The epidemiology of congenital and infantile cataract in the United Kingdom.

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ABSTRACT

Congenital and infantile cataract is an important cause of visual impairment and blindness in childhood. Its prevention, through primary, secondary and tertiary strategies, remains an important international goal, requiring epidemiological data which are currently lacking. The work which forms the basis of this thesis was undertaken to determine the incidence, mode of detection, and underlying or associated causes of congenital and infantile cataract in the United Kingdom.

A national cohort of incident cases of congenital and infantile cataract was identified through two national active surveillance schemes: a disorder-specific scheme in ophthalmology established specifically for this study, and an existing paediatric surveillance scheme for rare disorders. Capture-recapture analysis was used to assess level of ascertainment and derive ascertainment-adjusted incidence rates. In addition, completeness of notification of congenital cataract to the Congenital Anomaly System in England and Wales was assessed.

During one year from October 1995, 248 children with newly diagnosed congenital or infantile cataract were identified, of whom 65% had bilateral disease. Overall ascertainment of infants through the surveillance schemes was estimated to be 92% complete. In contrast, 10% of cases were notified to the national Congenital Anomaly System. The ascertainment-adjusted annual age specific incidence of cataract in infancy was 2.49 per 10,000 children, and is equivalent to cumulative incidence by one year of age. 47% of all cases had been detected through the national programme of routine examination of young infants,
while 34% presented symptomatically. Only 57% of cases had been examined by an ophthalmologist by three months of age. Associated ocular disorders occurred in 47% of unilateral and 14% of bilateral cases (p<0.001) whereas 25% of bilateral and 6% of unilateral cases had associated systemic disorders (p<0.001). No cause for cataract was found in 92% of unilateral and 38% of bilateral cases. However possible contributing factors were noted in some of these idiopathic cases, including prematurity, low birthweight, and peri-natal hypoxia and hypoglycaemia. In contrast, hereditary disease accounted for 56% of bilateral cases. Prenatal infections and other systemic or environmental disorders were implicated in 5% of all cases.

From this work, the observed incidence of congenital and infantile cataract is higher than previously reported, with evidence of under-ascertainment through existing routine sources. Nationally, the proportion of cases detected through screening is low, and could be improved. A higher than expected proportion of cases are idiopathic, suggesting a limited scope for primary prevention. Aetiological hypotheses, suggested by the findings of this research, warrant further exploration, as do factors associated with good visual outcome in later childhood. Active surveillance, combined with capture-recapture analysis, is an effective method for identifying children with congenital or infantile cataract and for determining its frequency, and thus merits application to the study of other rare ophthalmic disorders in the future.
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1. INTRODUCTION

Globally, cataract in infancy is a major and avoidable cause of visual impairment in childhood. It has been estimated that the 200,000 children currently blind from congenital cataract represent 12 million person years of blindness, compared with 75 million due to adult cataract-related blindness, the most prevalent blinding disorder in adults. However these estimates provide only a limited assessment of total disease burden, as congenital and infantile cataract can also result in lesser degrees of impairment. Furthermore, as most children with cataract in both industrialised and developing countries would be expected to have a normal life expectancy, congenital and infantile cataract has a continuing impact throughout childhood and adult life. The prevention of visual impairment and blindness due to congenital and infantile cataract is a priority of the World Health Organisation’s international programme for the elimination of avoidable blindness. Epidemiological data are required as a foundation for preventive strategies but have been derived mainly from the study of selected populations, which may not be representative.

While the prevalence of cataract, reflecting both incidence and duration, provides a useful indicator of disease burden, incidence data are required to evaluate the effectiveness of preventive strategies over time, to plan intervention studies, and to assess current and future requirements for health and other services for affected children. Such incidence data are currently not available in the United Kingdom.
Early detection of cataract is important for optimal management, irrespective of the treatment undertaken. Consequently, in the UK and elsewhere, all infants receive routine ocular examination to detect cataract and other ophthalmic disorders. The national programme in the UK, comprising an examination shortly after birth and again at six to eight weeks, has not been evaluated at a national level. In particular, the proportion of cases of cataract detected through these screening examinations is not known.

Congenital and infantile cataract has been reported to occur in association with a number of ocular and systemic disorders, many of which are rare. However, the risk factors for idiopathic congenital and infantile cataract have not been characterised. This contrasts with adult cataract, for which a number of risk factors have been proposed as a result of extensive basic scientific and epidemiological research. The aetiology of congenital and infantile cataract in the UK, as well as the proportion due to preventable causes, are not known.

Thus information is lacking with which to evaluate the potential contribution of primary, secondary and tertiary preventive strategies to the reduction of visual impairment attributable to congenital and infantile cataract. In view of this, a programme of work, reported in this thesis, was undertaken, to ascertain the incidence, mode of detection and aetiology of congenital and infantile cataract in the UK.
The epidemiological data which are currently available for congenital and infantile cataract in the UK are reviewed and issues relevant to the epidemiological study of congenital cataract appraised, as a basis for the research described in this thesis. (Chapter 2) Methods used to establish a disorder-specific active surveillance scheme amongst ophthalmologists are reported. This scheme, and an existing paediatric surveillance scheme, were used to ascertain a national cohort of children with newly diagnosed congenital and infantile cataract. The assumptions underlying capture-recapture analysis are examined, and its application, to estimate level of ascertainment by surveillance, is reported. The extent to which cases of congenital and infantile cataract are notified to the national Congenital Anomaly System is assessed. The methods used to ascertain current practices and the previous training of paediatricians responsible for routine ophthalmic examination of infants are reported. (Chapter 3) The findings regarding the incidence, detection and aetiology of congenital and infantile cataract in the UK are reported in Chapter 4. This work is critically appraised and interpreted with reference to the methodology and findings of other published studies in Chapter 5. The thesis concludes with a discussion of the implications of this research for clinical practice, as well as the future research agenda for congenital and infantile cataract.
2. BACKGROUND

Issues relevant to the epidemiological study of visual impairment in children are discussed in this chapter, with an emphasis on congenital and infantile cataract. An overview is presented of the available epidemiological data on congenital and infantile cataract, in the UK and elsewhere, and sources available for its study are discussed. Areas of incomplete information are identified and appropriate methods to ascertain such information reviewed, as a basis for the research described in this thesis.

2.1 THE PUBLIC HEALTH IMPACT OF VISUAL IMPAIRMENT IN CHILDHOOD.

Normal vision is important for the general development of children as much of their knowledge of their environment is derived through the visual system. Visual impairment has significant implications, throughout life, for the affected child and her family in terms of education, future employment and personal and social welfare. A reduction of the incidence of childhood blindness is thus a priority of the World Health Organisation’s (WHO) Global Initiative for the Elimination of Avoidable Blindness by the year 2020.8

Globally, about one child in a thousand is severely visually impaired or blind, using the World Health Organisation (WHO) classification of levels of visual
loss.\(^4^3\) (Table 2-1, page 18) Although this is less than one tenth of the prevalence in adults,\(^1^5\) the estimated 1.5 million blind children in the world account for about 75 million person years of blindness.\(^1^2,^4^5,^8\) This is equivalent to the burden of adult cataract-related blindness, which is the leading cause of blindness amongst adults.\(^4^8\) As low vision in childhood (Table 2-1, page 18) is estimated to be three to ten times more common than blindness\(^1^5\) the total burden of childhood visual impairment is considerable.

It has been estimated recently that the global cost arising from childhood blindness, in terms of care and lost productivity, is between US$ 6 and 27 thousand million.\(^4^4\) Most of this is accounted for by children in high income countries, where childhood blindness is less common, but life expectancy and earning capacity greater, than in low income countries. The reduction of avoidable visual impairment and blindness in childhood remains an important international public health and economic goal.\(^8\)
Table 2-1 World Health Organisation Classification of levels of visual impairment.

(Source: International Classification of Diseases 10th Revision 43)

<table>
<thead>
<tr>
<th>Level of visual impairment</th>
<th>Category of vision</th>
<th>Visual acuity in better eye with optical correction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slight if visual acuity &lt; 6/7.5</td>
<td>Normal vision</td>
<td>6/18 or better</td>
</tr>
<tr>
<td>Visual impairment (VI)</td>
<td>Low vision</td>
<td>less than 6/18 to 6/60</td>
</tr>
<tr>
<td>Severe visual impairment (SVI)</td>
<td>Low vision</td>
<td>less than 6/60 to 3/60</td>
</tr>
<tr>
<td>Blind (BL)</td>
<td>Blindness</td>
<td>less than 3/60 to no light perception or visual field ≤ 10 degrees around central fixation</td>
</tr>
</tbody>
</table>
2.2 Classification of visual impairment in childhood.

A precise case definition is essential for the epidemiological study of any disorder. Inconsistent classification of levels of visual loss and the underlying disorders responsible for visual impairment in children has considerably limited the usefulness of many previous studies. More recently, standard systems for categorising visual impairment and its causes have been devised and their increasing use has improved the comparability and generalisability of studies, although some difficulties remain. Visual impairment can be categorised according to the functional consequences or according to the underlying aetiology and ocular structures affected.

2.2.1 Functional classification - levels of visual loss.

Normal vision depends on the synthesis of a number of different visual functions including distance and near visual acuity, colour vision, visual fields, binocularity and contrast sensitivity. All may be assessed individually and may be relevant to overall function in a given child. In the clinical setting, visual acuity is the most commonly measured visual function. Most systems currently used to classify visual loss are based on acuity. The WHO classification of visual impairment (Table 2-1, page 18) is based on the distance visual acuity in the better eye, measured wearing the best optical correction where necessary. This classification applies to individuals with
bilateral visual loss and excludes those with reduced acuity due to refractive errors alone. However the WHO definitions differ from other systems, for example, those used to classify blindness and partial sight for the purposes of registration in Britain,\(^{46,47}\) which illustrates the difficulties of extrapolating from, or making direct comparisons with, studies employing different taxonomies.

The categorisation of visual impairment in children is considerably more difficult than in adults. Visual functions mature throughout childhood, so prediction of final visual outcome, which is dependent on both visual maturation and the natural history of the ophthalmic disorder, can be difficult in young children. In addition assessment may be impeded by a young child’s inability to co-operate with testing. Although measurement of visual acuity is less problematic in older children, the methods used to test adults are generally appropriate only for children of school age or above. Young children are increasingly assessed using psychophysical tests, based on preferential looking techniques, and electrophysiological tests. These tests, based on different principles, are not directly comparable with each other or with methods used in older children.\(^{40}\) Thus, despite recent advances in the development and refinement of age-appropriate methods for testing vision, the assessment of acuity remains difficult in infants and pre-school children, as well as in those with other disabilities.

The effect of a given visual deficit depends, amongst other factors, on whether the child has any additional disabilities. A key unresolved problem is the
classification of visually impaired children with multiple disabilities in whom acuity cannot be measured easily.\textsuperscript{40,41,48,49} This difficulty is not specific to visual impairment, as the general classification of childhood disabilities is problematic.\textsuperscript{50} The commonly used WHO paradigm of impairments, disabilities and handicap,\textsuperscript{51} is based on a medical model of disability and does not readily provide an epidemiologically useful classification of childhood visual impairment.

Thus whilst new classifications systems have been developed, and increasingly applied, thereby allowing more meaningful interpretation and comparison of published studies, some issues regarding the functional categorisation of visual impairment in childhood remain unresolved.

2.2.2 Structural and aetiological classification - the causes of visual loss.

For epidemiological studies, causal factors have been classified in a number of ways.\textsuperscript{52,53} Two major categories are 'necessary' causes, which must always precede the effect, although that effect can have several causes, and 'sufficient' causes, which inevitably initiate or produce a given effect.\textsuperscript{53} All causes may be either necessary or sufficient, or both.

The aetiological mechanisms in many ophthalmic disorders in children are unclear but causal factors can often be identified. In response to the difficulties in classifying the underlying or associated causes of visual loss in children, the
WHO Prevention of Blindness Committee has developed the taxonomy\textsuperscript{45} shown in Table 2-2, page 23. Causes are categorised according to both the anatomical site affected and the timing of the insult leading to the visual defect. This system, developed for use in the WHO Eye Examination Record For Children with Low Vision and Blindness,\textsuperscript{45} is aimed at highlighting preventable or treatable causes, which is reflected in the algorithm for its use when more than one anatomical or aetiological cause is identified or there are differences between the two eyes. This form has been used to standardise data collection in a number of studies in developing countries\textsuperscript{3,6,54-56} but experience in industrialised countries is limited.\textsuperscript{1}
Table 2-2 Classification of underlying or associated causes of blindness and low vision.

(Source: WHO / Prevention of Blindness Committee Eye Examination Record^)

<table>
<thead>
<tr>
<th>I Anatomical Classification *</th>
<th>II Aetiological Classification ^</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole globe</td>
<td>Prenatal</td>
</tr>
<tr>
<td>Cornea</td>
<td>Perinatal</td>
</tr>
<tr>
<td>Lens</td>
<td></td>
</tr>
<tr>
<td>Retina</td>
<td>Childhood</td>
</tr>
<tr>
<td>Optic Nerve</td>
<td></td>
</tr>
<tr>
<td>Glaucoma</td>
<td>Unclassified ^ c</td>
</tr>
<tr>
<td>Other</td>
<td></td>
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</tbody>
</table>

Key

* according to primary anatomical site affected

^ according to timing of insult resulting in ocular or vision disorder

^ c if an aetiological category cannot be definitely assigned or determined
2.3 DEVELOPMENT OF THE LENS AND PATHOGENESIS OF CATARACT.

2.3.1 Normal development of the human lens.

2.3.1.1 Embryology and prenatal growth of the lens.

The structures of the human eye are derived from neuroectoderm, neural crest, surface ectoderm and mesoderm. Ocular embryogenesis starts with the development of the optic vesicle in the 3rd week of gestation. The development of the lens is a key component of this process, and recent evidence indicates that lens induction may be influenced by factors present before the formation of the optic vesicle.\textsuperscript{32,57,58}

The earliest event in the formation of the lens is the development of the lens placode, between the 3\textsuperscript{rd} and 4\textsuperscript{th} weeks of gestation, from the surface ectoderm adjacent to the developing optic vesicle. The lens placode invaginates, forming the lens vesicle which separates from the surface ectoderm and is filled by primary lens fibres which start to appear from the 6\textsuperscript{th} week. These fibres subsequently degenerate, forming the embryonic nucleus of the lens and secondary lens fibres appear from the 7\textsuperscript{th} week. By the 3\textsuperscript{rd} month of gestation, the lens comprises embryonic and fetal nuclei. The vascular network of the eye, the tunica vasculosa lentis, develops from the 7\textsuperscript{th} week, completely surrounds the eye by the 3\textsuperscript{rd} month and begins to regress from the 4\textsuperscript{th} month, disappearing completely by the 7\textsuperscript{th} month of gestation. By this time the lens diameter is 5 mm.\textsuperscript{59}
2.3.1.2 Postnatal growth of the lens.

At birth, the crystalline lens has a biconvex structure with an equatorial diameter of 6.5mm and an antero-posterior diameter of 3.5mm at its poles. Further secondary lens fibres are added throughout life, forming the adult nucleus, which surrounds the embryonic and fetal nuclei, and which is itself surrounded by the newly developing cortical lens fibres. By adulthood, the lens measures 9 mm at its equator and has a depth of 5 mm.

The normal crystalline lens is a clear optical structure which functions as part of the refractive and accommodative apparatus of the eye. It retains its clarity through active metabolic processes.

2.3.2 Pathogenesis of congenital and infantile cataract.

Opacification of the lens is termed cataract. When present from birth, this results from either anomalous development or degenerative changes in normally formed lenticular tissue. Evidence from animal experiments indicates that the defect may involve either abnormal maturation of the lens cells or abnormal interaction of secondary lens fibres within the fetal nucleus. The variable morphology of congenital cataract is determined by the timing of the cataractogenic insult, irrespective of its nature. Thus it is possible to ascribe the onset of cataract from its morphology.
The histo-pathological and biochemical study of cataract in infancy has been limited, by contrast to its study in adults.\textsuperscript{57,58} This may be attributable to the limited availability of lens material from infants, as well as to a greater scientific interest in the more common problem of cataract in adulthood. Experimental work indicates that opacification of the lens in adults results from altered lens proteins,\textsuperscript{60} which may involve glycation or oxidative damage.\textsuperscript{33,36,37,61,62} The role of these processes in infantile cataract is not known.\textsuperscript{33,61,62}

\section*{2.4 Normal and Abnormal Visual Development in Childhood.}

\subsection*{2.4.1 Normal Visual Development.}

The visual system is immature at birth. Maturation depends on both structural and functional changes. Development is particularly rapid in the first year of life, although some changes continue into late childhood, so that a child with normal vision only achieves adult levels of visual function at about 5 years.\textsuperscript{40,41,48,65}

A number of anatomical and physiological changes occur in the visual system in childhood. At birth, the length and volume of the eye are approximately 70\% and 50\% respectively, of their adult dimensions.\textsuperscript{59} Further differentiation and growth
of the retina occurs after birth, such that differentiation of the fovea, subserving central and colour vision, may not be complete until end of the first year of life.\textsuperscript{40}

In parallel with ocular growth, there are structural changes in the central nervous system. Differentiation of areas of the visual cortex which integrate visual input from the two eyes occurs in the early post-natal period and myelination of the visual pathways occurs in the second year.\textsuperscript{40}

2.4.2 Abnormal visual development.

During the process of maturation, the visual system is highly susceptible to external agents. This 'plasticity' of the developing visual system is a key principle in the management of ophthalmic disease in children.\textsuperscript{40,64} In early life there are 'sensitive periods' of varying lengths, during which visual function can be profoundly, and sometimes irreversibly, impaired by a variety of insults which impede the transmission of normal visual input from both eyes to the brain. One type of insult is stimulus or form deprivation, such as that resulting from cataract in infancy, which precludes the formation of a distinct image by the affected eye(s), thereby generating abnormal input to the visual cortex.\textsuperscript{24,64-66} Equally, 'critical periods' exist during which treatment should be instituted to have maximal, or sometimes any, effect. Some adverse changes in the visual system become largely irreversible outside these critical periods.\textsuperscript{64-68}
2.4.3 Visual impairment due to cataract.

The derivation of the medical use of the word cataract is uncertain, but it is likely to originate from *katarrhaktes* or *cataracta*, the Greek and Latin respectively, for waterfall or portcullis which provide an apt description of the effect of opacification of the lens in obscuring and / or distorting normal vision.

Visual loss in congenital and infantile cataract is largely attributable to amblyopia, arising in a number of related ways. Stimulus-deprivation amblyopia is the most important mechanism and is most severe when treatment is undertaken late or, if detected late in childhood, not at all.

The natural history of untreated cataract was well described in 1808 by John Cunningham Saunders, the first British surgeon to specialise in the treatment of diseases of the eye:

"How great the advantage of an early cure is a question of no difficult solution. Eyes originally affected with cataracts contract an unsteady and rolling motion, which remains after their removal, and retards, even when it does not ultimately prevent, the full benefit of the operation. A person cured at a late period cannot overcome this awkward habit by the utmost exertion......but the actions of an infant are instinctive: surrounding objects attract attention and the eye naturally follows them. The management of the eye is readily acquired as vision rapidly improves and the infant will most probably be susceptible of education about the usual period."
Other mechanisms of visual impairment include amblyopia secondary to anisometropia, arising from incomplete post-operative correction of aphakia or other refractive error, and the continued effects of the initial stimulus deprivation, particularly in unilateral cases. Visual loss can also arise secondarily from complications associated with cataract surgery, such as posterior capsular opacification or aphakic glaucoma.

Recent experimental and clinical research on stimulus deprivation amblyopia suggests that the 'critical period' for surgical treatment of dense congenital cataract lies within the first three months of life. In unilateral cataract, where ocular rivalry is also a factor, the critical period may be as early as the first six weeks, as the relative disadvantage adds to the absolute effect of stimulus deprivation in the cataractous eye.

### 2.5 Clinical assessment of cataract.

In adults, the lens is examined using the slit-lamp biomicroscope which allows the morphology, density and other characteristics of the cataract to be assessed in detail. Although increasing use of portable, hand-held slit-lamps has made this examination easier, it still requires some co-operation on the part of the patient, to maintain visual fixation, and therefore is inappropriate for routine use in most young children. Therefore a thorough examination is generally only possible if
the child undergoes a general anaesthetic or sedation, either specifically for that purpose or at the time of cataract surgery.

Increasingly, in clinical and epidemiological studies, clinical grading systems are used to classify lens opacity, some of which require other methods of examination, including the use of cameras to image the lens. These methods also require the patient’s co-operation, thereby precluding their routine use in young children. Therefore, at present, there is no standardised objective method of evaluating or grading cataract in young children.

Thus in young children, routine evaluation of the lens most commonly involves inspection of the pupillary red reflex, using a direct ophthalmoscope, to ascertain whether this reflex is normal. This technique is used for screening infants for the presence of cataract.
2.6 ISSUES IN THE EPIDEMIOLOGICAL STUDY OF CONGENITAL AND INFANTILE CATARACT.

A number of issues are relevant to the design and interpretation of epidemiological studies of congenital and infantile cataract, including the choice of case definition and the rarity of the disorder, and these are discussed below.

The selection of an appropriate case definition is not straightforward. Many routine data sources\textsuperscript{81,82} use standard disease classification systems\textsuperscript{42} in which congenital and infantile cataract are categorised separately and cataract associated with ocular or systemic disorders may be further assigned to other categories. It can be difficult to assign some cases to such categories. Moreover, in clinical practice, the terms congenital and infantile are often used interchangeably, because the management of cataract in infancy requires an approach which is different to that in older children.\textsuperscript{14,16} However, as discussed below, children with congenital and infantile cataract are a heterogeneous group, in terms of cause and morphology of cataract, as well as in severity and therefore, treatment required. Case definitions based on either morphology, aetiology, treatment category or visual outcome, will have specific limitations, which are discussed further in the next chapter of this thesis reporting study methodology.

Another issue relevant to study design, is that cataract in infancy is uncommon. Its study requires high and unbiased ascertainment of eligible cases to allow
precise estimates of frequency and meaningful analysis of aetiology and outcome.

It is recognised that the method of identification or reporting of a disorder can influence estimates of its frequency, reflecting differences in ascertainment.\textsuperscript{83-86} Single sources and/or sources of routinely collected data are unlikely to achieve the necessary level of ascertainment, detail or representativeness required to effectively study the epidemiology of congenital and infantile cataract.

The management of infants with cataract, described below, is complex, usually involving detection by one group of health professionals and subsequent treatment by others. Therefore, ascertainment of cases is likely to be improved, and more complete information about the different components of care, may be collected by identifying cases through more than one source.

Finally, as visual development continues throughout childhood, a long follow up is required to allow meaningful assessment of visual, educational and other relevant outcomes in children with congenital and infantile cataract.
2.7 FREQUENCY, AETIOLOGY AND MANAGEMENT OF CONGENITAL AND INFANTILE CATARACT: A GLOBAL VIEW.

There have been few population-based studies of the prevalence of visual impairment in childhood and incidence data are even more limited.\textsuperscript{1,3,5,87} While both prevalence and causes of visual impairment in childhood vary between industrialised and developing countries, cataract in infancy is a major and avoidable cause of visual impairment in childhood throughout the world.\textsuperscript{1-3} In many developing countries, childhood blindness is associated with increased mortality, due to the underlying or associated causes, such as vitamin A deficiency or measles.\textsuperscript{1,3} However, the majority of children with cataract in both industrialised and developing countries would be expected to have a life expectancy similar to those without this disorder.\textsuperscript{1} Therefore, unlike some visually disabling disorders, congenital and infantile cataract has an impact throughout childhood and in to adult life, as indicated by population based data from industrialised countries showing congenital cataract contributes to the prevalence of blindness in adults, accounting for 4% of blind adults in one study in the United States.\textsuperscript{4,7}

2.7.1 Prevalence.

It is estimated that childhood cataract, predominantly congenital and infantile, accounts for 10-15\% of childhood blindness worldwide. The estimated 200,000 children blind from congenital cataract represent a burden of 12 million person
years of blindness, compared with 75 million due to adult cataract blindness.\textsuperscript{1,2,4-6}

As congenital and infantile cataract may result in lesser degrees of visual impairment, measuring severe visual impairment and blindness alone will underestimate the magnitude of the problem.

Few published prevalence studies of childhood visual impairment include formal ophthalmic examination of subjects randomly selected from the whole population. The prevalence of childhood cataract, mainly of infantile onset, has been estimated from the findings of those studies meeting these criteria and, as shown in Table 2-3 page 35, the estimates range from 1.7 per 10,000 children in Nepal in 1985 to 4.0 per 10,000 in USA in 1971.

Prevalence of cataract, dependent on incidence and duration, is a useful indicator of the burden of disease and can be useful in comparing different populations. However, incidence data are necessary to plan preventive strategies and allocate resources.
Table 2-3  Prevalence of childhood cataract reported in population-based prevalence studies of visual impairment.

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Number surveyed (N)</th>
<th>Number affected (n)</th>
<th>Age (years)</th>
<th>Prevalence of cataract per 10,000 children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh²⁸</td>
<td>1982</td>
<td>22,335</td>
<td>5</td>
<td>0 - 5</td>
<td>2.2 ²</td>
</tr>
<tr>
<td>Nepal²⁹</td>
<td>1980</td>
<td>12,143</td>
<td>2</td>
<td>&lt;10</td>
<td>1.7 ²</td>
</tr>
<tr>
<td>Malawi³⁰</td>
<td>1983</td>
<td>5415</td>
<td>2</td>
<td>&lt;6</td>
<td>3.7 ³</td>
</tr>
<tr>
<td>Ethiopia³¹</td>
<td>1994</td>
<td>3433</td>
<td>1</td>
<td>0-15</td>
<td>2.9 ³</td>
</tr>
<tr>
<td>Jamaica³²</td>
<td>1987</td>
<td>5468</td>
<td>2</td>
<td>2 - 9</td>
<td>3.7 ³</td>
</tr>
<tr>
<td>Saudi Arabia³³</td>
<td>1986</td>
<td>10,383</td>
<td>nr*</td>
<td>0-19</td>
<td>3.0 ³</td>
</tr>
<tr>
<td>United States³⁴</td>
<td>1971</td>
<td>nr*</td>
<td>4</td>
<td>0-5</td>
<td>4.0 ³</td>
</tr>
</tbody>
</table>

Key

*nr = not reported

² all cases bilateral and blind

³ all cases unilateral and blind

bilateral and unilateral cases and all levels of visual impairment
2.7.2 Incidence.

In some industrialised countries, the incidence of congenital cataract has been reported from longitudinal studies involving repeated examination of children to ascertain congenital anomalies. In the United States, the cumulative incidence of congenital cataract detected by 1 year of age was 20.9 per 10,000 births amongst infants born in 1946 and 18.9 per 10,000 by age 7 years in infants born between 1959 and 1965. However, these incidence rates are likely to reflect the high frequency, at that time, of relevant aetiological factors, in particular, congenitally acquired rubella. There have been no similar studies subsequently from which the incidence of congenital and infantile cataract can be determined.

In the absence of incidence estimates, by extrapolating from available data, the Committee of the WHO Prevention of Blindness Programme has suggested that, in developing countries, 10 children per million total population per year will be born with bilateral congenital cataract. This is likely to be at least twice the incidence in industrialised countries, given both a higher birth rate and a higher likely exposure to preventable aetiological factors in developing countries.

2.7.3 Aetiology.

As a consequence of the extensive basic scientific and epidemiological research undertaken, a number of putative risk factors for adult cataract have been proposed. These include increasing age, female sex, diabetes, exposure to
ultra-violet light, smoking, hypertension and hyperlipidaemia. Risk factors for congenital and infantile cataract remain unclear\(^9,11,12,19,22,32,34,35\) although much been learned from experimental animal studies of metabolic and endocrinological abnormalities, as well as observation of specific systemic disorders in humans.\(^13,19,97\)

The limited epidemiological information about congenital cataract has been derived almost exclusively from a few hospital-based case series, many including small numbers of cases, which may be prone to ascertainment bias and thus may not be representative.\(^9-22\) Moreover, the use of different systems of classifying the causes of cataract, together with the limited disaggregated information reported, makes direct comparison of these studies difficult. However the findings indicate changes in the relative contribution of different aetiological factors in industrialised countries over time, with a reduction in the proportion of cases attributable to causes amenable to primary prevention, such as prenatal infections or other known teratogens, such as drugs.\(^9-21,98,99\) By comparison, in countries currently at an intermediate level of development, the reported causes today are similar to those seen 30 or more years ago in industrialised countries.\(^9-21,98\) This is illustrated by the causes reported in the 3 largest published case series, shown aggregated for ease of comparison, in Table 2-4, page 38.
Table 2-4: Secular trends in reported causes of congenital and infantile cataract in published case series.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Canada(^{14}) (1950-68)</th>
<th>North India(^{15}) (1980-87)</th>
<th>South India(^{18}) (1993-4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (% all cases(^{a}))</td>
<td>n (% all cases(^{b}))</td>
<td>n (% of all cases(^{c}))</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>123 (32)</td>
<td>62 (31)</td>
<td>47 (47)</td>
</tr>
<tr>
<td>Isolated hereditary</td>
<td>32 (8)</td>
<td>28 (14)</td>
<td>18 (18)</td>
</tr>
<tr>
<td>Associated ocular disorder</td>
<td>23 (6)</td>
<td>nr</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Associated systemic disorder</td>
<td>208 (54)</td>
<td>110 (55)</td>
<td>29 (29)</td>
</tr>
<tr>
<td>hereditary</td>
<td>33 (9)</td>
<td>25 (13)</td>
<td>-</td>
</tr>
<tr>
<td>congenital rubella</td>
<td>74 (19)</td>
<td>43 (21)</td>
<td>25 (25)</td>
</tr>
<tr>
<td>other non-hereditary</td>
<td>101 (26)</td>
<td>42 (21)</td>
<td>4 (4)</td>
</tr>
</tbody>
</table>

Key

\(^{a}\) 386 cases
\(^{b}\) 200 cases
\(^{c}\) 100 cases
nr not reported separately
Numerous aetiological factors or processes, many of which are rare, have been implicated in congenital and infantile cataract in humans and further factors have been reported from experimental studies in animals. Those underlying or associated causes reported in published clinical studies have been collated and are summarised in Table 2-5, page 40. This taxonomy demonstrates the considerable aetiological heterogeneity of this disorder, which, in some cases, may be attributable to more than one factor: for example, cataract associated with microphthalmos which is genetically determined. The system also assigns cases in to the clinically relevant categories of isolated cataract, cataract associated with ocular disease and cataract associated with systemic diseases, grouped by the principal system affected.
Table 2-5  Summary of reported underlying or associated causes of congenital and infantile cataract.

**Idiopathic**

**Intra-uterine infection / maternal infection embryopathy**
- rubella, cytomegalovirus, varicella-herpes zoster, herpes simplex, toxoplasmosis, syphilis, EB virus, measles, poliomyelitis

**Intra-uterine drug exposure**
- chlorpromazine, corticosteroids, sulphonamides, vitamin D, vitamin A

**Intra-uterine ionizing radiation**

**Metabolic disorder**
- galactosaemia, galactokinase deficiency, hyperglycinuria, sialidosis, alpha-mannosidosis
- sorbitol dehydrogenase deficiency, hypocalcaemia - idiopathic, or hypoparathyroidism or pseudohypoparathyroidism, marginal maternal galactokinase deficiency, maternal diabetes

**Ocular disease**
- microphthalmia, persistent hyperplastic primary vitreous, aniridia, aniridia plus anterior chamber dysgenesis syndromes, retinopathy of prematurity, ectopia lentis posterior lenticonus, intra-ocular tumour

**Hereditary without systemic abnormality**
- autosomal dominant
- autosomal recessive
- X-linked recessive

**Hereditary with systemic abnormality**

a. Chromosomal
- trisomy 21, Turner's syndrome, trisomy 13-15, trisomy 16-18, deletion ch'some 5

b. With skeletal disease
- Conradi - Hunermann syndrome, rhizomelic chondrodysplasia punctata, Stickler syndrome, campak syndrome

c. With syndactyly, polydactyly, or other digital syndrome
- Rubinstein-Taybi syndrome, Ellis van Creveld syndrome, Bardet-Biedl syndrome

d. With central nervous system abnormalities
- cerebro-oculo-facial-skeletal syndrome, Martsolf syndrome, Zellweger syndrome
- Marinesco-Sjogren syndrome, Smith-Lemli-Opitz syndrome, Norrie’s disease

e. With muscle disease
- myotonic dystrophy, cataract, lactic acidosis and cardiomyopathy

f. With renal disease
- Lowe's syndrome, Alport's syndrome

g. Mandibulo-facial syndromes
- Hallerman - Streiff syndrome, Nance- Horan cataract-dental syndrome

h. Dermatological disease
- congenital ichthyosis, cataract, alopecia, & sclerodactyly, Schafer syndrome, Siemens syndrome, incontinentia pigmenti
Although many of the systemic disorders listed in Table 2-5 are individually and collectively rare, their study can offer specific insights into pathogenesis, for example, disorders of sugar or cholesterol metabolism. There has been considerable basic scientific research to identify the genes involved in hereditary cataract, both isolated and associated with systemic diseases, as well as their products and the role of these gene products, many structural lens fibre proteins, in cataractogenesis. ^ However, possible risk factors for idiopathic cataract, which accounts for between one and two thirds of cases in most series, ^ have received far less attention. Putative risk factors include adverse pre- and peri-natal events: preterm birth, low birth weight, peri-natal hypoglycaemia, hypoxia and hypothermia, as well as pre-eclampsia. ^ The mechanisms of lenticular damage are not known although transient lens vacuoles, postulated to be due to local osmotic changes, have been reported in infants born prematurely or of low birthweight. ^

2.7.4 Management.

Effective management requires co-ordination between ophthalmic, paediatric and other clinical, as well as educational and social services, to ensure early detection and prompt provision of specialist treatment. The process of visual rehabilitation is costly and time-consuming and requires long-term intensive clinical and parental input.
The origin of the surgical treatment of cataract is attributed to Susruta in India but, as recorded by the oral tradition, the exact date is not known, and may be as early as 1000 B.C. However, written records of 'couching', involving posterior displacement of the cataractous lens, and other surgical procedures in adults have existed since at least the 3rd century B.C. There are few such early references to surgery for childhood cataract. Detailed descriptions of paediatric cataract techniques used by European surgeons in the 19th century indicate the forerunners of current procedures. The surgical and optical techniques for treatment of congenital and infantile cataract have changed significantly in the past three decades with the development of micro-surgical techniques, the use of lasers as an adjunct to surgery, the evolution of optical correction using contact lenses and, more recently, an increasing interest in the use of intra-ocular lens implants. There remains some disagreement about the surgical technique of choice and the optimal method of optical correction following surgery.

