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Using Active Medical Record Review and Capture-Recapture Methods to Investigate the Prevalence of Down Syndrome among Live-Born Infants in Colorado

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ABSTRACT

Background: In a 1994 comparison of Down Syndrome (DS) birth prevalence rates between 17 states (CDC '94), the average rate for the 17 states was 9.2 per 10,000 live–born infants. Colorado residents had the highest birth prevalence rate (12.3 per 10,000). We investigated the accuracy of this report.

Methods: All children born to Colorado residents during 1989–1991 and reported to CRCSN as having DS went through an active medical record review to eliminate false-positive cases. To adjust for case underascertainment, we used capture-recapture methods to estimate the number of cases missed during surveillance activities. After eliminating false-positive cases and adjusting for case underascertainment, we estimated a new prevalence rate.

Results: A total of 198 children born to Colorado residents during 1989–1991 were reported to CRCSN as having DS. Of these, 151 (76%) were definite cases, 25 (13%) were false-positive cases, and 22 (11 %) were inconclusive. A log-linear capture-recapture model applied to the definite cases resulted in an estimate of three missing cases. Therefore, the estimated total number of definite DS cases in Colorado was 155 (95% CI = (153–160)) and the new prevalence rate for 1989–1991 was 9.6 per 10,000 live-born infants.

Conclusions: Identifying false-positive cases and applying capture-recapture methods can help identify problems with birth defects surveillance efforts and provide direction for improvements. In Colorado, these techniques identified a problem of false-positive and inconclusive reports of DS. Case underascertainment was discovered not to be a problem.

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INTRODUCTION

In a 1994 comparison of Down Syndrome (DS) birth prevalence rates among 17 states (CDC '94), the average rate for the 17 states was 9.2 per 10,000 live–born infants. Colorado residents had the highest birth prevalence rate (12.3 per 10,000).

The data for Colorado were provided by Colorado Responds to Children with Special Needs (CRCSN), Colorado's birth defects monitoring and prevention program located at the Colorado Department of Public Health and Environment. Part of CRCSN's objective in monitoring and characterizing the prevalence of birth defects is to identify the potential for prevention activities and respond to public concern, which requires understanding of and ability to explain rates that may appear high. Therefore, CRCSN staff investigated the DS rate reported in the 1994 study using methods that resulted in a more accurate prevalence rate for live-born infants.

Accurate prevalence rates are essential to birth defects monitoring and surveillance programs. Two key steps in obtaining accurate rates for reporting and comparison purposes are minimizing false-positive cases and minimizing case underascertainment. All surveillance systems are vulnerable to false-positive case reports that will result in inaccurate rates. Additionally, accurate counts of cases that account for case underascertainment are key to monitoring efforts (LaPorte et al. '96). No surveillance program should assume their surveillance activities have ascertained all cases, and no prevalence study should be reported without attempts to estimate case underascertainment (Hook and Regal, '92). Accounting for both false-positive reports and case underascertainment increases the accuracy of prevalence rates.

For passive surveillance systems such as CRCSN, a common way to minimize false-positive cases is to identify them through an active medical record review of all reported cases and then eliminate them from any prevalence estimates. After eliminating false-positive

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TABLE 1. Three-source multiple recapture history

		Source 1			
		Present		Absent	
		Source 2		Source 2	
		Present	Absent	Present	Absent
Source 3	*Present*	A	B	C	D
	Absent	E	F	G	?

cases, one can adjust for case underascertainment by using capture-recapture methods to estimate the number of cases missed by surveillance activities. Capture-recapture methods were once used primarily to estimate wildlife populations, such as the number of fish in a certain lake (Pollock, '91), but have recently been adapted for use in epidemiology. Traditional methods for calculating prevalence rates include aggregating the data by eliminating duplicate case reports and using the total number of unduplicated case reports as the numerator and the total population as the denominator. Capture-recapture methods allow the overlapping data reports to be used to estimate the number of cases missed by surveillance activities, thereby adjusting for case underascertainment (McCarty et al., '93). Capture-recapture methods have been used to evaluate the completeness of cancer registries, sources of traumatic spinal cord injury data, and surveillance of specific congenital anomalies such as congenital rubella syndrome and fetal alcohol syndrome (Robles et al., '88; Johnson et al., '97; Cochi et al., '89; Egeland et al., '95). We report how these methods were combined with an active medical record review to aid in an investigation of an increased prevalence of DS in Colorado.

