

Maternal use of cough medications during early pregnancy and selected birth defects: a US multisite, case-control study

Supplemental Materials

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Supplemental Table 1. Interview items for an indication (cold or flu) episode and medication use for the episode, NBDPS, 1997-2011

Category	Item
Indication	<ul style="list-style-type: none"> From 3 months before you became pregnant to the end of your pregnancy, did you have a cold or flu? (IF YES) How many episodes did you have? When did your (1st/2nd/3rd) cold or flu episode start? When did the illness stop? How long did the illness last? When you were ill on this occasion, did you have respiratory symptoms, such as a cough, congestion, or runny nose; diarrhea or vomiting; muscle aches; fever?
	<ul style="list-style-type: none"> Did you take any medications or remedies for this illness? What did you take? / Did you take anything else? (LIST ALL.) When did you start using (medicine) for this illness? When did you stop using (medicine) OR How long did you take it? How often did you use (medicine)?

Abbreviation: NBDPS, National Birth Defects Prevention Study.

Supplemental Table 2. Cough medication use exposure algorithm, NBDPS, 1997-2011

Reported			Calculated		
Start Date	Stop Date	Duration	Start Date	Stop Date	
Full date	Full date	Unreported	Reported start date	Reported stop date	
	Unreported	Reported		Reported start date+duration-1	
		Unreported		Missing	
	Partial date	Reported		Reported start date+duration-1	
	Partial date	Beginning of calendar month		Unreported	10th of calendar month
		Middle of calendar month		Unreported	20th of calendar month
		End of calendar month		Unreported	30th (or 28th, 31st) of calendar month
		Unreported calendar month period		Unreported	15th of calendar month
Beginning/ Middle/ End of calendar year		Unreported	Missing		
Partial date*	Full date	Reported	Reported stop date+1-duration	Reported stop date	
		Unreported		Reported stop date	
	Unreported	Reported	1st of calendar month if start date reported as "beginning" 11th of calendar month if start date reported as "middle" 21st of calendar month if start date reported as "end" 15th of calendar month if start month reported without start day "Missing" if start date reported as "beginning/ middle/end" of calendar year	Calculated start date+(reported duration-1)	
		Unreported		Missing	
	Partial date	Beginning of calendar month		Reported/ Unreported	10th of calendar month
		Middle of calendar month		Reported/ Unreported	20th of calendar month
		End of calendar month		Reported/ Unreported	30th (or 28th, 31st) of calendar month
		Unreported calendar month period		Reported/ Unreported	15th of calendar month
		Beginning/ Middle/ End of calendar year		Reported/ Unreported	Missing
	Unreported	Full date		Reported	Reported stop date+1-duration
Unreported				Missing	Reported stop date
Unreported		Reported/ Unreported		Missing	Missing
		Partial date	Beginning of calendar month	Reported	Calculated stop date+1-duration
Unreported			Missing		
Middle of calendar month			Reported	Calculated stop date+1-duration	20th of calendar month
Unreported			Missing		
End of calendar month			Reported	Calculated stop date+1-duration	30th (or 28th, 31st) of calendar month
Unreported		Missing			
Unreported calendar month period		Reported	Calculated stop date+1-duration	15th of calendar month	
Unreported		Missing			
Beginning/ Middle/ End of calendar year		Reported	Missing	Missing	
	Unreported	Missing			

Abbreviation: NBDPS, National Birth Defects Prevention Study.

*Beginning, middle, end, or unreported day of a calendar month OR beginning, middle, or end of a calendar year

Supplemental Box 1. Examples of cough medication exposure assessment**Full Start Date, Full Stop Date, and No Duration**

A mother reported a start date of September 15th, 1999, a stop date of September 20th, 1999; the duration was not queried. The calculated start and stop dates were the same as the reported dates.

Full Start Date, No Stop Date, and Duration

A mother reported a start date of December 20th, 1999, no stop date (i.e. missing), and a duration of 10 days. The respective calculated start and stop dates were December 20th, 1999 and December 29th, 1999.

Full Start Date, Partial Stop Date, and No Duration

A mother reported a start date of November 21st, 1999, a stop date of the end of December 1999, and no duration (i.e. missing). The respective calculated start and stop dates were November 21st, 1999 and December 31st, 1999.

Partial Start Date, Partial Stop Date, and No Duration

A mother reported a start date of the end of November 1999, a stop date of the end of December, 1999, and no duration (i.e. missing). The respective calculated start and stop dates were November 21st, 1999 and December 31st, 1999.

Partial Start Date, No Stop Date, and Duration

A mother reported a start date of the beginning of April 1999, no stop date (i.e. missing), and a duration of 1 week. The respective calculated start and stop dates were April 1st, 1999 and April 7th, 1999.

Partial Start Date, Partial Stop Date, and Duration

A mother reported a start date of the beginning of November 1999, a stop date of the middle of November, 1999, and a duration of 3 weeks. The respective calculated start and stop dates were November 1st, 1999 and November 20th, 1999.

Supplemental Table 3. Distribution of selected child and maternal characteristics and exposures for analysis of NTD subtypes, NBDPS, 1997-2011

