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Complete List of Authors:	Köberlein, Juliane; University of Wuppertal, Beifus, Karolina Schaffert, Corinna Finger, Robert; University of Bonn, Dept of Ophthalmology
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THE ECONOMIC BURDEN OF SEVERE VISUAL IMPAIRMENT AND BLINDNESS - A Systematic Review

Juliane Köberlein[1], Karolina Beifus[1*], Corinna Schaffert[1], Robert P. Finger[2]*

Contact Address:
Juliane Köberlein, PhD
Karolina Beifus
Department of Health Economics und Health Care Management
University of Wuppertal
Rainer-Gruenter-Str. 21
42119 Wuppertal
Tel: +49 (0)202 439 1388
Fax: +49 (0)202 439 1384
e-mail: koeberlein@wiwi.uni.wuppertal.de

[1]Department of Health Economics und Health Care Management
University of Wuppertal
Germany

[2]University of Bonn
Department of Ophthalmology
Germany
and
University of Melbourne
Centre of Eye Research Australia
Royal Victorian Eye and Ear Hospital
Australia

*JK and KB contributed equally to this article

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ABSTRACT

Objectives

Visual impairment and blindness (VI&B) cause a considerable and increasing economic burden in all high income countries due to population ageing. Thus we conducted a review of the literature to better understand all relevant costs associated with VI&B and to develop a multi-perspective overview.

Design

Systematic review. Two independent reviewers searched relevant literature and assessed studies for inclusion and exclusion criteria as well as quality aspects

Eligibility criteria for included studies

Interventional, non-interventional and cost of illness studies, conducted prior May 2012 investigation direct and indirect costs as well as intangible effects related to visual impairment and blindness, were included.

Methods

We followed the PRISMA statement approach to identify relevant studies. A meta-analysis was not performed, due to the variability of reported cost categories.

Results

A total of 22 studies were included. Hospitalization and use of medical services around diagnosis and treatment at the onset of VI&B were the largest contributor to direct medical costs. Mean annual expenses were found to be US$ PPP 12,175-14,029 for moderate visual impairment, US$ PPP 13,154-16,321 for severe visual impairment, and US$ PPP 14,882-24,180 for blindness, almost twofold the costs for non-blind patients. Informal care was the major contributor to other direct costs, with the time spent by caregivers increasing from 5.8 hours/week (or US$ PPP 263) for persons vision > 20/32 up to 94.1 hours/week (or US$ PPP 55,062) for persons with vision ≤ 20/250. VI&B caused considerable indirect costs due to productivity losses, premature mortality, and dead weight losses.

Conclusions

VI&B cause a considerable economic burden for affected persons, their care givers and society at large, which increases with the degree of visual impairment. This review provides insight into the distribution of costs and the economic impact of VI&B.

ARTICLE SUMMARY

Article Focus

- To explore all relevant costs associated with visual impairment and blindness.

Key Message

- We could demonstrate a considerable impact of visual impairment and blindness in terms of the associated direct and indirect costs, as well as intangible effects such as loss of well-being, independence and excess mortality.
- A large proportion of the direct costs reported in reviewed studies are not directly related to eye-related medical care, but to falls and other accidents due to visual impairment, exacerbation of diabetes due to a reduced ability to self-manage, depression related to loss of vision and further excess morbidity.
- All identified costs as well as intangible effects correlated with the degree of visual impairment with highest expenditures associated with blindness.

Strengths and limitations

- This is the first review exploring an international and multi-perspective overview of costs and intangible effects associated with visual impairment as well as blindness.
- The study synthesis of reviewed literature was limited as no two studies used the same methodology, reported exactly the same outcomes or used the same sample population. Therefore a meta-analysis was not conducted.

INTRODUCTION

Visual impairment and blindness are foremost a problem of older age in all high-income countries, and constantly increasing due to the ageing of populations in these countries [1]. Globally, the burden of disease related to vision disorders has increased by 47% from 12,858,000 Disability Adjusted Life Years (DALYs) in 1990 to 18,837,000 DALYs in 2010 [2]. Health-related quality of life in severely visually impaired persons has been shown to be similar or even lower and emotional distress higher compared with other serious chronic health conditions such as stroke or metastasised solid tumours [3]. Blindness and visual impairment impact not only the affected individual but also the family, caregivers and the community, leading to a significant cost burden. In Australia, the overall cost placed visual disorders seventh among diseases, ahead of coronary heart disease, diabetes, depression, and stroke in terms of economic burden on the health system [4].

As demands on healthcare continue to increase in all high-income countries, economic evaluations of disease, impairment and interventions have also become increasingly important [5]. This necessitates a clear understanding of all aspects of the direct and indirect costs and intangible effects related to blindness and severe visual impairment, as almost all interventions in this area are aiming to prevent these and are often measured as an incremental cost effectiveness ratio (ICER), i.e. the difference in cost compared to the difference in effectiveness. Similarly, faced with increasing demand and limited resources in healthcare, these resources need to be prioritized which again calls for a clear understanding of the economic impact of a disease or disorder. Against this background we conducted a systematic review of the literature, collating all data available on the economic impact of visual impairment and blindness.

METHODS

Literature search

All economical and medical databases were searched from May to June 2012 via PubMed and OVID using the following terms:

"low vision", "visual impairment", "visually impaired", "blindness", "blind", "visual loss", "costs", "costs of illness".

Subsequently, a second search was conducted using the main causes of visual impairment and blindness. Search terms were: *"low vision", "visual impairment", "visually impaired", "blindness", "blind", "visual loss", "costs"* combined with "*age-related macular degeneration", "glaucoma", "diabetic retinopathy", "cataract", "corneal opacities", "childhood blindness"* separated by *"or".*

Supplemental sources including references contained in identified articles were used in addition.

Two independent researchers screened identified articles using the following inclusion or exclusion criteria:

Inclusion:

- data for direct and indirect costs related to visual impairment and blindness,
- studies with outcomes related to intangible effects due to visual impairment and blindness,
- overall data for burden of illness related to affected persons and carers.

Exclusion:

- costs pertaining to underlying diseases only with no specification of visual impairment levels,
- economic studies conducted in developing countries.

Data extraction strategy & cost classification

All included articles were assessed as to which cost aspects they reported. Broadly, costs were divided into direct costs, indirect costs, and intangible effects [6].

Direct costs are defined as the actual expenses related to an illness and contain medical costs, non-medical costs and other direct costs [5]. Medical costs measure the cost of resources used for treating a particular illness. Non-medical costs are costs caused by the disease but not attributed to medical treatment. In case of visual impairment and blindness these are supporting services, assistive devices, home care, residential care or transportation (travel expenses). Other direct costs comprise informal care, time spent in treatment by patients or caregivers, or time spent in rehabilitation, training, self-help groups or preventative activities [5].

Indirect costs are defined as the value of lost output caused by reduced productivity due to illness or disability [7]. Both, patients and caregivers are affected by indirect costs due to allowances (financial support for income, residence, benefits), productivity losses (absenteeism, salary losses, part-time employment, loss of work), and dead weight losses or years of life lost.

Intangible costs or effects refer to the burden of illness of affected persons and caregivers, and comprise loss of well being or loss of quality of life. It can be captured using questionnaires and expressed in DALYs. As this aspect of costs is difficult to quantify, DALYs or other measures of intangible effects are rarely assigned a monetary value.

Commonly, cost categories considered in a particular study depend on the perspective the study is conducted from, i.e. a healthcare payer's (direct costs only) or the patient's perspec-

tive, or a societal perspective (all costs). Cost-of-illness – or in this case cost-of-impairment – studies can be divided into disease-specific and general studies. Both types of studies were included if they contained relevant data.

Quality of included studies

A checklist, based on the assessment tool of Emmert and colleagues [8] and extended by several questions covering relevant cost-of-illness aspects (see **Appendix 1**), was generated to assess the overall quality of included studies. The checklist contained sections on the study design, population, definition and specification of cost data and its limitations, including a total of 25 questions. Studies were rated from 0 – 100 for each of these categories. Two independent reviewers conducted the assessment and interrater-reliability was assessed using Kappa (κ_n) as suggested by Brennan and Prediger [9] for every study. The interpretation of agreement was based on the agreement scale by Landis and Koch [10].

Conversion of Cost-of-illness study results

For better comparison of costs across studies, the data were transformed: (1) costs were inflated to 2011 using country specific gross domestic product deflator, which takes fluctuating exchange rates, different purchasing power of currencies and the rate of inflation into account [11], and (2) converted to USD using purchasing power parities (PPP) [12]. Purchasing power parities account for differences in price levels between countries, and convert local currencies into international dollars taking purchasing power of different national currencies into account and eliminating differences in price levels between countries. The transformed values are presented in million units (million US$-PPP) for total expenditures reported and in US$-PPP for costs per person.

RESULTS

The search yielded a total of 389 articles. After applying all inclusion and exclusion criteria, 22 studies were included in the systematic review (**Figure 1**). Altogether there were eight studies conducted in the USA, six studies conducted in Australia, two studies from France, and one study from each of the following countries: Germany, Canada, the UK, Japan, India and one study with a global perspective. All included studies are summarized in **Table 1.**

Table 1: Characteristics of included studies

Author	Country	Design and Population	Cost components evaluated	Objective	Vision categories
Bramley et al. 2008 [13]	USA	retrospective cohort analysis of nationally representative Medicare 5% random sample; patients older than 65 years with newly diagnosed glaucoma; regression analysis	direct medical costs, intangible effects	to measure costs of visual impairment due to progressing glaucoma	no vision loss, moderate vision loss, severe vision loss, blindness
Brezin et al. 2005 [14]	France	national survey of a random stratified sample; 16, 945 affected persons answered questionnaires; 4,091 caregiver answered questionnaires;	indirect costs; intangible effects	to document the prevalence of self-reported visual impairment and its association with disabilities, handicaps, and socioeconomic consequences.	blind or light perception only, low vision, other visual problems, and no visual problems
Chou et al. 2006 [15]	Australia	150 persons completed cost diaries for 12 months and were evaluated; costs categorized into four sections: 1. medicines, products and equipment, 2. health and community services, 3. informal care and support, 4. other expenses	direct medical costs, direct non-medical costs	to describe and evaluate the process used to collect personal costs (out-of pocket) associated with vision impairment using diaries	≥ 6/12with restricted fields; <612–6/18; <6/18–6/60; <6/60–3/60; <3/60
Clarke et al. 2003 [16]	UK	regression-based approach to estimate the short-term and long- term annual hospital and non-hospital costs associated with seven major diabetes-related complications in the UK Prospective Diabetes Study (UKPDS): myocardial infarction (MI); stroke, angina or ischemic heart disease (IHD); heart failure; blindness in one eye; amputation and cataract extraction; 5102 patients with newly diagnosed type 2 diabetes	direct medical costs	to estimate the immediate and long-term health- care costs associated with seven diabetes-related complications	blind in one eye
Cruess et al. 2011 [17] (in combination with Gordon et al. 2011 [18])	Canada	prevalence-based approach, population projections for the whole population were compiled using data from the Statistics Canada 2006 Population Projections for Canada, Provinces and Territories 2001-2031	direct medical costs, direct non medical costs, indirect costs, intangible effects	to investigate costs of vision loss in Canada to inform healthcare planning	no details
Frick et al. 2008 [19]	USA	retrospective cohort study; patients with blindness matched to non-blind selected from managed care claims database	direct medical costs	to evaluate total and condition related charges incurred by blind patients in a managed care population in the	blind, non blind

				US	
Javitt et al. 2007 [20]	USA	retrospective cohort analysis of nationally representative Medicare 5% random sample, excluding Medicare managed-care enrollees	direct medical costs	to assess and identify the costs to the Medicare program for patients with either stable or progressive vision loss and estimate the impact on eye-related and non-eye related care	mild, moderate, severe vision loss (VA ≤20/200), blindness (VA ≤ 20/400)
Keeffe et al. 2009 [21]	Australia	114 participants of the Melbourne Visual Impairment Project completed diaries for 12 month; the burden of caregiver and opportunity costs for losses in work time was calculated (in combination with methods and data from Chou et.al.)	other direct costs	to analyse prospective data on providers, types and costs of care for people with impaired vision in Australia	VA < 20/40
Kymes et al. 2010 [22]	USA	decision analytic approach; Markov model to replicate health events over the remaining lifetime of someone newly diagnosed with glaucoma	incremental costs of illness	to evaluate the incremental cost of primary open-angle glaucoma considering both visual and non-visual medical costs over a lifetime	no details
Lafuma et al. 2006 [23]	France	interviews with sample population (665,000) from a national survey of persons living in institutions or in the community (with caregiver at home)	direct non medical costs, other direct costs, indirect costs	to estimate the annual national non medical costs due to visual impairment and blindness	blind (light perception), low vision (better than light perception??, low vision, and controls
McCarty et al. 2001 [24]	Australia	population-based study; evaluation of the data from Melbourne Visual impairment project; population ≥40 years was analyzed in causes of death	intangible effects	to describe predictors of mortality in the 5 year follow up of Melbourne Visual impairment project;	visual acuity < 6/12
Morse et al. 1999 [25]	USA	2.552.350 discharges from hospital in state of NY -> 5.764 patients had visual impairment	direct medical costs	to assess whether visual impairment contributes to average length of stay within inpatient care facilities	no details
Porz et al. 2010 [26]	Germany	retrospective study of 66 patients using a cost and a vision-related quality of life questionnaire (Impact of vision Impairment questionnaire)	direct non medical costs, intangible ef-	to capture costs for medicines, aids and equipment, support in everyday	Visual acuity (VA) ≥ 0,3, Visual acuity < 0,3

			fects	life and social benefits, as well as vision- related quality of life	
Rein, et al. 2006 [27]	USA	private insurance and Medicare claims data	direct non medical costs, indirect costs	to estimate the societal economic burden and the governmental budg-etary impact of the following visual disorders among US adults aged 40 years and older:	refractive errors
Roberts et al. 2010 [28]	Japan	prevalence-based approach; adopted using data on visual impairment, the national health system, and indirect costs	direct medical costs, direct non medical costs, other direct costs and intangible effects	to quantify the total economic cost of visual impairment in Japan	low vision 6/12-6/60; blind < 6/60; visual impairment = >6/12
Schmier et al. 2009 [29]	USA	using a questionnaire that included items on demographic and clinical characteristics and on the use of services, assistive devices, and care-giving; 761 persons were included	direct non medical costs, other direct costs	to assess the use of devices and caregiving among individuals with diabetic retinopathy and to evaluate the impact of visual acuity on use	group 1 (20/20 or better), group 2 (20/ 25–20/30), group 3 (20/40–20/50), group 4 (20/60–20/70), or group 5 (20/80 or worse)
Schmier et al. 2006 [30]	USA	survey with interviews on Daily Living Tasks Dependent on Vision Questionnaire;803 respondents	other direct costs,	to assess the patient-reported use of caregiving among individuals with age-related macular degeneration (AMD) and evaluation of impact of visual impairment level on this use	1. VA > 20/32; 2. VA 20/32 - > 20/50; 3. VA 20/50 - >20/80; 4. VA 20/80 - > 20/150; 5. 20/150 - >20/250; 6. VA ≤ 20/250
Vu, et al. 2005 [31]	Australia	stratified random sample of 3040 participants from the Melbourne Visual Impairment Project; 2530 attended the follow-up study	intangible effects	to investigate whether unilateral vision loss reduces any aspects of quality of life in comparison with normal vision	unilateral and bilateral vision loss (correctable and non-correctable)

Wong et al. 2008 [32]	Australia	prospective cohort study; participants of any age to complete a diary for 12 months answering four categories: 1) medicines, products and equipment, 2) health and community services, 3) informal care and support and 4) other expenses	direct costs (medical and non medical), other direct costs	to determine the personal out-of-pocket costs of visual impairment and to ex-amine the expenditure pattern related to eye diseases and the severity of visual impairment	visual acuity ≥6/18 with constricted. fields; < 6/18-6/60; < 6/60
Wood et al. 2011 [33]	Australia	76 community-dwelling individuals with a range of severity of AMD; completing a diary for 12 month	intangible effects; costs of adverse events	to explore the relationship between AMD, fall risk, and other injuries and identified visual risk factors for these adverse events	binocular visual acuity, contrast sensitivity, and merged visual fields

All studies were rated above 50 for all four main quality aspects, indicating a sufficient level of quality, and consequently were included into the review (see **Figure 2**). The interrater-reliability was consistently high and only a few discrepancies had to be settled by a discussion between the two raters. Kappa scores ranged from 0.34 to 0.76 (**Figure 3)**.

Of all included studies eleven captured direct medical cost, seven direct non-medical costs, and six other direct costs. Seven studies report data on indirect costs and ten on intangible effects. All cost components reported by studies within each cost category are summarized in **Appendix 2,** highlighting the considerable variability in obtaining and reporting cost aspects related to visual impairment and blindness between all studies.

Direct medical costs

Direct medical costs occurred mostly due to hospitalization, the use of medical services and medical products, and were reported either as incremental costs or, in some studies, provided as the length of hospital stay (**Table 2**).

At the onset of visual impairment and blindness, the two major contributors to direct medical costs are hospitalizations and costs due to increased use of medical services around diagnosis and treatment [16, 17, 19, 25, 28]. Costs related to recurrent hospitalizations and ongoing, but less frequent use of medical services, remain major cost components in persons with visual impairment and blindness in the long term. Costs related to drugs, however, did not emerge as a major direct cost factor [15, 32]. All identified costs correlated with the degree of visual impairment leading to the highest expenditures being associated with blindness. The considerable differences in study methods and reported outcomes makes a head to head comparison of results by study or country or aggregation of data in terms of met-analyses for direct medical costs very difficult. Several studies based on representative samples of Medicare beneficiaries in the USA reported mean annual expenses to be US$ PPP 12,175-14,029 for moderate visual impairment, US$ PPP 13,154-16,321 for severe visual impairment, and US$ PPP 14,882-24,180 for blindness, which is almost a 100% excess of the estimated mean annual cost for non-blind patients at the upper end of the range (**Table 2**).

Table 2: Outcomes for direct medical costs.

