article

Maternal reports of family history from the National Birth Defects Prevention Study, 1997–2001

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Purpose: To assess usefulness of family history information obtained in pediatric practice, we evaluated maternally reported family history data. **Methods:** We analyzed family history responses from the National Birth Defects Prevention Study using interview data from mothers of children with birth defects (n = 9,331) and of unaffected liveborn children (n = 3,390) with 1997–2001 estimated delivery dates. We examined the effects of demographic factors, case–control status, and type of defect on birth defect family history reports. Interview information was compared with occurrence of prenatal testing. **Results:** Among case mothers, 1,577 (17%) reported a first- or second-degree relative with a birth defect, compared with 327 (10%) control mothers (odds ratio = 1.91, 95% confidence interval = 1.68–2.16). Reports of affected relatives were also more frequent among mothers who were non-Hispanic white, were 25 years or older, had more than 12 years of education, had an annual household income greater than $20,000, were born in the United States, and completed an English-language interview. **Conclusion:** Reporting a family history of birth defects might be influenced by maternal demographic factors, which should be considered in developing pediatric family history tools. ***Genet Med* 2008:10(1):37–45.**

Key Words: *National Birth Defects Prevention Study, family history, birth defects, maternal interview, congenital heart defects*

Family history is an important risk factor for many disorders, including certain birth defects.[1] Increasingly, tools are being developed to determine the risk of disease based on family history information collected in settings ranging from prenatal care visits to adult health care.[2] Knowledge of family history can guide decisions on genetic screening, preventive care, and early intervention.[3] In pediatric settings, most family history information is obtained from parents, and evaluating the quality of this information is essential. Many family history validity studies have looked at chronic diseases, but only two have focused on birth defects.[4,5] These reports have shown that maternal responses may be of questionable accuracy, with low sensitivity indicating that there was under ascertainment. Furthermore, Rasmussen et al.[4] found that accuracy of maternal reporting of a child's birth defect varied greatly, depending on the type of defect. Rasmussen et al.[4] showed that demographic factors such as maternal race, education, and age-affected sensitivity, with higher sensitivity associated with white race, more education, and increasing age. Romitti et al.[5] found that responses from mothers of children with birth defects showed higher sensitivity than those from mothers of unaffected children. They also observed higher sensitivity with increasing maternal age and education for mothers of children with birth defects, but the opposite trend for mothers of unaffected children.

To expand on these studies, we analyzed family history reports from the National Birth Defects Prevention Study (NBDPS), an ongoing, multisite case–control study initiated to identify genetic and environmental risk factors for birth defects.[6] The NBDPS includes extensive maternal interviews to assess exposures, and buccal swab collection for genetic studies. We evaluated which factors were associated with interview reports of a family history of birth defects, and how reports varied by defect and by which family member was affected. We could not independently validate family histories, so differences in accuracy could not be determined. We explored one example of how family history awareness might affect behavior. Knowledge of a family history of birth defects might influence the level of prenatal testing, especially because family history of certain birth defects might be an indication for additional prenatal testing. Therefore, we examined whether reports of family history of birth defects or genetic disorders were associated with increased prenatal testing.

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This assessment provides a better understanding of what type of family history information can be expected from interviewing mothers of both case and control children.

MATERIALS AND METHODS

Study population

Case infants with specific types of major structural birth defects were identified through National Birth Defects Prevention Network surveillance programs in Arkansas, California, Georgia, Iowa, Massachusetts, New Jersey, New York, and Texas. Case infants included liveborn infants, stillborn infants, and pregnancies with birth defects diagnosed prenatally that were terminated. Infants with recognized or strongly suspected single-gene disorders and chromosomal abnormalities were excluded from the study. Control infants were a random sample of livebirths with no major birth defects from the same locations who were identified through hospital records or vital records from the general population. The mean age at maternal interview was 11 months for case children and 8 months for control children. Mothers of case and control infants were interviewed by telephone in English or Spanish by trained interviewers at the centers. The NBDPS was approved by the institutional review boards of the participating study centers and the Centers for Disease Control and Prevention, and informed consent was obtained from all mothers. Yoon et al.[6] provided a more detailed description of the study methods.

Participating infants were born on or after October 1, 1997, had an estimated delivery date on or before December 31, 2001, and had complete maternal interviews. For evaluation of the relationship between prenatal testing and reports of family history of birth defects, only mothers of control children were considered because the indication for prenatal testing in case children might have been abnormalities detected through standard prenatal care (e.g., polyhydramnios).

Coding of family history responses

We coded the responses to the NBDPS family history questions, which asked whether the child's mother, father, or any other relative had ". . . a health problem at birth or a birth defect that was diagnosed in childhood?," and, if so, "What was it?" For relatives other than the mother or father, questions were asked to determine the sex and relationship to the index child. Interviewers were instructed to record responses verbatim. Coding of responses was done after the interview by R.F.G. and R.S.O.