Characteristic or exposure	Individuals, No. (%)*			
	Controls (n = 10 409)	Anencephaly (n = 502)	Encephalocele (n = 139)	Spina bifida (n = 1003)
Child characteristic				
Sex				
Male	5309 (51.1)	205 (47.2)	59 (43.7)	496 (50.5)
Female	5089 (48.9)	229 (52.8)	76 (56.3)	487 (49.5)
Missing	11	68	4	20
First-degree family history of NTDs				
Yes	17 (0.2)	2 (0.4)	2 (1.4)	17 (1.7)
No	10 392 (99.8)	500 (99.6)	137 (98.6)	986 (98.3)
Missing	0	0	0	0
Study site				
Arkansas	1282 (12.3)	62 (12.4)	17 (12.2)	118 (11.8)
California	1136 (10.9)	111 (22.1)	17 (12.2)	195 (19.4)
Georgia	1098 (10.5)	58 (11.6)	24 (17.3)	125 (12.5)
Iowa	1149 (11.0)	54 (10.8)	14 (10.1)	123 (12.3)
Massachusetts	1248 (12.0)	18 (3.6)	8 (5.8)	59 (5.9)
New Jersey	501 (4.8)	4 (0.8)	6 (4.3)	33 (3.3)
New York	874 (8.4)	12 (2.4)	6 (4.3)	65 (6.5)
North Carolina	894 (8.6)	64 (12.7)	17 (12.2)	83 (8.3)
Texas	1221 (11.7)	70 (13.9)	16 (11.5)	117 (11.7)
Utah	1006 (9.7)	49 (9.8)	14 (10.1)	85 (8.5)
Missing	0	0	0	0
Maternal characteristic				
Race/ethnicity				
Non-Hispanic White	5969 (57.4)	247 (49.2)	61 (43.9)	532 (53.0)
Non-Hispanic Black	1143 (11.0)	36 (7.2)	24 (17.3)	82 (8.2)
Hispanic	2614 (25.1)	182 (36.3)	44 (31.7)	335 (33.4)
Other	676 (6.5)	37 (7.4)	10 (7.2)	54 (5.4)
Missing	7	0	0	0
Age at delivery (years)				
<25	3449 (33.1)	163 (32.5)	51 (36.7)	321 (32.0)
25-34	5528 (53.1)	277 (55.2)	67 (48.2)	541 (53.9)
≥35	1432 (13.8)	62 (12.4)	21 (15.1)	141 (14.1)
Missing	0	0	0	0
Educational level at delivery (years)				
<12	1736 (17.2)	108 (22.2)	33 (24.6)	178 (18.2)
12-15	5067 (50.2)	256 (52.6)	71 (53.0)	546 (55.8)
≥16	3298 (32.7)	123 (25.3)	30 (22.4)	254 (26.0)
Missing	308	15	5	25
Prepregnancy BMI (kg/m ²)				
<18.5	549 (5.5)	23 (4.9)	6 (4.8)	27 (2.9)
18.5-24.9	5359 (54.1)	233 (49.2)	71 (56.3)	431 (46.8)
25.0-29.9	2240 (22.6)	115 (24.3)	21 (16.7)	221 (24.0)
≥30	1752 (17.7)	103 (21.7)	28 (22.2)	242 (26.3)
Missing	509	28	13	82
Maternal exposure				
Hypertension†				
Yes	918 (8.9)	33 (6.7)	16 (11.8)	77 (7.7)
No	9404 (91.1)	463 (93.3)	120 (88.2)	920 (92.3)
Missing	87	6	3	6
Cigarette smoking‡				
No active or passive	7153 (70.7)	344 (70.8)	87 (64.4)	671 (68.4)
Active only	772 (7.6)	26 (5.3)	11 (8.1)	67 (6.8)
Passive only	1199 (11.9)	89 (18.3)	23 (17.0)	153 (15.6)
Active and passive	987 (9.8)	27 (5.6)	14 (10.4)	90 (9.2)
Missing	298	16	4	22

Characteristic or exposure	Individuals, No. (%) [*]			
	Controls (n = 10 409)	Anencephaly (n = 502)	Encephalocele (n = 139)	Spina bifida (n = 1003)
Alcohol consumption [‡]				
Yes	3551 (35.1)	129 (26.6)	45 (33.6)	316 (32.2)
No	6557 (64.9)	356 (73.4)	89 (66.4)	666 (67.8)
Missing	301	17	5	21
Fever [‡]				
Yes	493 (5.1)	32 (7.0)	12 (9.5)	72 (7.9)
No	9126 (94.9)	422 (93.0)	114 (90.5)	842 (92.1)
Missing	790	48	13	89
Use of a supplement containing folic acid [‡]				
Yes	5500 (54.2)	265 (54.5)	74 (56.1)	509 (52.3)
No	4643 (45.8)	221 (45.5)	58 (43.9)	464 (47.7)
Missing	266	16	7	30

Abbreviations: BMI, body mass index; NBDPS, National Birth Defects Prevention Study; NTD, neural tube defect.

^{*}Percentages within each column may not total 100 due to rounding.

[†]Diagnosed before or during pregnancy.

[‡]One month before pregnancy through the first month of pregnancy.

Supplemental Table 4. Distribution of selected child and maternal characteristics and exposures for analysis of hydrocephalus and anotia/microtia, NBDPS, 1997-2011

Characteristic or exposure	Individuals, No. (%)*		
	Controls (n=10 671)	Hydrocephalus (n=305)	Anotia/Microtia (n=421)
Child characteristic			
Sex			
Male	5443 (51.1)	172 (56.4)	246 (58.4)
Female	5217 (48.9)	133 (43.6)	175 (41.6)
Missing	11	0	0
First-degree family history of same defect			
Yes	--†	8 (2.6)	9 (2.1)
No	--	297 (97.4)	412 (97.9)
Missing	0	0	0
Study site			
Arkansas	1318 (12.4)	39 (12.8)	28 (6.7)
California	1162 (10.9)	34 (11.1)	106 (25.2)
Georgia	1131 (10.6)	32 (10.5)	23 (5.5)
Iowa	1178 (11.0)	51 (16.7)	21 (5.0)
Massachusetts	1268 (11.9)	22 (7.2)	34 (8.1)
New Jersey	517 (4.8)	13 (4.3)	34 (8.1)
New York	892 (8.4)	29 (9.5)	27 (6.4)
North Carolina	916 (8.6)	29 (9.5)	21 (5.0)
Texas	1264 (11.8)	34 (11.1)	79 (18.8)
Utah	1025 (9.6)	22 (7.2)	48 (11.4)
Missing	0	0	0
Maternal characteristic			
Race/ethnicity			
Non-Hispanic White	6127 (57.5)	194 (63.6)	131 (31.1)
Non-Hispanic Black	1169 (11.0)	34 (11.1)	6 (1.4)
Hispanic	2672 (25.1)	64 (21.0)	251 (59.6)
Other	696 (6.5)	13 (4.3)	33 (7.8)
Missing	7	0	0
Age at delivery (years)			
<25	3532 (33.1)	115 (37.7)	151 (35.9)
25-34	5666 (53.1)	151 (49.5)	210 (49.9)
≥35	1473 (13.8)	39 (12.8)	60 (14.3)
Missing	0	0	0
Educational level at delivery (years)			
<12	1765 (17.0)	61 (20.6)	123 (29.9)
12-15	5211 (50.3)	158 (53.4)	189 (45.9)
≥16	3381 (32.6)	77 (26.0)	100 (24.3)
Missing	314	9	9
Pre-pregnancy BMI (kg/m ²)			
<18.5	558 (5.5)	22 (7.5)	17 (4.6)
18.5-24.9	5487 (54.0)	154 (52.6)	192 (52.2)
25.0-29.9	2306 (22.7)	66 (22.5)	92 (25.0)
≥30.0	1810 (17.8)	51 (17.4)	67 (18.2)
Missing	510	12	53
Maternal exposure			
Hypertension‡			
Yes	944 (8.9)	48 (15.7)	42 (10.0)
No	9640 (91.1)	257 (84.3)	377 (90.0)
Missing	87	0	2
Cigarette smoking§			
No active or passive	7253 (70.0)	184 (62.2)	302 (73.3)
Active only	783 (7.6)	23 (7.8)	22 (5.3)
Passive only	1292 (12.5)	51 (17.2)	59 (14.3)
Active and passive	1039 (10.0)	38 (12.8)	29 (7.0)

