

interview question about birth defects did not specify a time period. Thus, a positive 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 in 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 <sup>a</sup> | 90.7        | 1577 <sup>a</sup> |

<sup>a</sup> 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 Records and Distribution Among Participating Children, by Cohort Status of Fathers – General Birth Defects Study**

| Characteristic<br>(of Mother) | Analysis Category | Children in Category |     |             |     |
|-------------------------------|-------------------|----------------------|-----|-------------|-----|
|                               |                   | Vietnam              |     | Non-Vietnam |     |
|                               |                   | %                    | 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<br>(of Veteran)             | Analysis Category  | Children in Category |      |             |      |
|--|--------------------|----------------------|------|-------------|------|
|  |                    | Vietnam              |      | Non-Vietnam |      |
|  |                    | %                    | 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)<br>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<br>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<br>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<br>(of Veteran)  | Analysis Category | Children in Category |      |             |      |
|---|-------------------|----------------------|------|-------------|------|
|   |                   | Vietnam              |      | Non-Vietnam |      |
|   |                   | %                    | No.  | %           | No.  |
| Smoking history<br>(average number of<br>cigarettes per day)                | <10               | 33.7                 | 604  | 37.0        | 584  |
|   | 10-39             | 51.9                 | 930  | 47.8        | 753  |
|   | 40+               | 14.3                 | 256  | 14.8        | 234  |
|   | missing           | 0.1                  | 2    | 0.4         | 6    |
| Alcohol use<br>(average number of drinks<br>per month)                      | <30               | 56.9                 | 1019 | 57.6        | 908  |
|   | 30-89             | 26.0                 | 465  | 29.2        | 460  |
|   | 90+               | 15.2                 | 273  | 12.4        | 195  |
|   | missing           | 2.0                  | 35   | 0.9         | 14   |
| Educational attainment<br>(in years)  | <12               | 12.6                 | 226  | 9.6         | 152  |
|   | 12-15             | 70.0                 | 1255 | 68.2        | 1076 |
|   | 16+               | 17.4                 | 311  | 21.9        | 346  |
|   | missing           | 0.0                  | 0    | 0.2         | 3    |
| Marital status<br>(current)   | Married           | 84.5                 | 1515 | 85.8        | 1353 |
|   | Not married       | 15.5                 | 277  | 14.2        | 224  |
| Regular drug use in Army<br>(at least once a week<br>for at least 3 months) | None              | 74.0                 | 1326 | 80.6        | 1271 |
|   | Marijuana only    | 17.9                 | 320  | 12.6        | 198  |
|   | 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<br>Population     | 100.0   | 154 | 100.0       | 112 |
| Nonparticipants                        |         |     |             |     |
| Unable to locate or<br>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         | 4   |
| Participants – Records<br>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 first child                  | ≤25                | 36.6                      | 48.5            |
|  | 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                       | 11.8            |
| General Technical (GT) test score            | 40-89              | 24.9                      | 42.6            |
|  | 90-109             | 31.0                      | 39.7            |
|  | 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 occupational specialty      | Tactical           | 33.8                      | 20.6            |
|  | Other              | 66.2                      | 79.4            |
| Year of entry into Army                      | 1965-66            | 38.5                      | 39.7            |
|  | 1967-69            | 51.6                      | 41.2            |
|  | 1970-71            | 9.9                       | 19.1            |
| Years between entry and birth of first child | ≤5                 | 33.3                      | 41.1            |
|  | 6-10               | 37.1                      | 42.6            |
|  | 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<br>(average number of cigarettes<br>per day)                | <10               | 33.8                      | 29.4            |
|   | 10-39             | 52.6                      | 58.8            |
|   | 40+               | 13.6                      | 11.8            |
| Alcohol use<br>(average number of drinks<br>per month)                      | <30               | 56.3                      | 50.0            |
|   | 30-89             | 23.0                      | 22.1            |
|   | 90+               | 19.2                      | 27.9            |
|   | missing           | 1.4                       | —               |
| Educational attainment<br>(in years)  | <12               | 11.3                      | 25.0            |
|   | 12-15             | 70.9                      | 66.2            |
|   | 16+               | 17.8                      | 8.8             |
| Marital status<br>(current)   | Married           | 89.2                      | 70.6            |
|   | Not married       | 10.8                      | 29.4            |
| Regular drug use in Army<br>(at least once a week<br>for at least 3 months) | None              | 78.4                      | 75.0            |
|   | Marijuana only    | 14.6                      | 17.6            |
|   | 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<br>(of Mother) | Analysis Category | Children in Category |     |             |     |
|-------------------------------|-------------------|----------------------|-----|-------------|-----|
|                               |                   | Vietnam              |     | Non-Vietnam |     |
|                               |                   | %                    | No. | %           | No. |
| Maternal age                  | ≤24               | 44.9                 | 57  | 39.4        | 57  |
|                               | 25-29             | 29.1                 | 37  | 39.4        | 57  |
|                               | 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<br>(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)<br>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<br>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<br>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<br>(of Veteran)  | Analysis Category | Children in Category |     |             |     |
|---|-------------------|----------------------|-----|-------------|-----|
|   |                   | Vietnam              |     | Non-Vietnam |     |
|   |                   | %                    | No. | %           | No. |
| Smoking history<br>(average number of<br>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<br>(average number of drinks<br>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<br>(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<br>(current)   | Married           | 86.6                 | 110 | 92.6        | 87  |
|   | Not married       | 13.4                 | 17  | 7.5         | 7   |
| Regular drug use in Army<br>(at least once a week<br>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   |

