HHS Public Access

Author manuscript

Genet Med. Author manuscript; available in PMC 2015 June 18.

Published in final edited form as:

Genet Med. 2014 April ; 16(4): 329–337. doi:10.1038/gim.2013.143.

Factors affecting maternal participation in the genetic component of the National Birth Defects Prevention Study—United States, 1997–2007

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Abstract

Purpose—As epidemiological studies expand to examine gene–environment interaction effects, it is important to identify factors associated with participation in genetic studies. The National Birth Defects Prevention Study is a multisite case–control study designed to investigate environmental and genetic risk factors for major birth defects. The National Birth Defects Prevention Study includes maternal telephone interviews and mailed buccal cell self-collection kits. Because subjects can participate in the interview, independent of buccal cell collection, detailed analysis of factors associated with participation in buccal cell collection was possible.

Methods—Multivariable logistic regression models were used to identify the factors associated with participation in the genetic component of the study.

Results—Buccal cell participation rates varied by race/ethnicity (non-Hispanic whites, 66.9%; Hispanics, 60.4%; and non-Hispanic blacks, 47.3%) and study site (50.2–74.2%). Additional monetary incentive following return of buccal cell kit and shorter interval between infant's

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SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/gim

DISCLOSURE

The authors declare no conflict of interest.

estimated date of delivery and interview were associated with increased participation across all racial/ethnic groups. Higher education and delivering an infant with a birth defect were associated with increased participation among non-Hispanic whites and Hispanics.

Conclusion—Factors associated with participation varied by race/ethnicity. Improved understanding of factors associated with participation may facilitate strategies to increase participation, thereby improving generalizability of study findings.

Keywords

birth defects; data collection; epidemiologic methods; ethnic groups; risk factors

INTRODUCTION

Understanding the contribution of genetic variants and gene–environment interactions to disease susceptibility and treatment response has the potential to enhance medical treatments and public health interventions. As technologies advance, more epidemiological studies will have the capacity to investigate genetic susceptibilities to environmental exposures and diseases and may include the collection of a biological sample.[1–3] Although follow-up measures can be applied to an epidemiological study to encourage participation, it is still not clear what characteristics may influence a subject's decision to participate or not to participate in a study that includes the collection of biological specimens.[4–9] Therefore, defining the differences between those who participate and those who do not participate will have important benefits for future epidemiological research. However, the inclusion of a genetic component might affect study participation and thereby causing selection bias due to concern about the risks of collecting genetic information.[5,10–12] Differences between those who participate and those who do not participate can be used to predict characteristics that influence participation and can be used to develop strategies to increase participation rates in a genetic component of a study. Furthermore, the potential biases that arise as a result of low participation rates can also be better evaluated.[4] The few previous studies that have investigated differences between participants who provided biological samples and those who declined to do so[6,8,13,14] demonstrated that race/ethnicity, age, health status, education, and other demographic factors are associated with participation.[8,9,14–17] A previous analysis of buccal cell participation at 1 of 10 study sites of the National Birth Defects Prevention Study (NBDPS) found that non-Hispanic white race, higher maternal education, and the addition of monetary incentives were associated with higher participation in buccal cell collection.[14]

Our objective was to determine what factors were associated with participation in buccal cell collection of the NBDPS, an ongoing population-based case–control study of risk factors for major birth defects across nine study sites. In a 1 hour NBDPS telephone interview study, personnel obtained information on the mother's demographic characteristics, lifestyle, and health behaviors. The NBDPS requires self-collection of DNA through the completion and return of a buccal cell collection kit with a written consent. This staged consent allows for detailed analysis to determine if demographic characteristics, lifestyle, and health behaviors of the individuals who participated in the interview are associated with participation in buccal cell collection. Better understanding of factors potentially associated with

participation could facilitate strategies to increase participation, thereby improving generalizability of study findings.