Outcomes have been reported, almost exclusively, in hospital based case series, which although often detailed, involve retrospective collection of management and outcome data and are prone to selection bias. Nationally representative information on outcome, including educational and other non-clinical outcome measures, are lacking. Factors associated with good visual outcome, and those associated with adverse outcomes, such as complications of treatment, have not been systematically studied.
2.8 PREVENTION OF VISUAL IMPAIRMENT DUE TO CONGENITAL AND INFANTILE CATARACT.

Current primary, secondary and tertiary preventive strategies to combat visual impairment due to congenital and infantile cataract\textsuperscript{1,2,5,6} are outlined in Table 2-6 and require epidemiological data which are currently lacking in many regions of the world.\textsuperscript{1,6,8}
Table 2-6 Current preventive strategies against congenital and infantile cataract.

<table>
<thead>
<tr>
<th>Primary prevention strategies:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Public health education programmes to improve awareness and understanding of hereditary eye diseases and to promote avoidance of known teratogens, such as drugs and infectious agents during pregnancy.</td>
</tr>
<tr>
<td>2. Provision of pre-conceptional genetic counselling services for families affected by hereditary cataract.</td>
</tr>
<tr>
<td>3. Antenatal care to evaluate and advise pregnant women at risk of having an affected child.</td>
</tr>
<tr>
<td>4. Appropriate rubella immunisation programmes in countries where this is a significant problem.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary prevention strategies:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Early detection of cataract by routine examination of the red reflex in all newborn and young infants and prompt referral of children with an abnormality to an ophthalmologist.</td>
</tr>
<tr>
<td>2. Routine ophthalmic examination of children at ‘high risk’, such as those with a family history of ocular disease, to ensure early detection.</td>
</tr>
<tr>
<td>3. Public health education programmes to improve parental understanding of the importance of early detection and treatment of cataract.</td>
</tr>
<tr>
<td>4. Management of referred cases by ophthalmologists with special expertise, ideally, working within an appropriate multi-disciplinary team.</td>
</tr>
<tr>
<td>5. Provision of prompt surgical treatment, adequate correction of aphakia and maintenance treatment for amblyopia.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tertiary prevention strategies:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Long term follow up of cases to detect and treat post-operative complications, such as posterior capsular opacification and glaucoma.</td>
</tr>
<tr>
<td>2. Assessment and provision of low vision optical aids to maximise residual vision in appropriate cases.</td>
</tr>
<tr>
<td>3. Assessment and provision of appropriate education for visually impaired children.</td>
</tr>
<tr>
<td>4. Where appropriate, surgical treatment of cases detected or presenting late in order to restore navigational vision or improve cosmesis.</td>
</tr>
</tbody>
</table>
2.9 REVIEW OF EXISTING EPIDEMIOLOGICAL DATA ABOUT CONGENITAL AND INFANTILE CATARACT IN THE UNITED KINGDOM.

Information about children with ophthalmic disorders has been derived from various sources in the United Kingdom (UK), including special surveys, studies of birth cohorts and other defined populations, routine disorder-specific sources, such as registers of visual impairment and other disabilities, and routine sources of data on ophthalmic services. Most provide prevalence data but, as in many other countries, there are few incidence data on childhood visual impairment in the UK. As all ophthalmic disorders which cause severe visual impairment or blindness in children are uncommon, high and unbiased ascertainment in any study is important and is a particular issue in studies relying on a single source of cases.

2.9.1 Prevalence studies.

2.9.1.1 Surveys of disability in childhood.

The national prevalence of disability in children is not measured routinely in the UK. In the 1974 General Household Survey, the prevalence of parental or self-reported blindness amongst children aged < 16 years was 3.6 per 10,000. Of the 3 affected children, 2 had congenital cataract, from which the prevalence of blindness due to congenital cataract can be estimated as 2.4 per 10,000. Two
national surveys of disability undertaken by the Office of National Statistics (formerly the Office of Population Censuses and Surveys), in 1985 and 1988, reported one or more specific disabilities in 32 per 1000 children aged under 16 in Great Britain. A seeing disability (defined on the basis of vision dependent tasks rather than acuity) affected 2 per 1000 children overall: 6% of disabled children living in private homes and 16% of those in communal establishments. None of the 112 children with a seeing disability in the survey had cataract.

2.9.1.2 Population based prevalence studies.

There have been a few population-based prevalence studies of visual impairment in childhood in the UK. The 1958 \textsuperscript{117} and 1970 \textsuperscript{118} birth cohorts are the only large studies from which the prevalence of visual impairment and its causes can be determined on a national basis. (Table 2-7, page 48) From the reported findings, the estimated prevalence of partial sight or blindness due to cataract was 1.9 per 10,000 children in the 1958 birth cohort (National Child Development Study). \textsuperscript{117} The estimated prevalence of bilateral cataract (all partially sighted or blind) was 3.3 per 10,000 and of unilateral cataract was 2.0 per 10,000 children in the 1970 Birth Cohort Study. \textsuperscript{118} The number of affected children in both cohorts was small, but congenital cataract was the most important cause of partial sight and blindness in the 1970 cohort and of equal first ranking with optic atrophy in the 1958 birth cohort. Differences in prevalence in these studies may be attributable, in part, to differences in methodology, ascertainment, or survival patterns of children with
multiple disabilities. These estimates are similar to the prevalence of visually significant cataract in Northern Ireland in 1977 of 3 per 10,000 children based on a multiple source survey of visually handicapped children.119
Table 2-7  Prevalence of visual impairment and its main causes in England, Scotland and Wales.

<table>
<thead>
<tr>
<th></th>
<th>1958 Birth Cohort</th>
<th>1970 Birth Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 15,275</td>
<td>N = 14,907</td>
</tr>
<tr>
<td></td>
<td>age 11 years</td>
<td>age 10 years</td>
</tr>
<tr>
<td><strong>Prevalence per 1000 (95% CI)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ocular or vision disorder</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partial sight</td>
<td>0.46 (0.12, 0.79)</td>
<td>0.54 (0.17, 0.91)</td>
</tr>
<tr>
<td>Blindness</td>
<td>0.13 (0.05, 0.31)</td>
<td>0.34 (0.04, 0.64)</td>
</tr>
<tr>
<td>Congenital cataract</td>
<td>0.19</td>
<td>0.33</td>
</tr>
<tr>
<td>Optic atrophy</td>
<td>0.19</td>
<td>0.13</td>
</tr>
<tr>
<td>Retinal dystrophy/albinism</td>
<td>0.13</td>
<td>0.13</td>
</tr>
<tr>
<td>Retinopathy of prematurity</td>
<td>-</td>
<td>0.07</td>
</tr>
<tr>
<td>Retinoblastoma</td>
<td>-</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Key

a  CI = confidence interval
b 3 bilateral cases and includes 1 case with dislocated cataract
c 5 bilateral cases and excludes 3 cases with unilateral cataract
At least half of all visually impaired children have other disabilities. Of those groups of children known to have a higher risk of ocular and vision disorders, those born preterm or of low birth weight have specific problems. The reported prevalence of congenital cataract in children born preterm (<32 weeks gestation) or of low birth-weight (<2000g), is estimated to be between 0.2% and 1%, which is higher than in children born at term and of normal birthweight. In most of these population based studies, the underlying or associated causes of congenital cataract are reported but the small number of cases involved limits the usefulness of this information in making recommendations about clinical practice, public health policy or further aetiological research.

2.9.2 Disorder-specific routine sources.

2.9.2.1 Registers of visual impairment.

Since 1851, the number of blind people in Britain has been recorded through the Census returns. In 1920, through the Blind Persons Act, statutory benefits for blind people were introduced and a register of blind persons established. The current system, involving certification by a consultant ophthalmologist and administration of statutory services and disability registers by local authorities, was established following the 1948 National Assistance Act. Routine examination of the causes of blindness using these notifications was initiated in
1950 by Sorsby whose analyses for the period 1948 to 1968 were based on his own system of classification of cause.\textsuperscript{125,126} Thereafter, the WHO International Statistical Classification of Diseases (ICD)\textsuperscript{43} was adopted for these analysis.

Thus, the national registers of partial sight and blindness have been the main source of incidence data on visual impairment in childhood in Britain.\textsuperscript{46,49,70,98,104,120,127-130} Registration of eligible individuals is voluntary and is not a prerequisite for assessment of special educational needs or provision of relevant services for visually impaired children. In addition, certification in children does not offer the same financial advantages as in adults. Variation in registration practices,\textsuperscript{129} together with under-certification and imprecision of information on causes have been documented.\textsuperscript{46,47,99,124,128,129,131,131-135} Thus certification rates provide only minimum estimates of the incidence of severe visual impairment and blindness in children.

Between 1969 and 1991 the percentage of new registrations of children with blindness due to congenital cataract fell from 13\% to 3\% and of partial sight registrations fell from 20\% to 6\%.\textsuperscript{136-139} (Figure 2-1, page 52 and Figure 2-2, page 53) However analysis of registrations in 1990/91 shows that less than a quarter of all registrations due to congenital cataract were of children aged 15 years or less.\textsuperscript{46} This indicates variation in certification practices as many eligible children with congenital cataract were not registered in childhood. Therefore, whilst the relative contribution of congenital cataract to new partial sight or blindness
registrations has decreased, this does not necessarily indicate declining incidence, as changes in management and outcome, as well as registration practice, may account for some of the observed differences over time. Registration data necessarily exclude children with unilateral cataract or those with better visual outcome, who are not eligible for certification. Furthermore, data regarding underlying or associated cause of cataract are not collected. Finally, although certification continues, regular analysis and reporting by the Office of National Statistics (ONS, formerly OPCS) of partial sight and blindness registration data, has recently been discontinued, making these data less accessible. (Personal communication, R Wormald, Institute of Ophthalmology)
Figure 2-1
Causes of blindness amongst newly registered children, aged 15 years or less, in England and Wales between 1969 and 1990.

- cataract
- retinopathy of prematurity
- retinal dystrophies
- visual pathways
- optic atrophy
- congenital eye anomalies
Figure 2-2

Causes of partial sight amongst newly registered children, aged 15 years or less, in England and Wales between 1969 and 1990. 136-139
2.9.2.2 Systems for monitoring congenital anomalies.

National congenital malformation monitoring systems and registers exist in many countries and mainly rely on passive notifications at birth or discharge from hospital.\[35,81,140-146\] Estimates of the incidence of congenital cataract have been derived from such systems. The National Congenital Anomaly System, run by the Office of National Statistics (ONS), was established in 1964, initially as a rapid surveillance system in England and Wales, following the epidemic of congenital anomalies occurring in children whose mothers had been treated with thalidomide during pregnancy.\[81\] Reporting of congenital anomalies is passive and voluntary and, until 1995, included only those abnormalities detected within 10 days of birth. There is now no upper age limit for reporting.\[81\] Cases are notified through the statutory birth notification system, itself now often derived from the maternity form completed for the hospital episode system, together with notifications from any home births or those occurring in private institutions. Reported anomalies are categorised using the WHO International Classification of Diseases system\[41\] and underlying aetiology is not reported separately. Minimum identifying information is collected on notified cases and there is no routine confirmation of notifications or verification of reported data.

The incidence of congenital cataract is not reported routinely in the ONS system, but one study using these data reported a rate of congenital cataract of 0.33 per 10,000 live births in singletons and 0.13 per 10,000 in twins between 1979 and 1985 in England and Wales.\[147\] Other regional systems in the United Kingdom,
contributing to the European congenital anomaly reporting system (EUROCAT) have reported rates of congenital cataract between 1.1 per 10,000 live births in the Belfast register to 2.1 per 10,000 in the Glasgow register.

The ONS Congenital Anomaly System is the only source of routine incidence data on congenital ocular anomalies at national level. Under-ascertainment of even major anomalies, as well as inaccuracies in reported data, in this system have been documented, including by direct comparison with independent regional congenital anomaly reporting systems. There have been no validation studies, at national level, of ascertainment of congenital ocular anomalies through this passive surveillance scheme and thus their reliability in monitoring secular and other trends in incidence is not known.

2.9.2.3 Oxford Region Register of Early Childhood Impairment.

The relative contribution of different disorders to visual impairment, particularly amongst groups of children at higher risk, can be ascertained from disorder-specific registers. The Oxford Region Register of Early Childhood Impairments is a unique population-based register which uses multiple sources to identify children with early onset visual and other neuro-sensory impairments. The rate of severe vision loss (acuity ≤ 6/18 in better eye) between 1984-1991 was estimated to be 1.4 per 1000 live births. Bilateral cataract accounted for 6% of these cases, a rate of visual impairment due to cataract by age 5 years of 0.9 per
10,000 live births during this eight year period. Temporal trends are of interest but as the number of children with individual disorders is small and restricted to subgroups with certain levels of vision, the interpretation of disorder-specific analysis is difficult.

2.9.3 Ophthalmic or other clinical services data.

2.9.3.1 Multi-disciplinary visual assessment teams.

Multi-disciplinary visual assessment teams exist in many areas of the UK, which often serve defined populations. The relative importance of difference causes of visual impairment amongst children assessed by such teams have been reported. Amongst children referred to the Liverpool vision assessment team, 12% of those with visual impairment alone had congenital cataract compared with 5% of those with multiple disabilities. The prevalence of visual impairment (visual acuity ≤ 6/18) due to cataract was 1.3 per 10,000 children aged 0-16 years in Liverpool in 1995. Secular trends are of interest and, if all children in a defined population are referred to such teams, then the prevalence of different disorders can be estimated. Although advocated, such teams do not exist in all districts. Furthermore, children with visual impairment which is less severe, or unassociated with other disabilities or due to purely ocular disorders may be managed principally or solely by an ophthalmic team and therefore may be less readily identified in a community through systems primarily designed to ascertain
children with multiple disabilities. Therefore data about congenital cataract from this source may not be representative.

2.9.3.2 Hospital Episode Statistics (HES)

Hospital in-patient statistics have been compiled in England and Wales since 1929. The introduction of the National Health Service in 1948 provided the opportunity for a national scheme for collecting hospital morbidity data. In 1987, the Hospital Episode Statistics (HES) system replaced the Hospital In-Patient Enquiry system (HIPE), as the source of routinely collected data about in-patient clinical activity.

The primary purpose of the HES system is to provide routine data on hospital in-patient services, out-patient clinical activity being specifically excluded, and these are reported by individual hospitals to the Department of Health. The unit of measurement is a completed consultant episode and thus these data provide information about hospital activity but cannot provide estimates of disease frequency in a population. Disorders are coded according to the WHO International Classification of Diseases (ICD), in which congenital cataract is coded amongst congenital eye anomalies while infantile cataract is included as a subset of other categories of cataract. Operative procedures are categorised using the ONS (formerly OPCS) coding system, in which some of the procedures used in paediatric cataract surgery do not have individual codes. The operative
and diagnostic codes are assigned, usually by administrative rather than clinical staff, before reporting to the Department of Health.

Routine analyses are published but are insufficiently detailed for assessment of in-patient activity related to congenital and infantile cataract. Unpublished data, made available by the Department of Health, (Personal communication, S Maslen, HES project) indicate 176 episodes, in children aged 0-15 years, in England and Wales in 1993-4, in which the primary operation code was a form of lens surgery and congenital eye anomaly was one of the diagnostic codes. It is not possible to establish, from these aggregated data, the number of children involved, whether they had bilateral or unilateral cataract and whether they were incident or prevalent cases.

Incomplete reporting of various disorders through such systems has been documented and verification of notifications by reference to the original medical records is considered essential.\textsuperscript{55,157,158} Completeness of reporting of paediatric ophthalmic disorders has not been validated. Thus data derived from the HES or equivalent systems elsewhere in the UK can provide useful information about the management of cases requiring surgery, but are of limited use in the broader study of the epidemiology of congenital and infantile cataract.
2.10 Screening for Cataract in Infancy: Policy and Practice in the UK.

Congenital cataract is one of the few causes of severe visual impairment and blindness in children which is amenable to specific treatment. As early detection is essential for optimal management, irrespective of the need for surgery, routine examination of young infants to detect cataracts and other less common ophthalmic disorders, is undertaken, as part of the child health surveillance programme in the UK, and elsewhere. In the UK, national recommendations include evaluation of the pupillary red reflex in newborn children and again in infants aged 6-8 weeks, when examination for the presence of squint and assessment of visual behaviour are also recommended. Formal ophthalmic assessment of children considered to be at high risk, such as those with a family history of ocular disease or relevant neuro-developmental disorders, is also recommended. Little is known about the detection rate of the UK national screening programme, as it has not been specifically evaluated at national level and its process and outcomes are not routinely monitored.
2.11 **Summary of aims of this epidemiological study of congenital and infantile cataract in the UK.**

Although an uncommon disorder, the prevention of childhood visual impairment and blindness due to congenital and infantile cataract is now a priority of the World Health Organisation’s international programme for the elimination of avoidable blindness. This is in recognition of the potential for prevention and the consequences of untreated cataract. As discussed in this chapter, the epidemiological data necessary for planning appropriate preventive strategies, to achieve this aim, are currently lacking.

Within the UK, the available sources of data, reviewed previously, have provided estimates of the prevalence of visual impairment due to congenital and infantile in the UK cataract. However, incidence data are currently lacking, with which to evaluate the effectiveness of preventive strategies and to plan appropriate provision of services. Similarly, the aetiology of congenital and infantile cataract in the UK has not been adequately characterised and the proportion due to preventable causes remains unknown. This information is important for clinical practice, and for future epidemiological and basic scientific research, and for the evaluation of existing, and the development of future, primary preventive strategies. The effectiveness of the current national programme of screening young infants to detect cataract is not known, despite its importance to the implementation of effective secondary preventive strategies.
Consequently, this study was established to determine the incidence, mode of detection and aetiology of congenital and infantile cataract in the UK. Consideration of the specific epidemiological issues relevant to the study of cataract in infancy, as well as the limited scope and completeness of available routinely collected sources of data, led to the development of the methods used in this research to ascertain a nationally representative cohort of incident cases. These methods are described in the following chapter of this thesis.
3. METHODS

In this chapter, surveillance methodology is reviewed and its application to ascertain a nationally representative cohort of children with newly diagnosed congenital and infantile cataract in the UK is described. The technique of capture-recapture analysis is reviewed and its use to estimate completeness of ascertainment of incident cases through active surveillance is presented. The methods used to examine the completeness with which cases are identified through two national external sources of data are described. The design of a national survey of the practice and training of paediatricians responsible for routine ophthalmic screening and surveillance examinations of infants is reported. The methods used to calculate incidence and determine mode of detection and aetiology are described.

3.1 THE SURVEILLANCE STUDY.

3.1.1 Overview of the history, principles and methods of surveillance.

3.1.1.1 History and definitions.

Public health surveillance has a long history, with rudimentary systems for monitoring individuals with illness being established in Europe in the Middle Ages.\textsuperscript{160,161} Disease surveillance of whole populations, adopted more recently, was initially used for the control and prevention of communicable diseases.\textsuperscript{160-162}
This activity was defined in 1963 by Langmuir as:

"...continued watchfulness over the distribution and trends of incidence through systematic collection, consolidation and evaluation of morbidity reports and other relevant data..." together with "...regular dissemination of the basic data and the interpretations to all who have contributed and to all others who need to know."

Subsequently, surveillance methods were also used to study non-communicable diseases and to examine other population characteristics relevant to health, such as risk factors, disability, and health practices. This broadening of the application of surveillance is reflected in its definition by the World Health Organisation as:

"The systematic measurement of health and environmental parameters, recording and transmission of data" together with "the comparison and interpretation of data in order to detect possible changes in the health and environmental status of populations".

Population-based surveillance can address the specific difficulties of studying uncommon diseases, which require a representative, and ideally large, sample of cases of the disorder of interest to allow unbiased and meaningful analysis.
3.1.1.2 Methods of population-based surveillance.

Various models of surveillance have been described to ascertain a range of health related events.\textsuperscript{145,146,156,160-162,164,169,173,175-179} Surveillance can be undertaken of a whole population or of an appropriate subgroup only.\textsuperscript{145,146} The latter, sentinel surveillance, is appropriate when it is not necessary to identify all eligible cases, rather to ensure accurate and timely reporting of sufficient cases to detect changing trends in the population. Sentinel health event surveillance, involving identification of avoidable (preventable or treatable) adverse health events, is applied to assess the quality of medical care.\textsuperscript{163,180} Sentinel surveillance can be less costly than surveillance of whole populations.

A fundamental distinction is made in all surveillance between systems with passive and active reporting. In passive surveillance schemes, only positive reports of cases of the disorder of interest are sought. By comparison, in active surveillance, null reports, confirming absence of disease, are sought explicitly from the notifying source as the alternative to positive reports, and where necessary, non-responders are prompted for these null reports. The effectiveness of both types of surveillance relies on accurate notification by respondents, but in active reporting schemes, an assessment of compliance with the notification system can be made. Thus, if null reporting is assumed to be accurate, then the degree to which reported cases or data are representative of eligible cases can be evaluated.\textsuperscript{175}
Most routine surveillance schemes rely on passive reporting, as this is generally more easily administered and therefore less costly to maintain.\textsuperscript{145,146} However, it is recognised that active surveillance can achieve substantially higher levels of ascertainment than passive reporting,\textsuperscript{145,146,160,181} even though the difficulties and costs involved in their establishment and maintenance can be considerable. Thus the overall benefit to cost ratio may favour active surveillance.\textsuperscript{182}

Passive surveillance is used, on a national basis, to monitor communicable diseases,\textsuperscript{156} adverse drug reactions\textsuperscript{156,169} and congenital anomalies\textsuperscript{81,146,156} in the UK. As discussed previously, (section 2.9.2.2, page 54) under-ascertainment has been reported in the UK\textsuperscript{81,148-152} and other similar systems for monitoring congenital anomalies.\textsuperscript{143,145,146} As notification in these systems is passive, compliance with reporting cannot be routinely assessed. Estimation of ascertainment through these systems requires specific comparison with cases identified independently from other sources.

3.1.1.3 Requirements of a surveillance scheme.

Certain factors are essential for the success of any surveillance scheme. The use of clear and easily applied case definitions,\textsuperscript{145,146,162,178,183,184} together with the identification of a well-defined study population,\textsuperscript{164,185} are important. A fundamental requirement is the response of contributing clinicians and this can be
enhanced by selecting those most appropriate for the study, as well as by
minimising the work involved in their contribution. Provision of regular
and relevant feedback to respondents is also likely to improve motivation and
compliance Specific surveillance schemes are reported to be more
accurate.

3.1.1.4 Applications of active population-based surveillance.

Active surveillance has proved to be an effective method of case identification for
a number of uncommon disorders, with the use of
multiple sources further improving ascertainment. In the UK, the appropriateness and effectiveness of this method of study is recognised: it has been used to study a wide range of conditions affecting children at a national
level, and more recently has been applied to neurology, dermatology and
gastroenterology. However the use of active surveillance in ophthalmological research has been limited.

The national paediatric scheme, run by the British Paediatric Surveillance Unit (BPSU) was established in 1986 to "...improve the surveillance of ... conditions in children which could not be monitored throughout existing data collection systems..." This active surveillance scheme, which can enable up to 12 disorders to be surveyed concurrently, has facilitated a number of studies of uncommon conditions in the past decade. Monthly reporting
cards, listing the disorders being studied, are sent to over 1300 respondents, comprising members of the Royal College of Paediatrics and Child Health (formerly the British Paediatric Association) and paediatrician members of the Royal College of Physicians in Ireland. Case reporting is active, with null reports specifically requested. It has been reported that over 90% of case notification cards are returned each month. This scheme has been the model for surveillance schemes in other specialities in the UK, as well as paediatric schemes in other countries.

3.1.1.5 Use of active surveillance to study congenital and infantile cataract.

As discussed in the previous chapter, existing sources of data were not sufficient for the purpose of identifying a nationally representative cohort of incident cases. Therefore an active surveillance study was conducted. In the UK ophthalmologists treat children with this disorder while paediatricians are responsible for the routine examination of infants to detect cataract and for the management of associated systemic diseases. Thus national surveillance was undertaken through a new disorder-specific ophthalmic scheme and, in parallel but independently, through the existing paediatric scheme.
3.1.2 The ophthalmic surveillance scheme.

An active reporting scheme for congenital and infantile cataract was established in May 1995 through a collaborative group specifically formed to facilitate this study, the British Congenital Cataract Interest Group (BCCIG). (Appendix A, page 259)

3.1.2.1 Establishing a new, disorder-specific ophthalmic surveillance scheme.

The management of cataract in infants is recognised to be a highly specialised area of ophthalmology, requiring multi-disciplinary expertise.\textsuperscript{19,32} Thus eight ophthalmologists in the UK, recognised within the ophthalmic community as having particular expertise in this field, were specifically approached and asked to help to establish the active reporting base and form the study collaborative group (BCCIG). The aims and methods of the research programme were discussed with these ophthalmologists.

Relevant manpower census data, including information on subspecialty interests, were lacking with which to identify other eligible ophthalmologists. In view of this, a postal questionnaire survey was carried out in March 1995 to identify those eligible ophthalmologists in the UK who managed infants and young children with cataract. Regional lists were obtained from the Royal College of Ophthalmologists of all consultant ophthalmologists in England, Scotland, Wales and Northern Ireland. To assess their completeness, these were compared with the lists of consultant posts per region in the Directory of Training Posts in
All listed ophthalmologists were sent a letter outlining the study and inviting them to join the ophthalmic reporting base and the BCCIG. This was accompanied by a questionnaire asking for details about their clinical practice. They were also invited to share information about the study with any relevant colleagues. The eight ophthalmologists already included in the ophthalmic reporting base, as well as those known to work entirely in subspecialties precluding referral to them of children with cataract, were excluded from the survey.

Respondents were asked if they were involved, in any way, in the management of children with cataract, the approximate number of new cases managed annually and the number on whom they operated personally each year. Those who did not manage children with cataract were asked to identify the ophthalmologists to whom they referred new cases. All respondents involved, in any way, in managing children with cataract were invited to join the ophthalmic reporting base, with the aim of maximising the sensitivity of this disorder-specific surveillance scheme.

All respondents indicating an interest in the study joined either the active reporting base or the mailing list of the BCCIG. The latter category comprised those ophthalmologists not actively involved in managing children with cataract, but who had an interest in the study for other reasons and wished to receive reports on study progress.
Detailed information about the study, including the operation of the active reporting scheme, together with drafts of the data collection proformas were sent to all members of the reporting base. These were discussed subsequently at the first annual meeting of the BCCIG in May 1995.

Six consultant ophthalmologists in the Republic of Ireland joined the BCCIG. However, as it proved impossible to develop a formal active reporting base in this country, incident cases from the Republic of Ireland were not included.

3.1.2.2 Maintaining the ophthalmic reporting base.

At the start of the case ascertainment period in October 1995, the active reporting base comprised 86 respondents. (Section 4.1.1.1, page 102) All new consultants appointed during the case ascertainment period were systematically identified through the Royal College of Ophthalmologists. They were sent information about the study and invited to join the group, if eligible, irrespective of whether they had new cases to report. Consultants who reported that they were retiring from practice during the case ascertainment period were removed from the active reporting base but could continue to receive progress reports through the BCCIG mailing list if they wished.
3.1.2.3 Case definition.

A clinical case definition, encompassing visually significant congenital and infantile cataract, was considered appropriate for this study. However an agreed clinical definition for cataract occurring in infancy did not exist. In many published studies the case definition used was not explicitly reported\textsuperscript{20,22,74} while in others, age at surgery or at detection were given as the inclusion criteria.\textsuperscript{9,15,17,21,68,73,78,194} Where specifically reported, differing definitions had been applied, depending on the purpose of the study. For example, a definition of ‘dense fetal nuclear cataract of \textgreater{} 5mm diameter’ was used in a neurophysiological study of the critical period for surgery for unilateral cataract,\textsuperscript{79} and of ‘cataract developing in the first 18 months of life’ for a review of management and aetiology of infantile cataract.\textsuperscript{34}

For the purposes of the present study, a definition based on treatment category was inappropriate, as it was important to identify any children diagnosed and under review, but not undergoing surgical or non-surgical (occlusion and/or mydriatics) treatment to improve their vision. It was important that such cases were not excluded from the assessment of age and context of detection and estimates of incidence.
The case definition adopted for this research was:

"any child in the UK, aged 15 years or less, with newly diagnosed congenital or infantile cataract, irrespective of the treatment undertaken"

This included all cases in which cataract was present in infancy, or due to a congenital cause, or detected outside infancy, but with strong clinical evidence of earlier onset, including cataract morphology, the presence of nystagmus, or the occurrence of other congenital ocular anomaly. As the reference population was children born in the UK, those born outside it were not eligible for inclusion.

All cases with minor lens opacities not requiring further follow up or assessment were specifically excluded, as were all cases with cataract which was possibly or definitely acquired, for example, as a result of trauma, drugs or other childhood ocular or systemic diseases. Before being adopted finally, this case definition was discussed and approved by members of the BCCIG.

3.1.2.4 Surveillance period.

Surveillance was undertaken for 12 months from 1st October 1995 to 30th September 1996.
3.1.2.5 Notification of cases by ophthalmologists.

All ophthalmologists included in the reporting base were sent case notification forms at the end of the first and second months of the study to familiarise them with the scheme, and subsequently at two monthly intervals. (Appendix B, page 260) Respondents were asked to notify all cases, as defined above, seen by them for the first time for any reason, in the preceding two months. Brief identifying and clinical details about the notified case(s) were requested on the notification form. The respondent was also asked to indicate, on this form, the number of proformas required for collection of follow up data. A reply-paid envelope was provided for return of the notification form.

Throughout the ascertainment period, ad hoc case notifications, for example by telephone, were accepted without the respondents being asked to complete a notification form. Similarly, respondents could report cases directly by completing data collection proformas without formal notification using the notification form.

3.1.2.6 Development of study proformas.

Proformas were developed for collection of detailed information about each case. (Appendix C, page 261) These were pre-tested amongst ophthalmic respondents and comments were also sought from epidemiologists with expertise in questionnaire design. The proformas were amended appropriately.
Detailed information was requested on each case regarding:

*Presentation or detection and first ophthalmic assessment*
- specifically, who first suspected the child had an ocular or vision defect and at what age; the first health professional to detect cataract, together with the date and context of detection; and the age at referral to, and date of first assessment by, an ophthalmologist.

*Underlying or associated cause of cataract*
- including the findings of all investigations and non-ophthalmic clinical assessments undertaken.

*Clinical (ophthalmic and non-ophthalmic) findings*
- including visual function, morphology of cataract and other ophthalmic and systemic (non-ophthalmic) abnormalities.

*Identifying details, necessary for assessing eligibility and matching cases*
- including the child’s name, date of birth, whether born in the UK, address, NHS number, the managing hospital(s) and date of detection.

In addition, detailed data about initial management undertaken or planned were collected together with short term clinical follow-up information.
A combination of open-ended and closed-ended questions were used. To avoid inconsistencies, wherever possible, forced-choice tick boxes were used for ease of completion. The data collection proformas for each case were printed on self-carbonised paper and bound together to form booklets. Respondents were asked to complete and detach the top copy of each page, retaining the carbon copies in the booklet, as their record of the information reported about each case.

3.1.2.7 Data collection.

Before the start of the surveillance study, data collection proformas, together with short instructions on their completion, were distributed to ensure that each respondent had one booklet. Those expected to notify several cases were sent a proportionately larger number. Further proformas were sent to respondents on notification of a case and also as requested by them. Available identifiers on the reported case were entered on to the proformas before they were sent, to ensure that if any were returned without these identifiers, the case to which they referred could be determined.

When a completed proforma was received, a letter was sent to the reporting ophthalmologist to thank her/him for completing and returning it, and to confirm its receipt.
Respondents were prompted, as necessary, for return of proformas on notified cases: they were regularly sent lists of the data forms received to date for each of their reported cases and general reminders were included in the quarterly study progress report sent to all ophthalmologists.

At the end of the case ascertainment period, all ophthalmologists on the reporting base were sent a list of the cases notified by them in the preceding 12 months. They were asked to confirm that they had no further cases to be included in the study. Those respondents who had not notified a case were asked to confirm that they did not have a case to report over the study period.

3.1.2.8 Encouraging response.

A number of measures were adopted to encourage respondents to notify cases and provide information about them.

Respondents, as members of the study collaborative group (BCCIG), were consulted at an early stage about the proposed methods of study, including the means by which notification of cases or collection of data could be improved, particularly to reduce their workload. In addition, the final data proformas incorporated respondents' suggestions. Throughout the study a high level of communication was maintained with ophthalmic respondents through quarterly study progress reports, which included interim analysis, as well as other, ad hoc,
Annual meetings of the BCCIG were held to discuss study progress and findings, to which all ophthalmologists, irrespective of whether they were on the active reporting base, were invited. At the first annual meeting, in May 1995, the research programme was finalised. The second annual meeting was held at the midpoint of the case ascertainment period. This provided an opportunity to discuss interim analyses and to prompt members to notify any unreported cases and return outstanding data proformas on those already reported. All members of the BCCIG were sent a detailed annual summary report on study progress and findings prior to the annual meeting.