**Table 16. 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 Category of Defect**

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

<sup>a</sup> Model 1 contains the primary covariates, maternal age, and gravidity.

<sup>b</sup> Model 2 contains the primary and secondary covariates, maternal age, and gravidity.

<sup>c</sup> Standardized for race. Stratum-specific ORs are presented in Table 17.

<sup>d</sup> 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 groups (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 3,370 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). For early neonatal deaths (deaths before discharge from the hospital of birth), the rates are 8.9 and 4.4 per 1,000 total births, respectively (crude OR = 2.0, 95% CI = 0.8-4.9). The adjusted OR for 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 small, 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 category 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 |     | Non-Vietnam |     | Crude Results |          | Multivariate Results |          |                      |          |
|--------------------------|---------|-----|-------------|-----|---------------|----------|----------------------|----------|----------------------|----------|
|                          | Rate    | No. | Rate        | No. | OR            | 95% CI   | Model 1 <sup>a</sup> |          | Model 2 <sup>b</sup> |          |
|                          |         |     |             |     |               |          | OR                   | 95% CI   | OR                   | 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   | —             | —        | —                    | —        | —                    | —        |

<sup>a</sup> Model 1 contains the primary covariates, maternal age, and gravidity.

<sup>b</sup> 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   |                                      | Non-Vietnam |                                      |
|-------|-----------|--------------------------------------|-------------|--------------------------------------|
|       | No. Cases | Defect                               | No. Cases   | 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) |     | Non-Vietnam (N=1575) |     | Crude Results |         |
|-----------------|------------------|-----|----------------------|-----|---------------|---------|
|                 | Rate             | No. | Rate                 | No. | OR            | 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 Summary, Crude Rates per 100 Total Births Among Vietnam and Non-Vietnam Veterans and Crude Odds Ratio, by Category of Defect**

| Defect Category | Vietnam<br>(N=1791) |     | Non-Vietnam<br>(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 <sup>c</sup> | Vietnam<br>(N=1791) |     | Non-Vietnam<br>(N=1575) |     | Crude Results |         | Multivariate Results |         |                      |         |
|---------------------------|---------------------|-----|-------------------------|-----|---------------|---------|----------------------|---------|----------------------|---------|
|                           | Rate                | No. | Rate                    | No. | OR            | 95% CI  | Model 1 <sup>a</sup> |         | Model 2 <sup>b</sup> |         |
|                           |                     |     |                         |     |               |         | 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                  | 0.5-1.6 |
| 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   | —             | —       | —                    | —       | —                    | —       |

<sup>a</sup> Model 1 contains the primary covariates, maternal age, and gravidity.