MATERIALS AND METHODS

The NBDPS is an ongoing, population-based, case–control study based on birth defects surveillance systems within specified geographic areas in Arkansas, California, Georgia, Iowa, Massachusetts, New Jersey, New York, North Carolina, Texas, and Utah. One of the 10 NBDPS sites (New Jersey) was excluded from this analysis as they participated in the study for a limited time period (1997–2002). The NBDPS is a multisite case–control study designed to investigate environmental and genetic risk factors for major birth defects. Case infants are identified from each state's birth defects surveillance system and have one or more of over 30 eligible birth defects and include liveborn or stillborn infants and electively terminated fetuses. Mothers can be excluded from the NBDPS due to social reasons (child in foster care, adoption). Controls are unaffected liveborn infants randomly selected from the same base population as case infants using either birth certificates or birth hospitals delivery logs.[18] Following initial identification and medical record abstraction, medical information is reviewed by clinical geneticists. Eligible case and control mothers are mailed an introductory letter, a fact sheet about the NBDPS, and a $20 incentive (check or money order) which the mother is advised she can keep, regardless of whether or not she chooses to participate in the NBDPS. This packet, available in English and Spanish, is mailed to the mother not earlier than 6 weeks after her infant's estimated date of delivery (EDD). Mothers are then contacted via telephone by trained interviewers, who described the NBDPS according to a standardized script and asked the mother for her verbal consent to participate in the interview. Mothers are interviewed using a computer-assisted telephone interview from 6 weeks to 24 months after the EDD.[18] Interviews are completed in English or Spanish, according to the preference of the mother. At the end of the interview, the mother is informed that a buccal cell collection kit will be sent to her address. The kit contains: a letter, collection instructions, three color-coded envelopes each containing two brushes for the mother, father, and infant; a consent form; and a second $20 incentive. After receiving the kit, the mother decides whether or not to participate in buccal cell collection and is again informed that the $20 can be kept regardless of whether she chooses to participate. A mother receives up to two reminder calls and three reminder letters asking if she has any questions and encouraging her to return buccal cell samples. Mothers were only eligible to participate in buccal cell collection if they completed the telephone interview. Nonparticipants were not asked to indicate why they would not participate in buccal cell collection. To increase participation in the NBDPS, incentive strategies changed over time with varying dates of implementation at each NBDPS study site. For the current analysis, incentive strategies that were compared were: (i) $20 incentive with invitation to interview and $20 incentive with buccal cell collection kit and (ii) $20 incentive with invitation to interview, $20 incentive with buccal cell collection kit, and an additional $20 incentive after return of completed buccal cell samples. One of the NBDPS sites (site 9) implemented incentive packages one and two (as above) simultaneously. Therefore, site 9 was excluded from analyses that assessed monetary incentives.

Our analyses were limited to mothers who completed the interview and therefore were eligible for buccal cell collection. Sociodemographic and health characteristics among mothers who provided buccal cell samples were compared with those who did not. Buccal cell sample participation was defined as return of any of the buccal brushes and a signed consent form. Nonparticipants included both those who actively declined participation (provided an explicit refusal statement) and those who did not return the kit (passive refusals). Because the dates of implementation of buccal cell collection varied by NBDPS site, this analysis was limited to subjects with an EDD after the date that buccal cell collection was added to the local study protocol.

Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using manual backward multiple logistic regression to identify factors potentially associated with participation in buccal cell collection. The Hosmer–Lemeshow test was used to assess goodness of fit. Nonsignificant factors were eliminated unless there was a reduction in the fit of the model.

The factors that were assessed were grouped into four categories: modifiable study design characteristics, demographic characteristics, pregnancy/infant characteristics, and lifestyle characteristics. Variables were dichotomized to minimize the number of degrees of freedom in the statistical models, and to be consistent with other published analyses, if possible. Most of the cut points are used consistently in NBDPS analyses and are based on how the question is asked ($50,000 cut point) or convention (<37 vs. ≥37 weeks). The modifiable study design characteristics included: receipt of the third $20 incentive after buccal cell sample participation versus receipt of two monetary incentives ($20 incentive with invitation to interview and $20 incentive with buccal cell collection kit), time between baby's EDD and maternal interview (<12 vs. ≥12 months), and language of interview (English versus Spanish) among Hispanic mothers). The demographic characteristics included: NBDPS site (study site 7 referent), maternal age (≥25 vs. <25 years), maternal race/ethnicity (non-Hispanic white referent), maternal education (≥12 vs. <12 years), household income (≥ $50,000 vs. <$50,000), mother employed outside the home (yes versus no), and mother born in the United States (yes versus no). The pregnancy/infant characteristics included: case versus control infants, preterm delivery (<37 vs. ≥37 weeks), gravidity (primigravid versus multigravid), outcome of the pregnancy (fetal death/pregnancy termination versus live birth), and pregnancy intendedness (wanting to become pregnant at the time of conception and/or stopped using contraception versus not wanting to become pregnant or wanting to wait until later stages). The lifestyle characteristics included: use of folic acid/multivitamins (any use during the month before conception and the first month of pregnancy versus no use during this period), maternal drinking (any alcohol use from 3 months before pregnancy through the end of pregnancy—yes versus no), maternal smoking (any smoking from 3 months before pregnancy through the end of pregnancy—yes versus no).

We also assessed patterns in participation over time. Calendar year was colinear with many of the covariates, and the overall participation rate for buccal cell collection rate varied over time; therefore, calendar year was not included in the statistical models.

To address the strong correlation of race/ethnicity, NBDPS site, and monetary incentive, we performed a generalized estimating equation model analysis using study site as a repeated measure. The results of the generalized estimating equation model were similar to the manual backward logistic regression model; therefore, the results of the backward logistic regression model are presented in this paper.

