interview question about birth defects did not specify a time period. Thus, a positve report by a veteran about the presence of a defect in a child that cannot be validated by a medical record could mean one of two things: (1) a false-positive response; or (2) a true positive response, but the defect was not present or diagnosed at birth. On the other hand, a negative response by a veteran for a child with a confirmed birth defect in the medical record may be considered a truly false-negative response.

The lack of a "gold standard" does not prohibit a misclassification analysis because our main interest is in comparing misclassification between the two cohorts, rather than the absolute magnitude of misclassification within either cohort.

Criteria for Matching Record and Interview Results

We considered the following three levels of matching, which range from general to specific.

1. Level 1 corresponds to the presence of any birth defect on the medical record if the veteran mentioned any birth defect for the child in the interview. For matching purposes, a birth defect is defined as any condition that was coded in the ICD-9 range of 740.0-759.9, for both interview responses and conditions listed on a medical record. This very general kind of matching shows the degree of agreement on the presence of defects.
2. Level 2 corresponds to a match of the organ system involved. Veterans may not remember the actual medical diagnosis, but may remember the specific organ system affected (such as gastrointestinal or cardiac). This is an intermediate level of matching. Organ systems for this level of matching are defined in Part A, Table 2.
3. Level 3 corresponds to a match of the exact condition (i.e. identical four-digit ICD-9 codes for both the interview response and the diagnosis from the medical records). This is the most specific degree of matching.

Measures of Misclassification

At each level of matching, two overall measures of misclassification were computed.

1. Percent agreement is defined as the number of interview-record pairs that match, divided by the total number of pairs compared.
2. Because birth defects are infrequent outcomes, percent agreement was corrected for chance agreement using the kappa statistic.

Percent chance agreement was computed using the product of marginals as described by Fleiss (1981).

At each level of matching, two kappa statistics were computed: one for Vietnam veterans and one for non-Vietnam veterans. These kappas were compared statistically using the method described by Fleiss (1981).

In addition to overall measures of agreement, two components of agreement were computed and compared between the cohorts:

1. Predictive value of a positive interview response (PPV). This corresponds to the proportion of positive interview responses that were confirmed upon examination of medical records. A PPV was computed for each cohort at each level of matching.
2. Predictive value of a negative interview response (NPV). This corresponds to the proportion of negative interview responses that were confirmed upon examination of medical records. Again, NPVs were computed for each cohort at each level of matching.

4.3.3 Analysis of Cerebrospinal Malformations

The objective of the analysis of cerebrospinal malformations is to examine, for children within each cohort, the extent of agreement between the interview response and the medical record(s) on the presence of a cerebrospinal malformation.

Because the numbers of both reported cerebrospinal malformations and records-based cerebrospinal malformations are small, we conducted a case-by-case review. For each cerebrospinal malformation case (including both reported cases and records-based cases), we have presented data from all available sources.

All children in the CSM Study were initially selected, on the basis of interview reports, as probable or possible cases. Consequently, the PPV was the only measure of agreement computed for the CSM Study. This is defined as the proportion of children in the CSM Study who were found to have a cerebrospinal malformation upon examination of the medical records. The PPVs were computed separately for stillbirths and live births in each cohort. Because the number of cases in each cohort is small, we did no statistical testing of differences between PPVs.

5. RESULTS

5.1 ANALYSIS OF PARTICIPANTS AND NONPARTICIPANTS

5.1.1 General Birth Defects Study

Of all children eligible for participation in the GBD Study, we received hospital records for 92.1% of the children whose fathers served in Vietnam and for 90.7% of the children whose fathers served elsewhere (Table 3). Refusal rates were very low in both cohorts; most of the nonparticipation was due to the inability to locate and retrieve hospital records.

The number of children per veteran (excluding veterans who reported no children) in the GBD Study is slightly greater than two. This is true in both cohorts for children reported at LMF, eligible children, and children with records received.

Participants and nonparticipants differ with regard to some of the primary and secondary covariates (Tables 4 and 5). A greater percentage of the fathers of nonparticipants are black (26.1%) and Hispanic (12.0%) than are the fathers of participants (9.7% and 6.9%, respectively). Fathers of nonparticipants also have lower General Technical (GT) test scores and less cumulative educational attainment. Many more fathers of participants were married at the time of the interview (83.1%) than were fathers of nonparticipants (69.3%). Finally, fathers of nonparticipants were younger than fathers of participants and had entered the Army more recently when their children were born.

The distributions of participating children by maternal and paternal characteristics show very similar patterns for children of Vietnam and non-Vietnam veterans (Tables 6-8). We found no important differences between the two cohorts.

5.1.2 Cerebrospinal Malformations Study

The participation rates in the CSM Study vary considerably by veteran cohort status (Table 9). We obtained hospital records for 82.5% of the eligible children of Vietnam veterans and for 67.1% of the eligible children of non-Vietnam veterans. This difference n cohort participation is primarily due to a large difference in the rates of veteran or mother refusal and also to a difference in the ability to locate and contact veterans. Non-Vietnam veterans were more difficult to locate and contact and more likely to refuse participation than were Vietnam veterans. In both cohorts, the percent of records received is higher for live-born children than for stillborn children (Table 10).

Table 3. Distribution of Nonparticipating and Participating Children, by Cohort Status of Fathers — General Birth Defects Study

	Vietnam		Non-Vietnam	
	%	No.	%	No.
Final Eligible Study Population	100.0	1945	100.0	1738
Nonparticipants				
Veteran or mother refusal	1.2	24	1.6	28
Records not located	6.6	129	7.7	133
Participants — Records Received	92.1	1792[a]	90.7	1577[a]

[a] Birth records were received for 1791 children of Vietnam veterans and 1575 children of non-Vietnam veterans. For the additional three children, a transfer hospital record was received but a birth record could not be obtained.

Table 4. Distribution of Primary Covariates Among Participating and Nonparticipating Veterans — General Birth Defects Study

Characteristic	Analysis Category	% of Veterans in Category	
		Participants	Nonparticipants
Age at birth of first child	≤25	45.3	53.9
	26-30	37.3	34.9
	31+	17.4	11.2
Race	White	83.5	61.8
	Black	9.7	26.1
	Hispanic and other	6.9	12.0
General Technical (GT) test score	40-89	20.2	35.7
	90-109	33.4	34.4
	110-129	33.2	22.8
	130-160	12.1	5.8
	missing	1.1	1.2
Enlistment status	Drafted	64.5	68.9
	Enlisted	35.5	31.1
Primary military occupational specialty	Tactical	30.1	29.9
	Other	69.9	70.1
Year of entry into Army	1965-66	37.9	37.3
	1967-69	46.2	46.9
	1970-71	15.9	15.8
Years between entry and birth of first child	≤5	45.9	58.9
	6-10	37.4	31.5
	11+	16.7	9.5

Table 5. Distribution of Secondary Covariates Among Participating and Nonparticipating Veterans — General Birth Defects Study

Characteristic	Analysis Category	% of Veterans in Category	
		Participants	Nonparticipants
Smoking history (average number of cigarettes per day)	<10	34.8	31.1
	10-39	50.6	53.9
	40+	14.4	14.5
	missing	0.2	0.4
Alcohol use (average number of drinks per month)	<30	56.7	51.0
	30-89	27.4	28.6
	90+	14.5	18.3
	missing	1.4	2.1
Educational attainment (in years)	<12	11.3	20.3
	12-15	68.8	69.3
	16+	19.9	10.0
	missing	0.1	0.4
Marital status (current)	Married	83.1	69.3
	Not married	16.9	29.9
	missing	—	0.8
Regular drug use in Army (at least once a week for at least 3 months)	None	76.2	70.5
	Marijuana only	15.8	17.4
	Hard drugs	7.5	11.2
	missing	0.4	0.8

The number of children per veteran in the CSM Study is just slightly greater than one. This is true in both cohorts for children reported in the VES interview, eligible children, and children with records received.