Initial review indicated that many chronic conditions and developmental disabilities, in addition to birth defects, were included in the responses; thus, each response was coded by the type of condition: birth defect, genetic disorder, developmental disability, prematurity or low birth weight, congenital cancer, exposure to teratogens, or other condition. To be as inclusive as possible, we included all birth defects ascertained by the Metropolitan Atlanta Congenital Defects Program.[7] For birth defects and genetic disorders, a level of detail was assigned to each response (high, medium, or low). For example, for heart defects, "ventricular septal defect" was assigned a high level of detail, "hole in heart" a medium level, and "heart defect" a low level (see Appendix for criteria for level of detail coding). This coding was done separately for each relative and blinded to case–control status, except when responses included information about the case–control status of the infant (e.g., defect indicated to be same as the proband). When multiple birth defects or genetic disorders were reported for a single individual, the level of detail was assigned to reflect the median for all defects or disorders mentioned.

For case children, responses were coded according to whether a family history of the same birth defect was present. For all family histories consistent with NBDPS-eligible defects, responses were also coded according to defect anatomic category (e.g., eye, ear). A variable was also created to indicate whether the birth defect occurred in a first-, second-, or third- or more degree family member.

We investigated whether reported family history of any birth defect or genetic disorder showed an association with prenatal testing in mothers of control children, including maternal serum screening, amniocentesis, and chorionic villus sampling. We also assessed the association between family history of congenital heart defects and fetal echocardiography among control infants.

Data management and analysis

Quantitative analysis was performed using SPSS and SABER, and logistic regression was performed using SPSS.[8] Although family histories for all biological relatives were included in our original analysis, we limited most of the results to first- (mother, father, and full siblings) and second-degree (half-siblings, grandparents, aunts, and uncles) relatives.

Factors assessed were case or control status, maternal race and ethnicity, paternal race and ethnicity, maternal age at delivery ($<$25 years, $\geq$25 years), maternal education (0–12 years, $>$12 years), paternal education (0–12 years, $>$12 years), household income ($<$\$20,000, $\geq$\$20,000), language of interview (English, Spanish), language spoken at home (English, other), maternal birthplace (United States, outside United States), paternal birthplace (United States, outside United States), maternal alcohol use during pregnancy (yes, no), maternal smoking during pregnancy (yes, no), maternal medication use during pregnancy (yes, no), interview quality, and whether the father contributed to the interview (yes, no). Race and ethnicity were defined categorically and also dichotomously as non-Hispanic white and all other races and ethnicities. As shown by Yoon et al.,[6] demographic characteristics were similar for case and control mothers. Interview quality was a subjective measure provided by the interviewer at the completion of the maternal interview. For our analysis, interview quality was defined as good for interviewer ratings of "high quality" or "generally reliable," and poor for interviewer ratings of "questionable" or "unsatisfactory."

RESULTS

Of the 12,721 respondents with completed interviews, 5,229 (41%) reported a family history of any condition in any relative, 2,709 (21%) reported birth defects, 903 (7%) genetic disorders, 1,349 (11%) developmental disabilities, 505 (4%) prematurity or low birth weight, and 1,482 (12%) other conditions (including congenital cancers and exposure to teratogens). Overall, mothers of control children reported family history less often for all categories, but significantly less for birth defects. Among mothers of case children, 1,577 (17%) reported a family history of birth defects in a first- or second-degree relative, compared with 327 (10%) mothers of control children.

Reports of birth defects in mothers and fathers were nearly equal ($n = 443$ vs. $n = 491$). Defects were reported for first-degree ($n = 1{,}318$), second-degree ($n = 1{,}014$), and third-degree or more distant ($n = 1{,}362$) relatives. To reduce the potentially confounding effect of degree of closeness, further analyses focused on first- and second-degree relatives, unless otherwise noted.

Level of detail of family history responses by defect

We examined the level of detail of family history reports by birth defect category (Table 1). Mothers most often reported relatives with heart defects ($n = 535$), orofacial clefts ($n = 314$), or limb deficiencies ($n = 199$). The level of detail varied substantially by defect. A high level of detail was seen for orofacial clefts (93%) and hypospadias (89%). In contrast, reports of heart or gastrointestinal (GI) defects tended to be of either medium (42% for heart, 23% for GI) or low (29% for heart, 27% for GI) level of detail. We also analyzed the level of detail by defect separately for case and control infants and did not observe a significant difference between the two groups (data not shown).

