Avoidable childhood blindness in a high-income country: findings from the British Childhood Visual Impairment and Blindness Study 2 (BCVIS2)

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Financial Support: This work was funded directly by a Fight for Sight grant (1525/26) and was supported by funding from the Ulverscroft Foundation for the Ulverscroft Vision Research Group. AL Solebo received support from the National Institute for Health Research Biomedical Research Center (NIHR BRC) based at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, and an NIHR Lectureship, and is

supported by an NIHR Clinician Scientist award (CS-2018-18-ST2-005). JS Rahi is supported in part by the NIHR BRC based at Moorfields Eye Hospital NHS Foundation Trust and by the UCL Institute of Ophthalmology, and an NIHR Senior Investigator award. This work was undertaken at UCL Institute of Child Health / Great Ormond Street Hospital for children which received a proportion of funding from the Department of Health's NIHR Biomedical Research Centers funding scheme. The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

Conflict of Interest: There are no disclosures to report.

Word count: 2688

Synopsis/Precis

In the UK, more than two-thirds of case of childhood visual impairment are due to disorders for which there is no preventative or therapeutic intervention. There is considerable need for new prevention and treatment approaches.

What is already known on this topic:

Childhood visual impairment, severe visual impairment and blindness (VI/SVIBL) confers significant individual and societal burden. There is an unmet informational need around the contribution of treatable or preventable versus unavoidable disease to childhood visual disability within different care settings.

What this study adds:

Within a high-income country, the majority of children with VI/SVIBL have disorders that are not treatable or preventable with current knowledge. However, a sizeable minority (1 in 6) children have treatable disorders causing their vision impairment, and a further 1 in 8 have disorders which are potentially preventable, although in the main these were complex, multifactorial disorders such as hypoxic ischaemic encephalopathy (HIE), with very few instances of 'simple' disorders for which evidence based preventive interventions are already widely available

How this study might affect research, practice or policy:

Attention is still required to ensuring effective implementation of existing prevention strategies and treatment approaches in high income countries, whilst also developing novel therapies in order to address the burden of currently unavoidable childhood visual disability.

Abstract

Background / Aims

Addressing childhood visual disability is an international priority, with data on causes needed to plan, implement and evaluate public health and clinical care. We have examined the contribution of 'avoidable' blinding disorders to childhood visual impairment, severe visual impairment and blindness (VI/SVIBL) in the UK.

Methods

National prospective observational longitudinal study, the British Childhood Visual Impairment and Blindness Study, BCVIS2, of children (aged 18 years or under) newly diagnosed with vision worse than 0.48 LogMAR or equivalent in both eyes Proportions of children with an 'avoidable' disorder comprising either a *potentially preventable* (isolated disorders with an effective intervention which reduces disease incidence) or *treatable (*isolated eye or vision disorders for which there are routinely available effective interventions able to improve vision or halt progressive visual loss) are reported.

Results

Of the 784 children within BCVIS2, isolated potentially preventable disorders were present in only 17% (132/784) and treatable disorders in an additional 13% (99/784). The most common treatable causes were cataract, retinopathy of prematurity and glaucoma. Of the 132 children with potentially preventable disease, 64 had hypoxic-ischaemic encephalopathy (HIE). Non-accidental injury accounted for almost two thirds (11/16, 69%) of those with VI/SVIBL due to injury.

Conclusion

Despite significant progress in the past decades in high income countries there remains a need to be vigilant about implementing preventive strategies and treatments. Attention to disorders

that are currently neither preventable or treatable remains a priority in these settings and will become increasingly important in lower-income countries undergoing economic transition.

