Capture–Recapture Analysis of Ascertainment in the British Congenital Cataract Study

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PURPOSE. Active surveillance has not been widely used in ophthalmologic research. The use of capture-recapture analysis to determine completeness of case ascertainment by active surveillance in a national study of congenital cataract is reported.

METHODS. In 1 year in the United Kingdom, all incident diagnoses of congenital and infantile cataract were notified through independent ophthalmic and pediatric active surveillance schemes. Two-source capture-recapture analysis was applied to assess the level of ascertainment of infants (age ≤12 months) by these two schemes.

RESULTS. In a 12-month period, 161 infants with newly diagnosed congenital or infantile cataract were notified. Overall ascertainment was estimated to be 92% complete and higher in the ophthalmic (85%) than in the pediatric (45%) scheme. Comparison with the number of cases expected, from disease frequency reported in existing national congenital anomaly notification systems, suggests previous underascertainment of congenital cataract in such passive reporting systems.

CONCLUSIONS. This study shows the effectiveness of two-source active surveillance in identifying a nationally representative cohort that will provide better information about this disorder than has been available from sources of routinely collected data. (Invest Ophthalmol Vis Sci. 1999; 40:236–239)

Congenital cataract is an important treatable cause of severe visual impairment or blindness in children in industrialized countries. Estimates of incidence have been based on single sources of routinely collected data, such as registers of visual impairment and passive reporting systems for congenital anomalies, in which incomplete ascertainment has been documented.2,3 Active surveillance is an effective method for studying uncommon disorders, and ascertainment can be further improved by using multiple reporting systems. It has been used to study various childhood disorders.4–6

Capture-recapture analysis addresses the problem of underascertainment in epidemiologic studies by providing a method for adjusting derived estimates of disease frequency appropriately.7,8 Adapted from the original two-sample methods used in studying fish and wildlife populations, the technique has been used in studies of various congenital disorders.7,8

We report the application of capture-recapture analysis to determine completeness of case ascertainment by active surveillance in the British Congenital Cataract Study: This national study was established to measure the frequency of congenital cataract and to describe its mode of detection, causes, management, and outcome in the United Kingdom.6 Although ophthalmologists undertake treatment in the United Kingdom, pediatricians are responsible for identifying affected children through the routine ocular examination of all infants (performed nationally in the newborn period and again at 6 to 8 weeks), which includes assessment of the pupillary red reflex with a direct ophthalmoscope.9 They are also responsible for the assessment of children for the presence of associated systemic disorders and for the management of such disorders. There is universal and cost-free access to ophthalmic (treatment) and pediatric (screening) services in the United Kingdom through the National Health Service. Accordingly, newly diagnosed cases were identified through ophthalmologists and pediatricians.

METHODS

For 12 months (October 1995 through September 1996) all newly diagnosed cases of congenital or infantile cataract in the United Kingdom were notified by ophthalmologists participating in a new disorders-specific surveillance scheme established for the study through the British Congenital Cataract Interest Group and comprising 89% of all ophthalmologists identified through a national survey to be involved in the management of infants with cataract. In parallel, but independently, cases were notified by pediatricians through a national scheme previously established by the British Paediatric Surveillance Unit of the Royal College of Paediatrics and Child Health,6 which has facilitated the study of a number of uncommon childhood conditions and has a reporting base that is 92% complete.10 Reporting cards, with which to notify new cases or to confirm that no new cases had been seen, were sent to pediatricians monthly and to ophthalmologists every second month. The two schemes were independent throughout, so each eligible case could be notified through either or both schemes. The reporting bases were also maintained independently, as was communication with participating clinicians in each scheme.

A case was defined as any child, aged 15 years or less, newly diagnosed with congenital or infantile cataract by an ophthalmologist or a pediatrician. This included all new cases known to be present in infancy, or of a congenital cause, or those with salient clinical features indicating early onset, such as morphology, or the presence of other congenital anomalies or nystagmus,11 but diagnosed after infancy.

Once a case was notified, the reporting clinician was sent a form requesting information about mode of detection, cause of cataract, and management undertaken. Identifying details, necessary for matching, including the child’s initials, date of
birth, gender, and eye affected, were also obtained. Successful matching of cases notified to both surveillance schemes required agreement on all four criteria.

