

Clinical Research on the Leading Causes of Severe Sight Impairment in the UK General and Working Populations

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Purpose: Clinical research brings the potential of improved diagnostics, sight-saving treatments, and more accessible services to those suffering with severe sight impairment (SSI). This report investigates whether registered ophthalmology clinical studies address the leading causes of SSI in the general and working populations of the United Kingdom (UK).

Methods: The latest statistics on the leading causes of SSI in the UK general and working populations were identified by searching PubMed, Cochrane Library, and TRIP databases. Clinical study registries were searched to identify registered clinical studies (on or prior to 1st December 2022) on the leading causes of SSI. The relationship between the number of clinical studies on leading causes of SSI and the percentage of SSI certifications they account for was analyzed.

Results: In the UK general population, the number of registered clinical studies on the leading causes of SSI is statistically significantly correlated (Spearman's $\rho = 0.86$, $p < 0.01$) with the percentage of SSI certifications they account for. However, there is no correlation between the two in the UK working population (aged 16–64) (Spearman's $\rho = 0.15$, $p = 0.70$). Eye conditions accounting for the most SSI certifications in individuals of working age have significantly less clinical research activity than those that cause the most SSI certifications in the general population. Out of the leading causes of SSI certifications studied, disorders of the visual cortex and congenital anomalies of the eye have the least clinical research activity.

Conclusion: Clinical research into the leading causes of SSI in the general population is essential. However, it is important to consider eye conditions that cause the most severe visual impairment in individuals of working age due to the significant health and socioeconomic implications of sight loss in this population.

Keywords: ophthalmology, blindness, clinical study, healthcare

Introduction

Over two million people live with vision loss in the United Kingdom (UK).¹ Severe sight impairment (SSI) is defined as being “so blind that they cannot do any work for which eyesight is essential” (1948 National Assistance Act).² To be certified as severely sight impaired, individuals generally must have a visual acuity on the Snellen scale that falls into one of the following categories: less than 3/60 with a full visual field, between 3/60 and 6/60 with a reduced visual field, or 6/60 or above but with clinically significant reduced field of vision.³ Beyond the detrimental effects on physical and mental health, vision loss is estimated to cost the UK economy £25.2 billion a year, and this figure is expected to rise as the population ages.^{4,5} The majority of costs lie outside direct health and social care costs, reflecting the loss of productivity resulting from barriers to the workplace experienced by visually impaired individuals of working age.⁶ The leading causes of SSI certifications in the working population (aged 16–64) differ to those in the general population. Hereditary retinal disorders are the leading cause of SSI certification in the UK working population. Meanwhile, degeneration of the macula and posterior pole is the leading cause of SSI certification in the general population, but accounts for a small percentage of SSI certifications in the working population.^{7,8}

Clinical research is crucial to enhance understanding, diagnosis, treatment, and prevention of sight-threatening eye diseases.^{6,9} All research is meaningful, but with limited resources, research priorities must meet clinical need.^{5,6,10} Determining clinical need is difficult: whilst it is important that clinical research addresses the most prevalent conditions, it is essential that conditions causing the most SSI and the highest disease burden are not overlooked. This report analyzes data from clinical study registries to investigate whether registered clinical studies address the leading causes of SSI in the general and working populations of the UK. We aim to highlight gaps in ophthalmology clinical research and inform future research strategies.

Materials and Methods

PubMed, Cochrane Library, and TRIP databases were searched (December 2022) to identify the most current statistics on the leading causes of SSI in the UK general and working populations. Statistics on the leading causes of SSI in the UK general and working populations were reported by Quartilho et al (2016) and Liew et al (2014), respectively. Data on the percentage of SSI certifications accounted for by each disease category were extracted from these reports and used in our statistical analysis.^{7,8}

Clinical study registries (ClinicalTrials.gov, the ISRCTN registry, the EU clinical trials register, and the NIHR Clinical Research Network (CRN) portfolio managed by Ophthalmology) were searched to identify registered clinical studies (on or prior to 1st December 2022) on the leading causes of SSI certification. This aims to yield a comprehensive search of interventional clinical trials, which must be registered, as well as registered clinical studies (eg, observational studies). Search terms for each cause were defined with the aid of the International Classification of Diseases (ICD)-10 (Version: 2019) and are listed in [Supplementary Table 1](#).¹¹ Studies were filtered for those conducted in the UK. Studies of all types, phases, statuses, and results were included. Certain causes of SSI certification were excluded from statistical analysis due to difficulties to define and search ([Supplementary Table 1](#)). Following title and summary screening and exclusion of duplicates, studies investigating the specified conditions were collated and counted.