Participants and nonparticipants in the CSM Study differ in several ways (Tables 11 and 12). Compared with fathers of participants, fathers of nonparticipants are more likely to be

Table 6. Definition and Categorization of Covariates Obtained From Hospital Recor s and Distribution Among Participating Children, by Cohort Status of Fathers — General Birth Defects Study

Characteristic (of Mother)	Analysis Category	Children in Category			
		Vietnam		Non-Vietn m	
		%	No.	%	No.
Maternal age	≤24	32.1	576	32.6	514
	25-29	28.4	508	26.6	419
	30+	14.4	258	17.7	279
	missing	25.1	450	23.2	365
Gravida	1	27.8	498	27.0	426
	2	30.2	541	29.7	468
	3+	27.9	500	29.0	458
	missing	14.1	253	14.3	225

Table 7. Distribution of Primary Covariates Among Participating Children, by Cohort Status of Fathers — General Birth Defects Study

Characteristic (of Veteran)	Analysis Category	Children in Category			
		Vietnam		Non-Vie nam	
		%	No.	%	No.
Age at birth of child	≤25	28.7	515	28.3	446
	26-30	39.8	714	40.1	632
	31+	31.4	563	31.6	499
Race	White	84.5	1515	82.3	1298
	Black	7.9	142	11.6	183
	Hispanic and other	7.5	135	6.1	96
General Technical (GT) test score	040-089	20.2	361	19.9	314
	090-109	35.4	634	31.4	495
	110-129	32.4	581	34.9	551
	130-160	11.0	197	13.1	207
	missing	1.1	19	0.6	10
Enlistment status	Drafted	63.6	1140	64.6	1019
	Enlisted	36.4	652	35.4	558
Primary military occupational specialty	Tactical	33.1	593	26.5	418
	Other	66.9	1199	73.5	1159
Year of entry into Army	1965-66	37.5	672	39.0	615
	1967-69	53.2	954	39.0	615
	1970-71	9.3	166	22.0	347
Years between entry and birth	≤5	26.4	473	29.1	459
	6-10	40.8	731	38.9	614
	11+	32.8	588	32.0	504

nonwhite, unmarried at the time of the VES interview, less educated, and younger at the time of their child's birth, and they are more likely to have lower GT test scores.

The distributions of covariates among participants show some differences between children of Vietnam and non-Vietnam veterans with regard to maternal and paternal characteristics (Tables 13-15). Compared with Vietnam veterans, non-Vietnam veterans were better educated, scored higher on the GT test, were more likely to be married, were older when their child was born, were more likely to have had a nontactical primary military occupational specialty (MOS) in the Army, to have served in the Army during both earlier and later years, and to have used alcohol less.

Table 8. Distribution of Secondary Covariates Among Participating Children, by Cohort Status of Fathers — General Birth Defects Study

Characteristic (of Veteran)	Analysis Category	Children in Category			
		Vietnam		Non-Vietnam	
		%	No.	%	No.
Smoking history	<10	33.7	604	37.0	584
(average number of	10-39	51.9	930	47.8	753
cigarettes per day)	40+	14.3	256	14.8	234
	missing	0.1	2	0.4	6
Alcohol use	<30	56.9	1019	57.6	908
(average number of drinks	30-89	26.0	465	29.2	460
per month)	90+	15.2	273	12.4	195
	missing	2.0	35	0.9	14
Educational attainment	<12	12.6	226	9.6	152
(in years)	12-15	70.0	1255	68.2	1076
	16+	17.4	311	21.9	346
	missing	0.0	0	0.2	3
Marital status	Married	84.5	1515	85.8	1353
(current)	Not married	15.5	277	14.2	224
Regular drug use in Army	None	74.0	1326	80.6	1271
(at least once a week	Marijuana only	17.9	320	12.6	198
for at least 3 months)	Hard drugs	7.5	135	6.5	103
	missing	0.6	11	0.3	5

Table 9. Distribution of Nonparticipating and Participating Children, by Cohort Status of Fathers — Cerebrospinal Malformations Study

	Vietnam		Non-Vietnam	
	%	No.	%	No.
Final Eligible Study Population	100.0	154	100.0	113
Nonparticipants				
Unable to locate or contact veteran	2.6	4	5.7	3
Veteran or mother refusal	7.8	12	22.1	31
Records not located	4.5	7	2.1	3
Other	2.6	4	2.9	1
Participants—Records Received	82.5	127	67.1	94

5.2 DIRECT COMPARISON OF HOSPITAL RECORDS FROM THE GENERAL BIRTH DEFECTS STUDY

5.2.1 BIRTH DEFECTS

Using data from hospital birth records only, we found 130 children of Vietnam veterans and 112 children of non-Vietnam veterans with one or more stated or suspected birth defects, yielding rates of 7.3% and 7.1%, respectively (crude OR = 1.0, 95% CI = 0.8-1.3) (Table 16). When defects are classified as major, minor, and suspected (Table 16), the crude ORs for Vietnam service are 1.2 (95% CI = 0.8-1.9), 0.9 (95% = CI 0.6-1.4), and 0.9 (95% CI = 0.5-1.6), respectively.

Table 17 shows a crude and adjusted analysis of birth defects, stratified by race. The crude

Table 10. Number and Percent of Records Received, by Birth Status and Cohort Status of Fathers — Cerebrospinal Malformations Study

	Vietnam			Non-Vietnam		
	Requested	Received	%	Requested	Received	%
Stillbirths	99	78	78.8	114	74	64.9
Live births	55	49	89.1	26	20	76.9
Total	154	127	82.5	140	94	67.1

Table 11. Distribution of Primary Covariates Among Participating and Nonparticipating Veterans — Cerebrospinal Malformations Study

Characteristic	Analysis Category	% of Veterans in Category	
		Participants	Nonparticipants
Age at birth of	≤25	36.6	48 5
first child	26-30	35.7	36 8
	31+	27.2	14 7
	missing	0.5	--
Race	White	85.4	60 3
	Black	9.4	27 9
	Hispanic and other	5.2	1 8
General Technical (GT)	40-89	24.9	42 6
test score	90-109	31.0	30 7
	110-129	31.0	14 7
	130-160	11.7	2 9
	missing	1.4	--
Enlistment status	Drafted	69.5	63 2
	Enlisted	30.5	36 8
Primary military	Tactical	33.8	20 6
occupational specialty	Other	66.2	79 4
Year of entry into Army	1965-66	38.5	39 7
	1967-69	51.6	4 2
	1970-71	9.9	19 1
Years between entry	≤5	33.3	44 1
and birth of first	6-10	37.1	42 6
child	11+	29.6	13 2

OR for total defects among children of black veterans is 3.4 compared with 0.9 for children of white veterans and 0.4 for children of veterans of other races. This trend is also present for major, minor, and suspected defects.

Because of the apparent association of Vietnam service and birth defects among children of black veterans, we examined more closely the types of abnormalities in these infants. The stated major and minor defects are listed in Table 18. No single category of major defect occurred more than once in each veteran group. None of the infants with major defects among Vietnam veterans or non-Vietnam veterans had identical anomalies or any patterns of multiple anomalies suggestive of a syndrome. Of the 13 infants of black Vietnam veterans with minor defects, four had polydactyly (two of whom were siblings), and two siblings had supernumerary nipples; none of the infants of non-Vietnam veterans had polydactyly or supernumerary nipples. No other minor anomalies occurred more than once.

Table 12. Distribution of Secondary Covariates Among Participating and Nonparticipating Veterans — Cerebrospinal Malformations Study

Characteristic	Analysis Category	% of Veterans in Category	
		Participants	Nonparticipants
Smoking history	<10	33.8	29.4
(average number of cigarettes	10-39	52.6	58.8
per day)	40+	13.6	11.8
Alcohol use	<30	56.3	50.0
(average number of drinks	30-89	23.0	22.1
per month)	90+	19.2	27.9
	missing	1.4	—
Educational attainment	<12	11.3	25.0
(in years)	12-15	70.9	66.2
	16+	17.8	8.8
Marital status	Married	89.2	70.6
(current)	Not married	10.8	29.4
Regular drug use in Army	None	78.4	75.0
(at least once a week	Marijuana only	14.6	17.6
for at least 3 months)	Hard drugs	7.0	5.9
	missing	—	1.5

Table 13. Definition and Categorization of Covariates Obtained From Hospital Records and Distribution Among Participating Children, by Cohort Status of Fathers — Cerebrospinal Malformations Study

Characteristic (of Mother)	Analysis Category	Children in Category			
		Vietnam		Non-Vietnam	
		%	No.	%	No.
Maternal age	≤24	44.9	57	39.4	37
	25-29	29.1	37	39.4	37
	30+	16.5	21	16.0	15
	missing	9.5	12	5.3	5
Gravida	1	37.8	48	38.3	36
	2	26.8	34	31.9	30
	3+	24.4	31	20.2	19
	missing	11.0	14	9.6	9

When we considered transfer records in the analysis (Table 19), the number of children in each defect category either remained the same or changed by only one or two cases. The crude ORs are virtually identical to those based on birth records only.