The study was publicised through the Royal College of Ophthalmologists' quarterly newsletter. Throughout the case ascertainment period, further opportunities were taken to publicise the study at relevant academic meetings.
3.1.3 The paediatric surveillance scheme (British Paediatric Surveillance Unit).

Surveillance for an ocular disorder had not previously been undertaken through the BPSU. It was carried out, in this study, for three reasons: to enhance overall ascertainment of cases, to allow level of ascertainment to be estimated, and to minimise any possible under-representation of children with systemic diseases or multiple disabilities, or those in whom surgery was not undertaken for any reason.

3.1.3.1 Establishing surveillance for congenital and infantile cataract through the BPSU.

The methods used to establish and maintain this paediatric active surveillance system have been reported previously by the BPSU\textsuperscript{168,178,183,186} and were not within the control of this study. Surveillance for congenital and infantile cataract was undertaken following the formal application procedure, which included final approval of the questionnaires to be sent to paediatricians to collect information on reported cases.

3.1.3.2 Case definition.

To avoid the possibility of under-reporting of cases in whom the aetiology or onset of cataract were unknown or unclear to the reporting paediatrician, a simplified and broader case definition was adopted for the paediatric surveillance scheme, and was approved by the BPSU.
Thus paediatricians were asked to notify

"any child in the UK, aged 15 years or less, with newly diagnosed cataract of any severity and irrespective of treatment undertaken."

However, all communications about the study, including the study protocol distributed by the BPSU before the surveillance started, clarified that congenital and infantile cataract was the disorder of interest. Furthermore, the number of children with acquired cataract seen by paediatricians was expected to be small.

3.1.3.3 Notification of cases by paediatricians.

The case ascertainment period for surveillance through the BPSU was concurrent with that of the ophthalmic scheme, from October 1995 to September 1996 inclusive.

Notification cards were returned directly to the BPSU with respondents indicating the number of new cases seen in the preceding month. As with all studies facilitated by the BPSU, no identifying information was provided by the clinician on the notification card. Contact details of clinicians notifying cases of congenital and infantile cataract were forwarded by the BPSU to the study researcher who communicated with them directly to gather further information. The BPSU were responsible for reminding paediatricians with notification cards outstanding for three consecutive months.
3.1.3.4 Data collection.

Once a case was notified, the reporting paediatrician was sent a questionnaire to gather further information, accompanied by a covering letter explaining the purpose of the study and identifying the principal investigator, who could be contacted to answer any queries about the study in general or the information sought.

Information was sought about detection, aetiology, clinical findings and initial management undertaken. (Appendix D, page 276) To ensure comparability of data, the sections of the questionnaire on detection and aetiology, including investigations and clinical assessments, were identical to those in the data collection proformas used in the ophthalmic scheme. The section on management was modified for paediatricians as they may have had limited access to this information. Respondents were also invited to provide copies of relevant information in other forms, such as copies of correspondence, investigation results or relevant sections of the case notes, if they wished to. The same unique identifiers (section 3.1.2.6, page 73) were sought from reporting paediatricians as from ophthalmologists to allow matching of cases notified by both sources. A summary of underlying or associated causes of congenital and infantile cataract described previously (Table 2-5, page 40) was appended to the questionnaire, to help clinicians complete the section on aetiology. A reply-paid envelope was provided for return of the questionnaire.
On receipt of a completed questionnaire, a letter was sent to the reporting paediatrician to thank her/him for completing and returning it, and as confirmation that it had been received.

Up to three reminders, at eight weekly intervals, were sent to paediatricians from whom completed questionnaires about notified cases had not been received.

The study identification number allocated to each case report by the BPSU, using a sequential coding system combining year, month and number of reports, was assigned to each questionnaire before it was sent. This ensured that any completed questionnaires returned without the respondent’s name could be traced, to allow her/him to be thanked and to avoid reminders being sent inappropriately. The use of a consistent identification number also facilitated the regular feedback undertaken to the BPSU about study progress.

Reporting paediatricians were also asked to identify, on the questionnaire, the ophthalmologist(s) involved in the management of the case, with the understanding that they would be contacted only if they were not already respondents in the ophthalmic scheme. Thus if a child was under the care of an ophthalmologist who was not on the ophthalmic reporting base, she/he was contacted. A letter was sent outlining the study, inviting her/him to join the ophthalmic scheme and asking whether she/he would be willing to provide
information on the case notified by the paediatrician, irrespective of whether she/he would be joining the reporting base. Data collection proformas were also sent with this initial correspondence. On receipt of a completed proforma, a letter was sent to thank the ophthalmologist. A single reminder was sent to ophthalmologists who did not reply to the initial letter.

3.1.3.5 Encouraging response.

A summary of the surveillance study was published in the BPSU monthly bulletin before the start of the case ascertainment period.\textsuperscript{178} Subsequently, case ascertainment was reported through this bulletin each month. A more detailed progress report was included in each annual report of the BPSU.\textsuperscript{183} The study was publicised through the newsletter of the British Association for Community Child Health. In addition, as required, both written and verbal communications were made with reporting paediatricians throughout the case ascertainment period.
3.2 Evaluation of the surveillance schemes.

The surveillance schemes were evaluated to assess compliance of clinicians with the notification system, specificity of reporting and level of ascertainment achieved.

3.2.1 Compliance with reporting.

The acceptability and representativeness of a scheme can be assessed by measuring the compliance of respondents.\textsuperscript{184,196} In the present study, this was estimated as the percentage of all notification forms returned every two months by ophthalmologists and each month by paediatricians.

3.2.2 Specificity of reporting.

The proportion of notified cases which are eligible is often referred to as the positive predicative value of a surveillance scheme.\textsuperscript{196} As it is an indicator of the efficiency of the scheme, i.e. how infrequently false positive notifications occurred, this attribute is referred to as the specificity of the system throughout this thesis. This differs from its conventional definition as a measure of the ability of a test to correctly identify individuals as disease-free. Thus the specificity of reporting through each scheme was estimated as the percentage of all reported cases subsequently confirmed as eligible.
3.2.3 Ascertainment by active surveillance.

Complete ascertainment in epidemiological studies is unlikely to be achieved by reliance on a single source. Although the use of multiple sources enhances ascertainment, it is recognised that, even in seemingly exhaustive epidemiological studies, there is a need to formally evaluate the completeness of reporting. Ascertainment by the two active surveillance schemes used in the present study was assessed using two source capture-recapture analysis.

3.2.3.1 Overview of history and methods of capture-recapture analysis.

Capture-recapture or multiple record system analysis has been developed to address the problem of under-ascertainment in epidemiological studies and provides a method for adjusting derived estimates of disease frequency appropriately. The technique originates from two sample methods used to study fish and wildlife populations and only recently has been adopted in epidemiology. Since a description by Sekar and Deming in 1949 of its use in estimation of birth and death rates and the extent of registration of these events in India, capture-recapture analysis has been used in a range of studies of human populations. An early application was in estimation of the incidence of adverse drug reactions amongst in-patients in the US in 1968. Subsequently, among other applications, capture-recapture analysis has been used in studies of congenital defects and other disorders affecting children. Its use in the study of a congenital ocular disorder has not been described previously.
Valid application of capture-recapture analysis requires that the following conditions are fulfilled:\textsuperscript{198,201,206}

1. The study population is closed.
2. All individuals identified by each source are true cases, which are readily matched from capture to recapture.
3. Capture in each sample is independent of capture in any other sample.
4. The probability of capture in each sample is the same for all individuals in the population.

It can be difficult to prove these assumptions.\textsuperscript{199,202,207} Variable catchability may exist in any natural population\textsuperscript{199} and complete independence of reporting sources is rare.\textsuperscript{199} Knowledge is required of the specific disorder, the sources of data, and the mechanisms of reporting, to identify possible deviations from these assumptions.\textsuperscript{199,206} Where multiple sources are available, statistical modelling may be used to attempt to overcome biases introduced by dependency of sources and heterogeneity in capture probabilities.\textsuperscript{198,199,201,206}

3.2.3.2 Application of two source capture-recapture analysis.

To ensure the criteria for its use were met, capture-recapture analysis was restricted to the subgroup of cases born in 1995 or 1996 and who were detected within infancy (age $\leq$ 12 months). This secured a closed population, effectively a birth cohort, within which any individual could be identified, with equal
probability, by either the ophthalmic or paediatric scheme.

The rationale for restriction of the analysis to this sub-group was that routine ocular examinations to detect cataract are conducted in infancy only in the UK\textsuperscript{26,27} therefore children detected later, may have been identified in a wider range of contexts, making the assumption of uniform probability of detection by paediatricians of these older children more debatable. Therefore the analysis was restricted to the group in which this assumption was secure, i.e. infants aged one year or less at detection.

The analysis was carried out using Chapman’s adaptation of the Lincoln-Peterson method for capture-recapture analysis in two record systems.\textsuperscript{199-201} (Equation 3-1, page 87) This also allows for the situation where one surveillance system surveys only a subset of the second system.\textsuperscript{205} Confidence intervals around the estimate were derived using the goodness-of-fit model.\textsuperscript{208} (Equation 3-2, page 88)
Equation 3-1 Method of calculation of ascertainment corrected number of cases using two source capture-recapture analysis.\(^{199-201}\)

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

where

\(N\) = total (ascertainment corrected) number of cases in the population and

\(a\) = cases reported by both schemes

\(b\) = cases reported by the paediatric scheme only

\(c\) = cases reported by the ophthalmic scheme only

as shown below

<table>
<thead>
<tr>
<th></th>
<th>Reported by ophthalmic scheme</th>
<th>Reported by the paediatric scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>(a)</td>
<td>(b)</td>
</tr>
<tr>
<td>No</td>
<td>(c)</td>
<td>(d)</td>
</tr>
</tbody>
</table>

(true unidentified cases)
Equation 3-2 Goodness of fit based confidence intervals for ascertainment adjusted estimate of total number of cases.\textsuperscript{208}

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

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

The level of ascertainment achieved by surveillance was calculated as:

\[
\frac{\text{observed cases} \; (\text{identified in the surveillance study})}{\text{expected cases} \; (N, \text{derived from capture-recapture analysis})} \times 100\%
\]

Characteristics of cases notified through each scheme were compared for evidence of heterogeneity in ascertainment probability.
3.3 Data management.

3.3.1 Monitoring progress of the surveillance study and sources of reporting.

Day to day monitoring of notification of cases by ophthalmologists and paediatricians and receipt of data proformas was undertaken using a spreadsheet developed in Microsoft Excel. On receipt of a completed proforma about a notified case, the relevant entry, listing the information received to date, was updated. The spreadsheet was also used to generate the regular audits of data received on each case which were sent, as prompts, to individual ophthalmologists.

As sources of notification of each case were also recorded in this spreadsheet, it was also used to generate the tabulation of reporting through different sources which was necessary for capture-recapture analysis.

3.3.2 Management of data reported by ophthalmologists and paediatricians.

3.3.2.1 Verification of data.

All completed proformas and questionnaires from ophthalmologists and paediatricians were scrutinised for consistency and validity of the reported information. As necessary, further information was sought from the respondent about missing or inconsistent data items. Where a case had been reported from
both sources, reported information was compared and any discrepancies were
resolved through further enquiry directly to the reporting ophthalmologist and
paediatrician.

Two ophthalmologists at one hospital (Great Ormond Street Hospital) were
expected, on the basis of a review of previous outpatient activity, to report a large
proportion of all cases. Proformas for all their cases were completed by the study
researcher and data verified by reference to the hospital case notes. Funds were
not available to allow systematic verification of data reported from all other
centres. However, whenever additional sources of information were provided by
the respondent, such as copies of correspondence, investigation results or relevant
sections of the case notes, these were used to verify the data recorded on the
proformas.

3.3.2.2 Data entry.

Numerical or categorical codes were assigned to data items on the study
proformas. Free text responses and some descriptive data were entered as
provided, without coding, for example clinical descriptions regarding ocular
abnormalities other than cataract or complex details of management.

Data from ophthalmologists and paediatricians were entered into two separate
databases, each developed in Microsoft Access. Both were relational databases,
in which data on detection, aetiology and initial management were stored in identical formats. That developed for information reported by ophthalmologists also included fields for data on subsequent management and follow up. To facilitate ease of entry and minimise inaccuracies, the interface for inputting data was designed to resemble the proformas and questionnaires used for collecting them. Internal checks were included in the database to preclude entry of value of variables outside the acceptable ranges. In addition, wherever possible, precoded variables, within pull-down menus, were used in the database for entry of responses to closed-ended questions on the proformas.

All data were entered on the databases and checked by one clerical assistant. Subsequently, each database was scrutinised independently by the study researcher to identify erroneous or inconsistent entries.

The databases were backed up to floppy disks after each session of data entry. A full back up of the personal computer, to tape, was carried out every 2 weeks.
3.4 ASCERTAINMENT OF CONGENITAL AND INFANTILE CATARACT BY EXTERNAL SOURCES.

The methods used to assess completeness of reporting of congenital and infantile cataract through external national sources are described below.

3.4.1 The Congenital Anomaly System of Office of National Statistics.

As discussed in the preceding chapter (section 2.9.2.2, page 54), the ONS congenital anomaly system in England and Wales is the only routine source of national incidence data about congenital eye anomalies but their ascertainment, at a national level, through this passive reporting system has not been assessed previously.

Following approval by ONS, a collaboration was established to conduct a validation study of notification of congenital and infantile cataract. All relevant ICD 10 codes for congenital or infantile cataract, occurring in isolation or in conjunction with a systemic disorder, were tabulated. This list was used to search all new notifications received by the congenital anomaly system in 1995 and 1996. All notifications which included the relevant codes were extracted. Quarterly meetings were held to allow manual matching of notifications to ONS with those cases identified by the surveillance study in England and Wales who were born in 1995 or 1996 and detected in infancy. Cases were matched on the basis of initials, gender, date of birth, laterality of cataract and the presence of
other congenital ocular or systemic malformations. A successful match required agreement on four of these criteria. This procedure was repeated at the end of the case ascertainment period to determine the proportion of cases ascertained by active surveillance which had also been notified to the ONS system.

3.4.2 The National Congenital Rubella Surveillance Programme.

This on-going programme uses multiple sources, including active reporting through the BPSU, to identify new cases of congenitally acquired rubella. A collaboration was established to evaluate reporting of incident cases of congenital cataract due to congenital acquired rubella. At the end of the case ascertainment period, all new notifications to the NCRSP of children born in the UK with congenital rubella were compared with such cases identified by the ophthalmic and paediatric surveillance schemes. Cases were matched on four of any of the following five criteria: initials, gender, date of birth, laterality, and the presence of other ocular and systemic anomalies. The proportion of children with cataract identified by each source were compared.

3.4.3 Hospital Episode Statistic (HES) system.

An application to conduct a validation study was accepted and disaggregated data were to be examined and compared. However, considerable delays in inputting of data for the relevant period in the HES system meant that these were not available within the time framework of the study.
3.5 Data analysis.

3.5.1 Incidence.

3.5.1.1 Unadjusted age-specific and cumulative incidence rates.

The annual age specific and cumulative incidence rates of congenital and infantile cataract were estimated using the method of Breslow and Day.\textsuperscript{209}

The age specific incidence (equivalent to the cumulative incidence of congenital and infantile cataract in the first year of life), was derived from the ratio of newly diagnosed cases in each age group to the mid year population of children within those age groups in the UK.\textsuperscript{210} Cumulative incidence of new diagnosis of congenital and infantile cataract by age 5 and by age 15 were also estimated. Confidence intervals for all incidence rates were similarly constructed using the methods of Breslow and Day.\textsuperscript{209} All analyses were carried out using SAS V6.11 (SAS Institute, North Carolina, USA) and the programme for these analyses is shown in Appendix E, page 282.

3.5.1.2 Ascertainment-adjusted incidence rates.

Incidence rates were subsequently adjusted for ascertainment by increasing the point estimates appropriately. As this adjustment was post hoc, and not based on knowledge of real cases, it was considered inappropriate to also adjust the
confidence intervals in the same way, as they reflected the sampling error of true cases.

3.5.1.3 Regional distribution.

The distribution of cases by health service region in which management was undertaken was determined. This included the number of ophthalmologists involved in each region, as well as the number of cases managed by each of them.

3.5.2 Detection and ophthalmic assessment.

Descriptive analyses were undertaken to determine: the age at which an ocular problem was first suspected, cataract was detected and first ophthalmic assessment took place, as well as the context of, and health professional responsible for, detection. Bilateral and unilateral cases were analysed separately, and together, and within the following clinically relevant but not mutually exclusive, age-groups: neonates (≤ 1 month), infants aged ≤ 3 months, infants aged ≤ 12 months, and children aged ≥ 13 months. Descriptive analyses were carried out using SPSS v 7.5 (SPSS Inc). Observed differences between unilateral and bilateral cases were examined using tests for the significance of the difference in two proportions.212
3.5.3 Aetiology.

Descriptive analyses were carried out using the mutually exclusive, and clinically relevant, categories of isolated cataract, cataract associated with another ocular disorder, or cataract associated with a systemic disorder, irrespective of the presence of another ocular disorder. Bilateral and unilateral cases were analysed separately. Descriptive analyses were carried out using SPSS v7.5 (SPSS Inc.).

Observed differences between unilateral and bilateral cases were evaluated using tests of significance of the difference in two proportions.\textsuperscript{212}
3.6 National survey of practices and training of paediatricians in routine ocular examination of infants.

This survey was carried out to determine current practice and training of UK paediatricians in routine ocular examination of infants to detect ophthalmic disorders.

3.6.1 Background.

In the United Kingdom and elsewhere,²⁶-²⁹,³¹ routine examinations are carried out to detect major ophthalmic disorders in infants. In the UK, national recommendations about practice are made in Health For All Children²⁶ and Ophthalmic Services For Children²⁷ the reports of two national joint working parties. However, little is known about the extent to which these recommendations have been adopted and the training of those involved. Therefore this survey was conducted to provide information necessary for the interpretation of the detection of children with congenital and infantile cataract in this research.
3.6.2 Survey methods.

A postal questionnaire survey was conducted in September 1995, a month before the start of the surveillance study.

3.6.2.1 Selection of respondents.

Two hundred and fifty hospital and community consultant paediatricians, 150 hospital-based trainees and 100 clinical medical officers were selected randomly from membership lists of the Royal College of Paediatrics and Child Health, the British Association of Perinatal Medicine, the British Association of Community Child Health and the Society for Public Health. Consultants were surveyed because, even when not personally undertaking routine examinations, they would be responsible for the provision of the service, including the training of junior hospital-based colleagues, who currently perform the majority of newborn examinations. The junior hospital-based trainees were randomly sampled from those working in the departments in which the selected hospital-based consultants were based.

3.6.2.2 Development and distribution of survey questionnaire.

A semi-structured questionnaire was developed for the study, comprising open-ended and closed-ended questions. (Appendix F, page 283) The questionnaire was modified after pre-testing on a selected sample of paediatricians, who were not subsequently surveyed.
Respondents were asked to indicate if they were involved, personally or through supervision of colleagues, in routine examinations of neonates and infants aged 6-8 weeks. For each age-group applicable to their practice, respondents were asked to list the ophthalmic abnormalities and disorders they specifically sought. These questions were intentionally open-ended to avoid any bias which might have been introduced if specific disorders had been highlighted. Closed-ended questions enquired about previous training received in ophthalmic assessment of infants. Specifically, respondents were asked whether they had received any previous training and at which stage(s) of their career, as well as the health professional(s) who had trained them and the form of training given, for example, lectures or practical demonstrations. Respondents were asked to indicate their requirements for further training, including the form of training sought and whether they considered they had access to an ophthalmologist for this. Respondents were also invited to include additional comments or information at the end of the questionnaire.

The questionnaires were distributed with a covering letter explaining the purpose of the survey and identifying the investigator who could be contacted for further information about the survey or the questionnaire.

A survey identification number was assigned to each questionnaire before distribution. A single reminder questionnaire was sent to non-responding
paediatricians six weeks after the first questionnaire had been distributed.
Postage-paid reply envelopes were included with the questionnaires to enhance completion and return.

3.6.3 Analysis.

On receipt of completed questionnaires, data were entered into a database in Epi-Info v6 (Atlanta). All descriptive analysis of training and of practice, by comparison with recommendations made in national guidelines,\textsuperscript{26,27} were carried out using this statistical software.
3.7 Ethics Approval.

This study was approved by the Great Ormond Street Hospital / Institute of Child Health local research ethics committee on the undertaking that patients and their families would not be contacted directly during the study.
4. RESULTS

4.1 SURVEILLANCE STUDY.

4.1.1 The ophthalmic surveillance scheme.

4.1.1.1 Composition of the active reporting base.

Questionnaires were returned by 296 (64%) consultant ophthalmologists contacted to establish whether they managed children with cataract within six weeks of mailing. (Table 4-1, page 103) Of these respondents, 193 (65%) were ineligible for inclusion in the ophthalmic reporting base: 164 (55%) referred all cases to colleagues for further management, 20 (7%) worked exclusively in non-surgical or adult subspecialties, and the remaining 9 (3%) worked in related subspecialties but did not undertake primary management of cataract.

Of the 103 (35%) eligible respondents, 88 (30%) were involved in all aspects of management, most of whom (55) reported they managed >1 case each year, and the remaining 15 (5%) were not responsible for primary treatment but had some involvement in non-surgical management. (Table 4-1, page 103)
Table 4-1 Practices of responding ophthalmologists according to membership of the ophthalmic surveillance scheme.

<table>
<thead>
<tr>
<th>Usual practice regarding management of new cases of congenital and infantile cataract</th>
<th>Number (%) of respondents</th>
<th>Number joining reporting base</th>
</tr>
</thead>
<tbody>
<tr>
<td>Involved in management</td>
<td>103 (35)</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>all aspects of primary management (&gt;1 case per year seen)</td>
<td>55 (19)</td>
</tr>
<tr>
<td></td>
<td>all aspects of primary management (≤ 1 case per year seen)</td>
<td>33 (11)</td>
</tr>
<tr>
<td></td>
<td>non-surgical or post operative management only</td>
<td>15 (5)</td>
</tr>
<tr>
<td>Not involved in management</td>
<td>193 (65)</td>
<td>not eligible</td>
</tr>
<tr>
<td></td>
<td>Refer all cases for management (&gt;1 case per year seen)</td>
<td>121 (41)</td>
</tr>
<tr>
<td></td>
<td>Refer all cases for management (≤ 1 case per year seen)</td>
<td>43 (14)</td>
</tr>
<tr>
<td></td>
<td>No cases seen / not applicable&lt;sup&gt;c&lt;/sup&gt;</td>
<td>20 (7)</td>
</tr>
<tr>
<td></td>
<td>Other relevant subspecialty&lt;sup&gt;d&lt;/sup&gt; (not primary management cataract)</td>
<td>9 (3)</td>
</tr>
</tbody>
</table>

Key

<sup>a</sup> total 296 respondents

<sup>b</sup> all joined BCCIG mailing list

<sup>c</sup> ophthalmologists in non-surgical or solely adult subspecialty

<sup>d</sup> ophthalmologists responsible for management of related disorders, such as glaucoma, retinal detachment, but not primary management of cataract
Thus overall, 88 (30%) respondents in the survey were eligible for inclusion in the active reporting base. Of these, 78 (87%) ophthalmologists joined the ophthalmic scheme, adding to the 8 ophthalmologists, approached prior to the survey, who had agreed to join it. A further 15 joined the BCCIG mailing list. (Table 4-1)

As no information was available about the practices of the non-responding ophthalmologists, it was not possible to evaluate the effect of non-response to this questionnaire survey on the completeness and composition of the reporting base. Had the same proportion of non-responding as responding ophthalmologists been responsible for the management of at least one child with cataract each year, then a further 50 ophthalmologists may have been eligible for inclusion in the reporting base. However, as will be discussed in the following chapter, this is unlikely to be the case and it is probable that the majority of eligible ophthalmologists were identified by this survey.

27 of 44 (61%) ophthalmologists newly appointed during the study period responded to letters enquiring about their practice and inviting them to join the ophthalmic reporting base. Of these, 7 were eligible and all joined. One member of the reporting base retired during the study period.

Thus the ophthalmic reporting base comprised 86 ophthalmologists at the start of the study period, in October 1995, and had increased to 98 respondents by September 1996, as shown in Table 4-2, page 105.
Table 4-2  Composition of ophthalmic reporting base by source of identification.

<table>
<thead>
<tr>
<th>Source</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At start of study period</strong></td>
<td>86</td>
</tr>
<tr>
<td>by invitation, to establish the scheme</td>
<td>8</td>
</tr>
<tr>
<td>through survey of ophthalmologists</td>
<td>78</td>
</tr>
<tr>
<td><strong>During study period</strong></td>
<td></td>
</tr>
<tr>
<td>new appointment</td>
<td>7</td>
</tr>
<tr>
<td>identified by reporting paediatricians</td>
<td>4</td>
</tr>
<tr>
<td>identified by other ophthalmologists</td>
<td>2</td>
</tr>
<tr>
<td><strong>At end of study period</strong></td>
<td>98 a</td>
</tr>
</tbody>
</table>

Key

* excludes 1 ophthalmologist who retired during study period
4.1.1.2 Case notification by ophthalmologists.

Ophthalmologists reported 278 cases in total, which are shown, according to means of reporting and eligibility, in Table 4-3, page 108.

Of 166 cases notified formally using the 2 monthly notification form, 160 (96%) were eligible cases for inclusion in the study. (Table 4-3, page 108 and Table 4-4, page 110). A further 18 cases, all eligible, were notified by other means, for example by letter or telephone. Throughout the case ascertainment period, data proformas were received without prior notification of the case using the notification form, or in lieu of it. Of 93 cases identified in this way, 57 (61%) were eligible. (Table 4-3, page 108)

At the end of the case ascertainment period, 96 (89%) respondents on the ophthalmic active reporting base completed and returned the final audit form which asked them to confirm the completeness of their reported cases or that they had no cases to report. All previously notified cases were confirmed and 1 new eligible case, not previously reported, was identified.

Of 278 cases reported by ophthalmologists, five (2%) were ineligible as they did not meet the case definition. A further 31 (11%) cases were ineligible as they were prevalent rather than incident cases, being first diagnosed outside the ascertainment period although first assessed by the reporting ophthalmologist.
within it. As outlined earlier, 6 cases reported by ophthalmologists from the Republic of Ireland were also excluded from the analysis. Thus 236 (85%) cases reported by ophthalmologists were eligible for inclusion. Data were available for all cases reported by ophthalmologists.
Table 4-3  Cases notified by ophthalmologists according to means of reporting and eligibility.

<table>
<thead>
<tr>
<th>Means of reporting</th>
<th>Number of cases notified</th>
<th>Number (%) of notified cases which were eligible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notification form</td>
<td>166</td>
<td>160 (96)</td>
</tr>
<tr>
<td>Other method of notification *</td>
<td>18</td>
<td>18 (100)</td>
</tr>
<tr>
<td>Data collection proforma sent without prior notification</td>
<td>93</td>
<td>57 (61)</td>
</tr>
<tr>
<td>Audit at end of study period</td>
<td>1</td>
<td>1 (100)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>278</strong></td>
<td><strong>236 (85)</strong></td>
</tr>
</tbody>
</table>

Key

* formal notification by other means, such as by letter or by telephone
4.1.1.3 Compliance with active reporting.

Of 236 eligible cases identified through the ophthalmic surveillance scheme, only 160 (68%) were formally reported using the notification form system.

Between 63% and 79% (median 70%) of 2 monthly notification forms were returned by ophthalmologists. All ophthalmologists returned a notification form at least once and the number of cases notified each month using these forms is shown in Table 4-4, page 110.

4.1.1.4 Specificity of the ophthalmic surveillance scheme.

The overall specificity of the ophthalmic surveillance scheme, measured as the percentage of reported cases which were eligible, was 85% (236/278). It was higher for cases notified formally than for those cases for whom data collection proformas were sent without prior notification. (Table 4-3, page 108) The percentage of all notifications through the ophthalmic scheme which met its reporting criteria was even higher, 98% (273/278).

A high level of specificity of reporting was achieved using the ophthalmic surveillance scheme, although compliance with the formal notification system was not high.
Table 4-4  Case notification and compliance with the notification system in the ophthalmic scheme.

<table>
<thead>
<tr>
<th>Reporting period</th>
<th>% (n) notification forms returned</th>
<th>number of cases notified by reporting form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oct 1995</td>
<td>72 (62)</td>
<td>21</td>
</tr>
<tr>
<td>Nov 1995</td>
<td>70 (60)</td>
<td>19</td>
</tr>
<tr>
<td>Dec 1995- Jan 1996</td>
<td>68 (59)</td>
<td>27</td>
</tr>
<tr>
<td>Feb - March 1996</td>
<td>63 (55)</td>
<td>24</td>
</tr>
<tr>
<td>April - May 1996</td>
<td>79 (73)</td>
<td>23</td>
</tr>
<tr>
<td>June - July 1996</td>
<td>72 (73)</td>
<td>28</td>
</tr>
<tr>
<td>August - September 1996</td>
<td>70 (69)</td>
<td>24</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td><strong>166</strong> a</td>
</tr>
</tbody>
</table>

Key

a  Includes 6 ineligible cases (1 not meeting case definition, 5 not incident cases)
4.1.2 The paediatric surveillance scheme.

4.1.2.1 Case notification by paediatricians.

Paediatricians notified 197 cases in total. Of these, 38 (19%) cases were ineligible as they did not meet the case definition adopted for the paediatric scheme, either because they were not incident cases or the child did not have cataract. A further 55 (28%) cases, which met the BPSU definition and were thus appropriately notified by paediatricians, were excluded subsequently as they did not meet the narrower case definition used for the study overall (and in the ophthalmic surveillance scheme): 54 had been diagnosed outside the study period, and in 1 case the cataract was acquired. One further case was ineligible as it was reported from the Republic of Ireland. The remaining 13 (7%) cases were excluded as no further follow up information could be collected about them from the reporting paediatrician: in six cases the reporting paediatrician had not recorded the child’s name or other identifying information and therefore was unable trace the case and in seven cases the questionnaire was not returned. Thus 90 of 197 (46%) cases reported by paediatricians were eligible for inclusion.

4.1.2.2 Compliance with active reporting.

During the study period, between 89% and 95% (median 92%) of monthly reporting cards were returned to the BPSU, as shown in Table 4-5, page 112.
<table>
<thead>
<tr>
<th>Reporting period</th>
<th>% BPSU cards returned</th>
<th>Number of cases notified</th>
<th>Confirmed cases</th>
<th>Notified but unconfirmed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>meet BPSU case definition</td>
<td>no cataract</td>
</tr>
<tr>
<td>Oct-95</td>
<td>95</td>
<td>37</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>Nov-95</td>
<td>94</td>
<td>19</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Dec-95</td>
<td>94</td>
<td>10</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Jan-96</td>
<td>95</td>
<td>21</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Feb-96</td>
<td>93</td>
<td>11</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Mar-96</td>
<td>92</td>
<td>14</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Apr-96</td>
<td>94</td>
<td>11</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>May-96</td>
<td>92</td>
<td>22</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>Jun-96</td>
<td>92</td>
<td>15</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Jul-96</td>
<td>89</td>
<td>14</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Aug-96</td>
<td>92</td>
<td>11</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Sep-96</td>
<td>92</td>
<td>12</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>197</strong></td>
<td><strong>146</strong></td>
<td><strong>13</strong></td>
<td><strong>25</strong></td>
</tr>
</tbody>
</table>

Key
- **a** excludes duplicate notifications
- **b** prevalent rather than incident cases
- **c** no information available from reporting paediatrician either because the paediatrician did not respond (7) or reported case could not be traced by the respondent (6)
4.1.2.3 Specificity of the paediatric surveillance scheme.

The specificity of the paediatric scheme, the percentage of reported cases which were eligible, was 46% (90/197) although 74% (146/197) of all notifications by paediatricians met the reporting criteria for this scheme.

Thus a lower specificity but higher compliance with the reporting system were attained in the paediatric than in the ophthalmic scheme.

4.1.3 Comparison of paediatric and ophthalmic surveillance schemes.

The ophthalmic and paediatric schemes are compared with respect to compliance with the formal notification system, percentage of notifications meeting reporting the criteria and specificity of reporting, in Table 4-6, page 114. Thus, although paediatricians were more successful in returning their notification cards each month, ophthalmologists were more likely to notify cases meeting the reporting criteria for their scheme and eligible for the study.
Table 4-6  Comparison of process and outcome of notification through the ophthalmic and paediatric schemes.

<table>
<thead>
<tr>
<th></th>
<th>Ophthalmic scheme</th>
<th>Paediatric scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compliance with notification system $^a$</td>
<td>63-79% (median 70%)</td>
<td>89-95% (median 92%)</td>
</tr>
<tr>
<td>Cases meeting reporting criteria $^b$</td>
<td>96% (273/278)</td>
<td>74% (146/197)</td>
</tr>
<tr>
<td>Specificity $^c$</td>
<td>84% (236/278)</td>
<td>46% (90/197)</td>
</tr>
</tbody>
</table>

Key

$^a$ Percentage of notification forms / cards returned in each reporting period.

$^b$ Percentage of all notifications meeting reporting criteria for the scheme.

$^c$ Percentage of all notified cases which were eligible for inclusion.
4.1.4 Summary of cases ascertained by surveillance by source of reporting.

Over the 12 month study period, 248 new cases of congenital and infantile cataract in the UK were identified by active surveillance through the two independent schemes. Of these 78 (31%) were notified by both sources, 158 (64%) through the ophthalmic scheme alone and 12 (5%) solely through the paediatric scheme. (Table 4-7, page 116.)

Of twelve children reported by paediatricians alone, seven were under the care of ophthalmologists outside the ophthalmic scheme, and three were each under the care of, but not reported by, ophthalmologists within the ophthalmic reporting base. The remaining two children died before formal assessment by an ophthalmologist.