<sup>b</sup> Model 2 contains the primary and secondary covariates, maternal age, and gravidity.

<sup>c</sup> 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 <sup>a</sup>        | Vietnam<br>(N=1791) |     | Non-Vietnam<br>(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   |

<sup>a</sup> 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<br>(N=1771) <sup>a</sup> |     | Non-Vietnam<br>(N=1561) <sup>a</sup> |     | Crude Results |         | Multivariate Results |         |                      |         |
|------------------|----------------------------------|-----|--------------------------------------|-----|---------------|---------|----------------------|---------|----------------------|---------|
|                  | Rate                             | No. | Rate                                 | No. | OR            | 95% CI  | Model 1 <sup>b</sup> |         | Model 2 <sup>c</sup> |         |
|                  |                                  |     |                                      |     |               |         | 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 |

<sup>a</sup> 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.

<sup>b</sup> Model 1 contains the primary covariates, maternal age, and gravidity.

<sup>c</sup> 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<br>(N=1791) |     | Non-Vietnam<br>(N=1575) |     | Crude Results |         | Multivariate Results |         |                      |        |
|-----------------------|---------------------|-----|-------------------------|-----|---------------|---------|----------------------|---------|----------------------|--------|
|                       | Rate                | No. | Rate                    | No. | OR            | 95% CI  | Model 1 <sup>a</sup> |         | Model 2 <sup>b</sup> |        |
|                       |                     |     |                         |     |               |         | 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 | —                    | —       | —                    | —      |

<sup>a</sup> Model 1 contains the primary covariates, maternal age, and gravidity.

<sup>b</sup> 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           | 0.0-1.8  |
| 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 |
|--------------------------------------|---------|-------------|
| <b>Stillbirths</b>                   |         |             |
| 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           |
| <b>Neonatal Deaths</b>               |         |             |
| Prematurity/low birth weight related | 8       | 3           |
| <b>Birth defects</b>                 | 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 |
| <b>Reported Birth Defects</b> |                  |               |                  |               |                  |               |
| 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           |
| <b>Reported Infant Deaths</b> |                  |               |                  |               |                  |               |
| 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**

| Experience                               | Rate | No. <sup>c</sup> | Crude Results |         | Multivariate Results |         |                      |          |
|--|------|------------------|---------------|---------|----------------------|---------|----------------------|----------|
|  |      |                  | OR            | 95% CI  | Model 1 <sup>a</sup> |         | Model 2 <sup>b</sup> |          |
|  |      |                  |               |         | OR                   | 95% CI  | OR                   | 95% CI   |
| <u>Non-Vietnam</u>                       |      |                  |               |         |                      |         |                      |          |
|  | 2.3  | 37               | —             | —       |                      |         |                      |          |
| <u>Vietnam</u>                           |      |                  |               |         |                      |         |                      |          |
| Reported Combat Exposure <sup>d</sup>    |      |                  |               |         |                      |         |                      |          |
| 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 <sup>d</sup> |      |                  |               |         |                      |         |                      |          |
| 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  |

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

<sup>b</sup> Model 2 contains the primary and secondary covariates.

<sup>c</sup> Sum of cases over strata may be less than total numbers presented in previous analyses because of missing values for covariates.

<sup>d</sup> 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. <sup>c</sup> | Crude Results |         | Multivariate Results |         |                      |         |
|--|------|------------------|---------------|---------|----------------------|---------|----------------------|---------|
|  |      |                  | OR            | 95% CI  | Model 1 <sup>a</sup> | 95% CI  | Model 2 <sup>b</sup> | 95% CI  |
| <u>Non-Vietnam</u>                       |      |                  |               |         |                      |         |                      |         |
|  | 3.4  | 54               | —             | —       |                      |         |                      |         |
| <u>Vietnam</u>                           |      |                  |               |         |                      |         |                      |         |
| Reported Combat Exposure <sup>d</sup>    |      |                  |               |         |                      |         |                      |         |
| 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 <sup>d</sup> |      |                  |               |         |                      |         |                      |         |
| 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 |

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

<sup>b</sup> Model 2 contains the primary and secondary covariates.