Reporting of family history of same birth defect

Among case children, reports of a family history of the same defect were evaluated (Table 2). For all relatives, reports of a family history of the same defect were more common for some defects, most notably orofacial clefts, where one in five case infants had a reported family history. This may reflect a stronger family history risk for some defects; however, we could not confirm whether there was underreporting or overreporting of defects. Some defects were reported more often in third-degree or more distant relatives, including orofacial clefts (50%), neural tube defects (61%), and central nervous system defects excluding neural tube defects (73%), whereas others were reported more often in first-degree relatives like craniosynostosis

Table 1
Level of detail by defect for maternal reports of birth defects in first- and second-degree relatives of case and control infants in the National Birth Defects Prevention Study, 1997–2001

Reported defect in first- or second-degree relatives of case and control infants	Level of detail, *N* (% total)			
	High	Medium	Low	Total
Amnion rupture	2 (100%)	0 (0%)	0 (0%)	2
NTD	75 (84%)	9 (10%)	5 (6%)	89
CNS (excluding NTDs)	29 (64%)	13 (29%)	3 (7%)	45
Eye	68 (85%)	8 (10%)	4 (5%)	80
Ear	17 (46%)	10 (27%)	10 (27%)	37
Heart	154 (29%)	227 (42%)	154 (29%)	535
Choanal atresia	0 (0%)	2 (100%)	0 (0%)	2
Orofacial clefts	291 (93%)	18 (6%)	5 (2%)	314
All GI defects	40 (49%)	19 (23%)	22 (27%)	81
Hypospadias	76 (89%)	7 (8%)	2 (2%)	85
Renal agenesis	25 (58%)	6 (14%)	12 (28%)	43
All limb deficiencies	134 (67%)	39 (20%)	26 (13%)	199
Craniosynostosis	25 (78%)	3 (9%)	4 (13%)	32
Sacral agenesis	3 (43%)	3 (43%)	1 (14%)	7
Diaphragmatic hernia	10 (91%)	1 (9%)	0 (0%)	11
Abdominal wall defects	17 (61%)	11 (39%)	0 (0%)	28
Multiple defects	17 (81%)	4 (19%)	0 (0%)	21
Total	983	380	248	

NTD, neural tube defect; CNS, central nervous system; GI, gastrointestinal.

Table 2
Maternal reports of family history of same birth defect as case child in first-, second-, and third- or more degree relatives from the National Birth Defects Prevention Study, 1997–2001

Defect in case infant	Degree closeness of relative reported to have same defect			Total reporting (% case infants)
	1st degree	2nd degree	≥3rd degree	
Amnion rupture	0 (0%)	0 (0%)	3 (100%)	3 (2%)
NTD	9 (15%)	14 (24%)	36 (61%)	59 (9%)
CNS (excluding NTDs)	2 (13%)	2 (13%)	11 (73%)	15 (4%)
Eye[a]	21 (70%)	4 (13%)	5 (17%)	30 (13%)
Ear	9 (41%)	5 (23%)	8 (36%)	22 (10%)
Heart	132 (30%)	140 (32%)	167 (38%)	439 (12%)
Orofacial clefts	81 (27%)	69 (23%)	152 (50%)	302 (20%)
All GI defects	15 (44%)	6 (18%)	13 (38%)	34 (4%)
Hypospadias	36 (50%)	19 (26%)	17 (24%)	72 (10%)
Renal agenesis	1 (33%)	2 (67%)	0 (0%)	3 (4%)
All limb deficiencies	12 (27%)	12 (27%)	21 (47%)	45 (9%)
Craniosynostosis	13 (50%)	5 (19%)	8 (31%)	26 (7%)
Diaphragmatic hernia	1 (13%)	4 (50%)	3 (38%)	8 (3%)
Gastroschisis	4 (24%)	5 (29%)	8 (47%)	17 (5%)
Omphalocele	1 (50%)	1 (50%)	0 (0%)	2 (1%)
Total	337	288	452	

[a]Cataracts, glaucoma, and related eye defects were exceptional in that they were not excluded if the affected child had a first-degree relative with the same defect and the defect showed inheritance consistent with a single-gene mutation.
NTD, neural tube defect; CNS, central nervous system; GI, gastrointestinal.

(50%) and hypospadias (50%). Unlike all other defects, some eye defects were not excluded from the NBDPS if the affected child had a first-degree relative with the same defect and if the defect showed inheritance consistent with a single-gene mutation. Thus, eye defects in the study were much more likely to be inherited. This might explain the high percentage (70%) of reports of first-degree relatives with eye defects.

Associations of case–control status and demographics with number of reports of birth defects family history

Mothers of case children reported a family history of birth defects more often than mothers of control children. Case status was associated with reports of birth defects in first- and second-degree relatives (odds ratio [OR] = 1.91, 95% confidence interval [CI] = 1.68–2.16) and in first-degree relatives only (OR = 1.71, 95% CI = 1.47–2.00) (Table 3).