When we considered only defects recorded in the final diagnosis or discharge summary of the birth record in the analysis, the rate of total defects dropped to less than half of the rate for defects recorded anywhere on the birth record (Table 20). ORs also changed. For major defects, the crude OR is 0.8 (95% CI = 0.5-1.5) and for minor defects, the crude OR is 1.6 (95% CI = 0.9-3.2).

Table 21 shows an analysis of stated defects on birth records by major organ systems. While the numbers of cases are quite small in some categories, most of the ORs are close to 1.0. The largest excess is seen for digestive system anomalies (crude OR = 2.1, 95% CI = 0.9-4.6). Table 22 shows the numbers and crude rates for selected congenital anomalies (mostly major). The number of affected infants is too small for formal analysis.

Table 14. Distribution of Primary Covariates Among Participating Children, by Cohort Status of Fathers — Cerebrospinal Malformations Study

Characteristic (of Veteran)	Analysis Category	Children in Category			
		Vietnam		Non-Vietnam	
		%	No.	%	No.
Age at birth of child	≤25	39.4	50	33.0	31
	26-30	35.4	45	35.1	33
	31+	24.4	31	31.9	30
	missing	0.8	1	0.0	0
Race	White	87.4	111	83.0	78
	Black	8.7	11	10.6	10
	Hispanic and other	3.9	5	6.4	6
General Technical (GT) test score	040-089	27.6	35	21.3	20
	090-109	33.9	43	25.5	24
	110-129	27.6	35	37.2	35
	130-160	9.5	12	14.9	14
	missing	1.6	2	1.1	1
Enlistment status	Drafted	70.1	89	69.2	65
	Enlisted	29.9	38	30.9	29
Primary military occupational specialty	Tactical	42.5	54	24.5	23
	Other	57.5	73	75.5	71
Year of entry into Army	1965-66	31.5	40	45.7	43
	1967-69	62.2	79	37.2	35
	1970-71	6.3	8	17.0	16
Years between entry and birth	≤5	33.1	42	33.0	31
	6-10	40.9	52	31.9	30
	11+	26.0	33	35.1	33

Table 15. Distribution of Secondary Covariates Among Participating Children, by Cohort Status of Fathers — Cerebrospinal Malformations Study

Characteristic (of Veteran)	Analysis Category	Children in Category			
		Vietnam		Non-Vietnam	
		%	No.	%	No.
Smoking history (average number of cigarettes per day)	<10	30.7	39	36.2	34
	10-39	56.7	72	47.9	45
	40+	12.6	16	16.0	15
Alcohol use (average number of drinks per month)	<30	54.3	69	61.7	58
	30-89	22.1	28	23.4	22
	90+	22.8	29	12.8	12
	missing	0.8	1	2.1	2
Educational attainment (in years)	<12	13.4	17	9.6	9
	12-15	72.4	92	68.1	64
	16+	14.2	18	22.3	21
Marital status (current)	Married	86.6	110	92.6	87
	Not married	13.4	17	7.5	7
Regular drug use in Army (at least once a week for at least 3 months)	None	77.2	98	79.8	75
	Marijuana only	12.6	16	18.1	17
	Hard drugs	10.2	13	2.1	2

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Table 16. Number of Children With Birth Defects Recorded on Birth Records, Crude R.ites per 100 Total Births Among Vietnam and Non-Vietnam Veterans, and Crude and Adjusted Odds Ratios, by Category of Defect

| Defect Category | Vietnam (N = 1791) | | Non-Vietnam (N = 1575) | | Crude Results | | Multivariate Result; | | | |
| | | | | | | | Model 1[a] | | Mod(i 2[b] | |
	Rate	No.	Rate	No.	OR	95% CI	OR	95% CI	OR	!i;% CI
Total	7.3	130	7.1	112	1.0	0.8-1.3	1.0[c]	0.8-1.4	1.0[c]	·)8-1.3
Major	2.9	51	2.4	37	1.2	0.8-1.9	1.1	0.7-1.8	1.2	·)8-1.9
Minor	3.2	58	3.4	54	0.9	0.6-1.4	1.0[c]	0.7-1.5	0.9[d]	·)6-1.3
Suspected	1.2	21	1.3	21	0.9	0.5-1.6	0.9	0.5-1.7	—	—

[a] Model 1 contains the primary covariates, maternal age, and gravidity.
[b] Model 2 contains the primary and secondary covariates, maternal age, and gravidity.
[c] Standardized for race. Stratum-specific ORs are presented in Table 17.
[d] Standardized for alcohol use.

5.2.2 Other Perinatal Outcomes

Low Birth Weight

As Table 23 shows, the rates of low birth weight (<2500 g) are similar for both ci oups (5.6% and 5.5%, respectively). The crude OR is 1.0 (95% CI = 0.8-1.4). The mean birth weights of children of Vietnam and non-Vietnam veterans are 3,366 g and 3,:i70 g, respectively.

Perinatal Mortality

The rates of stillbirth are 5.6 and 5.7 per 1,000 total births for children of Vietnam and non-Vietnam veterans, respectively (crude OR = 1.0, 95% CI = 0.4-2.4) (Table 24). Fo early neonatal deaths (deaths before discharge from the hospital of birth), the rates are 8.9 a d 4.4 per 1,000 total births, respectively (crude OR = 2.0, 95% CI = 0.8-4.9). The adjusted OF ior all perinatal deaths is somewhat larger than the crude OR, but the 95% CIs for both the crude and the adjusted ORs include unity.

Because of the racial differences in ORs for birth defects, we conducted a stratified analysis of perinatal mortality by race (Table 25). While the numbers of cases are sma l, the excess in early neonatal deaths seems to be primarily among children of white veterans.

In Table 26, the causes of stillbirths and early neonatal deaths among children of white Vietnam and white non-Vietnam veterans are listed. Among stillbirths, the largest categ ory in both cohorts is death due to unknown causes. Among early neonatal deaths, prematurity/ low birth weight and congenital malformations account for all the deaths in both groups. There are eight cases of prematurity-related death among children of Vietnam veterans and three cases among children of non-Vietnam veterans. There are six neonatal deaths associated with congenital malformations among children of Vietnam veterans and none among children of non-Vietnam veterans.

5.2.3 Comparison of the General Birth Defects Study Subsample to the VES Interview Sample

We compared the rates and crude ORs of reported birth defects and reported infant deaths in the entire VES interview population (Part A) with the rates and ORs in that portion of the interview population that makes up the GBD Study sample (Table 27). Our purpose was to determine if the GBD subsample (in total and within each race group) is representative of the interview population for these two outcomes.