As a subanalysis, among families with a liveborn infant, multivariable logistic regression was used to assess the association between buccal cell participation and case/control status. The phenotypes that were assessed were selected a priori based on the level of severity and potential hesitancy of collection of an oral buccal cell sample. The following isolated defects/defect groups were assessed: spina bifida, eye defects (anophthalmos/microphthalmos, glaucoma/anterior chamber defects, and cataracts), anotia/microtia, heart defects, critical congenital heart defects (hypoplastic left heart syndrome, pulmonary atresia (with intact septum), transposition of the great arteries, truncus arteriosus, tricuspid atresia, tetralogy of Fallot, and total anomalous pulmonary venous return), any orofacial cleft, cleft lip with cleft palate, cleft lip without cleft palate, cleft palate alone, esophageal atresia, hypospadias, any limb deficiency, and gastroschisis. In addition, to assess if participation in buccal cell collection varied by phenotype, we also compared participation of case infants with isolated defects affecting the mouth (any orofacial cleft, cleft lip with cleft palate, cleft lip without cleft palate, and cleft palate) to case infants with isolated limb deficiencies. Estimates of associations were adjusted for preterm delivery, NBDPS study site, maternal race/ethnicity, education, folic acid use, drinking, smoking, pregnancy intendedness, provision of an additional $20 incentive, and time interval from EDD to telephone interview.

All statistical analyses were performed using SAS 9.3 (SAS Institute, Cary, NC).

RESULTS

Among mothers who were eligible to complete the NBDPS interview, the overall interview participation rate was 64.8% among cases and 64.7% among controls. The overall interview participation rate was highest among Non-Hispanic whites (68.9%), followed by Hispanics (60.3%) and non-Hispanic blacks (59.2%) (Table 1).

A total of 26,715 mothers who completed the telephone interview were eligible to receive a buccal cell collection kit (19,710 cases and 7,005 controls). Buccal cell sample collection was completed by 62.9% of the interviewed mothers (Figure 1). Participation rates were highest at study site 6 (74.2%) and lowest at site 2 (50.2%). Participation rates were highest among non-Hispanic whites (67.2%), followed by Hispanics (60.2%) and non-Hispanic blacks (46.6%) (Table 1).

Crude ORs showed that modifiable study design characteristics, demographic characteristics, pregnancy/infant characteristics, and lifestyle characteristics were associated with changes in participation in buccal cell collection (Table 2; Supplementary Table S1 online). NBDPS site and maternal race/ethnicity were strongly associated with participation in buccal cell collection as well as with many of the factors that were assessed; therefore, further analyses were stratified by site and maternal race/ethnicity.

Modifiable study design characteristics

Associations with modifiable study design characteristics and buccal cell collection did not vary by race/ethnicity and varied only slightly by NBDPS site (Table 3; Supplementary Tables S2–S5 online). Combining all race/ethnicities, participation increased with the receipt of an additional $20 incentive after the return of buccal cell samples (adjusted OR (aOR) = 1.52; 95% CI = 1.42, 1.62); six of the eight NBDPS sites showed statistically significant increases in participation with the extra incentive. Similarly, participation in buccal cell collection increased among mothers of all race/ethnicities (aOR = 1.32; 95% CI = 1.24, 1.40) when the woman was interviewed within 12 months; for seven of the nine study sites, participation was statistically significantly higher (Supplementary Table S2 online).

Demographic characteristics

Associations of demographic characteristics and participation in buccal cell collection remained consistent across race/ethnic groups and NBDPS sites (Table 3; Supplementary Tables S2–S5 online). Non-Hispanic black mothers (aOR = 0.47; 95% CI = 0.42, 0.52) and Hispanic mothers (aOR = 0.71; 95% CI = 0.65, 0.78) were less likely to participate in buccal cell collection compared with non-Hispanic white mothers. Overall, maternal education ≥12 years was associated with an increase in participation (aOR = 1.21; 95% CI = 1.14, 1.29); results were similar between non-Hispanic white and Hispanic mothers, but for non-Hispanic black mothers, no significant association was found between maternal education and participation. Overall, mothers born in the United States were less likely to participate in buccal cell collection (aOR = 0.89; 95% CI = 0.82, 0.96) compared with those born elsewhere. When stratified by race/ethnicity, Hispanic mothers that were born in the United States were less likely to participate in buccal cell collection (aOR = 0.72; 95% CI = 0.64, 0.81) than Hispanic mothers that were not born in the United States (Table 3). No significant association in buccal cell participation was found among non-Hispanic white and non-Hispanic black mothers born in the United States versus elsewhere. The lack of a significant finding may be due to small sample size within the subgroups.

Pregnancy/infant characteristics

Associations between pregnancy/infant characteristics and participation in buccal cell collection did not vary by NBDPS site or by race/ethnicity (Table 3; Supplementary Tables S2–S5 online). Mothers of case infants were more likely to participate in buccal cell collection than mothers of control infants (aOR = 1.37; 95% CI = 1.29, 1.46) (Table 3).

Lifestyle characteristics

Associations between lifestyle characteristics and buccal participation varied by race/ethnicity and by NBDPS site (Table 3; Supplementary Tables S2–S5 online). Overall, mothers who used folic acid or multivitamins at any time in the month before pregnancy or the first month of pregnancy were more likely to participate than those who did not use folic acid or multivitamins. Overall, mothers who consumed alcohol at any point during pregnancy were more likely to participate than those who did not consume alcohol (aOR = 1.10; 95% CI = 1.03, 1.16) (Table 3); this finding was consistent among all sites except site

8, where maternal drinking was found to have a decreased association with buccal cell collection (aOR = 0.73; 95% CI = 0.59, 0.91) (Supplementary Table S2 online). Mothers who smoked during pregnancy were less likely to participate (aOR = 0.83; 95% CI = 0.77, 0.89) (Table 3); findings were reversed for site 3 (aOR = 1.23; 95% CI = 1.01, 1.51) (Supplementary Table S2 online).

