The Decreasing Prevalence of Nonrefractive Visual Impairment in Older Europeans

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The decreasing prevalence of non-refractive visual impairment in older Europeans: a meta-analysis of published and unpublished data

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CD is consultant for Allergan, Bausch+Lomb, Laboratoires Théa, Novartis, and Roche, and has received grants from Laboratoires Théa, all outside the submitted work. RS is member of Advisory Board for Allergan, Alimera, Bayer, Alcon, Novartis, and THEA, outside the submitted work. AK is consultant for Novartis and Allergan, outside the present work. All other authors declare no competing interests .

Running head:

Prevalence of visual impairment in Europe

ABBREVIATIONS:

AMD: age-related macular degeneration

BCVA: best-corrected visual acuity

E3: European Eye Epidemiology consortium

GBD: Global Burden of Diseases, Injuries and Risk Factors

PVA: presenting visual acuity

VEGF: vascular endothelial growth factor

WHO: World Health Organization

ABSTRACT

Topic: Our objective was to estimate the prevalence of non-refractive visual impairment and blindness in European subjects aged 55 years and older.

Clinical relevance: Few visual impairment and blindness prevalence estimates are available for the European population. In addition, many of the data collected in European population-based studies are currently unpublished and have not been included in previous estimates.

Methods: Fourteen European population-based studies participating in the European Eye Epidemiology (E3) consortium (N=70,723) were included. Each study provided non-refractive visual impairment and blindness prevalence estimates stratified by age (10 years strata) and gender. Non-refractive visual impairment and blindness were defined as best-corrected visual acuity (BCVA) worse than 20/60 and 20/400 in the better eye, respectively. Using random effects meta-analysis, prevalence rates were estimated according to age, gender, geographical area and time period (1991-2006; 2007-2012). Since no data were available for Central and Eastern Europe, population projections for numbers of affected people were estimated using Eurostat population estimates for European high-income countries in 2000 and 2010.

Results: The age-standardized prevalence of non-refractive visual impairment in people aged 55 years or older decreased from 2.22% (95% confidence interval (CI): 1.34-3.10) in 1991-2006, to 0.83% (95% CI: 0.38-1.28) in 2007-2012. It strongly increased with age in both time periods (up to 15.69 % and 4.39% in subjects aged 85 or more in 1991-2006 and 2007-2012, respectively). Age-standardized prevalence of visual impairment tended to be higher in women than men in 1991-2006 (2.67% versus 1.88%), but not in 2007-2012 (0.87% versus 0.88%). No differences were observed between Northern, Western and Southern regions of Europe. The projected numbers of affected older inhabitants in European high-income countries decreased from 2.5 million affected subjects in 2000 to 1.2 million in 2010. Of those, 584,000 were blind in 2000, by comparison with 170,000 in 2010.

Conclusions: Despite the increase in the European older population, our study indicates that the number of visually impaired people has decreased in European high-income countries in the last twenty years. This may be due to major improvements in eye care and prevention and/or decreasing prevalence of eye diseases.

Visual impairment and blindness have profound human and socioeconomic consequences in all societies. People with vision loss experience a reduced quality of life,[1, 2] greater difficulty with daily living and social dependence,[3, 4] higher rates of depression [5, 6] and an increased risk of falls and related hip fractures.[7, 8] Worldwide, vision loss is a leading cause of disability. [9] The costs of lost productivity, rehabilitation, and education of the blind constitute a considerable economic burden for the individuals, their family, and society. Vision loss also incurs both direct health care costs and indirect costs of lost productivity, welfare, and informal care[10]. The global annual cost of visual impairment was estimated to be 3000 billion US dollars (563 billion US dollars for Europe).[11] Since 1999, prevention of visual impairment and blindness has been a priority of the World Health Organization (WHO), through its joint program with the International Agency for the Prevention of Blindness, known as "VISION2020 –the Right to Sight".[12] In 2013, the World Health Assembly adopted a new global action plan for the prevention of avoidable blindness and visual impairment for the period 2014–2019.[13]