For reported birth defects, the GBD Study sample appears to be very representative of the interview population for both the total sample and for white children (Table 27); ORs for the

Table 17. Number of Children With Birth Defects Recorded on Birth Records, Crude Rates per 100 Total Births Among Vietnam and Non-Vietnam Veterans, and Crude and Adjusted Odds Ratios, by Race and Category of Defect

Defect Category and Race	Vietnam Rate	Vietnam No.	Non-Vietnam Rate	Non-Vietnam No.	Crude Results OR	Crude Results 95% CI	Model 1[a] OR	Model 1[a] 95% CI	Model 2[b] OR	Model 2[b] 95% CI
Total										
White	6.8	103	7.2	93	0.9	0.7-1.3	0.9	0.7-1.2	0.9	0.7-1.2
Black	14.8	21	4.9	9	3.4	1.5-7.6	3.3	1.5-7.5	3.2	1.4-7.4
Hispanic and other	4.4	6	10.4	10	0.4	0.1-1.1	0.4	0.1-1.2	0.4	0.1-1.2
Major										
White	2.8	42	2.4	31	1.2	0.7-1.9	1.1	0.7-1.7	1.1	0.7-1.8
Black	4.2	6	1.1	2	4.0	0.8-20.1	3.9	0.8-19.8	4.1	0.8-21.0
Hispanic and other	2.2	3	4.2	4	0.5	0.1-2.4	0.5	0.1-2.4	0.5	0.1-2.5
Minor										
White	2.9	44	3.2	42	0.9	0.6-1.4	0.9	0.6-1.4	0.8	0.5-1.3
Black	9.2	13	3.3	6	3.0	1.1-8.0	2.9	1.1-8.0	2.5	0.9-7.2
Hispanic and other	0.7	1	6.3	6	–	–	0.1	0.0-1.0	0.1	0.0-0.9
Suspected										
White	1.1	17	1.5	20	0.7	0.4-1.4	–	–	–	–
Black	1.4	2	0.5	1	2.6	0.2-29.0	–	–	–	–
Hispanic and other	1.5	2	0.0	0	–	–	–	–	–	–

[a] Model 1 contains the primary covariates, maternal age, and gravidity.
[b] Model 2 contains the primary and secondary covariates, maternal age, and gravidity.

Table 18. Listing of Major and Minor Birth Defects Recorded on Birth Records of Children of Black Vietnam and Non-Vietnam Veterans

	Vietnam No. Cases	Vietnam Defect	Non-Vietnam No. Cases	Non-Vietnam Defect
Major	1	Patent ductus arteriosus	1	Coarctation of aorta
	1	Microcephaly	1	Microcephaly
	1	Imperforate anus		
	1	Congenital hip dislocation		
	1	Clubfoot		
	1	Pes valgus		
Minor	1	Unspecified congenital heart disease	1	Unspecified congenital heart disease
	4	Polydactyly (2 sibs)	1	Macrostomia
	2	Supernumerary nipples (sibs)	1	Macroglossia
	1	Thick tongue	1	Low set ears
	1	Short palpebral tissue	1	Undescended testicle
	1	Single umbilical artery	1	Inversion of left foot
	2	Birthmarks (skin)		
	1	Undescended testicle		

Table 19. Number of Children With Birth Defects Recorded on Either the Birth Record or Transfer Record, Crude Rates per 100 Total Births Among Vietnam and Non-Vietnam Veterans, and Crude Odds Ratio, by Category of Defect

Defect Category	Vietnam (N=1791) Rate	Vietnam (N=1791) No.	Non-Vietnam (N=1575) Rate	Non-Vietnam (N=1575) No.	Crude Results OR	Crude Results 95% CI
Total	7.2	129	7.1	111	1.0	0.8-1.3
Major	2.9	52	2.4	37	1.2	0.8-1.9
Minor	3.2	58	3.4	53	1.0	0.7-1.4
Suspected	1.1	19	1.3	21	0.8	0.4-1.5

Table 20. Number of Children With Birth Defects Recorded Only on the Discharge Sun nary, Crude Rates per 100 Total Births Among Vietnam and Non-Vietnam Veterans and Crude Odds Ratio, by Category of Defect

Defect Category	Vietnam (N=1791)		Non-Vietnam (N=1575)		Crude Results	
	Rate	No.	Rate	No.	OR	95% CI
Total	3.0	54	2.9	45	1.1	0.7-1 6
Major	1.3	23	1.5	24	0.8	0.5-1 5
Minor	1.5	26	0.9	14	1.6	0.9-3 2
Suspected	0.3	5	0.4	7	0.6	0.2-2 0

Table 21. Number of Children With Birth Defects Stated on Birth Records, Crude Rates per 1000 Total Births Among Vietnam and Non-Vietnam Veterans, and Crude and Adjusted Odds Ratios, by Organ System of Defect

Organ System[c]	Vietnam (N=1791)		Non-Vietnam (N=1575)		Crude Results		Multivariate Results			
							Model 1[a]		Model 2[b]	
	Rate	No.	Rate	No.	OR	95% CI	OR	95% CI	OR	95% CI
Nervous system	2.2	4	1.3	2	—	—	—	—	—	—
Eye	0.6	1	0.0	0	—	—	—	—	—	—
Ear, face, neck	5.6	10	7.0	11	0.8	0.3-1.9	—	—	—	—
Cardiovascular	5.6	10	5.1	8	1.1	0.4-2.8	—	—	—	—
Respiratory	0.6	1	0.6	1	—	—	—	—	—	—
Digestive	10.1	18	5.1	8	2.0	0.9-4.6	2.0	0.8-4.8	—	—
Genital	8.9	16	8.3	13	1.1	0.5-2.3	0.9	0.4-2.0	—	—
Urinary	1.1	2	0.6	1	—	—	—	—	—	—
Musculoskeletal	20.7	37	20.3	32	1.0	0.6-1.6	1.0	0.6-1.6	1.0	0.3-1.6
Integument	15.1	27	12.7	20	1.2	0.7-2.1	1.2	0.7-2.3	—	—
Chromosomal	1.1	2	1.3	2	—	—	—	—	—	—
Other/unspecified	0.6	1	0.0	0	—	—	—	—	—	—

[a] Model 1 contains the primary covariates, maternal age, and gravidity.
[b] Model 2 contains the primary and secondary covariates, maternal age, and gravidity.
[c] Children with suspected defects are not included. A child may be counted in more than one organ system.

Table 22. Number of Children With Selected Birth Defects Stated on Birth Records and Crude Rates per 1000 Total Births Among Vietnam and Non-Vietnam Veterans

Defect[a]	Vietnam (N=1791)		Non-Vietnam (N=1575)	
	Rate	No.	Rate	No.
Anencephaly	0.6	1	0.0	0
Spina bifida	0.0	0	0.6	1
Hydrocephalus	1.1	2	0.0	0
Cleft palate	0.0	0	0.6	1
Cleft lip/palate	2.2	4	1.3	2
Esophageal atresia	0.0	0	0.0	0
Anorectal atresia	1.1	2	0.0	0
Polydactyly	3.4	6	1.9	3
Limb reduction defects	0.6	1	0.0	0
Hypospadias (males only)	4.3	4	1.3	1
Congenital hip dislocation	2.2	4	3.2	5
Down's syndrome	0.0	0	1.3	2

[a] Children with suspected defects are not included. A child may be counted in more than one defect category.

two populations are virtually identical. In contrast, the OR for black children in the GBD subsample is higher (1.8) than the OR for black children in the interview population (1.3).

For reported infant deaths, the GBD Study sample does not appear to be representative of the interview population. The OR for white children in the GBD subsample is 5.5 compared

Table 23. Number of Children With Low Birth Weight (<2500 Grams), Crude Rates per 100 Total Births Among Vietnam and Non-Vietnam Veterans, and Crude and Adjusted Odds Ratios

Condition	Vietnam (N=1771)[a]		Non-Vietnam (N=1561)[a]		Crude Results		Model 1[b]		Model 2[c]	
	Rate	No.	Rate	No.	OR	95% CI	OR	95% CI	OR	95% CI
Low birth weight	5.6	99	5.5	85	1.0	0.8-1.4	1.1	0.8-1.4	1.1	0.8-1.5

a For 20 children of Vietnam veterans and 14 children of non-Vietnam veterans, birth weight was not recorded on the hospital birth record; these children have been omitted from this analysis.
b Model 1 contains the primary covariates, maternal age, and gravidity.
c Model 2 contains the primary and secondary covariates, maternal age, and gravidity.