Introduction

Children with visual impairment, severe visual impairment and blindness, when compared to their normally sighted peers, are at risk of poorer health, educational, socioeconomic and psychosocial later life outcomes.[1 2] As the ability to see well is central to how children learn about themselves, others and their place in the world around them, visual impairment has a significant adverse impact on all aspects of development.[3] For the majority of affected children, visual disability starts early, caused by disorders arising in the 'First 1001 days' of post-conceptional life.[4 5]

Addressing childhood visual disability is a priority for the World Health Organization, which has developed supranational guidance on the planning and implementation of community and hospital-based eye and visual healthcare.[6] This guidance, the Package of Eye Care Interventions includes preventative public health interventions, treatments for the key blinding disorders of childhood, and management of established poor vision in childhood. The relative importance of these different strategies varies across the world, reflecting the transitions in healthcare that accompany economic development. For example, in some low-income countries, effective primary prevention such as rubella immunisation programmes are yet to be implemented universally.[7] The focus in many high income countries, however, where primary preventive strategies such as whole population vaccination programmes were introduced some time ago, is effective implementation of evidence-based secondary prevention strategies such as screening and treatment for retinopathy of prematurity or congenital cataract.[8] Tertiary prevention, such as the use of low vision aids, provision of support for parents to optimise their child's early learning through adapted play and care routines, and habilitation training to minimise the impact of established impaired vision, is important in all settings.[9]

To monitor the effectiveness of existing public health or clinical care strategies, and to identify areas where new strategies are needed, it is necessary to examine the contribution of 'avoidable' – that is preventable or treatable – disorders to negative health outcomes. For childhood visual disability, these data are lacking for many countries, and there is also no consensus on the definition of avoidable, preventable or treatable blinding disorders.

We addressed this unmet information need through the British Childhood Visual Impairment and Blindness Study 2, developing a consensus-based classification system for disorders which cause avoidable visual disability applied to quantify the current burden of avoidable childhood visual impairment, severe visual impairment and blindness in the United Kingdom.

Methods

The British Childhood Visual Impairment and Blindness Study 2 (BCVIS2) is a unique population-based cohort study of all children (aged ≤18 years) newly diagnosed with visual impairment, severe visual impairment or blindness (VI/SVIBL) as defined by the WHO's International Classification of Disease (WHO ICD-10).[10] This comprises individuals with best achievable corrected vision in their better seeing eye of worse than 0.48 logMAR (6/18 Snellen equivalent). This WHO definition excludes unilateral vision impairment of any severity and also those with 'presenting' reduced acuity due purely to uncorrected refractive error in the absence of irreversible amblyopia Details of BCVIS2 study methods have been published elsewhere.[4] Within BCVIS2, disorders of the cerebral visual pathways, retina and optic nerve are those most commonly seen, affecting 48% (378/784), 36% (286), and 28% (222) of children respectively. The rich study dataset includes detailed information on the

conditions causing VI/SVIBL reported by their managing clinicians, and on the management of this condition.

Avoidable VI/SVIBL was identified and categorised by the multi-disciplinary clinical research team, comprising two paediatric consultant ophthalmologists, and one consultant paediatric neurodisability specialist (ALS, JS, JSR, figure 1) as follows:

a) *treatable*: comprising an isolated eye or vision disorder for which there were routinely available effective interventions able to improve vision or halt progressive visual loss. These comprised cataract (or lens disorder), glaucoma, ocular inflammatory disorders, retinopathy of prematurity, and ocular or visual pathway tumours.

b) *potentially preventable*: comprising an isolated disorder for which there is an effective intervention which reduces disease incidence, or potentially reduces the population at risk. These comprised nutritional deficiency related ocular disorders (Vitamin A deficiency), injury (non-accidental or accidental), congenital infections such as primary maternal prenatal rubella, prematurity related visual pathway disorders (eg periventricular leukomalacia (PVL), in the absence of other structural defect) and autosomal inherited disorders affecting children born to families with an established family history.