A common cause of visual impairment is refractive error (such as myopia, hyperopia, astigmatism or presbyopia), which can be corrected using optical correction (spectacles or contact lenses).[14] Thus, visual impairment due to refractive error is often termed "correctable visual impairment", while visual impairment from other causes is often termed "uncorrectable visual impairment" or "non-refractive visual impairment". Worldwide, major causes of non-refractive visual impairment currently are age-related eye diseases (cataract, age-related macular degeneration (AMD), glaucoma, and diabetic retinopathy).[15] For this reason, visual impairment is much more frequent in older individuals. Globally, 65% of visually impaired and 82% of the blind subject are aged 50 years or more.[15]

While estimates of the prevalence of visual impairment and blindness are regularly published for the USA,[16-19] such estimates are less reported for the European population. Although many epidemiological studies have been conducted in Europe,[2, 20-24] there have been few attempts to harmonize these studies in order to provide estimations of the prevalence of visual impairment throughout the continent. In 2011, the EUREYE study suggested that the prevalence of visual impairment and blindness may be higher in Southern Europe than in Northern Europe (with the exception of Tallinn, Estonia, demonstrating prevalence rates as high as in Southern Europe) and that European women may be more affected than European men.[2] However, this study was performed in 6

cities from 6 European countries (Bergen, Norway; Tallinn, Estonia; Belfast, UK; Paris-Créteil, France; Verona, Italy; Thessaloniki, Greece), with a total of 4166 participants, and may not be representative of the whole European continent. In 2014, prevalence rates for the European continent were estimated in a systematic review and meta-analysis performed by the expert group convened for the Global Burden of Diseases, Injuries and Risk Factors (GBD).[25, 26] This meta-analysis suggests that the prevalence of visual impairment and blindness has decreased in recent decades in all continents, and in particular in Europe. It also showed higher prevalence rates of visual impairment in Central and Eastern Europe compared with Western Europe, and somewhat higher prevalence of visual impairment in women compared with men. However, because this meta-analysis relied on published data, the definitions (thresholds, type of optical correction) and reporting (in particular age groups) of visual impairment differed widely among the included studies, although these differences were in part addressed by the authors using complex statistical modeling. In addition, many European population-based studies have collected data on visual impairment without publishing prevalence estimates, and thus could not be included in this meta-analysis.

The European Eye Epidemiology (E^3) consortium is a collaborative initiative between 41 epidemiological studies across Europe to share and meta-analyze epidemiological data on ocular health.[27] The aim of the present study was to provide more precise estimates of the prevalence of non-refractive visual impairment in older Europeans and to assess potential temporal trends and geographical variations.

POPULATIONS AND METHODS

Studies and participants

To date, E^3 comprises data from 41 studies with a range of ophthalmic data on approximately 170,000 individuals from population-based and other studies (case-control, cases only, randomized trials).[27] The present study was based on the fourteen E^3 population-based studies that collected best-corrected visual acuity (BCVA) data (n=70,723). Studies in the E^3 consortium were eligible for inclusion in this analysis if they were population-based, and had available data on BCVA, together with sex, age at measurement, and year of measurement.

As described in Table 1, participants included in this meta-analysis were mainly of middle to late age. Because only few studies included subjects younger than 55 years, we estimated prevalence of visual impairment and blindness only in subjects above this age. Visual acuity measurements were performed between 1991 and 2012. Designs and methods of included studies are described in Supplementary Online material (available at aaojournal.org). All studies adhered to the tenets of the Declaration of Helsinki, and relevant local ethical committee approvals with specific study consent were obtained.