Study	*cost outcomes*	*US$ PPP in 2011*
Bramley et al. 2008[11]	annual costs per patient compared in degrees of vision impairment from no vision loss and onset of moderate or severe vision impairment or blindness	
	no vision loss **US$ 8,157**	**8,695**
	moderate visual impairment **US$13,162**	**14,029**
	severe visual impairment **US$ 15,312**	**16,321**
	blindness **US$ 18,670**	**19,900**
Frick et al. 2008[17]	cohort with legally blind patients matched to equal sample cohort with non-blind patients (annual costs per patient in the first year)	
	blind persons mean costs **US$ 20,677**	**24,180**
	median costs **US$ 6,854**	**8,015**
	non blind mean costs **US$ 13,321**	**15,578**
	median costs **US$ 371**	**434**
Javitt et al. 2007[18]	patients with normal vision compared to moderate or severe visual impairment or blindndess regarding eye-related and non-eye-related care	
	mean annual costs for eye-related care	
	normal vision **US$ 370**	**445**
	moderate visual impairment **US$ 345**	**415**
	severe visual impairment **US$ 407**	**490**
	blindness **US$ 237**	**285**
	mean annual values for non eye related costs	
	normal vision **US$ 7,928**	**9,537**
	moderate visual impairment **US$ 2,193**	**2,638**
	severe visual impairment **US$ 3,301**	**3,971**
	blindness **US$ 4,443**	**5,345**
Kymes et al. 2010[20]	lifetime costs of POAG (primary open-angle glaucoma) to non POAG patients	
	incidence costs **US$ 41,039**	**46,456**
	prevalence costs **US$ 19,268**	**21,811**
	drug costs **US$ 7,098**	**8,035**
	incremental incidence costs **US$ 27,326**	**30,933**
	incremental prevalence costs **US$ 5,555**	**6,288**
	incremental drug costs **US$ 4,179**	**4,731**
Morse et al. 1999[23]	extension of average length of stay in hospitals due to visual impairment	
	5.2 days longer stay	
Cruess et al. 2011[15]	financial burden of vision loss to Canadian health care system	
	hospital **CAN$ 1,497.7 million**	**1,934.72 million**
	physicans **CAN$ 866.5 million**	**1,119.34 million**
	vision care **CAN$ 3,483.7 million**	**4,500.24 million**
Chou et al. 2006[13]	the out-of-pocket expenses for medicines and products per person annually	
	AUS $ 206	**456**
Wong et al. 2008[30]	annual costs for medicine and products per patient	
	Visual acuity (VA) ≥ 6/18 with restr. field **AUS$ 285**	**632**
	< 6/18 – 6/60 = **AUS$ 233**	**516**
	< 6/60 = **AUS$ 147**	**326**
Clarke et al. 2003[14]	short-term and long-term annual hospital and non-hospital costs due to major diabetes-related complications	
	blindness in one eye (in 20% of patients) **£ 4,370**	**4,086**
	mean hospital in-patient costs **£ 872**	**815**
Roberts et al. 2010[26]	total economic costs of visual impairment	
	General medical expenditure **US$ 8.102 billion**	**8,636 million**
	Inpatient **US$ 1.808 billion**	**1,927 million**
	Outpatient **US$ 6.294 billion**	**6,709 million**
	Drugs **US$ 1.395 billion**	**1,487 million**

Direct non medical costs

Assistive devices and aids, home modifications, costs for health care services like home-based nursing or nursing home placements were the major contributors to direct non-medical costs (**Table 3**). With worsening visual acuity direct non-medical costs for support services and assistive devices increased, from US$ PPP 53.90 for a person with visual acuity ≥ 20/20 up to US$ PPP 608.71 for a person with visual acuity ≤ 20/80 [29] . Nursing home-placements and professional care costs incurred the highest expenditures followed by domestic modifications. These costs however, were highest initially shortly after the loss of vision and in the majority only a one-off (**Table 3**).

Table 3: Outcomes for direct non medical costs.

Study	*cost outcomes*		*US$ PPP in 2011*	
Rein et al. 2006[25]	total annual costs for visual impairment and blindndess for adults ≥40 years			
	nursing placements of **US$ 10.96 billion**		**12,818 million**	
	guide dogs **US$ 0.062 billion**		**72.5 million**	
	independent living **US$ 0.029 billion**		**33.9 million**	
Schmier et al. 2009[27]	annual costs for use of services and devices related to the degree of visual impairment per person			
	devices (glasses, sticks, computer software, etc. **US$ 109.79**		**120**	
	rehabilitation **US$ 7.09**		**7.78**	
Chou et al. 2006[13]	annual costs for health and community services per person			
	health care, home help, personal affairs, personal care, communication, transport, social activities **AUS $ 872**		**1,932.50**	
	expenditure for taxi, public transport, education expenses, guide dog **AUS $ 321**		**711**	
Cruess et al. 2011[15]	financial burden of vision loss to Canadian health care system			
	care costs **CAN$ 693 million**		**895.21 million**	
	aids and modification **CAN$ 305 million**		**394 million**	
Wong et al. 2008 [30]	annual personal costs for health and community services and other expenses per patient			
	median total costs **AUS$ 1,768**		**3,919**	
	mean total costs **AUS $ 3,376**		**7,482**	
Roberts et al. 2010[26]	total economic costs of visual impairment			
	meal service on admission **US$ 0.149 billion**		**158.81 million**	
	home-visit nursing **US$ 0.013 billions**		**13.86 million**	
	health care administration **US$ 0.475 billion**		**506.30 million**	
	Community care **US$ 6.608 billion**		**7,043 million**	
	Institutional care **US$ 0.238 billion**		**253.68 million**	
	Vision aids **US$ 0.2 billion**		**213.18 million**	
Porz et al. 2010[24]	financial and psychological burden of retinal diseases divided into health economic relevant categories; annual expenses per person			
	aids for VA ≥ 0.3 = **€ 96.65**		**77.39**	
	VA < 0.3 = **€ 83.58**		**66.92**	
	personal assistance VA ≥ 0.3 = **€ 454.96**		**364.28**	
	VA < 0.3 = **€ 667.77**		**534.68**	
Lafuma et al. 2006[21]	national survey with estimation on costs of low vision and blindness for persons living in institutions[1] or in the community [2] (declared annually per person and total expenditures)			
	low vision	**blindness**	**low vison**	**blindness**
	home modifications [1] **€ 36.65 pp/ year**	**€ 926.96 pp/ y**	**37.87**	**957.90**
	€ 3.27 million total	**€ 9.63 million total**	**3.375 million**	**9.95 million**
	devices [1] **€184.14 pp/ year**	**€ 387.35 pp/ y**	**190.29**	**400.28**
	€ 16.43 million total	**€4.03 million total**	**16.98 million**	**4.165 million**
	home modification [2] **€ 42.23 pp/ y**	**€ 121.12 pp/y**	**43.64**	**125.16**
	€ 16.43 million total	**€ 7.02 million total**	**16.98 million**	**7.25 million**
	devices [2] **€ 376.39**	**€ 363.14 pp/ y**	**388.95**	**375.26**
	€ 420 million total	**€ 21.04 million total**	**434.02 million**	**21.74 million**
	paid assistance [2] **€ 1,463.59 pp/ y**	**€ 6750.66 pp/ y**	**1,512.44**	**6,976**
	€ 1,635 million	**€ 391 million total**	**1,690 million**	**404 million**

Other direct costs

Six of the included studies reported costs caused by informal care. Time spent on caring for or assisting visually impaired persons was related to the degree of visual impairment, with blind persons requiring the most assistance. The time spent by caregivers ranged from 5.8 hours per week for a person with a visual acuity of > 20/32 and a cost of US$ PPP 263 up to 94.1 hours per week and costs of US$ PPP 55,062 for persons with a visual acuity of ≤ 20/250 [30]. All studies differed slightly as to the nature of direct costs assessed. Some studies reported on governmental, out-of-pocket expenses as well as opportunity costs, others considered only one or two of these. The wide range of time and resources spent on informal care provision demonstrates the broad economic impact and considerable burden of informal care provision with concurrent expenses at a personal and societal level. Again, reported cost aspects and methodologies differ considerably, with, for example, Keeffe and colleagues[21] reporting out-of-pocket expenses and Lafuma and colleagues[23] reporting time spent on caring using an hourly rate. The multitude of differing approaches in each study does not allow for a head-to-head comparison but gives a comprehensive impression of the complex cost situation and highlights the importance of providing assistance to visually impaired and blind persons (**Table 4**).

Table 4: Outcomes for other direct costs.

Study	*cost outcomes*		*US$ PPP in 2011*	
Schmier et al. 2009[27]	annual costs for caregiver time spent in supporting patients with macular degeneration			
	US$ 5,038		**5,526**	
Schmier et al. 2006[28]	annual costs for quantity of caregiver time addicted to the degree of visual impairment per patient diabetic retinopathy			
	mean 5.7 hours a day 5 days a week			
	overall amount of **US$ 9572.77**		**11,194.40**	
Keeffe et al. 2009[19]	personal out-of-pocket expenses regarding the burden of caregiver			
	median annual opportunity costs for worktime spent on caregiving **AUS$ 915**		**2,244.60**	
Wong et al. 2008[30]	annual median personal costs for informal care and assistance in activities of daily living			
	e.g. meal preparing, dressing, shopping, transportation **AUS$ 2,911**		**6,451**	
Lafuma et al. 2006[21]	national survey with estimation on costs for time caregiver spent on of low vision and blindness for persons in the community (declared annually per person and total expenditures)			
	low vision	**blindness**	**low vison**	**blindness**
	informal care **€ 1881.80 pp/ year**	**€ 7,316.26 pp/ y**	**1,944**	**7,560.48**
	€ 2,101 million total	**€ 424 million total**	**2,171 million**	**438 million**

Indirect costs

Studies of indirect costs demonstrate high expenditures related to productivity losses, changes in employment (employer and/or area of work), loss of income, premature mortality, and dead weight losses (**Table 5**). Received social allowances were detailed in one study, but not counted towards the overall costs as they were considered transfer costs.[26] One study included the loss of caregivers' time, which is spent on support in terms of productivity loss but also as a loss of personal time and time to engage in leisure activities.[23] Equal to other cost components indirect costs correlated with the degree of visual impairment, with the highest indirect costs reported for blind persons. Compared to all other cost categories indirect costs due to productivity losses, lower employment rates and losses of income in patients as well as caregivers caused the highest economic burden. Annual estimates of productivity losses and absenteeism due to visual impairment and blindness in the USA and Canada range from US$ PPP 4,974-5,724 million, and are estimated to be US$ PPP 7,367 million for an overall decrease in workforce participation in the US (**Table 5**).

Table 5: Outcomes for indirect costs

Study	*cost outcomes*		*US$ PPP in 2011*	
Rein et al. 2006[25]	total annual indirect costs caused by visual disorders			
	decreased work force participation **US$ 6.3 billion**		**7,367 million**	
	decreased wages **US$ 1.73 billion**		**2,023 million**	
Roberts et al. 2010[28]	indirect costs for visual impairment and blindness			
	productivity losses **US$ 4.667 billion**		**4,974 million**	
	lower employment **US$ 4.230 billion**		**4,509 million**	
	absenteeism **US$ 0.384 billion**		**409 million**	
	premature mortality **US$ 0.053 billion**		**56.5 million**	
	dead weight losses **US$ 1.609 billion**		**1,715 million**	
Lafuma et al. 2006[21]	national survey with estimation on indirect costs for losses of income in persons with low vision and blindness living in institutions [1] or in the community [2] (declared annually per person and total expenditures)			
	low vision	**blindness**	**low vison**	**blindness**
	losses of incomes[1] **€ 120.00 pp/y**	**€ 180.00 pp/y**	**124**	**186**
	€ 10.71 million total	**€ 1.87 million total**	**11.07 million**	**1.93 million**
	losses of incomes [2] **€ 3,912.00 pp/y**	**€ 3,168.00 pp/y**	**4,042**	**3,273**
	€ 4,369 million total	**€ 183.6 million total**	**4,515 million**	**189.72 million**
Brezin et al. 2005[12]	prevalence and burden of blindness, lo sion and visual impairment in the French community (estimation of monthly average value)			
	low vision	**blindness**	**low vison**	**blindness**
	social allowances **€ 87**	**€ 364**	**92**	**384**
	total household income **€ 1,525**	**€ 1,587**	**1,607**	**1,673**
	household income no VI **€ 1,851**		**1,951**	
Cruess et al. 2011[15]	indirect costs for Canada caused by vision loss			
	employment participation, absenteeism, presenteeism **CAN $ 4,431 million**		**5,724 million**	
	dead weight losses **CAN$ 1,757 million**		**2,270 million**	

Intangible effects

Most studies used personal burden such as depression, emotional distress, loss of independency, loss of quality of life, limitations in activities of daily living or hazards such as falls and injuries to capture intangible effects of visual impairment and blindness. Two studies, set in Japan and Canada, reported a loss of well being as DALYs and an associated cost of US$ PPP 51.8 billion and US$ PPP 15.11 billion per year respectively.[17, 28] Every reviewed study reported a high burden caused by multiple individual restrictions in patients and also in caregivers, which was found to be increasing with the degree of visual impairment (**Table 6**). Mortality associated with visual impairment was reported to increase linearly from 4.5% in persons with normal visual acuity (≥20/20) to 22.2% in blind persons (visual acuity of < 20/200) [24]. Measured as a restriction in care givers, Brezin and colleagues [14] reported a increases from 1.6% of caregivers of non-visually impaired persons, who reported restrictions in going out during the day, up to 12% for caregivers of blind patients.

Table 6: Outcomes for intangible effects

Study	*Outcomes*
Bramley et al. 2008[11]	incidences of depression occur in 17% more than patients with no vision loss, placements in nursing homes are demanded in 25.3% more, injuries happen in 33.4% more cases and femur fractures in 67.4% more cases
Cruess et al. 2011[15]	loss of well-being and loss in quality of life evokes 77,306 DALYs or rather CAN$ 11.7 billion in 2007 (US$ PPP 15.11 billion in 2011)
Vu et al. 2005[29]	non-correctable unilateral vision loss was addicted to independent living and reduced safety; bilateral non-correctable vision loss was associated with nursing homes, emotional wellbeing, use of community services, and activities of daily living
Wood et al. 2008[31]	increased visual impairment was significantly associated with an increased incidence of falls and other injuries. 54% of participants had at least one fall, 30% had more than fall, and 63% of falls ended in injuries
McCarty et al. 2001[22]	a linear increase of 5-year mortality correlating with degree of visual impairmen was detected; even mild visual impairment is related to a more than twofold risk of death
Brezin et al. 2005[12]	burden in patients occurs because of inability to undertake daily activities; need of assistance correlates with degree of visual impairment; burden on caregiver was caused by limited by restricted possibilities for going out for different periods or losing social contacts, affected physical and mental welfare and modified professional activities
Porz et al. 2010[24]	in a questionnaire with score scale 0-100 points patients with VA ≥ 0.3 achivede 79.32 for mobility and independency, 69.64 for emotional well-being and 73.86 for reading and achievement of information; persons with VA < 0.3 were rated with scores 46.84, 61.43, 44.25 respectively
Roberts et al. 2010[26]	loss of well-being was measured in DALYs; converted into a monetary value this results in total annual costs of US$ 48.598 billion (US$ PPP 51.8 billion in 2011) and costs per capita of US$ 29,690 per year (US$ PPP 31,647)

DISCUSSION

In this first systematic review of costs associated with visual impairment and blindness we could demonstrate a considerable impact of visual impairment and blindness in terms of the associated direct and indirect costs, as well as intangible effects such as loss of well-being, independence and excess mortality. The highest costs are caused by productivity losses in visually impaired and blind persons as well as their carers, followed by formal and informal care giving, recurrent hospitalizations and the use of medical and supportive services in the visually impaired and blind. A much larger economic impact was due to intangible effects

such as loss of independence, quality of life and excess morbidity. However, these are very difficult to quantify in monetary terms and only a small number of studies attempted this. All highlighted cost components as well as intangible effects which contribute to the overall economic impact of visual impairment and blindness need to be considered in economic evaluations not only of visual impairment and blindness but also of interventions aimed at averting these, depending on the focus of the economic evaluation.

A large proportion of the direct costs reported in reviewed studies are not directly related to eye-related medical care, but to falls and other accidents due to visual impairment, exacerbation of diabetes due to a reduced ability to self-manage, depression related to loss of vision and further excess morbidity.[20] Drug costs were not a major contributor to overall costs, which is mirrored in studies investigating chronic diseases such as diabetes mellitus, where – despite its ongoing use – hypoglycaemic drugs constitute only a small proportion of overall direct medical costs.[34] Annual mean costs of other potentially incapacitating chronic diseases such as diabetes mellitus (Euros 5,262 or USD 6,889)[34] or the first year after a stroke (USD 14,361)[35] were much lower for diabetes and similar for the stroke estimate compared to mean annual costs of severe visual impairment and blindness.[13, 20] This is likely due to the average diabetic not requiring professional care giving of a scale required during the first year after a stroke or in severely visually impaired and blind persons. In severely visually impaired or blind persons, however, these costs are incurred every year following the loss of vision, and do not decrease significantly over the following years unlike reported annual costs for stroke.[35] Javitt and colleagues report all direct medical cost caused by visual impairment to amount to US$ 2.14 million in 2003 in all non-institutionalized Medicare beneficiaries 69 years and older, and postulate a much higher cost for the whole of the US population.[20] With the introduction of anti-Vascular-Endothelial-Growth-Factor treatment for a number of potentially blinding eye diseases such as neovascular age-related macular degeneration, diabetic macular edema or macular edema in retinal vein occlusions since all reviewed studies were conducted, the overall direct medical costs associated with visual impairment can be expected to be much higher today. This increase in cost is exacerbated by the ageing of populations in all developed countries as all major blinding diseases are age-related.[27]

Our finding that indirect costs are much higher than direct costs caused by visual impairment and blindness is mirrored by virtually all other cost-of-illness studies assessing the economic impact of diseases or impairments which result in absenteeism and reduced ability to work. Back pain, for example, was found to cause considerable absenteeism and disablement, which – despite its significant hospital cost – lead to indirect cost constituting 93% of the

overall cost in 1991 in the Netherlands.[36] Even in treatment and healthcare resource intensive chronic diseases such as diabetes mellitus, indirect costs pose more than half of the overall costs caused by the illness.[37]

All studies which assessed intangible effects in economic terms reported these to be the largest contributor to the overall economic impact of visual impairment and blindness. Considering the adverse impact of loosing vision on quality of life, independence and the ability to participate in society, this is not surprising. We and others have previously reported that even mild visual impairment (0.3<LogMAR<0.5) has a significant and independent impact on vision-specific functioning.[38-40] Similarly, emotional well-being is affected in patients with even mild vision impairment.[39] Depression is considered to result in further functional decline in this group by reducing motivation, initiative and resiliency[41] and people with depression are less likely to access vision rehabilitation services than those not depressed.[42, 43] Even unilateral vision loss had a measurable impact on falling and some other activities of independent living, with increased odds of having problems in many activities of daily life in the study conducted by Vu and colleagues.[31] All this very adversely impacts the ability to participate in society, and contributes to the considerable economic impact of intangible effects caused by visual impairment and blindness.