Thus 236 of 248 (95%) eligible cases were identified through the ophthalmic scheme compared with 90 of 248 (36%) for the paediatric scheme.
Table 4-7 Summary of 248 new cases ascertained by surveillance by source of reporting.

<table>
<thead>
<tr>
<th>Notified through the ophthalmic scheme</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notified through the paediatric scheme</td>
<td>Yes</td>
<td>78</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>158</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>236</td>
<td></td>
</tr>
</tbody>
</table>


4.2 ASSESSMENT OF ASCERTAINMENT BY ACTIVE SURVEILLANCE USING CAPTURE-RECAPTURE ANALYSIS.

4.2.1 Capture-recapture analysis of cases detected in infancy.

Active surveillance by ophthalmologists and paediatricians identified 161 children with newly diagnosed congenital cataract, who were born in 1995 or 1996 and detected in infancy (age <13 months). These are shown, by source of reporting, in Figure 4-1, page 118. To meet the conditions for its valid use, two source capture-recapture analysis was restricted to these cases. (Equation 3-1, page 87 and Equation 3-2, page 88)

Thus:

\[
N = \left[ \left( 67 + 12 + 1 \right) \left( 67 + 82 + 1 \right) / (67 + 1) \right] - 1
\]

and

\[
\text{Var} \left( N \right) = \left( \left( 67 + 12 + 1 \right) \left( 67 + 82 + 1 \right) (12) (82) \right) / \left( (67 +1)^2 (67 +2) \right)
\]

gives an ascertainment corrected total of 175 (163-187, 95% confidence interval) as shown in Figure 4-1. Thus it was estimated that 14 infants had not been identified by either scheme.

Thus overall 92% (161/175) of all infants were estimated to have been ascertained by active surveillance, with 85% (149/175) ascertainment through the ophthalmic scheme and 45% (79/175) through the paediatric scheme.
Figure 4-1 Source of notification of 161 children with cataract born in 1995 or 1996 and detected aged 12 months or under, with capture-recapture analysis of ascertainment.

\[ N = \text{Ascertainment corrected number of cases in the population (95\% C.I.)} \]

\[ = 175 \ (163-187) \]
The characteristics of these children, according to source of notification, are summarised in Table 4-8, page 120. Cases reported to the two schemes were similar with respect to laterality, requirement for surgery, and age at, and context of detection, thus meeting the assumption of uniform probability of ascertainment required for application of capture-recapture analysis. The majority of cases reported through both schemes had ocular disease only, and a higher proportion of such cases were identified through the ophthalmic scheme. Conversely, a higher proportion of cases notified through the paediatric scheme had associated systemic disorders and were detected by hospital based paediatricians. Of twelve infants reported by paediatricians only, two died before assessment by an ophthalmologist. All cases reported by paediatricians were referred to ophthalmologists.
Table 4-8  Comparison of characteristics of children with cataract born in 1995 or 1996 and detected aged 12 months or under, according to source of notification.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases identified through the ophthalmic scheme n (% total)</th>
<th>Cases identified through the paediatric scheme n (% total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral</td>
<td>94 (63)</td>
<td>54 (68)</td>
</tr>
<tr>
<td>Undergoing surgery</td>
<td>98 (66)</td>
<td>51 (65)</td>
</tr>
<tr>
<td>First presenting to:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. hospital based paediatrician</td>
<td>82 (55)</td>
<td>57 (72)</td>
</tr>
<tr>
<td>b. community based paediatrician</td>
<td>6 (4)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>c. general practitioner</td>
<td>45 (31)</td>
<td>17 (21)</td>
</tr>
<tr>
<td>Detected in context of a routine child surveillance examination</td>
<td>101 (68)</td>
<td>55 (70)</td>
</tr>
<tr>
<td>Detected during neonatal period (aged ≤ 1 month)</td>
<td>86 (58)</td>
<td>53 (67)</td>
</tr>
</tbody>
</table>

Cause of cataract:

a. category
- cataract +/- other ocular disorder 119 (80) 52 (66)
- cataract +/- other ocular disorder and associated / underlying systemic disorder 30 (20) 27 (34)

b. underlying cause
- idiopathic 80 (54) 41 (52)
- hereditary +/- ocular disorder 39 (26) 11 (14)
- hereditary systemic disorder 22 (15) 17 (21)
- other (non-hereditary) systemic disease /disorder 8 (5) 10 (13)

Key

a 149 cases
b 79 cases
4.3 ASCERTAINMENT OF CONGENITAL AND INFANTILE CATARACT THROUGH EXTERNAL SOURCES.

4.3.1 Ascertainment through the Congenital Anomaly System of the Office of National Statistics.

Twenty-one notifications of infants with congenital cataract in England and Wales were made to the ONS congenital anomaly system between January 1995 and December 1996. Of these, 15 (71%) were incident during the study period and were matched on the basis of 4 or more identifying details with cases ascertained through the active surveillance schemes. Three cases, also reported through the paediatric surveillance scheme, were ineligible as they did not have cataract. One case, with multiple congenital anomalies, had died in the early neonatal period and could not be confirmed, but had not been identified through either the ophthalmic or paediatric scheme. In the remaining two cases the information provided in the notification to ONS was insufficient for matching.

By comparison, the surveillance study identified 149 children, born in 1995 or 1996 and detected in infancy, in England or Wales. Of these, 15 (10%) were notified to the congenital anomaly system, indicating a low level of ascertainment through this passive reporting system.
4.3.2 Ascertainment by the National Congenital Rubella Surveillance Programme.

Two cases of congenital cataract were notified during the study period to the National Congenital Rubella Surveillance Programme (NCRSP) amongst six children with congenital rubella born in the UK. Each was notified through both ophthalmic and paediatric surveillance schemes and, additionally, one was notified to the ONS Congenital Anomaly System.

4.4 Verification and completeness of reported data.

Reported data were checked by comparing with information in the case notes of the 64 (26%) cases notified by the two ophthalmologists at Great Ormond Street Hospital and 29 (12%) cases notified by other respondents. No discrepancies in reported data were found.

Complete data regarding detection were available in 235 (95%) cases and regarding aetiology in 243 (98%) cases. Variable data items were available in the remaining cases.
4.5 INCIDENCE OF CONGENITAL AND INFANTILE CATARACT IN THE UK.

4.5.1 Unadjusted incidence of congenital and infantile cataract.

Of 248 newly diagnosed cases identified by the surveillance study, 161 (65%) had bilateral and 45 (18%) left-sided unilateral cataract, and 118 (48%) were girls. In ten (4%) cases, neither age at detection or at ophthalmic assessment were available so they were excluded from estimates of incidence.

The distribution of age at detection of unilateral and bilateral cases is shown in Figure 4-2, page 124. (Discussed further in section 4.6.2, page 143)
Figure 4-2  Age at detection of children with congenital and infantile cataract in one year in the UK
Estimates of the annual age specific and cumulative incidence of congenital and infantile cataract in the UK, unadjusted for ascertainment, are shown in Table 4-9 and Table 4-10. The annual age specific incidence in the first year of life (equivalent to the cumulative incidence in the first year) was 2.29 per 10,000 children, which was considerably higher than in later childhood.

However, a child’s unadjusted annual risk of diagnosis of congenital and infantile cataract increased from 2.29 per 10,000 by the age of 1 year to 3.19 per 10,000 by 15 years. If the ten cases with missing data regarding age at detection are assumed to have been diagnosed by age 15 years (the upper age limit used in the case definition), then annual cumulative incidence of diagnosis of congenital or infantile cataract by 15 years in the UK is 3.33 per 10,000 children.
### Table 4-9  Annual unadjusted age specific incidence of congenital and infantile cataract in the UK.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Number of cases of congenital and infantile cataract</th>
<th>Annual age-specific incidence per 10,000 children</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 1</td>
<td>168</td>
<td>2.29</td>
<td>1.94 to 2.64</td>
</tr>
<tr>
<td>&gt;1 - 5</td>
<td>50</td>
<td>0.16</td>
<td>0.10 to 0.22</td>
</tr>
<tr>
<td>&gt;5 - 15</td>
<td>20</td>
<td>0.03</td>
<td>0.02 to 0.04</td>
</tr>
</tbody>
</table>

### Table 4-10  Annual unadjusted cumulative incidence of congenital and infantile cataract in the UK.

<table>
<thead>
<tr>
<th>By age (years)</th>
<th>Number of cases of congenital and infantile cataract</th>
<th>Annual cumulative incidence per 10,000 children</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>168</td>
<td>2.29</td>
<td>1.94 to 2.64</td>
</tr>
<tr>
<td>5</td>
<td>218</td>
<td>2.93</td>
<td>2.54 to 3.31</td>
</tr>
<tr>
<td>15</td>
<td>238*</td>
<td>3.19*</td>
<td>2.79 to 3.59</td>
</tr>
</tbody>
</table>

**Key**

* If 10 cases with missing age at diagnosis are included, then annual cumulative incidence by age 15 years is 3.33 per 10,000 children.
4.5.2 Incidence by laterality.

The unadjusted annual age specific and cumulative incidence of congenital and infantile cataract in the UK for bilateral and unilateral cases are shown in Table 4-11 and Table 4-12, page 128. Both age specific and cumulative incidence of bilateral cataract are higher than of unilateral cataract.

4.5.3 Incidence by sex.

The unadjusted annual age specific and cumulative incidence rates of congenital and infantile cataract in the UK amongst girls and boys are similar, as shown in Table 4-13 and Table 4-14, page 129.
Table 4-11 Annual unadjusted age-specific incidence of congenital and infantile cataract in the UK by laterality.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Bilateral</th>
<th>Unilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of cases</td>
<td>Rate per 10,000 (95% CI a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(95% Cl a)</td>
</tr>
<tr>
<td>0-1</td>
<td>108</td>
<td>1.47</td>
</tr>
<tr>
<td></td>
<td>1.19-1.74</td>
<td>0.07-0.15</td>
</tr>
<tr>
<td>&gt;1-5</td>
<td>60</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>0.60-1.04</td>
<td>0.03-0.07</td>
</tr>
</tbody>
</table>

Key

a 95% confidence interval

Table 4-12 Annual unadjusted cumulative incidence of congenital and infantile cataract in the UK by laterality.

By age (years)

<table>
<thead>
<tr>
<th>By age (years)</th>
<th>1</th>
<th>5</th>
<th>15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral</td>
<td>108</td>
<td>141</td>
<td>156</td>
</tr>
<tr>
<td></td>
<td>1.47</td>
<td>1.90</td>
<td>2.10</td>
</tr>
<tr>
<td></td>
<td>1.19-1.74</td>
<td>1.59-2.21</td>
<td>1.77-2.43</td>
</tr>
<tr>
<td>Unilateral</td>
<td>60</td>
<td>77</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>0.82</td>
<td>1.04</td>
<td>1.10</td>
</tr>
<tr>
<td></td>
<td>0.60-1.04</td>
<td>0.80-1.28</td>
<td>0.86-1.34</td>
</tr>
</tbody>
</table>

Key

a 95% confidence interval
Table 4-13 Annual unadjusted age-specific incidence of congenital and infantile cataract in the UK by sex.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of cases</td>
<td>Rate per 10,000 (95% CI a)</td>
</tr>
<tr>
<td>0 - 1</td>
<td>85</td>
<td>2.26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.31</td>
</tr>
</tbody>
</table>

Key

a 95% confidence interval

Table 4-14 Annual unadjusted cumulative incidence of congenital and infantile cataract in the UK by sex.

<table>
<thead>
<tr>
<th>By age (years)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of cases</td>
<td>Rate per 10,000 (95% CI a)</td>
</tr>
<tr>
<td>1</td>
<td>85</td>
<td>2.26</td>
</tr>
<tr>
<td></td>
<td>1.79 - 2.73</td>
<td>2.37 - 3.47</td>
</tr>
<tr>
<td>5</td>
<td>83</td>
<td>2.31</td>
</tr>
<tr>
<td></td>
<td>1.81 - 2.81</td>
<td>2.38 - 3.52</td>
</tr>
</tbody>
</table>

Key

a 95% confidence interval
4.5.4 Incidence by country.

The annual unadjusted age specific and cumulative incidence of congenital and infantile cataract by country of residence are shown in Table 4-15, page 131 and Table 4-16, page 132 respectively.

As with incidence rates for the UK as a whole, age specific incidence was greatest in infancy. The annual incidence of congenital cataract in infancy varied from 2.47 per 10,000 children in England to 0.86 per 10,000 in Wales. However although the point estimates of both age-specific and cumulative incidence in England were higher than in Scotland, Wales and Northern Ireland, the 95% confidence intervals for these estimates overlapped. As the majority of cases were reported in England, the estimated rates in the other countries were subject to greater sampling variation, which was reflected in the wider confidence intervals observed. However, as the number of cases reported outside England were small, it was not possible to statistically evaluate the observed differences in rates.
Table 4-15 Annual unadjusted age-specific incidence of congenital and infantile cataract in the UK by country of residence.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>England</th>
<th>Scotland</th>
<th>Wales</th>
<th>Northern Ireland</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of cases</td>
<td>Rate per 10,000 (95% CI)</td>
<td>Number of cases</td>
<td>Rate per 10,000 (95% CI)</td>
</tr>
<tr>
<td>0 - 1</td>
<td>152</td>
<td>2.47 (2.08 - 2.86)</td>
<td>43</td>
<td>0.17 (0.12 - 0.22)</td>
</tr>
<tr>
<td>&gt;1 - 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5 - 15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key

*a* 95% confidence interval

*b* Negative rate rounded up to zero
Table 4-16 Annual unadjusted cumulative incidence of congenital and infantile cataract in the UK by country of residence.

<table>
<thead>
<tr>
<th>Country</th>
<th>1 (Number of cases)</th>
<th>Rate per 10,000 (95% CI a)</th>
<th>5 (Number of cases)</th>
<th>Rate per 10,000 (95% CI a)</th>
<th>15 (Number of cases)</th>
<th>Rate per 10,000 (95% CI a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>England</td>
<td>152</td>
<td>2.47 (2.08 - 2.86)</td>
<td>195</td>
<td>3.14 (2.71 - 3.57)</td>
<td>211</td>
<td>3.39 (2.94 - 3.84)</td>
</tr>
<tr>
<td>Scotland</td>
<td>10</td>
<td>1.64 (0.62 - 2.66)</td>
<td>13</td>
<td>2.10 (0.97 - 3.23)</td>
<td>15</td>
<td>2.41 (1.19 - 3.53)</td>
</tr>
<tr>
<td>Wales</td>
<td>3</td>
<td>0.86 (0.0b - 1.82)</td>
<td>5</td>
<td>1.39 (0.18 - 2.62)</td>
<td>5</td>
<td>1.39 (0.18 - 2.62)</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>3</td>
<td>1.25 (0.0b - 2.66)</td>
<td>5</td>
<td>2.03 (0.25 - 3.81)</td>
<td>7</td>
<td>2.79 (0.73 - 4.85)</td>
</tr>
</tbody>
</table>

Key

a  95% confidence interval
b  Negative rate rounded up to zero
4.5.5 Ascertainment adjusted incidence of congenital and infantile cataract.

Capture-recapture analysis indicated that the 92% of eligible infants had been ascertained. (Figure 4-1, page 118) Thus the ascertainment-adjusted annual age-specific and cumulative incidence of cataract in infancy in the UK was estimated to be 2.49 per 10,000 children, as shown Figure 4-3, page 134 and Figure 4-4, page 135 respectively.

Age specific and cumulative incidence after the first year were adjusted for ascertainment by the same factor. Ascertainment-adjusted age-specific incidence rates are shown in Figure 4-3. The ascertainment adjusted risk (cumulative incidence) of new diagnosis of congenital and infantile cataract by age 5 years was estimated to be 3.19 per 10,000, increasing to 3.48 per 10,000 by age 15 years. (Figure 4-4) If the cases with missing data regarding age at detection are assumed to have been diagnosed by age 15 years, then annual ascertainment adjusted cumulative incidence of diagnosis of congenital or infantile cataract by 15 years is 3.62 per 10,000 children.
Figure 4-3  Annual age specific incidence of congenital and infantile cataract in the UK, adjusted for ascertainment.
Figure 4-4 Annual cumulative incidence of congenital and infantile cataract in the UK, adjusted for ascertainment.
4.5.6 The distribution of cases by region in the UK.

The distribution of cases by health service region in which treatment was undertaken is shown in Table 4-17, together with the total number of ophthalmologists responsible for the management of these cases within each region.

The highest percentage of all cases (34%, 84/248) were reported from North Thames. Smaller percentages were reported from South and West (11%, 27/248), Northern and Yorkshire (9%, 23/248), North West (9%, 22/248) and Trent (8%, 19/248). Less than 7% of cases were reported from each other region, with at least one case reported from every health service region.
Table 4-17 Distribution of congenital and infantile cataract by health service region, ranked by percentage of cases reported.

<table>
<thead>
<tr>
<th>Region</th>
<th>Number (% total cases (^\ast))</th>
<th>Number of ophthalmologists</th>
</tr>
</thead>
<tbody>
<tr>
<td>North Thames</td>
<td>84 (34)</td>
<td>13</td>
</tr>
<tr>
<td>South and West</td>
<td>27 (11)</td>
<td>7</td>
</tr>
<tr>
<td>Northern and Yorkshire</td>
<td>23 (9)</td>
<td>8</td>
</tr>
<tr>
<td>North West</td>
<td>22 (9)</td>
<td>4</td>
</tr>
<tr>
<td>Trent</td>
<td>19 (8)</td>
<td>6</td>
</tr>
<tr>
<td>Scotland</td>
<td>15 (6)</td>
<td>6</td>
</tr>
<tr>
<td>West Midlands</td>
<td>13 (5)</td>
<td>3</td>
</tr>
<tr>
<td>Anglia and Oxford</td>
<td>12 (5)</td>
<td>5</td>
</tr>
<tr>
<td>South Thames</td>
<td>11 (4)</td>
<td>7</td>
</tr>
<tr>
<td>Mersey</td>
<td>9 (4)</td>
<td>5</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>7 (3)</td>
<td>3</td>
</tr>
<tr>
<td>Wales</td>
<td>5 (2)</td>
<td>2</td>
</tr>
<tr>
<td>Wessex</td>
<td>1 (&lt;1)</td>
<td>1</td>
</tr>
</tbody>
</table>

**Total** 248 (100) 70

Key

\(^\ast\) 248 cases
4.5.7 The distribution of cases amongst ophthalmologists in the UK.

The distribution of all 248 cases amongst ophthalmologist is shown in Table 4-18.

Sixty four (26%) cases were reported by two ophthalmologists at Great Ormond Street Hospital (North Thames). A further 102 (41%) cases were reported by twelve ophthalmologists, each with between 5 and 20 cases. Only 39 (16%) cases were managed by ophthalmologists with a single case each during the 12 month study period. All 12 cases reported only through the paediatric scheme were in this group.

Of note, the eight ophthalmologists who had been approached individually to establish the ophthalmic reporting base notified 127 (51%) cases in total.

102 (42%) cases were under the care of ophthalmologists to whom they had been secondarily referred by another ophthalmologist. All these cases were managed by ophthalmologists within the reporting scheme.
Table 4-18 Distribution of cases amongst ophthalmologists in the UK.

<table>
<thead>
<tr>
<th>Number of cases per ophthalmologist</th>
<th>Number of ophthalmologists</th>
<th>Total number (% all cases *)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;20</td>
<td>2</td>
<td>64 (26)</td>
</tr>
<tr>
<td>10-20</td>
<td>4</td>
<td>53 (21)</td>
</tr>
<tr>
<td>5-9</td>
<td>8</td>
<td>49 (20)</td>
</tr>
<tr>
<td>2-4</td>
<td>17</td>
<td>43 (17)</td>
</tr>
<tr>
<td>1</td>
<td>39</td>
<td>39 (16)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>70</strong></td>
<td><strong>248 (100)</strong></td>
</tr>
</tbody>
</table>

Key

* 248 cases
4.6 DETECTION AND OPHTHALMIC ASSESSMENT OF CONGENITAL AND INFANTILE CATARACT IN THE UK.

In this section, the findings of the survey about current practice of screening for ocular disorders in infants are reported, to provide a context for the findings of the surveillance study regarding detection and ophthalmic assessment of children with congenital and infantile cataract in the UK.

4.6.1 Survey of practice and training of paediatricians in routine ocular examination of infants.

4.6.1.1 Current practice.

After one reminder, 365 (73%) paediatricians returned completed questionnaires: 205 consultants, 102 junior hospital paediatricians and 58 clinical medical officers (CMOs). Of these, 272 indicated that they were responsible for examinations of neonates and 200 were responsible for examinations of infants aged 6 to 8 weeks.

The percentage of these respondents who reported seeking the ophthalmic disorders specified in the national recommendations\textsuperscript{26,27} for infants aged up to 8 weeks is shown in Figure 4-5, page 142. Congenital cataract was the most frequently sought disorder: 241 (89%) respondents reported they specifically examined for this in the neonatal period and 186 (93%) in infants aged 6-8 weeks. Congenital eye anomalies and abnormal visual behaviour were sought, in children aged 6-8 weeks, by more than half of all respondents, whereas less than half
reported seeking the other ocular disorders specified in the national recommendations. There were no substantial or consistent differences in the practices of consultants compared with hospital based trainees or CMOs nor between community versus hospital based paediatricians.

4.6.1.2 Training.

A fifth of all respondents (75) and a third (32) of junior hospital paediatricians reported receiving no training in the ophthalmological examination of infants. Of 279 paediatricians reporting some training, 158 (57%) received this at postgraduate level only and 44 (16%) at undergraduate level only. Training in ophthalmic examination had been by given by a senior paediatrician (223, 80%), an ophthalmologist (115, 41%), an orthoptist (50, 18%) or a junior paediatric colleague (12, 4%), with a quarter receiving training from more than one source. The majority of these respondents (259, 92%) had received some practical training with 46% (130) reporting receiving some formal teaching in addition.

Overall 71% (248) of all responding paediatricians (57% of consultants, 81% of hospital juniors and CMOs) considered they would benefit from further training by an ophthalmologist. Most sought practical training only (49%) or in combination with formal teaching (40%). Amongst respondents reporting a requirement for further training by an ophthalmologist, 85 (40%) did not have access to such training.
Figure 4-5  The percentage of paediatricians seeking specific abnormalities in neonates and infants aged 6-8 weeks.

Key

# includes all congenital eye anomalies e.g. microphthalmos and coloboma
## not applicable in newborn
4.6.2 Age at detection and at first ophthalmic assessment.

Complete data regarding detection and ophthalmic assessment were available in 235 (95%) cases, and denominators for specific data items are reported separately. Age at detection and at ophthalmic assessment are reported for all cases and according to laterality, gender and cause of cataract.

The median age (range) at first assessment by an ophthalmologist was 10 weeks (birth to 15 years). By 3 months of age, 137 (57%) children had undergone formal ophthalmic assessment but 78 (33%) cases had not been examined by an ophthalmologist until after one year of age. (Figure 4-6, page 144) Although an ocular or vision defect had been suspected in 121 (51%) cases by one month, only 87 (36%) had been assessed by an ophthalmologist by this age. (Figure 4-7, page 145 and Table 4-19, page 146)
Figure 4-6  Cumulative percentage of cases of congenital and infantile cataract assessed by an ophthalmologist by age 15 years.
Figure 4-7 Detection and ophthalmic assessment of cases of congenital and infantile cataract by age.

- Suspected by anyone (238)
- Detected by health professional (237)
- Examined by ophthalmologist (241)
Table 4-19  Age at presentation or detection and at ophthalmic assessment of children with congenital and infantile cataract in the UK.

<table>
<thead>
<tr>
<th>Age group</th>
<th>% (n)(^a) cases in whom ocular or vision disorder suspected</th>
<th>% (n)(^b) cases presenting to or detected by a health professional</th>
<th>% (n)(^c) cases seen by an ophthalmologist</th>
</tr>
</thead>
<tbody>
<tr>
<td>By 1 month</td>
<td>51 (121)</td>
<td>40 (95)</td>
<td>36 (87)</td>
</tr>
<tr>
<td>By 3 months</td>
<td>66 (157)</td>
<td>61 (144)</td>
<td>57 (138)</td>
</tr>
<tr>
<td>By 12 months</td>
<td>74 (176)</td>
<td>71 (168)</td>
<td>67 (161)</td>
</tr>
<tr>
<td>By 5 years</td>
<td>94 (223)</td>
<td>92 (218)</td>
<td>91 (217)</td>
</tr>
<tr>
<td>By 10 years</td>
<td>99 (236)</td>
<td>99 (234)</td>
<td>99 (238)</td>
</tr>
</tbody>
</table>

Key

\(^a\) n = 238, includes 2 cases suspected antenatally and confirmed at birth

\(^b\) n = 237

\(^c\) n = 241
Bilateral and unilateral cases did not differ significantly in age at detection or at ophthalmic assessment. (Figure 4-8, page 148) Similarly, there were no significant differences between males and females in terms of age at detection, although a greater proportion of girls than boys were detected by 12 months (73%, 68% respectively, 95% CI for difference -7% to 12%, p = 0.5) as shown in Figure 4-9, page 149.

The median age (range) at first ophthalmic assessment of cases of cataract associated with a systemic disorder was 1 month (0 to 139) by comparison with 2.5 months (0 to 98) for cataract associated with another ocular disorder and 2.5 months (0 to 180) for isolated cataract.

The percentage of different categories of cases undergoing ophthalmic assessment within infancy is shown in Figure 4-10, page 150. A smaller percentage of both unilateral and bilateral isolated cases were examined by ophthalmologists in infancy than of cases with associated ocular or systemic disorders.
Figure 4-8
Age at detection of congenital and infantile cataract by laterality.

Cumulative proportion

- 0.98
- 0.96
- 0.9
- 0.74
- 0.69
- 0.64
- 0.59
- 0.5
- 0.41
- 0.38
- 0.3
- 0.2
- 0.1
- 0

By 1 month: 0.41
By 3 months: 0.59
By 1 year: 0.64
By 5 years: 0.9
By 10 years: 0.98

□ Bilateral  □ Unilateral
Figure 4-9
Age at detection of congenital and infantile cataract by sex.
Figure 4-10
Percentage of unilateral and bilateral cases examined by an ophthalmologist by age 12 months

<table>
<thead>
<tr>
<th>Condition</th>
<th>Bilateral</th>
<th>Unilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated cataract</td>
<td>55</td>
<td>25</td>
</tr>
<tr>
<td>Associated ocular disorder</td>
<td>20</td>
<td>26</td>
</tr>
<tr>
<td>Associated systemic disorder</td>
<td>30</td>
<td>5</td>
</tr>
</tbody>
</table>

- Isolated cataract 64%
- Associated ocular disorder 67%
- Associated systemic disorder 73%
There was good evidence supporting infantile onset of cataract in cases detected after the age of 12 months. In 25 (36%) cases cataract was due to confirmed, and in a further nine (13%) due to suspected, prenatal aetiological factors. While six (9%) idiopathic cases had established amblyopia of a severity which precluded surgical treatment and strongly suggested an infantile onset. In eight of the remaining 29 cases, the parents had suspected an ocular problem from infancy, and in the remaining 21 the clinical features, such as morphology, were consistent with infantile onset.

Overall, 92 % (178/193) of cases were referred to an ophthalmologist within one month of first presentation to a non-ophthalmic health professional and 88% (195/221) were seen by ophthalmologists within one month of referral to them.

4.6.3 The role of families and non-health professionals in detection.

The parents or other family members of 91 (38%) cases were the first to suspect an ocular or vision defect. Among 53 cases in whom parents suspected an ocular problem within the 3 months of life, 13 (25%) were diagnosed after this age and 24 (45%) had established ocular symptoms or signs at diagnosis. An ocular problem was first noted by the affected child in four cases (3 bilateral) or by a teacher in two bilateral cases.
4.6.4 Context of detection.

Overall 135 (57%) children were identified through the UK child health surveillance or screening programme, 83 (35%) at the neonatal and a further 30 (12%) at the 6-8 week examination. (Table 4-20, page 154) A further seven (3%) cases were identified during other routine examinations in the first two years of life and 15 (7%) during preschool or school entry vision screening. A similar percentage of unilateral and bilateral cases were detected during these routine examinations (62%, 53% respectively, p=0.23), or with prior concerns about ophthalmic signs or symptoms or known risk factors (17%, 21%, respectively, p=0.56).

Eighty two (34%) cases were detected as a result of established ophthalmic symptoms or signs, usually reduced vision, strabismus or nystagmus. (Table 4-20, page 154) This included one fifth (34) of all cases presenting in infancy, in the majority of whom (29), the parents had suspected an ocular defect before a diagnosis of cataract was made.

Thirteen (5%) cases, including nine detected in infancy, were identified through clinical examination of otherwise asymptomatic children with a family history of cataract or other ocular disease, or of pre-term infants at risk of retinopathy of prematurity. (Table 4-20, page 154) Although the median age (range) at first detection of children with hereditary cataract unassociated with systemic disease
was six weeks (birth to 8 years), 17 (28%) of these were detected after the age of one year.

A further eight (3%) cases, all bilateral, were identified during assessment or primary management of a systemic disorder. In all cases with underlying or associated systemic disorders, the non-ophthalmic features had been noted prior to detection of cataract although in one, the definitive systemic diagnosis was first suggested by the findings of the ophthalmic examination.
Table 4-20 Context of detection of congenital and infantile cataract.

<table>
<thead>
<tr>
<th>Context of Detection</th>
<th>n (%) all cases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Child health screening or surveillance</strong></td>
<td></td>
</tr>
<tr>
<td>Neonatal examination</td>
<td>83 (35)</td>
</tr>
<tr>
<td>6-8 weeks examination</td>
<td>30 (12)</td>
</tr>
<tr>
<td>8-9 month examination</td>
<td>3 (1)</td>
</tr>
<tr>
<td>13-18 month examination</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Preschool vision screening</td>
<td>4 (2)</td>
</tr>
<tr>
<td>School entry vision screening</td>
<td>11 (5)</td>
</tr>
<tr>
<td><strong>Presentation with ophthalmic symptoms or signs</strong></td>
<td>82 (34)</td>
</tr>
<tr>
<td><strong>Targeted examination of high risk groups by ophthalmic professionals b</strong></td>
<td>13 (5)</td>
</tr>
<tr>
<td>Sibling with ocular or systemic disease</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Other ocular or systemic family history</td>
<td>3 (1)</td>
</tr>
<tr>
<td><strong>Detection during assessment or management of a systemic disorder</strong></td>
<td>8 (3)</td>
</tr>
<tr>
<td><strong>Routine eye examination</strong></td>
<td>1 (&lt;1)</td>
</tr>
</tbody>
</table>

**Key**

a n = 239

b Includes cases detected by:
a geneticist (1) screening for an unrelated systemic disorder
a general practitioner (1) and a community paediatrician (1) examining children with a family history of ocular disease

154
4.6.5 Health professionals involved in detection.

The majority of cases were detected by a non-ophthalmic health professionals, usually a hospital paediatrician (41%) or a general practitioner (27%), as shown in Table 4-21, page 156. A range of ophthalmic professionals identified the remaining cases. Finally, two bilateral hereditary cases, first suspected by an obstetrician during antenatal ultrasound examination, were subsequently confirmed by a paediatrician.
Table 4-21  First health professional to detect congenital cataract.

<table>
<thead>
<tr>
<th>Health professional</th>
<th>n ( % of all cases *)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Non-ophthalmic</strong></td>
<td></td>
</tr>
<tr>
<td>Hospital paediatrician</td>
<td>96 (41)</td>
</tr>
<tr>
<td>General practitioner</td>
<td>63 (27)</td>
</tr>
<tr>
<td>Community paediatrician</td>
<td>13 (5)</td>
</tr>
<tr>
<td>Health visitor</td>
<td>10 (4)</td>
</tr>
<tr>
<td>School nurse or doctor</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Other (^b)</td>
<td>2 (1)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ophthalmic</strong></td>
<td></td>
</tr>
<tr>
<td>Optometrist</td>
<td>17 (7)</td>
</tr>
<tr>
<td>Ophthalmologist</td>
<td>14 (6)</td>
</tr>
<tr>
<td>Orthoptist</td>
<td>11 (5)</td>
</tr>
</tbody>
</table>

Key

\(^a\) n = 235

\(^b\) 1 midwife, 1 geneticist
4.7 Underlying and Associated Causes of Congenital and Infantile Cataract in the UK.

Complete data regarding underlying or associated cause were available in 243 (98%) cases of which 160 had bilateral and 83 had unilateral cataract.

4.7.1 Categories of cataract.

Isolated cataract was significantly more prevalent in children with bilateral disease, accounting for 97 (61%) bilateral and 39 (47%) unilateral cases (95% CI for difference 1% to 27%, p=0.05). Associated ocular disorders were more common amongst those with unilateral cataract, occurring in 39 (47%) unilateral and 22 (14%) bilateral cases (95% CI for difference 22% to 44%, p<0.001).

Conversely, associated systemic disorders were present in 41 (25%) bilateral but only 5 (6%) unilateral cases (95% CI for difference 12% to 34%, p<0.001) as shown in Figure 4-11, page 158. In all cases with associated systemic disorders, the non-ophthalmic clinical findings had been noted prior to detection of cataract.

Although more bilateral than unilateral cases occurred in boys (54%, 49% respectively) this was not statistically significant. (95% CI for difference -8% to 18%, p=0.5). Similarly, a male excess (23, 59%) amongst unilateral cases with associated ocular anomaly was not statistically significant (p=0.26).

Table 4-22, page 159)
Figure 4-11  Categories of cases of congenital and infantile cataract by laterality.

- Bilateral (160) cases:
  - Associated systemic disorder: 25%
  - Associated ocular disorder: 61%
  - Isolated: 14%

- Unilateral (83) cases:
  - Associated systemic disorder: 6%
  - Associated ocular disorder: 47%
  - Isolated: 47%
Table 4-22  Number (percentage) of boys in each category of congenital and infantile cataract.