Types of defects

As a subanalysis, we examined participation in buccal cell collection by phenotype. Among mothers of children with selected isolated birth defects, non-Hispanic white and Hispanic mothers were more likely to participate than non-Hispanic black mothers. Non-Hispanic black mothers of infants with critical congenital heart defects were more likely to participate than non-Hispanic white and Hispanic mothers (Table 4). The association between participation in buccal cell collection by case/control status did not vary by birth defect phenotype. Similarly, participation among families affected by orofacial clefts was similar to that among families affected by isolated limb deficiencies.

DISCUSSION

Among women enrolled in the NBDPS, provision of buccal cell samples was associated with several demographic and study-specific characteristics. Race/ethnicity was strongly associated with participation in buccal cell collection; non Hispanic black and Hispanic mothers had lower participation rates than non-Hispanic white mothers. The association of race/ethnicity with participation in buccal cell collection was consistent with recent findings of other studies.[14,19,20] Our expanded analysis produced findings consistent with a 2006 paper on participation in buccal cell collection at the Atlanta NBDPS site including data from 1999 to 2002.[14] This study found that non-Hispanic black mothers had lower participation rates than non-Hispanic white and Hispanic mothers.[14] In the 1999–2000 National Health and Nutrition Examination Survey, non-Hispanic blacks were less likely to consent to have a blood sample saved for genetic research than non-Hispanic whites and Mexican Americans.[15] In the 2003–2004 National Health and Nutrition Examination Survey, when the item mentioning about the date of DNA collection was removed from the continuing studies consent document, there was no longer a significant decrease in consent by non-Hispanic blacks, and racial/ethnic differences were no longer observed.[21] A number of studies have indicated a lower level of trust of medical research among the African–American population in comparison with other racial/ethnic groups.[22–24]

Our data suggest that participation in buccal cell collection is affected by several characteristics. Across all race/ethnicities, the addition of a $20 incentive after the return of the buccal cell samples increased participation, with participation of non-Hispanic black mothers considerably improved by the additional incentive. This finding is consistent with previous studies that have shown that monetary incentives improve study participation rates.[14,19,20] We also found participation increased when the time from EDD to telephone interview was <12 months. Although each NBDPS site has varying protocols for data abstraction, case ascertainment, medical record review by a clinical geneticist, and maternal contact, the time from EDD to telephone interview is comparable across sites.

Case mothers were more likely to participate in buccal cell collection than control mothers. This could indicate that mothers with an infant with a health problem are more likely to participate in research than those without. This finding is consistent with a recent study on participation in cancer genetics research, where those who had a first-degree relative with cancer were significantly more likely to provide a blood specimen for DNA analysis (OR = 1.57; $P = 0.005$).[25]

Our findings suggested that mothers with positive health behaviors were more likely to participate in buccal cell collection than mothers with negative health behaviors. Mothers who took folic acid or multivitamin supplements during the month before pregnancy or the first month of pregnancy were more likely to participate, whereas those mothers who smoked during pregnancy were less likely to participate. These findings are consistent with another study which found that subjects with favorable lifestyle factors such as regular exercise, nonsmokers, and nondrinkers were more likely to participate in buccal cell collection.[8] We did find, however, that overall and in Hispanic mothers, those who consumed alcohol were more likely to participate in buccal cell collection. It is hypothesized that consumption of alcohol could be an indicator of higher socioeconomic status. A recent study showed that pregnant women who reported any alcohol use during pregnancy were more likely to be employed and have a college degree.[26] Previous studies have shown that higher income individuals are more likely to participate in genetic research than those with lower income.[16,17] In our data, mothers with household income ≥$50,000 were more likely to participate in buccal cell collection at two of the nine study sites than those with household income <$50,000 per year.

One of the strengths of this study is enrollment of a large, diverse population-based sample enabling comparisons by race/ethnicity, and geographic regions. Cases and controls were enrolled from the same base population. A recent study found that control participants in the NBDPS generally are representative of their base populations.[27] An additional strength is that participants were interviewed before the buccal cell kits were mailed and thus had an opportunity to consent separately to the two different components of the study. We were therefore able to analyze data on many characteristics provided by the participant in the telephone interview enabling us to characterize nonparticipants.

Some limitations of this study were that nonparticipants included those that both actively (provided an explicit refusal statement) and passively refused (did not return the buccal cell collection kit, with no reason given). A recent study assessed attitudes regarding DNA collection in the NBDPS through focus groups of mothers who had participated in the buccal cell component of the study and those who had not.[12] The primary reasons focus group respondents would choose not to participate in buccal cell collection included distrust of the government, concerns or skepticism regarding how DNA specimens and genetic information would be used, and paternal skeptism about sharing specimens and genetic information.[12] The primary reasons focus group respondents would choose to participate in buccal cell collection included wanting to help prevent or find cures for birth defects, to help advance science in general, or both.