Among case and control reports, we observed several differences in reporting of birth defects in first- and second-degree relatives by maternal demographic characteristics (Table 3). More mothers who were non-Hispanic white (18.7%) reported a family history of birth defects compared with mothers who were non-Hispanic black (8.9%), Hispanic (9.0%), Asian/Pacific Islander (8.8%), or all other races/ethnicities (8.8%). We observed a similar pattern for paternal race and ethnicity. Mothers who were 25 years of age or older reported a family history of birth defects more often than those younger than 25. Statistically significantly more family history reports were provided by higher educated mothers. Mothers with an annual household income of $20,000 or more showed increased odds of reporting a family history compared with those with incomes of <$20,000. Maternal alcohol use, smoking, and medication use during pregnancy also showed an association with reports of a family history of birth defects.

Language may have been a factor in the reporting of a family history of birth defects, because we observed fewer reports for those whose interviews were conducted in Spanish, for those who spoke a language other than English at home, for mothers born outside the United States, and for fathers born outside the United States.

Not surprisingly, aspects that affected the interview itself also showed associations with family history reports of birth defects. Those with poor interview quality showed decreased odds of reporting a family history of birth defects, whereas the father contributing to the interview increased the odds of reporting a family history of birth defects.

Similar results were found when we limited our analyses to control infants only, to reduce recall bias (data not shown).

We performed logistic regression analysis for maternal reports of family history of birth defects among case and control children. Maternal race and ethnicity, age, income, education, case–control status, alcohol use, smoking, and medication use during pregnancy were included in the model, along with interview quality and whether the father contributed to the interview. Although when we simultaneously controlled for these factors, we continued to see associations for non-Hispanic white maternal race and ethnicity compared with all

Table 3
Demographic and other associations with maternal reports of birth defects in first- or second-degree relatives of case and control infants from the National Birth Defects Prevention Study, 1997–2001

	Respondents reporting 1st or 2nd degree relative with birth defect *N* (% within group)	OR	95% CI	*P*
Case status				
Case	1577 (16.9%)	1.91	1.68–2.16	<0.001
Control	327 (9.6%)		—	
Cases and controls				
Maternal race and ethnicity				
Non-Hispanic White	1439 (18.7%)		—	
Non-Hispanic Black	122 (8.9%)	0.43	0.35–0.52	<0.001
Hispanic	259 (9.0%)	0.43	0.37–0.49	<0.001
Asian/Pacific Islander	28 (8.8%)	0.42	0.28–0.62	<0.001
All other races/ethnicities[a]	424 (8.8%)	0.42	0.38–0.47	<0.001
Paternal race and ethnicity				
Non-Hispanic White	1373 (18.8%)		—	
Non-Hispanic Black	148 (9.6%)	0.46	0.38–0.55	<0.001
Hispanic	254 (9.2%)	0.44	0.38–0.50	<0.001
Asian/Pacific Islander	19 (6.8%)	0.32	0.20–0.50	<0.001
All other races/ethnicities[a]	531 (9.8%)	0.47	0.42–0.52	<0.001
Maternal age (yr)				
Younger than 25	604 (13.9%)		—	
25 or older	1300 (15.5%)	1.14	1.03–1.27	0.014
Maternal education				
0–12 yr	777 (13.7%)		—	
More than 12 yr	1127 (16.0%)	1.20	1.08–1.32	<0.001
Paternal education				
0–12 yr	841 (13.7%)		—	
More than 12 yr	1014 (16.5%)	1.25	1.13–1.38	<0.001
Household income				
Under $20,000	507 (13.3%)		—	
$20,000 or more	1210 (16.1%)	1.25	1.12–1.40	<0.001
Language of interview				
English	1864 (15.6%)		—	
Spanish	40 (5.4%)	0.31	0.23–0.43	<0.001
Language spoken at home				
English	1760 (16.6%)		—	
Other	144 (6.8%)	0.36	0.31–0.43	<0.001
Maternal birthplace				
US	1732 (16.5%)		—	
Outside US	172 (7.7%)	0.42	0.36–0.49	<0.001

(*Continued*)