METHODS

We identified DS cases from CRCSN. CRCSN collected data on children who were born to a Colorado resident and in whom a congenital anomaly or medical or environmental risk factor for delay was diagnosed before their third birthday. Diagnostic data were collected passively from multiple sources such as vital records (birth and death certificates), hospital discharge records, voluntary physician reports, genetics clinics and other specialty medical clinics, and other epidemiologic surveillance systems. Data were also collected actively through medical record review for special studies, although the method of case ascertainment was primarily passive. We then linked data to identify unique cases and retain all reported diagnoses and reporting sources for each case. We obtained demographic data by linking the diagnostic data collected by CRCSN to a Colorado birth certificate using a unique identifier.

Medical record review of DS cases

To identify false-positive reports of DS, a trained medical record abstractor reviewed medical records of all children born to Colorado residents during 1989–1991 who were reported to CRCSN as having DS. All reported cases were in live born infants. For a given DS case, the abstractor searched the medical records from each source that reported the case until a confirming laboratory test was found or the list of data sources was exhausted. If no confirming laboratory test was found in the medical records, the abstractor contacted physicians identified from the medical records and requested the information. A reported DS case was considered a definite case only if documentation of a laboratory test confirming a karyotype of Trisomy 21 was found in a medical record. Reported cases were classified as false-positive if there were no confirming laboratory reports and no documentation of any characteristic of DS was discovered during the medical records review. Cases were considered inconclusive if one or more characteristics of DS were documented but no confirming laboratory test was found.

Capture-recapture estimate of case underascertainment

After we completed medical record reviews and eliminated false-positive cases, we used capture-recapture methods to evaluate the completeness of reported DS for children born to Colorado residents during 1989–1991. One implicit assumption of capture-recapture is that all the cases have been diagnosed accurately (Hook and Regal, '95). Therefore, it was necessary to complete the active reviews and eliminate false-positive cases before using capture-recapture methods to estimate the number of cases missed by surveillance activities.

To use capture-recapture methods, data must be collected by at least two sources that overlap in their reporting of cases. The data are first placed into a 2^k contingency table, where k is the number of sources used to ascertain the cases. The data in the contingency table represent the full multiple recapture history of the cases, and the empty cell in the table represents the number of cases not ascertained by any of the sources (Wittes, '74). The data in the nonempty cells are used to estimate the empty cell. An example of a three-source combination is provided in Table 1. Each of the eight cells (2^3) represents the number of cases reported by each of those sources (i.e., "A" represents the number of cases reported by sources 1, 2, and 3). The cell containing "?" represents the number of cases not reported by any of the sources.

The number of cases in the missing cell can be estimated using simple, straightforward mathematical equations when only two sources are used to collect the data. When more than two sources are used, log-linear models can be fit to the 2^k cells of data to estimate the empty cell (Egeland, '95). Because capture-recapture estimates are influenced by the probabilistic relations between reporting sources, failure to assess the dependencies between sources can result in a biased estimate of the number of missing cases.

We used methods similar to those used by Fienburg ('72) and Wittes ('74) to identify dependencies between the data sources reporting DS. First, all independent models containing each of the two, three, four, and five source combinations were fit to the data using log-linear modeling to estimate the total number of cases in the population. We then graphed these estimates so we could observe any extreme underestimates or overestimates of the known population. Models that resulted in extreme underestimates indicated a possible positive dependency between the sources in the model, and extreme overestimates indicated a possible negative dependency. Chi-square statistics were used to identify statistically significant dependencies between pairs of sources. Each of the models containing the independent sources and one two-source interaction term were then fit to the data. We identified models that resulted in a statistically significant improvement over the independent model using likelihood ratio tests. The same method was repeated to test for statistically significant three- and four-source interactions.

We adjusted for significant dependencies identified using the above methods by including the appropriate interaction term(s) in the log-linear model. The log likelihood ratio chi-squared statistic G^2 was used to assess the fit of the log-linear model to the data. The model was then fit to the data to provide an estimate for the missing cell. Finally, the 95% goodness-of-fit based confidence interval (CI) was calculated for the new estimate of the total number of DS cases (Regal and Hook, '84). All analysis was accomplished using SAS, 6.12 ('88). For a detailed example of SAS code and output used to accomplish such an analysis see Orton et al. ('99).

Using the capture-recapture estimate of the total number of DS cases, we calculated a new birth prevalence rate on the basis of a total of 159,974 live births for Colorado residents during 1989–1991. A case-ascertainment rate was also calculated by dividing the total number of definite cases ascertained by the new estimate of the number of DS cases.

RESULTS

Medical record review

A total of 198 children born to Colorado residents during 1989–1991 were reported to CRCSN as having DS. Of these, 151 (76%) were definite cases, 25 (13%) were false-positive cases, and 22 (11%) were inconclusive.