We considered time interval between EDD and the maternal interview a modifiable study characteristic. However, in some instances, the time interval from the EDD to interview is dependent on phenotype and other external factors not under the control of study staff. Some phenotypes do not present until later and/or require lengthy hospitalizations delaying the time between the EDD and the time the neonatal or infant discharge record is available for case identification. Data from three of the nine sites were not stratified by race/ethnicity due to the small sample size of non-Hispanic black mothers at those sites. It was not possible to determine why the participation rate varied by study center. We believe that demographic differences account for the variance in participation. Given that the study population is women who were recently pregnant, we are unsure if the results are generalizable to the average epidemiological research population. However, as data are generally collected 6 months after pregnancy, this may not be a substantially limiting factor.

For researchers conducting genetic epidemiological studies, it is encouraging that some modifiable study characteristics were associated with increased participation. Other variables associated with participation had less to do with field operations. Participation among non-Hispanic whites was substantially higher than other racial-ethnic groups. Lower participation among other racial-ethnic groups could limit the generalizability of study findings and adversely affect statistical power. We suggest the researchers to utilize evidence from our study and others to develop strategies and protocols to target those groups less likely to participate in the genetic component of the study, and to invest in outreach to understand hesitancies and concerns.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank the many participating families, study investigators, and staff at the National Birth Defects Prevention Study sites for their important contributions. The authors thank Owen Devine, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, for statistical guidance and support.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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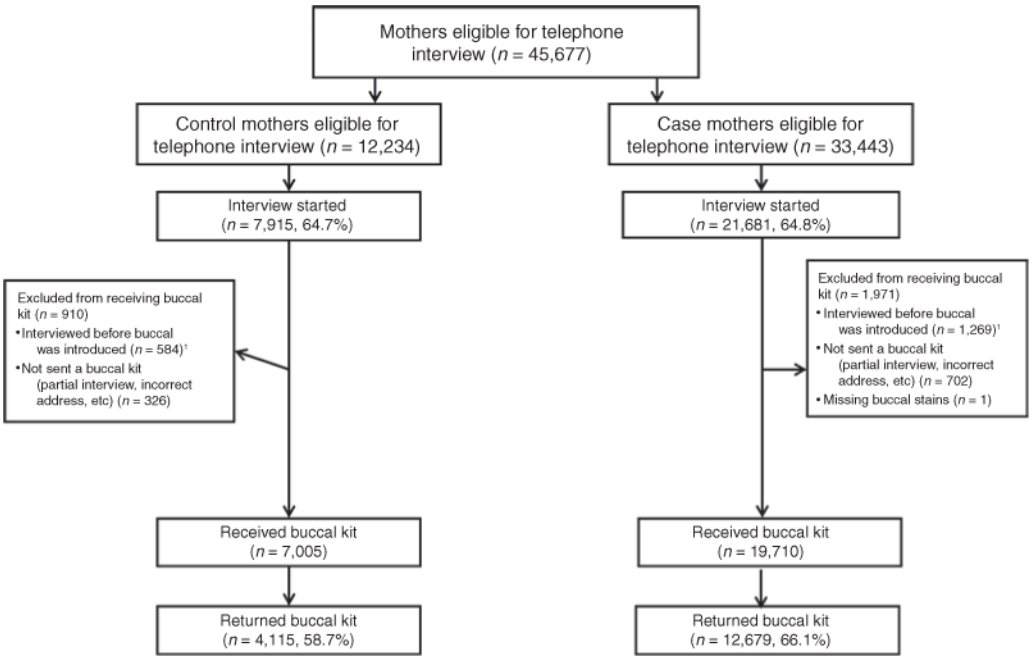

Figure 1. National Birth Defects Prevention Study: rates of participation in interview and buccal cell collection, 1997–2007

[1]Centers did not start sending buccal collection kits until October 1999, more than 18 months after the start of the interviews.

Table 1

National Birth Defects Prevention Study: rates of participation in interview and buccal cell collection by site, race/ethnicity, and estimated date of delivery, 1997–2007