For each population, the number of clinical studies on each disease category was correlated to the percentage of SSI certifications caused by that category. Spearman's rank correlation studies and data analysis were conducted using SPSS (IBM SPSS Statistics for Macintosh, Version 29.0. Armonk, NY: IBM Corp).

Results

Clinical Research on the Leading Causes of SSI in the General Population

The largest number of registered clinical studies have been counted on degeneration of the macula and posterior pole ([Table 1](#)). Amongst the conditions studied, disorders of the visual cortex and congenital anomalies of the eye demonstrate the least research activity. When analyzing the general population, the number of registered clinical studies on the leading causes of SSI is

Table 1 The Leading Causes of SSI Certifications in the UK General Population and the Corresponding Number of Clinical Studies Registered (on or Prior to 1st December 2022). Data on SSI Certifications were Reported by Quartilho et al (2016) and are Presented to the Nearest 1 Decimal Point⁷

Cause of SSI Certifications	% of SSI Certifications	Number of Clinical Studies
Degeneration of macula and posterior pole	50.0	190
Glaucoma	11.0	184
Hereditary retinal disorders	8.2	61
Diabetic retinopathy/maculopathy	5.4	104
Optic atrophy	4.9	12
Disorders of the visual cortex	2.6	3
Retinal vascular occlusion	2.0	23
Congenital anomalies of the eye	1.5	8

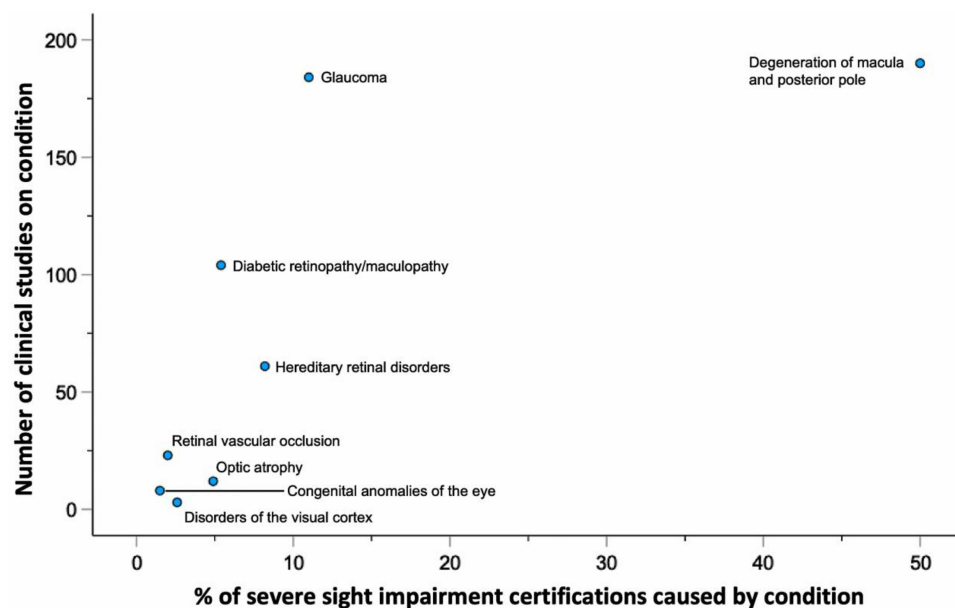


Figure 1 The number of registered clinical studies on the leading causes of SSI correlated significantly with the percentage of SSI certifications they account for in the UK general population (Spearman's $Rho = 0.86$, $p < 0.01$, $n = 8$). Data on SSI certifications were reported by Quartilho et al.⁷

statistically significantly correlated (Spearman's $\rho = 0.86$, $p < 0.01$) with the percentage of SSI certifications they account for (Figure 1). This indicates that clinical research activity is largely in accordance with disorders causing the most SSI. However, there is a similar number of clinical studies registered on glaucoma and degeneration of the macula and posterior pole, despite the former accounting for a significantly smaller percentage of SSI certifications (11%) than the latter (50%).