Table 24. Numbers of Perinatal Deaths, Stillbirths, and Early Neonatal Deaths, Crude Rates per 1000 Total Births Among Vietnam and Non-Vietnam Veterans, and Crude and Adjusted Odds Ratios

Condition	Vietnam (N=1791)		Non-Vietnam (N=1575)		Crude Results		Model 1[a]		Model 2[b]	
	Rate	No.	Rate	No.	OR	95% CI	OR	95% CI	OR	95% CI
Perinatal Deaths	14.5	26	10.2	16	1.4	0.8-2.7	1.6	0.8-3.1	–	–
Stillbirths	5.6	10	5.7	9	1.0	0.4-2.4	–	–	–	–
Early neonatal deaths	8.9	16	4.4	7	2.0	0.8-4.9	–	–	–	–

a Model 1 contains the primary covariates, maternal age, and gravidity.
b Model 2 contains the primary and secondary covariates, maternal age, and gravidity.

with an OR of 1.2 for white children in the entire interview population. This contributes to an OR for all GBD children of 1.8 compared with 1.0 for all interview children. The numbers of reported infant deaths among nonwhite children in the GBD subsample are very small, and the rates are difficult to interpret.

5.2.4 Special Analyses Among Subgroups of Vietnam Veterans

Analyses within subgroups of Vietnam veterans were done for major birth defects, minor birth defects, perinatal deaths, and low birth weight. Offspring of Vietnam veterans were categorized according to five components of their fathers' Vietnam experience: self-reported combat exposure, self-reported drug use in the Army, perceived herbicide exposure, year of entry into the Army, and primary MOS. Each multivariate OR is adjusted for all other components of the Vietnam experience.

Table 25. Number of Perinatal Deaths, Stillbirths, and Early Neonatal Deaths, Crude Rates Per 1000 Total Births Among Vietnam and Non-Vietnam Veterans, and Crude Odds Ratio, by Race

Characteristics	Vietnam		Non-Vietnam		Crude Results	
	Rate	No.	Rate	No.	OR	95% CI
Perinatal Deaths						
White	14.5	22	7.7	10	1.9	0.9-4.0
Black	7.0	1	32.8	6	0.2	0-1.8
Hispanic and other	22.2	3	0.0	0	–	–
Stillbirths						
White	5.3	8	5.4	7	1.0	0.4-2.7
Black	7.0	1	10.9	2	0.6	0.1-7.2
Hispanic and other	7.4	1	0.0	0	–	–
Early Neonatal Deaths						
White	9.2	14	2.3	3	4.0	1.2-14.0
Black	0.0	0	21.9	4	–	–
Hispanic and other	14.8	2	0.0	0	–	–

Table 26. Numbers of Perinatal Deaths, Including Stillbirths and Early Neonatal Deaths Among Children of White Vietnam and Non-Vietnam Veterans, by Cause of Death

	Vietnam	Non-Vietnam
Stillbirths		
Cord-related asphyxia	0	1
Maternal diabetes	1	0
Preeclampsia	2	0
Fetal malnutrition	1	0
Premature rupture of membranes	0	1
Placental abnormality	0	1
Unknown	4	4
Neonatal Deaths		
Prematurity/low birth weight related	8	3
Birth defects	6	0
Congenital heart defects	2	0
Chromosomal anomalies	1	0
Anencephaly	1	0
Polycystic kidneys	1	0
Multiple anomalies	1	0

There is little variability in the risk of major defects across the subgroups of Vietnam veterans examined (Table 28). With respect to minor defects (Table 29), children of Vietnam veterans with a tactical primary MOS had a lower risk of minor anomalies (crude OR = 0.5, 95% CI = 0.3-1.0). Crude ORs for perinatal deaths showed little variability across components of the Vietnam experience (Table 30). There is an excess risk of low birth weight among children of "hard drug" users (crude OR = 1.9, 95% CI = 1.0-3.6) (Table 31). Multivariate adjustment using Models 1 and 2 yields adjusted ORs of 2.2 and 2.6, respectively.

5.3 MISCLASSIFICATION ANALYSIS

We compared the veterans' responses about birth defects in children with the presence and type of defects recorded on hospital birth records. We included 1,758 children of Vietnam veterans and 1,544 children of non-Vietnam veterans in this misclassification

Table 27. A Comparison of Reported Birth Defects and Infant Deaths Among Children in the Entire VES Interview Sample and Children in the GBD Study Subsample: Crude Rates of Birth Defects per 100 Total Births and Crude Rates of Infant Deaths per 1000 Live Births Among Vietnam and Non-Vietnam Veterans, and Crude Odds Ratio, by Race

Race	Vietnam		Non-Vietnam		Crude Odds Ratio	
	Interview Sample	GBD Subsample	Interview Sample	GBD Subsample	Interview Sample	GBD Subsample
Reported Birth Defects						
Total	6.5	6.7	5.0	5.3	1.3	1.3
White	6.9	7.2	5.2	5.7	1.4	1.3
Black	5.1	5.0	3.9	2.8	1.3	1.8
Hispanic and other	3.2	2.3	4.3	4.4	0.8	0.5
Reported Infant Deaths						
Total	12.0	11.5	11.8	6.5	1.0	1.8
White	12.3	12.9	10.4	2.4	1.2	5.5
Black	9.9	0.0	17.2	34.3	0.6	--
Hispanic and other	12.4	7.8	17.8	11.1	0.7	0.7

Table 28. Number of Children With *Major Birth Defects* Recorded on Birth Records, Crude Rates per 100 Total Births Among Vietnam and Non-Vietnam Veterans, and Crude and Adjusted Odds Ratios for Children of Vietnam Veterans, by Component of Vietnam Experience

| | | | Crude Results | | Multivariate Results | | | |
| | | | | | Model 1[a] | | Model 2[b] | |
Experience	Rate	No.[c]	OR	95% CI	OR	95% CI	OR	95% CI
				Non-Vietnam				
	2.3	37	—	—				
				Vietnam				
Reported Combat Exposure[d]								
Low	2.7	13	1.0	—	1.0	—	1.0	—
Mid	3.6	17	1.4	0.7-2.8	1.1	0.5-2.5	1.1	0.5-2.5
High	2.6	10	1.0	0.4-2.2	0.8	0.3-2.0	0.8	0.3-2.0
Very high	2.6	10	1.0	0.4-2.2	0.7	0.3-1.8	0.7	0.3-1.9
Reported Drug Use in Army								
None	2.9	39	1.0	—	1.0	—	1.0	—
Marijuana only	2.8	9	1.0	0.5-2.0	1.0	0.5-2.1	1.1	0.5-2.3
Hard drugs	2.2	3	0.7	0.2-2.5	0.8	0.2-2.8	1.0	0.3-3.7
Reported Herbicide Exposure[d]								
None	2.8	23	1.0	—	1.0	—	1.0	—
Low	3.0	16	1.1	0.6-2.1	1.3	0.6-2.6	1.4	0.7-2.8
Mid	2.8	11	1.0	0.5-2.1	1.3	0.6-2.9	1.4	0.6-3.1
High	2.1	1	0.8	0.1-5.8	1.1	0.1-9.0	1.4	0.2-12.3
Year of Entry into Army								
1965-66	2.8	19	1.0	—	1.0	—	1.0	—
1967-69	3.0	29	1.1	0.6-1.9	1.0	0.5-1.8	0.9	0.5-1.8
1970-71	1.8	3	0.6	0.2-2.2	0.6	0.2-2.1	0.6	0.2-2.2
Primary Military Occupational Specialty								
Nontactical	2.6	31	1.0	—	1.0	—	1.0	—
Tactical	3.4	20	1.3	0.7-2.3	1.5	0.8-3.0	1.6	0.8-3.1

[a] Model 1 contains the primary covariates. Each multivariate result is also adjusted for the other components of the Vietnam experience. No interactions were assessed.
[b] Model 2 contains the primary and secondary covariates.
[c] Sum of cases over strata may be less than total numbers presented in previous analyses because of missing values for covariates.
[d] See Volume II, Appendix E, for methods used to create combat and herbicide exposure indices.

analysis. (Thirty-three children of Vietnam veterans and 31 of non-Vietnam veterans reported at Lovelace Medical Foundation (LMF) were not reported at Research Triangle Institute (RTI) and, consequently, could not be included in the misclassification analysis.) The basic results of the misclassification analysis for the presence or absence of a birth defect are shown in Table 32. Suspected defects were not included in this analysis. Several misclassification parameters are shown in Table 32 for Vietnam and non-Vietnam veterans; these include positive and negative predictive values (PPVs and NPVs), sensitivity and specificity, percent agreement, and the *kappa* index.