	Controls				Cases			
	Eligible mothers	Interview started (%)	Received buccal kit[a]	Buccal kit returned (%)	Eligible mothers	Interview started (%)	Received buccal kit[a]	Buccal kit returned (%)
NBDPS study site								
Study site 1	1,674	1,011 (60.4)	898	516 (57.5)	4,748	2,779 (58.5)	2,549	1,667 (65.4)
Study site 2	1,519	1,033 (68.0)	789	377 (47.8)	4,436	3,023 (68.1)	2,517	1,284 (51.0)
Study site 3	1,474	1,028 (69.7)	851	486 (57.0)	4,435	3,095 (69.8)	2,744	1,737 (63.3)
Study site 4	1,434	893 (62.2)	781	387 (49.5)	4,425	2,714 (61.3)	2,476	1,360 (55.7)
Study site 5	1,294	731 (56.5)	596	288 (48.3)	2,592	1,622 (62.6)	1,401	781 (55.7)
Study site 6	1,521	935 (61.5)	925	653 (70.6)	3,820	2,187 (57.3)	2,161	1,636 (75.7)
Study site 7	1,579	1,070 (67.8)	985	652 (66.2)	4,514	3,123 (69.1)	2,793	2,093 (74.9)
Study site 8	881	617 (70.0)	611	415 (67.9)	2,537	1,856 (73.2)	1,838	1,295 (70.5)
Study site 9	858	597 (69.6)	569	342 (60.1)	1,936	1,282 (62.2)	1,231	826 (67.1)
Maternal race/ethnicity								
Non-Hispanic white	6,818	4,699 (68.9)	4,216	2,643 (62.7)	18,806	12,950 (68.9)	11,731	8,022 (68.4)
Non-Hispanic black	1,469	898 (61.1)	784	355 (45.3)	3,876	2,265 (58.4)	2,054	986 (48.0)
Hispanic	2,494	1,455 (58.3)	1,338	745 (55.7)	7,901	4,817 (61.0)	4,400	2,723 (61.9)
Other	1,453	863 (55.9)	667	372 (55.8)	2,860	1,649 (57.7)	1,525	948 (62.2)
Year of estimated date of delivery								
1997–1998	1,189	746 (62.7)	173	84 (48.6)	3,114	1,871 (60.0)	613	305 (49.8)
1999	1,044	744 (71.3)	560	274 (48.9)	2,776	1,943 (70.0)	1,560	912 (58.5)
2000	1,006	759 (75.4)	749	427 (57.0)	3,003	2,126 (70.8)	2,091	1,265 (60.5)
2001	989	683 (69.1)	675	355 (52.6)	2,997	2,029 (67.7)	2,000	1,259 (63.0)
2002	973	631 (64.9)	622	363 (58.4)	2,748	1,882 (68.5)	1,850	1,178 (63.7)
2003	1,367	902 (66.0)	880	542 (61.6)	3,332	2,176 (65.3)	2,133	1,343 (63.0)
2004	1,416	901 (63.6)	872	515 (59.1)	4,319	2,741 (63.5)	2,687	1,731 (64.4)
2005	1,375	870 (63.2)	835	496 (59.1)	4,036	2,584 (64.0)	2,512	1,669 (66.4)

	Controls				Cases			
	Eligible mothers	Interview started (%)	Received buccal kit[a]	Buccal kit returned (%)	Eligible mothers	Interview started (%)	Received buccal kit[a]	Buccal kit returned (%)
2006	1,481	868 (58.6)	847	539 (63.6)	3,469	2,106 (60.7)	2,071	1,458 (70.4)
2007	1,394	811 (58.1)	792	520 (65.6)	3,649	2,223 (60.9)	2,193	1,559 (71.1)
Total	12,234	7,915 (64.7)	7,005	4,115 (58.7)	33,443	21,681 (64.8)	19,710	12,679 (66.1)

[a]The number of interviews started differs from the number of buccal kits received because of the following: (i) centers did not start sending buccal collection kits until October 1999, more than 18 months after the start of the interviews; (ii) women who did not complete interviews were not sent a kit; and (iii) buccal kits were sent to an incorrect address. Women who requested that a buccal kit not be sent to them are in the column together with those who received buccal kits, as they were eligible to receive the kit.

Table 2

National Birth Defects Prevention Study: association between participation in buccal cell collection and covariates, 1997–2007 (crude ORs and 95% CIs)

Variable	Responders/total	%	OR	95% CI
Total	16,794/26,715	62.9		
Additional $20 after return of the completed kit—yes[a]	5,136/7,863	65.3	1.15	1.09, 1.22
Additional $20 after return of the completed kit—no[a]	10,093/16,252	62.1		
Time to interview <12 months	11,039/17,284	63.9	1.13	1.07, 1.19
Time to interview ≥12 months	5,755/9,431	61.0		
English interview among Hispanics	2,505/4,226	59.3	0.89	0.81, 0.99
Spanish interview among Hispanics	1,405/2,268	61.9		
Maternal race/ethnicity				
Non-Hispanic white	10,564/15,710	67.2	Ref	
Non-Hispanic black	1,266/2,714	46.6	0.43	0.39, 0.46
Hispanic	3,910/6,494	60.2	0.74	0.69, 0.78
Other	1,054/1,797	58.7	0.69	0.63, 0.76
Study site				
Study site 1	2,183/3,447	63.3	0.65	0.59, 0.72
Study site 2	1,661/3,306	50.2	0.38	0.34, 0.42
Study site 3	2,222/3,595	61.8	0.61	0.55,0.67
Study site 4	1,747/3,257	53.6	0.44	0.39, 0.48
Study site 5	1,069/1,997	53.5	0.43	0.39, 0.49
Study site 6	2,289/3,086	74.2	1.08	0.97, 1.20
Study site 7	2,745/3,778	72.6	Ref	
Study site 8	1,710/2,449	69.8	0.87	0.78, 0.97
Study site 9	1,168/1,800	64.9	0.70	0.62, 0.79
Maternal age ≥25	11,057/17,432	63.4	1.07	1.02, 1.13
Maternal age <25	5,737/9,283	61.8		
Maternal education ≥12 years	9,748/14,953	61.2	1.25	1.19, 1.31
Maternal education <12 years	7,037/11,737	60.0		
Household income ≥$50, 000/year	5,228/8,137	64.2	1.09	1.03, 1.15
Household income <$50, 000/year	11,306/18,144	62.3		
Mother born in the United States	13,609/21,393	63.6	1.17	1.10, 1.25
Mother not born in the United States	3,179/5,312	59.8		
Child with birth defect (case)	12,679/19,710	64.3	1.27	1.20, 1.34
Child without birth defect (control)	4,115/7,005	58.7		