Table 3
Continued

	Respondents reporting 1st or 2nd degree relative with birth defect *N* (% within group)	OR	95% CI	*P*
Paternal birthplace				
US	1682 (16.7%)		—	
Outside US	207 (8.3%)	0.45	0.39–0.52	<0.001
Alcohol during pregnancy				
Yes	982 (16.5%)	1.24	1.13–1.37	<0.001
No	901 (13.7%)		—	
Smoking during pregnancy				
Yes	527 (18.5%)	1.40	1.25–1.56	<0.001
No	1358 (14.0%)		—	
Any medications during pregnancy				
Yes	1513 (15.9%)	1.37	1.21–1.54	<0.001
No	377 (12.1%)		—	
Interview quality				
Good	1861 (15.1%)		—	
Poor	41 (11.2%)	0.71	0.51–0.99	0.043
Father contribute				
Yes	170 (19.7%)	1.43	1.20–1.70	<0.001
No	1730 (14.7%)		—	

[a]This category (all other races/ethnicites) was used when race and ethnicity were defined as a dichotomous variable, with non-Hispanic white as the reference group.

other races (OR = 2.31, 95% CI = 2.05–2.59), case status (OR = 1.92, 95% CI = 1.69–2.19), maternal smoking during pregnancy (OR = 1.23, 95% CI = 1.10–1.38), and the father contributing to the interview (OR = 1.31, 95% CI = 1.09–1.57).

Associations of case–control status and demographics with level of detail of birth defects family history responses

We next examined whether factors that showed associations with reporting a family history of birth defects also correlated with the level of detail of the responses provided. Because the level of detail in responses varied widely between defects, analyzing all defects together might have obscured associations between demographics and the level of detail of the responses. Thus, we restricted our analyses to defects that were described with a lower level of detail: heart defects, GI defects, and renal agenesis (Table 4).

We did not see differences in the percentage of responses with high, medium, or low levels of detail for case infants compared with control infants (Table 4). Level of detail differed by selected maternal and paternal characteristics. A higher percentage of non-Hispanic white mothers responded with a high

Table 4
Demographic and other associations with level of detail of maternal reports of heart defects, gastrointestinal defects, or renal agenesis in first-degree relatives of case and control infants from the National Birth Defects Prevention Study, 1997–2001

	Level of detail (heart and gastrointestinal defects and renal agenesis only, 1st degree relatives only)				
	High	Medium	Low	Total	*P*
Case status					
Case	131 (48.0%)	85 (31.1%)	57 (20.9%)	273	
Control	21 (44.7%)	14 (29.8%)	12 (25.5%)	47	0.772
Maternal race and ethnicity					
Non-Hispanic White	136 (56.2%)	59 (24.4%)	47 (19.4%)	242	
All other races/ethnicities	15 (22.7%)	34 (51.5%)	17 (25.8%)	66	<0.001
Paternal race and ethnicity					
Non-Hispanic White	132 (55.5%)	61 (25.6%)	45 (18.9%)	238	
All other races/ethnicities	20 (24.4%)	38 (46.3%)	24 (29.3%)	82	<0.001
Maternal age (yr)					
Younger than 25	36 (35.3%)	35 (34.3%)	31 (30.4%)	102	
25 or older	116 (55.8%)	64 (30.8%)	28 (13.5%)	208	<0.001
Maternal education					
0–12 yr	50 (35.5%)	55 (39.0%)	36 (25.5%)	141	
More than 12 yr	102 (57.0%)	44 (24.6%)	33 (18.4%)	179	<0.001
Paternal education					
0–12 yr	64 (40.8%)	57 (36.3%)	36 (22.9%)	157	
More than 12 yr	87 (55.8%)	38 (24.4%)	31 (19.9%)	156	0.022
Household income					
Under $20,000	29 (34.5%)	34 (40.5%)	21 (25.0%)	84	
$20,000 or more	108 (54.8%)	50 (25.4%)	39 (19.8%)	197	0.006
Language of interview					
English	152 (48.3%)	96 (30.5%)	67 (21.3%)	315	
Spanish	0 (0%)	3 (60.0%)	2 (40.0%)	5	0.100
Language spoken at home					
English	148 (49.2%)	91 (30.2%)	62 (20.6%)	301	
Other	4 (21.1%)	8 (42.1%)	7 (36.8%)	19	0.050
Maternal birthplace					
US	142 (48.3%)	88 (29.9%)	64 (21.8%)	294	
Outside US	10 (38.5%)	11 (42.3%)	5 (19.2%)	26	0.419
Paternal birthplace					
US	147 (49.7%)	91 (30.7%)	58 (19.6%)	296	
Outside US	5 (20.8%)	8 (33.3%)	11 (45.8%)	24	0.004

(*Continued*)