TABLE 2. Number of Down syndrome cases among live-born infants of Colorado residents (n = 151) and ascertainment rates by data source: 1989–1991

Source	No. of cases identified	Ascertainment rate
Vital records (I)	72	47.7%
Hospital discharge data (II)	143	94.7%
Active review (III)	17	11.3%
Genetics clinics (IV)	44	29.1%
Other (V)	41	27.2%

Capture-recapture analysis

The following five data sources reported the definite DS cases to CRCSN: 1) vital records, 2) hospital discharge data, 3) active review (special study), 4) genetics clinics, and 5) other (physician report or the Handicapped Children's Program). These sources will be referred to as I, II, III, IV and V, respectively. Table 2 presents the counts of cases and the ascertainment rates for each source before adjusting for missing cases. Table 3 presents the data recapture history by source of ascertainment.

Hospital discharge data identified 95% of the cases (n=143); 35 cases (23%) were ascertained only by hospital discharge data. The only other single source of ascertainment for cases was vital records, which identified only three cases (2%) which no other sources identified. The majority of the cases (75%) were ascertained by at least two sources. The methods used to identify dependencies between the data sources indicated a statistically significant dependency between vital records and active review (source I and source III). We estimated the total population by fitting the 26 independent log-linear models for the two-, three-, four- and five-source combinations to the data. The estimates were graphed and compared with the total number of confirmed cases ascertained using all five sources (n=151) (Table 4). The high estimate produced by the model containing only sources IV and V indicated a possible negative dependency, and the low estimate produced by the model containing sources I and III indicated a possible positive dependency.

The results of the chi-square analyses used to test for dependencies between pairs of sources confirmed the statistically significant dependency between source I and source III ($p<0.01$). The test for the dependency between sources IV and V was not statistically significant, and no other pairs of sources resulted in statistically significant chi-square statistics.

For the independent model containing only the five sources and no interaction terms, the estimate of the number of missing cases was three, and G^2 was 35.35 with 25 degrees of freedom. Compared with this independent model, the only model that resulted in a statistically significant improvement was the model that included each of the five sources and the interaction between sources I and III (likelihood ratio chi-square(1) = 10.3, $p<0.05$). Therefore, the final log-linear model used to estimate the number of cases

TABLE 3. Number of Down syndrome cases identified among live-born infants of Colorado residents by all possible combinations of the five data sources: 1989–1991

			I yes		I no	
III	IV	V	II yes	II no	II yes	II no
yes	yes	yes	1	0	1	0
yes	yes	no	2	0	0	0
yes	no	yes	2	0	2	0
yes	no	no	7	2	0	0
no	yes	yes	3	0	2	1
no	yes	no	14	1	19	0
no	no	yes	9	1	19	0
no	no	no	27	3	35	?

I = vital records, II = hospital discharge data, III = active review, IV = genetics clinics, V = other, yes = cases identified by source, no = case not identified by source.

TABLE 4. Number of Down syndrome cases among live-born infants of Colorado residents (*n*) versus estimates of the total population from independent log-linear models (*N*): 1989–1991

# of sources	I	II	III	IV	V	*n*	*N*
5	X	X	X	X	X	151	153
4	X	X	X	X		151	155
4	X	X	X		X	151	155
4	X	X		X	X	151	154
4	X		X	X	X	116	154
4		X	X	X	X	148	152
3	X	X	X			150	156
3	X	X		X		151	156
3	X	X			X	151	156
3	X		X	X		97	131
3	X		X		X	97	136
3	X			X	X	116	175
3		X	X	X		147	154
3		X	X		X	147	154
3		X		X	X	146	149
3			X	X	X	86	193
2	X	X				150	158
2	X		X			75	87
2	X			X		95	150
2	X				X	97	184
2		X	X			145	162
2		X		X		145	149
2		X			X	145	150
2			X	X		57	187
2			X		X	52	116
2				X	X	77	225

I = vital records, II = hospital discharge data, III = active review, IV = genetics clinics, V = other.

missed during surveillance activities included each of the five sources and the interaction between sources I and III:

$$I + II + III + IV + V + (I*III)$$

This final model resulted in an estimate of three missing cases. Therefore, the estimated number of definite DS cases among infants born to Colorado residents during 1989–1991 was 154 (95% goodness-of-fit based confidence interval 152–159). The value of G^2 was 25.1 with 24 degrees of freedom ($p = 0.40$), indicating a good fit of the model to the data. Based on this estimate, the adjusted prevalence rate of DS was 9.6 per 10,000 live-born infants. The case-ascertainment rate for the time period was 98%.

DISCUSSION

Before this investigation, the estimated prevalence rate of DS for live-born infants of Colorado residents during 1989–1990 was 12.3 per 10,000 live births. This was the highest ranking birth prevalence rate in the 17 state comparison presented in the *MMWR* (CDC, '94). Even after statistical considerations, such a distinction is often the impetus for an investigation. Using an active medical record review and capture-recapture techniques, the estimated prevalence rate of DS for infants born during 1989–1991 to Colorado residents was 9.6 per 10,000 live- born infants. This rate is believed to be a more accurate estimate because it is corrected for false-positive reporting and case underascertainment.