Variable	Responders/total	%	OR	95% CI
Preterm delivery <37 weeks	3,833/6,162	62.2	0.97	0.91, 1.03
Term delivery ≥37 weeks	12,828/20,380	62.9		
Fetal death, pregnancy termination[b]	575/814	70.6	1.35	1.16, 1.57
Live birth	12,096/18,885	62.6		
Primigravid	5,178/8,080	64.1	1.08	1.02, 1.14
Multigravid	11,614/18,632	62.3		
Mother worked during pregnancy	11,975/18,924	65.5	1.06	1.00, 1.12
Mother did not work during pregnancy	4,815/7,777	61.9		
Folic acid/multivitamin use[c]	8,857/13,442	65.9	1.30	1.24, 1.36
No folic acid/multivitamin use	7,937/13,273	59.8		
Maternal drinking[d]	7,432/11,691	63.6	1.06	1.00, 1.11
No maternal drinking	9,321/14,960	62.3		
Maternal smoking[e]	3,427/5,624	60.9	0.90	0.85, 0.96
No maternal smoking	13,363/21,081	63.4		
Intended pregnancy	10,084/15,637	64.5	1.18	1.12, 1.24
Unintended pregnancy	6,666/10,991	60.6		

CI, confidence interval; OR, odds ratio; Ref, referent.

[a] Limited to participants that received $20 with invitation to interview and additional $20 after the return of the kit.

[b] Only cases included.

[c] Any folic acid use during the month before conception and the first month of pregnancy versus no use during this period.

[d] Any alcohol use from 3 months before pregnancy through the end of pregnancy—yes versus no.

[e] Any smoking from 3 months before pregnancy through the end of pregnancy—yes versus no.

Table 3

National Birth Defects Prevention Study: association between participation in buccal cell collection and covariates stratified by race/ethnicity, 1997–2007

	Total		Non-Hispanic white		Non-Hispanic black		Hispanic		Other	
Variable[a]	**aOR**	**95% CI**	**aOR**[b]	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**
Additional $20 after return of the completed kit	1.52	1.42 1.62	1.49	1.36, 1.63	1.88	1.56, 2.27	1.46	1.29, 1.65	1.47	1.15, 1.88
Time to interview <12 vs. ≥12 months	1.32	1.24, 1.40	1.33	1.24, 1.45	1.24	1.04, 1.49	1.22	1.10, 1.37	1.52	1.22, 1.91
Maternal race/ethnicity										
Non-Hispanic black vs. non-Hispanic white	0.47	0.42, 0.52	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Hispanic vs. non-Hispanic white	0.71	0.65, 0.78	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Other vs. non-Hispanic white	0.67	0.59, 0.75	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Study site										
Study site 1 vs. study site 7	0.72	0.64, 0.81	0.79	0.66, 0.95	0.78	0.48, 1.26	0.59	0.43, 0.79	0.98	0.57, 1.71
Study site 2 vs. study site 7	0.29	0.26, 0.33	0.30	0.26, 0.33	0.36	0.26, 0.53	0.24	0.16, 0.35	0.28	0.18, 0.45
Study site 3 vs. study site 7	0.65	0.58, 0.72	0.55	0.46, 0.64	1.02	0.67, 1.54	0.56	0.41, 0.75	0.58	0.38, 0.86
Study site 4 vs. study site 7	0.37	0.33, 0.42	0.39	0.33, 0.45	0.43	0.34, 0.53	0.31	0.22, 0.42	0.29	0.19, 0.44
Study site 5 vs. study site 7	0.33	0.29, 0.27	0.33	0.28, 0.38	0.38	0.26, 0.53	0.28	0.19, 0.41	0.33	0.20, 0.54
Study site 6 vs. study site 7	1.21	1.07, 1.37	1.27	1.10, 1.46	0.75	0.43, 1.32	0.81	0.51, 1.31	0.98	0.55, 1.75
Study site 8 vs. study site 7	0.65	0.57, 0.73	0.63	0.55, 0.73	1.10	0.27, 5.47	0.41	0.28, 0.60	0.55	0.34, 0.88
Maternal education ≥12 vs. <12 years	1.21	1.14, 1.29	1.35	1.24, 1.47			1.23	1.09, 1.39		
Mother born in the United States vs. not born in the United States	0.89	0.82, 0.96					0.72	0.64, 0.81		
Child with birth defect (case vs. control)	1.37	1.29, 1.46	1.41	1.30, 1.54			1.39	1.23, 1.56		
Preterm (<37 weeks) vs. term (≥37 weeks) delivery	1.07	1.00, 1.15								
Primigravid vs. multigravid	1.06	1.00, 1.13								
Folic acid/multivitamin use vs. no folic acid/multivitamin use[c]	1.14	1.08, 1.21	1.20	1.11, 1.30						
Maternal drinking vs. no maternal drinking[d]	1.10	1.03, 1.16					1.18	1.05, 1.32		