<table>
<thead>
<tr>
<th></th>
<th>Isolated cataract n (% cases a)</th>
<th>Associated ocular disorder n (% cases b)</th>
<th>Associated systemic disorder n (% cases c)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unilateral</strong></td>
<td>16 (41)</td>
<td>23 (59)</td>
<td>2 (40)</td>
</tr>
<tr>
<td><strong>Bilateral</strong></td>
<td>54 (56)</td>
<td>9 (41)</td>
<td>23 (56)</td>
</tr>
<tr>
<td><strong>All</strong></td>
<td>70 (51)</td>
<td>32 (52)</td>
<td>46 (54)</td>
</tr>
</tbody>
</table>

Key

a  39 unilateral, 97 bilateral isolated cataract

b  39 unilateral, 22 bilateral cataract associated with an ocular disorder

c  5 unilateral, 41 bilateral cataract associated with a systemic disorder
4.7.2 Causes of cataract.

There were significant differences in the aetiology of unilateral and bilateral cases, as shown in Figure 4-12, page 161 and Table 4-23, page 162. Seventy six (92%) unilateral cases were idiopathic, almost half with an associated ocular disorder, compared with 60 (38%) bilateral idiopathic cases with predominantly isolated cataract. By contrast 90 (56%) bilateral cases but only 5 (6%) unilateral cases were due to hereditary disease. Non-hereditary systemic disorders accounted for 10 (6%) bilateral and 2 (2%) unilateral cases. These differences are discussed in detail in this section.
Figure 4-12 Causes of congenital and infantile cataract by laterality.

- Bilateral (160): Other aetiological factor - 38%, Hereditary - 56%, Idiopathic - 6%
- Unilateral (83): Other aetiological factor - 2%, Hereditary - 92%, Idiopathic - 6%
<table>
<thead>
<tr>
<th>Cause</th>
<th>Bilateral (160) n (%)</th>
<th>Unilateral (83) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>isolated</td>
<td>60 (38)</td>
<td>76 (92)</td>
</tr>
<tr>
<td>with ocular disorder</td>
<td>53 (34)</td>
<td>37 (44)</td>
</tr>
<tr>
<td></td>
<td>7 (4)</td>
<td>39 (48)</td>
</tr>
<tr>
<td>Hereditary</td>
<td>90 (56)</td>
<td>5 (6)</td>
</tr>
<tr>
<td>isolated</td>
<td>44 (28)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>with ocular disorder</td>
<td>15 (9)</td>
<td>-</td>
</tr>
<tr>
<td>with systemic disorder</td>
<td>31 (19)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Other systemic aetiological factor</td>
<td>10 (6)</td>
<td>2 (2)</td>
</tr>
</tbody>
</table>
4.7.2.1 Hereditary disease.

A higher percentage of bilateral than unilateral cases were due to hereditary
disease (56%, 6% respectively, 95% CI for difference 38% to 62%, p <0.001),
as shown in Figure 4-12, page 161. There were also differing patterns of
inheritance, as shown in Table 4-24, page 164.

Bilateral cataract was caused by a number of uncommon hereditary systemic
disorders, including PEHO syndrome and Odho syndrome. Four children in this
group died shortly after presentation: one with Marfan’s syndrome, one with
Odho’s syndrome, one with Cockayne syndrome, and one with Rhizomelic
chondrodysplasia punctata. Of unilateral hereditary cases, three had underlying
systemic disease and two had isolated autosomal dominant cataract. (Table 4-24
page 164)

Cataract was attributed to Down syndrome in twelve of thirteen children with this
disorder. Of these, eleven had bilateral cataract and eight were detected in the
early neonatal period. One of the bilateral cases had posterior lenticous which
has not commonly been reported in Down syndrome. In the remaining child with
trisomy 21, cataract was attributed to autosomal recessive inheritance.
Table 4-24  Hereditary causes of congenital and infantile cataract in the UK.

<table>
<thead>
<tr>
<th>Category and hereditary cause</th>
<th>Bilateral (160)</th>
<th>Unilateral (83)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td><strong>Isolated cataract</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>autosomal dominant</td>
<td>40 (25)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>autosomal recessive</td>
<td>4 (2)</td>
<td></td>
</tr>
<tr>
<td><strong>Associated ocular disorder</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>autosomal dominant</td>
<td>13 (8)</td>
<td></td>
</tr>
<tr>
<td> 5 microphthalmos, 1 persistent hyperplastic  primary vitreous, 1 posterior lenticonus,  6 anterior segment dysgenesis</td>
<td>                           </td>
<td>                           </td>
</tr>
<tr>
<td>autosomal recessive</td>
<td>2 (1)</td>
<td></td>
</tr>
<tr>
<td> 1 persistent hyperplastic  primary vitreous,  1 anterior segment dysgenesis</td>
<td>                           </td>
<td>                           </td>
</tr>
<tr>
<td><strong>Associated systemic disorder</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>chromosomal - trisomy 21</td>
<td>11 (7)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>autosomal recessive (+ trisomy 21)</td>
<td>1 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td>autosomal dominant (+ Marfan)</td>
<td>1 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td>X-linked recessive - Lowe’s syndrome</td>
<td>1 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td>autosomal recessive</td>
<td>17 (11)</td>
<td>2 (2)</td>
</tr>
<tr>
<td> Rhizomelic chondrodysplasia punctata</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td> Atypical galactosaemia</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td> Smith-Lemli-Optiz syndrome</td>
<td>1</td>
<td>1 (1)</td>
</tr>
<tr>
<td> PEHO syndrome</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td> Ohdo syndrome</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td> COFS syndrome</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td> Cockayne syndrome</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td> Congenital ichthyosis</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td> Walker Warburg syndrome</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td> Other autosomal recessive syndromes</td>
<td>6</td>
<td>1</td>
</tr>
</tbody>
</table>
4.7.2.2 Prenatal infection.

Prenatal infections were implicated in six cases, with varying degrees of certainty. Prenatal rubella infection resulted in unilateral cataract in two children: one with microphthalmos, the other with retinopathy. Prenatal toxoplasma infection was implicated in one child with bilateral cataract whose twin had chorioretinal disease. Prenatal infections were the probable cause in a further three bilateral cases who had salient systemic features but in whom investigations were inconclusive.

4.7.2.3 Other systemic/environmental aetiological factors.

Specific systemic aetiological factors were confirmed or strongly suspected in a small number of bilateral cases. (Table 4-23, page 162) Severe perinatal hypoxia was the probable cause of bilateral cataract in one child who died shortly after birth from its complications. Two children with bilateral cataract had cerebral palsy, amongst other non-ocular features, and an underlying systemic aetiological factor was suspected. Similarly, an underlying metabolic syndrome was strongly suspected but could not be confirmed in three bilateral cases with relevant systemic findings.
4.7.2.4 Unknown aetiological factors (idiopathic cataract).

Cataract of unknown aetiology accounted for 76 (92%) of unilateral cases and 60 (38%) of bilateral cases (CI for difference 41% to 67%, p<0.001), as shown in Figure 4-12, page 161. Of note, 39 (51%) of those with unilateral idiopathic cataract had an associated ocular anomaly compared with 7 (12%) of bilateral idiopathic cases (95% CI for difference 23% to 55%, p<0.001; Table 4-23, page 162).

Possible contributing aetiological factors were reported in a small number of bilateral and unilateral idiopathic cases. Nine (15%) bilateral and 5 (7%) unilateral cases were born pre-term (< 37 weeks) and/or of low birth-weight (<2500g). Peri-natal hypoxia was also reported in one unilateral case who was born preterm. Prolonged maternal hyperglycaemia occurred in one (1%) unilateral case. One child with bilateral cataract had peri-natal hypoglycaemia resulting in fits. Although of uncertain significance, in six cases (five bilateral) maternal ingestion, from early pregnancy, of the following drugs was reported: methadone and phenobarbitone (1), sodium valproate (1) in child who was also preterm, thyroxine (2), atenolol (1), and fluoxetine hydrochloride (Prozac) (1) in a child with unilateral cataract. In four isolated bilateral cases, which were categorised as idiopathic, an autosomal recessive (2) or autosomal dominant (2) inheritance was suspected but could not be confirmed.
Six (2%) children in the study cohort were twins and there were no other higher order multiple births. Five (7%) unilateral idiopathic cases, of whom two were also born preterm, had unaffected twins and one bilateral case had a twin with toxoplasma chorioretinitis.
5. DISCUSSION

In this first national epidemiological study of congenital and infantile cataract in the UK, surveillance through two independent reporting schemes was undertaken to identify a representative cohort of affected children. A high level of ascertainment of eligible cases, estimated by capture-recapture analysis, was achieved. The observed incidence of congenital and infantile cataract in the UK is higher than previously reported from routine sources. A large proportion of children with this disorder are not detected through the existing national screening programme and consequently are not first examined by an ophthalmologist until after their first birthday. Bilateral and unilateral cases differ considerably in terms of their underlying or associated causes. The proportion of congenital and infantile cataract in the UK currently amenable to primary prevention is small, as most unilateral cases, and a large proportion of bilateral cases, are of unknown aetiology.

In this chapter, the research methodology is critically appraised: the findings of each component of this research are summarised and their internal validity assessed. These findings are interpreted in the light of relevant existing knowledge and the implications of this body of work for clinical practice and future research are discussed.
5.1 SURVEILLANCE METHODS.

5.1.1 Summary of findings.

Surveillance was undertaken independently through two national schemes: one, a newly devised, disorder-specific scheme in ophthalmology, and the other, an existing UK scheme in paediatrics covering a range of disorders. Ophthalmic respondents were less compliant with the notification system than their paediatric counterparts but reported a higher proportion of all eligible cases, as well as fewer ineligible cases. Using capture-recapture analysis, it was estimated that overall 92% of infants were ascertained, with the level of ascertainment being higher in the ophthalmic than the paediatric scheme (85% and 45% respectively).

5.1.2 Case definition.

In the absence of an appropriate existing definition, a new clinical case definition for congenital and infantile was adopted for this study. This was intended to encompass children with visually significant cataract of infantile onset, who form a clinically relevant group, distinct from other children with cataract. Its validity was assumed in this study, in the absence of a ‘gold standard’ against which to evaluate it formally.

The case definition adopted had been agreed, before the study commenced, with ophthalmologists participating in the surveillance scheme. The majority of cases
were reported by a small number of these respondents with particular expertise in
the management of young children with cataract. Only 2% of cases notified by
ophthalmologists were ineligible because they did not meet the case definition.
Thus it is reasonable to assume that the case definition was reliably applied by
ophthalmic respondents. This assumption is supported indirectly by published
evaluations of inter-observer variation in large epidemiological studies which
have shown that most ophthalmic diagnoses made clinically are reliable.213

Ease of application of the case definition is recognised to be an important factor in
successful surveillance.160,162,165,178,184 Therefore a simplified case definition was
adopted for the paediatric scheme, to minimise under-reporting of cases in which
the aetiology or age at onset of cataract were unknown to the reporting
paediatrician. Of cases reported by paediatricians which did not meet the case
definition, two thirds were ineligible because they were prevalent cases and only
one child with acquired cataract was notified. This suggests that the use of a
broader case definition did not adversely affect specificity of reporting by
paediatricians.

The eligibility of all notified cases was carefully assessed from the details
provided. As discussed in the preceding chapter (section 4.6.2), there was
evidence supporting infantile onset in those cases detected outside infancy. This
included morphology, associated congenital ocular anomalies, nystagmus and
established amblyopia. Thus they were included in the study as they were
considered to be valid cases of cataract of congenital or infantile onset.

5.1.3 Completeness of the reporting bases of the surveillance schemes.

Surveillance has not previously been used widely in ophthalmology. At the time the research reported in this thesis was initiated, a national surveillance scheme in ophthalmology did not exist. Therefore it was necessary to establish a new disorder-specific scheme.

The management of congenital and infantile cataract is recognised to be a highly specialised area of ophthalmic practice. Eight ophthalmologists in the UK known to have particular expertise in this area were specifically approached to establish the surveillance scheme: they subsequently reported more than half of all eligible cases.

Most other respondents were identified through the survey of self-reported practice as a result of which, 87% of replying eligible ophthalmologists joined the reporting base. However, in the absence of appropriate census data about ophthalmic practice in the UK, formal validation of the ophthalmic reporting base was not conducted. Although it is possible that there was biased recruitment of respondents to the reporting base, a higher than expected number of ophthalmologists reported managing infants with cataract and it is likely that most eligible respondents were included. Evidence to support this comes from the
finding that only 7 (3%) eligible cases were under the care of an ophthalmologist outside the scheme.

An ocular disorder has not previously been included in the BPSU surveillance scheme. The composition of the paediatric reporting base, comprising over 1300 respondents, was not within the control of this study. The surgical (ophthalmic) management of infants with cataract is more highly specialised than the detection of affected children by screening or their general (paediatric) assessment. Therefore it is likely that many of the respondents on the paediatric reporting base would have been involved, in some way, in the management of children with congenital and infantile cataract. However the findings of one study to validate the paediatric reporting base suggest some previous under-representation of neonatologists, community paediatricians and paediatric neurologists, some of whom might be responsible for the care of infants with cataract. The effect of this potential bias is discussed further in the context of ascertainment by the paediatric scheme. (Section 5.1.6, page 175)

Surveillance through the paediatric scheme was undertaken to minimise under-representation of children with lethal or systemic diseases or multiple disabilities, or those in whom surgery was not undertaken for any reason, as well as to allow ascertainment to be estimated. That paediatricians notified two children who died before ophthalmic assessment could take place was evidence that this aim was likely to have been realised.
5.1.4 Compliance with the notification systems.

Although modelled on the paediatric scheme to function as an active surveillance system with formal notification of cases and confirmation of null reports, compliance with the 2 monthly reporting system in the ophthalmic scheme was not high. However, the notification form return rates achieved were similar to those obtained in the early months of the BPSU scheme and those reported in the first year of a recently established national ophthalmic surveillance scheme, run by the British Ophthalmological Surveillance Unit. (Personal communication, B. Foot, Scientific Co-ordinator, BOSU)

Throughout the study, passive as well as active surveillance occurred in the ophthalmic scheme, as clinicians were allowed to report cases through other means than the two-monthly notification forms. Thus the formal reporting system appears to have served simply as a prompt to some ophthalmologists, who preferred to report cases directly rather than use this system, whereas, other respondents actively notified null reports. This hybrid model may be relevant to other schemes, as it demonstrates that surveillance can be effective without strict adherence to only one paradigm and that flexibility within a system may improve compliance and ascertainment.

Surveillance through the paediatric scheme for congenital and infantile cataract, as one of 12 disorders being surveyed concurrently, met the requirements of an active surveillance system. High card return rates were reported by the BPSU
throughout the study period, indicating good compliance with the reporting system, and greater than in the ophthalmic scheme.

5.1.5 Specificity of reporting.

Card return rates can be used as a measure of compliance with a surveillance scheme, but do not necessarily correlate with specificity of reporting or completeness of ascertainment. Low ascertainment, despite high compliance with the notification system, has been reported by others. A high level of specificity, the percentage of notified cases which were eligible, was achieved in the ophthalmic scheme, supporting the efficiency of this disorder-specific scheme in identifying eligible children.

Whilst the specificity of the paediatric scheme was lower, the percentage of cases appropriately notified was of a level which suggests other disorders principally managed by non-paediatricians might be successfully studied through this scheme. The most common reason for ineligibility in the study was that notified cases were prevalent rather than incident, reflecting the temporal sequence of their detection and referral. It is of note, however, that despite reminders to reporting paediatricians, 7% of all notifications were unconfirmed, often because the paediatrician had not retained the child's identifying details at the time of notification and was unable to the case to trace the case subsequently. This problem has been similarly encountered in other studies using the BPSU
scheme and highlights the vulnerability of active notification systems. Such non-response in a surveillance scheme can potentially give rise to misleading conclusions about the disorder being studied. This emphasises the importance of careful attention to minimising difficulties in the process of notification and collection of follow-up data from respondents. As specificity and sensitivity (detection rate) of surveillance schemes are inter-dependent, both are also relevant to ascertainment by the paediatric scheme, and are discussed further in that context in the following section.

5.1.6 Ascertainment by the surveillance schemes.

Capture-recapture analysis is a recognised method for quantifying completeness of ascertainment. Although previously used in the study of congenital anomalies, its application to the study of ophthalmic disorders has not been described before. The technique was applied here in its two-source method which, to be valid, requires that certain conditions are fulfilled, namely that all cases are drawn from a closed population, are identifiable for matching, and have a uniform probability of being ascertained by each source, which are independent of each other. (Section 3.2.3.1, page 84)

In this study, by restricting the capture-recapture analysis to cases born in 1995 or 1996 and detected in infancy, a subgroup effectively forming a birth cohort, was identified as the closed population of interest.
Accurate matching was ensured by the availability of more detailed information on all reported cases.

The issue of uniform ascertainment probabilities was more complex. It was reasonably assumed for reporting by ophthalmologists, with the only probable exception being infants identified by paediatricians but not referred to ophthalmologists for treatment and there were no such reports. The two infants who died before ophthalmic assessment could take place were still reported by paediatricians and added strength to the belief that, as intended, children with systemic disorders associated with cataract had been adequately ascertained by surveillance through the paediatric scheme. Thus a uniform probability of identification by paediatricians, who are involved in both detection and management of infants with cataract, was likely to have existed but is difficult to prove.

Comparison of cases reported through the ophthalmic and paediatric schemes showed that they were similar with respect to factors which might have influenced ascertainment: laterality, treatment undertaken and age at, and context of, detection (in particular, detection through screening in infancy). Whilst the percentage of notified cases with idiopathic cataract was similar in the two schemes, a higher percentage of infants notified through the paediatric than the ophthalmic scheme had associated systemic disorders and the converse was true.
for infants with isolated ocular disease. As it is recognised that some level of variable catchability exists in any natural population, these differences were not considered to be sufficient to preclude the use of capture-recapture analysis.

Complete independence of reporting sources is rare. Consequently, although paediatricians and ophthalmologists notified their cases through entirely separate systems, the possibility that paediatricians did not report cases they knew had been notified by their ophthalmic colleagues, or the converse situation, cannot be entirely discounted. Thus some dependency between the two sources cannot be excluded. Had positive dependence in reporting existed, whereby a case was more likely to be identified in one system if also reported in another, this would result in an overestimate of the completeness of ascertainment. An assessment of the order of magnitude of such an error can be made by assuming the estimated 95th centile of the true number of infants in the population to be correct: this would suggest that overall ascertainment had been 86% (161/187) rather than 92% (161/175). Conversely, had negative dependence of sources existed, resulting in under-estimation of ascertainment, of generally of much greater magnitude, this would imply that overall ascertainment had been higher than 92%. Neither positive or negative dependence, or the existence of both, in this study can be excluded.

In the absence of other data sources, and given the small number of cases reported through the paediatric scheme alone, assumptions about uniform ascertainment
probabilities and source independence could not be tested statistically in a meaningful way. However, from knowledge of the role of the ophthalmologists and paediatricians in the UK in the management of congenital and infantile cataract, as well as of the two reporting schemes, it is reasonable to suggest that use of capture-recapture analysis to estimate ascertainment of infants was valid. Thus the derived estimate of detection rates of the two surveillance schemes are considered accurate.

The high level of ascertainment achieved by the ophthalmic scheme, established within five months specifically for this study, concurs with the experiences of other investigators and demonstrates that effective surveillance can be achieved by clinicians without prior experience of the methods. The high ascertainment is likely to reflect the motivation of participating ophthalmologists who, as members of the study collaborative group, were committed to the longer-term assessment of outcome in the study cohort. Their participation in the surveillance scheme is also likely to have been encouraged by the high level of communication maintained with them throughout the study period, as well as by the combination and flexibility of methods of reporting, which are reported to be important components of successful surveillance schemes.

However, although effective, had there been sole reliance on the ophthalmic scheme, 5% of all cases would have been missed, which re-emphasises the value of using multiple appropriate sources, wherever available, to enhance
ascertainment in epidemiological studies of rare disorders. Furthermore, without two sources, estimates of the completeness of ascertainment would not have been possible.

As surveillance has not been widely applied in ophthalmological research, experience of its use in this study, as a disorder-specific and versatile reporting model, strengthens the initiative by others to establish a new national active surveillance scheme in ophthalmology, run by the British Ophthalmological Surveillance Unit (BOSU), and may also have implications for its methods.

Flexibility is recognised to be an important attribute of successful surveillance schemes and in the present study, allowing respondents to report cases by means other than the formal notification system improved ascertainment. Thus flexibility and adaptability of the notification system may be important to the success of specific studies undertaken through the BOSU scheme in the future. Recognition of passive reporting within a system that it intended to be active is also important in evaluating and interpreting compliance and ascertainment.

Specific surveillance systems are reported to be more accurate, which is supported by the findings of the present study. Thus, it is possible to suggest that those rare ophthalmic disorders managed by a small number of sub-specialists on the BOSU reporting base, may be more efficiently and thoroughly ascertained by
surveying only the relevant subset of respondents. These and other possible benefits, such as reduced administrative requirements and costs, would have to be weighed against the potential disadvantage of ascertainment bias which might be introduced by failing to identify any eligible cases under the care of ophthalmologists who individually only manage a very small number of affected individuals, for example one case per year.

Surveillance through the paediatric scheme improved ascertainment overall, and in particular, helped to identify children with systemic disorders and those not undergoing treatment. Thus one main purpose of surveying through this scheme was served. However ascertainment through this scheme was low despite high compliance with the notification system. Assuming that null reports were accurate, this might have reflected other factors which it would be important to address in future studies of ocular disorders using this scheme.

Since its establishment over 10 years ago, the scheme has facilitated the concurrent surveillance of a number of uncommon disorders. Where specifically assessed, the level of case ascertainment has varied with the disorder being studied. For example, higher ascertainment was reported for children with diabetes, and for babies with vertically transmitted HIV, both disorders in which paediatricians have a greater role in primary management, than for cataract in this study. Differences in ascertainment are likely therefore to reflect the pattern of presentation and management of the disorder studied, as well as
the composition and completeness of the reporting base with respect to subspecialty interests. As previously discussed, all these factors may have been relevant in the present study, as both community paediatricians and neonatologists, reported to be under-represented in the paediatric reporting base might be expected to be involved in the detection of children with cataract.

As prevalent cases, identified by either scheme, were ineligible, it is probable that the temporal sequence of detection and referral of some cases was of greatest importance to the ascertainment of cataract by the paediatric scheme. Cases first detected within the study period but subsequently examined by paediatricians outside it, would not have been notified through both schemes and this accounted for 28% of cases correctly notified by paediatricians.

It is possible that all the notified but unconfirmed cases were eligible, and thus their exclusion reduced the sensitivity (detection rate) of the scheme. Difficulties in tracing notified cases subsequently have been reported previously and in the present study might have been avoided by providing paediatricians with data collection questionnaires at the start of the study, just as ophthalmologists were given data proformas.

Lastly, it is possible that some cases known to paediatricians may not have been reported, which is supported by the experiences of other investigators using this scheme. In this context, paediatricians may have been less motivated to report
cases than ophthalmologists. Their response might have been encouraged by providing regular individual feedback on study progress, in a similar way as to ophthalmologists. This would be important to consider in any future studies through this scheme of disorders not primarily managed by paediatricians.

As ophthalmic disorders have not previously been surveyed through this, or other national schemes in paediatrics the findings regarding ascertainment of congenital and infantile cataract may be relevant to similar studies in the future. A number of measures can be taken to maximise the specificity and sensitivity of reporting of ocular disorders in such schemes. These include the use of an easily applied case definition, an understanding of the clinical workload of different groups of respondents, the characterisation of the role of paediatricians in the management of affected children, together with the temporal sequence of their involvement, and the maintenance of appropriate communication to improve the motivation of respondents to notify cases and provide data about them.

5.1.7 Data verification.

Detailed data were collected from ophthalmologists and paediatricians about each case they notified. In order to minimise observer and measurement biases in this study, a number of measures were taken to enhance accurate reporting of data, as well as to assess their validity.
To allow direct comparison, the format of the questionnaires sent to paediatricians was identical to that of the data collection proformas used by ophthalmologists. To ensure they were appropriate and acceptable, ophthalmologists on the reporting base were consulted in the development of the proformas and the BPSU executive committee assessed the questionnaires sent to paediatricians. Both proformas and questionnaires were distributed with instructions about their completion. Forced choice questions were used, wherever possible, to avoid inaccuracies. Consistent unique identifiers were used for matching of cases.

All proformas and all questionnaires were carefully scrutinised by the same observer for consistency and validity of the reported information. Further information was sought, when necessary, from the respondent about missing or inconsistent data items or to resolve discrepancies. Reported data for 38% of cases were verified by reference to the case notes but logistic and budgetary constraints precluded this being undertaken for all cases.

Thus complete data were available for the majority of cases and reported information is therefore considered to be accurate and representative.
5.1.8 Conclusion.

The mode of identification or source of reporting of cases can influence the resulting estimate of prevalence of congenital malformations. Specific, intensive investigation tends to be more complete than reliance on hospital or other clinical records which, in turn, are generally more complete than routinely recorded health service data.\(^3,4\) This is particularly relevant to the study of uncommon disorders since incomplete or differential ascertainment will influence estimates of disease frequency and such selection bias could lead to a misleading interpretation of determinants or outcome.\(^8\)

Surveillance methods have been used in the study of large number of uncommon health events.\(^8,14,145,146,160-162,166,173,174,178,189,211\) In recognition of the diverse models of surveillance used and their purposes, in 1971 Langmuir coined the phrase "epidemiological intelligence" to encapsulate these diverse activities.\(^216\) Despite their widespread use for routine monitoring of temporal trends of various health events of public health importance, such as notifiable communicable diseases,\(^14,145,146,162\) adverse drug reactions,\(^14,15,160\) and congenital anomalies,\(^14,145,146,165\) as well as their application in specific studies, many reporting systems have not been systematically evaluated.\(^162\) For example, in one of the few published studies to use active surveillance methods to ascertain ophthalmic disorders, cases of acute toxoplasma chorioretinitis were identified through a single source, precluding formal evaluation of completeness of reporting.\(^189\)
Regular review and modification of established public health surveillance systems, based on the explicit criteria of quality, usefulness and cost, have been recommended.\textsuperscript{145,160} A proposed systematic method of evaluation of quality is based on the inter-dependent characteristics of sensitivity, specificity, predictive value positive, representativeness, timeliness, simplicity, flexibility and acceptability.\textsuperscript{184,190} One approach to judging the usefulness of surveillance system has been to assess the impact of information derived from it on policies and interventions, allowing for the influence of other factors, such as public opinion or economic constraints.\textsuperscript{145,160,218}

A similar approach is appropriate for the assessment of the effectiveness of surveillance methods in individual studies. In the present study, the key parameters of ascertainment, specificity, compliance and representativeness have been evaluated. This assessment suggests that by using two independent active surveillance schemes, a high level of ascertainment was achieved and a nationally representative cohort identified of children with newly diagnosed congenital and infantile cataract in the UK. Thus the findings regarding incidence, detection and aetiology, discussed later in this chapter, provide more complete information about this disorder than has been previously available.
5.2 ASCERTAINMENT OF CONGENITAL AND INFANTILE CATARACT BY EXTERNAL SOURCES.

5.2.1 Congenital Anomaly System of the Office of National Statistics.

5.2.1.1 Summary of findings.

Only 10% of eligible cases identified through the surveillance schemes were notified to the congenital anomaly system. Of 21 notifications to the ONS system, 15 were true cases, whilst three did not have cataract. Two notifications for whom there was insufficient information for matching, and one of a child who died in early infancy, could not be confirmed as having cataract.

5.2.1.2 Interpretation and implications of findings.

Ascertainment of congenital cataract through this passive reporting system was found to be low. In addition, the findings indicated a need for, but difficulties in undertaking, routine validation of notifications to establish whether cases have been correctly reported.

National congenital malformation monitoring systems and registers exist in many countries and mainly rely on passive notifications at birth or discharge from hospital. These data are used in planning services, for identification of public health hazards and in aetiological research. Under-ascertainment through them of even major congenital anomalies has been
documented, together with false positive notification errors.\textsuperscript{143,148-151} The ONS system is the only routinely available source of incidence data for congenital ocular anomalies in the UK. However notifications to ONS are not confirmed and reported data are not verified routinely. Completeness of ascertainment of ocular anomalies by this system has not previously been assessed at a national level.

In one important validation study, congenital anomaly notifications between 1972 and 1978 to a local scheme in Birmingham\textsuperscript{152} were compared with those made independently to the national ONS system. The latter was found to have an overall sensitivity of 34\% for anomalies of the eye and of 15\% (2 of 13 children) for congenital cataract.\textsuperscript{149} Furthermore, half of all eye anomalies notified to ONS were false positives, including one false notification of anophthalmia. The investigators in this and other subsequent studies, concluded that major deficiencies in both design and implementation contributed to the inaccuracies in the ONS system.\textsuperscript{148,149} Despite a recent review and redesign of the ONS system,\textsuperscript{81} almost two decades later, under-ascertainment of congenital cataract, at national level, has been found to be of a similar magnitude, and more marked than under-ascertainment of other non life-threatening congenital anomalies.\textsuperscript{149}

These findings suggest the current ONS system is of limited use in monitoring temporal trends in the incidence of congenital and infantile cataract, as it is likely to be insensitive to small but important changes, such as those due to an epidemic of congenital rubella described below.(Section 5.2.2, page 190) Other major
congenital anomalies of the eye, such as anophthalmia, are more easily diagnosed and may therefore be better ascertained by this system. However the completeness with which such anomalies are ascertained has not been determined nationally. This question may be addressed by an on-going study of anophthalmia and microphthalmia in the UK which has used passive reporting from multiple sources to establish a register of prevalent cases.\textsuperscript{220,221}

A recent review by the working group of the Registrar General's Medical Advisory Committee of the ONS system concluded improvements were required as a rapid surveillance system was still needed.\textsuperscript{81} The adoption of new methods of increasing and extending early ascertainment, such as use of electronic capture of relevant data from birth notifications, was recommended. It was also advocated that the system be developed to establish a more complete database of major congenital anomalies through improvements to ensure late diagnoses and better validated data were included. The latter recommendations are supported by the findings of this study regarding ascertainment of congenital cataract.

However, such measures may be insufficient in themselves to improve ascertainment of congenital ocular anomalies by such routine reporting systems. Evaluations of notifications at birth or discharge from hospital, on which these systems rely, have shown that these have both low sensitivity and low specificity.\textsuperscript{157,222,223} The presence of multiple defects has been shown to predict under-reporting of anomalies,\textsuperscript{222} so it possible that congenital cataract may go
undiagnosed in children with multiple anomalies. Alternatively, it may be more carefully ascertained, as it is may be one of the more readily treatable disorders in some children with multiple anomalies. Children with isolated congenital ocular anomalies may not be detected until the functional consequences of the structural abnormality become obvious, by which time notification of a disorder which is likely to have been present from birth, may be considered inappropriate. Thus, although the upper age limit for notifications to the ONS system, previously 10 days, no longer applies, the system may still significantly under-ascertain later diagnosed anomalies. Reporting to the ONS system remains voluntary. Adoption of statutory notification, which was not advocated in the review, might improve notification of identified cases but would not necessarily guarantee it.

Major congenital anomalies of the eye together accounted for one in six of new registrations of blindness in children in England and Wales in 1991. Thus an effective method of monitoring these disorders remains important to the public health of children. The proposed changes to the current national system may improve completeness of reporting, but it is possible to speculate that even higher ascertainment might be achieved through a system specifically designed to identify children with those ophthalmic disorders which cause severe visual impairment or blindness. As discussed previously, the national registers of partial sight and blindness are currently unsuitable for this purpose. (Section 2.9.2.1, page 49) An alternative routine source is required, as it is recognised that “to maintain surveillance over a disease in the community, recourse has to be
made to routine data-collecting systems." One approach, to be implemented shortly, is to embed a passive surveillance system within a regional liaison and support service for newly diagnosed visually impaired children and their families. (Unpublished, J Rahi and D Taylor, Great Ormond Street Hospital) As those providing this service must necessarily be informed of all eligible children, irrespective of diagnosis or treatment undertaken, and have access to the relevant information about them, they are well placed to notify cases to a regional system. The evaluation of this new service should provide evidence of the effectiveness of undertaking such epidemiological surveillance within this health service context.

5.2.2 The National Congenital Rubella Surveillance Programme.

5.2.2.1 Summary of findings.

Both children with cataract due to congenitally acquired rubella identified by the surveillance study were notified to the National Congenital Rubella Surveillance Programme (NCRSP) and no other cases of cataract were reported to the NCRSP. Thus ascertainment of this rare cause of congenital cataract by both the NCRSP and the present surveillance study appeared to be complete.

5.2.2.2 Interpretation and implications of findings.

On the basis of reported incidence over the past decade, at most one incident case of cataract due to congenital rubella had been expected during the study
period in the UK. An epidemic of rubella in the UK in 1996 (Personal communication, P Tookey, Institute of Child Health) accounts for the two unexpected cases of cataract among the higher than usual number of notifications to the NCRSP of confirmed or suspected congenital rubella during the study period.

The National Congenital Rubella Surveillance Programme was established to monitor the effectiveness of the rubella vaccination policy in the UK. The findings of the present study support its use of appropriate, multiple sources and active reporting to ensure that small fluctuations in incidence of congenital rubella are identified, which can alert public health professionals to deficiencies in the vaccination programme.

5.2.3 Conclusion.

The cohort of children with congenital and infantile cataract identified by active surveillance has been compared with those identified by the national passive surveillance reporting system for congenital anomalies and with the national, active, disorder-specific surveillance programme for congenital rubella. The high level of ascertainment which can be achieved through multiple source active reporting has been demonstrated.
By comparison, the main routine source of incidence data about children with serious congenital ocular disorders in the UK has been found to be unsatisfactory. As the limitations of the current system of registration of visually impaired children render it unsuitable for monitoring purposes, it is therefore suggested that new systems are necessary for monitoring these and other disorders which cause severe visual impairment and blindness in children. Their design needs to address the specific problems of ascertaining disorders which are individually and collectively rare and which, although present from early infancy, may not be detected or become functionally significant until later in childhood. A model for such a system, involving surveillance within the context of health service provision, is proposed.
5.3 INCIDENCE OF CONGENITAL AND INFANTILE CATARACT IN THE UK.