Table 4
Continued

	Level of detail (heart and gastrointestinal defects and renal agenesis only, 1st degree relatives only)				
	High	Medium	Low	Total	*P*
Alcohol during pregnancy					
Yes	83 (49.7%)	52 (31.1%)	32 (19.2%)	167	
No	66 (44.3%)	46 (30.9%)	37 (24.8%)	149	0.438
Smoking during pregnancy					
Yes	37 (41.1%)	34 (37.8%)	19 (21.1%)	90	
No	112 (49.6%)	64 (28.3%)	50 (22.1%)	226	0.239
Any medications during pregnancy					
Yes	126 (47.9%)	79 (30.0%)	58 (22.1%)	263	
No	26 (47.3%)	18 (32.7%)	11 (20.0%)	55	0.905
Interview quality					
Good	150 (49.2%)	92 (30.2%)	63 (20.7%)	305	
Poor	2 (14.3%)	6 (42.9%)	6 (42.9%)	14	0.028
Father contribute					
Yes	14 (66.7%)	3 (14.3%)	4 (19.0%)	21	
No	137 (46.1%)	95 (32.0%)	65 (21.9%)	297	0.149

level of detail, compared with all other races and ethnicities ($P < 0.001$). Similar results were seen for paternal race and ethnicity ($P < 0.001$). We also observed a high level of detail for mothers 25 years of age or older ($P < 0.001$), maternal education of more than 12 years ($P < 0.001$), paternal education of more than 12 years ($P = 0.022$), and an annual household income of $20,000 or more ($P = 0.006$). A high level of detail was found more often when the interview was conducted in English, when English was the language spoken at home, when the mother was born in the United States, and when the father was born in the United States, although only the last comparison was statistically significant ($P = 0.004$).

Association between prenatal screening and family history of birth defects or genetic disorders among control children

We next investigated whether reports of family history of birth defects correlated with increased prenatal testing or procedures, including maternal serum screening, chorionic villus sampling, and amniocentesis. We considered only mothers of control children, because the indication for prenatal testing in mothers of case children might have been abnormalities detected during routine prenatal care. Although we did not find associations with maternal serum screening, chorionic villus sampling, or amniocentesis, prenatal tests specified as "other," which included fetal echocardiography, showed an association with reports of a family history of birth defects in a first-degree relative (OR = 4.09, 95% CI = 2.39–7.01) and in a first- or second-degree relative (OR = 3.37, 95% CI = 2.05–5.55). Focusing further, we found an association between reports of fetal echocardiograms and family history of congenital heart defects in a first-degree relative (OR = 14.56, 95% CI = 5.78–36.65) and in a first- or second-degree relative (OR = 7.72, 95% CI = 3.16–18.82). As might be expected, family history of genetic disorders correlated with amniocentesis for mothers younger than 35 years of age (OR = 1.67, 95% CI = 1.38–2.01), although not with maternal serum screening or chorionic villus sampling.

DISCUSSION

In our analysis of family history responses from the NBDPS maternal interviews, we found that the level of detail of responses varied by defect, as did reports of family history of the same birth defect. The level of detail finding has implications for development of tools to collect information on birth defects family histories. For some defects, such as orofacial clefts, more detailed explanations may not be needed, whereas others, such as heart defects, may require more extensive descriptions and may even warrant obtaining medical records to clarify the nature of the defect present in the relative. Furthermore, more complex birth defects, such as heart defects, might not be explained to families as comprehensively by clinicians or might be described using simplified terminology such as "hole in the heart," so that families might be reporting the information they received. Reports of family history of the same defect could reflect the heritable nature of the defect as well as differences in reporting between defects. For example, easily visible defects, such as orofacial clefts and limb deficiencies, were reported more often in third-degree relatives. This may reflect an increased awareness of this type of defect in less closely related family members or may indicate overreporting of such defects by those mothers with an affected child.

In this case–control study, we observed that reports of family history were associated with case status, non-Hispanic white maternal race and ethnicity, maternal smoking, and paternal participation in the interview. These characteristics did not seem to have as strong an effect on the level of detail of family history responses, although we did detect significant differences in percentages of high level of detail responses by race and ethnicity, age, education, income, and paternal birthplace. The association of case status with increased reporting of family history of birth defects was expected, both because genetic and other birth defect risk factors present in case children may be inherited or more common among other relatives and because of recall bias. Also, mothers of case children might have had increased awareness of other relatives with birth defects and might have made more effort to research occurrence of such conditions among family members in response to having an affected child. Surprisingly, the level of detail in responses was not significantly higher for mothers of case children, although this is consistent with findings by Rasmussen et

al.,[4] in which mothers often failed to correctly report the birth defect present in their child. The demographic associations with reports of birth defects family history indicate that these factors should be considered in collection and interpretation of family history information. Adjustment for covariates in multivariate logistic regression in the analysis did not make a substantive difference, because the adjusted and unadjusted odds ratios for case status were virtually identical. However, in other situations, covariates might well have a confounding influence. Although one or more of these demographic factors might be associated with an actual increase or decrease in the number of affected relatives, it is also possible that the reporting itself is affected.