To ensure that the assumptions underlying capture-recapture techniques were met, we undertook capture-recapture analysis in the subgroup of newly diagnosed cases in infants born in 1995 or 1996 and diagnosed at age 12 months or less. This secured a closed population, effectively a birth cohort, in which any infant could be identified by either scheme with equal probability. The equations used for calculating the ascertainment-corrected number of cases7,8 and the 95% confidence interval9 of this number are shown.

The method of calculation of the ascertainment-corrected number of cases was the two-source capture-recapture analysis 7,10:

\[
(N) = \left[\frac{(a + b + 1)(a + c + 1)(a + 1)}{a + 1}\right] - 1 \tag{1}
\]

where \( N \) is the total (ascertainment-corrected) number of cases in the population, \( a \) is the cases reported by both schemes, \( b \) is the cases reported by the pediatric scheme only, and \( c \) is the cases reported by the ophthalmic scheme only:

\[
\text{Reported by the ophthalmic scheme} \quad \begin{array}{ll}
\text{Reported by the pediatric scheme} & \text{Yes} & a \\
& \text{No} & c
\end{array}
\]

*True unidentified cases.

The method for calculating confidence intervals for ascertainment-adjusted estimate of the total number of cases was7,12

\[
\text{Var}(N) = \frac{(a + b + 1)(a + c + 1)(b)(c)}{(a + 1)^2(a + 2)} \tag{2}
\]

and 95% confidence intervals were \( N \pm 1.96(\sqrt{\text{Var}(N)}) \).

We calculated the level of ascertainment as the proportion of total expected cases actually notified, expressed as a percentage. The characteristics of cases notified through each source were compared for any evidence of variable ascertainment.

**RESULTS**

Active surveillance by ophthalmologists and pediatricians identified 161 children with newly diagnosed congenital cataract born in 1995 or 1996 and detected in infancy, as shown by source of reporting in Figure 1. Using capture-recapture analysis, it was estimated that 14 cases had not been not identified by either scheme, yielding an ascertainment-adjusted total of 175 (163-187, 95% confidence interval). Overall, ascertainment by active surveillance using both schemes was estimated to be 161 (92%) of 175.

A higher percentage of incident cases were notified through the ophthalmic than through the pediatric surveillance scheme (149 [85%] and 79 [45%], respectively). However, cases reported through the two schemes were similar in laterality, requirement for surgery, age, and context of detection (Table 1). Of the 12 children notified by pediatricians alone, 7 were under the care of ophthalmologists outside the ophthalmic scheme, and 3 were each under the care of, but not notified by, ophthalmologists within the ophthalmic reporting base. The remaining two children died before formal assessment by an ophthalmologist.

**DISCUSSION**

A high level of ascertainment was achieved by two-source active surveillance in this national study of congenital cataract. Capture-recapture analysis is a recognized method for quantifying completeness of ascertainment.7,8,10,11,12 Its valid application requires that certain conditions be fulfilled: the study population must be closed; all people identified by each source must be true cases, randomly ascertained and readily matched from capture to recapture; capture in each sample must be independent of capture in any other sample; and the probabili-
ity of capture in each sample is the same for all subjects in the population.\textsuperscript{7,8} It may be difficult to prove these assumptions.\textsuperscript{8} Variable catchability may exist in any natural population,\textsuperscript{8} and complete independence of reporting sources is rare.\textsuperscript{7} Knowledge of the specific disorder, the sources of data, and the mechanisms of reporting, is required to identify possible deviations from the assumptions.\textsuperscript{14} In addition, in multiple source studies, statistical modeling may be used to attempt to overcome some known biases.\textsuperscript{8}

In the present study, we restricted analysis to a subgroup to identify the closed population of interest, and matching was achieved. There was no evidence of variable catchability (Table 1). Notification of cases by ophthalmologists and pediatricians was independent. Positive dependence in reporting, whereby a case was more likely to be identified in one system if also reported in another, would have resulted in an overestimate of the completeness of ascertainment.\textsuperscript{14} Conversely, negative dependence of sources would have resulted in the reverse error, which is generally of much greater magnitude\textsuperscript{14} and in the present study would imply that more than 92% of cases had been ascertained. Neither positive nor negative dependence, nor both, can be excluded with certainty.\textsuperscript{8,14}