There are several limitations which necessitate a careful interpretation of the overall findings. Using key words to identify relevant literature always bears the potential of a too narrow focus, and not all relevant literature may have been included. However, based on the searches conducted, as well as the cross-searching performed based on references, the authors are confident that the vast majority of relevant literature could be included. To the authors' knowledge, a standardized quality checklist has not been used to assess economic evaluations of the impact of visual impairment and blindness prior to inclusion into a systematic review to date. This further increases the overall quality of our review. The study synthesis of reviewed literature was limited as no two studies used the same methodology, reported exactly the same outcomes or used the same sample population. These problems have been reported for cost-of-illness - or in this case cost-of-impairment – studies in other areas, and adherence to existing cost-of-illness study guidelines recommended.[11, 44] Unfortunately, none of the reviewed studies seem to have adhered to any of the available international standards, and thus the overall comparability is limited. Similar to cost-of-illness studies in other areas, studies are summarized mostly descriptively, or at a high level of aggregation.[11] The same applies to the chosen categories of visual impairment used in all studies which differ considerably (**Table 1**). The perspective (affected person, healthcare payer, societal) of the study was only described in a minority of reports, and as highlighted in

the results section, most studies were conducted in the USA and Australia, making inferences to other countries and healthcare systems difficult. However, this is the only systematic review of the economic impact of visual impairment and blindness to date, highlighting the very broad economic impact and outlining the considerable scope a comprehensive economic evaluation in this area should ideally have.

In conclusion, visual impairment and blindness cause a considerable economic burden for affected persons, their care givers and society at large, which increases with the degree of visual impairment for all assessed cost categories as well as intangible effects. This review highlights a large amount of cost categories which should be considered in economic evaluations in eye health, and future cost-of illness or cost-of-impairment studies should adhere to available guidelines to improve comparability. The review highlights the considerable amount of resources spent on caring for visually impaired and blind persons in the absence of a cure.

FINANCIAL DISCLOSURE

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COMPETING INTERESTS

Authors declared that there are no competing interests.

AUTHORS' CONTRIBUTION

All authors contributed to the design of the review, KB and CS searched databases and extracted references, KB, CS and JK collated studies, and drafted the manuscript, all authors critically revised the manuscript.

DATA SHARING

There are no additional unpublished data from the study available.

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FIGURES

Figure 1: Inclusion of articles

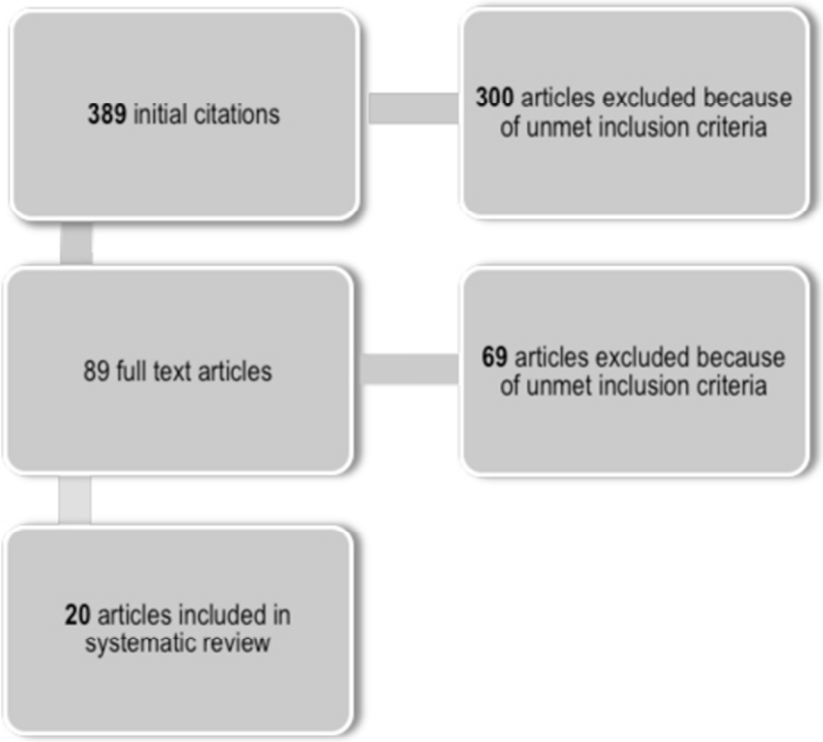
Figure 2: Quality rating of included studies

Figure 3: Kappa-index per study

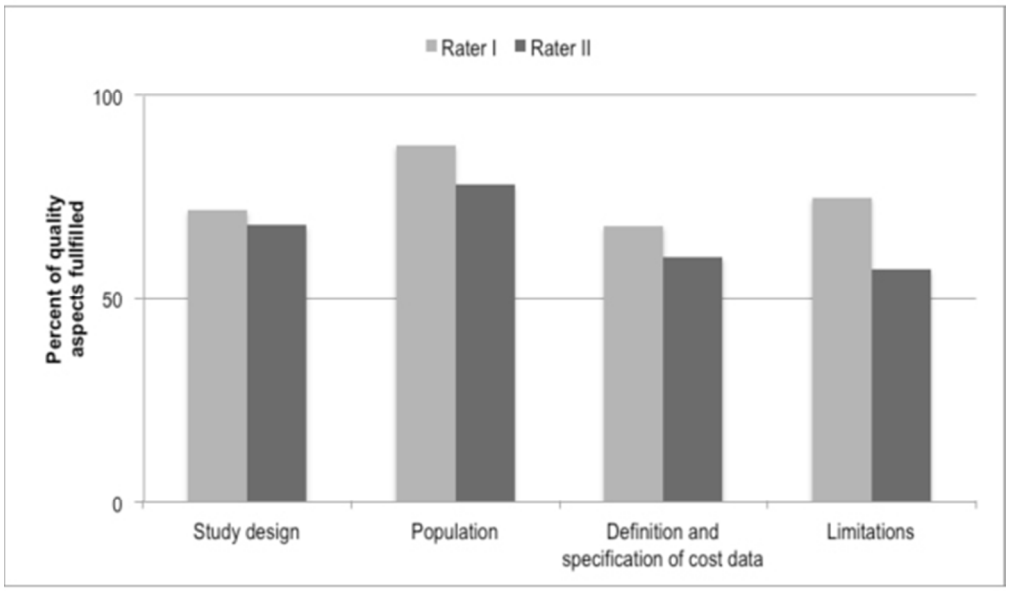
APPENDIX

Appendix 1: Quality checklist

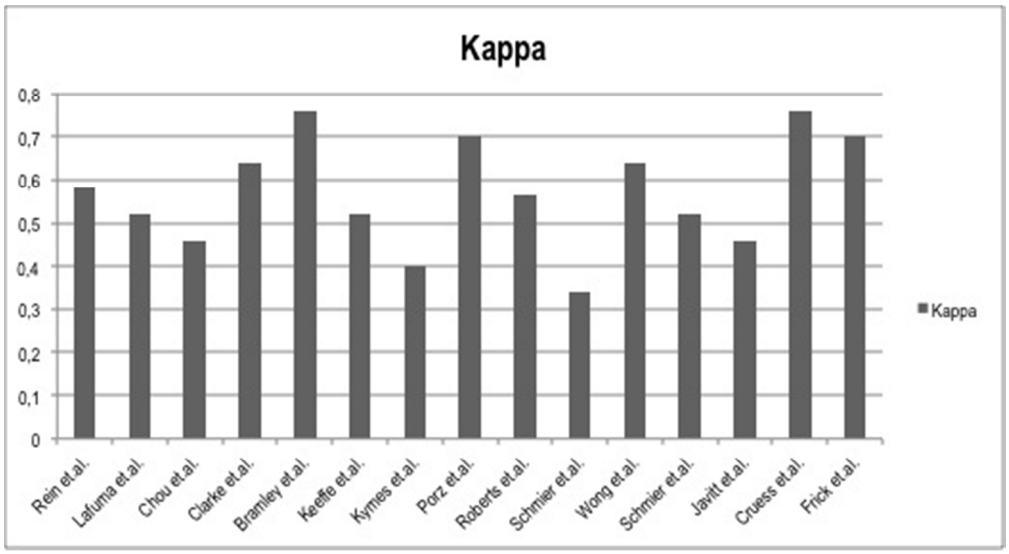
Appendix 2: Cost categories reported in included studies.



Inclusion of articles



Quality rating of included studies
208x169mm (72 x 72 DPI)



Kappa-index per study
184x100mm (72 x 72 DPI)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3-4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3-4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	3
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	3-4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3-4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	3-4, 7-10
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Not done
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	3-4
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Not done

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Not done
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not done
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5-6
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7-10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	NA
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	NA
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	19-22
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	21-22
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19-22
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	22

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Study design

1. Was the issue of research defined in a well answerable form?
2. Was the economic relevance of the research stated?
3. Was the medical context described well?
4. Were the perspectives of the study clearly described and justified?
5. Was the type of economic evaluation defined?
6. Was the valuation method stated (top-down, bottom-up, prevalence-based, incidence-based)?

Population

7. Was the study population described in detail?
8. Was the method of data acquisition explained (including evaluation of health states and further benefits)?
9. In case of estimations from subgroups, were the subgroups defined clearly in the beginning of the study?

Definition and specification of cost data

10. Were sources of data for consumption of resources exposed?
11. Was a justification stated for the selection of data sources?
12. Were all relevant (relating to the present issue of research) cost units identified?
13. Was the quantity of consumption and relevant prices mentioned separately?
14. Was the source of all relevant cost units exposed?
15. Were costs valued appropriately?
16. Were currencies and prices specified?
17. Were currency translations and price adjustments stated in detail?
18. Were price adjustments for inflation and deflation conducted adequately?
19. Is the year of currency declared?
20. Were economic productivity changes stated separately?
21. Were the changes in economic productivity changes discussed referred to the issue of research?
22. Is the data for productivity losses implicated correctly into the analysis?

Limitations

23. Were limitations stated and discussed?
24. Is the quality of data discussed critically?
25. Are biases described and discussed in manner and degree?

		Bramley, T. et al.	Brézin, A.P. et al.	Chou, S.-L. et al.	Clarke, P. et al.	Cruess, A.F. et al.	Frick, K.D. et al.	Javitt, J.C. et al.	Keeffe, J.E. et al.	Kymes, S.M. et al.	Lafuma, A. et al.	McCarty, C.A. et al.	Morse, A.R. et al.	Porz, G. et al.	Rein, D.B. et al.	Roberts, C.B. et al.	Schmier, J.K. et al. (2006)	Schmier, J.K. et al. (2009)	Vu, H.T.V. et al.	Wong, E.Y.H. et al.	Wood, J.M. et al.
direct medical costs																					
	physician, outpatient	x			x	x	x	x								x	x				
	hospital, inapatient	x		x	x	x		x								x	x				
	rehabilitation	x				x													x		
	hospice	x						x													
	counselling			x															x		
	prescription drugs, vitamins and other medications	x		x		x	x	x							x	x	x				x
	laboratory	x							x												
direct nonmedical costs																					
living in institutions	excess of stay in institutions											x									
	long-term Care, nursing homes, skilled nursing facilty	x							x							x					
support in homely environment	paid assistance / social support services / personal care services / home delivery services / home health care / independent living services / home-visit nursing	x		x					x			x			x	x	x	x			x
aids and devices	stick											x									
	white stick											x							x		
	guide dogs / guide dog registration			x								x				x					x
	walking aids											x									
	wheelchair											x									
	optical assistance / low vision devices			x		x						x			x				x		x
	television magnifier																		x		
	low vision equipments																				x
	eye care products			x																	
	eye care research					x											x				
adaptation of living environment	furniture (toilet, kitchen, table, seat, bed, ramps, door opening device)											x									
	extra lights / lamps																		x		
	home modifications											x									
	move due to impairment											x									
communication and media	computer interface											x									
	software adapted for blindness				x							x							x		
	computer hardware / braille printer / talking books / tape recorder				x							x							x		
	technical assistance											x									
	national library service, library costs						x									x					
	american printing house large print materials															x			x		
transportation	taxi				x																x
	public transport				x																x
	transportation service																		x		x
	travel reimbursement														x						
national budget	disabilty benefits and pension / aid to the blind														x						
	supplemental security income															x					
	food stamps															x					
	committee for purchase from people who are blind or severely disabled															x					
	social security payments						x														
	accommodation allowance														x						
insurances	long-term care insurance																x				
	social security disability insurance															x					
other	education expenses				x																x
	job training service																		x		
	recreational services																		x		
other direct costs																					
	informal care									x		x						x	x		x
indirect costs																					
	productivity losses						x									x					
	decreased workforce participation, employment participation						x									x					
	decreased wages															x					
	Tax losses, Steuernachlass						x								x	x					
	loss of family revenue											x									
	loss of income											x									
	time-losses of caregivers						x					x									
	absenteeism/presenteeism						x														
intangible effects																					
							x						x				x			x	

THE ECONOMIC BURDEN OF VISUAL IMPAIRMENT AND BLINDNESS - A Systematic Review

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THE ECONOMIC BURDEN OF VISUAL IMPAIRMENT AND BLINDNESS - A Systematic Review

Juliane Köberlein[1], Karolina Beifus[1*], Corinna Schaffert[1], Robert P. Finger[2]*

Contact Address:
Juliane Köberlein, PhD
Karolina Beifus
Department of Health Economics und Health Care Management
University of Wuppertal
Rainer-Gruenter-Str. 21
42119 Wuppertal
Tel: +49 (0)202 439 1388
Fax: +49 (0)202 439 1384
e-mail: koeberlein@wiwi.uni.wuppertal.de

[1]Department of Health Economics und Health Care Management
University of Wuppertal
Germany

[2] Department of Ophthalmology, University of Bonn, Bonn, Germany
and
Centre of Eye Research Australia, Royal Victorian Eye and Ear Hospital,
University of Melbourne, Melbourne, Australia

*JK and KB contributed equally to this article

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ABSTRACT

Objectives

Visual impairment and blindness (VI&B) cause a considerable and increasing economic burden in all high income countries due to population ageing. Thus we conducted a review of the literature to better understand all relevant costs associated with VI&B and to develop a multi-perspective overview.

Design

Systematic review. Two independent reviewers searched relevant literature and assessed studies for inclusion and exclusion criteria as well as quality.

Eligibility criteria for included studies

Interventional, non-interventional and cost of illness studies, conducted prior to May 2012, investigating direct and indirect costs as well as intangible effects related to visual impairment and blindness were included.

Methods

We followed the PRISMA statement approach to identify relevant studies. A meta-analysis was not performed due to the variability of reported cost categories and varying definition of visual impairment.

Results

A total of 22 studies were included. Hospitalization and use of medical services around diagnosis and treatment at the onset of VI&B were the largest contributor to direct medical costs. Mean annual expenses per patient were found to be US$ PPP 12,175-14,029 for moderate visual impairment, US$ PPP 13,154-16,321 for severe visual impairment, and US$ PPP 14,882-24,180 for blindness, almost twofold the costs for non-blind patients. Informal care was the major contributor to other direct costs, with the time spent by caregivers increasing from 5.8 hours/week (or US$ PPP 263) for persons with vision > 20/32 up to 94.1 hours/week (or US$ PPP 55,062) for persons with vision ≤ 20/250. VI&B caused considerable indirect costs due to productivity losses, premature mortality, and dead weight losses.

Conclusions

VI&B cause a considerable economic burden for affected persons, their care givers and society at large, which increases with the degree of visual impairment. This review provides insight into the distribution of costs and the economic impact of VI&B.

ARTICLE SUMMARY

Article Focus

- To explore all relevant costs associated with visual impairment and blindness.

Key Message

- We could demonstrate a considerable impact of visual impairment and blindness in terms of the associated direct and indirect costs, as well as intangible effects such as loss of well-being, independence and excess mortality.
- A large proportion of the direct costs reported in reviewed studies are not directly related to eye-related medical care, but to falls and other accidents due to visual impairment, exacerbation of diabetes due to a reduced ability to self-manage, depression related to loss of vision and further excess morbidity.
- All identified costs as well as intangible effects correlated with the degree of visual impairment with highest expenditures associated with blindness.

Strengths and limitations

- This is the first international and multi-perspective overview of costs and intangible effects associated with visual impairment as well as blindness.
- The study synthesis of reviewed literature was limited as no two studies used the same methodology, reported exactly the same outcomes or used the same sample population. Therefore a meta-analysis could not be conducted.

INTRODUCTION

Visual impairment and blindness are foremost a problem of older age in all high-income countries, and constantly increasing due to the ageing of populations [1]. Globally, the burden of disease related to vision disorders has increased by 47% from 12,858,000 Disability Adjusted Life Years (DALYs) in 1990 to 18,837,000 DALYs in 2010 [2]. In high-income countries, health-related quality of life in severely visually impaired persons has been shown to be similar or even lower and emotional distress higher compared with other serious chronic health conditions such as stroke or metastasised solid tumours [3]. Blindness and visual impairment impact not only the affected individual but also the family, caregivers and the community, leading to a significant cost burden. In Australia, the overall cost placed visual disorders seventh among diseases, ahead of coronary heart disease, diabetes, depression, and stroke in terms of economic burden on the health system [4].

As demands on healthcare continue to increase in all high-income countries, economic evaluations of disease, impairment and interventions have also become increasingly important [5]. This necessitates a clear understanding of all aspects of the direct and indirect costs and intangible effects related to blindness and severe visual impairment, as almost all interventions in this area are aiming to prevent these and are often measured as an incremental cost effectiveness ratio (ICER), i.e. the difference in cost compared to the difference in effectiveness. Similarly, faced with increasing demand and limited resources in healthcare, these resources need to be prioritized which again calls for a clear understanding of the economic impact of a disease or disorder. Against this background we conducted a systematic review of the literature, collating all data available on the economic impact of visual impairment and blindness.

METHODS

The systematic review was conducted as suggested in the PRISMA statement which aims to improve the quality of systemtic reviews by providing guidance and a 27-item checklist to aid in structuring methods and improving the reporting of results. It focuses on randomized trials, but can also be used as a basis for reporting systematic reviews of other types of research, for example health economic evaluation studies. However the checklist should not be used as a quality assessment instrument to measure the quality of included studies or the performed systematic review [47]. The completed PRISMA checklist for this review can be found in appendix three.

Literature search

All economical and medical databases were searched from May to June 2012 via PubMed and OVID using the following terms:

"low vision", "visual impairment", "visually impaired", "blindness", "blind", "visual loss", "costs", "costs of illness".