Characteristic or exposure	Individuals, No. (%) [*]		
	Controls (n=10 671)	Hydrocephalus (n=305)	Anotia/Microtia (n=421)
Missing	304	9	9
Alcohol consumption [§]			
Yes	3818 (36.8)	97 (32.8)	124 (30.0)
No	6546 (63.2)	199 (67.2)	290 (70.0)
Missing	307	9	7
Fever [§]			
Yes	1054 (10.7)	34 (12.0)	40 (10.3)
No	8803 (89.3)	250 (88.0)	350 (89.7)
Missing	814	21	31
Use of a supplement containing folic acid [§]			
Yes	9100 (87.5)	259 (87.2)	332 (80.2)
No	1296 (12.5)	38 (12.8)	82 (19.8)
Missing	275	8	7

Abbreviations: BMI, body mass index; NBDPS, National Birth Defects Prevention Study.

^{*}Percentages within each column may not total to 100 due to rounding.

[†]Control totals for first-degree family history: hydrocephalus (n=6, 0.1%); anotia/microtia (n=6, 0.1%).

[‡]Diagnosed before or during pregnancy.

[§]One month before pregnancy through the first three months of pregnancy.

Supplemental Table 5. Distribution of selected child and maternal characteristics and exposures for analysis of craniofacial defects, NBDPS, 1997-2011

Characteristic or exposure	Individuals, No. (%)*		
	Controls† (n=10 553)	Cleft lip with/without cleft palate (n=2471)	Cleft palate (n=1158)
Child characteristic			
Sex			
Male	5389 (51.1)	1624 (65.8)	479 (41.4)
Female	5153 (48.9)	843 (34.2)	678 (58.6)
Missing	11	4	1
First-degree family history of orofacial clefts			
Yes	34 (0.3)	147 (5.9)	66 (5.7)
No	10 519 (99.7)	2324 (94.1)	1092 (94.3)
Missing	0	0	0
Study site			
Arkansas	1318 (12.5)	288 (11.7)	132 (11.4)
California	1162 (11.0)	398 (16.1)	147 (12.7)
Georgia	1131 (10.7)	256 (10.4)	128 (11.1)
Iowa	1178 (11.2)	256 (10.4)	114 (9.8)
Massachusetts	1268 (12.0)	289 (11.7)	190 (16.4)
New Jersey	517 (4.9)	87 (3.5)	54 (4.7)
New York	892 (8.5)	194 (7.9)	104 (9.0)
North Carolina	916 (8.7)	179 (7.2)	98 (8.5)
Texas	1264 (12.0)	267 (10.8)	100 (8.6)
Utah	907 (8.6)	257 (10.4)	91 (7.9)
Missing	0	0	0
Maternal characteristic			
Race/ethnicity			
Non-Hispanic White	6026 (57.1)	1524 (61.7)	761 (65.7)
Non-Hispanic Black	1168 (11.1)	132 (5.3)	72 (6.2)
Hispanic	2662 (25.2)	637 (25.8)	239 (20.6)
Other	690 (6.5)	177 (7.2)	86 (7.4)
Missing	7	1	0
Age at delivery (years)			
<25	3489 (33.1)	879 (35.6)	343 (29.6)
25-34	5599 (53.1)	1248 (50.5)	619 (53.5)
≥35	1465 (13.9)	344 (13.9)	196 (16.9)
Missing	0	0	0
Educational level at delivery (years)			
<12	1756 (17.1)	485 (20.1)	175 (15.6)
12-15	5142 (50.2)	1274 (52.7)	607 (54.0)
≥16	3343 (32.6)	657 (27.2)	343 (30.5)
Missing	312	55	33
Pre-pregnancy BMI (kg/m ²)			
<18.5	556 (5.5)	147 (6.3)	75 (6.7)
18.5-24.9	5416 (53.9)	1265 (54.1)	573 (51.3)
25.0-29.9	2283 (22.7)	496 (21.2)	265 (23.7)
≥30.0	1790 (17.8)	431 (18.4)	203 (18.2)
Missing	508	132	42
Maternal exposure			
Hypertension‡			
Yes	927 (8.9)	259 (10.5)	100 (8.7)
No	9539 (91.1)	2197 (89.5)	1047 (91.3)
Missing	87	15	11
Cigarette smoking§			
No active or passive	7154 (69.8)	1516 (62.8)	730 (64.9)
Active only	778 (7.6)	221 (9.2)	103 (9.2)

Characteristic or exposure	Individuals, No. (%) [*]		
	Controls [†] (n=10 553)	Cleft lip with/without cleft palate (n=2471)	Cleft palate (n=1158)
Passive only	1286 (12.5)	331 (13.7)	152 (13.5)
Active and passive	1033 (10.1)	347 (14.4)	140 (12.4)
Missing	302	56	33
Alcohol consumption [§]			
Yes	3804 (37.1)	890 (36.8)	449 (39.9)
No	6444 (62.9)	1526 (63.2)	677 (60.1)
Missing	305	55	32
Fever [§]			
Yes	1041 (10.7)	280 (12.3)	119 (11.5)
No	8709 (89.3)	1995 (87.7)	914 (88.5)
Missing	803	196	125
Use of a supplement containing folic acid [§]			
Yes	8989 (87.4)	2083 (85.7)	979 (87.0)
No	1291 (12.6)	348 (14.3)	146 (13.0)
Missing	273	40	33

Abbreviations: BMI, body mass index; NBDPS, National Birth Defects Prevention Study.

^{*}Percentages within each column may not total to 100 due to rounding.

[†]Control total excludes those from Utah delivered in 2003 (n=118) because Utah did not contribute data on children with cleft lip with/without cleft palate or cleft palate during that year.

[‡]Diagnosed before or during pregnancy.

[§]One month before pregnancy through the first three months of pregnancy.