Family history risk assessments using algorithms developed for one group might not be appropriate for another, and assumptions that the number of relatives reported reflect the number affected equally across all groups might not be valid. For example, algorithms to assess family history risk developed using data on non-Hispanic white participants might not be directly applicable to all other races and ethnicities, not only because of differences in actual risk, but also because of differences in reporting of family history. These results also support development of culturally sensitive approaches to family history collection and interpretation, rather than a one-size-fits-all approach.

For mothers of control infants, birth defects family history reports were associated with specific types of prenatal testing, which might be warranted given a particular family history. For instance, fetal echocardiography was associated with a family history of congenital heart defects, especially if a first-degree relative was affected, consistent with recommendations in the literature.[9] The association with amniocentesis in women younger than 35 years of age, presumably for genetic testing, was expected. These results also suggest that women with a family history of birth defects did not seem to be undergoing a larger number of invasive procedures, such as chorionic villus sampling and amniocentesis, which are not indicated by their family histories. In some cases, this might be due to the requirement for informed consent and genetic counseling before undergoing these invasive procedures.

Our study did have some significant limitations. Most importantly, we had no mechanism to confirm the validity of family history reports, so we could not address issues related to the sensitivity, specificity, or positive predictive value of reports of family history of birth defects. Thus, our focus was on the type of information that could be obtained through maternal interviews, rather than on the accuracy of this information. For the same reason, we could not assess whether the demographic associations observed, such as those for race and ethnicity, represented actual differences in prevalence between races and ethnicities rather than differences in sensitivity and specificity of reports, as observed by Rasmussen et al.[4] Because of this limitation, the data from our study should not be directly applied to modify risk algorithms based on family history. Also, coding the level of detail of responses had a subjective component; however, we attempted to standardize the coding as much as possible, as indicated in the Appendix.

Public health initiatives to use family history risk for health promotion and in clinical settings rely on reports provided by patients or their parents. Our level-of-detail results indicated that ascertainment of the precise nature of defects in some systems, such as the heart, might be more difficult than for other defects, such as orofacial clefts. Furthermore, reporting of a family history of the same birth defect may also vary by defect category. Tools designed to collect family history information on defects such as orofacial clefts may not require much explanation of the defect, whereas those for heart defects may require further details and possibly confirmation through medical records or other means. Assessing risk of a condition based on family history is a key component of use of family history information, with algorithms designed to facilitate risk assessment.[10] Although these algorithms might account for demographic factors such as race and ethnicity as they relate to genetic susceptibilities in calculating risk, the effect that these factors might have on reporting has not been considered. Our results suggested that demographic factors may affect reporting and should be considered in the design of family history risk assessment tools. As one approach, the Genetic Alliance's Coalition for Accessible Family Health History Tools[11] is currently creating a guide to aid different communities in the use and development of family history tools for their specific populations. Clinicians should be sensitive to the effect of demographics on reporting of family history, and professional education on this issue might be needed. Furthermore, research studies using family history information based on patient reports might need to consider the effects of demographics on reporting. In addition, the association of reports of family history of birth defects with the father contributing to the interview suggested that attempts should be made to obtain information from both sides of the family when feasible.