Subsequently, a second search was conducted using the main causes of visual impairment and blindness. Search terms were: *"low vision", "visual impairment", "visually impaired", "blindness", "blind", "visual loss", "costs"* combined with "*age-related macular degeneration", "glaucoma", "diabetic retinopathy", "cataract", "corneal opacities", "childhood blindness"* separated by *"or"*.

Supplemental sources including references contained in identified articles were used in addition.

Two independent researchers screened identified articles using the following inclusion or exclusion criteria:

Inclusion:

- data for direct and indirect costs related to visual impairment and blindness. Cost-of-illness – or in this case cost-of-impairment – studies can be divided into disease-specific and general studies. Both types of studies were included if they contained relevant data,
- studies with outcomes related to intangible effects due to visual impairment and blindness,
- overall data for burden of illness related to affected persons and carers.

Exclusion:

- costs pertaining to underlying diseases only with no specification of visual impairment levels,
- economic studies conducted in developing countries.

As we were interested in the burden of VI&B in high-income countries only, we excluded economic studies conducted in developing countries. Health services provision and treatment options differ vastly between high-income and middle- or low-income countries, making a comparison of cost categories unfeasible.

Cost classification

All included articles were assessed as to which cost aspects they reported. Broadly, costs were divided into direct costs, indirect costs, and intangible effects [6].

Direct costs are defined as the actual expenses related to an illness and contain medical costs, non-medical costs and other direct costs [5]. Medical costs measure the cost of resources used for treating a particular illness. Non-medical costs are costs caused by the disease but not attributed to medical treatment. In case of visual impairment and blindness these are supporting services, assistive devices, home care, residential care or transportation (travel expenses). Other direct costs comprise informal care, time spent in treatment by patients or caregivers, or time spent in rehabilitation, training, self-help groups or preventative activities [5].

Indirect costs are defined as the value of lost output caused by reduced productivity due to illness or disability [7]. Both, patients and caregivers are affected by indirect costs due to allowances (financial support for income, residence, benefits), productivity losses (absenteeism, salary losses, part-time employment, loss of work), and dead weight losses as well as years of life lost. Dead weight loss, also known as an excess burden, is not a clearly defined concept. In a purely economic sense, deadweight loss describes the costs to society created by market inefficiency. In the context of our study we refer to it as an excess financial burden on society caused by VI&B.

Intangible costs or effects refer to the burden of illness of affected persons and caregivers, and comprise amongst others loss of well being or loss of quality of life. It can be captured using questionnaires and expressed in DALYs. As this aspect of costs is difficult to quantify, DALYs or other measures of intangible effects are rarely assigned a monetary value.

Commonly, cost categories considered in a particular study depend on the perspective the study is conducted from, i.e. a healthcare payer's (direct medical and non-medical costs only) or the patient's perspective, or a societal perspective (all costs).

As cost categories varied considerably between all cost-of-illness studies all different direct and indirect cost categories were listed in appendix two prior to being categorized into our broader categories as outlined above.

Quality of included studies

A checklist, based on the assessment tool of Emmert and colleagues [8] and extended by several questions covering relevant cost-of-illness aspects (see **Appendix 1**), was generated to assess the overall quality of included studies reporting direct or indirect costs of illness. The checklist contained sections on the study design, population, definition and specification of cost data and its limitations, including a total of 25 questions. Studies were rated from 0 – 100 for each of these categories. Two independent reviewers conducted the assessment and interrater-reliability was assessed using Kappa (κ_n) as suggested by Brennan and Prediger [9] for every study. The interpretation of agreement was based on the agreement scale by

Landis and Koch [10]. which indicates fair agreement at Kappa levels between 0.21 and 0.40, moderate agreement between 0.41 and 0.60, substantial between 0.61 and 0.80 and almost perfect agreement 0.81 and above.

Conversion of Cost-of-illness study results

For better comparison of costs across studies, the data were transformed: (1) costs were inflated to 2011 using country specific gross domestic product deflator, which takes fluctuating exchange rates, different purchasing power of currencies and the rate of inflation into account [11 12], and (2) converted to USD using purchasing power parities (PPP) [13]. Purchasing power parities account for differences in price levels between countries, and convert local currencies into international dollars taking purchasing power of different national currencies into account and eliminating differences in price levels between countries. The transformed values are presented in million units (million US$-PPP) for total expenditures reported and in US$-PPP for costs per person.

RESULTS

The search yielded a total of 390 articles. After applying all inclusion and exclusion criteria, 22 studies were included in the systematic review (**Figure 1**). Altogether there were nine studies conducted in the USA, six studies conducted in Australia, two studies from France and Canada, and one study from each of the following countries: Germany,, the UK, Japan.. All included studies are summarized in **Table 1.**

Table 1: Characteristics of included studies

Author	Country	Design and Population	Cost components evaluated	Objective	Vision categories
Bramley et al. 2008 [14]	USA	retrospective cohort analysis of nationally representative Medicare 5% random sample; patients older than 65 years with newly diagnosed glaucoma; regression analysis	direct medical costs, intangible effects	to measure costs of visual impairment due to progressing glaucoma	no vision loss, moderate vision loss, severe vision loss, blindness
Brezin et al. 2005 [15]	France	national survey of a random stratified sample; 16, 945 affected persons answered questionnaires; 4,091 caregiver answered questionnaires;	indirect costs; intangible effects	to document the prevalence of self-reported visual impairment and its association with disabilities, handicaps, and socioeconomic consequences.	blind or light perception only, low vision, other visual problems, and no visual problems
Chou et al. 2006 [16]	Australia	150 persons completed cost diaries for 12 months and were evaluated; costs categorized into four sections: 1. medicines, products and equipment, 2. health and community services, 3. informal care and support, 4. other expenses	direct medical costs, direct non-medical costs	to describe and evaluate the process used to collect personal costs (out-of pocket) associated with vision impairment using diaries	≥ 6/12with restricted fields; <612–6/18; <6/18–6/60; <6/60–3/60; <3/60
Clarke et al. 2003 [17]	UK	regression-based approach to estimate the short-term and long-term annual hospital and non-hospital costs associated with seven major diabetes-related complications in the UK Prospective Diabetes Study (UKPDS): myocardial infarction (MI); stroke, angina or ischemic heart disease (IHD); heart failure; blindness in one eye; amputation and cataract extraction; 5102 patients with newly diagnosed type 2 diabetes	direct medical costs	to estimate the immediate and long-term healthcare costs associated with seven diabetes-related complications	blind in one eye
Cruess et al. 2011 [18] (in combination with Gordon et al. 2011 [19])	Canada	prevalence-based approach, population projections for the whole population were compiled using data from the Statistics Canada 2006 Population Projections for Canada, Provinces and Territories 2001-2031	direct medical costs, direct non medical costs, indirect costs, intangible effects	to investigate costs of vision loss in Canada to inform healthcare planning	no details
Frick et al. 2008 [20]	USA	retrospective cohort study; patients with blindness matched to non-blind selected from managed care claims database	direct medical costs	to evaluate total and condition related charges incurred by blind patients in a managed care population in the US	blind, non blind

Frick et al. 2007 [21]	USA	data from the medical expenditure panel survey 1996 – 2002 for adults older than 40 years with visual impairment or blindness	direct medical costs; direct non medical costs; other direct costs; intangible effects	to estimate the economic impact of visual impairment and blindness in persons aged 40 years and older in the US	visual impairment; blindness
Javitt et al. 2007 [22]	USA	retrospective cohort analysis of nationally representative Medicare 5% random sample, excluding Medicare managed-care enrollees	direct medical costs	to assess and identify the costs to the Medicare program for patients with either stable or progressive vision loss and estimate the impact on eye-related and non-eye related care	mild, moderate, severe vision loss (VA ≤20/200), blindness (VA ≤ 20/400)
Keeffe et al. 2009 [23]	Australia	114 participants of the Melbourne Visual Impairment Project completed diaries for 12 month; the burden of caregiver and opportunity costs for losses in work time was calculated (in combination with methods and data from Chou et.al.)	other direct costs	to analyse prospective data on providers, types and costs of care for people with impaired vision in Australia	VA < 20/40
Kymes et al. 2010 [24]	USA	decision analytic approach; Markov model to replicate health events over the remaining lifetime of someone newly diagnosed with glaucoma	incremental costs of illness	to evaluate the incremental cost of primary open-angle glaucoma considering both visual and non-visual medical costs over a lifetime	no details
Lafuma et al. 2006 [25]	France	interviews with sample population (665,000) from a national survey of persons living in institutions or in the community (with caregiver at home)	direct non medical costs, other direct costs, indirect costs	to estimate the annual national non medical costs due to visual impairment and blindness	blind (light perception), low vision (better than light perception??, low vision, and controls
McCarty et al. 2001 [26]	Australia	population-based study; evaluation of the data from Melbourne Visual impairment project; population ≥40 years was analyzed in causes of death	intangible effects	to describe predictors of mortality in the 5 year follow up of Melbourne Visual impairment project;	visual acuity < 6/12
Morse et al. 1999 [27]	USA	2.552.350 discharges from hospital in state of NY -> 5.764 patients had visual impairment	direct medical costs	to assess whether visual impairment contributes to average length of stay within inpatient care facilities	no details
Porz et al. 2010 [28]	Germany	retrospective study of 66 patients using a cost and a vision-related quality of life questionnaire (Impact of vision Impairment	direct non medical costs, intangible	to capture costs for medicines, aids and equipment, support in everyday life and social bene-	Visual acuity (VA) ≥ 0,3, Visual acuity < 0,3

		questionnaire)	effects	fits, as well as vision- related quality of life	
Rein, et al. 2006 [29]	USA	private insurance and Medicare claims data	direct non medical costs, indirect costs	to estimate the societal economic burden and the governmental budgetary impact of the following visual disorders among US adults aged 40 years and older: visual impairment, blindness, refractive error, age-related macular degeneration, cataracts, diabetic retinopathy, and primary open angle glaucoma	refractive errors
Roberts et al. 2010 [30]	Japan	prevalence-based approach; adopted using data on visual impairment, the national health system, and indirect costs	direct medical costs, direct non medical costs, indirect costs and intangible effects	to quantify the total economic cost of visual impairment in Japan	low vision 6/12-6/60; blind < 6/60; visual impairment = >6/12
Schmier et al. 2009 [31]	USA	using a questionnaire that included items on demographic and clinical characteristics and on the use of services, assistive devices, and caregiving; 761 persons were included	direct non medical costs, other direct costs	to assess the use of devices and caregiving among individuals with diabetic retinopathy and to evaluate the impact of visual acuity on use	group 1 (20/20 or better), group 2 (20/ 25–20/30), group 3 (20/40–20/50), group 4 (20/60–20/70), or group 5 (20/80 or worse)
Schmier et al. 2006 [32]	USA	survey with interviews on Daily Living Tasks Dependent on Vision Questionnaire;803 respondents	other direct costs,	to assess the patient-reported use of caregiving among individuals with age-related macular degeneration (AMD) and evaluation of impact of visual impairment level on this use	1. VA > 20/32; 2. VA 20/32 - > 20/50; 3. VA 20/50 - >20/80; 4. VA 20/80 - > 20/150; 5. 20/150 - >20/250; 6. VA ≤ 20/250
Vu, et al. 2005 [33]	Australia	stratified random sample of 3040 participants from the Melbourne Visual Impairment Project; 2530 attended the follow-up study	intangible effects	to investigate whether unilateral vision loss reduces any aspects of quality of life in comparison with normal vision	unilateral and bilateral vision loss (correctable and non-correctable)
Wong et al. 2008 [34]	Australia	prospective cohort study; participants of any age to complete a diary for 12 months answering four categories: 1) medicines, products and equipment, 2) health and community services, 3) informal care and support and 4) other expenses	direct costs (medical and non medical), other direct costs	to determine the personal out-of-pocket costs of visual impairment and to ex-amine the expenditure pattern related to eye diseases and the severity of visual impairment	visual acuity ≥6/18 with constricted. fields; < 6/18-6/60; < 6/60

Wood et al. 2011 [35]	Australia	76 community-dwelling individuals with a range of severity of AMD; completing a diary for 12 month	intangible effects; costs of adverse events	to explore the relationship between AMD, fall risk, and other injuries and identified visual risk factors for these adverse events	binocular visual acuity, contrast sensitivity, and merged visual fields

All 17 of 22 studies dealing with direct or indirect costs of illness were rated above 50 for all four main quality aspects, indicating a sufficient level of quality, and consequently were included into the review (see **Figure 2**). The interrater-reliability was consistently high and only a few discrepancies had to be settled by a discussion between the two raters. Kappa scores ranged from 0.34 to 0.76 (**Figure 3)**.

Of all included studies twelve captured direct medical cost, ten direct non-medical costs, and six other direct costs. Six studies report data on indirect costs and ten on intangible effects. All cost components reported by studies within each cost category are summarized in **Appendix 2,** highlighting the considerable variability in obtaining and reporting cost aspects related to visual impairment and blindness between all studies.

Direct medical costs

Direct medical costs occurred mostly due to hospitalization, the use of medical services and medical products, and were reported either as incremental costs or, in some studies, provided as the length of hospital stay (**Table 2**).

At the onset of visual impairment and blindness, the two major contributors to direct medical costs are hospitalizations and costs due to increased use of medical services around diagnosis and treatment [17 18 20 21 27 30]. Costs related to recurrent hospitalizations and ongoing, but less frequent use of medical services, remain major cost components in persons with visual impairment and blindness in the long term. Costs related to drugs, however, did not emerge as a major direct cost factor [16 34]. All identified costs correlated with the degree of visual impairment leading to the highest expenditures being associated with blindness. The considerable differences in study methods and reported outcomes makes a head to head comparison of results by study or country or aggregation of data in terms of meta-analyses for direct medical costs very difficult. Several studies based on representative samples of Medicare beneficiaries in the USA reported mean annual expenses per patient to be US$ PPP 12,175-14,029 for moderate visual impairment, US$ PPP 13,154-16,321 for severe visual impairment, and US$ PPP 14,882-24,180 for blindness, which is almost a 100% excess of the estimated mean annual cost for non-blind patients at the upper end of the range (**Table 2**).

Table 2: Results for direct medical costs.

Study	*cost outcomes*	*US$ PPP in 2011*
Bramley et al. 2008[14]	annual costs per patient compared in degrees of vision impairment from no vision loss and onset of moderate or severe vision impairment or blindness	
	no vision loss **US$ 8,157**	**8,695**
	moderate visual impairment **US$13,162**	**14,029**
	severe visual impairment **US$ 15,312**	**16,321**
	blindness **US$ 18,670**	**19,900**
Frick et al. 2007[21]	total expenditures on health care in blind and visual impaired persons ≥ 40 years	
	blindness individual excess medical expenditures **US$ 2,157**	**2,621**
	total excess medical expenditures **US$ 2,454 million**	**2,982 million**
	visual impairment individual excess medical exp. **US$ 1,037**	**1,260**
	total excess medical expenditure **US$ 2,661 million**	**3,233 million**
	total annual monetary impact for VI and blindness (primary owing to home care) **US$ 5,100 million**	**6,197 million**
Frick et al. 2008[20]	cohort with legally blind patients matched to equal sample cohort with non-blind patients (annual costs per patient in the first year)	
	blind persons mean costs **US$ 20,677**	**24,180**
	median costs **US$ 6,854**	**8,015**
	non blind mean costs **US$ 13,321**	**15,578**
	median costs **US$ 371**	**434**
Javitt et al. 2007[22]	patients with normal vision compared to moderate or severe visual impairment or blindndess regarding eye-related and non-eye-related care	
	mean annual costs for eye-related care	
	normal vision **US$ 370**	**445**
	moderate visual impairment **US$ 345**	**415**
	severe visual impairment **US$ 407**	**490**
	blindness **US$ 237**	**285**
	mean annual values for non eye related costs	
	normal vision **US$ 7,928**	**9,537**
	moderate visual impairment **US$ 2,193**	**2,638**
	severe visual impairment **US$ 3,301**	**3,971**
	blindness **US$ 4,443**	**5,345**
Kymes et al. 2010[24]	lifetime costs of POAG (primary open-angle glaucoma) to non POAG patients	
	incidence costs **US$ 41,039**	**46,456**
	prevalence costs **US$ 19,268**	**21,811**
	drug costs **US$ 7,098**	**8,035**
	incremental incidence costs **US$ 27,326**	**30,933**
	incremental prevalence costs **US$ 5,555**	**6,288**
	incremental drug costs **US$ 4,179**	**4,731**
Morse et al. 1999[27]	extension of average length of stay in hospitals due to visual impairment	
	5.2 days longer stay	
Cruess et al. 2011[18]	financial burden of vision loss to Canadian health care system	
	hospital **CAN$ 1,497.7 million**	**1,934.72 million**
	physicans **CAN$ 866.5 million**	**1,119.34 million**
	vision care **CAN$ 3,483.7 million**	**4,500.24 million**
Chou et al. 2006[16]	the out-of-pocket expenses for medicines and products per person annually	
	AUS $ 206	**456**
Wong et al. 2008[34]	annual costs for medicine and products per patient	
	Visual acuity (VA) ≥ 6/18 with restr. field **AUS$ 285**	**632**
	< 6/18 – 6/60 = **AUS$ 233**	**516**
	< 6/60 = **AUS$ 147**	**326**
Clarke et al. 2003[17]	short-term and long-term annual hospital and non-hospital costs due to major diabetes-related complications	
	blindness in one eye (in 20% of patients) **£ 4,370**	**4,086**
	mean hospital in-patient costs **£ 872**	**815**
Roberts et al. 2010[30]	total economic costs of visual impairment	
	General medical expenditure **US$ 8.102 billion**	**8,636 million**
	Inpatient **US$ 1.808 billion**	**1,927 million**
	Outpatient **US$ 6.294 billion**	**6,709 million**
	Drugs **US$ 1.395 billion**	**1,487 million**

Direct non medical costs

Assistive devices and aids, home modifications, costs for health care services like home-based nursing or nursing home placements were the major contributors to direct non-medical costs (**Table 3**). With worsening visual acuity direct non-medical costs for support services and assistive devices increased, from US$ PPP 53.90 for a person with visual acuity ≥ 20/20 up to US$ PPP 608.71 for a person with visual acuity ≤ 20/80 [31]. Nursing home-placements and professional care costs incurred the highest expenditures followed by domestic modifications. These costs however, were highest initially shortly after the loss of vision and in the majority only incurred once (**Table 3**).

Table 3: Results for direct non medical costs.