Clinical Research on the Leading Causes of SSI in the Working Population

Amongst the leading causes of SSI certifications in the working population, degeneration of the macula and posterior pole has the greatest number of clinical studies registered (Table 2). Hereditary retinal disorders account for the most SSI

Table 2 The Leading Causes of SSI Certifications in the UK Working Population and the Corresponding Number of Clinical Studies Registered (on or Prior to 1st December 2022). Data on SSI Certifications were Reported by Liew et al (2014) and are Presented to the Nearest 1 Decimal Point⁸

Cause of SSI Certifications	% of SSI Certifications	Number of Clinical Studies
Hereditary retinal disorders	20.2	61
Diabetic retinopathy/maculopathy	14.4	104
Optic atrophy	14.1	12
Glaucoma	5.9	184
Congenital anomalies of the eye	5.1	8
Disorders of the visual cortex	4.1	3
Degeneration of macula and posterior pole	3.0	190
Myopia	2.8	55
Corneal disorders	2.6	40

Abbreviations: SSI, severe sight impairment; ICD, International Classification of Diseases.

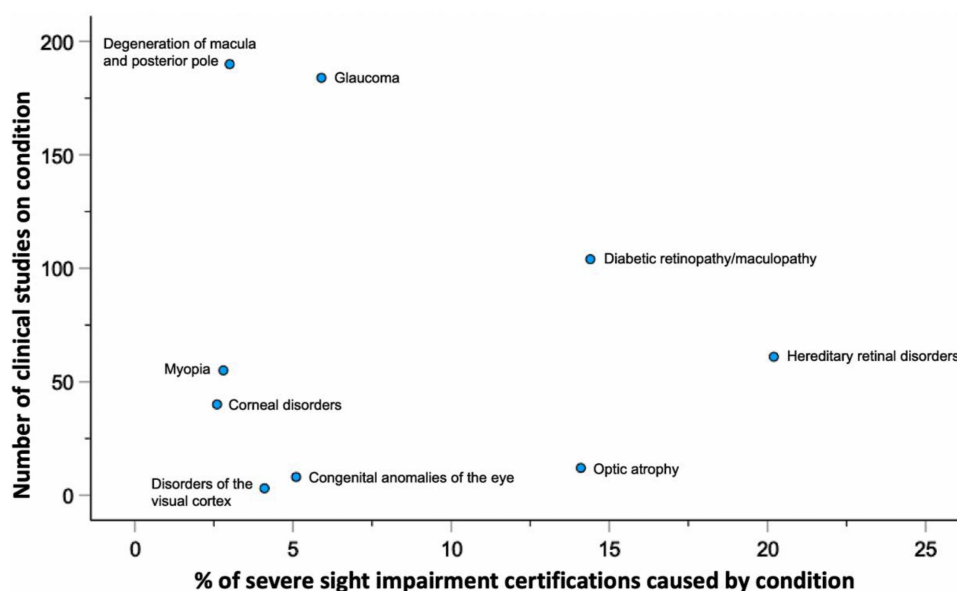


Figure 2 The relationship between the number of registered clinical studies on the leading causes of SSI and the percentage of SSI certifications they account for in the UK working population (Spearman's $Rho = 0.15$, $p = 0.70$, $n = 9$). Data on SSI certifications were reported by Liew et al.⁸

certifications in individuals of working age, but the number of clinical studies on hereditary retinal disorders is approximately one-third that on degeneration of the macula and posterior pole. In comparison to the general population, there is no correlation (Spearman's $\rho = 0.15$, $p = 0.70$) between the number of registered clinical studies on the leading causes of SSI and the percentage of SSI certifications they account for in the UK working population (Figure 2). These data suggest that eye conditions accounting for the most SSI certifications in individuals of working age are not the most clinically researched.

Discussion

In the UK general population, clinical research activity on the leading causes of SSI is positively correlated to the percentage of SSI certifications they account for. However, this relationship is not seen for the working population where conditions accounting for the most SSI certifications are less clinically researched than those causing the most SSI in the general population. Degeneration of the macula and posterior pole showed the greatest levels of clinical research activity; this corresponds to macular degeneration being the most common cause of irreversible vision loss in the UK, despite being largely a disease of the elderly.^{6,12}

Whilst it is fundamental to address conditions that severely impair vision in the general population, appreciation of vision loss and its causes in the working population is essential. Burden of disease is significant: 40% of working-age individuals with severe vision loss are unable to work due to their eye condition and barriers to the work-place, which is costing the UK economy up to £7.4 billion annually.^{6,13,14}