Overall, the interview responses were not highly predictive of the presence of a defect in the hospital birth record for either group of veterans. The PPV among Vietnam veterans is lower than that among non-Vietnam veterans (24.8% versus 32.9%). Sensitivity is also slightly lower in the Vietnam group (27.1% versus 30.3%), as was the *kappa* index of agreement (20.9% versus 27.6%). The crude OR is 1.3 based on the interview data (117 X 1462/82 X 1641). On the other hand, the crude OR is 1.1 (107 X 1455/89 X 1651) based on

Table 29. Number of Children With *Minor Birth Defects* Recorded on Birth Records, Crude Rates per 100 Total Births Among Vietnam and Non-Vietnam Veterans, and Crude and Adjusted Odds Ratios for Children of Vietnam Veterans, by Component of Vietnam Experience

Experience	Rate	No.[c]	Crude Results OR	Crude Results 95% CI	Model 1[a] OR	Model 1[a] 95% CI	Model 2[b] OR	Model 2[b] 95% CI
Non-Vietnam								
	3.4	54	—	—				
Vietnam								
Reported Combat Exposure[d]								
Low	3.7	18	1.0	—	1.0	—	1.0	—
Mid	3.0	14	0.8	0.4-1.6	1.1	0.5-2.3	1.2	0.5-2.5
High	3.4	13	0.9	0.4-1.9	1.3	0.6-2.8	1.1	0.5-2.6
Very high	2.6	10	0.7	0.3-1.5	1.2	0.5-3.1	1.3	0.5-3.4
Reported Drug Use in Army								
None	2.9	39	1.0	—	1.0	—	1.0	—
Marijuana only	4.4	14	1.5	0.8-2.8	1.6	0.8-3.1	1.7	0.8-3.4
Hard drugs	3.7	5	1.3	0.5-3.3	1.1	0.4-3.0	0.8	0.2-2.9
Reported Herbicide Exposure[d]								
None	3.7	31	1.0	—	1.0	—	1.0	—
Low	2.3	12	0.6	0.3-1.2	0.6	0.3-1.2	0.7	0.3-1.5
Mid	3.6	14	1.0	0.5-1.8	0.9	0.4-1.8	0.8	0.4-1.8
High	2.1	1	0.6	0.1-4.2	0.5	0.1-4.0	0.7	0.1-6.1
Year of Entry into Army								
1965-66	3.6	24	1.0	—	1.0	—	1.0	—
1967-69	2.9	28	0.8	0.5-1.4	0.9	0.5-1.7	1.0	0.5-1.8
1970-71	3.6	6	1.0	0.4-2.5	1.1	0.4-2.9	1.0	0.3-3.1
Primary Military Occupational Specialty								
Nontactical	3.8	46	1.0	—	1.0	—	1.0	—
Tactical	2.0	12	0.5	0.3-1.0	0.4	0.2-0.9	0.4	0.2-1.0

[a] Model 1 contains the primary covariates. Each multivariate result is also adjusted for the other components of the Vietnam experience. No interactions were assessed.
[b] Model 2 contains the primary and secondary covariates.
[c] Sum of cases over strata may be less than total numbers presented in previous analyses because of missing values for covariates.
[d] See Volume II, Appendix E, for methods used to create combat and herbicide exposure indices.

the birth records data. Although the overall agreement between records and interviews for the presence of defects is relatively poor for both groups of veterans, the slightly poorer agreement for Vietnam veterans explains the lower records-based OR. Although Vietnam veterans' responses were less predictive than those of non-Vietnam veterans for the presence of any defect or a defect of the same organ system, the two cohorts were equally predictive in naming a specific condition that resulted in a perfect agreement of the ICD-9 codes from the interview and the birth record (16.2% versus 15.9%) (Table 33).

In Table 34, we present an analysis of sensitivity for total, major, and minor defects. Of the defects documented in birth records, 27.1% were also reported by Vietnam veterans and 30.3% were reported by non-Vietnam veterans. Sensitivity is higher for major defects in both groups (40.8% versus 44.4%) and much lower for minor or unspecified defects (15.5% versus 20.8%).

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Table 30. Number of *Perinatal Deaths* Recorded on Birth Records, Crude Rates per ⁻000 Total Births Among Vietnam and Non-Vietnam Veterans, and Crude and Adjusted Odds Ratios for Children of Vietnam Veterans, by Component of Vietnam Experience

| | | | | | Multivariate Results | | | |
| | | | Crude Results | | Model 1[a] | | Model 2[b] | |
Experience	Rate	No.[c]	OR	95% CI	OR	95% CI	OR	95% CI
					Non-Vietnam			
	10.2	16	—	—				
					Vietnam			
Reported Combat Exposure[d]								
Low	20.8	10	1.0	—	—[e]	—	—	—
Mid	8.5	4	0.4	0.1-1.3				
High	13.0	5	0.6	0.2-1.8				
Very high	12.9	5	0.6	0.2-1.8				
Reported Drug Use in Army								
None	13.6	18	1.0	—	—	—	—	—
Marijuana only	12.5	4	0.9	0.3-2.7				
Hard drugs	29.6	4	2.2	0.7-6.7				
Reported Herbicide Exposure[d]								
None	10.9	9	1.0	—	—	—	—	—
Low	24.7	13	2.3	1.0-5.4				
Mid	10.3	4	0.9	0.3-3.1				
High	0.0	0	—	—				
Year of Entry into Army								
1965-66	16.4	11	1.0	—	—	—	—	
1967-69	11.5	11	0.7	0.3-1.6				
1970-71	24.2	4	1.5	0.5-4.7				
Primary Military Occupational Specialty								
Nontactical	13.4	16	1.0	—	—	—	—	
Tactical	16.9	10	1.3	0.6-2.8				

[a] Model 1 contains the primary covariates. Each multivariate result is also adjusted for the other components of the Vietnam experience. No interactions were assessed.
[b] Model 2 contains the primary and secondary covariates.
[c] Sum of cases over strata may be less than total numbers presented in previous analyses because of missing values for covariates.
[d] See Volume II, Appendix E, for methods used to create combat and herbicide exposure indices.
[e] Number of cases too small for multivariate modeling.

5.4 CEREBROSPINAL MALFORMATIONS

In Tables 35 and 36, we present the veterans' descriptions of their children's birth defects along with the information obtained from hospital birth records (if the record was received) for all live-born children in the CSM Study and for those stillborn children with either a reported or records-based cerebrospinal malformation. These listings and Table 2 show that more than twice the number of potential live-born cases were initially selected for inclusion in the CSM Study among children of Vietnam veterans (55 children) than among children of non-Vietnam veterans (26 children). This is because Vietnam veterans reported more children with CSMs and possible CSMs in the original VES interview than did non-Vietnam veterans. This discrepancy is not apparent among stillbirths, which were reported similarly in both cohorts.