5.3.1 Summary of findings.

The ascertainment adjusted annual cumulative and age-specific incidence of cataract in infancy is 2.49 per 10,000 children in the United Kingdom, being higher for bilateral than unilateral disease. Age-specific incidence rates of diagnosis of both bilateral and unilateral congenital and infantile cataract decrease considerably after the first year of life. The cumulative incidence of congenital and infantile cataract into later childhood has also been determined: an infant in the UK has a risk of being diagnosed with congenital cataract of 3.19 per 10,000 by five years, increasing to 3.48 per 10,000 by the age of fifteen.

5.3.2 Sources of bias.

Unadjusted incidence estimates, with 95% confidence intervals, reported in the previous chapter (section 3.5.1.1, page 94) were based on 238 cases identified by surveillance for whom age at detection was known. Adjustment of measures of disease frequency for the level of ascertainment has been advocated.\textsuperscript{199,201} Therefore point estimates were adjusted appropriately for the 92% ascertainment of eligible cases in the surveillance study, as discussed in section 5.1.6, page 175.
Incidence rates for each constituent country were based on country of residence rather than country of birth, as the latter was not specifically sought. The observed differences in incidence between countries need to be interpreted in light of this, as some children may have been born in a different country to the one in which they were living at the time of diagnosis. The distribution of cases within the UK, according to health service region of the hospital at which ophthalmic treatment was undertaken, was examined to assess the likely representativeness of the ophthalmic reporting base and the cohort of cases ascertained. Thus this does not measure true geographical differences in incidence.

5.3.3 Interpretation and implications of findings.

There are few incidence data with which to compare the rates estimated in the current study. The total number of incident cases identified was greater than had been expected on the basis of birth prevalence previously reported from routinely collected data in the UK.\textsuperscript{147,224-229} The current birth prevalence of congenital cataract in Europe, reported from the constituent registers of the European Congenital Anomaly system (EUROCAT), is between 2.6 per 10,000 live births in Strasbourg to 0.2 per 10,000 in Zagreb.\textsuperscript{142} Of note, the highest prevalence, reported from Strasbourg, was based on a defined birth cohort of children who were specifically examined to ascertain those with any congenital anomalies.\textsuperscript{35}
Thus the considerable variation in reported prevalence in Europe is likely to reflect differences in ascertainment.

There are few published data with which to directly compare incidence rates according to laterality in the present study. However the estimated higher incidence of bilateral cataract is supported by the findings of the 1970 UK Birth Cohort Study in which five of the eight children with congenital cataract had bilateral disease. In the present study, the incidence of cataract amongst boys and girls was similar, which concurs with the findings of other investigations of congenital ocular anomalies.

There are no appropriate data in the UK with which to directly compare the estimated cumulative incidence of congenital and infantile cataract. Comparison with longitudinal studies of defined cohorts in North America in the 1950s, when congenitally acquired rubella was more common, indicates that the cumulative incidence has decreased. The observed cumulative incidence rates demonstrate that reliance on measures of birth prevalence alone, particularly when derived from routinely collected data, will underestimate the total burden of disease in the population and thus the requirement for specialist services.

The observed variation in point estimates of incidence by country within the UK is unlikely to be due principally to true geographic variation, as the confidence limits of these estimates were similar. This is supported by the similarity of birth
prevalence estimates reported from the British registers within EUROCAT, of between 1.1 per 10,000 live births in Belfast to 2.1 per 10,000 live births in Glasgow. Rather, in the current study, the incidence estimates were subject to sampling error produced by the small number of cases reported outside England. This in turn, may reflect differences in ascertainment, but with the small numbers available, it was not possible to assess these differences statistically by stratification of cases according to country. As congenital and infantile cataract is aetiologically heterogeneous, further investigation of the observed geographical variation of individual causes would require better actual or proxy measures of putative environmental exposures and other geographically distributed risk factors, than available in this study, as well as the use of appropriate techniques for analysis, for example, evidence for clustering based on place of birth.

The distribution of cases according to health service region showed that 71% of all cases in the UK were reported from five of thirteen regions. About half of all cases were managed by eight ophthalmologists and 42% by ophthalmologists to whom they had been secondarily referred. Taken together these findings support the fact that management of cataract in infancy in the UK is primarily undertaken by a small number of sub-specialists. This is relevant to planning future studies, especially those designed to assess interventions.
Six infants in the study cohort died shortly after detection of cataract, two before ophthalmic assessment could take place. No estimate can be made of deaths before diagnosis of cataract, including stillbirths, and therefore birth prevalence of congenital cataract cannot be estimated from the present study. Longer-term follow up will ascertain the mortality experience of the study cohort. Although uncommon, congenital and infantile cataract confers life-long morbidity, which highlights its public health significance. As data become available about survival of children in the cohort identified, it will be possible to evaluate how appropriate and accurate estimates of prevalence in later childhood are for planning services.

5.3.4 Conclusion.

The prevalence of congenital and infantile cataract, dependent on incidence and duration, is a useful measure of the burden of this disease in the population. However, knowledge of the incidence of this disorder is important for planning of services and development of preventive strategies, as well for monitoring of specific trends, for example, over time.

This research has provided the first national estimates of the incidence of congenital and infantile cataract in the UK, as well as of the distribution of cases by health service region. The findings suggest that at least one infant would be expected to be diagnosed with cataract each year in an average sized health
district of 5000 annual births. Many of these children are likely to be secondarily referred for management to an ophthalmologist with particular expertise in this field, usually based at a regional centre.

These incidence data are important for the assessment of outcome of the national screening programme to detect cataract. In addition, as the management of cataract in infancy requires specialist, multi-disciplinary care, these data are relevant to regional provision of services. They are also the first reliable data from which information necessary for the planning of future aetiological or interventional studies can be derived. Lastly, they provide previously unavailable base-line estimates of incidence for evaluation of secular and other trends.
5.4 DETECTION AND OPHTHALMIC ASSESSMENT OF CONGENITAL AND INFANTILE CATARACT.

5.4.1 Survey of training and practices of paediatricians.

5.4.1.1 Summary of findings.
Congenital cataract was the most frequently sought disorder, in both neonates and infants aged 6-8 weeks, by senior and junior, as well as community and hospital based, paediatricians. One fifth of all respondents reported receiving no training in the ophthalmological examination of infants and 71% of paediatricians reported they would benefit from further training by an ophthalmologist but of these, 40% reported that they did not have access to such training.

5.4.1.2 Sources of bias.
This survey assessed reported practice, which may vary from actual practice, and may also have been subject to biased recall of previous training. A representative sample of paediatricians were surveyed of whom 73% returned the survey questionnaire. It is probable that non-responding paediatricians were dissimilar to those who responded, but the overall effect of this non-response bias is difficult to assess. It is possible that those whose practice differed from current recommendations were less likely to respond. Conversely those who considered their previous training inadequate might have been more likely to respond to draw attention to this problem. Questions about practice were open-
ended, to avoid prompting respondents, and those about training were closed-ended, for clarity.

5.4.1.3 Interpretation and implications of findings.

The findings indicate important variation exists in the implementation of current recommendations about screening and surveillance for ophthalmic disorders in infancy in the UK. The degree of clinical experience of the respondents surveyed and the setting in which they worked did not appear to be factors in this variation in practice.

The findings raise concerns about the extent and content of both undergraduate and postgraduate medical training in ophthalmic examination of infants, especially the low reported frequency of training received from ophthalmologists and other ophthalmic professionals. Perhaps most importantly, the majority of paediatricians, including consultants, considered they would benefit from further training. This is consistent with the reported training needs of general practitioners involved in child health surveillance, who are increasingly responsible for the routine examination at six to eight weeks of age, and some of whom may not have received appropriate undergraduate training in ophthalmic assessment. Variation in current postgraduate training provision for general practitioners and others involved in child health surveillance has been identified.
More than 90% of paediatricians specifically reported seeking congenital cataract routinely at both the newborn examination and that at 6-8 weeks of age. The implications of this finding are discussed in conjunction with those specifically about the detection and ophthalmic assessment of cataract in the surveillance study.

5.4.2 Detection and ophthalmic assessment of children with congenital and infantile cataract in the UK.

5.4.2.1 Summary of findings.

Although 57% of children were formally assessed by an ophthalmologist by three months of age, 33% were not examined until after the age of one year. While 35% of cases were detected through the routine newborn, and 12% through the six to eight week examination, 34% presented symptomatically. In 38% of cases, the child’s parents or other carers, suspected an ocular defect before cataract was diagnosed, and in more than half of these cases, this was in the first three months of life. Those health professionals principally involved in routine screening of infants, hospital-based paediatricians and family practitioners, detected the majority of cases, but 18% were detected by an ophthalmic professional. There was no evidence of serious delays in the chain of referral to an ophthalmologist.
5.4.2.2 Sources of bias.

Although collected retrospectively, information regarding detection and ophthalmic assessment was sought, in a standardised way, and independently from ophthalmologists and paediatricians. Complete data were available for the majority of cases. As discussed earlier, there was evidence of infantile onset in those cases detected later. Thus it is likely that cataract had been overlooked in these cases, but the possibility that initially less severe lens opacity may have progressed, becoming clinically more apparent, cannot be excluded.

5.4.2.3 Interpretation and implications of findings.

The current national screening programme to detect ocular disorders in children has not been evaluated previously. As neither the process nor the outcome of the current UK screening programme are routinely monitored at national level, little is known about the detection through screening of children with congenital and infantile cataract. Furthermore, there has been little systematic study to determine how children with cataract or other major ophthalmic disorders are identified and the pathways leading to assessment by an ophthalmologist. Few studies in the UK have examined this question, and it has been assumed that such children are usually first identified in early infancy and mostly by family members, such that later formal vision screening examinations contribute little to early detection. Whilst comparison is not straightforward, because of differences in methodology and populations studied,
the findings of the present study challenge these assumptions, as congenital and infantile cataract was not suspected or diagnosed before the first birthday in a substantial proportion of cases in this nationally representative cohort.

The findings regarding the detection and ophthalmic assessment of children with congenital and infantile cataract, together with the reported practice of paediatricians discussed earlier, allow the detection rate of the current national screening programme to be assessed. As information is only available on true cases, the specificity of this screening programme cannot be assessed from these findings. As the disorder is rare, knowledge of the specificity of the programme is particularly important in its overall evaluation.

Despite a national screening programme based on routine examination of all newborn and young infants to specifically detect congenital cataract and other serious ocular disorders, cataract was not diagnosed before the first birthday in 29% of all cases, which is similar to the percentage detected by this age in countries without universal screening. The aims of the current infant screening programme in the UK, and other similar programmes elsewhere, are to prevent visual loss due to treatable disorders, as well as to ensure prompt provision of relevant services for affected children and their families. Thus the proportion of children with congenital cataract undergoing ophthalmic assessment by three months of age is a useful indicator of its performance. However in the current study, only 47% of children were identified through screening, with 57%
being assessed by an ophthalmologist, by this age. This may represent some improvement over the past decade, although direct comparison with published case series,\textsuperscript{20,21} which may be prone to ascertainment bias, is difficult. Nevertheless, the proportion of children undergoing ophthalmic assessment in early infancy requires improvement. There was little evidence of delay in referral to, and subsequent examination by, an ophthalmologist in the present study, suggesting that delays in detection, rather than in the referral pathway, contributed to the low proportion of cases examined by three months. Furthermore, the survey of paediatricians’ practice showed that congenital cataract was the disorder most frequently sought during routine examination of young infants. Together these findings suggest that difficulties with actual examination, rather than a lack of awareness of the disorder, are contributing to delayed diagnosis.

As the largest percentage of children with congenital and infantile cataract were detected through screening of newborn and young infants, this suggests the best opportunity for enhancing early detection of this disorder lies in improving the effectiveness of these screening examinations. There is increasing interest in standardising the content of the routine neonatal examination and in identifying the most appropriate health care professional to undertake this task.\textsuperscript{243,244} This presents an important opportunity to review the ophthalmic component of this examination and also that at six to eight weeks of age.
The clinical evaluation of the pupillary red reflex, to detect cataract and other media opacities, remains the advocated technique, although it has not been systematically evaluated. From a single published study of the ability of inexperienced examiners to detect such abnormalities, using this technique, in eight subjects and eight controls aged 3 to 30 years, the sensitivity of this examination was reported to be 98% and its specificity 94%. Similar data are lacking for the sensitivity and specificity of this examination in young infants and would be difficult to obtain, but given the low prevalence of the relevant disorders, the positive predictive value is likely to be low. However systematic recording of all components of routine infant screening examinations, which is not currently undertaken, would allow routine audit and research which could contribute to assessing the performance of the examination of the pupillary red reflex as a screening test.

There may also be some benefit in evaluating the role of alternative health technologies to detect cataract. For example, the role of photorefraction in detection of ocular abnormalities in infants able to co-operate with this examination could be evaluated, possibly within the context of existing studies of the use of this technique to screen for significant refractive errors. Longitudinal studies, involving repeated imaging from infancy through to the pre-school years might also offer further insight into the natural history of initially small lens opacities.
A small but important percentage of cases were detected through clinical examination of otherwise asymptomatic children at high risk, including those with a family history of cataract or ocular disease, those born preterm or those with relevant systemic disorders. Recommendations about the value of formal ophthalmic assessment of such children already exist^26,27 and should continue to be promoted. Liaison between paediatric, primary care and ophthalmic health professionals and services is crucial to the success of this strategy. Interestingly, two infants in the present study with bilateral hereditary cataract were diagnosed antenatally by ultrasound examination. Detection of cataract, either hereditary or in association with a relevant systemic disorder, by this method has been reported previously,^248 and may contribute to early ophthalmic referral in selected high risk groups but is not a strategy for universal screening.

In more than one third of cases, parents suspected an ocular problem prior to diagnosis. As lens opacity per se is difficult to identify by simple inspection, it is likely that these parents were alerted by abnormal visual behaviour or features, such as strabismus or nystagmus, arising secondarily from reduced visual function. However such parental concern did not always ensure prompt detection, suggesting parental uncertainty about the significance of the features noticed and/or a failure of health professionals to elicit or respond to these concerns. ^236,237,237-240,240,240,244,249-251 Previous studies have indicated that parents are most likely to note or report the most obvious ophthalmic abnormalities, such as
manifest squint.\textsuperscript{236,237,239,241,252} Thus the role of parents in the early detection of serious ophthalmic disorders could be strengthened by improving their knowledge about abnormal clinical features and the need to seek medical attention if they are noted, in addition to ensuring that health professionals actively elicit such concerns. This approach could be enhanced by systematic qualitative study of knowledge, awareness and attitudes amongst parents and other carers of children with ocular disorders.

Ophthalmic examination of young infants is demanding and requires specific knowledge and practical training. Variation in, and dissatisfaction with, undergraduate and postgraduate training in ophthalmology have been documented and its content and purpose have been increasingly questioned.\textsuperscript{235,253-255} Further evidence for this was provided by the findings of the survey of paediatricians reported earlier.\textsuperscript{242} Specific teaching on paediatric ophthalmic disorders and visual assessment of children within the national postgraduate training programme of paediatricians has been advocated but not yet implemented in the UK.\textsuperscript{27} All health professionals involved in child health surveillance, should receive appropriate training and be aware of the importance of relevant features, such as strabismus or nystagmus, as well as the value of enquiring actively about a family history of ocular disease.\textsuperscript{238,241}

In the future, the detection rate of children with cataract and other major ocular disorders might be more easily measured if the process and outcome of the
screening programme were routinely monitored, using appropriate performance indicators and with data aggregated at national level. Such information should allow the specificity as well as the sensitivity of the programme to be measured.

5.4.3 Conclusion.

The routine ocular examination of young infants is part of a continuum of ophthalmic screening throughout childhood and is of particular relevance to the identification of disorders causing serious visual loss. Thus, as the purpose and value of vision screening in later childhood are being reviewed in the UK,256 it is appropriate that ophthalmic screening and surveillance in young children is also assessed. The findings of this study suggest that it is important that measures are taken now to improve the effectiveness of this programme.
5.5 AETIOLOGY OF CONGENITAL AND INFANTILE CATARACT IN THE UK.

5.5.1 Summary of findings.

The causes of cataract differ considerably between bilateral and unilateral cases. The majority of unilateral cases have idiopathic cataract, whereas more than half of bilateral cases have hereditary cataract. Prenatally acquired infections are responsible in a few cases. In the rest, non-hereditary systemic disorders, perinatal hypoxia or hypoglycaemia are implicated. Possible contributing prenatal or perinatal factors are also noted in a few idiopathic cases.

5.5.2 Sources of bias.

Detailed information regarding aetiology, was collected using an agreed taxonomy. Although a standardised clinical investigation protocol was not used, it is unlikely that any underlying or associated systemic disorders were not identified. Complete data regarding aetiology were available for the majority of cases. However, the analysis of aetiology is descriptive only as controls, with which to make comparisons, were not sought. Thus the risks associated with different determinants have not been estimated.
5.5.3 Interpretation and implications of findings.

The findings of this study demonstrate that the aetiology of congenital cataract in the UK is diverse. This complexity has implications both for assessment and management of affected children, as well as for further aetiological research.

Comparison with the findings of other studies, in different regions of the world, is problematic: many are based on hospital or other selected populations or routinely collected data, which may be unrepresentative, while others have not examined aetiology separately for unilateral and bilateral cases and some have used treatment or outcome categories to define cases, thereby introducing selection bias. However, as discussed previously (section 2.7.3, page 36) it does appear that the aetiology of congenital cataract in industrialised countries has evolved over the past few decades. The implementation of specific primary preventive strategies, such as rubella immunisation, and avoidance of known teratogens, such as drugs or irradiation, have reduced the contribution of preventable aetiological factors which continue to be important in some developing countries.

Although methodologically different, a more meaningful comparison can be made with the recently published findings of the Spanish Collaborative Study of Congenital Malformations (ECEMC), in which a specific examination by paediatricians of infants in the first 3 days of life was undertaken to ascertain congenital anomalies. 414 children with ocular anomalies were identified from
more than 1 million births between 1980 and 1995. Of these, 71 were diagnosed
with congenital cataract, giving a birth prevalence of cataract in this study of 0.63
per 10,000 (0.49 to 0.79 95% CI). This is lower than reported in the European
congenital anomaly register\textsuperscript{42} and less than might be predicted from the incidence
in infancy observed in the present study, suggesting that ascertainment may not
have been complete. However, comparison of the broad findings regarding
aetiology with those of the present study\textsuperscript{258} are of interest and are summarised in
Table 5-1, page 212. Despite differences in ascertainment and aetiological
taxonomy, the aggregated data about aetiology are remarkably similar in these
two population based studies, with cataract of unknown aetiology accounting for
more than half of the cases and hereditary cataract for the majority of the
remainder.
Table 5-1 Comparison of aetiology in population based studies of congenital cataract in the United Kingdom and Spain.

<table>
<thead>
<tr>
<th>Cause of cataract</th>
<th>Present study (British Congenital / Infantile Cataract Study)</th>
<th>Spanish Collaborative Study of Congenital Malformations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (% all cases a)</td>
<td>n (% all cases b)</td>
</tr>
<tr>
<td>Hereditary</td>
<td>95 (39)</td>
<td>25 (35)</td>
</tr>
<tr>
<td>Environmental / systemic agents</td>
<td>12 (5) c</td>
<td>5 (7) d</td>
</tr>
<tr>
<td>Unknown</td>
<td>136 (56)</td>
<td>41 (58)</td>
</tr>
</tbody>
</table>

Key

a 243 cases with available data (bilateral and unilateral cases combined)

b 71 cases (bilateral and unilateral cases reported together)

c systemic aetiological factors in the present study are reported in Table 4-23, page 162, and Table 4-24, page 164.

d specific causes for cataract not reported
In the vast majority of unilateral cases in the present study, no apparent cause for the cataract was identified. This suggests that if clinical assessment by a paediatrician of a child with isolated unilateral cataract indicates there is no underlying systemic abnormality, then further investigations are unlikely to reveal an aetiological agent.

In contrast, in more than one third of bilateral cases hereditary cataract was diagnosed, either alone or in association with another ocular disorder. This emphasises the importance of ophthalmic examination of parents, siblings and other family members of otherwise healthy children with bilateral cataract to ensure hereditary cases are not overlooked and that appropriate genetic counselling is provided.19

Rare multi-system hereditary disorders accounted for almost a fifth of bilateral cases, reflecting the wide range of systemic disorders in which congenital cataract has been reported to occur.19,33,34,259,260 Of note, cataract was diagnosed in one child with PEHO syndrome261 and another with Ohdo’s syndrome,262 both being disorders in which cataract has not been reported commonly. In contrast to earlier reports,263 cataract was present from the neonatal period in the majority of children with Down syndrome in this study. These findings emphasise the importance of early formal ophthalmic evaluation of children with relevant systemic and hereditary diseases, who have a high risk of ocular disorders.26,27

(Table 2-5, page 40) Thus liaison between paediatricians and ophthalmologists is
crucial for the effective initial assessment, as well as subsequent management of children with congenital cataract.\textsuperscript{19}

In industrialised countries, autosomal dominant inheritance of isolated cataract has been reported more frequently than either autosomal recessive or X linked inheritance.\textsuperscript{101,102} Most genetic research has been aimed at identifying and understanding the genes responsible for autosomal dominant bilateral cataract\textsuperscript{101,102} in which phenotypic variability is recognised.\textsuperscript{100,102} Unilateral autosomal dominant cataract has not been commonly reported\textsuperscript{100,101} and its identification in two cases in the present study may be relevant to research in this field. Autosomal recessive inheritance was identified or suspected in 3\% of bilateral cases. This form of inheritance, which can be more difficult to identify, has been more commonly reported in populations with larger average family size and higher rates of consanguinity.\textsuperscript{18,56,264} Thus opportunities exist for collaborative research in this area which may have wide benefits. Follow up of the study cohort, to ascertain if any cases categorised as idiopathic subsequently have affected siblings, should contribute to further understanding of genetic defects in congenital cataract. This information will also be important for refining current estimates of recurrence risk given to families with one affected child.\textsuperscript{265}

The description by Gregg, an Australian ophthalmologist, in 1941 of congenital cataract occurring following rubella in pregnancy was one of the first clearly demonstrated risk factors for congenital anomalies in humans.\textsuperscript{266} Although they
continue to be important in many developing countries, particularly rubella, have become an uncommon cause of congenital cataract in industrialised countries. In the present study, six cases of congenital cataract were attributable to prenatal infections, of which rubella was the most common. This highlights the importance of appropriate public health measures against, and continuing public health surveillance for, these potentially preventable diseases in all countries.

By comparison with adult cataract, epidemiological research to identify risk factors for congenital cataract has been limited. One important study has involved investigation of a number of possible risk factors using data from a large, multiple source register of congenital anomalies among more than 350,000 children born in Birmingham between 1964 and 1984, of whom 62 had congenital cataract. Of these, cataract was found to be most strongly associated with proximity to factory chimneys, incinerators and gas works, suggesting a link with toxic combustion products. However, the authors cautioned that the finding, based on small numbers, was subject to large sampling error. Cataract was also found to be statistically associated with deprivation, measured using composite indicators based on electoral ward, but not social class when measured using father’s occupation. There were no associations with other factors evaluated, including maternal age, or birth rank, and only weak evidence for periodicity was found. Similarly, in another study, an observed trend of increasing risk of cataract with increasing paternal age was not statistically significant. Thus determinants of
idiopathic infantile cataract, identified as the major category in the present and other studies, remain unclear. Unless modifiable risk factors for idiopathic congenital cataract are identified, the scope of primary prevention of this disorder will remain limited.

As outlined earlier, children born preterm or of low birthweight are at greater risk of visual impairment than those of normal gestation or birthweight, mainly from disorders specifically associated with prenatal or perinatal events, such as cortical visual impairment, optic atrophy or retinopathy of prematurity. A specific iatrogenic, and readily identifiable, risk factor for cataract formation in these children is laser photocoagulation treatment for retinopathy of prematurity which should be better quantified through ongoing studies of outcome in treated infants. Transient lens opacities in preterm or low birth weight infants have been attributed to adverse perinatal events. However, in population based studies of these children, the prevalence of congenital cataract, unrelated to retinopathy of prematurity, is higher than in the whole population. Amongst idiopathic cases in the present study, 10% were born preterm (<37 weeks), which is higher than the percentage of births of this gestation nationally. Confirmation of this association and exploration of the underlying mechanisms may provide further insights into the basic processes involved in cataract formation.
Adverse perinatal events, particularly hypoglycaemia and hypoxia, as well as hypothermia and pre-eclampsia, have been reported to cause congenital cataract. In this study, cataract was attributed to severe hypoxia in one child, who subsequently died from its complications, and was a possible contributing factor in another case categorised as idiopathic. Maternal hyperglycaemia was reported in one idiopathic case. A variety of manifest and sub-clinical disorders of sugar metabolism have been reported in mothers of children with cataract and further work in this area is likely to provide clearer understanding of the effects of such altered metabolism on cataract formation in infants.

A range of ocular teratogens have been identified, including various drugs, irradiation and alcohol. Congenital cataract has been reported following ingestion of certain drugs in pregnancy but their role in six cases in the present study is unclear. In two, the mothers were taking anticonvulsants, known to have other ocular teratogenic effects and in one of these, the mother was also taking methadone and may also have ingested other teratogenic substances. In another case, the mother was hypertensive and treated with atenolol and either factor may be have been relevant, as both systemic hypertension and anti-hypertensive drugs have been implicated in adult cataract. The mothers of two bilateral idiopathic cases, were being treated with thyroxine, which is notable in the light of animal experiments demonstrating cataract associated with hypothyroidism.
Whilst cataract is the congenital ocular anomaly most likely to occur in isolation, its association with microphthalmia, without other non-ocular anomalies, has been demonstrated statistically to occur more frequently than expected by chance alone, supporting the hypothesis that a normal lens is important for the subsequent development of the globe. In the present study, anomalies of the globe, without associated systemic disorders, were three times as common in unilateral as bilateral cases, and in unilateral cases were all of unknown aetiology. Furthermore, two-thirds of these unilateral cases had some degree of microphthalmos compared with half of the bilateral cases. These findings are consistent with the occurrence of unilateral cataract associated with microphthalmos arising more frequently as a result of a local, rather than a general, insult during embryogenesis.

Various congenital abnormalities have been reported to occur more frequently in twins than singletons. It is therefore notable that whilst 1% of all maternities in the UK results in twins, 7% (4-9%, 95% CI ) of children with unilateral idiopathic cataract (4 isolated, 1 with associated ocular disorder) in the present study were one of a pair of twins, although two of these five children, were also born preterm. Previous studies, involving smaller numbers of cases, often ascertained from routine data sources, have not reported a higher frequency of congenital ocular anomalies in twins. It will be of interest to see whether future population studies of higher order births, for example using established
twin registers, report an increased frequency of isolated cataract or that associated with other ocular anomalies.

5.5.4 Conclusion.

The findings of this study regarding aetiology are relevant to clinical practice, public health policy and further research.

The importance of co-ordinated ophthalmic and paediatric services, to ensure appropriate assessment of affected children is highlighted.

As the first nationally representative descriptive aetiological data about congenital and infantile cataract, they are of importance in generating hypotheses for future aetiological research. The causes of cataract identified in this study, together with the current understanding of basic mechanisms of formation of congenital cataract, indicate that the scope for primary prevention of this disorder, an important international public health goal, is limited.

Epidemiological studies, to identify or confirm putative risk factors, are required to inform basic scientific research in this area and to develop effective primary preventive strategies. One approach would be through case control studies to explore risk factors already identified as relevant in causing cataract in
adults, and which may act through similar mechanisms in the intrauterine period. For example, the role of dietary factors or of smoking during pregnancy could be evaluated. Of possible risk factors identified in this study, low birthweight and prematurity are of interest, as they may be markers for, or predispose to, other prenatal or perinatal events that contribute to cataract formation, for example hypoxia. The higher than expected frequency of children with cataract and unaffected twins could also be explored, for example, through appropriately designed studies drawing on existing, population twin registers in Europe. It has recently been suggested that future epidemiological research on risk factors for cataract in adults should be based around interventions evaluated in clinical trials. The results of such studies may also be relevant to infantile cataract. However, this approach cannot be adopted currently as our epidemiological knowledge of risk factors for idiopathic cataract remains poor.
5.6 Further research on congenital and infantile cataract arising from the study.

The cohort of children identified in this study, effectively constituting a 'longitudinal observation register', offers unique opportunities for further research. Possible and planned investigations are discussed in this section.

Although the aetiological data about ascertained cases are more representative than those previously available, in the absence of information from unaffected control infants, the relative risks associated with individual factors cannot be estimated. Using the data on incidence and distribution of cases in the UK, it is now possible to assess the feasibility of prospectively recruiting sufficient subjects for a case control study from selected hospitals as well as assessing their representativeness. Such a case control study could be designed to both test and generate hypotheses. A number of risk factors could be evaluated, including nutrition or diet, smoking and drugs in pregnancy, low birthweight, prematurity, prenatal and perinatal hypoxia and hypoglycaemia, social deprivation, maternal and paternal age, and season of conception and birth. Knowledge of confirmed or newly identified risk factors would be relevant to basic scientific research on cataract and may be important to preventive strategies.

The outcome of congenital and infantile cataract in the study cohort is of particular interest. Detailed information regarding initial management has already
been collected and the opportunity exists to assess outcome longitudinally. To this end, the method of collection of data on further management and clinical outcome, using standard proformas, has been agreed. It is intended to assess factors associated with good visual outcome as well as those associated with adverse events, such as complications arising from surgery. The opportunity will also be taken to evaluate other important outcomes, which have not previously been systematically studied, such as the educational attainment and vision related quality of life of these children. This information may also have wider implications for the understanding of what constitutes visual handicap in children and whether unilateral visual loss is disabling, thereby contributing to other debates on areas of uncertainty in paediatric ophthalmic practice.

Lastly, as the cohort is representative, comprising children managed surgically and conservatively, a unique opportunity exists to undertake a total cost of illness study.273 This would provide currently unavailable information regarding the economic consequences of this disorder for affected families, as well as for the health care system.
6. CONCLUSION

Written descriptions of the surgical treatment of cataract, from as early as the 3rd century BC, attest to the long history of secondary prevention of visual impairment due to this disorder in adults. Attention to primary, secondary and tertiary preventive strategies against cataract in infancy is more recent. These strategies require epidemiological data which are currently lacking in the UK, as in other regions of the world.

Consequently, the research reported in this thesis was undertaken, to ascertain information about the incidence, aetiology and detection of congenital and infantile cataract in the UK. A body of work has been described which has identified specific epidemiological issues relevant to the study of cataract in infancy, as well as the limited scope of current routinely collected sources of data for such study. Research methods, not previously widely used in ophthalmology, have been applied to identify a nationally representative cohort of incident cases. Thus the findings provide more complete information about the epidemiology of this disorder than has been available previously in the UK.

The observed incidence of congenital and infantile cataract in the UK, higher than previously reported from routine sources, suggests that at least one child would be expected to be detected in infancy each year in an average sized health district of 5000 annual births. This has implications for provision of services for affected
children, as well as for planning further aetiological or interventional studies, and for monitoring trends.

The principal routine source of incidence data regarding congenital ocular disorders in the UK has been evaluated with respect to cataract and has been found to be unsatisfactory. New systems for monitoring these and other disorders which cause severe visual impairment and blindness in children are required. Their design will need to address the specific problems of ascertaining disorders which are individually and collectively rare and which, although present from early infancy, may not be detected or become functionally significant until later in childhood.

The detection rate of congenital and infantile cataract in the existing national infant screening programme is lower than has been assumed previously, such that one third of children with this disorder are first examined by an ophthalmologist after their first birthday. Measures are required to improve the effectiveness of this programme.

The causes of congenital and infantile cataract in the UK are diverse, and there are considerable differences between unilateral and bilateral cases. A cause for cataract cannot be identified in nine of every ten children with unilateral, and four out of ten children with bilateral disease. Effective primary prevention of this
disorder is an important goal, however the causes identified, together with our current understanding of basic mechanisms of pathogenesis of congenital cataract, indicate that the potential to achieve this in the UK is currently limited. Nevertheless, these findings are of importance to public health policy and to future analytical studies to identify or confirm putative risk factors.