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APPENDIX

Table A1
Criteria for level of detail coding

Level of detail		
High	Medium	Low
Medical term used correctly	Medical term but unclear usage (e.g., *left parietal encephla–hematoma hydrocele*) or modified with *partial, light case of, probably, semi, likely, ?, think it was, incomplete*	Congenital nonspecific or general defect (e.g., *multiple congenital anomalies*)
Precisely described in layman's terms: must mention exact anatomy and describe such that only one defect can be assigned	Description clear but not precise (e.g., *principal vessel blocked*)	Unclear what defect is (e.g., *birthmark behind eye; birth defect in nose, blood vessel in nose, had to put acid in nose to burn them off; does not have nerve endings in the left side of her face; descendent colon; right hip rotation; retroverted hip; blue baby*)
Use common colloquial term and describe standard treatment (e.g., *Had fluid in the brain or inside of the head, had to put a tube to drain the fluid from the head*)	Common colloquial term only	Give two options and unsure of which is correct
Club foot or hand	Indicate that defect is same as that of case child	*Underdeveloped, not developed, overgrowth, grew too fast*[a]
Cleft lip, palate, or foot	Nonspecific indication of defect (e.g., *deformed*) and surgery or other appropriate treatment (e.g., casting); indicate died; or mention specific structures (e.g., ear lobe, part of one vertebrae) or location (e.g., *vascular malformation behind eye*)	Nonspecific indication of defect (e.g., *malformed, misshaped, deformed, defect, grew improperly, not form right, different looking, damaged, odd*)
Indicate obstruction and say surgery to open, closed on its own, or clearly describe obstruction in lower gastrointestinal tract	Indicate obstruction (e.g., *blockage, blocked, clogged, closed, covered, not open, backup*); *artery from heart, that runs down left arm was 100% blocked off, it fixed itself by making an artery down the right arm*	Indicate that condition went away on its own (unless condition able to resolve itself)[b]
Displaced or *dislocated* hips	Specific surgery (only)	*Problem with* or *something wrong with* and surgery (nonspecific) or died[c]
Webbed or *fused* digits	Atrophied structure or organ (e.g., *withered, degenerative, weak, deterioration*); organ removed at birth due to lack of growth	Organ removed at birth (unless indicate due to lack of growth); *weak spinal cord (muscles were weak);* organ or structure *not working, not functioning*
Indicate duplication of specific structure (e.g., *extra, double, split*, give number)	Indicate duplication but exact structure or defect unclear (e.g., *nerve split between one vertebra; extra tube going into her bladder; double intestine; two fingers off elbow; 3rd breast; double hernia*)	Unclear description of chromosomal duplication: *extra digit, extra chromosome (stillborn)*, and *extra leg of chromosome*
Precise description of abnormal opening in organ or structure with outcome indicated (e.g., *hole in lung that did not develop but that eventually closed*)	Abnormal opening in organ or structure (e.g., *torn, hole in, not closed, open*)	Abnormal opening in organ or structure but location unclear (e.g., *hole in chest*)
Indicate complete absence of specific structure (e.g., *missing, no, without*)	Indicate absence of structure but description more general (e.g., *missing cartilage in nose; bone missing from head; missing part of auditory system; without side of his brain; piece missing from ear; born without pupils; no palate in mouth; baby died at birth "born with no skin"; missing teeth, born without a complete set of teeth; missing a valve; part of heart missing*)	Indicate absence of structure but description incorrect or unclear (e.g., *no muscles in eyelids; missing abdominal muscles; skin discoloration lack of pigment; missing chromosomes*)

(*Continued*)

Table A1
Continued

Level of detail		
High	Medium	Low
Positional or conformational description that includes information on specific anatomical parts relative to each other (e.g., *aorta wrapped around esophagus, heart on outside of body, tongue attached to palate, kidney did not drop into his abdomen, right kidney in pelvis, 4th toe on right foot is under the 3rd toe*)	Positional or conformational description such as *backwards, upside-down, not in normal position, twisted, crooked, outside, curled, does not go straight, folded, pinched, attached, connect to, stuck together, joined together, grown together, dropping, drooping, overhanging, tethered, with a notch, caved in, concave, in knots, curved, filled with, out of place, bent, went in/out, fused* (except digits)	Inaccurate description (e.g., ascribe defect to nearby organ instead of more likely one—e.g., intestine instead of stomach, *blockage in her eye* when likely mean tear duct, *tubes in stomach not connected*)
Size comparisons that are standard layman's description (e.g., *small rectal opening, narrow pulmonary valve*)	Size comparisons (e.g., *longer than, smaller than, enlarged, elongated, high, thickened, dilation, half*)[d]	Size comparisons that are unlikely or unclear (e.g., *one eye is smaller than the other, high palate, soft tissue on left shoulder; large brain (growing too fast), His back-one side was bigger than the other; small heart*)
Surgery and positional or size description	Surgery or other treatment and positional or size description if nonspecific or unclear (e.g., *legs were deformed when I was born. My knees went in and my feet went out. I had to have cast to fix them; Born with crooked legs, had to be broken and rejoined; could not bend knee, did surgery by age 2; projectile vomiting; twisted esophagus, surgery at 1 month; spine did not grow, he stayed tiny, lots of surgeries*)	Surgery or other treatment if nonspecific or unclear (e.g., *shunt put in head, not sure why, having seizures*)
Large birthmark or *skin tag* with location given	*Tumor, extra tissue* with unclear location given (e.g., *born with a tumor connected to her tail bone; extra piece of tissue on his intestine when he was born*)	*Skin tag, growth, extra tissue, tumor* (unless clear that tumor refers to cancer in which case not coded as birth defect) with no location given
Polycystic kidney, dermoid cyst, pilodinal cyst	Cysts (except *polycystic kidney, dermoid cyst, pilodinal cyst*)	

[a]Exception: *sphincter muscle overdeveloped*, given high level of detail, and *left side of heart did not develop*, assigned medium level of detail.
[b]*Heart murmur* not coded as birth defect unless indicate due to structural defect, for example, *heart murmur, closed on its own*.
[c]Not coded as family history of birth defect if only say problem with or something wrong with.
[d]*Enlarged heart* not coded as birth defect.

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