Supplemental Table 6. Distribution of selected child and maternal characteristics and exposures for analysis of gastrointestinal defects, NBDPS, 1997-2011

Characteristic or exposure	Individuals, No. (%)*		
	Controls (n=10 671)	Anorectal atresia/stenosis (n=397)	Small intestinal atresia/stenosis (n=358)
Child characteristic			
Sex			
Male	5443 (51.1)	249 (62.7)	173 (48.3)
Female	5217 (48.9)	148 (37.3)	185 (51.7)
Missing	11	0	0
First-degree family history of same defect			
Yes	--†	9 (2.3)	1 (0.3)
No	--	388 (97.7)	357 (99.7)
Missing	0	0	0
Study site			
Arkansas	1318 (12.4)	70 (17.6)	42 (11.7)
California	1162 (10.9)	58 (14.6)	62 (17.3)
Georgia	1131 (10.6)	41 (10.3)	44 (12.3)
Iowa	1178 (11.0)	26 (6.5)	29 (8.1)
Massachusetts	1268 (11.9)	45 (11.3)	40 (11.2)
New Jersey	517 (4.8)	35 (8.8)	30 (8.4)
New York	892 (8.4)	25 (6.3)	26 (7.3)
North Carolina	916 (8.6)	23 (5.8)	27 (7.5)
Texas	1264 (11.8)	51 (12.8)	36 (10.1)
Utah	1025 (9.6)	23 (5.8)	22 (6.1)
Missing	0	0	0
Maternal characteristic			
Race/ethnicity			
Non-Hispanic White	6127 (57.5)	209 (52.6)	153 (42.7)
Non-Hispanic Black	1169 (11.0)	39 (9.8)	59 (16.5)
Hispanic	2672 (25.1)	115 (29.0)	124 (34.6)
Other	696 (6.5)	34 (8.6)	22 (6.1)
Missing	7	0	0
Age at delivery (years)			
<25	3532 (33.1)	139 (35.0)	131 (36.6)
25-34	5666 (53.1)	200 (50.4)	164 (45.8)
≥35	1473 (13.8)	58 (14.6)	63 (17.6)
Missing	0	0	0
Educational level at delivery (years)			
<12	1765 (17.0)	73 (18.8)	82 (23.8)
12-15	5211 (50.3)	211 (54.2)	173 (50.1)
≥16	3381 (32.6)	105 (27.0)	90 (26.1)
Missing	314	8	13
Pre-pregnancy BMI (kg/m ²)			
<18.5	558 (5.5)	21 (5.5)	22 (6.6)
18.5-24.9	5487 (54.0)	173 (45.3)	172 (51.5)
25.0-29.9	2306 (22.7)	94 (24.6)	66 (19.8)
≥30.0	1810 (17.8)	94 (24.6)	74 (22.2)
Missing	510	15	24
Maternal exposure			
Hypertension‡			
Yes	944 (8.9)	39 (9.8)	41 (11.5)
No	9640 (91.1)	357 (90.2)	315 (88.5)
Missing	87	1	2
Cigarette smoking§			
No active or passive	7253 (70.0)	255 (65.4)	223 (64.5)
Active only	783 (7.6)	31 (7.9)	32 (9.2)
Passive only	1292 (12.5)	54 (13.8)	47 (13.6)

Characteristic or exposure	Individuals, No. (%) [*]		
	Controls (n=10 671)	Anorectal atresia/stenosis (n=397)	Small intestinal atresia/stenosis (n=358)
Active and passive	1039 (10.0)	50 (12.8)	44 (12.7)
Missing	304	7	12
Alcohol consumption [§]			
Yes	3818 (36.8)	148 (38.1)	107 (30.9)
No	6546 (63.2)	240 (61.9)	239 (69.1)
Missing	307	9	12
Fever [§]			
Yes	1054 (10.7)	37 (10.2)	49 (14.9)
No	8803 (89.3)	327 (89.8)	280 (85.1)
Missing	814	33	29
Use of a supplement containing folic acid [§]			
Yes	9100 (87.5)	336 (86.4)	295 (84.5)
No	1296 (12.5)	53 (13.6)	54 (15.5)
Missing	275	8	9

Abbreviations: BMI, body mass index; NBDPS, National Birth Defects Prevention Study.

^{*}Percentages within each column may not total to 100 due to rounding.

[†]Control totals for first-degree family history: anorectal atresia/stenosis (n=3, 0.0%); small intestinal atresia/stenosis (n=3, 0.0%).

[‡]Diagnosed before or during pregnancy.

[§]One month before pregnancy through the first three months of pregnancy.

Supplemental Table 7. Distribution of selected child and maternal characteristics and exposures for analysis of hypospadias, NBDPS, 1997-2011

Characteristic or exposure	Individuals, No. (%) [*]	
	Controls [†] (n=5443)	Hypospadias [‡] (n=1991)
Child characteristic		
First-degree family history of hypospadias		
Yes	10 (0.2)	102 (5.1)
No	5433 (99.8)	1889 (94.9)
Missing	0	0
Study site		
Arkansas	657 (12.1)	298 (15.0)
California	597 (11.0)	93 (4.7)
Georgia	576 (10.6)	226 (11.4)
Iowa	584 (10.7)	167 (8.4)
Massachusetts	653 (12.0)	416 (20.9)
New Jersey	238 (4.4)	244 (12.3)
New York	461 (8.5)	130 (6.5)
North Carolina	505 (9.3)	192 (9.6)
Texas	667 (12.3)	25 (1.3)
Utah	505 (9.3)	200 (10.0)
Missing	0	0
Maternal characteristic		
Race/ethnicity		
Non-Hispanic White	3106 (57.1)	1481 (74.4)
Non-Hispanic Black	593 (10.9)	231 (11.6)
Hispanic	1388 (25.5)	157 (7.9)
Other	352 (6.5)	121 (6.1)
Missing	4	1
Age at delivery (years)		
<25	1810 (33.3)	492 (24.7)
25-34	2894 (53.2)	1144 (57.5)
≥35	739 (13.6)	355 (17.8)
Missing	0	0
Educational level at delivery (years)		
<12	918 (17.4)	149 (7.7)
12-15	2674 (50.7)	914 (47.1)
≥16	1685 (31.9)	878 (45.2)
Missing	166	50
Pre-pregnancy BMI (kg/m ²)		
<18.5	294 (5.7)	101 (5.2)
18.5-24.9	2800 (54.0)	1052 (53.9)
25.0-29.9	1177 (22.7)	427 (21.9)
≥30.0	916 (17.7)	370 (19.0)
Missing	256	41
Maternal exposure		
Hypertension [§]		
Yes	485 (9.0)	334 (16.9)
No	4922 (91.0)	1644 (83.1)
Missing	36	13
Cigarette smoking [¶]		
No active or passive	3667 (69.5)	1413 (73.0)
Active only	397 (7.5)	134 (6.9)
Passive only	658 (12.5)	198 (10.2)
Active and passive	558 (10.6)	191 (9.9)
Missing	163	55
Alcohol consumption [¶]		
Yes	1970 (37.4)	842 (43.6)
No	3301 (62.6)	1091 (56.4)

Characteristic or exposure	Individuals, No. (%) [*]	
	Controls [†] (n=5443)	Hypospadias [‡] (n=1991)
Missing	172	58
Fever [¶]		
Yes	533 (10.6)	181 (10.3)
No	4504 (89.4)	1581 (89.7)
Missing	406	229
Use of a supplement containing folic acid [¶]		
Yes	4622 (87.3)	1815 (92.8)
No	673 (12.7)	141 (7.2)
Missing	148	35

Abbreviations: BMI, body mass index; NBDPS, National Birth Defects Prevention Study.