Study	*cost outcomes*		*US$ PPP in 2011*	
Frick et al. 2007[21]	total health care expenditures for adults ≥ 40 years (excess costs)			
	blindness home health agencies **US$ 4,988**		**6060**	
	low vision home health agencies **US$ 3,105**		**3,773**	
	expenditures for private home health providers was **US$ 1,200 more** for blind than visually impaired persons			
Rein et al. 2006[29]	total annual costs for visual impairment and blindndess for adults ≥40 years			
	nursing placements of **US$ 10.96 billion**		**12,818 million**	
	guide dogs **US$ 0.062 billion**		**72.5 million**	
	independent living **US$ 0.029 billion**		**33.9 million**	
Schmier et al. 2009[31]	annual costs for use of services and devices related to the degree of visual impairment per person			
	devices (glasses, sticks, computer software, etc. **US$ 109.79**		**120**	
	rehabilitation **US$ 7.09**		**7.78**	
Chou et al. 2006[16]	annual costs for health and community services per person			
	health care, home help, personal affairs, personal care, communication, transport, social activities **AUS $ 872**		**1,932.50**	
	expenditure for taxi, public transport, education expenses, guide dog **AUS $ 321**		**711**	
Cruess et al. 2011[18]	financial burden of vision loss to Canadian health care system			
	care costs **CAN$ 693 million**		**895.21 million**	
	aids and modification **CAN$ 305 million**		**394 million**	
Wong et al. 2008[34]	annual personal costs for health and community services and other expenses per patient			
	median total costs **AUS$ 1,768**		**3,919**	
	mean total costs **AUS $ 3,376**		**7,482**	
Roberts et al. 2010[30]	total economic costs of visual impairment			
	meal service on admission **US$ 0.149 billion**		**158.81 million**	
	home-visit nursing **US$ 0.013 billions**		**13.86 million**	
	health care administration **US$ 0.475 billion**		**506.30 million**	
	Community care **US$ 6.608 billion**		**7,043 million**	
	Institutional care **US$ 0.238 billion**		**253.68 million**	
	Vision aids **US$ 0.2 billion**		**213.18 million**	
Porz et al. 2010[28]	financial and psychological burden of retinal diseases divided into health economic relevant categories; annual expenses per person			
	aids for VA ≥ 0.3 = **€ 96.65**		**77.39**	
	VA < 0.3 = **€ 83.58**		**66.92**	
	personal assistance VA ≥ 0.3 = **€ 454.96**		**364.28**	
	VA < 0.3 = **€ 667.77**		**534.68**	
Lafuma et al. 2006[25]	national survey with estimation on costs of low vision and blindness for persons living in institutions[1] or in the community [2] (declared annually per person and total expenditures)			
	low vision	**blindness**	**low vison**	**blindness**
	home modifications [1] **€ 36.65 pp/ year**	**€ 926.96 pp/ y**	**37.87**	**957.90**
	€ 3.27 million total	**€ 9.63 million total**	**3.375 million**	**9.95 million**
	devices [1] **€184.14 pp/ year**	**€ 387.35 pp/ y**	**190.29**	**400.28**
	€ 16.43 million total	**€4.03 million total**	**16.98 million**	**4.165 million**
	home modification [2] **€ 42.23 pp/ y**	**€ 121.12 pp/y**	**43.64**	**125.16**
	€ 16.43 million total	**€ 7.02 million total**	**16.98 million**	**7.25 million**
	devices [2] **€ 376.39**	**€ 363.14 pp/ y**	**388.95**	**375.26**
	€ 420 million total	**€ 21.04 million total**	**434.02 million**	**21.74 million**
	paid assistance [2] **€ 1,463.59 pp/ y**	**€ 6750.66 pp/ y**	**1,512.44**	**6,976**
	€ 1,635 million	**€ 391 million total**	**1,690 million**	**404 million**

Other direct costs

Six of the included studies reported costs caused by informal care. Time spent on caring for or assisting visually impaired persons was related to the degree of visual impairment, with blind persons requiring the most assistance. The time spent by caregivers ranged from 5.8 hours per week for a person with a visual acuity of > 20/32 and a cost of US$ PPP 263 up to 94.1 hours per week and costs of US$ PPP 55,062 for persons with a visual acuity of ≤ 20/250 [32]. All studies differed slightly as to the nature of direct costs assessed. Some studies reported on governmental, out-of-pocket expenses as well as opportunity costs, others considered only one or two of these. The wide range of time and resources spent on informal care provision demonstrates the broad economic impact and considerable burden of informal care provision with concurrent expenses at a personal and societal level. Again, reported cost aspects and methodologies differ considerably, with, for example, Keeffe and colleagues[23] reporting out-of-pocket expenses and Lafuma and colleagues[25] reporting time spent on caring using an hourly rate. The multitude of differing approaches in each study does not allow for a head-to-head comparison but gives a comprehensive impression of the complex cost situation and highlights the importance of providing assistance to visually impaired and blind persons (**Table 4**).

Table 4: Results for other direct costs.

Study	*cost outcomes*		*US$ PPP in 2011*	
Frick et al. 2007[21]	the economic impact of blindness and visual impairment on adults ≥ 40 years			
	blindness causes mean individual excess informal care days 5.2			
	visual impairment causes mean individual excess informal care days 1.2			
	blindness causes total excess informal care costs **US$ 242 million**		**294.03 million**	
	visual impairment total excess informal care costs **US$ 124 million**		**150.66 million**	
Schmier et al. 2009[31]	annual costs for caregiver time spent in supporting patients with macular degeneration			
	US$ 5,038		**5,526**	
Schmier et al. 2006[32]	annual costs for quantity of caregiver time addicted to the degree of visual impairment per patient diabetic retinopathy			
	mean 5.7 hours a day 5 days a week			
	overall amount of **US$ 9572.77**		**11,194.40**	
Keeffe et al. 2009[23]	personal out-of-pocket expenses regarding the burden of caregiver			
	median annual opportunity costs for worktime spent on caregiving **AUS$ 915**		**2,244.60**	
Wong et al. 2008[34]	annual median personal costs for informal care and assistance in activities of daily living			
	e.g. meal preparing, dressing, shopping, transportation **AUS$ 2,911**		**6,451**	
Lafuma et al. 2006[25]	national survey with estimation on costs for time caregiver spent on of low vision and blindness for persons in the community (declared annually per person and total expenditures)			
	low vision	**blindness**	**low vison**	**blindness**
	informal care **€ 1881.80 pp/ year**	**€ 7,316.26 pp/ y**	**1,944**	**7,560.48**
	€ 2,101 million total	**€ 424 million total**	**2,171 million**	**438 million**

Indirect costs

Studies of indirect costs demonstrate high expenditures related to productivity losses, changes in employment (employer and/or area of work), loss of income, premature mortality, and dead weight losses (**Table 5**). Received social allowances were detailed in one study, but not counted towards the overall costs as they were considered transfer costs.[28] One study included the loss of caregivers' time, which is spent on support in terms of productivity loss but also as a loss of personal time and time to engage in leisure activities.[25] Equal to other cost components indirect costs correlated with the degree of visual impairment, with the highest indirect costs reported for blind persons. Compared to all other cost categories indirect costs due to productivity losses, lower employment rates and losses of income in patients as well as caregivers caused the highest economic burden. Annual estimates of productivity losses and absenteeism due to visual impairment and blindness in the USA and Canada range from US$ PPP 4,974-5,724 million, and are estimated to be US$ PPP 7,367 million for an overall decrease in workforce participation in the USA (**Table 5**).

Table 5: Results for indirect costs

Study	*cost outcomes*		*US$ PPP in 2011*	
Rein et al. 2006[29]	total annual indirect costs caused by visual disorders			
	decreased work force participation **US$ 6.3 billion**		**7,367 million**	
	decreased wages **US$ 1.73 billion**		**2,023 million**	
Roberts et al. 2010[30]	indirect costs for visual impairment and blindness			
	productivity losses **US$ 4.667 billion**		**4,974 million**	
	lower employment **US$ 4.230 billion**		**4,509 million**	
	absenteeism **US$ 0.384 billion**		**409 million**	
	premature mortality **US$ 0.053 billion**		**56.5 million**	
	dead weight losses **US$ 1.609 billion**		**1,715 million**	
Lafuma et al. 2006[25]	national survey with estimation on indirect costs for losses of income in persons with low vision and blindness living in institutions [1] or in the community [2] (declared annually per person and total expenditures)			
	low vision	**blindness**	**low vison**	**blindness**
	losses of incomes [1] **€ 120.00 pp/y**	**€ 180.00 pp/y**	**124**	**186**
	€ 10.71 million total	**€ 1.87 million total**	**11.07 million**	**1.93 million**
	losses of incomes [2] **€ 3,912.00 pp/y**	**€ 3,168.00 pp/y**	**4,042**	**3,273**
	€ 4,369 million total	**€ 183.6 million total**	**4,515 million**	**189.72 million**
Brezin et al. 2005[15]	prevalence and burden of blindness, lo sion and visual impairment in the French community (estimation of monthly average value)			
	low vision	**blindness**	**low vison**	**blindness**
	social allowances **€ 87**	**€ 364**	**92**	**384**
	total household income **€ 1,525**	**€ 1,587**	**1,607**	**1,673**
	household income no VI **€ 1,851**		**1,951**	
Cruess et al. 2011[18]	indirect costs for Canada caused by vision loss			
	employment participation, absenteeism, presenteeism **CAN $ 4,431 million**		**5,724 million**	
	dead weight losses **CAN$ 1,757 million**		**2,270 million**	

Intangible effects

Most studies used personal burden such as depression, emotional distress, loss of independency, loss of quality of life, limitations in activities of daily living or hazards such as falls and injuries to capture intangible effects of visual impairment and blindness. Two studies, set in Japan and Canada, reported a loss of well being as DALYs and an associated cost of US$ PPP 51.8 billion and US$ PPP 15.11 billion per year respectively.[18 30] Every reviewed study reported a high burden caused by multiple individual restrictions in patients and also in caregivers, which was found to be increasing with the degree of visual impairment (**Table 6**). Mortality associated with visual impairment was reported to increase linearly from 4.5% in persons with normal visual acuity (≥20/20) to 22.2% in blind persons (visual acuity of < 20/200) [26]. Measured as a restriction in care givers, Brezin and colleagues [15] reported a increases from 1.6% of caregivers of non-visually impaired persons, who reported restrictions in going out during the day, up to 12% for caregivers of blind patients.

Table 6: Results for intangible effects

Study	*Outcomes*
Bramley et al. 2008[14]	incidences of depression occur in 17% more than patients with no vision loss, placements in nursing homes are demanded in 25.3% more, injuries happen in 33.4% more cases and femur fractures in 67.4% more cases
Cruess et al. 2011[18]	loss of well-being and loss in quality of life evokes 77,306 DALYs or rather CAN$ 11.7 billion in 2007 (US$ PPP 15.11 billion in 2011)
Vu et al. 2005[33]	non-correctable unilateral vision loss was addicted to independent living and reduced safety; bilateral non-correctable vision loss was associated with nursing homes, emotional wellbeing, use of community services, and activities of daily living
Wood et al. 2008[35]	increased visual impairment was significantly associated with an increased incidence of falls and other injuries. 54% of participants had at least one fall, 30% had more than fall, and 63% of falls ended in injuries
McCarty et al. 2001[26]	a linear increase of 5-year mortality correlating with degree of visual impairmen was detected; even mild visual impairment is related to a more than twofold risk of death
Brezin et al. 2005[15]	burden in patients occurs because of inability to undertake daily activities; need of assistance correlates with degree of visual impairment; burden on caregiver was caused by limited by restricted possibilities for going out for different periods or losing social contacts, affected physical and mental welfare and modified professional activities
Porz et al. 2010[28]	in a questionnaire with score scale 0-100 points patients with VA ≥ 0.3 achivede 79.32 for mobility and independency, 69.64 for emotional well-being and 73.86 for reading and achievement of information; persons with VA < 0.3 were rated with scores 46.84, 61.43, 44.25 respectively
Roberts et al. 2010[30]	loss of well-being was measured in DALYs; converted into a monetary value this results in total annual costs of US$ 48.598 billion (US$ PPP 51.8 billion in 2011) and costs per capita of US$ 29,690 per year (US$ PPP 31,647)
Frick et al. 2007[21]	the cases of blindness and visual impairment more than 209,000 QALY were projected to lost each year, this amounts to a monetary value of US$ 10,000 million (US$ PPP 12,150 in 2011)

DISCUSSION

In this first systematic review of costs associated with visual impairment and blindness we could demonstrate a considerable impact of visual impairment and blindness in terms of the associated direct and indirect costs, as well as intangible effects such as loss of well-being, independence and excess mortality. The highest costs are caused by productivity losses in visually impaired and blind persons as well as their carers, followed by formal and informal care giving, recurrent hospitalizations and the use of medical and supportive services in the visually impaired and blind. A much larger economic impact was due to intangible effects such as loss of independence, quality of life and excess morbidity. However, these are very difficult to quantify in monetary terms and only a small number of studies attempted this. All highlighted cost components as well as intangible effects which contribute to the overall economic impact of visual impairment and blindness need to be considered in economic evaluations not only of visual impairment and blindness but also of interventions aimed at averting these, depending on the focus of the economic evaluation.

A large proportion of the direct costs reported in reviewed studies are not directly related to eye-related medical care, but to falls and other accidents due to visual impairment, exacerbation of diabetes due to a reduced ability to self-manage, depression related to loss of vision and further excess morbidity.[22] Drug costs were not a major contributor to overall costs, which is mirrored in studies investigating chronic diseases such as diabetes mellitus, where – despite its ongoing use – hypoglycaemic drugs constitute only a small proportion of overall direct medical costs.[36] Annual mean costs of other potentially incapacitating chronic diseases such as diabetes mellitus (Euros 5,262 or USD 6,889) [36] or the first year after a stroke (USD 14,361)[37] were much lower for diabetes and similar for the stroke estimate compared to mean annual costs of severe visual impairment and blindness.[14 22] This is likely due to the average diabetic not requiring professional care giving of a scale required during the first year after a stroke or in severely visually impaired and blind persons. In severely visually impaired or blind persons, however, these costs are incurred every year following the loss of vision, and do not decrease significantly over the following years unlike reported annual costs for stroke.[37] Javitt and colleagues report all direct medical cost caused by visual impairment to amount to US$ 2.14 million in 2003 in all non-institutionalized Medicare beneficiaries 69 years and older, and postulate a much higher cost for the whole of the US population.[22] With the introduction of anti-Vascular-Endothelial-Growth-Factor treatment for a number of potentially blinding eye diseases such as neovascular age-related macular degeneration, diabetic macular edema or macular edema in retinal vein occlusions since all reviewed studies were conducted, the overall direct medical costs associated with visual impairment can be expected to be much higher today. This increase in cost is exacer-

bated by the ageing of populations in all developed countries as all major blinding diseases are age-related.[29]

Our finding that indirect costs are much higher than direct costs caused by visual impairment and blindness is mirrored by virtually all other cost-of-illness studies assessing the economic impact of diseases or impairments which result in absenteeism and reduced ability to work [38-39]. Back pain, for example, was found to cause considerable absenteeism and disablement, which – despite its significant hospital cost – lead to indirect cost constituting 93% of the overall cost in 1991 in the Netherlands.[38] Even in treatment and healthcare resource intensive chronic diseases such as diabetes mellitus, indirect costs pose more than half of the overall costs caused by the illness.[39]

All studies which assessed intangible effects in economic terms reported these to be the largest contributor to the overall economic impact of visual impairment and blindness. Considering the adverse impact of loosing vision on quality of life, independence and the ability to participate in society, this is not surprising. We and others have previously reported that even mild visual impairment (0.3<LogMAR<0.5) has a significant and independent impact on vision-specific functioning.[40-42] Similarly, emotional well-being is affected in patients with even mild vision impairment.[41] Depression is considered to result in further functional decline in this group by reducing motivation, initiative and resiliency. [43-45] Even unilateral vision loss had a measurable impact on falling and some other activities of independent living, with increased odds of having problems in many activities of daily life in a study conducted by Vu and colleagues.[33] All this very adversely impacts the ability to participate in society, and contributes to the considerable economic impact of intangible effects caused by visual impairment and blindness.

There are several limitations which necessitate a careful interpretation of the overall findings. Using key words to identify relevant literature always bears the potential of a too narrow focus, and not all relevant literature may have been included. As we were interested in the economic burden of VI&B in high-income countries, we did not include (uncorrected) refractive error into our search terms as this is mostly a problem of middle- and low-income countries, and excluded studies conducted in middle- and low-income countries which limits our results to high-income countries. Based on the searches conducted, as well as the cross-searching performed based on references, the authors are confident that the vast majority of relevant literature could be included. To the authors' knowledge, a standardized quality checklist has not been used to assess economic evaluations of the impact of visual impairment and blindness prior to inclusion into a systematic review to date. This further increases

the overall quality of our review. The study synthesis of reviewed literature was limited as no two studies used the same methodology, lacking a standardized definition and specification of cost components (see Appendix 2). Furthermore no two studies reported exactly the same outcomes or used the same sample population. These problems have been reported for cost-of-illness - or in this case cost-of-impairment – studies in other areas, and adherence to existing cost-of-illness study guidelines recommended.[11 12 46] Unfortunately, none of the reviewed studies seem to have adhered to any of the available international standards, and thus the overall comparability is limited. Similar to cost-of-illness studies in other areas, studies are summarized mostly descriptively, or at a high level of aggregation.[11] The same applies to the chosen categories of visual impairment used in all studies which differ considerably and further limit our ability to collate results (**Table 1**).The perspective (affected person, healthcare payer, societal) of the study was only described in a minority of studies, and as highlighted in the results section, most studies were conducted in the USA and Australia, making inferences to other countries and healthcare systems difficult. However, this is the only systematic review of the economic impact of visual impairment and blindness to date, highlighting the very broad economic impact and outlining the considerable scope a comprehensive economic evaluation in this area should ideally have.

In conclusion, visual impairment and blindness cause a considerable economic burden for affected persons, their care givers and society at large, which increases with the degree of visual impairment for all assessed cost categories as well as intangible effects. This review highlights a large amount of cost categories which should be considered in economic evaluations in eye health, and future cost-of illness or cost-of-impairment studies should adhere to available guidelines to improve comparability. The review highlights the considerable amount of resources spent on caring for visually impaired and blind persons in the absence of a cure.

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COMPETING INTERESTS

Authors declared that there are no competing interests.

AUTHORS' CONTRIBUTION

All authors contributed to the design of the review, KB and CS searched databases and extracted references, KB, CS and JK collated studies, and KB, JK and RF drafted the manuscript, all authors critically revised the manuscript.

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FIGURES

Figure 1: Flow chart of the literature search

Figure 2: Quality rating of included studies

Figure 3: Kappa-index per study

APPENDIX

Appendix 1: Quality checklist

Appendix 2: Cost categories reported in included studies.

