
| Sex | |
| Male | 1.05 (0.95–1.16) |
| Female | 1.00 |
| Age at 9/11 (years) | |
| 18–24 | 1.00 |
| 25–44 | 1.56 (1.11–2.18) |
| 45–64 | 2.49 (1.77–3.50) |
| 65 + | 3.05 (2.00–4.64) |
| Race/ethnicity | |
| Non-Hispanic white | 1.00 |
| Non-Hispanic black | 1.70 (1.48–1.96) |
| Hispanic | 1.68 (1.47–1.92) |
| Asian | 3.38 (2.82–4.04) |
| Other | 1.50 (1.16–1.93) |
| Hypertension | |
| Yes | 2.41 (2.17–2.68) |
| No | 1.00 |
| High cholesterol ^b | |
| Yes | 1.98 (1.80–2.18) |
| No | 1.00 |
| BMI, kg/m ^{2b} | |
| Obese (≥30) | 3.96 (3.40–4.62) |
| Overweight (25–29.9) | 1.77 (1.51–2.07) |
| Normal/low (<25) | 1.00 |
| Education | |
| Less than high school | 1.08 (0.84–1.38) |
| High school graduate | 1.26 (1.12–1.41) |
| Some college | 1.27 (1.14–1.41) |
| College graduate | 1.00 |
| PTSD at enrollment | |
| Yes | 1.37 (1.23–1.52) |
| No | 1.00 |
| Time | 3.58 (3.39–3.79) |

PTSD, posttraumatic stress disorder. BMI, body mass index.

^a Excludes those <18 years at 9/11, those diagnosed with diabetes pre-W1, and those missing a year of diagnosis or diagnosis history.

^b Measured at W3.

odds of reporting new-onset diabetes at W3 compared with non-Hispanic white enrollees. Previous studies have also observed an elevated risk of diabetes among Asian populations (Gupta et al., 2011; Islam et al., 2013).

This study relied on self-reported data; therefore the type of diabetes, the year of diagnosis, and the validity of the diagnosis could not be confirmed. However, multiple studies have observed high levels of agreement between self-reported diabetes and medical records (Horton et al., 2010; Jackson et al., 2013; Okura et al., 2004). Numerous studies from the Registry, which have similarly relied on self-reported data for respiratory and mental health outcomes such as asthma and PTSD (Brackbill et al., 2009; Farfel et al., 2008) are remarkably consistent with clinical studies, including studies of NYC firefighters (Chiu et al., 2011; Prezant et al., 2002) as well as Registry studies in which objective measurements of pulmonary function were compared to reported respiratory symptoms (Friedman et al., 2011).

Loss to follow-up is a potential source of bias. We examined this by comparing study participants (all of whom completed at least one follow-up survey) with enrollees who completed only W1 and who did not report diabetes (i.e., nonparticipants in W2 and W3). The study sample had a slightly higher proportion of males compared to the nonparticipants (62% vs. 59%), and fewer enrollees in the youngest and oldest age categories, though these two groups comprise less than 10% of the total population at risk at W1. Additionally, proportionally fewer non-white enrollees participated in the follow-up surveys. These underrepresented populations (especially older adults) tend to be at increased risk for diabetes. We also found the prevalence of PTSD at W1 to be higher in non-participants compared with the study sample (18% vs. 14%), consistent with other reports of increased attrition among persons with PTSD followed over time (Koenen et al., 2003). These observations suggest that our findings are likely conservative.

Our study found that overweight and obese BMI categories showed two of the strongest associations with new-onset diabetes, which was expected. We only measured BMI at W3 and thus were only able to assess BMI as a co-occurring condition and time-invariant predictor, and not as a risk factor. However, it is very likely that the majority of overweight or obese enrollees at W3 were overweight or obese at earlier waves, as high levels of self-correlation have been observed between BMI measurements six years apart (Prospective Studies Collaboration et al., 2009).

Second generation antipsychotics, which are often used off-label to treat PTSD (Bauer et al., 2014), have been associated with an increased risk of metabolic syndrome and diabetes (Lambert et al., 2006; Newcomer, 2007). Heppner et al. (2012), however, did not observe an independent association between second generation antipsychotic use and metabolic syndrome when controlling for PTSD severity. We were unable to assess the possible relationship between medication side effects and diabetes in the current study because the Registry has not collected detailed data on medication use.

As a substantial proportion our WTC-exposed cohort continues to experience PTSD over a decade after the disaster, the observation of a weak but statistically significant association between PTSD and diabetes warrants further investigation. Clinicians treating WTC workers and survivors as well as other disaster-affected populations need to be aware of this phenomenon, and to consider PTSD in addition to established risk factors when screening for diabetes. Future studies could use trajectory analyses to examine the subgroups in which PTSD symptoms resolve, and others in which they persist or worsen, in relation to diabetes risk.

Conflict of interest statement

The authors declare that there are no conflicts of interests.

Uncited reference

Lukaschek et al., 2013

Since PTSD is one of the most common mental health outcomes observed in WTC-exposed populations (Brackbill et al., 2009; Galea et al., 2003; Perlman et al., 2011; Perrin et al., 2007), and has persisted among some enrollees for years after the event (Brackbill et al., 2009; Stelman et al., 2008), this population has a large number of individuals with an increased risk of diabetes. Our findings of an increased risk of new-onset diabetes in a civilian population complement those of the Millennium Cohort study's military population (Boyko et al., 2010); whether this extends to other types of trauma is unknown.

There are several theories regarding plausible biological mechanisms for a relationship between PTSD and diabetes. Activation of the hypothalamic–pituitary axis due to stress results in excess secretion of cortisol, leading to increases in blood glucose levels and, eventually, insulin resistance (Black, 2006; Golden, 2007). Additionally, activation of the sympathetic nervous system and the subsequent release of epinephrine and norepinephrine can lead to abdominal obesity and insulin resistance (Black, 2006; Golden, 2007). PTSD is also associated with unhealthy behaviors such as poor diet and physical inactivity, which are risk factors for diabetes (Dedert et al., 2010; Pietrzak et al., 2011).

Established diabetes risk factors, including non-white race/ethnicity, older age, lower educational attainment, and overweight/obesity, were highly associated with diabetes in this study, as were hypertension and high cholesterol. Although those with less than a high school education had nearly twice the proportion of new-onset diabetes compared with college graduates (8.2% vs. 4.4%, respectively), after adjustment for other variables, our results showed no statistically significant difference between them. However, we did observe significant differences between high school graduates and persons with some college compared to college graduates. Asian enrollees had greater than three times the

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