Table 31. Number of Children With *Low Birth Weight* (<2500 Grams) Recorded on Birth Records, Crude Rates per 100 Total Births Among Vietnam and Non-Vietnam Veterans, and Crude and Adjusted Odds Ratios for Children of Vietnam Veterans, by Component of Vietnam Experience

Experience	Rate	No.[c]	Crude Results OR	Crude Results 95% CI	Model 1[a] OR	Model 1[a] 95% CI	Model 2[b] OR	Model 2[b] 95% CI
				Non-Vietnam				
	5.4	85	—	—				
				Vietnam				
Reported Combat Exposure[d]								
Low	7.1	34	1.0	—	1.0	—	1.0	—
Mid	4.5	21	0.6	0.4-1.1	0.6	0.3-1.1	0.7	.4-1.4
High	5.5	21	0.8	0.4-1.3	0.8	0.4-1.4	0.9	.5-1.7
Very high	4.8	18	0.7	0.4-1.2	0.7	0.3-1.4	0.9	.4-1.9
Reported Drug Use in Army								
None	5.3	69	1.0	—	1.0	—	1.0	—
Marijuana only	5.3	17	1.0	0.6-1.7	1.1	0.6-2.0	1.1	.6-2.0
Hard drugs	9.6	13	1.9	1.0-3.6	2.2	1.1-4.4	2.6	1.3-5.4
Reported Herbicide Exposure[d]								
None	5.6	46	1.0	—	1.0	—	1.0	—
Low	6.0	31	1.1	0.7-1.7	1.2	0.7-2.1	1.2	.7-2.1
Mid	4.9	19	0.9	0.5-1.5	0.9	0.5-1.6	0.8	.4-1.6
High	6.5	3	1.2	0.4-3.9	1.2	0.3-4.4	1.4	.4-5.3
Year of Entry into Army								
1965-66	6.5	43	1.0	—	1.0	—	1.0	—
1967-69	5.1	48	0.8	0.5-1.2	0.8	0.5-1.3	0.7	.4-1.1
1970-71	4.8	8	0.7	0.3-1.6	0.6	0.3-1.3	0.6	.3-1.4
Primary Military Occupational Specialty								
Nontactical	6.0	71	1.0	—	1.0	—	1.0	—
Tactical	4.8	28	0.8	0.5-1.2	0.8	0.5-1.5	0.7	.4-1.2

[a] Model 1 contains the primary covariates. Each multivariate result is also adjusted for the other components of the Vietnam experience. No interactions were assessed.

[b] Model 2 contains the primary and secondary covariates.

[c] Sum of cases over strata may be less than total numbers presented in previous analyses because of missing values for covariates.

[d] See Volume II, Appendix E, for methods used to create combat and herbicide exposure indices.

Because negative responses were not verified and record retrieval rates varied considerably by cohort status, we did not calculate or compare rates of CSM cases in the two cohorts; the results are expressed as numbers of verified cases.

Among reported stillbirths, birth records documented five CSMs in children of Vietnam veterans (three cases of anencephaly, one of spina bifida, one of hydrocephalus) and six in children of non-Vietnam veterans (four cases of anencephaly, two of hydrocephalus) (Table 37). This yields a PPV (among records received) of 6.4% for children of Vietnam veterans and of 8.1% for children of non-Vietnam veterans. For 10 of these 11 CSM cases among reported stillbirths, the veteran, during the interview, did not mention a defect.

Birth records documented 21 CSMs (7 cases of anencephaly, 8 of spina bifida, and 6 of hydrocephalus) in live-born children of Vietnam veterans and 6 CSMs (3 cases of anencephaly, 2 of spina bifida, and 1 of hydrocephalus) among live-born children of non-Vietnam veterans (Table 38). These results yield PPVs of 42.9% and 30.0%, respectively.

Table 32. Results of Misclassification Analyses: Numbers of Children With and Without Birth Defects in the Interview and on Birth Records, Positive Predictive Value (PPV), Negative Predictive Value (NPV), Sensitivity, Specificity, Percent Agreement, and Kappa Index for Vietnam and Non-Vietnam Veterans

Vietnam				Non-Vietnam			
	Interview				Interview		
Birth Records	Defect	No Defect	Total	Birth Records	Defect	No Defect	Total
Defect[a]	29	78	107	Defect[a]	27	62	89
No defect	88	1563	1651	No defect	55	1402	1455
Total	117	1641	1758[b]	Total	82	1462	1544[b]

PPV:	24.8%		PPV:	32.9%	
NPV:	95.2%		NPV:	95.8%	
Sensitivity:	27.1%		Sensitivity:	30.3%	
Specificity:	94.7%		Specificity:	96.2%	
% Agreement:	90.6%		% Agreement:	92.4%	
Kappa index:	20.9%		Kappa index:	27.6%	

[a] Defined as major and minor defects; suspected defects were not included.
[b] Thirty-three children of Vietnam veterans and 31 children of non-Vietnam veterans were reported at LMF but not during the VES interview; their birth records could not be matched with the interview, and they have been omitted from this analysis.

When live-born and stillborn children are combined, there are 26 CSMs among children of Vietnam veterans and 12 among children of non-Vietnam veterans. The PPVs (among records received) for all children in the CSM Study are 20.5% for children of Vietnam veterans and 12.8% for children of non-Vietnam veterans.

There are no siblings among the cases listed in Tables 35 and 36. With the exception of two children in the Vietnam group, all records-based diagnoses were stated on hospital birth records. One exception was a case of hydrocephalus that was stated on a transfer hospital record on the day following the birth. The second exception was a case of spina bifida documented on a birth certificate. Case No. 15 in the non-Vietnam group (Table 36) was documented on the birth record as a "possible" spina bifida. This suspected case was later diagnosed as lipoma and has been classified under the "No CSM" category in Table 38.

Table 33. Positive Predictive Value (%) of the Interview Response for the Presence of Defects Recorded on Birth Records for Children of Vietnam and Non-Vietnam Veterans—Any Defect, a Defect in the Same Organ System, and the Same Defect (ICD-9) Code

	Vietnam		Non-Vietnam	
Level of Matching	%	No.	%	No.
Any defect	24.8	29	32.9	27
Same organ system	21.4	25	26.8	22
Same ICD-9 code	16.2	19	15.9	13

Table 34. Sensitivity (%) for Total, Major, and Minor Defects Stated on Birth Records Among Vietnam and Non-Vietnam Veterans

	Vietnam		Non-Vietnam	
Defect Category	%	No.	%	No.
Total	27.1	29	30.3	27
Major	40.8	20	44.4	16
Minor	15.5	9	20.8	11

Table 35. Children of *Vietnam Veterans* in Cerebrospinal Malformations Study: Includes Are Stillbirths With Cerebrospinal Malformations and All Live-Born Children

Child No.	Reported Status	Father's Description	Birth Defect(s) on Record
1	Stillborn	—	Anencephaly
2	Stillborn	—	Anencephaly
3	Stillborn	Baby was not developed from drug mom took	Anencephaly
4	Stillborn	—	Spina bifida
5	Stillborn	—	Hydrocephalus
6	Stillborn	Anencephaly	—[a]
7	Died <1 year	Anencephaly	Anencephaly
8	Died <1 year	Anencephaly	Anencephaly
9	Live-born	Spina bifida	Spina bifida
10	Died <1 year	Open spine, spina bifida	None
11	Live-born	Spina bifida	Spina bifida with hydrocephalus
12	Live-born	Spina bifida	Spina bifida with hydrocephalus
13	Live-born	Spina bifida	Spina bifida
14	Live-born	Spina bifida, hydrocephalus	Spina bifida with hydrocephalus
15	Live-born	Spina bifida, hydrocephalus	Spina bifida with hydrocephalus
16	Died <1 year	Open spine	Spina bifida
17	Live-born	Spina bifida, hydrocephalus	Spina bifida with hydrocephalus
18	Live-born	Water on the brain	—[a]
19	Live-born	Hydrocephalus	Hydrocephalus
20	Live-born	Hydrocephalus	None
21	Live-born	Hydrocephalus	Hydrocephalus
22	Live-born	Fluid, abnormal liquid on brain	None
23	Live-born	Hydrocephalus, water head	None
24	Live-born	Hydrocephalus	Hydrocephalus, schizencephaly
25	Live-born	Fluid on brain	None
26	Died <1 year	Hydrocephalus	Hydrocephalus
27	Live-born	Water lump on head	None
28	Live-born	Fluid on head	Hydrocephalus
29	Live-born	Water head	—[a]
30	Live-born	Large growth on top of head	None
31	Live-born	Tumor on back	None
32	Live-born	Meningocele cyst on back	—[a]
33	Live-born	Bump on back, caused blood vessel	None of nervous system
34	Died <1 year	Missing part of brain	Anencephaly, spina bifida
35	Died <1 year	Part of brain unformed, unattached	Anencephaly
36	Live-born	Underdeveloped nervous system	None
37	Died <1 year	Spinal cord deformities	None of nervous system
38	Died <1 year	Did not develop a brain sufficiently	Anencephaly
39	Live-born	Schizencephaly, brain malfunction	None
40	Live-born	Short neck, deformities	None
41	Live-born	Enlarged head	None
42	Died <1 year	Back of head caved in	Anencephaly
43	Live-born	Extended forehead	—[a]
44	Live-born	Deformed skull	None
45	Live-born	Abnormal cranium, flat on top	—[a]
46	Live-born	Part of vertabrae missing, back	—[a]
47	Live-born	Small opening at base of spine	None
48	Live-born	Hole base of spine, indentation	None
49	Live-born	Hole at base of tailbone	None
50	Live-born	Hole on rump	None
51	Live-born	Spine trouble	None
52	Died <1 year	Severe deformity to entire body	Hydrocephalus
53	Live-born	Multiple birth defects	None of nervous system
54	Died <1 year	Organs deformed	Multiple anomalies including congenital cerebral cyst
55	Died <1 year	Badly deformed	None
56	Live-born	Cyst on neck	None of nervous system
57	Live-born	Tethered cord	None
58	Live-born	Bone at back of head missing	None of nervous system
59	Live-born	Defect born structure of brain	None
60	Live-born	Extremely large head	None
61	Died <1 year	Underdeveloped, missing top of head	Anencephaly

[a] Birth record not obtained.