Impaired vision due to hypoxic ischaemic encephalopathy (HIE) was also considered as potentially preventable (in the absence of a co-existent cause of unavoidable blindness), given current understanding of pathogenesis and the availability of neuroprotection therapies which can limit longer term neurodevelopmental sequalae.[11 12,13]

Children with multiple disorders contributing to their disability were only considered to have avoidable causes of VI/SVIBL if all their contributing disorders met the criteria for either treatable or potentially preventable disease, and only considered to have treatable causes of disability if all their contributing disorders had a currently available treatment (fig 1). As

amblyopia occurs in the context of all of these disorders, amblyopia per se was not considered as a standalone treatable cause of VI/SVIBL, except those with irreversible amblyopia due solely to high refractive error in the absence of other unavoidable disorders (ametropic amblyopia).

Data were analysed using STATA statistical software (version 14.2, StataCorp LLC, College Station Texas). Descriptive analyses were undertaken, with categorical data expressed as counts and percentages with 95% confidence intervals (CI).

The British Childhood Visual Impairment and Blindness Study 2 was approved by the UK Health Research Authority (HRA reference 14/LO/1809), and use of data without individual consent has been approved by the UK HRA Confidentiality Advisory Group, (section 251 exemption, reference 14/CAG/1028).

Results

The BCVIS2 cohort comprises 784 children, of whom 356 (45%) were female. 313 children had moderate visual impairment (VI) and 471 had severe visual impairment or blindness (SVIBL). Of the 784, 439 children (56%, 95% CI 2.4 – 59.5%) had more than one underlying condition causing vision impairment. Isolated potentially preventable disorders were present in 17% (95% CI 14.0 – 19.4%) and treatable disorders in an additional 13% (95% CI 10.4 – 15.2%) of all children (figure 2, table 2).

Treatable disorders

Of the 99 children with purely isolated treatable eye disorders, 56 were children with SVIBL, and 45 with VI (table 2). The timing of the visually disabling 'insult' to the eye or visual system was identifiable in 87 children, with 79 of them (91%) having VI/SVIBL due to a congenital disorder. Amongst the 79 children with a congenital but treatable visually disabling disease, only 21 (27%) were identified through the universal newborn and infant physical screening examination), whilst most of the 57 children with VI/SVIBL 'plus' (ie additional non-ophthalmic impairments or conditions) were detected through clinical surveillance of a high- risk group.

The most common treatable causes of VI/SVIBL were cataract (or lens disorder), retinopathy of prematurity and glaucoma (table 1). Median age at diagnosis of vision impairment, and median time from diagnosis of the disorder to diagnosis of permanent VI/SVIBL varied by disorder: 0.5 years (range 0 to 14.4) and 2.8 years (range 1.8 to 14) for cataract; 0.1 years (0 to 0.7) and 2.8 (1.8 to 8.1) for retinopathy of prematurity; and 0.04 years (0 to 0.7) and 3.1 (range 2.3 to 6.8) for glaucoma. A range of medical and surgical interventions were implemented for treatable cause(s) (table 3).

Potentially preventable disorders

Within the cohort of 130 children with wholly avoidable VI/SVIBL, 64 children had hypoxic ischaemic encephalopathy (HIE), all of whom had cerebral visual impairment. Most children (52, 62%) were born preterm (gestational age <37 weeks: 32 children were born very or extremely preterm with gestational age <31 weeks). The use of therapeutic hypothermia for neuroprotective cooling was reported in six of these children with HIE. In 12 of the 64 infants, an associated hypoglycaemia was noted in 12 infants at birth, eight mothers had used drugs during pregnancy (illicit intravenous drug use in 2, prescribed insulin n=3,

antihypertensives n=3) and five mothers had smoked nicotine products during pregnancy. Maternal infections were reported in four cases of HIE, comprising three mothers with Group B streptococcus diagnosed in the third trimester, and one with recurrent UTI in the second trimester. Irreversible amblyopia solely due to refractive error accounted for VI in one child, who had delayed refractive treatment for bilateral hypermetropic astigmatism.