^{*}Percentages within each column may not total to 100 due to rounding.

[†]Control total excludes females (n=5,217) and children with missing data for sex (n=11).

[‡]Second or third degree.

[§]Diagnosed before or during pregnancy.

[¶]One month before pregnancy through the first three months of pregnancy.

Supplemental Table 8. Distribution of selected child and maternal characteristics and exposures for analysis of heart defects, NBDPS, 1997-2011

Characteristic or exposure	Individuals, No. (%)*									
	Controls (n=10 671)	Controls for PVS† (n=10 326)	AS (n=292)	AVSD (n=157)	CoA (n=482)	d-TGA (n=509)	HLHS (n=517)	PVS (n=914)	TAPVR (n= 232)	ToF (n=833)
Child characteristic										
Sex										
Male	5443 (51.1)	5229 (51.1)	217 (74.3)	66 (42.0)	345 (71.7)	359 (70.5)	351 (68.2)	380 (41.6)	150 (64.7)	486 (58.4)
Female	5217 (48.9)	4996 (48.9)	75 (25.7)	91 (58.0)	136 (28.3)	150 (29.5)	164 (31.8)	533 (58.4)	82 (35.3)	346 (41.6)
Missing	11	11	0	0	1	0	2	1	0	1
First-degree family history of heart defects										
Yes	120 (1.1)	117 (1.1)	10 (3.4)	8 (5.1)	26 (5.4)	9 (1.8)	26 (5.0)	37 (4.0)	4 (1.7)	39 (4.7)
No	10 551 (98.9)	10 119 (98.9)	282 (96.6)	149 (94.9)	456 (94.6)	500 (98.2)	491 (95.0)	877 (96.0)	228 (98.3)	794 (95.3)
Missing	0	0	0	0	0	0	0	0	0	0
Study site										
Arkansas	1318 (12.4)	1318 (12.9)	42 (14.4)	27 (17.2)	56 (11.6)	62 (12.2)	61 (11.8)	204 (22.3)	21 (9.1)	98 (11.8)
California	1162 (10.9)	727 (7.1)	23 (7.9)	10 (6.4)	44 (9.1)	74 (14.5)	70 (13.5)	55 (6.0)	42 (18.1)	101 (12.1)
Georgia	1131 (10.6)	1131 (11.0)	20 (6.8)	15 (9.6)	47 (9.8)	58 (11.4)	55 (10.6)	83 (9.1)	23 (9.9)	106 (12.7)
Iowa	1178 (11.0)	1178 (11.5)	42 (14.4)	18 (11.5)	53 (11.0)	48 (9.4)	56 (10.8)	113 (12.4)	12 (5.2)	71 (8.5)
Massachusetts	1268 (11.9)	1268 (12.4)	23 (7.9)	20 (12.7)	71 (14.7)	94 (18.5)	46 (8.9)	110 (12.0)	32 (13.8)	118 (14.2)
New Jersey	517 (4.8)	517 (5.1)	10 (3.4)	12 (7.6)	10 (2.1)	28 (5.5)	10 (1.9)	37 (4.0)	16 (6.9)	39 (4.7)
New York	892 (8.4)	892 (8.7)	27 (9.2)	13 (8.3)	37 (7.7)	43 (8.4)	47 (9.1)	59 (6.5)	24 (10.3)	78 (9.4)
North Carolina	916 (8.6)	916 (8.9)	13 (4.5)	17 (10.8)	33 (6.8)	28 (5.5)	33 (6.4)	56 (6.1)	15 (6.5)	81 (9.7)
Texas	1264 (11.8)	1264 (12.3)	17 (5.8)	8 (5.1)	46 (9.5)	38 (7.5)	51 (9.9)	50 (5.5)	24 (10.3)	89 (10.7)
Utah	1025 (9.6)	1025 (10.0)	75 (25.7)	17 (10.8)	85 (17.6)	36 (7.1)	88 (17.0)	147 (16.1)	23 (9.9)	52 (6.2)
Missing	0	0	0	0	0	0	0	0	0	0
Maternal characteristic										
Race/ethnicity										
Non-Hispanic White	6127 (57.5)	5981 (58.5)	235 (80.5)	115 (73.2)	335 (69.5)	348 (68.4)	334 (64.6)	556 (60.8)	120 (51.7)	467 (56.1)
Non-Hispanic Black	1169 (11.0)	1155 (11.3)	6 (2.1)	22 (14.0)	31 (6.4)	23 (4.5)	50 (9.7)	141 (15.4)	13 (5.6)	113 (13.6)
Hispanic	2672 (25.1)	2436 (23.8)	41 (14.0)	9 (5.7)	90 (18.7)	99 (19.4)	107 (20.7)	148 (16.2)	76 (32.8)	185 (22.2)
Other	696 (6.5)	657 (6.4)	10 (3.4)	11 (7.0)	26 (5.4)	39 (7.7)	26 (5.0)	69 (7.5)	23 (9.9)	68 (8.2)
Missing	7	7	0	0	0	0	0	0	0	0
Age at delivery (years)										
<25	3532 (33.1)	3320 (32.4)	85 (29.1)	51 (32.5)	113 (23.4)	153 (30.1)	155 (30.0)	289 (31.6)	97 (41.8)	253 (30.4)
25-34	5666 (53.1)	5488 (53.6)	163 (55.8)	92 (58.6)	295 (61.2)	279 (54.8)	292 (56.5)	500 (54.7)	103 (44.4)	435 (52.2)
≥35	1473 (13.8)	1428 (14.0)	44 (15.1)	14 (8.9)	74 (15.4)	77 (15.1)	70 (13.5)	125 (13.7)	32 (13.8)	145 (17.4)
Missing	0	0	0	0	0	0	0	0	0	0
Educational level at delivery (years)										
<12	1765 (17.0)	1613 (16.3)	26 (9.3)	20 (13.2)	65 (13.8)	76 (15.1)	90 (17.7)	130 (14.7)	53 (23.6)	115 (14.2)
12-15	5211 (50.3)	4984 (50.2)	159 (57.0)	79 (52.3)	232 (49.4)	254 (50.4)	257 (50.5)	479 (54.1)	111 (49.3)	438 (54.1)
≥16	3381 (32.6)	3329 (33.5)	94 (33.7)	52 (34.4)	173 (36.8)	174 (34.5)	162 (31.8)	277 (31.3)	61 (27.1)	256 (31.6)
Missing	314	310	13	6	12	5	8	28	7	24
Pre-pregnancy BMI (kg/m ²)										
<18.5	558 (5.5)	544 (5.6)	15 (5.3)	6 (3.9)	20 (4.3)	22 (4.5)	22 (4.5)	35 (4.0)	12 (5.6)	34 (4.3)