Demographic and outcome variables

All included studies measured distance visual acuity (mostly using Snellen or Early Treatment of Diabetic Retinopathy Study (ETDRS) charts), with optimal refractive correction. Definitions of visual impairment and blindness vary in the literature. According to the WHO, moderate to severe visual impairment is defined as a visual acuity in the better eye <6/18 but ≥3/60 while blindness is defined as a visual acuity <3/60. By contrast, in the United States, the threshold for visual impairment is 20/40. In order to be as comparable as possible with previous studies and use all available data in the participating studies, we used the following definitions of visual impairment and blindness:

- Non-refractive visual impairment (WHO standard): BCVA<6/18 (or 20/60) in better eye
- Non-refractive visual impairment (US standard): BCVA<6/12 (or 20/40) in better eye
- Non-refractive blindness: BCVA<3/60 (or 20/400) in better eye

Differences in visual impairment by age (in ten year age bands from 55-64 years to ≥85 years), sex, time period (1991-2006 and 2007-2012, using the median of study periods), and geographical European region were examined. Countries were divided into three regions (Northern, Western, and Southern Europe) according to the United Nations Geoscheme [28]. No data were available from Eastern Europe.

Statistical analysis

For each visual endpoint, the investigators from each study provided the number of individuals stratified by sex and age group (55-64 years, 65-74 years, 75-84 years, 85 years or older). Random effects meta-analyses were performed to estimate prevalence rates. Random effects modeling was chosen over a fixed effects model, to take into account heterogeneity in study design characteristics. Subgroups with less than 50 observations were excluded from the analyses.

We first evaluated the variation in prevalence of non-refractive visual impairment and blindness with sex, time period, and geographical area. Since non-refractive visual impairment and blindness strongly vary with age and the age range was quite different among studies, we estimated age-standardized prevalence rates for all aged ≥ 55 years, using the following steps: firstly, for each stratum of sex, period, and geographical area, prevalence rates were estimated using random-effect meta-analyses in each age group (55-64 years, 65-74 years, 75-84 years, 85 years or older). Secondly, an age-standardization to age-specific European population was performed using the European Standard Population 2010 [29]. This enabled prevalence estimates that are representative for the European population, with appropriate weighting to the age demographic distribution of Europe. Subsequently, random effects meta-analyses were performed with stratification by age, sex and time-period.

Finally, in order to estimate the numbers of people affected by visual impairment and blindness, we applied the age- and period-specific prevalence rates to the population of European high-income countries, as defined by the GBD (Andorra, Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom).[25] Population estimates were obtained from Eurostat. To obtain the estimates of numbers of people affected by visual impairment and blindness for the year 2000, we applied prevalence estimates of visual impairment and blindness for the 1991-2006 period to the Eurostat estimates of population for year 2000. Similarly, for the year 2010, we applied visual impairment and blindness prevalence estimates for the 2007-2012 period to the Eurostat population estimates for year 2010.

Statistical analysis was performed using R (R Development Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Fourteen studies were included in the statistical analysis (Table 1). They were conducted between 1991 and 2012 and included 70,723 participants. Age-specific prevalence estimates of the different visual endpoints in the participating studies are presented in Figure 1. The prevalence of non-refractive visual impairment strongly increased with age in all studies. For non-refractive blindness, increasing prevalence with age was not so obvious in some studies, but this was mainly due to low number of affected subjects, particularly in the older age groups. A significant inter-study variability in age-specific prevalence estimates was observed, again especially in the older age groups.

In Table 2, we estimated age-standardized prevalence rates of visual endpoints according to several factors (sex, period of eye examination, and geographical area). Prevalence of all visual endpoints tended to be somewhat higher in women, but the confidence intervals were largely overlapping with those of men. Age-standardized prevalence rates of all visual endpoints were much lower in the most recent time period (2007-2012) in comparison to the older studies (1991-2006). Indeed, the prevalence of non-refractive visual impairment (WHO standard) decreased from 2.22% to 0.83% (p=0.02). As shown in Figure 2, the differences were more pronounced in the older participants, and particularly striking in individuals aged 85 years or more: prevalence of non-refractive visual impairment (WHO standard) was 15.69 % before 2006 and less than 4.39% after 2006. Similarly, in this age group, prevalence of non-refractive blindness was about 3.26% before 2006 and 0.82% after 2006. By contrast, we observed no clear difference of prevalence of visual impairment and blindness between Northern, Western and Southern Europe (for instance, for non-refractive visual impairment 1.64 %, 1.55 % and 1.53 %, respectively, p=0.40).