Inherited autosomal dominant disorders with established family history

Inherited disorders were primarily retinal or vitreoretinal (21/46, 45.7%), including rod cone dystrophy / retinitis pigmentosa (n=4), inherited maculopathy, and / or cone dystrophy (n=7), congenital stationary night blindness (CSNB, n=3), and vitreoretinopathy (n=4). Other inherited visually disabling disorders affecting children born to families with an established family history included aniridia (with foveal hypoplasia, n=7) and chorioretinal coloboma (n=1). Cerebral visual pathway disease accounted for six of the 46 children, with microcephaly being the most common manifestation (5 children). Inherited optic nerve disorders accounted for six children (hypoplasia n=3, primary optic atrophy n=3). Congenital cataract affected 4/46, and anterior segment dysgenesis affected four children.

Trauma

Head injury resulting in cerebral visual impairment was the cause of vision impairment in 16 children, notably due to non-accidental injury (NAI) in 11 children.

Infectious disease

Maternal rubella infection during the first and second trimester, resulting in congenital cataract and pigmentary retinopathy, was the cause of congenital poor vision in two children, one of whom also had anterior segment dysgenesis. Congenital toxoplasmosis led to

bilaterally poor vision in two children. Including the four children with HIE in the context of maternal infection, a total of eight children had visual disability (partly or wholly) attributable to infectious disease.

Nutritional deficiency disorders

One child developed severe visual impairment because of acquired vitamin A deficiency related bilateral corneal opacity and retinal dysfunction.

Discussion

In this contemporary population-based cohort of all children newly diagnosed with visual impairment, severe visual impairment or blindness in a high-income country over a 12-month period, the majority have disorders that are not treatable or preventable with current knowledge. However, a sizeable minority (1 in 6) children did have treatable disorders causing their vision impairment. A further 1 in 8 children had disorders which were potentially preventable, although in the main these were complex, multifactorial disorders such as hypoxic ischaemic encephalopathy (HIE), with very few instances of 'simple' disorders for which evidence based preventive interventions are already widely available, such as immunisation to prevent prenatal rubella infection.

This study draws on a cohort of children with all-cause visual disability, capturing by design only those with the most adverse outcomes of a given disorder. For example, the majority of children with congenital cataract in the UK have better outcomes than VI/SVIBL after treatment.[14] Whilst ascertainment is presumed to be high (based on prior experience of studies conducted via BOSU and BPSU and the involvement of a longstanding study collaborative group), capture-recapture analysis could not be used to measure ascertainment

formally due to lack of independence in the data sources. The study also captures information within the first year of initial diagnosis of VI/SVI/BL so the theoretical possibility of a very small number of children developing new disorders causing impaired vision independently exists. The key strength of the BCVIS2 is its ability to present population level data (ie, data anchored in the denominator of the nation's childhood population) on potentially avoidable causes of childhood visual disability – as a measure of successful implementation of available interventions.

Hypoxic-ischemic encephalopathy (HIE), one of the most common causes of childhood disability worldwide,[8] accounts for half of all potentially preventable childhood VI/SVIBL in the UK, and globally accounts for 2.4% of all years of life lived with disability (YLD).[15] The complexity and heterogeneity of the population of children with perinatal insult may mean that not all children with HIE can be considered to have preventable disease.[16] Due to uncertainties around aetiopathogenesis, and the absence of clarity on disease phenotypes, there may be a number of affected children for whom improved maternal health may not have improved outcomes. However, for the majority of children with HIE, antenatal care and management of labour, delivery and perinatal infections all hold considerable scope for improvements in mother and child health outcomes,[8,15,17] with stratified care determined through earlier identification of maternal risk factors. There is promising evidence that this 'personalised' approach is particularly powerful in reducing the social inequities in health outcomes for infants and mothers.[18] Such approaches will be key to addressing the unequal distribution of VI/SVIBL across different socioeconomic and ethnic groups.[4] For those neonates identified as high risk for neurodevelopmental sequelae from hypoxic perinatal brain injury, therapeutic hypothermia (TH) with intracorporeal temperature monitoring is currently recommended by the UK's National Institute for Health and Care Excellence.[1719]