Characteristic or exposure	Individuals, No. (%) [*]									
	Controls (n=10 671)	Controls for PVS [†] (n=10 326)	AS (n=292)	AVSD (n=157)	CoA (n=482)	d-TGA (n=509)	HLHS (n=517)	PVS (n=914)	TAPVR (n= 232)	ToF (n=833)
18.5-24.9	5487 (54.0)	5276 (54.0)	152 (54.1)	88 (57.5)	243 (52.5)	271 (55.4)	258 (52.4)	407 (46.9)	112 (51.9)	401 (50.3)
25.0-29.9	2306 (22.7)	2203 (22.6)	59 (21.0)	32 (20.9)	119 (25.7)	117 (23.9)	120 (24.4)	236 (27.2)	44 (20.4)	196 (24.6)
≥30.0	1810 (17.8)	1745 (17.9)	55 (19.6)	27 (17.6)	81 (17.5)	79 (16.2)	192 (18.7)	190 (21.9)	48 (22.2)	167 (20.9)
Missing	510	468	11	4	19	20	25	46	16	35
Maternal exposure										
Hypertension [‡]										
Yes	944 (8.9)	912 (9.0)	40 (13.9)	15 (9.7)	65 (13.5)	39 (7.7)	40 (7.8)	137 (15.2)	18 (7.9)	95 (11.5)
No	9640 (91.1)	9238 (91.0)	248 (86.1)	140 (90.3)	415 (86.5)	470 (92.3)	470 (92.2)	767 (84.8)	211 (92.1)	731 (88.5)
Missing	87	86	4	2	2	0	7	10	3	7
Cigarette smoking [§]										
No active or passive	7253 (70.0)	6927 (69.7)	183 (65.4)	92 (60.5)	346 (73.6)	350 (69.6)	353 (69.4)	599 (67.5)	152 (67.3)	557 (68.6)
Active only	783 (7.6)	751 (7.6)	26 (9.3)	15 (9.9)	29 (6.2)	39 (7.8)	42 (8.3)	64 (7.2)	14 (6.2)	53 (6.5)
Passive only	1292 (12.5)	1242 (12.5)	38 (13.6)	20 (13.2)	61 (13.0)	58 (11.5)	68 (13.4)	129 (14.5)	36 (15.9)	126 (15.5)
Active and passive	1039 (10.0)	1015 (10.2)	33 (11.8)	25 (16.4)	34 (7.2)	56 (11.1)	46 (9.0)	95 (10.7)	24 (10.6)	76 (9.4)
Missing	304	301	12	5	12	6	8	27	6	21
Alcohol consumption [§]										
Yes	3818 (36.8)	3697 (37.2)	94 (33.8)	57 (37.5)	172 (36.8)	194 (38.4)	177 (34.7)	292 (33.0)	73 (32.4)	308 (38.2)
No	6546 (63.2)	6236 (62.8)	184 (66.2)	95 (62.5)	296 (63.2)	311 (61.6)	333 (65.3)	592 (67.0)	152 (67.6)	498 (61.8)
Missing	307	303	14	5	14	4	7	30	7	27
Fever [§]										
Yes	1054 (10.7)	1009 (10.7)	36 (14.0)	11 (7.9)	43 (10.1)	58 (12.7)	65 (13.8)	101 (12.2)	19 (9.1)	85 (11.2)
No	8803 (89.3)	8432 (89.3)	221 (86.0)	128 (92.1)	381 (89.9)	400 (87.3)	405 (86.2)	726 (87.8)	189 (90.9)	672 (88.8)
Missing	814	795	35	18	58	51	47	87	24	76
Use of a supplement containing folic acid [§]										
Yes	9100 (87.5)	8757 (87.8)	258 (92.1)	141 (92.8)	436 (91.6)	432 (86.2)	444 (88.3)	776 (88.0)	194 (86.6)	722 (88.5)
No	1296 (12.5)	1221 (12.2)	22 (7.9)	11 (7.2)	40 (8.4)	69 (13.8)	59 (11.7)	106 (12.0)	30 (13.4)	94 (11.5)
Missing	275	258	12	5	6	8	14	32	8	17

Abbreviations: AS, aortic stenosis; AVSD, atrioventricular septal defect; BMI, body mass index; CoA, coarctation of the aorta; d-TGA, dextro-rotated transposition of the great arteries; HLHS, hypoplastic left heart syndrome; NBDPS, National Birth Defects Prevention Study; PVS, pulmonary valve stenosis; TAPVR, total anomalous pulmonary venous return; ToF, tetralogy of Fallot.

^{*}Percentages within each column may not total to 100 due to rounding.

[†]Controls from California delivered prior to 2002 (n=345) were excluded because children with PVS in California were not routinely ascertained according to NBDPS criteria prior to 2002.

[‡]Diagnosed before or during pregnancy.

[§]One month before pregnancy through the first three months of pregnancy.

Supplemental Table 9. Distribution of selected child and maternal characteristics and exposures for and analysis of musculoskeletal defects, NBDPS, 1997-2011