In Table 3, we estimated the prevalence rates and their 95% confidence intervals, for each age- and sex-strata in 1991-2006 and in 2007-2012. Women showed higher prevalence rates of all visual endpoints in studies performed before 2006, in particular in the oldest-old (for instance, for non-refractive visual impairment, 21.45 % versus 13.11% in men, p=0.08). However, the difference was less pronounced in the more recent studies, with very similar prevalence rates in men and women in most age categories (for instance, for non-refractive visual impairment in the 85+ age category, 3.93% versus 4.03% in men, p=0.40).

In Table 4, we estimated the total number of inhabitants of European high income countries, affected by non-refractive visual impairment and blindness, in 2000 and 2010. Although the total number of subjects aged 55 years or more increased from 106 million in 2000 to 123 million in 2010, the number of subjects affected by non-refractive visual impairment decreased from 2.5 million to 1.2 million (5.2 million to 3.8 million when using the US standard). Similar decreases were observed for non-refractive blindness (584,000 to 170,000).

DISCUSSION

This study, which summarizes published and unpublished data from 14 studies performed in Europe from 1991 to 2012, provides evidence for a major decrease in the prevalence of non-refractive visual impairment and blindness in older Europeans in recent years. The age-standardized prevalence of non-refractive visual impairment in people aged 55 years or older decreased from 2.22% in 1991-2006, to 0.83% in 2007-2012. It tended to be higher in women than men in 1991-2006 (2.67% versus 1.88%), but not in 2007-2012 (0.87% versus 0.88%). No differences were observed according to geographical area. The projected numbers of affected older inhabitants in European high-income countries decreased from 2.5 million affected subjects in 2000 to 1.2 million in 2010.

In a meta-analysis of population-based studies from high-income countries (including United States, Australia, and Europe) performed in the 1990's, the prevalence rates for non-refractive visual impairment according to US standards (BCVA<20/40) were very similar to our estimates, varying from 0.56% in subjects aged 55 to 59 years to 23.73 % in subjects 80 years or older[16] (in comparison with 0.72 % in subjects aged 55-64 years to 28.95% in those age 85 years or more for the 1991-2006 period in the present study). In the National Health and Nutrition Examination Study (NHANES), the prevalence of non-refractive visual impairment (BCVA<20/40) in non-Hispanic whites aged 60 years or more was 3.9% (95% CI: 3.3 %-4.6 %) in 1999-2002, increasing to 4.5 % (95 % CI: 3.6%-5.3 %) in 2006-2008.[19] We observed a similar estimate in 1991-2006 (4.68 %, 95 % CI:2.68%-6.68%) for the

period 1991-2006, with largely overlapping confidence intervals, but a lower estimate in 2007-2012 (2.86%, 95% CI: 1.52%-4.20%).[19] This difference might be due to different temporal trends in Europe and the United States (with stability or even increase in the United States, contrasting with decrease in Europe) or to the fact that the decrease in prevalence of non-refractive visual impairment has happened after 2008, and thus was not observed in NHANES. To our knowledge, there are no available estimates of the prevalence of visual impairment in the United States after 2008. However, the GBD meta-analysis is also in favor of a decreasing prevalence of visual impairment in Northern America (from 3.5% in 1990 to 2.5% in 2010 for presenting visual acuity (PVA)<20/60).[26]

The results of the GBD meta-analysis are not directly comparable to the present study, since they were based on presenting visual acuity (PVA), thus including visual impairment due to refractive errors. However, the temporal trends were similar to our study. Indeed, in the GBD study, the prevalence of visual impairment and blindness (PVA<20/60 and PVA<20/400, respectively) decreased worldwide from 1990 to 2010.[25] This was in particular the case in European high-income countries, with a prevalence of visual impairment in subjects aged 50 years or more estimated at 6.2% (95% confidence interval (CI): 4.3%- 9.5%) in 1990 and 3.9% (95% CI: 2.8%- 6.6%) in 2010.[26] Since they estimated that 47% of visual impairment was due to refractive errors at both time points, their estimates appear somewhat higher than ours (2.22% and 0.83% for non-refractive visual impairment and blindness, respectively).