There is still an absence of consensus on the indications for treatment for at-risk children, with conflicting reports on the benefits of TH for those children with 'mild' neonatal encephalopathy or for preterm infants.[17] There is also a desperate need for additional therapies, as even with TH, there remains a high mortality and morbidity burden for children with moderate or severe HIE. Further work is needed to improve the tools used for HIE severity stratification, and to develop additional neuroprotection therapies.[20]

A large number of children within the BCVIS cohort were visually disabled due to genetic disease (265/784), with only a minority affected by disease amenable to genetic counselling (ie inherited disease within a family who were already aware of the risk to future children). The relative incidence of childhood VI/SVIBL due to inherited and sporadic genetic disease has increased over the past decade in the UK,[21] and the genetic therapies initially trumpeted as the new frontier for children with blinding disorders have yet to fulfil that promise.[22,23] Precision diagnostics and therapeutics remain critical areas for development in the fight to prevent disease and disability in children with genetic disorders.

Parental support, child protection policies and health and safety guidance are needed to reduce trauma related blindness. Strategies aimed at reducing health inequalities and health inequities within the UK, and strengthening support services for at risk families, are key to reducing the burden of childhood visual disability within high income countries. This pathway will be particularly needed at a time when the pandemic has further unbalanced the distribution of the key social determinants of health, such as parental education and employment, and family housing.

World Health Organization and the International Agency for the Prevention of Blindness joint global VISION 2020:The Right to Sight initiative sought to eliminate avoidable blindness, targeting disorders for which there were known treatments, and focused particularly on lower- and middle-income countries. This work, alongside the work of others,[24] led to the Package of Eye Care Interventions (PECI), the upcoming WHO supranational recommendations which supports the planning, commissioning and delivery of ophthalmic interventions.[6,24] As countries undergo economic transition, the relative importance of readily preventable and readily treatable disorders typically diminish,[6] which limits the scope for further reducing the frequency of childhood vision impairment in higher income countries. Our study suggests that there may be however greater scope for action than previously thought in terms of potentially preventable disorders. It also serves as reminder that even in a high-income country, where effective public health and therapeutic interventions exist and are accessible, some children will nevertheless have poor outcomes. This merits attention in preventative health care planning, parental education, clinical practices and research in such settings in order to lead to further innovations. Data from BCVIS2 also holds important data on 'lessons learned' for middle or lower income countries in transition, namely those facing the third pandemic of retinopathy of prematurity, as survival rates improve for children born very pre term, very low birthweight, and for children after term birth complicated by perinatal insult.[20] Whilst continued delivery of whole population preventive care for children is crucial, improvements in maternal health also hold potential for reducing the burden of childhood visual disability across all health settings, and should remain a public health priority. Trials of interventions to reduce brain injury in both preterm and term infants should also focus on lower- and middle-income countries, ahead of predicted greater and growing need. Finally, the BCVIS2 findings demonstrate, since the majority of affected children had disorders that were neither treatable nor preventable, the

significant evidence gaps in disease management that must be addressed if the world is to tackle the 'wicked problem'[25] of childhood blindness.