Characteristic or exposure	Individuals, No. (%)*						
	Controls (n=10 671)	Cranio- synostosis (n=1300)	Diaphragmatic hernia (n=590)	Gastroschisis (n=1,205)	Longitudinal limb deficiency (n=221)	Omphalocele (n=227)	Transverse limb deficiency (n=530)
Child characteristic							
Sex							
Male	5443 (51.1)	894 (68.8)	364 (61.7)	614 (51.1)	129 (58.6)	135 (60.0)	280 (52.8)
Female	5217 (48.9)	406 (31.2)	226 (38.3)	588 (48.9)	91 (41.4)	90 (40.0)	250 (47.2)
Missing	11	0	0	3	1	2	0
First-degree family history of same defect							
Yes	--†	51 (3.9)	7 (1.2)	13 (1.1)	4 (1.8)	2 (0.9)	8 (1.5)
No	--	1249 (96.1)	583 (98.8)	1,192 (98.9)	217 (98.2)	225 (99.1)	522 (98.5)
Missing	0	0	0	0	0	0	0
Study site							
Arkansas	1318 (12.4)	163 (12.5)	71 (12.0)	159 (13.2)	43 (19.5)	24 (10.6)	38 (7.2)
California	1162 (10.9)	114 (8.8)	67 (11.4)	239 (19.8)	25 (11.3)	28 (12.3)	71 (13.4)
Georgia	1131 (10.6)	98 (7.5)	88 (14.9)	124 (10.3)	22 (10.0)	30 (13.2)	55 (10.4)
Iowa	1178 (11.0)	137 (10.5)	55 (9.3)	111 (9.2)	26 (11.8)	20 (8.8)	46 (8.7)
Massachusetts	1268 (11.9)	194 (14.9)	83 (14.1)	104 (8.6)	29 (13.1)	26 (11.5)	59 (11.1)
New Jersey	517 (4.8)	32 (2.5)	29 (4.9)	44 (3.7)	8 (3.6)	13 (5.7)	43 (8.1)
New York	892 (8.4)	84 (6.5)	38 (6.4)	69 (5.7)	14 (6.3)	23 (10.1)	40 (7.5)
North Carolina	916 (8.6)	124 (9.5)	31 (5.3)	94 (7.8)	12 (5.4)	18 (7.9)	45 (8.5)
Texas	1264 (11.8)	80 (6.2)	64 (10.8)	144 (12.0)	20 (9.0)	23 (10.1)	59 (11.1)
Utah	1025 (9.6)	274 (21.1)	64 (10.8)	117 (9.7)	22 (10.0)	22 (9.7)	74 (14.0)
Missing	0	0	0	0	0	0	0
Maternal characteristic							
Race/ethnicity							
Non-Hispanic White	6127 (57.5)	954 (73.4)	354 (60.0)	600 (49.8)	134 (60.6)	132 (58.1)	300 (56.6)
Non-Hispanic Black	1169 (11.0)	48 (3.7)	44 (7.5)	99 (8.2)	30 (13.6)	33 (14.5)	41 (7.7)
Hispanic	2672 (25.1)	236 (18.2)	149 (25.3)	410 (34.0)	43 (19.5)	45 (19.8)	160 (30.2)
Other	696 (6.5)	62 (4.8)	43 (7.3)	96 (8.0)	14 (6.3)	17 (7.5)	29 (5.5)
Missing	7	0	0	0	0	0	0
Age at delivery (years)							
<25	3532 (33.1)	291 (22.4)	193 (32.7)	926 (76.8)	89 (40.3)	71 (31.3)	183 (34.5)
25-34	5666 (53.1)	760 (58.5)	317 (53.7)	262 (21.7)	107 (48.4)	111 (48.9)	285 (53.8)
≥35	1473 (13.8)	249 (19.2)	80 (13.6)	17 (1.4)	25 (11.3)	45 (19.8)	62 (11.7)
Missing	0	0	0	0	0	0	0
Educational level at delivery (years)							
<12	1765 (17.0)	146 (11.5)	83 (14.5)	321 (28.0)	33 (15.5)	29 (13.1)	92 (17.8)
12-15	5211 (50.3)	634 (49.8)	297 (51.9)	733 (63.9)	118 (55.4)	122 (55.0)	277 (53.7)
≥16	3381 (32.6)	494 (38.8)	192 (33.6)	93 (8.1)	62 (29.1)	71 (32.0)	147 (28.5)
Missing	314	26	18	58	8	5	14
Pre-pregnancy BMI (kg/m ²)							

Characteristic or exposure	Individuals, No. (%)*						
	Controls (n=10 671)	Cranio- synostosis (n=1300)	Diaphragmatic hernia (n=590)	Gastroschisis (n=1,205)	Longitudinal limb deficiency (n=221)	Omphalocele (n=227)	Transverse limb deficiency (n=530)
<18.5	558 (5.5)	67 (5.3)	27 (4.8)	106 (9.1)	6 (2.9)	9 (4.1)	33 (6.7)
18.5-24.9	5487 (54.0)	633 (50.0)	310 (55.6)	789 (68.0)	115 (55.3)	106 (48.6)	253 (51.0)
25.0-29.9	2306 (22.7)	311 (24.6)	119 (21.3)	205 (17.7)	61 (29.3)	54 (24.8)	123 (24.8)
≥30.0	1810 (17.8)	254 (20.1)	102 (18.3)	60 (5.2)	26 (12.5)	49 (22.5)	87 (17.5)
Missing	510	35	32	45	13	9	34
Maternal exposure							
Hypertension†							
Yes	944 (8.9)	139 (10.7)	58 (9.9)	68 (5.7)	19 (8.7)	23 (10.2)	57 (10.8)
No	9640 (91.1)	1155 (89.3)	526 (90.1)	1,127 (94.3)	200 (91.3)	203 (89.8)	471 (89.2)
Missing	87	6	6	10	2	1	2
Cigarette smoking§							
No active or passive	7253 (70.0)	924 (72.7)	385 (67.0)	549 (47.7)	133 (61.6)	151 (68.0)	343 (66.3)
Active only	783 (7.6)	97 (7.6)	53 (9.2)	143 (12.4)	19 (8.8)	16 (7.2)	49 (9.5)
Passive only	1292 (12.5)	133 (10.5)	78 (13.6)	198 (17.2)	28 (13.0)	33 (14.9)	70 (13.5)
Active and passive	1039 (10.0)	117 (9.2)	59 (10.3)	262 (22.7)	36 (16.7)	22 (9.9)	55 (10.6)
Missing	304	29	15	53	5	5	13
Alcohol consumption§							
Yes	3818 (36.8)	465 (36.6)	207 (36.1)	493 (42.7)	82 (38.0)	95 (42.8)	183 (35.3)
No	6546 (63.2)	807 (63.4)	367 (63.9)	661 (57.3)	134 (62.0)	127 (57.2)	336 (64.7)
Missing	307	28	16	51	5	5	11
Fever§							
Yes	1054 (10.7)	116 (10.2)	59 (11.0)	148 (13.2)	29 (14.5)	24 (11.5)	68 (14.0)
No	8803 (89.3)	1019 (89.8)	478 (89.0)	974 (86.8)	171 (85.5)	185 (88.5)	417 (86.0)
Missing	814	165	53	83	21	18	45
Use of a supplement containing folic acid§							
Yes	9100 (87.5)	1143 (90.6)	512 (88.7)	978 (83.7)	193 (88.5)	194 (87.4)	453 (87.8)
No	1296 (12.5)	119 (9.4)	65 (11.3)	190 (16.3)	25 (11.5)	28 (12.6)	63 (12.2)
Missing	275	38	13	37	3	5	14

Abbreviations: BMI, body mass index; NBDPS, National Birth Defects Prevention Study.