In the present study, the prevalence of non-refractive visual impairment was also halved in the most recent period (2.22% in 1991-2006 compared with 0.83% in 2007-2012). This suggests that visual impairment due to eye diseases has decreased with time. Unfortunately, causes of visual impairment and blindness were available only in some of the included studies, mainly because of incomplete eye examinations in many studies (in particular absence of assessment of lens opacities, impeding the diagnosis of cataract, and absence of visual field testing, impeding the diagnosis of glaucoma, which are leading causes of visual impairment). The decrease in non-refractive visual impairment is most

probably due to improvement in ophthalmological care over the last 20 years, with an easier access to eye care professionals in most European countries and a better reimbursement of medical expenses. In particular, surgical procedures for cataract surgery, and intraocular lenses, have improved over the last 20 years, increasing its availability, safety, and results in terms of visual acuity. Indeed, the proportion of visual impairment due to cataract has been reported to decrease in the last 20 years, worldwide, and in particular in industrialized countries.[14] Moreover, new ocular therapies have been developed in this period, including intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents for exudative macular diseases (neovascular AMD, diabetic macular edema, and macular edema due to retinal vein occlusion), which were introduced in 2006.[30-32] These therapies have led to major improvements in the visual prognosis of these diseases, and most probably contribute to a decrease in the overall prevalence of visual impairment.[34,35] For instance, a decrease of 50 % of the incidence of blindness due to AMD has been reported in Denmark, mainly after the introduction of intravitreal therapies for AMD in 2006.[33]

Finally, a decrease in the prevalence of eye diseases themselves may have contributed to a decrease in the prevalence of visual impairment. Indeed, it is now clear that the prevalence of diabetic retinopathy, and diabetic macular edema has decreased after year 2000, probably because of improvements in the management of diabetes (although this might be partly compensated by an increase in the prevalence of diabetes itself).[34] Two American studies, and a meta-analysis in Europe, based on the E3 consortium, have also suggested that the prevalence of AMD may be lower in new generations. [35-37]

Similar trends have been observed in the decrease of the prevalence of other age-related disorders, in particular dementia.[38-40] This suggests that recent generations are aging differently, which is probably due to multiple causes, such as changes in education, living conditions, lifestyle habits (smoking, nutrition, physical activity), and medical care. In particular, generations born after World War II, which are now entering old age, have experienced quite different living and nutritional

conditions than those born before, and may age differently. While it is usually projected that the number of disabled older individuals will dramatically grow in future years because of the aging population, these recent reports, including ours, suggest that these projections may be over-pessimistic. In this changing environment, epidemiological studies need to be repeated in order to monitor the trends in the prevalence of age-related disorders and related disability.

Similarly to other reports, women tended to have higher age-standardized prevalence rates of visual impairment and blindness, although this was mainly observed in the first time period (1991-2006). In the GBD meta-analysis, the prevalence of visual impairment was higher in women than in men in all world regions.[25] In the NHANES study, women had higher prevalence rates of visual impairment, both in 1999-2002 (1.5% versus 1.2% for males) and in 2006-2008 (1.9% versus 1.5%), but these differences did not reach statistical significance after adjustment for age, ethnicity, poverty, education, health insurance, and diabetes. Reasons for these potential differences in visual impairment among men and women are unclear, and the differences appear to have decreased in the more recent years in Europe.