	Total		Non-Hispanic white		Non-Hispanic black		Hispanic		Other	
Variable[a]	**aOR**	**95% CI**	**aOR**[b]	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**
Maternal smoking vs. no maternal smoking[e]	0.83	0.77, 0.89	0.77	0.71, 0.85						

aOR, adjusted odds ratio; CI, confidence interval; N/A, not applicable.

[a] The following variables were eliminated from all models during backward multiple logistic regression, and therefore omitted from the table: English versus Spanish interview among Hispanics, maternal age ≥25 vs. <25 years, household income ≥$50, 000/year vs. <$50,000/year, mother worked during pregnancy versus mother did not work during pregnancy, intended versus unintended pregnancy.

[b] Blank cell: not predicted, variable removed from model.

[c] Any folic acid use during the month before conception and the first month of pregnancy versus no use during this period.

[d] Any alcohol use from 3 months before pregnancy through the end of pregnancy—yes versus no.

[e] Any smoking from 3 months before pregnancy through the end of pregnancy—yes versus no.

Table 4

National Birth Defects Prevention Study: association between participation in buccal cell collection and case/control status stratified by isolated birth defect phenotypes and race/ethnicity, 1997–2007

	Total		Non-Hispanic white		Non-Hispanic black		Hispanic		Other	
Birth defect/defect group	**aOR**	**95% CI**	**aOR[a]**	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**	**aOR**	**95% CI**
All selected birth defects	1.35	1.26, 1.54	1.37	1.25, 1.50	1.18	0.95, 1.46	1.33	1.17, 1.52	1.17	0.89, 1.53
Spina bifida	1.58	1.30, 1.92	1.80	1.35, 2.42	0.77	0.39, 1.48	1.51	1.10, 2.09	2.42	0.93, 7.15
Eye defects (anophthalmos/microphthalmos, glaucoma/anterior chamber defects, cataracts)	1.29	1.02, 1.64	1.47	1.06, 2.07	1.28	0.73, 2.27	0.99	0.60, 1.65	1.53	0.56, 4.35
Anotia/microtia	1.41	1.09, 1.85	1.63	1.01, 2.71	1.83	0.32, 10.31	1.39	0.98, 1.98	1.04	0.41, 2.67
Heart defect (any)	1.28	1.19, 1.39	1.31	1.18, 1.46	1.21	0.96, 1.54	1.22	1.05, 1.43	1.22	0.89, 1.69
Critical congenital heart defects	1.48	1.31, 1.68	1.49	1.27, 1.75	1.75	1.17, 2.61	1.41	1.11, 1.80	1.20	0.74, 1.97
Orofacial cleft (any)	1.46	1.32, 1.62	1.43	1.24, 1.64	1.09	0.73, 1.62	1.67	1.36, 2.05	1.01	0.68, 1.50
Cleft lip with cleft palate	1.47	1.27, 1.70	1.44	1.18, 1.77	1.23	0.69, 2.21	1.53	1.18, 2.00	1.05	0.60, 1.86
Cleft lip without cleft palate	1.63	1.34, 1.97	1.62	1.27, 2.07	1.04	0.45, 2.38	1.71	1.15, 2.58	1.37	0.68, 2.81
Cleft palate	1.33	1.13, 1.58	1.29	1.04, 1.61	0.91	0.48, 1.69	1.92	1.34, 2.79	0.80	0.44, 1.43
Esophageal atresia	1.54	1.08, 2.23	1.50	0.98, 2.35	1.00	0.19, 4.69	0.95	0.39, 2.32	8.57	1.48, 75.69
Hypospadias	1.11	0.94, 1.32	1.15	0.94, 1.42	0.94	0.58, 1.51	0.99	0.60, 1.64	0.92	0.43, 1.98
Limb deficiency (any)	1.55	1.26, 1.91	1.30	1.21, 2.12	1.95	0.94, 4.20	1.50	1.04, 2.20	0.93	0.37, 2.37
Gastroschisis	1.29	1.07, 1.57	1.56	1.18, 2.06	1.13	0.55, 2.29	1.07	0.76, 1.50	0.68	0.33, 1.41

aOR, adjusted odds ratio; CI, confidence interval.

[a]Adjusted for preterm delivery, NBDPS study site, maternal race/ethnicity, education, folic acid use, drinking, smoking, pregnancy intendedness, additional $20 incentive, and shorter time interval from estimated date of delivery to telephone interview.