Table 1. Avoidable causes of childhood VI/SVIBL in BCVIS2

N, %	Total (n=784)	VI – all (n=313)	SVIBL – all (n=471)
Treatable			
Retinopathy of prematurity	27 (3.4%)	11 (3.5%)	16 (3.4%)
Cataract / other lens disorder*	42 (5.4%)	21 (6.7)	21 (4.5%)
Glaucoma	21 (2.7%)	8 (2.6%)	13 (2.8%)
Optic neuritis	5 (0.6%)	3 (1.0%)	2 (0.4%)
Uveitis	4 (0.5%)	2 (0.6%)	2 (0.4%)
Total treatable	***99 (12.6%)***	***45 (14.4%)***	***54 (11.5%)***
Potentially preventable			
Genetic:			
Autosomal dominant disorders	46 (5.9%)	22 (7.0%)	24 (5.1%)
Perinatal insult:			
Hypoxic ischaemic encephalopathy (term and pre-term infants)	64 (8.2%)	22 (7.0)	42 (8.9%)
Congenital infections:			
Prenatal rubella	2 (0.3%)	0 (0)	2 (0.4%)
Congenital toxoplasmosis (primary infection during pregnancy)	2 (0.3%)	0 (0)	2 (0.4%)
Injury:			
Non-accidental injury	11 (1.4%)	2 (0.6%)	9 (1.9%)
Accidental injury	5 (0.6%)	1 (0.3%)	4 (0.9%)
Nutritional:			
Vitamin A deficiency	1 (0.1%)	0 (0)	1 (0.2%)
Other:			
Hypermetropic astigmatic amblyopia	1 (0.1%)	1 (0.3%)	0
Total potentially preventable	***132 (16.8%)***	***48 (15.3%)***	***84 (17.8%)***

*One child had subluxed lenses, the remainder cataract

Table 2: Context of detection for treatable disorders by timing of causative insult

	Prenatal / perinatal insult n=80	Childhood insult n=8	Total n=88*
Routine health screening	32 (40%)	0	31 (36%)
Newborn physical examination programme	*21*	-	*21*
6 – 8 week infant examination programme	*4*	-	*4*
Other screening programme	*6*	*0*	*6*
Screening / surveillance of a high-risk group	24 (30%)	3 (38%)	27 (31%)
Symptoms	19 (24%)	4 (50%)	23 (26%)
Other	5 (6%)	1 (13%)	6 (7%)

*For a further 12 children the timing of the causative insult was unclear

Table 3: Interventions used in treatable causes of childhood visual impairment and blindness

	Medical interventions	Surgical interventions
Cataract / other lens*, n=42	Glaucoma drops, n=12 Anti-inflammatory/steroid drops,* n=5 Anti-VEGF treatment, n=1 Lubricating drops, n=2 **only including those used for recurrent / chronic inflammation (all children had steroid drops following surgery)*	Lensectomy, n=42 IoL insertion, n=6 Retinal detachment surgery, n=6 Other vitrectomy, n=4 Squint surgery, n=1 Pupilloplasty, n=2 Corneal graft/keratoplasty, n=1 Examination under anaesthetic (EUA), n=3
Glaucoma, n=21	Glaucoma drops, n=20 Antibiotic drops, n=1 Anti-inflammatory/steroid drops, n=20 Anti-VEGF treatment, n=1 Lubricating drops, n=1	Goniotomy, n=18 Lensectomy, n=10 Baerveldt tube insertion, n=9 Cyclodiode laser, n=8 Trabeculotomy, n=1 Vitrectomy, n=4 Pupilloplasty, n=1 EUA, n=5
Retinopathy of prematurity, n=27	Anti-VEGF treatment, n=4 Glaucoma drops, n=1 Antibiotic drops, n=1	ROP laser, n=21 Lensectomy, n=16 Squint surgery, n=5 Retinal detachment surgery, n=4 Other vitrectomy, n=4 Goniotomy, n=4 Cyclodiode laser, n=1 Trabeculotomy, n=1 EUA, n=2
Optic neuritis, n=5	Corticosteroid, n=1 Systemic immunosuppressive therapy, n=1	
Uveitis, n=4	Anti-inflammatory/steroid drops, n=3 Systemic immunosuppressive therapy, n=2 Glaucoma drops, n=1 Anti-VEGF treatment, n=1	Goniotomy, n=1 Lensectomy, n=1 Retinal detachment surgery, n=1 Vitrectomy, n=1

*One child had subluxed lenses managed with lensectomy

Figure 1. Classification scheme for avoidable, treatable and preventable disease

Figure 2. BCVIS2 participants flow chart

Acknowledgements: We thank the members of the British Paediatric Surveillance Unit and British Ophthalmic Surveillance Unit for their support for this study (case ascertainment and data acquisition).

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