<sup>c</sup> Sum of cases over strata may be less than total numbers presented in previous analyses because of missing values for covariates.

<sup>d</sup> 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%).



**Table 30. Number of Perinatal Deaths Recorded on Birth Records, Crude Rates per 1,000 Total Births Among Vietnam and Non-Vietnam Veterans, and Crude and Adjusted Odds Ratios for Children of Vietnam Veterans, by Component of Vietnam Experience**

| Experience                               | Rate | No. <sup>c</sup> | Multivariate Results |         |                      |        |                      |        |
|--|------|------------------|----------------------|---------|----------------------|--------|----------------------|--------|
|  |      |                  | Crude Results        |         | Model 1 <sup>a</sup> |        | Model 2 <sup>b</sup> |        |
|  |      |                  | OR                   | 95% CI  | OR                   | 95% CI | OR                   | 95% CI |
| <u>Non-Vietnam</u>                       |      |                  |                      |         |                      |        |                      |        |
|  | 10.2 | 16               | —                    | —       |                      |        |                      |        |
| <u>Vietnam</u>                           |      |                  |                      |         |                      |        |                      |        |
| Reported Combat Exposure <sup>d</sup>    |      |                  |                      |         |                      |        |                      |        |
| Low                                      | 20.8 | 10               | 1.0                  | —       | — <sup>e</sup>       | —      | —                    | —      |
| 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 <sup>d</sup> |      |                  |                      |         |                      |        |                      |        |
| 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 |                      |        |                      |        |

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

<sup>b</sup> Model 2 contains the primary and secondary covariates.

<sup>c</sup> Sum of cases over strata may be less than total numbers presented in previous analyses because of missing values for covariates.

<sup>d</sup> See Volume II, Appendix E, for methods used to create combat and herbicide exposure indices.

<sup>e</sup> 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. <sup>c</sup> | Crude Results |         | Multivariate Results |         |                      |         |
|--|------|------------------|---------------|---------|----------------------|---------|----------------------|---------|
|  |      |                  | OR            | 95% CI  | Model 1 <sup>a</sup> | 95% CI  | Model 2 <sup>b</sup> | 95% CI  |
| <b>Non-Vietnam</b>                       |      |                  |               |         |                      |         |                      |         |
|  | 5.4  | 85               | —             | —       |                      |         |                      |         |
| <b>Vietnam</b>                           |      |                  |               |         |                      |         |                      |         |
| Reported Combat Exposure <sup>d</sup>    |      |                  |               |         |                      |         |                      |         |
| 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                  | 0.4-1.4 |
| High                                     | 5.5  | 21               | 0.8           | 0.4-1.3 | 0.8                  | 0.4-1.4 | 0.9                  | 0.5-1.7 |
| Very high                                | 4.8  | 18               | 0.7           | 0.4-1.2 | 0.7                  | 0.3-1.4 | 0.9                  | 0.4-1.9 |
| 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                  | 0.6-2.0 |
| 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 <sup>d</sup> |      |                  |               |         |                      |         |                      |         |
| 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                  | 0.7-2.1 |
| Mid                                      | 4.9  | 19               | 0.9           | 0.5-1.5 | 0.9                  | 0.5-1.6 | 0.8                  | 0.4-1.6 |
| High                                     | 6.5  | 3                | 1.2           | 0.4-3.9 | 1.2                  | 0.3-4.4 | 1.4                  | 0.4-5.3 |
| 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                  | 0.4-1.1 |
| 1970-71                                  | 4.8  | 8                | 0.7           | 0.3-1.6 | 0.6                  | 0.3-1.3 | 0.6                  | 0.3-1.4 |
| 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                  | 0.4-1.2 |

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

<sup>b</sup> Model 2 contains the primary and secondary covariates.

<sup>c</sup> Sum of cases over strata may be less than total numbers presented in previous analyses because of missing values for covariates.