Further exploration of the findings of this observational study regarding detection and aetiology are warranted and opportunities exist to extend its scope through longitudinal assessment of outcomes.
7. REFERENCES


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8. APPENDICES

8.1 APPENDIX A MEMBERS OF THE BRITISH CONGENITAL CATARACT INTEREST GROUP.

Mr W Aclimandos Mr R Doran Mr A Moore
Ms G Adams Dr J Dudgeon Mr A Morrell
Mr S Armstrong Prof G Dutton Mr R Morris
Mr N Astbury Mr R Edwards Dr G Morrice
Mr A Assaf Mr A Evans Mr B Moriarty
Mr D Banerjee Mr N Evans Mr A Mushin
Miss L Beck Mr J Elston Mr C Munton
Mr A Beckingsale Mr H El-Kasaby Mr M Neugebauer
Mr G Bedford Miss B Enoch Mr J Nolan
Mr L Benjamin Mr ff Fisher Mr M O'Keefe
Miss B Billington Prof. A Fielder Mr G O'Connor
Miss T Blamires Mr B Fleck Miss R Ohri
Mr P Bloom Dr A Gaskell Mr C Peckar
Mr J Brazier Miss M Gibbens Mr S Perry
Mr D Brosnahan Mr B Greaves Mr R Phillips
Prof A Bron Mr R Gregson Mr N Price
Mr I Brown Mr P Gregory Mr A Quinn
Mr R Brown Mr S Haworth Mr I Quershi
Mr D Boase Mr MH Heravi Mr A Rahman
Mr J Bolger Mr R Holden Mr A Rennie
Mr R Bowell Mr R Humphry Mr A Ridgway
Miss M Boodhoo Mr C Hutchinson Mr M Roper-Hall
Mr J Bradbury Mr J Innes Mr E Rosen
Mr J Bryars Mr I K Jalili Miss I Russell Eggitt
Miss P Burgess Dr E Johnson Mr A Shun Shin
Mr J Burke Mrs N Kayali Dr V Thaller
Ms L Butler Mr N C Kaushik Mr R Taylor
Mr D Calver Mr S Kaye Mr D Taylor
Mr A Casswell Mr S Kotta Mr W Tormey
Mr A Chandra Mr T Lavy Mr J Twomey
Mr W Church Mr D Laws Mr S Verghese
Mr J Clarke Miss J Leitch Miss S Vickers
Mr M Clarke Mr C Liu Mr A Vijaykumar
Mr R Condon Mr I C Lloyd Mr A Vivian
Mr M Cole Miss C MacEwen Mr H Willshaw
Mr M Dang Mr G Mackintosh Mr G Woodruff
Mr S Daya Mr A Mandal Mr G Wright
Mr R Darvell Mr R Markham Mrs J Duvall Young
Dr P D Davies Mr G McGinnity Mr B Young
Mr C Dodd Mr B McCleod Dr J Young
Mr J McConnell Mr A Zaidi

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8.2 Appendix B Ophthalmic Surveillance Scheme Notification Form.

British Congenital and Infantile Cataract Study case notification form.

Please report all new cases:

Case definition: Any child, 15 years or less with newly diagnosed congenital or infantile cataract to include all cases known to be present from infancy, or due to a congenital cause, or with clinical evidence of infantile onset. Please report every new case if the child will not be undergoing surgery.

Name of notifying ophthalmologist:

Reporting period: —/-/-

Section I (please tick appropriate option boxes)

☐ NO CASES TO REPORT ⇒ please indicate in section II whether you require further data collection booklets before returning form

or

☐ CASES TO REPORT ⇒ please record available information on new cases below:

<table>
<thead>
<tr>
<th>Name of case</th>
<th>Date of birth</th>
<th>SURGERY?</th>
<th>if applicable, name of ophthalmologist to whom case has been referred</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Yes or No</td>
<td>n/a = not applicable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>□ yes □ no</td>
<td></td>
</tr>
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<td>□ yes □ no</td>
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please continue over if necessary or for any comments / suggestions

Section II

☐ No further data collection booklets required

or

☐ ________ further data collection booklets required

Thank you for completing this form. Please return it (envelope provided) to:

J S Rahi, Dept of Epidemiology, Institute of Child Health, London WC1N
Tel 0171-242-9789 x 2250

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## 8.3 Appendix C Ophthalmic Surveillance Scheme Data Collection Proformas

<table>
<thead>
<tr>
<th>Surname:</th>
<th>Forename:</th>
<th>Bilateral</th>
<th>Unilateral:</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address with Post-code</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date of birth:</td>
<td>/</td>
<td>Male</td>
<td>Female</td>
<td>Born in UK?</td>
<td>Yes</td>
</tr>
<tr>
<td>Hospital number</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHS number</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### PRESENTATION Date: ----/----/-----

*Please record age below with correction for gestational age if appropriate*

1) *Age at which an ocular or vision problem was suspected by anyone:

2) Who first suspected the problem:
- Mother
- Father
- Other relative
- Midwife
- Paediatrician
- GP
- Other (specify):

3) *Age at first presentation to a health professional:
   *(if different to question 1)*

4) To which health professional did the child first present:
   *(if different to question 2)*
- Midwife
- Health visitor
- Paediatrician
- General Practitioner
- Optometrist
- Orthoptist
- Ophthalmologist
- Other (specify):

5) Reason for first presentation:
- Poor vision
- White pupil
- Squint
- Nystagmus
- Known family history
- Screening / developmental test:
- Newborn
- Six weeks
- Other (specify):

6) *Age at first referral to an ophthalmologist:

7) *Age at first ophthalmic assessment:

8) Were you the first ophthalmologist to see the child: Yes No

9) Who referred the child to YOU:
- GP
- Hospital paediatrician
- Community paediatrician
- Optometrist
- Orthoptist
- Another ophthalmologist
- Other (specify):

10) *Age of child at first presentation to YOU:
   *(if different to question 7)*
### FIRST VISIT

#### 1 VISION ASSESSMENT

**1 FIXATION:** □ NOT APPLICABLE / RECORDED

<table>
<thead>
<tr>
<th></th>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>CENTRAL</td>
<td>□ Yes □ No</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>STEADY</td>
<td>□ Yes □ No</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>MAINTAINED</td>
<td>□ Yes</td>
<td>□ Yes</td>
</tr>
</tbody>
</table>

#### 2 VISUAL ACUITY

**a. DISTANCE:** □ NOT APPLICABLE / RECORDED

<table>
<thead>
<tr>
<th>Method (specify)</th>
<th>FCPL / acuity card procedure: Keeler □ Teller □ Other (specify): Kay’s pictures</th>
<th>Sheridan Gardner singles</th>
<th>Snellen optotypes</th>
<th>Sonksen Silver Acuity System</th>
<th>Other (specify):</th>
</tr>
</thead>
</table>

Test distance (if applicable):

<table>
<thead>
<tr>
<th>Visual acuity (actual measurement and with Snellen equivalent if possible)</th>
<th>□ without correction</th>
<th>□ with correction □ spectacles □ contact lens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Both eyes together</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**b NEAR:** □ NOT APPLICABLE / NOT RECORDED

<table>
<thead>
<tr>
<th>Method (specify)</th>
<th>Visual acuity □ without correction □ with correction □ spectacles □ contact lens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td></td>
</tr>
<tr>
<td>Both eyes together</td>
<td></td>
</tr>
</tbody>
</table>

#### 3 REFRACTION

**PRESCRIPTION (please subtract working distance only)**

<table>
<thead>
<tr>
<th></th>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycloplegic agent</td>
<td>□ YES (specify):</td>
<td>□ NO</td>
</tr>
</tbody>
</table>
### First Visit

#### Ocular Examination

<table>
<thead>
<tr>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

- **Cornea**
  - Including clarity & horizontal diameter (mm)
- **Anterior Chamber**
- **Iris / Pupil**
  - Including pupil reaction
- **Lens Morphology**
  - Please describe & draw the cataract(s)
- **Vitreous**
- **IOP (mmHg)**
  - Instrument used
- **Fundus Examination**
  - Disc
  - Macula
  - Vessels

#### Extraocular Movements

<table>
<thead>
<tr>
<th>Normal</th>
<th>Abnormal (Specify):</th>
</tr>
</thead>
</table>

#### Strabismus

- No
- Left / Right / Alt.
- Angle:
  - Constant
  - Intermittent
- Esotropia
- Exotropia
- Vertical
- Other:

#### Nystagmus

- Latent / Manifest
- Horizontal
- Vertical
- Combined
- Pendular
- Jerk
- Rotary
- Combined
- Other:
### FIRST VISIT

#### III OPHTHALMIC INVESTIGATIONS

Please record whether the investigation has been done and all the available results.

#### a ULTRASOUND EXAMINATION:

<table>
<thead>
<tr>
<th></th>
<th>Not done</th>
<th>Normal</th>
<th>Abnormal (specify) including axial length</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right eye</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left eye</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### b ELECTRORETINOGRAM:

<table>
<thead>
<tr>
<th></th>
<th>Not done</th>
<th>STIMULUS:</th>
<th>Normal</th>
<th>Abnormal (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td></td>
<td>☐ FLASH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td></td>
<td>☐ PATTERN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Binocular</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### c VISUAL EVOKED POTENTIAL:

<table>
<thead>
<tr>
<th></th>
<th>Not done</th>
<th>STIMULUS:</th>
<th>Normal</th>
<th>Abnormal (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td></td>
<td>☐ FLASH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td></td>
<td>☐ PATTERN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Binocular</td>
<td></td>
<td>☐ SWEEP</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
IV GENERAL PAEDIATRIC ASSESSMENT

a PREGNANCY:
1. Any specific illness? □ Yes □ No □ Unknown
details:
2. Any non-specific illness e.g. fever, skin rash? □ Yes □ No □ Unknown
details:
3. Any exposure to teratogens e.g. drugs, alcohol? □ Yes □ No □ Unknown
details:
4. Amniocentesis? □ Yes □ No □ Unknown
details:

b LABOUR & DELIVERY:
Gestation: Birth weight (kg): Mode of delivery:
Complications? □ Yes □ No □ Unknown
details:

c NEONATAL HISTORY:
Admission to SCBU / NICU? □ Yes □ No □ Unknown
main illnesses and treatment received:
Neonatal hypoglycaemia? □ Yes □ No □ Unknown details:

d DEVELOPMENTAL HISTORY:
□ NORMAL □ DELAYED □ UNKNOWN
main developmental delay: □ Motor □ Sensory □ Combined
please record details:
Surname: Forename: □ Bilateral □ Unilateral: □ Right □ Left

Date of birth
Hospital number
NHS number
Consultant:

IV GENERAL PAEDIATRIC ASSESSMENT continued

e FAMILY HISTORY (please draw a family pedigree if there is a positive family history)

1. family history of consanguinity? □ No □ Yes □ Unknown
details (or above on pedigree):

2. family history of cataract? □ No □ Yes □ Unknown
   if known, please record age at onset, age at surgery and present vision of each affected relative:

3. family history of other ocular disease? □ No □ Yes □ Unknown
   please report details:

4. family history of systemic disease? □ No □ Yes □ Unknown
   please report details:

f OCULAR EXAMINATION of RELATIVES
   please report whether any relatives have been examined and the findings:

i) mother: □ No □ Yes, findings: □ Normal □ Abnormal (specify):

ii) father: □ No □ Yes, findings: □ Normal □ Abnormal (specify):

iii) siblings: □ No □ Yes, findings: □ Normal □ Abnormal (specify):

iv) other(s): □ No □ Yes, findings: □ Normal □ Abnormal (specify):
Surnme:  Forename:  

☐ Bilateral  

☐ Unilateral:  ☐ Right  ☐ Left  

Consultant:  

Date of birth  
Hospital number  
NHS number  

IV GENERAL PAEDIATRIC ASSESSMENT continued  

| g  GROWTH |  
| --- | --- | ---  
| if available, please record current weight, length / height, head circumference with percentiles |  
|  

<table>
<thead>
<tr>
<th>Actual measurement</th>
<th>Percentile (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current weight</td>
<td></td>
</tr>
<tr>
<td>Current length / height</td>
<td></td>
</tr>
<tr>
<td>Current head circumference</td>
<td></td>
</tr>
</tbody>
</table>

| h  ASSESSMENT BY PAEDIATRICIAN(S) ? | ☐ No  ☐ Yes  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the child have any non-ocular disorder(s) ?</td>
<td>☐ No  ☐ Yes</td>
</tr>
<tr>
<td>please report the details:</td>
<td></td>
</tr>
</tbody>
</table>

| VI  ASSESSMENT BY GENETICIST ? | ☐ No  ☐ Yes  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the child have hereditary disease(s) ?</td>
<td>☐ No  ☐ Yes</td>
</tr>
<tr>
<td>please report the details &amp; include family tree if possible</td>
<td></td>
</tr>
</tbody>
</table>

| VII  OTHER ASSESSMENT(S) ? | ☐ No  ☐ Yes  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>please report the details:</td>
<td></td>
</tr>
</tbody>
</table>


| Surname: | Forename: | Bilateral │ Unilateral: Right □ Left □ |
|----------|-----------|-----------|---------------------------|
| Date of birth | Hospital number | NHS number | Consultant: |

**AETIOLOGY**

Please indicate below the **UNDERLYING or ASSOCIATED CAUSE** of the cataract(s).

1) □ **IDIOPATHIC**

2) □ **INTRA UTERINE INFECTION / MATERNAL INFECTION EMBRYOPATHY**

   - Rubella □ CMV □ Varicella □ Herpes Simplex □ Herpes Zoster
   - Toxoplasmosis □ Syphilis □ Infectious mononucleosis □ Measles □ Poliomyelitis
   - OTHER (specify): □

3) □ **INTRA UTERINE DRUG EXPOSURE**

   - Chlorpromazine □ Corticosteroids □ Sulphonamides □ Vitamin D □ Vitamin A
   - OTHER (specify): □

4) □ **INTRA UTERINE IONIZING RADIATION**

   details:

5) □ **METABOLIC DISORDER**

   - Galactosaemia □ Galactokinase deficiency □ Hyperglycinuria □ Sialidosis
   - Alpha-mannosidosis □ Sorbitol dehydrogenase deficiency □ Diabetes mellitus
   - Idiopathic hypocalcaemia □ Hypocalcaemia due to hypoparathyroidism or pseudohypoparathyroidism □ Marginal maternal galactokinase deficiency □ Maternal diabetes mellitus
   - OTHER (specify): □

6) □ **PREMATURITY**

   details:

7) □ **OCULAR DISEASE**

   - Microphthalmia □ Aniridia □ Aniridia plus □ Ectopia lentis □ Intra-ocular tumour: e.g. □ retinoblastoma or □ medulloepithelioma □ Persistent hyperplastic primary vitreous □ Anterior chamber dysgenesis syndromes □ Retinopathy of prematurity □ Posterior lenticus □ OTHER (specify): □
### Surname: [blank]  Forename:  

<table>
<thead>
<tr>
<th>Date of birth</th>
<th>Hospital number</th>
<th>NHS number</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Consultant: [blank]</th>
</tr>
</thead>
</table>

#### AETIOLOGY cont’d

8) **INHERITED WITHOUT SYSTEMIC ABNORMALITY**

- [ ] Autosomal dominant
- [ ] Autosomal recessive
- [ ] X-linked recessive

9) **INHERITED WITH SYSTEMIC ABNORMALITY**

- **a) CHROMOSOMAL**
  - [ ] Trisomy 21
  - [ ] Turner’s syndrome
  - [ ] Trisomy 13-15
  - [ ] Trisomy 16-18
  - [ ] Cri du chat

- **b) SKELETAL DISEASE**
  - [ ] Conradi-Hunermann syndrome
  - [ ] Stickler syndrome

- **c) SYNDACTYLY, POLYDACTYLY, or other DIGITAL SYNDROME**
  - [ ] Rubinstein-Taybi syndrome
  - [ ] Ellis van Creveld syndrome

- **d) CENTRAL NERVOUS SYSTEM ABNORMALITIES**
  - [ ] Cerboro-oculo-facial-skeletal syndrome
  - [ ] Martsolf syndrome

- **e) MUSCLE DISEASE**
  - [ ] Myotonic dystrophy

- **f) MANDIBULO-FACIAL SYNDROMES**
  - [ ] Hallerman-Streiff syndrome

- **g) RENAL DISEASE**
  - [ ] Lowe’s syndrome

- **h) DERMATOLOGICAL DISEASE**
  - [ ] Congenital ichthyosis including IBIDS / Tay / Pollitt
  - [ ] Schafer syndrome

10) **OTHER** please describe:

___

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### AETIOLOGICAL INVESTIGATIONS

Please report whether any of the following investigations have been done and the result(s) (it is not suggested that all of these tests should be carried out in every case).

#### 1) INTRA-UTERINE INFECTION SCREEN

<table>
<thead>
<tr>
<th>Serological tests</th>
<th>Not done</th>
<th>Normal</th>
<th>Abnormal (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubella</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syphilis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella Zoster</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infectious mononucleosis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### 2) GENETIC / HEREDITARY DISEASE

Chromosomal analysis: □Not done □Normal □Abnormal (specify):

Other DNA studies: □Not done □Normal □Abnormal (specify):

#### 3) METABOLIC or ENDOCRINE DISEASE

<table>
<thead>
<tr>
<th>Blood</th>
<th>Not done</th>
<th>Normal</th>
<th>Abnormal (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td>full blood count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>calcium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>phosphate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>amino acids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>liver function tests</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>glucose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>galactose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rbc GPIUT activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rbc G6PD activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rbc galactokinase activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>wbc alpha mannosiode activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>plasma phytanic acid activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fibroblast cystathione synthetase activity</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Urine</th>
<th>Not done</th>
<th>Normal</th>
<th>Abnormal (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td>reducing substances</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>amino acids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>organic acids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>proteins / blood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>copper</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**SUMMARY OF FIRST VISIT**

**Age:**
- □ Bilateral
- □ Unilateral
- □ Right eye
- □ Left eye

Underlying or associated CAUSE(S) of cataract(s):

**PLAN of MANAGEMENT:**

**I SURGICAL** if no surgical treatment is planned, please record the reason(s)

<table>
<thead>
<tr>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ NO</td>
<td>□ YES (specify):</td>
</tr>
<tr>
<td>□ NO</td>
<td>□ YES (specify):</td>
</tr>
</tbody>
</table>

**II OPTICAL CORRECTION**

<table>
<thead>
<tr>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ NO</td>
<td>□ YES (specify):</td>
</tr>
<tr>
<td>□ NO</td>
<td>□ YES (specify):</td>
</tr>
</tbody>
</table>

**III OCCLUSION THERAPY**

<table>
<thead>
<tr>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ NO</td>
<td>□ YES (specify):</td>
</tr>
<tr>
<td>□ NO</td>
<td>□ YES (specify):</td>
</tr>
</tbody>
</table>

**IV OTHER including INVESTIGATIONS**

| □ NO | □ YES (specify): |

**NEXT APPOINTMENT:**

<table>
<thead>
<tr>
<th>date:</th>
<th>for: □ SURGERY □ EUA □ OPD □ OTHER: (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

271
**PRIMARY OPERATION** (please use separate forms for the right & left eyes)

**DATE OF SURGERY:** / /  
**SURGEON:** □Consultant □Other

**I EUA:** □Not done □Done (please record the findings below)

<table>
<thead>
<tr>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>□Normal</td>
<td>□Normal</td>
</tr>
<tr>
<td>cornea (horiz. diameter mm)</td>
<td></td>
</tr>
<tr>
<td>□Normal</td>
<td>□Normal</td>
</tr>
<tr>
<td>anterior segment</td>
<td></td>
</tr>
</tbody>
</table>
| lens morphology  
please describe & draw the cataract(s) |  |
| IOP (mmHg) |  |
| instrument used |  |
| □Normal | □Normal |
| fundus examination |  |

**II SURGICAL PROCEDURE ON:** □RIGHT EYE □LEFT EYE

□ Lens aspiration  □ Lensectomy - vitrectomy: □pars plana □cornea  
□ Other (please specify):

Primary posterior capsulotomy □ NO □ YES  
if yes: □ surgical □ YAG laser

Primary intra-ocular lens: □ NO □ YES: Make and Power of lens:  
□ posterior chamber: □ bag □ sulcus □ unknown □ anterior chamber  
□ other (specify):

Per-operative complications □ NO □ YES  
if yes, specify:

Post-operative medication:

Early post-operative complications: □ NO □ YES  
if yes, specify:

Next appointment date: / /  
for □ Surgery □ EUA □ OPD □ Other (specify)
Surname: Forename: □Bilateral □Unilateral: □Right □Left

Date of birth
Hospital number
NHS number

Consultant:

FIRST POST-OPERATIVE VISIT

Date: / / Age:

I VISION ASSESSMENT

1 FIXATION □NOT APPLICABLE /Recorded

| Central | Right eye | □Yes □No | □Yes □No | □Yes □No |
| Steady | | □Yes □No | | □Yes □No |
| Maintained | | | | | |

2 CURRENT OPTICAL CORRECTION: □None □Spectacles □Contact lens □Other(specify):
Compliance: □Full □>50% □<50% □None
Main reason for poor compliance:

3 VISUAL ACUITY

a. DISTANCE □NOT APPLICABLE /Recorded

| Method (specify) | FCPL/acyuity card procedure: □Keeler □Teller □Other (specify): |
| Kay's pictures | Sheridan Gardner singles |
| Snellen optotypes | Sonksen Silver Acuity System |
| Other(specify): | |

Test distance (if applicable)

| Visual acuity (actual measurement and Snellen equivalent if possible) | □without correction | □with correction |
| Right | |
| Left | |
| Both eyes together | |

b NEAR □NOT APPLICABLE /Recorded

| Method (specify): | Visual acuity | □without correction | □with correction |
| Spectacles | Contact lens |
| Right | |
| Left | |
| Both eyes together | |

4 REFRACTION

| PRESCRIPTION (please subtract working distance only) |
| Right eye | |
| Left eye | |
| Cycloplegic agent □YES (specify) □NO | |
### FIRST POST-OPERATIVE VISIT

#### II OCULAR EXAMINATION

<table>
<thead>
<tr>
<th></th>
<th>Right eye</th>
<th></th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
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<td>Normal</td>
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<td></td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cornea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>horiz. diameter (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>anterior chamber</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>iris / pupil</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>lens</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>draw the cataract if applicable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>posterior capsule</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IOP (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>instrument used</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fundus examination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>disc, cup : disc ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>macula</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>vessels</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extra-ocular movements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td>Abnormal (specify):</td>
<td></td>
</tr>
<tr>
<td>Strabismus</td>
<td>No</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Angle:</td>
<td></td>
<td>Constant</td>
<td>Intermittent</td>
</tr>
<tr>
<td>Nystagmus</td>
<td>No</td>
<td>Latent</td>
<td>Manifest</td>
</tr>
<tr>
<td>Pendular</td>
<td></td>
<td>Rotary</td>
<td>Combined</td>
</tr>
<tr>
<td>Jerk</td>
<td></td>
<td>Other :</td>
<td></td>
</tr>
<tr>
<td>Vertical</td>
<td></td>
<td>Other :</td>
<td></td>
</tr>
<tr>
<td>Horizontal</td>
<td></td>
<td>Other :</td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td></td>
<td>Other :</td>
<td></td>
</tr>
</tbody>
</table>

#### III ANY OCCLUSION since surgery?     
- NO
- YES if yes, specify regime:

Right eye:

- Compliance: Full
- >50%
- <50%
- None

Compliance record: No Yes: checked with diary log book other:

Main reason for poor compliance:
**FIRST POST-OPERATIVE VISIT**

**PLAN OF MANAGEMENT:**

**I SURGICAL**

<table>
<thead>
<tr>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ NO</td>
<td>□ YES (specify):</td>
</tr>
<tr>
<td>□ NO</td>
<td>□ YES (specify):</td>
</tr>
</tbody>
</table>

**II OPTICAL CORRECTION:**

<table>
<thead>
<tr>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ NO</td>
<td>□ YES (specify):</td>
</tr>
<tr>
<td>□ NO</td>
<td>□ YES (specify):</td>
</tr>
</tbody>
</table>

**III OCCLUSION THERAPY:** recorded with: □ diary □ log book □ other:

<table>
<thead>
<tr>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ NO</td>
<td>□ YES (specify):</td>
</tr>
<tr>
<td>□ NO</td>
<td>□ YES (specify):</td>
</tr>
</tbody>
</table>

**IV MEDICATION:**

□ NO □ YES (specify):

**V OTHER including INVESTIGATIONS:**

□ NO □ YES (specify):

**NEXT APPOINTMENT:**

| date: / / | for: □ SURGERY □ EUA □ OPD □ OTHER: (specify) |
8.4 APPENDIX D PAEDIATRIC SURVEILLANCE SCHEME DATA COLLECTION

QUESTIONNAIRE.

BRITISH CONGENITAL / INFANTILE CATARACT STUDY

CONFIDENTIAL REPORTING QUESTIONNAIRE
Thank you for completing this questionnaire. Please complete all sections as fully as possible. If information is not available please indicate by N/K = not known. Appendix I may be helpful in answering some questions.

SECTION A: CASE IDENTIFICATION DETAILS (hospital identification sticker may be used)
Surname: Forename:
Address: Post code:
Hospital Number: NHS Number:
Date of birth: Sex: □ Male □ Female
Born in UK? □ Yes □ No

SECTION B: HISTORY

1) PREGNANCY:
a) Any maternal illnesses during the pregnancy?
If YES please specify illness / diagnosis & stage of pregnancy:
 □ YES □ NO □ UNKNOWN

b) Any maternal exposure to known teratogen(s)?
If YES, specify teratogen below:
 □Yes □ No □ Unknown

□ Intra uterine ionizing radiation, specify:
□ Intra uterine drug exposure: e.g. Chlorpromazine, Corticosteroids, Sulphonamides, Vitamin D, Vitamin A
specify:
□ Other (specify):

2) LABOUR & DELIVERY:
Gestation: Birth weight (kg):
Mode of delivery: □ SVD □ Assisted VD □ Elective LSCS □ Emergency LSCS

3) NEONATAL HISTORY:
b) Symptomatic neonatal hypoglycaemia?
If YES, specify: cause(s), if known, and treatment (oral / iv)
 □ Yes (specify: □ transient □ persistent ) □ No □ Unknown

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4) DEVELOPMENTAL HISTORY:
Any developmental delay? □ YES □ NO □ UNKNOWN
if Yes, specify:

5) FAMILY HISTORY: If response to any of the following questions is yes, please draw a PEDIGREE
a) Family history of consanguinity? □ YES □ NO □ UNKNOWN
if Yes, specify:

b) Family history of cataract? □ YES □ NO □ UNKNOWN
If Yes and information available, please record age at onset & age at surgery of each affected relative:


c) Family history of any other ocular disease? □ YES □ NO □ UNKNOWN
if Yes, specify:

5d) Is there a family history of any systemic disease(s)? □ YES □ NO □ UNKNOWN
if Yes, specify:
SECTION C: DETECTION / PRESENTATION OF CASE

Please record dates or exact age (corrected for gestational age if appropriate) below.

1) Age of child / date when an ocular or vision problem was first suspected by anyone?

2) Who first suspected a problem?
   □ Mother  □ Father  □ Other relative  
   □ Midwife  □ Health visitor  □ General practitioner  □ Community paediatrician  □ Hospital paediatrician  
   □ Other (specify):  

   *If answer is a health professional please go to question 4, otherwise go to question 3*

3a) To which health professional did the child first present with the problem?
   □ Midwife  □ Health visitor  □ Community paediatrician  □ Hospital paediatrician  □ General practitioner  
   □ Ophthalmologist  □ Orthoptist  □ Optometrist  □ Other (specify):  

3b) Age of child / date at first presentation to the health professional?

4) Reason for first presentation to health professional?  *(you may choose more than option)*
   □ Poor vision suspected by parents  □ Poor vision suspected by health professional  
   □ Routine screening / developmental examination, specify:  □ Newborn  □ Six weeks  □ Other (specify):  
   □ White pupil  □ Squint  □ Nyctagmus  □ Family history of cataract  □ Other (specify):  

5) Who referred the child to you?  □ Midwife  □ Health visitor  □ GP  □ No-one  □ Other (specify):  

6) Age of child / date when first seen by you?

SECTION D: EXAMINATION FINDINGS

1) GENERAL EXAMINATION:
   a) At presentation to you:  Weight:  Length / height:  Head circumference:  
   b) Any non-ocular DISORDER(S) or DISABILITIES?  □ YES  □ NO  □ UNKNOWN  
      If yes, specify:  □ hearing  □ speech  □ motor  □ other, specify:  
      OTHER:  

2) OCULAR EXAMINATION:  *(as an alternative to completing this section, if you have a written ophthalmic assessment which contains all the information sought in questions 1 to 4, you may prefer to enclose it)*
   a) Cataract(s):  □ Bilateral  or  □ Unilateral, specify:  □ Right eye  or  □ Left eye  
   b) Morphology of cataract(s):  □ complete  □ partial  □ not known  please describe if you have details:  

   c) Visual acuity measured?  □ YES  □ NO  □ UNKNOWN  
      If yes, specify:  date measured (most recent):  method used:  test distance:  
      tested wearing:  □ spectacles  □ contact lens  □ no optical correction  
      Distance visual acuity:  RIGHT eye:  LEFT eye:  BOTH eyes together:  

4) Any other ocular abnormalities?  □ YES  □ NO  □ UNKNOWN  
   If yes, specify:  

continued over
APPENDIX I gives a list of known underlying or associated causes of congenital cataract and may be helpful in completing this section.

1) Probable cause of cataract(s):  □ known CONGENITAL  or  □ presumed CONGENITAL  or □ ACQUIRED

If acquired, please go to question 3, if congenital, continue to question 2

2) Please specify below the most probable CONGENITAL CAUSE of the cataract(s): (appendix I may be helpful)

□ IDIOPATHIC

□ INTRA UTERINE DRUG EXPOSURE specify:

□ INTRA UTERINE IONIZING RADIATION specify:

□ INTRA UTERINE INFECTION specify:

□ PREMATURITY specify:

□ METABOLIC DISORDER specify:

□ HEREDITARY WITHOUT associated SYSTEMIC ABNORMALITY specify: □ Autosomal dominant □ Autosomal recessive □ X-linked recessive

□ HEREDITARY WITH associated SYSTEMIC ABNORMALITY specify:

□ Associated OCULAR DISEASE, specify:

□ OTHER, specify:

3) What is the ACQUIRED cause of the cataract(s)?
4) Please record below if any of the investigations have been carried out and the results.

Please note it is not suggested that any of these investigations should be carried out solely for this study.

British Congenital Cataract Study list of investigations which may be relevant in aetiological assessment of cases of congenital / infantile cataract

a) SCREEN for INTRA-UTERINE INFECTION? □ YES □ NO □ UNKNOWN

if Yes, specify:

<table>
<thead>
<tr>
<th>Serological tests</th>
<th>Maternal</th>
<th>Infant</th>
<th>Maternal</th>
<th>Infant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not done</td>
<td>Normal</td>
<td>Abnormal (specify)</td>
<td></td>
</tr>
<tr>
<td>Rubella</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syphilis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella Zoster</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infectious mononucleosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

b) Investigations for GENETIC/HEREDITARY DISEASE? □ YES □ NO □ UNKNOWN

Chromosomal analysis: □ Not done □ Normal □ Abnormal, specify:

Other DNA studies: □ Not done □ Normal □ Abnormal, specify:

c) Investigations on child for METABOLIC or ENDOCRINE DISEASE? □ YES □ NO □ UNKNOWN

if Yes, specify:

<table>
<thead>
<tr>
<th>BLOOD</th>
<th>Not done</th>
<th>Normal</th>
<th>Abnormal (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td>full blood count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>calcium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>phosphate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>amino acids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>liver function tests</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>glucose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>galactose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rbc G1PUT activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rbc G6PD activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rbc galactokinase activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>wbc alpha mannosidase activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>plasma phytanic acid activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fibroblast cystathione synthetase activity</td>
<td></td>
<td></td>
<td></td>
</tr>
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</table>

<table>
<thead>
<tr>
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<th>Not done</th>
<th>Normal</th>
<th>Abnormal (specify)</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>amino acids</td>
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<td></td>
</tr>
<tr>
<td>organic acids</td>
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<td></td>
</tr>
<tr>
<td>proteins / blood</td>
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<td></td>
</tr>
<tr>
<td>copper</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sediment</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1) Is the child already under the care of an ophthalmologist? □YES □NO □UNKNOWN
If YES please report:

a) age (or date) at which the child was referred to an ophthalmologist:

b) if known, age (or date) at which the first ophthalmic assessment took place:

2) Has the child already been treated? □YES □NO □UNKNOWN
If YES, and information available, please report the following: (alternatively, you may prefer to send copies of ophthalmic summaries, if they contain all the information sought, when returning the questionnaire)

a) surgical treatment(s) with dates

b) type of optical correction: □spectacles □contact lens □intra-ocular implant □other (specify)

3) If the child is not already under the care of an ophthalmologist, is the child to be referred to one? □YES □NO
If No, please go to box at end of questionnaire, if Yes, please specify:

a) age / date at which the child is to be referred (if this is known):

b) age / date at which the first ophthalmic assessment will take place (if this is known):

4) Please record the NAME and ADDRESS of any OPHTHALMOLOGIST(S) involved in the care of the child.

The ophthalmologist(s) will not be contacted unless the child is independently reported by him / her to the BCCSG.

NAME:

ADDRESS:

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE

NAME of person completing this questionnaire:

Please return the completed questionnaire (postage paid envelope provided) to:
Ms J S Rahi, Institute of Child Health, 30, Guilford Street, LONDON WCIN
Tel: 0171-242-9789 ext 2250 Fax 0171-813-8233

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8.5 Appendix E Method for calculation of age-specific and cumulative incidence rates and their 95\% confidence intervals using SAS.

data rates;
input age w pop events
atrisk=pop/10000;
rate=events/atrisk;
cumul+rate*w;
var+events*(w**2)/(atrisk**2);
se_cum=sqrt(var);
se_rate=sqrt(events)/atrisk;
drop var;
8.6 Appendix F Questionnaire used in survey of paediatricians' practices and training.

Survey of practice amongst paediatricians in screening / surveillance examinations for the detection of ocular disorders in infants.

Thank you completing this questionnaire.

Please answer all questions.
If a question does not apply to you please answer N/A = not applicable.
Where appropriate, please answer by ticking option boxes.

1. What is your clinical status?
   - □ Senior House Officer
   - □ Registrar
   - □ Senior Registrar
   - □ Consultant
   - □ Clinical Medical Officer
   - □ Senior Clinical Medical Officer
   - □ Other (specify):

2. Which setting do you work in? (you may tick more than one option)
   - □ Hospital
   - □ Community
   Sub-specialty if applicable:

3. Are you responsible for routine screening / surveillance examinations of
   a. neonates □ NO □ YES
   b. infants aged six weeks □ NO □ YES

4. Please report the ophthalmological disorder(s) you specifically seek to identify by screening / surveillance examinations of
   a) Neonates □ Not applicable
   b) Infants aged 6 weeks □ Not applicable
5. Please report the examination technique(s) and instrument(s) you use for the detection of the ophthalmological disorders you have recorded above.

a) Neonates

☐ Not applicable

b) Infants aged 6 weeks

☐ Not applicable

6. Who trained you in ocular examination of infants? *(you may tick more than one option)*

☐ No-one  ☐ Ophthalmologist  ☐ Paediatrician  ☐ Other (specify):

please now go to Question 9

7. What form did this training take? *(you may tick more than one option)*

☐ lecture  ☐ practical demonstration  ☐ other (specify):

8. When did you receive this training? *(you may tick more than one option)*

☐ Undergraduate training  ☐ Post-graduate paediatric training

at which grade?