Considering several assumptions is important when capture-recapture analysis is used to estimate the size of a population (Hook and Regal, '95; International Working Group for Disease Monitoring and Forecasting, '95). Implicitly, all cases are assumed to have been accurately diagnosed, appropriately matched between sources, and diagnosed within the time period and geographic boundaries under study. Explicitly, for each source, it is assumed that the probability of being ascertained by that source is the same for each case and that the ascertainment by each source is independent of the other sources. Finally, the population under study is assumed to be closed. We carefully considered each of these assumptions.

Only cases confirmed to be DS through an active review were included in the analysis, and cases were matched appropriately using unique identifiers. Also, only infants born to Colorado residents during 1989–1991 were included. Therefore, the implicit assumptions were met.

With respect to the explicit assumptions, for each of the five sources the probability of being ascertained by that source was assumed to be the same for each DS case. The probability of ascertainment must be equal for all cases within a source but can differ across sources. The assumption regarding independence of sources was dealt with by modeling the significant dependency between sources I and III in the final log-linear model. Meeting the assumption of closure when estimating the size of a human population it is difficult, if not impossible. However, in practicality, closure was assumed because the population was relatively stable with respect to births and infant deaths.

The statistically significant interaction between vital records and active review makes intuitive sense. In this analysis, most cases reported to CRCSN that were involved in an active medical record review as part of a special study were first identified by another reporting source such as vital records. Therefore, an alternative analysis could have been to eliminate the active medical record review as a source. In general, a subjective assessment of dependencies based on prior knowledge of sources and the grouping of sources is an important consideration. Not only should the model make sense, but known dependencies may also influence investigators' decisions about how sources are defined (Brenner, '95).

The results of the medical record review indicated a false-positive rate of almost 13%. However, 22 cases were inconclusive. Possible ways of handling these cases in the capture-recapture analysis included the following: 1) assume none of them were DS cases and exclude them from the analysis, 2) assume all of them were DS cases and include them in the analysis, or 3) assume about 13% of them were not Down syndrome cases and randomly choose 87% of the 22 unconfirmed cases (n = 19) to include in the analysis. For the main analysis reported above, none of the 22 cases were assumed to be DS. Therefore, all 22 cases were excluded from the capture-recapture analysis. The analysis was also done for the other two options described. When all 22 cases were assumed to be DS and were included in the analysis, the capture-recapture estimate of the number of missing cases was three, so the estimate of the total number of DS cases among infants born to Colorado residents during 1989–1991 was 176 (95% goodness-of-fit based confidence interval 174–182). When 19 of the unconfirmed cases were randomly chosen to be included in the capture-recapture analysis, the estimate of the number of cases missing was again three, so the estimate of the total number of DS cases among infants born to Colorado residents during 1989–1991 was 173 (95% goodness-of-fit based confidence interval 171–179). The prevalence rates calculated using the capture-recapture estimates obtained by including all unconfirmed cases and including 87% of the unconfirmed cases were 11.0 per 10,000 live born infants and 10.8 per 10,000 live-born infants respectively.

Using capture-recapture methods has both advantages and disadvantages. They can improve the accuracy of rates without the additional costs of case finding. They also provide a method for ascertaining the completeness of a registry that receives reports from multiple, overlapping sources and can be used to evaluate the usefulness of specific sources with respect to case ascertainment. However, confirming all reported diagnoses, which is necessary when using capture-recapture to estimate a population defined by the reported diagnoses, may be impractical. Capture-recapture techniques, especially those using many sources and log-linear modeling, may also be too complex for some situations. Two-source capture-recapture techniques, when appropriate, allow for more simplified analysis. One example of this type of analysis is found in Egeland et al. ('95). Additional discussions of the limitations of capture-recapture methodology are available from Brenner ('95) and Hook and Regal ('95).

Eliminating false-positive reports and applying capture-recapture methods can help identify problems with current surveillance efforts and provide direction for improvements. Although the Colorado investigation was prompted by an apparent high rate published in the literature, waiting for this kind of alarm is not necessary to trigger use of capture-recapture methods. Capture-recapture can also be used simply to evaluate the completeness of case ascertainment or efficacy of data reporting/collection sources. In Colorado, these techniques identified a problem of false-positive and inconclusive reports of DS. Case underascertainment was discovered not to be a problem. Examination of the false-positive cases identified through the active medical record review did not identify any consistent characteristics. To resolve the problem of false-positive and inconclusive reports, CRCSN has since added genetic laboratories as a reporting source.

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