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Table 36. Children of *Non-Vietnam Veterans* In Cerebrospinal Malformations Study: Included Are Stillbirths With Cerebrospinal Malformations and All Live-Born Children

Child No.	Reported Status	Father's Description	Birth Defect(s) on Record
1	Stillborn	—	Anencephaly, spina bifida
2	Stillborn	—	Anencephaly, spina bifida
3	Stillborn	—	Anencephaly
4	Stillborn	Head not developed from eyes up	Anencephaly
5	Stillborn	—	Hydrocephalus
6	Stillborn	—	Hydrocephalus
7	Died <1 year	Spina bifida, water on brain	—[a]
8	Died <1 year	Spina bifida	Spina bifida
9	Died <1 year	Spina bifida	Spina bifida with hydrocephalus
10	Live-born	Spina bifida	None
11	Live-born	Spina bifida, open spine	Multiple anomalies, none of nervous system
12	Live-born	Hydrocephalus	None of nervous system
13	Live-born	Hydrocephalus	Hydrocephalus
14	Died <1 year	Enlarged brain, tumor	None
15	Live-born	Tethered spine	Possible spina bifida
16	Live-born	Malformation in brain	None of nervous system
17	Died <1 year	Back of head never developed	Anencephaly
18	Live-born	Top of head open	None of nervous system
19	Live-born	Skull wasn't calcified	None of nervous system
20	Died <1 year	Skull not fully formed	Anencephaly
21	Live-born	Premature fusion of skull	None
22	Live-born	Opening on tailbone	None
23	Live-born	Indentation of skull	None
24	Live-born did not meet	Spinal cord and lumbar joint	None
25	Live-born	Opening in neck, hole	None
26	Died <1 year	Brain and head did not develop	Anencephaly
27	Live-born	Group of blood vessels, back of head	—[a]
28	Live-born	Open cyst on neck	None
29	Died <1 year	Underdeveloped skull	—[a]
30	Live-born	Rupture on back of skull	—[a]
31	Live-born	Cyst on top of head	—[a]
32	Live-born	Growth on side of head, blood	—[a]

[a] Birth record not obtained.

Table 37. Results of Agreement Analyses of Cerebrospinal Malformations Among Stillbirths, for Children of Vietnam and Non-Vietnam Veterans

	Vietnam					Non-Vietnam			
	Interview					Interview			
Birth Records	CSM	PCSM	No CSM	Total	Birth Records	CSM	PCSM	No CSM	Total
Anencephaly	—	—	3	3	Anencephaly	—	1	3	4
Spina bifida	—	—	1	1	Spina bifida	—	—	-	—
Hydrocephalus	—	—	1	1	Hydrocephalus	—	—	2	2
No CSM	—	—	73	73	No CSM	—	—	68	68
Not received	1[a]	1	19	21	Not received	—	—	40	40
Total	1	1	97	99	Total	—	1	113	114

Percent of records received having a CSM = 5/78 = 6.4%

Percent of records received having a CSM = 6/74 = 8.1%

CSM = Cerebrospinal malformation.
PCSM = Possible CSM.
[a] This child was a reported anencephalic.

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Table 38. Results of Agreement Analyses of Cerebrospinal Malformations Among *Live Births*, for Children of Vietnam and Non-Vietnam Veterans

Vietnam						Non-Vietnam					
	Interview						Interview				
Birth Records	AN	SB	HY	PCSM	Total	Birth Records	AN	SB	HY	PCSM	Total
Anencephaly	2	—	—	5	7	Anencephaly	—	—	—	3	3
Spina bifida	—	8	—	—	8	Spina bifida	—	2	—	—	2
Hydrocephalus	—	—	5[a]	1	6	Hydrocephalus	—	—	1	—	1
No CSM	—	1	5	22	28	No CSM	—	2	1	11	14
Not received	—	—	2	4	6	Not received	—	1	—	5	6
Total	2	9	12[a]	32	55	Total	0	5	2	19	26

Percent of records received having
a CSM = 21/49 = 42.9%

Percent of records received having
a CSM = 6/20 = 30.0%

AN = Anencephaly.
SB = Spina bifida.
HY = Hydrocephalus.
CSM = Cerebrospinal malformation.
PCSM = Possible CSM.
[a] One child included here was ineligible for inclusion in the interview analysis based on the date of birth reported in the interview. Consequently, the total number of hydrocephalus cases for the interview is 11 (Part A, Table 15).

6. DISCUSSION

6.1 GENERAL BIRTH DEFECTS STUDY

For most reproductive and child health outcomes studied in the interview (Part A) Vietnam veterans were more likely to report an adverse event than were non-Vietnam veterans. For birth defects, a second source of information not subject to differential reporting was available for a subgroup of children included in the GBD Study. This study had an 80% power to detect a relative risk of 1.4 for total birth defects in the subgroup of children for whom birth records were received. However, the study was not large enough to assess cohort differences for specific birth defects. For all races combined, there were no differences between children of Vietnam and non-Vietnam veterans in the prevalence of total, major, minor, or suspected birth defects documented in hospital birth records. This finding supports the explanation of differential reporting in the interview and the conclusion that (at least for birth defects evident at birth) children of Vietnam veterans were not at increased risk.

The reasons for the apparent racial variation in the association between Vietnam service and total birth defects found in the hospital records substudy are unclear. The findings in black children may be explained, in part, by the multiple occurrence of polydactyly and supernumerary nipples in two families; both defects have been suggested to have a strong genetic component, most likely autosomal dominant inheritance (McKusick, 1986). If the cases of polydactyly and supernumerary nipples are omitted, the excess is no longer significant for minor defects. Also, the results are based on small numbers of children among black and Hispanic veterans and may be due to sampling variability. The GBD Study had adequate power to detect an elevated risk for total birth defects in all races combined. The small number of black and Hispanic and other race children included in this study may not be representative of those children in the entire interview population. The difference in the OR for reported birth defects among black children in the GBD Study compared with the OR among black children in the entire interview population (Table 27) is consistent with this explanation.

Similarly, the results for early neonatal deaths are based on very small numbers show an apparent racial variation, and are difficult to interpret. For this outcome, there is a significant difference between children of white Vietnam veterans and children of white non-Vietnam veterans. This difference may, again, be due to sampling variability. Consistent with this explanation is the large difference with the OR for reported infant deaths among white children in the GBD Study compared with the OR among white children in the entire interview population (Table 27). The difference in these two ORs is due entirely to a very low (and nonrepresentative) rate of reported infant death among white children of non-Vietnam veterans in the GBD subsample.

The veterans in the GBD Study of total birth defects were selected from those veterans who completed the physical examination. Detailed analyses of the examination participants relative to the telephone interview participants did not show different characteristics or health histories (Volume III). In addition, participation in this study was very high in both cohorts, and, moreover, the two cohorts were similar with respect to various demographic and military covariates. Thus, there is no evidence of selection bias or participation bias in this study. Also, the selection of participants in this study was independent of interview reports and, consequently, was unlikely to be biased by potential differential reporting among the two veteran cohorts.