Collectively, inherited retinal disorders (IRDs) have a prevalence of approximately 1 in 2000 and are the leading cause of SSI in the UK working population.⁸ Amongst this genetically heterogeneous group of conditions, with over 270 causative genes identified to date, retinitis pigmentosa is the most common IRD and Stargardt disease the most common macular dystrophy.^{6,15,16} In comparison to degeneration of the macula and posterior pole, there are significantly fewer registered clinical studies on IRDs in the UK. Despite exciting developments, with numerous clinical trials on gene therapy and electronic retinal implants demonstrating promising results, it is important that clinical research continues to address the leading cause of SSI in the working population.^{17–20} With advances in genetic testing, research activity in IRDs has been exponential but much of this work remains in the pre-clinical stages, which were not considered in this study.¹⁷

Challenges to IRD clinical research include the experimental, lengthy, and costly nature of clinical studies; although gene-specific therapies have been revolutionary, this approach is likely limited by the time, available participants, and funding needed

to develop treatments for the relatively small numbers of individuals affected by each genetic subtype.¹⁶ Optimizing clinical study designs, such as employing umbrella and basket trials, and exploring mutation-independent approaches (eg, cell therapy, neuroprotection, and optogenetics) are important for clinical research that targets larger segments of the IRD population.^{16,21–23} In parallel, wider accessibility to genetic testing is essential for improved diagnosis and clinical research, with increasing recognition that understanding genetic etiology is crucial for all clinical trial participants, regardless of whether interventions are gene-specific.¹⁶

Notably, there appears to be a disproportionately large number of clinical studies conducted on glaucoma (Figure 1), with novel devices for sustained release medication delivery and minimally invasive surgery in the pipeline.^{24,25} This likely arises from well-understood pathophysiological mechanisms and identified modifiable risk factors (such as intraocular pressure) that lend themselves well to pharmacological and surgical intervention.²⁶ Furthermore, research has yielded revolutionary diagnostic tools and therapies that have likely contributed to the reduced prevalence of glaucoma-associated SSI.²⁷ In comparison, more complex poorly understood pathogenesis mechanisms may be a barrier to clinical research on other causes of severe visual loss.

Disorders of the visual cortex and congenital anomalies of the eye appear to have the least clinical research activity, despite being the leading causes of visual impairment in children.^{28–30} This is likely due, at least in part, to insufficient understanding of embryological development, neurobiology, and disease pathogenesis thus far. Although these conditions account for a small percentage of SSI certifications in the UK, they still touch the lives of many, particularly in the working population where they collectively account for 9% of SSI certifications.^{7,8} More clinical research into visual cortex disorders and congenital anomalies of the eye is required.

Limitations and Future Directions

Despite conducting a comprehensive search of clinical study registries, any studies not registered on these databases were not included in this analysis. Study sample sizes were not considered when analyzing research activity. Often, only estimated enrolment numbers are listed by registered studies that are currently recruiting and we had concerns this may not always be achieved. There is a lack of current data on the main causes of SSI in the UK and our analysis is based on certifications from over a decade ago and only includes England and Wales. Up-to-date epidemiological studies would enable more accurate tracking of the main causes of disease across the population. Certificates of vision impairment were used to reflect causes of SSI. Whilst these represent some of the best available epidemiological data on sight impairment and are regarded as a major public health indicator, SSI certifications are not equivalent to SSI rates as not all eligible individuals are registered.^{8,31}

SSI causes were categorized according to the ICD-9 codes in the studies conducted by Quartilho (2016) and Liew (2014).^{7,8,32} ICD-10 codes were used to determine the search terms of this study due to improved accessibility, clinical relevance, and easy comparability to the ICD-9 codes.¹¹ Although a useful method of classifying diseases, categorizing SSI causes and search terms using ICD codes presents limitations. For instance, optic atrophy is a disease category reported to account for a significant percentage of SSI certifications.^{7,8} However, optic atrophy is often an end-stage that arises from a multitude of optic nerve diseases.³³ The search for clinical studies on optic atrophy may not identify studies on conditions that feature optic atrophy and thus may represent an incomplete picture of the clinical research landscape on optic atrophy.

Conclusion

Whilst it is crucial to research the leading causes of SSI in the general population, more clinical research into eye conditions that severely affect working-age individuals is important due to the significant health and socioeconomic impacts. Addressing conditions with low clinical research activity, such as disorders of the visual cortex and congenital anomalies of the eye, is essential in ensuring that leading causes of SSI are well researched. This work aims to inform future clinical research priorities to address current gaps and areas of clinical need.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Disclosure

The authors report no conflicts of interest in this work.

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