Appendix 3: PRISMA checklist

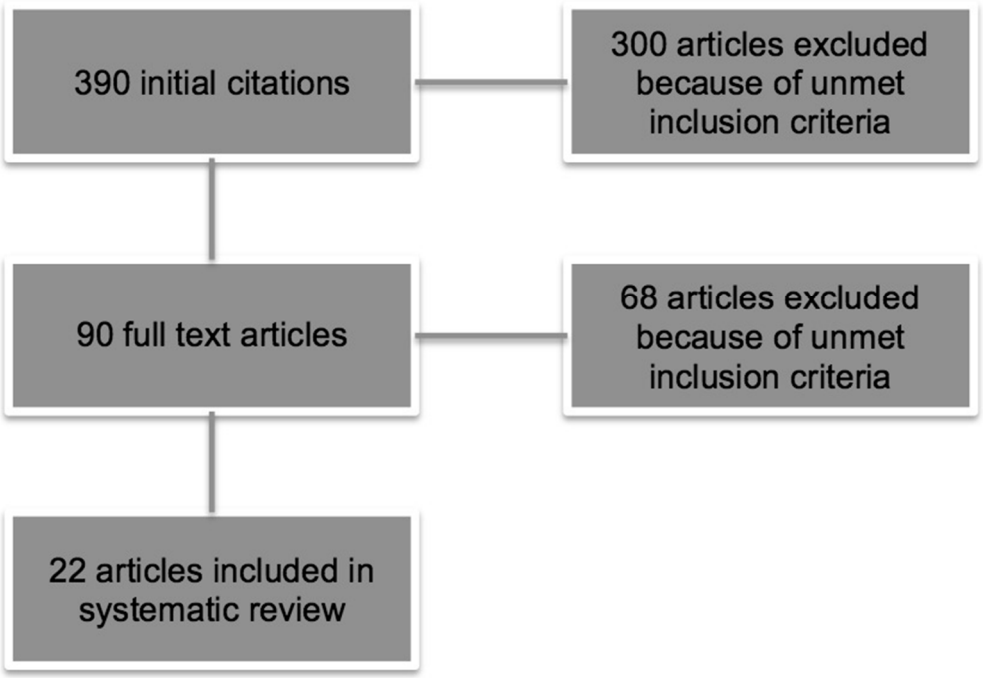

Figure 1: Flow chart of the literature search
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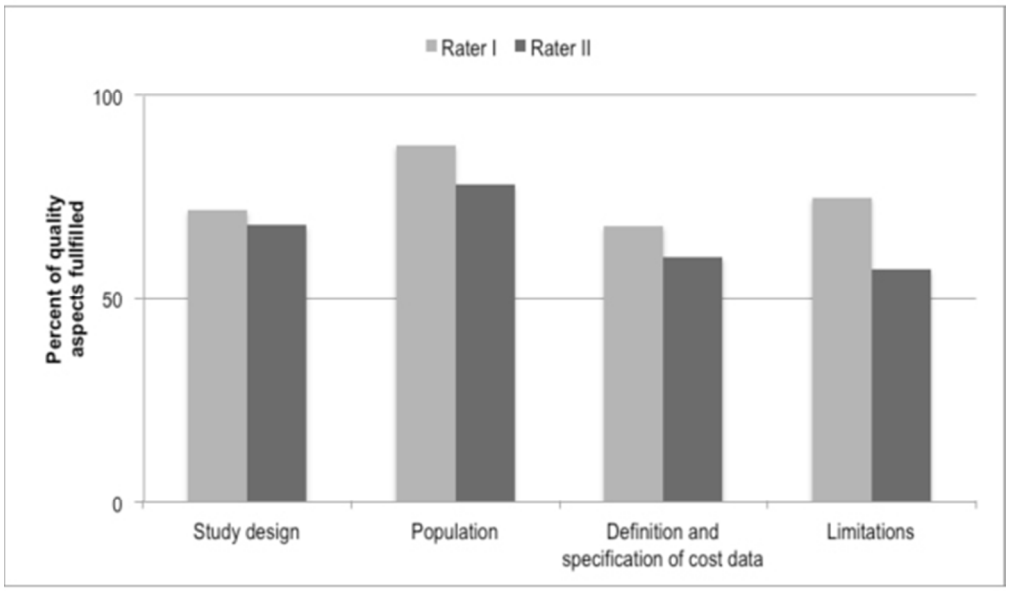

Figure 2: Quality rating of included studies
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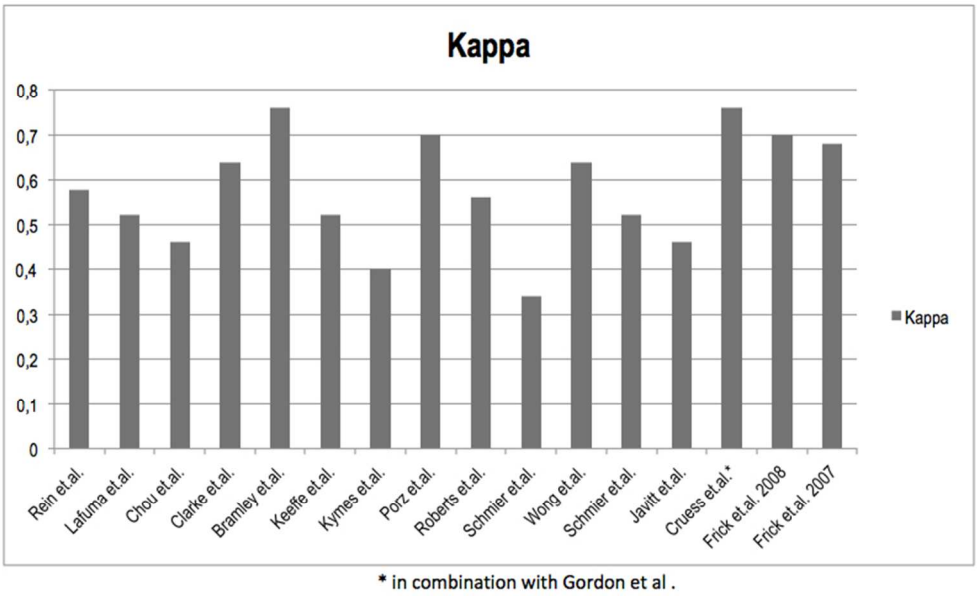

Figure 3: Kappa-index per study
286x174mm (72 x 72 DPI)

Study design

1. Was the issue of research defined in a well answerable form?
2. Was the economic relevance of the research stated?
3. Was the medical context described well?
4. Were the perspectives of the study clearly described and justified?
5. Was the type of economic evaluation defined?
6. Was the valuation method stated (top-down, bottom-up, prevalence-based, incidence-based)?

Population

7. Was the study population described in detail?
8. Was the method of data acquisition explained (including evaluation of health states and further benefits)?
9. In case of estimations from subgroups, were the subgroups defined clearly in the beginning of the study?

Definition and specification of cost data

10. Were sources of data for consumption of resources exposed?
11. Was a justification stated for the selection of data sources?
12. Were all relevant (relating to the present issue of research) cost units identified?
13. Was the quantity of consumption and relevant prices mentioned separately?
14. Was the source of all relevant cost units exposed?
15. Were costs valued appropriately?
16. Were currencies and prices specified?
17. Were currency translations and price adjustments stated in detail?
18. Were price adjustments for inflation and deflation conducted adequately?
19. Is the year of currency declared?
20. Were economic productivity changes stated separately?
21. Were the changes in economic productivity changes discussed referred to the issue of research?
22. Is the data for productivity losses implicated correctly into the analysis?

Limitations

23. Were limitations stated and discussed?
24. Is the quality of data discussed critically?
25. Are biases described and discussed in manner and degree?

		Bramley, T et al.	Brezin, A.P. et al.	Chou, S.-L et al.	Clarke, P. et al.	Cruess, A.F. et al.	Gordon, K.D. et al.	Frick, K.D. et al. 2008	Frick, K.D. et al. 2007	Javitt, J.C. et al.	Keeffe, J.E. et al.	Kymes, S.M. et al.	Lafuma, A. et al.	McCarty, C.A. et al.	Morse, A.R. et al.	Porz, G. et al.	Rein, D.B. et al.	Roberts, C.B. et al.	Schmier, J.K. et al.	Schmier, J.K. et al. (2006)	Vu, H.T.V. et al. (2009)	Wong, E.Y.H. et al.	Wood, J.M. et al.
direct medical costs																							
	physician, outpatient	x				x	x	x	x	x	x									x			
	hospital, inpatient	x			x	x	x	x		x	x		x				x*			x			
	rehabilitation	x					x	x					x										
	hospice	x									x												
	counselling				x																		
	prescription drugs, vitamins and other medications	x			x		x	x	x	x	x		x							x			x
	laboratory	x									x												
direct non-medical costs																							
living in institutions	excess of stay in institutions													x									
	long-term Care, nursing homes, skilled nursing facilty																	x					
support in homely environment	paid assistance / social support services / personal care services / home delivery services / home health care / independent living services / home-visit nursing				x				x					x			x	x	x				x
aids and devices	stick													x									
	white stick													x							x		
	guide dogs / guide dog registration				x									x				x					x
	walking aids													x									
	wheelchair													x									
	optical assistance / low vision devices				x		x	x		x				x			x				x		x
	television magnifier																				x		
	low vision equipments								x														x
	eye care products				x																		
	eye care research						x	x												x			
adaptation of living environment	furniture (toilet, kitchen, table, seat, bed, ramps, door opening device)													x									
	extra lights / lamps																				x		
	home modifications													x									
	move due to impairment													x									
communication and media	computer interface													x									
	software adapted for blindness				x									x							x		
	computer hardware / braille printer / talking books / tape recorder				x									x							x		
	technical assistance													x									
	national library service, library costs						x	x										x					
	american printing house large print materials																	x			x		
transportation	taxi				x																		x
	public transport				x																		x
	transportation service																				x		x
	travel reimbursement																x						
national budget	disabilty benefits and pension / aid to the blind																x						
	supplemental security income																	x					
	food stamps																	x					
	committee for purchase from people who are blind or severely disabled																	x					
	social security payments						x	x															
	accommodation allowance																x						
insurances	long-term care insurance																		x				
	social security disability insurance																	x					
other	education expenses				x																		x
	job training service																				x		
	recreational services																				x		
other direct costs																							
	informal care								x		x			x						x	x		x	
indirect costs																							
	productivity losses						x	x										x	x				
	decreased workforce participation, employment participation						x	x										x					
	decreased wages																	x					
	Tax losses						x	x										x	x				
	loss of family revenue													x									
	loss of income			x										x									
	time-losses of caregivers						x	x						x									
	absenteeism/presenteeism						x	x											x				
intangible effects																							
		x	x				x	x		x						x		x			x		x

* inpatient costs were reported in days not in cost units

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3-4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3-4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	3
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	3-4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3-4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	3-4, 7-10
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Not done
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	3-4
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Not done

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Not done
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not done
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5-6
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7-10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	NA
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	NA
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	19-22
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	21-22
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	19-22
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	22

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

THE ECONOMIC BURDEN OF ~~SEVERE~~ VISUAL IMPAIRMENT AND BLINDNESS - A Systematic Review

Juliane Köberlein[1], Karolina Beifus[1*], Corinna Schaffert[1], Robert P. Finger[2]*

Contact Address:
Juliane Köberlein, PhD
Karolina Beifus
Department of Health Economics und Health Care Management
University of Wuppertal
Rainer-Gruenter-Str. 21
42119 Wuppertal
Tel: +49 (0)202 439 1388
Fax: +49 (0)202 439 1384
e-mail: koeberlein@wiwi.uni.wuppertal.de

[1]Department of Health Economics und Health Care Management
University of Wuppertal
Germany

[2] Department of Ophthalmology, University of Bonn, Bonn, Germany
and
Centre of Eye Research Australia, Royal Victorian Eye and Ear Hospital,
University of Melbourne, Melbourne, Australia

*JK and KB contributed equally to this article

Keywords: visual impairment, blindness, costs of illness, health economics
Word Count: 3450

ABSTRACT

Objectives

Visual impairment and blindness (VI&B) cause a considerable and increasing economic burden in all high income countries due to population ageing. Thus we conducted a review of the literature to better understand all relevant costs associated with VI&B and to develop a multi-perspective overview.

Design

Systematic review. Two independent reviewers searched relevant literature and assessed studies for inclusion and exclusion criteria as well as quality. ~~aspects~~

Eligibility criteria for included studies

Interventional, non-interventional and cost of illness studies, conducted prior to May 2012, investigating ~~on~~ direct and indirect costs as well as intangible effects related to visual impairment and blindness~~,~~ were included.

Methods

We followed the PRISMA statement approach to identify relevant studies. A meta-analysis was not performed~~,~~ due to the variability of reported cost categories and varying definition of visual impairment.

Results

A total of 22 studies were included. Hospitalization and use of medical services around diagnosis and treatment at the onset of VI&B were the largest contributor to direct medical costs. Mean annual expenses per patient were found to be US$ PPP 12,175-14,029 for moderate visual impairment, US$ PPP 13,154-16,321 for severe visual impairment, and US$ PPP 14,882-24,180 for blindness, almost twofold the costs for non-blind patients. Informal care was the major contributor to other direct costs, with the time spent by caregivers increasing from 5.8 hours/week (or US$ PPP 263) for persons with vision > 20/32 up to 94.1 hours/week (or US$ PPP 55,062) for persons with vision ≤ 20/250. VI&B caused considerable indirect costs due to productivity losses, premature mortality, and dead weight losses.

Conclusions

VI&B cause a considerable economic burden for affected persons, their care givers and society at large, which increases with the degree of visual impairment. This review provides insight into the distribution of costs and the economic impact of VI&B.

ARTICLE SUMMARY

Article Focus

- To explore all relevant costs associated with visual impairment and blindness.

Key Message

- We could demonstrate a considerable impact of visual impairment and blindness in terms of the associated direct and indirect costs, as well as intangible effects such as loss of well-being, independence and excess mortality.
- A large proportion of the direct costs reported in reviewed studies are not directly related to eye-related medical care, but to falls and other accidents due to visual impairment, exacerbation of diabetes due to a reduced ability to self-manage, depression related to loss of vision and further excess morbidity.
- All identified costs as well as intangible effects correlated with the degree of visual impairment with highest expenditures associated with blindness.

Strengths and limitations

- This is the first ~~review exploring an~~ international and multi-perspective overview of costs and intangible effects associated with visual impairment as well as blindness.
- The study synthesis of reviewed literature was limited as no two studies used the same methodology, reported exactly the same outcomes or used the same sample population. Therefore a meta-analysis ~~was~~ could not be conducted.

INTRODUCTION

Visual impairment and blindness are foremost a problem of older age in all high-income countries, and constantly increasing due to the ageing of populations ~~in these countries~~ [1]. Globally, the burden of disease related to vision disorders has increased by 47% from 12,858,000 Disability Adjusted Life Years (DALYs) in 1990 to 18,837,000 DALYs in 2010 [2]. In high-income countries, ~~H~~health-related quality of life in severely visually impaired persons has been shown to be similar or even lower and emotional distress higher compared with other serious chronic health conditions such as stroke or metastasised solid tumours [3]. Blindness and visual impairment impact not only the affected individual but also the family, caregivers and the community, leading to a significant cost burden. In Australia, the overall cost placed visual disorders seventh among diseases, ahead of coronary heart disease, diabetes, depression, and stroke in terms of economic burden on the health system [4]. As demands on healthcare continue to increase in all high-income countries, economic evaluations of disease, impairment and interventions have also become increasingly important [5]. This necessitates a clear understanding of all aspects of the direct and indirect costs and intangible effects related to blindness and severe visual impairment, as almost all interventions in this area are aiming to prevent these and are often measured as an incremental cost effectiveness ratio (ICER), i.e. the difference in cost compared to the difference in effectiveness. Similarly, faced with increasing demand and limited resources in healthcare, these resources need to be prioritized which again calls for a clear understanding of the economic impact of a disease or disorder. ~~-~~Against this background we conducted a systematic review of the literature, collating all data available on the economic impact of visual impairment and blindness.

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METHODS

The systematic review was conducted as suggested in the ~~We followed the~~ PRISMA statement which aims to improve the quality of systemtic reviews by providing guidance and a 27-item checklist to aid in ~~statement approach to conduct this systematic review. This statement consists amongst others of a 27 item checklist and intends to help authors of systematic reviews to~~ structure~~e~~ing ~~their~~ methods and improving the~~e~~ reporting of results. It focuses on randomized trials, but can also be used as a basis for reporting systematic reviews of other types of research, for example health economic evaluation studies. However the checklist should not be used as a quality assessment instrument to measure the quality of ~~a systematic review~~included studies or the performed systematic review [47]. The completed ~~For higher transparency Appendix 3 displays the~~ PRISMA checklist ~~which we completed alongside our review process~~for this review can be found in appendix three.

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Literature search

All economical and medical databases were searched from May to June 2012 via PubMed and OVID using the following terms:

"low vision", "visual impairment", "visually impaired", "blindness", "blind", "visual loss", "costs", "costs of illness".

Subsequently, a second search was conducted using the main causes of visual impairment and blindness. Search terms were: *"low vision", "visual impairment", "visually impaired", "blindness", "blind", "visual loss", "costs"* combined with "*age-related macular degeneration", "glaucoma", "diabetic retinopathy", "cataract", "corneal opacities", "childhood blindness"* separated by *"or".*

Supplemental sources including references contained in identified articles were used in addition.

Two independent researchers screened identified articles using the following inclusion or exclusion criteria:

Inclusion:

- ~~-~~data for direct and indirect costs related to visual impairment and blindness.~~,~~ Cost-of-illness – or in this case cost-of-impairment – studies can be divided into disease-specific and general studies. Both types of studies were included if they contained relevant data.~~,~~
- ~~-~~
- ~~s~~
- ~~s~~tudies with outcomes related to intangible effects due to visual impairment and blindness,
- overall data for burden of illness related to affected persons and carers.

Exclusion:

- costs pertaining to underlying diseases only with no specification of visual impairment levels,
- economic studies conducted in developing countries.

As we were interested in the burden of VI&B in high-income countries only, we ~~We have ex~~cluded economic studies conducted in developing countries. Health services provision and treatment options differ vastly between high-income and middle- or low-income countries, making a comparison of cost categories unfeasible. ~~because generally treatment pathways show a high degree of heterogeneity and assess to care is highly different. Both aspects make comparisons to developed countries more difficult.~~

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~~Data extraction strategy &~~ Cost classification

All included articles were assessed as to which cost aspects they reported. Broadly, costs were divided into direct costs, indirect costs, and intangible effects [6].