<sup>d</sup> 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**

| Birth Records       | Vietnam   |           |                   | Non-Vietnam         |           |           |                   |
|---------------------|-----------|-----------|-------------------|---------------------|-----------|-----------|-------------------|
|                     | Interview |           |                   | Birth Records       | Interview |           |                   |
|                     | Defect    | No Defect | Total             |                     | Defect    | No Defect | Total             |
| Defect <sup>a</sup> | 29        | 78        | 107               | Defect <sup>a</sup> | 27        | 62        | 89                |
| No defect           | 88        | 1563      | 1651              | No defect           | 55        | 1402      | 1457              |
| Total               | 117       | 1641      | 1758 <sup>b</sup> | Total               | 82        | 1464      | 1544 <sup>b</sup> |
| 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%     |           |                   |

<sup>a</sup> Defined as major and minor defects; suspected defects were not included.

<sup>b</sup> 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 PPV (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**

| Level of Matching | Vietnam |     | Non-Vietnam |     |
|-------------------|---------|-----|-------------|-----|
|                   | %       | 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**

| Defect Category | Vietnam |     | Non-Vietnam |     |
|-----------------|---------|-----|-------------|-----|
|                 | %       | 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: Include: 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                               | — <sup>a</sup>  |
| 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                        | — <sup>a</sup>  |
| 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                                | — <sup>a</sup>  |
| 30        | Live-born       | Large growth on top of head               | None  |
| 31        | Live-born       | Tumor on back                             | None  |
| 32        | Live-born       | Meningocele cyst on back                  | — <sup>a</sup>  |
| 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                         | — <sup>a</sup>  |
| 44        | Live-born       | Deformed skull                            | None  |
| 45        | Live-born       | Abnormal cranium, flat on top             | — <sup>a</sup>  |
| 46        | Live-born       | Part of vertebrae missing, back           | — <sup>a</sup>  |
| 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   |

<sup>a</sup> Birth record not obtained.

**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              | — <sup>a</sup>                             |
| 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       | Spinal cord and lumbar joint did not meet | 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      | — <sup>a</sup>                             |
| 28        | Live-born       | Open cyst on neck                         | None                                       |
| 29        | Died <1 year    | Underdeveloped skull                      | — <sup>a</sup>                             |
| 30        | Live-born       | Rupture on back of skull                  | — <sup>a</sup>                             |
| 31        | Live-born       | Cyst on top of head                       | — <sup>a</sup>                             |
| 32        | Live-born       | Growth on side of head, blood             | — <sup>a</sup>                             |

<sup>a</sup> Birth record not obtained.

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

| Birth Records | Vietnam        |      |        |       | Non-Vietnam   |     |      |        |       |
|---------------|----------------|------|--------|-------|---------------|-----|------|--------|-------|
|               | Interview      |      |        |       | Interview     |     |      |        |       |
|               | 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 <sup>a</sup> | 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.

<sup>a</sup> This child was a reported anencephalic.

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

| Birth Records   | Vietnam   |    |                 |      |       | Birth Records  | Non-Vietnam |    |    |      |       |
|---|-----------|----|-----------------|------|-------|--|-------------|----|----|------|-------|
|   | Interview |    |                 |      |       |  | Interview   |    |    |      |       |
|   | AN        | SB | HY              | PCSM | Total |  | AN          | SB | HY | PCSM | Total |
| Anencephaly   | 2         | —  | —               | 5    | 7     | Anencephaly  | —           | —  | —  | 3    | 3     |
| Spina bifida  | —         | 8  | —               | —    | 8     | Spina bifida   | —           | 2  | —  | —    | 2     |
| Hydrocephalus   | —         | —  | 5 <sup>a</sup>  | 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 <sup>a</sup> | 32   | 55    | Total  | 0           | 5  | 2  | 19   | 26    |
| Percent of records received having<br>a CSM = 21/49 = 42.9% |           |    |                 |      |       | Percent of records received having<br>a CSM = 6/20 = 30.0% |             |    |    |      |       |

AN = Anencephaly.

SB = Spina bifida.

HY = Hydrocephalus.

CSM = Cerebrospinal malformation.

PCSM = Possible CSM.

<sup>a</sup> 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.