Surveillance has not been widely used in the study of ophthalmologic disorders.\textsuperscript{15} The high level of ascertainment achieved by the ophthalmic surveillance scheme, established within 5 months specifically for this study, suggests that good compliance can be achieved by clinicians without prior experience of active reporting. It may also reflect that participating ophthalmologists were members of the cooperative group responsible for the study. Response may have been further encouraged by maintaining a high level of communication with reporting ophthalmologists through study progress reports, periodic meetings, and personal contact. Although effective, had there been sole reliance on the ophthalmic scheme, 7% of cases would have been missed. This emphasizes the value of using multiple sources to enhance ascertainment.

Begun in 1986, the British Pediatric Surveillance: Unit scheme, on which the ophthalmic scheme in the present study was modeled, has been adopted in other countries and has been applied to other clinical specialties in Britain.\textsuperscript{5,6,16} The level of case ascertainment by this national pediatric scheme has varied with the disorder under study, reflecting each disorder’s pattern of manifestation and management, the composition and completeness of the reporting base regarding subspecialty interests, and the ease of application of the study case definition.\textsuperscript{5,7,11} Such factors may have been relevant in the present study. It is likely that ascertainment of cataract by the pediatric scheme also reflected the temporal sequence of detection and referral of some cases: Those first attended to by ophthalmologists within the ascertainment period and subsequently referred to pediatricians outside it would not have been notified in both schemes. Because the capture-recapture analysis is confined to incident cases, the high proportion of prevalent cases also reported by pediatricians\textsuperscript{8} is not included.

National congenital malformation monitoring systems and registers exist in many countries and mainly rely on passive notifications at birth or discharge from the hospital.\textsuperscript{17,18} Underascertainment of even major congenital anomalies has been documented.\textsuperscript{2} Congenital cataract might have been expected to be diagnosed in infancy in approximately 75 children, on the basis of the European birth prevalence, derived from the European congenital anomaly reporting system\textsuperscript{17} and applied to the 753,000 annual live births in the United Kingdom during this period.\textsuperscript{19} By comparison, 161 cases were identified by active surveillance in the present study. This suggests previous underascertainment of this ocular disorder in passive reporting systems.

Epidemiologic studies of rare conditions require complete case ascertainment to allow accurate measurement of disease frequency and unbiased assessment of determinants and outcome. Although active surveillance has been an effective method of identifying people with uncommon disorders,\textsuperscript{4,5,7,8,17} it remains important to quantify undercounting, even in seemingly exhaustive epidemiologic studies.\textsuperscript{2} The application of capture-recapture analysis in this study has allowed the ascertainment achieved by two independent active surveillance schemes to be assessed. We have shown that ophthalmic surveillance is an effective method of identifying congenital ocular disease, in this case cataract, and that ascertainment can be further improved by additional surveillance through a pediatric scheme. Because an estimated 92% of affected infants were identified, the study cohort is considered to be nationally representative and will provide more complete information than was previously possible about children with this disorder.

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References

H-7 Increases Trabecular Facility and Facility after Ciliary Muscle Disinsertion in Monkeys

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Purpose. To determine the effects of the serine-threonine kinase inhibitor H-7 on total outflow facility in iridectomized + ciliary muscle (CM)-disinserted, and on trabecular facility in normal, monkey eyes.

Methods. Total outflow facility was determined by two-level constant pressure perfusion of the anterior chamber. Trabecular outflow facility was determined from accumulation in blood of intracamerally infused radioiodinated albumin at two intraocular pressure levels.

Results. Three-hundred micromoles of intracameral H-7 doubled facility in iridectomized + CM-disinserted monkeys compared with contralateral vehicle-treated eyes. Four 5-μl drops of 400 mM H-7 applied topically followed 2 hours later by anterior chamber exchange for 10 minutes and intracameral infusion for 90 minutes with 100 μM H-7 increased trabecular and total outflow facility by 135% ± 29% and 105% ± 35% (n=5, P<0.01, P<0.05), respectively, compared with contralateral vehicle-treated eyes.

Conclusions. H-7 increases total outflow facility in monkeys by a mechanism independent of the CM, presumably acting directly on the trabecular meshwork.