☐ SHO  ☐ Registrar  ☐ Senior Registrar  ☐ Other (specify):
9. Do you think you would benefit from further formal training from an ophthalmologist?

☐ Yes ☐ No ☐ Don’t know

If yes,

a. what form of training? ☐ lecture ☐ practical demonstration ☐ other (specify):

b. what would be the most appropriate setting for such training:

☐ special course ☐ component of post-graduate training programme

☐ other (specify):

c. do you have access to an ophthalmologist for such training? ☐ Yes ☐ No

Please use this space for any comments or suggestions you may have:

Thank you for completing this questionnaire.

Please return in the envelope provided to:
Ms JS Rahi, Dept of Epidemiology
Institute of Child Health, 30 Guilford Street, LONDON WC1N

If you have any queries, contact: 0171-242-9789 ext 2250
Epidemiology of visual impairment in Britain

Jugnoo S Rahi, Carol Dezateux

Since vision is the major sensory modality in humans, normal vision is important for the general development of a child. Visual impairment has significant implications for the affected child and family in terms of education, future employment, and personal and social welfare throughout life.

Using the World Health Organisation (WHO) classification of levels of visual impairment (shown in table 1 and used throughout this paper), it is estimated that globally almost one in 1000 children are blind, which is less than a tenth of the prevalence in adults. However, the 1.5 million blind children in the world account for about 75 million person years of blindness, equivalent to the burden due to cataract related blindness, which accounts for 40% of adult blindness worldwide. As the combined categories of low vision in childhood (table 1) are three to 10 times more common than blindness, the total burden of childhood visual impairment is considerable. It has been estimated that globally, the financial costs of childhood blindness incurred by countries, in terms of care and productivity lost, are between 6 and 27 thousand million US dollars. Most of this is accounted for by children in high income countries where childhood blindness is less common but life expectancy and earning capacity are greater than in low income countries. Reduction of avoidable visual impairment remains an important international public health goal.

Knowledge of the magnitude and causes of childhood visual impairment is important to the planning, provision, and evaluation of educational and health services for affected children. This is also essential information for all strategies to reduce visual disability in the population. The purpose of this paper is to review the available data, highlighting relevant sources, on the incidence, prevalence, and causes of childhood visual impairment in Britain which are relevant to both hospital and community based child health.

Normal visual development
The visual system is relatively immature at birth. Maturation depends on both structural and functional changes. Development is particularly rapid in the first year of life, although some changes continue into late childhood. As a child with normal vision only achieves adult levels of visual function at about 5 years, it is difficult to predict final visual outcome in younger children with visual defects.

The plasticity of the visual system is a key principle in the management of ophthalmic disease in children. In early life there are "sensitive periods", of varying length, during which visual function can be profoundly impaired by a variety of insults such as stimulus deprivation arising from congenital cataract. Additionally "critical periods" exist during which treatment must be instituted to have maximal, or sometimes any effect. Some adverse changes in the visual system become largely irreversible outside these critical periods.

Measuring visual function
The visual function most frequently measured is distance acuity. However other visual functions, such as visual fields, contrast sensitivity, colour vision, and binocularity may be particularly relevant to overall functional assessment. Despite recent advances in the development and refinement of age appropriate methods for testing vision, the assessment of acuity remains difficult in infants and preschool children as well as those with other disabilities. Young children are increasingly assessed using psychophysical tests based on preferential looking techniques and electrophysiological tests. These are based on different principles and are not directly comparable with each other or with methods used in older children. Acuity measurement is less problematic in older children with normal vision only achieving adult levels of visual function at about 5 years, it is difficult to predict final visual outcome in younger children with visual defects. As a child with normal vision only achieves adult levels of visual function at about 5 years, it is difficult to predict final visual outcome in younger children with visual defects.

<table>
<thead>
<tr>
<th>Level of visual impairment</th>
<th>Category of vision</th>
<th>Visual acuity in better eye with optical correction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slight if visual acuity &lt; 6/7.5</td>
<td>Normal vision</td>
<td>6/18 or better</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>Low vision</td>
<td>&lt; 6/18 to 6/60</td>
</tr>
<tr>
<td>Severe visual impairment</td>
<td>Blindness</td>
<td>&lt; 6/60 to 3/60</td>
</tr>
<tr>
<td>Blind</td>
<td>Visual field ≤ 10 degrees around central fixation</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Aetiological classification</th>
<th>Underlying or associated causes of blindness and low vision (adapted from the WHO Preventive of Blindness Committee eye examination record)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cornea</td>
<td>Prenatal</td>
</tr>
<tr>
<td>Lens</td>
<td>Perinatal</td>
</tr>
<tr>
<td>Retina</td>
<td>Childhood</td>
</tr>
<tr>
<td>Optic nerve</td>
<td>Unspecified</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>Other</td>
</tr>
</tbody>
</table>

*According to timing of insult resulting in ocular or vision disorder.
†If an aetiological category cannot be definitely assigned or determined.

Table 1: WHO classification of levels of visual impairment (adapted from International Classification of Diseases, 10th revision).

Table 2: Classification of underlying or associated causes of blindness and low vision (adapted from the WHO Preventive of Blindness Committee eye examination record).
children but systems used in testing adults are generally inappropriate for children of less than school age.

Classification of visual impairment
The categorisation of levels and causes of childhood visual impairment is difficult. While the use of standard functional, anatomical, and aetiological classifications has increased, allowing more meaningful interpretation and comparison of studies, some issues remain unresolved.

The impact on a child of a given visual deficit depends, among other factors, on whether the child has any additional disabilities. The current WHO paradigm of impairments, disabilities and handicaps, based on a medical model of disability, does not readily provide an epidemiologically useful classification of childhood visual impairment. The WHO classification of levels of visual impairment and blindness in children in the UK and Ireland.

Size of the problem in the UK INCIDENCE
There are few data on the incidence of childhood visual impairment in any region of the world, including Britain. Most serious ophthalmic disorders in children which result in visual impairment are present or become manifest in early childhood. The new occurrence of serious bilateral visual loss in later childhood is uncommon by contrast with adults in whom the incidence of visual impairment is highest among those over 65 years.

In England and Wales in 1990–91, the combined incidence of certification of partial sight and blindness was eight per 100 000 children aged 0 to 15 years. However serious underascertainment and imprecision of information on causes have been documented in this voluntary certification system. The direct benefits of registration for a child differ to those for an adult, in particular there are no financial advantages and special educational needs can be assessed and met without registration. Consequently, in many cases there may be no additional real or perceived gain from registration of eligible children. Therefore, although registration data have traditionally been an important source of information, certification rates provide only general, minimum estimates of the incidence of severe visual impairment and blindness.

The Oxford Register of Early Childhood Impairments is a unique source of information

### Table 3 Prevalence of visual impairment and its main causes in England, Scotland, and Wales; results are prevalence per 1000 (95% confidence interval)

<table>
<thead>
<tr>
<th>Ocular or vision disorder</th>
<th>1958 Birth cohort: n=15 275, age 11 years</th>
<th>1970 Birth cohort: n=14 907, age 10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial sight</td>
<td>0.46 (0.12 to 0.79)</td>
<td>0.54 (0.17 to 0.91)</td>
</tr>
<tr>
<td>Blindness</td>
<td>0.13 (0.05 to 0.31)</td>
<td>0.34 (0.04 to 0.64)</td>
</tr>
<tr>
<td>Congenital cataract</td>
<td>0.19</td>
<td>0.33</td>
</tr>
<tr>
<td>Optic atrophy</td>
<td>0.10</td>
<td>0.13</td>
</tr>
<tr>
<td>Retinal dystrophy/Albinism</td>
<td>0.13</td>
<td>0.07</td>
</tr>
<tr>
<td>Retinopathy of prematurity</td>
<td></td>
<td>0.07</td>
</tr>
<tr>
<td>Retinoblastoma</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level of visual loss</th>
<th>Prevalence per 1000</th>
<th>Age (years)</th>
<th>Area and year</th>
<th>Source of data</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVI or blind</td>
<td>0.16</td>
<td>0–16</td>
<td>Eire, 1991</td>
<td>Multiple source national survey</td>
</tr>
<tr>
<td>6/18 or less</td>
<td>0.81</td>
<td>0–20</td>
<td>Northern Ireland, 1977</td>
<td>Multiple source national survey</td>
</tr>
<tr>
<td>6/18 or less</td>
<td>1.81 (all)</td>
<td>0–16</td>
<td>Liverpool, 1996</td>
<td>Multidisciplinary visual assessment team</td>
</tr>
<tr>
<td>0.63 visual loss</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.18 with other</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SVI = severely visually impaired.
Table 5  Aetiology (%) of low vision and blindness in childhood in Britain

<table>
<thead>
<tr>
<th>Region</th>
<th>Year</th>
<th>No</th>
<th>Data source</th>
<th>Prevalent</th>
<th>Unclassified*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hereditary</td>
<td>Intrauterine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Prevalent</td>
<td>Childhood</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pressed</td>
<td>Unknown</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td>1977</td>
<td>486</td>
<td>Multiple source national survey</td>
<td>51</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>11</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>22</td>
</tr>
<tr>
<td>Scotland</td>
<td>1987</td>
<td>99</td>
<td>School for visually impaired</td>
<td>48</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Eire</td>
<td>1991</td>
<td>172</td>
<td>Multiple source national survey</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*If an aetiological category cannot be definitely assigned or determined.
†Individuals <20 years with visual acuity of 6/18 or less.

About young children with early onset visual and other neurological impairments which uses multiple community and hospital sources to achieve high ascertainment. Between 1984 and 1991 the reported rate of visual loss (≤ 6/18) was 1.4 per 1000 live births.

During the same period in the 1984 Oxfordshire Health District Birth Cohort, the average annual incidence of presentation to a hospital eye clinic with ocular or vision disorders was 11 per 1000 in children under 2 years and 17 per 1000 in 2 to 5 year olds. However many of these children had uncorrected refractive errors or ocular disorders without visual impairment. Consultation rates provide information on ocular morbidity which, while important in planning eye services, cannot provide estimates of the incidence of visual impairment in the population.

**PREVALENCE**

In many low income countries, about half the severely visually impaired and blind children die in childhood as a consequence of the blinding disorder or as a result of the disadvantages associated with visual handicap.

By contrast, in Britain, only those visually impaired children with serious systemic disorders are at increased risk of dying in childhood. Therefore prevalence, dependent on both disease incidence and duration, is a useful measure of the burden of childhood visual impairment in Britain and is important in identifying groups at high risk and in assessing the impact of interventions.

The national prevalence of disability in children is not measured routinely in Britain. Two national surveys in 1985 and 1988 reported one or more specific disabilities in 36 per 1000 children aged under 16. A seeing disability (defined on the basis of vision dependent tasks rather than acuity) affected two per 1000 children overall and 6% of disabled children living in private homes and 16% of those in communal establishments. The 1958 and 1970 birth cohorts are the only large studies from which national estimates of the prevalence of visual impairment and its causes can be determined (table 3). The higher prevalence of partial sight and blindness in the later cohort may be due, among other factors, to differences in methodology or changes in survival patterns of children with multiple disabilities.

Prevalence estimates for a variety of different levels of visual impairment in other geographically defined populations in the British Isles are shown in table 4. The range of reported prevalence reflects varying case definitions, sources, methods, and completeness of ascertainment in these studies. This limits the scope for generating a summary estimate but it is probable that at least one child in a thousand in Britain is visually impaired, severely visually impaired, or blind (table 1). On-going studies of other defined populations, such as the ALSPAC cohort study, should provide information on incidence and causes of visual disability in the future.

The long established Liverpool visual assessment team reported the prevalence of visual impairment in the context of other disabilities to be about twice that of isolated visual loss (≤ 6/18 in either eye, table 4). Assessment of all children with serious visual loss by a district multidisciplinary team has been advocated recently but is not, as yet, available in all districts. Children with visual impairment which is less severe, isolated, or purely due to ocular disorders, may be managed principally or solely by the ophthalmic team and may be less readily identified in a community through systems primarily designed to ascertain children with multiple disabilities.
In Britain, the principal causes of serious visual loss are congenital cataract, cortical visual impairment, and optic atrophy together with disorders of the retina and congenital ocular anomalies (table 3 and fig 1). Trauma is an important and preventable cause of ocular morbidity in children, being more common in boys, school age children, and in the setting of the home. However, ocular injuries are often unilateral and mild, so trauma rarely causes visual impairment.

The changes in the relative importance of different causes of blindness in newly registered children between 1969 and 1990 are shown in fig 2. The relative contributions of disorders of visual pathways, the inherited retinal dystrophies and albinism, congenital ocular anomalies, and retinopathy of prematurity have increased whilst cataract and optic atrophy have decreased. A similar pattern is seen in new registrations of partial sight. The interpretation of these time trends is difficult because they are influenced by changes in case ascertainment and registration practices as well as available treatment for and incidence of different disorders.

Traditionally registers of visual impairment and other national reporting systems have been the main sources of information on ophthalmic and vision disorders in children. However it is difficult to derive reliable estimates from single sources, particularly those dependent on routine collection of data. For example, in a recent national study, fewer than a quarter of infants with congenital cataract ascertained by active surveillance involving both paediatricians and ophthalmologists had been notified through existing national systems.

Children at higher risk of visual impairment At least half of all visually impaired children have other disabilities and they are a special group for three reasons. Firstly, the impact of visual loss may be greater than in children without other disabilities, especially in hearing impaired children. Secondly, there may be a common underlying cause, such as hereditary disease or prenatal infection, and the recognition of such associations may be relevant to the diagnostic process. Thirdly, the prevalence and pattern of causes differ in children with other disabilities compared with those with isolated visual loss and this is relevant both to the management of individual cases and to policies aimed at early detection of ocular and vision defects.

Nearly half of the children referred to the Liverpool visual assessment team with additional disorders had cortical visual impairment whereas 41% with isolated visual loss had inherited retinal dystrophies (fig 3). UK case series reporting ocular and vision defects in children with hearing impairment, cerebral palsy, and intellectual impairment in the UK are shown in fig 4. In Down's syndrome high refractive errors, cataract, glaucoma, and strabismus occur more frequently than in the

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Figures and tables are not included in the text representation.
Epidemiology of visual impairment

Loss not reported in intellectual impairment.

Figure 4 Ocular and vision defects in children with other disorders in Britain; * = visual loss not reported in intellectual impairment.

A variety of ocular and vision defects occur more frequently in children born preterm or of low birth weight, especially among those with neonatal periventricular haemorrhage or leucomalacia. Varying visual assessment techniques and duration of follow up have limited useful comparison of some reported studies of these children. A standard minimum dataset for follow up studies, including information on visual morbidity, has been advocated and would improve knowledge about visual outcomes in these children. The major ocular and vision defects in survivors of three cohorts of general population and may not be detected early without routine full ophthalmic assessment.

Areas of future research
This review has highlighted some gaps in the epidemiological data regarding childhood visual impairment in Britain. Better information on the incidence, prevalence, and causes of visual impairment is required to inform and assess health, education, and social services for visually impaired children. The value of much of the currently available epidemiological information is limited by methodological difficulties as well as by the scope and completeness of routinely collected data. The further development and consistent use of standardised approaches to the classification of levels and causes of visual impairment would require better data on the incidence of different disorders and the distribution and importance of known risk factors. Furthermore, the scope for primary prevention is limited by our present understanding of underlying mechanisms in disorders such as microphthalmos or idiopathic congenital cataract and by the availability of effective means of prenatal diagnosis of and early intervention for inherited disorders such as the retinal dystrophies. Nevertheless, there are a number of effective primary, secondary, and tertiary preventive strategies aimed at reducing visual impairment in the community. Some current and future strategies, together with examples of target disorders, are summarised in table 7. Their successful implementation requires a coordinated multidisciplinary approach involving geneticists, obstetricians, neonatologists, hospital and community paediatricians, as well as ophthalmologists and other ophthalmic professionals and those with expertise in the educational needs of the visually impaired.

Table 7 Current and future strategies to prevent childhood visual impairment in Britain

<table>
<thead>
<tr>
<th>Primary prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strategies (examples of target disorders)</td>
</tr>
<tr>
<td>Prevention of prenatal infections such as rubella and prenatal exposure to known teratogens such as drugs and alcohol. (e.g. measles, leprosy, rubella, poliomyelitis, citrate).</td>
</tr>
<tr>
<td>Provision of preconceptional genetic counselling to families with known hereditary eye disease. (e.g. retinopathy of prematurity, congenital cataract, glaucoma).</td>
</tr>
<tr>
<td>Further development and future provision of prenatal diagnostic tests and possible gene therapies for inherited eye diseases. (e.g. retinopathy of prematurity, retinoblastoma).</td>
</tr>
<tr>
<td>Promotion and further development of strategies to reduce low birth weight and preterm birth. (e.g. retinopathy of prematurity, conjunctival visual impairment, optic atrophy).</td>
</tr>
<tr>
<td>Screening of children at high risk of specific disorders: preterm infants, specific systemic diseases, for example juvenile chronic arthritis, diabetes. (e.g. retinopathy of prematurity, optic atrophy).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early detection through child health surveillance to ensure prompt referral of all children with ocular disorders.</td>
</tr>
<tr>
<td>Early detection through routine ophthalmological assessment of children at high risk, for example family history of eye disease; those with hearing impairment, neurodevelopmental or neurological disorders.</td>
</tr>
<tr>
<td>Assessment and management of children with serious visual loss by specific multidisciplinary teams.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tertiary prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of special educational needs and appropriate educational placement.</td>
</tr>
<tr>
<td>Assessment for, and provision of, low vision aids and rehabilitation services to optimise residual vision of children with disorders not amenable to specific treatment (e.g. congenital eye anomalies, retinal dystrophies).</td>
</tr>
<tr>
<td>Partial sight or blindness registration to maximise access to appropriate services.</td>
</tr>
</tbody>
</table>
improvement are required together with more effective routine data systems for the collection of information on all children with visual loss in specified populations. Measures of disability associated with vision loss in children, including quality of life, are currently lacking but are particularly relevant to formal evaluation of different treatment options. Finally, there is a need for continued research to enhance understanding of human visual development, as well as natural history and causal pathways, if preventive strategies are to be strengthened and developed.

Conclusion

The prevention of childhood visual impairment in Britain poses an important challenge to clinicians and researchers alike. Effective secondary and tertiary preventive strategies exist and their successful implementation will continue to depend on coordinated services for affected children and their families. Further reduction in the burden of visual impairment will only be achieved by strengthening the scientific basis of primary preventive strategies.

Jugnue Rahi is a Medical Research Council clinical training fellow; Carol Dezateux was supported by the Wellcome Trust.

A survey of paediatricians’ practice and training in routine infant eye examination

Jugnoo S Rahi, Richard Lynn

Abstract
A survey of a sample of UK paediatricians was carried out to identify the practices and determine the training of those involved in routine surveillance examinations to detect ophthalmic disorders in infants. The findings indicate important variation in current practices and raise concerns about both undergraduate and postgraduate training in ophthalmic assessment of infants.

Keywords: screening; surveillance; vision

Early detection of treatable sight or life threatening ophthalmic disorders in infants is essential for their optimal management. Consequently, routine examinations to identify them, during the neonatal period and again at 6-8 weeks of age, are an established component of child health surveillance in Britain. Recommendations about practice are made in Health for All Children and Ophthalmic Services for Children, the reports of two national joint working parties. Careful inspection, evaluation of the red reflex, examination for the presence of squint, and assessment of visual behaviour are advised for the detection of serious sight threatening disorders, notably congenital eye anomalies such as microphthalmos and coloboma, congenital cataract, glaucoma, and retinoblastoma. However, little is known about the extent to which these recommendations have been adopted and the training of those involved.

Methods
In 1995, a survey of a representative sample of UK paediatricians was carried out to identify the practices and describe the training of those currently responsible for the routine examinations of young infants. After a pilot study, an anonymised semistructured questionnaire was sent to hospital and community consultants (250), hospital based trainees (150), and clinical medical officers (CMOs) (100) selected randomly from membership lists of the Royal College of Paediatrics and Child Health, the British Association of Perinatal Medicine, the British Association of Community Child Health, and the Society for Public Health. Consultant paediatricians were surveyed because, even when not personally involved in routine examinations of infants, they would be responsible for the provision of the service, including the training of junior colleagues.

Results
After one reminder, 365 (73%) paediatricians returned completed questionnaires (205 consultants, 102 hospital paediatric trainees, and 58 CMOs). Of these respondents, 272 indicated that they were responsible for examination of infants aged up to 8 weeks; the percentage of these respondents reporting seeking the ophthalmic disorders specified in the national recommendations for infants aged 6-8 weeks: the percentage of these respondents reporting seeking the ophthalmic disorders specified in the national recommendations for infants aged up to 8 weeks is shown in fig 1 (consultants) and fig 2 (hospital and community paediatricians). There were no substantial or consistent differences between the two groups or between community and hospital based paediatricians. Congenital cataract was the most frequently sought disorder at both examinations in all groups.

A fifth of all respondents (75) and a third (32) of hospital paediatric trainees reported receiving no training in the ophthalmological examination of infants. Of those reporting some training, 57% had received this only as postgraduates and 16% only while undergraduates. Respondents had been trained in ophthalmic examination by a senior paediatrician (80%), an ophthalmologist (41%), an orthoptist (18%), or a paediatric trainee colleague (4%) with a quarter receiving training from more than one source. The majority (92%) of these respondents had received some practical training with 46% reporting receiving...
Paediatricians' practice and training in routine infant eye examination

Figure 2 Percentage of hospital based paediatric trainees and CMOs seeking specific anomalies, for example microphthalmos and coloboma; not applicable in neonates.

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Infants aged 6-8 weeks</th>
<th>Neonates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buphthalmos glaucoma</td>
<td>21</td>
<td>27</td>
</tr>
<tr>
<td>Congenital eye anomalies*</td>
<td>50</td>
<td>45</td>
</tr>
<tr>
<td>Retinoblastoma</td>
<td>26</td>
<td>37</td>
</tr>
<tr>
<td>Congenital cataract</td>
<td>96</td>
<td>92</td>
</tr>
<tr>
<td>Squint*</td>
<td>58</td>
<td>24</td>
</tr>
<tr>
<td>Abnormal visual behaviour*</td>
<td>30</td>
<td>54</td>
</tr>
</tbody>
</table>

Discussion

Serious sight or life threatening ocular disorders, such as congenital cataract, congenital eye anomalies, retinoblastoma and glaucoma, are uncommon, with a combined prevalence of the order of 0.5 per 1000 births. The main purpose of routinely examining young infants to detect such disorders is to ensure that effective treatment and relevant medical and educational advice and support for the family of the affected child, are provided at the earliest opportunity. The effectiveness of these examinations is assumed in ophthalmic surveillance or vision screening programmes for older children, which are primarily intended to confirm normal visual development and to detect disorders such as squint or amblyopia which may develop during childhood.

The survey findings indicate important variation in the implementation of current recommendations about screening and surveillance for ophthalmic disorders in infancy. The degree of clinical experience of respondents and the setting in which they work do not appear to be the main factors influencing the variation in practice, as this did not differ substantially between consultants and trainees or hospital and community based paediatricians. Ophthalmic assessment of infants is difficult and requires specific knowledge and practical training to do effectively. At the time of this survey, routine neonatal examinations were carried out by junior hospital based trainee paediatricians but recently, in some areas, this has become the responsibility of general practitioners or midwives, who were not surveyed. There is increasing interest in standardising the content of the routine neonatal examination and in identifying the most appropriate health care professionals to undertake it; this presents a good opportunity to review the ophthalmic component and to develop appropriate training programmes for those undertaking it.

The survey findings raise serious concerns about the extent and content of both undergraduate and postgraduate medical training in ophthalmic examination of infants, especially the low reported frequency of training received from ophthalmologists and other ophthalmic professionals. Perhaps most important is the finding that most paediatricians, even consultants, considered they would benefit from further training. This is consistent with the reported training needs of general practitioners involved in child health surveillance, who are increasingly responsible for the routine examination at 6-8 weeks of age, some of whom may not have received appropriate undergraduate training in ophthalmic assessment. Variation in current postgraduate training programmes for general practitioners and others involved in child health surveillance has already been identified. Undergraduate ophthalmology training, traditionally during a separate clinical attachment, might be improved by greater integration with the main medical specialties: for example, undergraduates could attend paediatric ophthalmology clinics during their attachment to the paediatric department. Increased integration would enhance understanding of the relevance of ophthalmology to other disciplines, improve knowledge about specific ophthalmic disorders and provide greater opportunities to practise examination techniques. Postgraduate training for all doctors involved in screening and surveillance examinations should include specific teaching on paediatric ophthalmic disorders and visual assessment of children together with an evaluation of the skills acquired. The interdisciplinary discussions necessary for the development of such programmes for paediatricians have already been advocated. This is an opportunity to explore the possible role of orthoptists as trainers, given their expertise in the assessment of vision and ocular motility in children. A minority of respondents reported receiving any training from an orthoptist despite the scope which exists in both community and hospital settings, especially where secondary screening of referred children is undertaken by orthoptists. While development of undergraduate and postgraduate training programmes is a long-term process, closer liaison between paediatric and ophthalmology departments could create training opportunities in the short term: for example, joint assessment clinics for children with visual impairment, already advocated to improve overall management, offer excellent scope for further training of paediatricians and ophthalmologists alike.

We suggest that optimal ophthalmic surveillance of newborn and young infants nationally requires more specific guidance on the purpose and content of examinations as well as the programmes for training and assessment of all those involved, both now and in the future. In order to strengthen and develop such
programmes it will be necessary to gather the research evidence to inform practice which, as in some other areas of infant screening, is currently lacking: there is significant scope for this at a time when other aspects of child surveillance are being re-evaluated.

Conflict of interest: None

We thank all the paediatricians who took part in the survey, for completing the questionnaire and for providing helpful suggestions; Dr Waterston (British Association of Community Child Health) and Dr Gardner (Society for Public Health) for help with distribution of questionnaires; Dr Carol Daveretx and Professor Catherine Peckham (Institute of Child Health, London) for their comments.

Jugnoo Rahi is supported by the Medical Research Council.

3 Court S. Examination of the newborn—for what and by whom? Changing Childbirth Update September 1995:3-3 (paper).
Epidemiology of cataract in childhood: A global perspective

Allen Foster, FRCOphth, Clare Gilbert, FRCOphth, Jugnoo Rahi, FRCOphth

ABSTRACT

Cataract is the most important cause of treatable childhood blindness. There are an estimated 200,000 children blind from cataract worldwide; 20,000 to 40,000 children with developmental bilateral cataract are born each year. Rubella is still an important cause of preventable disease in many countries. In the developing world, there is a need to improve early case detection and referral services and to establish centers with expertise in the assessment, surgical treatment, and long-term management of the child with cataract.

It is estimated that there are 1.5 million blind (corrected visual acuity less than 20/400 in the better eye) children in the world, with a prevalence of between 1 to 4/10,000 children in industrialized countries and 5 to 15/10,000 children in developing countries. The incidence is not known, although the figure of 500,000 children per year going blind is often quoted. The mortality rate for blind children in developing countries is high because of the underlying cause of blindness (e.g., malnutrition, measles, or rubella) and a lack of support services for families with blind children.

Studies indicate that the causes of visual loss in children vary greatly from place to place. In countries with low income and inadequate health care, malnutrition, particularly vitamin A deficiency, and infections are responsible for more than half of all cases. In middle income countries, congenital anomalies, cataract, and glaucoma are important. In the urban centers of some middle income countries, retinopathy of prematurity is a cause because of the survival of large numbers of preterm and low-birth-weight babies as a consequence of increased availability of neonatal intensive care. In the industrialized countries, hereditary diseases predominate; this is also true for societies in which intermarriage is common practice.

Magnitude of Cataract in Childhood

The prevalence of cataract in childhood has been reported as 1 to 15/10,000 children (Table 1). The wide range is due to the variety of methodologies, the different age groups, and case definitions that have been used in the studies, as well as true differences between populations.

The available information suggests that the birth prevalence of bilateral cataract in industrialized countries is 1 to 3/10,000 births. This is likely to be higher in developing countries because of the survival of large numbers of preterm and low-birth-weight babies as a consequence of increased availability of neonatal intensive care. In the industrialized countries, hereditary diseases predominate; this is also true for societies in which intermarriage is common practice.

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Given a birth rate of 2% (that is, 20,000/million population), approximately 4 children/million total population/year will be born with bilateral cataract in industrialized countries. Because of the higher birthrate and increased prevalence, the figure for developing countries is likely to be 10/million total population/year.
### Table 1. Prevalence data on developmental cataract in children

<table>
<thead>
<tr>
<th>Country</th>
<th>Study</th>
<th>Method</th>
<th>Year of Study</th>
<th>Number of Cataract</th>
<th>Number Examined</th>
<th>Age Group</th>
<th>Prev./10,000 Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe/North America</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>BDMP*10</td>
<td>National surveillance</td>
<td>1988-91</td>
<td>214</td>
<td>1.76 million (approx)</td>
<td>Neonates</td>
<td>1.2</td>
</tr>
<tr>
<td>UK</td>
<td>1970 National Birth Cohort11</td>
<td>Cohort</td>
<td>1980</td>
<td>4 bilateral</td>
<td>12,853</td>
<td>10 years</td>
<td>3.3</td>
</tr>
<tr>
<td>UK</td>
<td>1984 Oxford Birth Cohort12</td>
<td>Cohort</td>
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<td>Jensen and Goldschmidt14</td>
<td>Population-based prevalence</td>
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<td>8784</td>
<td>5-13 years</td>
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<td>France</td>
<td>Stoll and coauthors15</td>
<td>Surveillance</td>
<td>1979-88</td>
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<tr>
<td>Nepal</td>
<td>Brilliant et al.17</td>
<td>Population-based survey</td>
<td>1980</td>
<td>2</td>
<td>12,143</td>
<td>&lt;10</td>
<td>1.7</td>
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<td>China</td>
<td>Hu18</td>
<td>Population-based survey</td>
<td>1987</td>
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<td>0-18</td>
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<td>Malawi</td>
<td>Population-based survey</td>
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<td>2 unilateral</td>
<td>5415</td>
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*Birth Defects Monitoring Programme
*National Collaborative Perinatal Project

The prevalence of blindness (best corrected visual acuity less than 3/60) from cataract in children in developing countries is probably 1 to 4/10,000, and approximately 0.1 to 0.6/10,000 children in the industrialized countries. This difference reflects the better prognosis for vision obtained when children are diagnosed early and managed by pediatric ophthalmologists. Globally, an estimated 200,000 children are blind from bilateral cataract.

### Etiology of Developmental Cataract in Childhood

The known underlying or associated causes of cataract in children are numerous, and many are rare. They have been reviewed in other papers. In industrialized countries, an underlying cause cannot be determined in approximately 50% of bilateral cases and in virtually all unilateral cases. Approximately 20% have a positive family history of isolated cataract, with autosomal dominant disease being more commonly diagnosed than X-linked or autosomal recessive disease. Autosomal dominant cataract is a collection of disorders, with several different phenotypes. To date there are six known genetic loci (linked to chromosomes 1, 2, 16, and 17). The underlying cause in the remaining 30% is chromosomal abnormalities, systemic abnormalities, metabolic disorders, intrauterine infection, prematurity, or in association with other ocular abnormalities.

There have been few reports from developing countries, but a recent prospective hospital-based study, which used saliva antibody immunoassay to detect rubella specific IgM, showed that 26% (25/95) of cataracts presenting to a large eye unit in South India in the first year of life were due to congenitally acquired rubella. The total study population included 366 children aged 0 to 15 years with nontraumatic cataract. In 25%, the cataract was due to genetic factors (mainly autosomal-dominant inheritance), in 15% to rubella; in half the
children, the underlying cause could not be determined. To summarize, in most cases the causes of childhood cataract remain unknown, but hereditary disease is important and rubella remains a significant preventable cause in developing countries.

Control

To reduce the amount of blindness from cataract in childhood, a variety of interventions can be considered:

1. In countries in which rubella is a significant cause, rubella immunization (together with measles) of girls aged 12 to 13 years or of all children younger than 1 year can be considered. The strategy to immunize infants should only be adopted if national coverage rates of 90% can be guaranteed.

2. Advice to families with autosomal dominant congenital cataract is important and can help parents decide about family planning and also ensure that affected children are diagnosed and treated early.

3. Screening of newborn babies should be taught to and practiced by all health workers responsible for the newborn. Examination of the eye to detect a white reflex (leucocoria) is easily taught and performed.

4. Early assessment and surgical treatment, when indicated, is essential to minimize visual loss from amblyopia. Surgical treatment should be performed by pediatric-oriented ophthalmologists who are experienced in anterior segment surgery and who have been trained and regularly perform cataract surgery in children.

5. Full correction of refractive errors must be achieved and regularly maintained with spectacles, contact lenses, or intraocular lenses (IOLs). Early use of an IOL may be justified in developing countries where parental compliance and follow-up may be particularly difficult to achieve since regular spectacle or contact lens wear is difficult to maintain. Studies are required to evaluate this question.

6. Long-term, regular follow-up with assessment and treatment of capsule opacification, glaucoma, refractive error, and amblyopia is necessary if good visual outcome is to be achieved.

7. For children with poor visual outcome, from amblyopia or surgical complications, low-vision aids and services with appropriate special education is important in obtaining maximum function and integration.

References

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