Direct costs are defined as the actual expenses related to an illness and contain medical costs, non-medical costs and other direct costs [5]. Medical costs measure the cost of resources used for treating a particular illness. Non-medical costs are costs caused by the disease but not attributed to medical treatment. In case of visual impairment and blindness these are supporting services, assistive devices, home care, residential care or transportation (travel expenses). Other direct costs comprise informal care, time spent in treatment by patients or caregivers, or time spent in rehabilitation, training, self-help groups or preventative activities [5].

Indirect costs are defined as the value of lost output caused by reduced productivity due to illness or disability [7]. Both, patients and caregivers are affected by indirect costs due to allowances (financial support for income, residence, benefits), productivity losses (absenteeism, salary losses, part-time employment, loss of work), and dead weight losses ~~or~~ as well as years of life lost.

Dead weight loss, also known as an excess burden, is not a clearly defined concept. In a purely economic sense, deadweight loss describes the costs to society created by market inefficiency. In the context of our study we refer to it as an excess financial burden on society caused by VI&B.

~~Dead weight loss is defined …~~

Intangible costs or effects refer to the burden of illness of affected persons and caregivers, and comprise amongst others loss of well being or loss of quality of life. It can be captured using questionnaires and expressed in DALYs. As this aspect of costs is difficult to quantify, DALYs or other measures of intangible effects are ~~rarely~~ rarely assigned a monetary value.

Commonly, cost categories considered in a particular study depend on the perspective the study is conducted from, i.e. a healthcare payer's (direct medical and non-medical costs only) or the patient's perspective, or a societal perspective (all costs).

As cost categories varied considerably between all~~Furthermore~~ cost-of-illness studies ~~were varying within reported cost components~~all different direct and indirect cost categories were listed in appendix two prior to being categorized into our broader categories as outlined above. ~~For example whereas one study reported all components of direct costs another cost of illness study described only outpatient cost and rehabilitation expenditures. To achieve a transparent reporting of costs we provide in **Appendix 2** a schedule of all included studies dealing with direct and indirect costs and their reported cost categories.~~

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~~Cost-of-illness – or in this case cost-of-impairment – studies can be divided into disease-specific and general studies. Both types of studies were included if they contained relevant data.~~

Quality of included studies

A checklist, based on the assessment tool of Emmert and colleagues [8] and extended by several questions covering relevant cost-of-illness aspects (see **Appendix 1**), was generated to assess the overall quality of ~~all 16~~ included studies ~~dealing with~~reporting direct or indirect costs of illness. The checklist contained sections on the study design, population, definition and specification of cost data and its limitations, including a total of 25 questions. Studies were rated from 0 – 100 for each of these categories. Two independent reviewers conducted the assessment and interrater-reliability was assessed using Kappa (κ_n) as suggested by Brennan and Prediger [9] for every study. The interpretation of agreement was based on the agreement scale by Landis and Koch [10]. ~~According to these authors Kappa values~~which indicates fair agreement at Kappa levels between 0.21 and 0.40, ~~-~~ moderate agreement ~~are correlated to a fair agreement, values~~ between 0.41 and 0.60, substantial ~~to a moderate, values~~ between 0.61 and 0.80 and almost perfect agreement ~~to a substantial and a score of more than~~ 0.81 ~~to an almost perfect agreement~~and above.

Conversion of Cost-of-illness study results

For better comparison of costs across studies, the data were transformed: (1) costs were inflated to 2011 using country specific gross domestic product deflator, which takes fluctuating exchange rates, different purchasing power of currencies and the rate of inflation into account [11,12], and (2) converted to USD using purchasing power parities (PPP) [13]. Purchasing power parities account for differences in price levels between countries, and convert local currencies into international dollars taking purchasing power of different national currencies into account and eliminating differences in price levels between countries. The transformed values are presented in million units (million US$-PPP) for total expenditures reported and in US$-PPP for costs per person.

RESULTS

The search yielded a total of ~~389~~ 390~~400~~ articles. After applying all inclusion and exclusion criteria, 22 studies were included in the systematic review (**Figure 1**). Altogether there were nine~~eight~~ studies conducted in the USA, six studies conducted in Australia, two studies from France and Canada, and one study from each of the following countries: Germany, ~~, Canada~~,

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the UK, Japan, India and one study with a global perspective. All included studies are summarized in **Table 1.**

Table 1: Characteristics of included studies

Author	Country	Design and Population	Cost components evaluated	Objective	Vision categories
Bramley et al. 2008 [14]	USA	retrospective cohort analysis of nationally representative Medicare 5% random sample; patients older than 65 years with newly diagnosed glaucoma; regression analysis	direct medical costs, intangible effects	to measure costs of visual impairment due to progressing glaucoma	no vision loss, moderate vision loss, severe vision loss, blindness
Brezin et al. 2005 [15]	France	national survey of a random stratified sample; 16, 945 affected persons answered questionnaires; 4,091 caregiver answered questionnaires;	indirect costs; intangible effects	to document the prevalence of self-reported visual impairment and its association with disabilities, handicaps, and socioeconomic consequences.	blind or light perception only, low vision, other visual problems, and no visual problems
Chou et al. 2006 [16]	Australia	150 persons completed cost diaries for 12 months and were evaluated; costs categorized into four sections: 1. medicines, products and equipment, 2. health and community services, 3. informal care and support, 4. other expenses	direct medical costs, direct non-medical costs	to describe and evaluate the process used to collect personal costs (out-of pocket) associated with vision impairment using diaries	≥ 6/12with restricted fields; <612–6/18; <6/18–6/60; <6/60–3/60; <3/60
Clarke et al. 2003 [17]	UK	regression-based approach to estimate the short-term and long- term annual hospital and non-hospital costs associated with seven major diabetes-related complications in the UK Prospective Diabetes Study (UKPDS): myocardial infarction (MI); stroke, angina or ischemic heart disease (IHD); heart failure; blindness in one eye; amputation and cataract extraction; 5102 patients with newly diagnosed type 2 diabetes	direct medical costs	to estimate the immediate and long-term healthcare costs associated with seven diabetes-related complications	blind in one eye
Cruess et al. 2011 [18] (in combination with Gordon et al. 2011 [19])	Canada	prevalence-based approach, population projections for the whole population were compiled using data from the Statistics Canada 2006 Population Projections for Canada, Provinces and Territories 2001-2031	direct medical costs, direct non medical costs, indirect costs, intangible effects	to investigate costs of vision loss in Canada to inform healthcare planning	no details
Frick et al. 2008 [20]	USA	retrospective cohort study; patients with blindness matched to non-blind selected from managed care claims database	direct medical costs	to evaluate total and condition related charges incurred by blind patients in a managed care population in the US	blind, non blind

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Frick et al. 2007 [21]	USA	data from the medical expenditure panel survey 1996 – 2002 for adults older than 40 years with visual impairment or blindness	direct medical costs; direct non medical costs; other direct costs; intangible effects	to estimate the economic impact of visual impairment and blindness in persons aged 40 years and older in the US	visual impairment; blindness
Javitt et al. 2007 [22]	USA	retrospective cohort analysis of nationally representative Medicare 5% random sample, excluding Medicare managed-care enrollees	direct medical costs	to assess and identify the costs to the Medicare program for patients with either stable or progressive vision loss and estimate the impact on eye-related and non-eye related care	mild, moderate, severe vision loss (VA ≤20/200), blindness (VA ≤ 20/400)
Keeffe et al. 2009 [23]	Australia	114 participants of the Melbourne Visual Impairment Project completed diaries for 12 month; the burden of caregiver and opportunity costs for losses in work time was calculated (in combination with methods and data from Chou et.al.)	other direct costs	to analyse prospective data on providers, types and costs of care for people with impaired vision in Australia	VA < 20/40
Kymes et al. 2010 [24]	USA	decision analytic approach; Markov model to replicate health events over the remaining lifetime of someone newly diagnosed with glaucoma	incremental costs of illness	to evaluate the incremental cost of primary open-angle glaucoma considering both visual and non-visual medical costs over a lifetime	no details
Lafuma et al. 2006 [25]	France	interviews with sample population (665,000) from a national survey of persons living in institutions or in the community (with caregiver at home)	direct non medical costs, other direct costs, indirect costs	to estimate the annual national non medical costs due to visual impairment and blindness	blind (light perception), low vision (better than light perception??, low vision, and controls
McCarty et al. 2001 [26]	Australia	population-based study; evaluation of the data from Melbourne Visual impairment project; population ≥40 years was analyzed in causes of death	intangible effects	to describe predictors of mortality in the 5 year follow up of Melbourne Visual impairment project;	visual acuity < 6/12
Morse et al. 1999 [27]	USA	2.552.350 discharges from hospital in state of NY -> 5.764 patients had visual impairment	direct medical costs	to assess whether visual impairment contributes to average length of stay within inpatient care facilities	no details
Porz et al. 2010 [28]	Germany	retrospective study of 66 patients using a cost and a vision-related quality of life questionnaire (Impact of vision Impairment	direct non medical costs, intangible ef-	to capture costs for medicines, aids and equipment, support in everyday life and social bene-	Visual acuity (VA) ≥ 0,3, Visual acuity < 0,3

		questionnaire)	fects	fits, as well as vision- related quality of life	
Rein, et al. 2006 [29]	USA	private insurance and Medicare claims data	direct non medical costs, indirect costs	to estimate the societal economic burden and the governmental budgetary impact of the following visual disorders among US adults aged 40 years and older: visual impairment, blindness, refractive error, age-related macular degeneration, cataracts, diabetic retinopathy, and primary open angle glaucoma	refractive errors
Roberts et al. 2010 [30]	Japan	prevalence-based approach; adopted using data on visual impairment, the national health system, and indirect costs	direct medical costs, direct non medical costs, indirect costs , ~~other direct costs~~ and intangible effects	to quantify the total economic cost of visual impairment in Japan	low vision 6/12-6/60; blind < 6/60; visual impairment = >6/12
Schmier et al. 2009 [31]	USA	using a questionnaire that included items on demographic and clinical characteristics and on the use of services, assistive devices, and caregiving; 761 persons were included	direct non medical costs, other direct costs	to assess the use of devices and caregiving among individuals with diabetic retinopathy and to evaluate the impact of visual acuity on use	group 1 (20/20 or better), group 2 (20/ 25–20/30), group 3 (20/40–20/50), group 4 (20/60–20/70), or group 5 (20/80 or worse)
Schmier et al. 2006 [32]	USA	survey with interviews on Daily Living Tasks Dependent on Vision Questionnaire;803 respondents	other direct costs,	to assess the patient-reported use of caregiving among individuals with age-related macular degeneration (AMD) and evaluation of impact of visual impairment level on this use	1. VA > 20/32; 2. VA 20/32 - > 20/50; 3. VA 20/50 - >20/80; 4. VA 20/80 - > 20/150; 5. 20/150 - >20/250; 6. VA ≤ 20/250
Vu, et al. 2005 [33]	Australia	stratified random sample of 3040 participants from the Mel-bourne Visual Impairment Project; 2530 attended the follow-up study	intangible effects	to investigate whether unilateral vision loss reduces any aspects of quality of life in compar-ison with normal vision	unilateral and bilateral vision loss (correctable and non-correctable)
Wong et al. 2008 [34]	Australia	prospective cohort study; participants of any age to complete a diary for 12 months answering four categories: 1) medicines, products and equipment, 2) health and community services, 3) informal care and support and 4) other expenses	direct costs (medical and non medical), other direct costs	to determine the personal out-of-pocket costs of visual impairment and to ex-amine the expendi-ture pattern related to eye diseases and the severity of visual impairment	visual acuity ≥6/18 with constricted. fields; < 6/18-6/60; < 6/60

Wood et al. 2011 [35]	Australia	76 community-dwelling individuals with a range of severity of AMD; completing a diary for 12 month	intangible effects; costs of adverse events	to explore the relationship between AMD, fall risk, and other injuries and identified visual risk factors for these adverse events	binocular visual acuity, contrast sensitivity, and merged visual fields

All 17~~6~~ of 22 studies dealing with direct or indirect costs of illness were rated above 50 for all four main quality aspects, indicating a sufficient level of quality, and consequently were included into the review (see **Figure 2**). The interrater-reliability was consistently high and only a few discrepancies had to be settled by a discussion between the two raters. Kappa scores ranged from 0.34 to 0.76 (**Figure 3)**.

Of all included studies ~~eleven~~ twelve captured direct medical cost, ten~~seven~~ direct non-medical costs, and six other direct costs. ~~Seven~~ Six studies report data on indirect costs and ten on intangible effects. All cost components reported by studies within each cost category are summarized in **Appendix 2,** highlighting the considerable variability in obtaining and reporting cost aspects related to visual impairment and blindness between all studies.

Direct medical costs

Direct medical costs occurred mostly due to hospitalization, the use of medical services and medical products, and were reported either as incremental costs or, in some studies, provided as the length of hospital stay (**Table 2**).

At the onset of visual impairment and blindness, the two major contributors to direct medical costs are hospitalizations and costs due to increased use of medical services around diagnosis and treatment [17 18 20 21 27 30]. Costs related to recurrent hospitalizations and ongoing, but less frequent use of medical services, remain major cost components in persons with visual impairment and blindness in the long term. Costs related to drugs, however, did not emerge as a major direct cost factor [16 34]. All identified costs correlated with the degree of visual impairment leading to the highest expenditures being associated with blindness. The considerable differences in study methods and reported outcomes makes a head to head comparison of results by study or country or aggregation of data in terms of meta-analyses for direct medical costs very difficult. Several studies based on representative samples of Medicare beneficiaries in the USA reported mean annual expenses per patient to be US$ PPP 12,175-14,029 for moderate visual impairment, US$ PPP 13,154-16,321 for severe visual impairment, and US$ PPP 14,882-24,180 for blindness, which is almost a 100% excess of the estimated mean annual cost for non-blind patients at the upper end of the range (**Table 2**).

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Table 2: ~~Outcomes~~ Results for direct medical costs.

Study	*cost outcomes*	*US$ PPP in 2011*
Bramley et al. 2008[14]	annual costs per patient compared in degrees of vision impairment from no vision loss and onset of moderate or severe vision impairment or blindness	
	no vision loss **US$ 8,157**	**8,695**
	moderate visual impairment **US$13,162**	**14,029**
	severe visual impairment **US$ 15,312**	**16,321**
	blindness **US$ 18,670**	**19,900**
Frick et al. 2007[21]	total expenditures on health care in blind and visual impaired persons ≥ 40 years	
	blindness individual excess medical expenditures **US$ 2,157**	**2,621**
	total excess medical expenditures **US$ 2,454 million**	**2,982 million**
	visual impairment individual excess medical exp. **US$ 1,037**	**1,260**
	total excess medical expenditure **US$ 2,661 million**	**3,233 million**
	total annual monetary impact for VI and blindness (primary owing to home care) **US$ 5,100 million**	**6,197 million**
Frick et al. 2008[20]	cohort with legally blind patients matched to equal sample cohort with non-blind patients (annual costs per patient in the first year)	
	blind persons mean costs **US$ 20,677**	**24,180**
	median costs **US$ 6,854**	**8,015**
	non blind mean costs **US$ 13,321**	**15,578**
	median costs **US$ 371**	**434**
Javitt et al. 2007[22]	patients with normal vision compared to moderate or severe visual impairment or blindndess regarding eye-related and non-eye-related care	
	mean annual costs for eye-related care	
	normal vision **US$ 370**	**445**
	moderate visual impairment **US$ 345**	**415**
	severe visual impairment **US$ 407**	**490**
	blindness **US$ 237**	**285**
	mean annual values for non eye related costs	
	normal vision **US$ 7,928**	**9,537**
	moderate visual impairment **US$ 2,193**	**2,638**
	severe visual impairment **US$ 3,301**	**3,971**
	blindness **US$ 4,443**	**5,345**
Kymes et al. 2010[24]	lifetime costs of POAG (primary open-angle glaucoma) to non POAG patients	
	incidence costs **US$ 41,039**	**46,456**
	prevalence costs **US$ 19,268**	**21,811**
	drug costs **US$ 7,098**	**8,035**
	incremental incidence costs **US$ 27,326**	**30,933**
	incremental prevalence costs **US$ 5,555**	**6,288**
	incremental drug costs **US$ 4,179**	**4,731**
Morse et al. 1999[27]	extension of average length of stay in hospitals due to visual impairment	
	5.2 days longer stay	
Cruess et al. 2011[18]	financial burden of vision loss to Canadian health care system	
	hospital **CAN$ 1,497.7 million**	**1,934.72 million**
	physicans **CAN$ 866.5 million**	**1,119.34 million**
	vision care **CAN$ 3,483.7 million**	**4,500.24 million**
Chou et al. 2006[16]	the out-of-pocket expenses for medicines and products per person annually	
	AUS $ 206	**456**
Wong et al. 2008[34]	annual costs for medicine and products per patient	
	Visual acuity (VA) ≥ 6/18 with restr. field **AUS$ 285**	**632**
	< 6/18 – 6/60 = **AUS$ 233**	**516**
	< 6/60 = **AUS$ 147**	**326**
Clarke et al. 2003[17]	short-term and long-term annual hospital and non-hospital costs due to major diabetes-related complications	
	blindness in one eye (in 20% of patients) **£ 4,370**	**4,086**
	mean hospital in-patient costs **£ 872**	**815**
Roberts et al. 2010[30]	total economic costs of visual impairment	
	General medical expenditure **US$ 8.102 billion**	**8,636 million**
	Inpatient **US$ 1.808 billion**	**1,927 million**
	Outpatient **US$ 6.294 billion**	**6,709 million**
	Drugs **US$ 1.395 billion**	**1,487 million**

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Direct non medical costs

Assistive devices and aids, home modifications, costs for health care services like home-based nursing or nursing home placements were the major contributors to direct non-medical costs (**Table 3**). With worsening visual acuity direct non-medical costs for support services and assistive devices increased, from US$ PPP 53.90 for a person with visual acuity ≥ 20/20 up to US$ PPP 608.71 for a person with visual acuity ≤ 20/80 [31]. Nursing home-placements and professional care costs incurred the highest expenditures followed by domestic modifications. These costs however, were highest initially shortly after the loss of vision and in the majority only ~~a one off~~incurred once (**Table 3**).

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Table 3: ~~Outcomes~~ Results for direct non medical costs.