*Percentages within each column may not total to 100 due to rounding.

†Control totals for first-degree family history: craniosynostosis (n=4, 0.0%); diaphragmatic hernia (n=1, 0.0%); gastroschisis (n=6, 0.1%); limb reduction defects (n=18, 0.2%); omphalocele (n=1, 0.0%).

‡Diagnosed before or during pregnancy.

§One month before pregnancy through the first three months of pregnancy.

Supplemental Table 10. Associations for maternal respiratory symptoms during early pregnancy with NTDs, NBDPS, 1997-2011*

Study Group	No. of non-exposed (referent)	No. (%) of exposed†	cOR (95%CI)	aOR‡ (95%CI)
Controls	8324	938 (10.1)	NA	NA
NTDs	1253	167 (11.8)	1.2 (1.0 to 1.4)	1.1 (0.8 to 1.3)
Anencephaly	385	56 (12.7)	1.3 (1.0 to 1.7)	1.2 (0.8 to 1.8)
Encephalocele	99	15 (13.2)	1.3 (0.8 to 2.3)	1.2 (0.6 to 2.4)
Spina bifida	769	96 (11.1)	1.1 (0.9 to 1.4)	1.0 (0.7 to 1.3)

Abbreviations: aOR, adjusted OR; cOR, crude OR; DM, dextromethorphan; GG, guaifenesin (glyceryl guaiacolate); NA, not applicable; NBDPS, National Birth Defects Prevention Study; NTDs, neural tube defects.

*Includes mothers who did not report using medications containing DM or GG during the three months before or the duration of their pregnancy.

†Exposure during the one month before pregnancy through the first month of pregnancy.

‡Adjusted for child sex, first-degree family history of NTDs and study site; maternal race/ethnicity, age and education level at delivery, pre-pregnancy body mass index and hypertension diagnosed before or during pregnancy; and maternal cigarette smoking, alcohol consumption, fever and folic acid-containing supplement use during the one month before pregnancy through the first month of pregnancy.

Supplemental Table 11. Associations for maternal respiratory symptoms during early pregnancy with non-NTDs, NBDPS, 1997-2011*

Study Group	No. of non-exposed (referent)	No. (%) of exposed†	cOR (95%CI)	aOR‡ (95%CI)
Controls for non-NTDs	7233	2102 (22.5)	NA	NA
Central nervous system				
Hydrocephalus	202	63 (23.8)	1.1 (0.8 to 1.4)	1.1 (0.8 to 1.6)
Ear				
Anotia/microtia	279	80 (22.3)	1.0 (0.8 to 1.3)	1.1 (0.8 to 1.5)
Craniofacial				
Cleft lip with/without cleft palate§	1672	449 (21.2)	0.9 (0.8 to 1.0)	0.9 (0.8 to 1.0)
Cleft palate§	733	234 (24.2)	1.1 (0.9 to 1.3)	1.1 (0.9 to 1.3)
Gastrointestinal				
Anorectal atresia/stenosis	284	65 (18.6)	0.8 (0.6 to 1.0)	0.9 (0.6 to 1.2)
Small intestinal atresia/stenosis	250	56 (18.3)	0.8 (0.6 to 1.0)	0.7 (0.5 to 1.0)
Genitourinary				
Hypospadias¶,**	1318	368 (21.8)	1.0 (0.9 to 1.1)	1.0 (0.8 to 1.1)
Heart				
AS	178	55 (23.6)	1.1 (0.8 to 1.4)	0.9 (0.6 to 1.3)
AVSD	106	21 (16.5)	0.7 (0.4 to 1.1)	0.8 (0.5 to 1.3)
CoA	323	91 (22.0)	1.0 (0.8 to 1.2)	0.9 (0.7 to 1.2)
d-TGA	348	92 (20.9)	0.9 (0.7 to 1.2)	0.8 (0.6 to 1.1)
HLHS	344	98 (22.2)	1.0 (0.8 to 1.2)	0.8 (0.6 to 1.1)
PVS††	584	186 (24.2)	1.1 (0.9 to 1.3)	1.1 (0.9 to 1.3)
TAPVR	168	32 (16.0)	0.7 (0.4 to 1.0)	0.7 (0.4 to 1.0)
ToF	543	167 (23.5)	1.1 (0.9 to 1.3)	1.1 (0.9 to 1.3)
Musculoskeletal				
Craniosynostosis	829	250 (23.2)	1.0 (0.9 to 1.2)	1.0 (0.9 to 1.2)
Diaphragmatic hernia	396	109 (21.6)	0.9 (0.8 to 1.2)	0.9 (0.7 to 1.2)
Gastroschisis	842	211 (20.0)	0.9 (0.7 to 1.0)	0.8 (0.7 to 1.0)
Longitudinal limb deficiency	146	38 (20.7)	0.9 (0.6 to 1.3)	0.9 (0.6 to 1.3)
Omphalocele	148	43 (22.5)	1.0 (0.7,1.4)	1.0 (0.7 to 1.5)
Transverse limb deficiency	355	99 (21.8)	1.0 (0.8 to 1.2)	0.9 (0.7 to 1.2)

Abbreviations: aOR, adjusted OR; AS, aortic stenosis; AVSD, atrioventricular septal defect; CoA, coarctation of the aorta; cOR, crude OR; DM, dextromethorphan; d-TGA, dextro-rotated transposition of the great arteries; GG, guaifenesin (glyceryl guaiaacolate); HLHS, hypoplastic left heart syndrome; NA, not applicable; NBDPS, National Birth Defects Prevention Study; NTDs, neural tube defects; PVS, pulmonary valve stenosis; TAPVR, total anomalous pulmonary venous return; ToF, tetralogy of Fallot. *Includes mothers who did not report using medications containing DM or GG during the three months before or the duration of their pregnancy.

†Exposure during the one month before pregnancy through the third month of pregnancy.

‡Adjusted for child sex, first-degree family history of same defect and study site; maternal race/ethnicity, age and education level at delivery, pre-pregnancy body mass index and hypertension diagnosed before or during pregnancy; and maternal cigarette smoking, alcohol consumption, fever and Use of a supplement containing folic acid during the one month before pregnancy through the third month of pregnancy.

§Controls from Utah delivered in 2003 (n=115) were excluded because Utah did not contribute data on children with cleft lip with/without cleft palate or cleft palate during that year.

¶Second or third degree.

**Female controls (n=5017) were excluded.

††Controls from California delivered prior to 2002 (n=413) were excluded because children with PVS in California were not routinely ascertained according to NBDPS criteria prior to 2002.