The E3 consortium has provided a large data set to meta-analyze temporal trends for prevalence of visual impairment across Europe. One of the strengths is that this meta-analysis was built not only on published data, but also on unpublished data, which have not been included in previous estimates. The size of the dataset is much larger than in previous meta-analyses of European subjects, in particular for the most recent time period (2007-2012). For instance, the GBD meta-analysis included only 2 European studies conducted in this time period, both performed in Spain and totaling 1600 participants, while for the same time period, the present-meta-analysis included 6 studies from 7 European countries, totaling more than 36,000 participants. The estimates were also derived from raw data provided by each study following standardized procedures, in particular in the definition of the different visual endpoints.

Limitations of this consortium meta-analysis include heterogeneity between studies. Contributing studies inherently differed in study design and cohort sampling. To overcome this, we performed a random-effect rather than a fixed-effect meta-analysis, assuming no different true effect between studies. There are also differences between European countries in terms of urbanization, economy, social class, education and lifestyle, which are known to influence eye diseases. Data on these variables at an individual or study-specific level were not uniformly available, and therefore could not be included in the present study.

Representativeness of the population samples is probably also heterogeneous among studies. In order to assess whether the lower prevalence rates observed in the most recent studies might be due to a lower representativeness of those studies, we performed analyses limited to the 3 most representative studies of the 2007-2012 period (Rotterdam III, Tromsø 6th, and Coimbra Eye Study). Prevalence of non-refractive visual impairment was similar in this subgroup (1.17%, 95% CI: 0.66% - 1.67%) as in the main analysis for the 2007-2012 period (0.83%, 95% CI: 0.38%-1.28%), and lower than in the studies performed in 1991-2006 (2.22%, 95% CI: 1.34%-3.10%).

While the E3 consortium strives to include a maximum of European research groups involved in ophthalmic epidemiology, participating studies were mostly from European high-income countries, while no studies from Central and Eastern Europe could be included, except for a small sample from Estonia. To our knowledge, only very few epidemiological studies including measurements of visual acuity have been conducted in Central and Eastern Europe. For instance, only three such studies were included in the GBD meta-analysis (including the sample from Estonia which is also included in our meta-analysis).[26] However, the available data suggest that the prevalence of visual impairment and blindness may be higher in Central and Eastern Europe than in European high-income countries.[26] Thus, we decided not to extrapolate our findings to those areas of Europe. Epidemiological studies conducted in these areas of Europe would be particularly informative.

In addition, as shown in Table 1, the majority of participating studies collected data only in subjects aged 55 years or more. We therefore could not estimate the prevalence of visual impairment below

this age. Finally, most participating studies included only measures of best-corrected visual acuity, but not of presenting visual impairment, so it was only possible to estimate the prevalence of non-refractive visual impairment. The causes of visual impairment were also generally not available. Future European epidemiological studies should strive to include measures of presenting visual acuity and to determine the causes of visual impairment, in order to give a more complete description of the epidemiology of visual impairment in Europe. In particular, uncorrected refractive errors represent a major cause of visual impairment and blindness worldwide, including in Europe [14].

In conclusion, this meta-analysis supports a decrease in the prevalence and numbers of older Europeans affected by non-refractive visual impairment and blindness in the last twenty years. This decrease may be due to major improvements in eye care and/or to a generation effect on eye disease incidence. These findings underline the need for continuing epidemiological monitoring of the temporal trends of ocular health in Europe.

Author contributions:

CD led the statistical analysis and drafted the manuscript. MLG performed the statistical analyses. All authors contributed to study design, data collection, data interpretation, revised the manuscript for important intellectual content and approved the final version of the manuscript.

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Figures legends:

Figure 1. Prevalence (in %) of non-refractive visual impairment according to age, in studies participating to the E3 consortium (A: non-refractive visual impairment (best-corrected visual acuity<20/60); B: non-refractive visual impairment (best-corrected visual acuity<20/40); C: non-refractive blindness (best-corrected visual acuity<20/400))

Figure 2. Prevalence (in %) of non-refractive visual impairment according to age and period (non refractive visual impairment (A: non-refractive visual impairment (best-corrected visual acuity<20/60); B: non-refractive visual impairment (best-corrected visual acuity<20/40); C: non-refractive blindness (best-corrected visual acuity<20/400))