Study	*cost outcomes*	*US$ PPP in 2011*
Frick et al. 2007[21]	total health care expenditures for adults ≥ 40 years (excess costs)	
	blindness home health agencies **US$ 4,988**	**6060**
	low vision home health agencies **US$ 3,105**	**3,773**
	expenditures for private home health providers was **US$ 1,200 more** for blind than visually impaired persons	
Rein et al. 2006[29]	total annual costs for visual impairment and blindndess for adults ≥40 years	
	nursing placements of **US$ 10.96 billion**	**12,818 million**
	guide dogs **US$ 0.062 billion**	**72.5 million**
	independent living **US$ 0.029 billion**	**33.9 million**
Schmier et al. 2009[31]	annual costs for use of services and devices related to the degree of visual impairment per person	
	devices (glasses, sticks, computer software, etc. **US$ 109.79**	**120**
	rehabilitation **US$ 7.09**	**7.78**
Chou et al. 2006[16]	annual costs for health and community services per person	
	health care, home help, personal affairs, personal care, communication, transport, social activities **AUS $ 872**	**1,932.50**
	expenditure for taxi, public transport, education expenses, guide dog **AUS $ 321**	**711**
Cruess et al. 2011[18]	financial burden of vision loss to Canadian health care system	
	care costs **CAN$ 693 million**	**895.21 million**
	aids and modification **CAN$ 305 million**	**394 million**
Wong et al. 2008[34]	annual personal costs for health and community services and other expenses per patient	
	median total costs **AUS$ 1,768**	**3,919**
	mean total costs **AUS $ 3,376**	**7,482**
Roberts et al. 2010[30]	total economic costs of visual impairment	
	meal service on admission **US$ 0.149 billion**	**158.81 million**
	home-visit nursing **US$ 0.013 billions**	**13.86 million**
	health care administration **US$ 0.475 billion**	**506.30 million**
	Community care **US$ 6.608 billion**	**7,043 million**
	Institutional care **US$ 0.238 billion**	**253.68 million**
	Vision aids **US$ 0.2 billion**	**213.18 million**
Porz et al. 2010[28]	financial and psychological burden of retinal diseases divided into health economic relevant categories; annual expenses per person	
	aids for VA ≥ 0.3 = **€ 96.65**	**77.39**
	VA < 0.3 = **€ 83.58**	**66.92**
	personal assistance VA ≥ 0.3 = **€ 454.96**	**364.28**
	VA < 0.3 = **€ 667.77**	**534.68**
Lafuma et al. 2006[25]	national survey with estimation on costs of low vision and blindness for persons living in institutions[1] or in the community [2] (declared annually per person and total expenditures)	
	low vision / **blindness**	**low vison** / **blindness**
	home modifications [1] **€ 36.65 pp/ year** / **€ 926.96 pp/ y**	**37.87** / **957.90**
	€ 3.27 million total / **€ 9.63 million total**	**3.375 million** / **9.95 million**
	devices [1] **€184.14 pp/ year** / **€ 387.35 pp/ y**	**190.29** / **400.28**
	€ 16.43 million total / **€4.03 million total**	**16.98 million** / **4.165 million**
	home modification [2] **€ 42.23 pp/ y** / **€ 121.12 pp/y**	**43.64** / **125.16**
	€ 16.43 million total / **€ 7.02 million total**	**16.98 million** / **7.25 million**
	devices [2] **€ 376.39** / **€ 363.14 pp/ y**	**388.95** / **375.26**
	€ 420 million total / **€ 21.04 million total**	**434.02 million** / **21.74 million**
	paid assistance [2] **€ 1,463.59 pp/ y** / **€ 6750.66 pp/ y**	**1,512.44** / **6,976**
	€ 1,635 million / **€ 391 million total**	**1,690 million** / **404 million**

Other direct costs

Six of the included studies reported costs caused by informal care. Time spent on caring for or assisting visually impaired persons was related to the degree of visual impairment, with blind persons requiring the most assistance. The time spent by caregivers ranged from 5.8 hours per week for a person with a visual acuity of > 20/32 and a cost of US$ PPP 263 up to 94.1 hours per week and costs of US$ PPP 55,062 for persons with a visual acuity of ≤ 20/250 [32]. All studies differed slightly as to the nature of direct costs assessed. Some studies reported on governmental, out-of-pocket expenses as well as opportunity costs, others considered only one or two of these. The wide range of time and resources spent on informal care provision demonstrates the broad economic impact and considerable burden of informal care provision with concurrent expenses at a personal and societal level. Again, reported cost aspects and methodologies differ considerably, with, for example, Keeffe and colleagues[23] reporting out-of-pocket expenses and Lafuma and colleagues[25] reporting time spent on caring using an hourly rate. The multitude of differing approaches in each study does not allow for a head-to-head comparison but gives a comprehensive impression of the complex cost situation and highlights the importance of providing assistance to visually impaired and blind persons (**Table 4**).

Table 4: ~~Outcomes~~ Results for other direct costs.

Study	*cost outcomes*		*US$ PPP in 2011*	
Frick et al. 2007[21]	the economic impact of blindness and visual impairment on adults ≥ 40 years			
	blindness causes mean individual excess informal care days 5.2			
	visual impairment causes mean individual excess informal care days 1.2			
	blindness causes total excess informal care costs **US$ 242 million**		**294.03 million**	
	visual impairment total excess informal care costs **US$ 124 million**		**150.66 million**	
Schmier et al. 2009[31]	annual costs for caregiver time spent in supporting patients with macular degeneration			
	US$ 5,038		**5,526**	
Schmier et al. 2006[32]	annual costs for quantity of caregiver time addicted to the degree of visual impairment per patient diabetic retinopathy			
	mean 5.7 hours a day 5 days a week			
	overall amount of **US$ 9572.77**		**11,194.40**	
Keeffe et al. 2009[23]	personal out-of-pocket expenses regarding the burden of caregiver			
	median annual opportunity costs for worktime spent on caregiving **AUS$ 915**		**2,244.60**	
Wong et al. 2008[34]	annual median personal costs for informal care and assistance in activities of daily living			
	e.g. meal preparing, dressing, shopping, transportation **AUS$ 2,911**		**6,451**	
Lafuma et al. 2006[25]	national survey with estimation on costs for time caregiver spent on of low vision and blindness for persons in the community (declared annually per person and total expenditures)			
	low vision	**blindness**	**low vison**	**blindness**
	informal care **€ 1881.80 pp/ year**	**€ 7,316.26 pp/ y**	**1,944**	**7,560.48**
	€ 2,101 million total	**€ 424 million total**	**2,171 million**	**438 million**

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Indirect costs

Studies of indirect costs demonstrate high expenditures related to productivity losses, changes in employment (employer and/or area of work), loss of income, premature mortality, and dead weight losses (**Table 5**). Received social allowances were detailed in one study, but not counted towards the overall costs as they were considered transfer costs.[28] One study included the loss of caregivers' time, which is spent on support in terms of productivity loss but also as a loss of personal time and time to engage in leisure activities.[25] Equal to other cost components indirect costs correlated with the degree of visual impairment, with the highest indirect costs reported for blind persons. Compared to all other cost categories indirect costs due to productivity losses, lower employment rates and losses of income in patients as well as caregivers caused the highest economic burden. Annual estimates of productivity losses and absenteeism due to visual impairment and blindness in the USA and Canada range from US$ PPP 4,974-5,724 million, and are estimated to be US$ PPP 7,367 million for an overall decrease in workforce participation in the USA (**Table 5**).

Table 5: ~~Outcomes~~ Results for indirect costs

Study	*cost outcomes*		*US$ PPP in 2011*	
Rein et al. 2006[29]	total annual indirect costs caused by visual disorders			
	decreased work force participation **US$ 6.3 billion**		**7,367 million**	
	decreased wages **US$ 1.73 billion**		**2,023 million**	
Roberts et al. 2010[30]	indirect costs for visual impairment and blindness			
	productivity losses **US$ 4.667 billion**		**4,974 million**	
	lower employment **US$ 4.230 billion**		**4,509 million**	
	absenteism **US$ 0.384 billion**		**409 million**	
	premature mortality **US$ 0.053 billion**		**56.5 million**	
	dead weight losses **US$ 1.609 billion**		**1,715 million**	
Lafuma et al. 2006[25]	national survey with estimation on indirect costs for losses of income in persons with low vision and blindness living in institutions [1] or in the community [2] (declared annually per person and total expenditures)			
	low vision	**blindness**	**low vison**	**blindness**
	losses of incomes [1] **€ 120.00 pp/y**	**€ 180.00 pp/y**	**124**	**186**
	€ 10.71 million total	**€ 1.87 million total**	**11.07 million**	**1.93 million**
	losses of incomes [2] **€ 3,912.00 pp/y**	**€ 3,168.00 pp/y**	**4,042**	**3,273**
	€ 4,369 million total	**€ 183.6 million total**	**4,515 million**	**189.72 million**
Brezin et al. 2005[15]	prevalence and burden of blindness, lo sion and visual impairment in the French community (estimation of monthly average value)			
	low vision	**blindness**	**low vison**	**blindness**
	social allowances **€ 87**	**€ 364**	**92**	**384**
	total household income **€ 1,525**	**€ 1,587**	**1,607**	**1,673**
	household income no VI **€ 1,851**		**1,951**	
Cruess et al. 2011[18]	indirect costs for Canada caused by vision loss			
	employment participation, absenteeism, presenteeism **CAN $ 4,431 million**		**5,724 million**	
	dead weight losses **CAN$ 1,757 million**		**2,270 million**	

Intangible effects

Most studies used personal burden such as depression, emotional distress, loss of independency, loss of quality of life, limitations in activities of daily living or hazards such as falls and injuries to capture intangible effects of visual impairment and blindness. Two studies, set in Japan and Canada, reported a loss of well being as DALYs and an associated cost of US$ PPP 51.8 billion and US$ PPP 15.11 billion per year respectively.[18 ,30] Every reviewed study reported a high burden caused by multiple individual restrictions in patients and also in caregivers, which was found to be increasing with the degree of visual impairment (**Table 6**). Mortality associated with visual impairment was reported to increase linearly from 4.5% in persons with normal visual acuity (≥20/20) to 22.2% in blind persons (visual acuity of < 20/200) [26]. Measured as a restriction in care givers, Brezin and colleagues [15] reported a increases from 1.6% of caregivers of non-visually impaired persons, who reported restrictions in going out during the day, up to 12% for caregivers of blind patients.

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Table 6: ~~Outcomes~~ Results for intangible effects

Study	*Outcomes*
Bramley et al. 2008[14]	incidences of depression occur in 17% more than patients with no vision loss, placements in nursing homes are demanded in 25.3% more, injuries happen in 33.4% more cases and femur fractures in 67.4% more cases
Cruess et al. 2011[18]	loss of well-being and loss in quality of life evokes 77,306 DALYs or rather CAN$ 11.7 billion in 2007 (US$ PPP 15.11 billion in 2011)
Vu et al. 2005[33]	non-correctable unilateral vision loss was addicted to independent living and reduced safety; bilateral non-correctable vision loss was associated with nursing homes, emotional wellbeing, use of community services, and activities of daily living
Wood et al. 2008[35]	increased visual impairment was significantly associated with an increased incidence of falls and other injuries. 54% of participants had at least one fall, 30% had more than fall, and 63% of falls ended in injuries
McCarty et al. 2001[26]	a linear increase of 5-year mortality correlating with degree of visual impairmen was detected; even mild visual impairment is related to a more than twofold risk of death
Brezin et al. 2005[15]	burden in patients occurs because of inability to undertake daily activities; need of assistance correlates with degree of visual impairment; burden on caregiver was caused by limited by restricted possibilities for going out for different periods or losing social contacts, affected physical and mental welfare and modified professional activities
Porz et al. 2010[28]	in a questionnaire with score scale 0-100 points patients with VA ≥ 0.3 achivede 79.32 for mobility and independency, 69.64 for emotional well-being and 73.86 for reading and achievement of information; persons with VA < 0.3 were rated with scores 46.84, 61.43, 44.25 respectively
Roberts et al. 2010[30]	loss of well-being was measured in DALYs; converted into a monetary value this results in total annual costs of US$ 48.598 billion (US$ PPP 51.8 billion in 2011) and costs per capita of US$ 29,690 per year (US$ PPP 31,647)
Frick et al. 2007[21]	the cases of blindness and visual impairment more than 209,000 QALY were projected to lost each year, this amounts to a monetary value of US$ 10,000 million (US$ PPP 12,150 in 2011)

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DISCUSSION

In this first systematic review of costs associated with visual impairment and blindness we could demonstrate a considerable impact of visual impairment and blindness in terms of the associated direct and indirect costs, as well as intangible effects such as loss of well-being, independence and excess mortality. The highest costs are caused by productivity losses in visually impaired and blind persons as well as their carers, followed by formal and informal care giving, recurrent hospitalizations and the use of medical and supportive services in the visually impaired and blind. A much larger economic impact was due to intangible effects such as loss of independence, quality of life and excess morbidity. However, these are very difficult to quantify in monetary terms and only a small number of studies attempted this. All highlighted cost components as well as intangible effects which contribute to the overall economic impact of visual impairment and blindness need to be considered in economic evaluations not only of visual impairment and blindness but also of interventions aimed at averting these, depending on the focus of the economic evaluation.

A large proportion of the direct costs reported in reviewed studies are not directly related to eye-related medical care, but to falls and other accidents due to visual impairment, exacerbation of diabetes due to a reduced ability to self-manage, depression related to loss of vision and further excess morbidity.[22] Drug costs were not a major contributor to overall costs, which is mirrored in studies investigating chronic diseases such as diabetes mellitus, where – despite its ongoing use – hypoglycaemic drugs constitute only a small proportion of overall direct medical costs.[36] Annual mean costs of other potentially incapacitating chronic diseases such as diabetes mellitus (Euros 5,262 or USD 6,889) [36] or the first year after a stroke (USD 14,361)[37] were much lower for diabetes and similar for the stroke estimate compared to mean annual costs of severe visual impairment and blindness.[14 22] This is likely due to the average diabetic not requiring professional care giving of a scale required during the first year after a stroke or in severely visually impaired and blind persons. In severely visually impaired or blind persons, however, these costs are incurred every year following the loss of vision, and do not decrease significantly over the following years unlike reported annual costs for stroke.[37] Javitt and colleagues report all direct medical cost caused by visual impairment to amount to US$ 2.14 million in 2003 in all non-institutionalized Medicare beneficiaries 69 years and older, and postulate a much higher cost for the whole of the US population.[22] With the introduction of anti-Vascular-Endothelial-Growth-Factor treatment for a number of potentially blinding eye diseases such as neovascular age-related macular degeneration, diabetic macular edema or macular edema in retinal vein occlusions

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since all reviewed studies were conducted, the overall direct medical costs associated with visual impairment can be expected to be much higher today. This increase in cost is exacerbated by the ageing of populations in all developed countries as all major blinding diseases are age-related.[29]

Our finding that indirect costs are much higher than direct costs caused by visual impairment and blindness is mirrored by virtually all other cost-of-illness studies assessing the economic impact of diseases or impairments which result in absenteeism and reduced ability to work [38-39]. Back pain, for example, was found to cause considerable absenteeism and disablement, which – despite its significant hospital cost – lead to indirect cost constituting 93% of the overall cost in 1991 in the Netherlands.[38] Even in treatment and healthcare resource intensive chronic diseases such as diabetes mellitus, indirect costs pose more than half of the overall costs caused by the illness.[39]

All studies which assessed intangible effects in economic terms reported these to be the largest contributor to the overall economic impact of visual impairment and blindness. Considering the adverse impact of loosing vision on quality of life, independence and the ability to participate in society, this is not surprising. We and others have previously reported that even mild visual impairment (0.3<LogMAR<0.5) has a significant and independent impact on vision-specific functioning.[40-42] Similarly, emotional well-being is affected in patients with even mild vision impairment.[41] Depression is considered to result in further functional decline in this group by reducing motivation, initiative and resiliency. [43-45] ~~and people with depression are less likely to access vision rehabilitation services than those not depressed.[44,45]~~ Even unilateral vision loss had a measurable impact on falling and some other activities of independent living, with increased odds of having problems in many activities of daily life in ~~the~~ a study conducted by Vu and colleagues.[33] All this very adversely impacts the ability to participate in society, and contributes to the considerable economic impact of intangible effects caused by visual impairment and blindness.

There are several limitations which necessitate a careful interpretation of the overall findings. Using key words to identify relevant literature always bears the potential of a too narrow focus, and not all relevant literature may have been included. As we were interested in the economic burden of VI&B in high-income countries, we did not include (uncorrected) refractive error into our search terms as this is mostly a problem of middle- and low-income countries, and excluded studies conducted in middle- and low-income countries which limits our results to high-income countries. ~~However, b~~Based on the searches conducted, as well as the cross-searching performed based on references, the authors are confident that the vast

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majority of relevant literature could be included. To the authors' knowledge, a standardized quality checklist has not been used to assess economic evaluations of the impact of visual impairment and blindness prior to inclusion into a systematic review to date. This further increases the overall quality of our review. The study synthesis of reviewed literature was limited as no two studies used the same methodology, ~~particularly~~lacking a standardized definition and specification of cost components (see Appendix 2). ~~:~~ Furthermore no two studies~~,~~ reported exactly the same outcomes or used the same sample population. These problems have been reported for cost-of-illness - or in this case cost-of-impairment – studies in other areas, and adherence to existing cost-of-illness study guidelines recommended.[11 12 46] Unfortunately, none of the reviewed studies seem to have adhered to any of the available international standards, and thus the overall comparability is limited. Similar to cost-of-illness studies in other areas, studies are summarized mostly descriptively, or at a high level of aggregation.[11] The same applies to the chosen categories of visual impairment used in all studies which differ considerably and further limit our ability to collate results (**Table 1**). ~~-~~The perspective (affected person, healthcare payer, societal) of the study was only described in a minority of ~~reports~~studies, and as highlighted in the results section, most studies were conducted in the USA and Australia, making inferences to other countries and healthcare systems difficult. However, this is the only systematic review of the economic impact of visual impairment and blindness to date, highlighting the very broad economic impact and outlining the considerable scope a comprehensive economic evaluation in this area should ideally have.

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In conclusion, visual impairment and blindness cause a considerable economic burden for affected persons, their care givers and society at large, which increases with the degree of visual impairment for all assessed cost categories as well as intangible effects. This review highlights a large amount of cost categories which should be considered in economic evaluations in eye health, and future cost-of illness or cost-of-impairment studies should adhere to available guidelines to improve comparability. The review highlights the considerable amount of resources spent on caring for visually impaired and blind persons in the absence of a cure.

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COMPETING INTERESTS

Authors declared that there are no competing interests.

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AUTHORS' CONTRIBUTION

All authors contributed to the design of the review, KB and CS searched databases and extracted references, KB, CS and JK collated studies, and KB, JK and RF drafted the manuscript, all authors critically revised the manuscript.

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FIGURES

APPENDIX

Appendix 1: Quality checklist

Appendix 2: Cost categories reported in included studies.

Appendix 3: PRISMA ~~Statement~~checklist

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