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The Decreasing Prevalence of Nonrefractive Visual Impairment in Older Europeans

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1 **The decreasing prevalence of non-refractive visual impairment in older**

2 **Europeans: a meta-analysis of published and unpublished data**

3

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13

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130 CD is consultant for Allergan, Bausch+Lomb, Laboratoires Théa, Novartis, and Roche, and has
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134 competing interests .

135

136 **Running head:**

137 Prevalence of visual impairment in Europe

138

139

140 **ABBREVIATIONS:**

141 AMD: age-related macular degeneration

142 BCVA: best-corrected visual acuity

143 E3: European Eye Epidemiology consortium

144 GBD: Global Burden of Diseases, Injuries and Risk Factors

145 PVA: presenting visual acuity

146 VEGF: vascular endothelial growth factor

147 WHO: World Health Organization

148

149 **ABSTRACT**

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

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154 are currently unpublished and have not been included in previous estimates.

155 Methods: Fourteen European population-based studies participating in the European Eye
156 Epidemiology (E3) consortium (N=70,723) were included. Each study provided non-refractive visual
157 impairment and blindness prevalence estimates stratified by age (10 years strata) and gender. Non-
158 refractive visual impairment and blindness were defined as best-corrected visual acuity (BCVA) worse
159 than 20/60 and 20/400 in the better eye, respectively. Using random effects meta-analysis,
160 prevalence rates were estimated according to age, gender, geographical area and time period (1991-
161 2006; 2007-2012). Since no data were available for Central and Eastern Europe, population
162 projections for numbers of affected people were estimated using Eurostat population estimates for
163 European high-income countries in 2000 and 2010.

164 Results: The age-standardized prevalence of non-refractive visual impairment in people aged 55
165 years or older decreased from 2.22% (95% confidence interval (CI): 1.34-3.10) in 1991-2006, to 0.83%
166 (95% CI: 0.38-1.28) in 2007-2012. It strongly increased with age in both time periods (up to 15.69 %
167 and 4.39% in subjects aged 85 or more in 1991-2006 and 2007-2012, respectively). Age-standardized
168 prevalence of visual impairment tended to be higher in women than men in 1991-2006 (2.67% versus
169 1.88%), but not in 2007-2012 (0.87% versus 0.88%). No differences were observed between
170 Northern, Western and Southern regions of Europe. The projected numbers of affected older
171 inhabitants in European high-income countries decreased from 2.5 million affected subjects in 2000
172 to 1.2 million in 2010. Of those, 584,000 were blind in 2000, by comparison with 170,000 in 2010.

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

177 Visual impairment and blindness have profound human and socioeconomic consequences in all
178 societies. People with vision loss experience a reduced quality of life,^{1, 2} greater difficulty with daily
179 living and social dependence,^{3, 4} higher rates of depression ^{5, 6} and an increased risk of falls and
180 related hip fractures.^{7, 8} Worldwide, vision loss is a leading cause of disability. ⁹ The costs of lost
181 productivity, rehabilitation, and education of the blind constitute a considerable economic burden for
182 the individuals, their family, and society. Vision loss also incurs both direct health care costs and
183 indirect costs of lost productivity, welfare, and informal care¹⁰. The global annual cost of visual
184 impairment was estimated to be 3000 billion US dollars (563 billion US dollars for Europe).¹¹ Since
185 1999, prevention of visual impairment and blindness has been a priority of the World Health
186 Organization (WHO), through its joint program with the International Agency for the Prevention of
187 Blindness, known as “VISION2020 –the Right to Sight”.¹² In 2013, the World Health Assembly adopted
188 a new global action plan for the prevention of avoidable blindness and visual impairment for the period
189 2014–2019.¹³

190 A common cause of visual impairment is refractive error (such as myopia, hyperopia, astigmatism or
191 presbyopia), which can be corrected using optical correction (spectacles or contact lenses).¹⁴ Thus,
192 visual impairment due to refractive error is often termed “correctable visual impairment”, while visual
193 impairment from other causes is often termed “uncorrectable visual impairment” or “non-refractive
194 visual impairment”. Worldwide, major causes of non-refractive visual impairment currently are age-
195 related eye diseases (cataract, age-related macular degeneration (AMD), glaucoma, and diabetic
196 retinopathy).¹⁵ For this reason, visual impairment is much more frequent in older individuals. Globally,
197 65% of visually impaired and 82% of the blind subject are aged 50 years or more.¹⁵

198
199 While estimates of the prevalence of visual impairment and blindness are regularly published for the
200 USA,¹⁶⁻¹⁹ such estimates are less reported for the European population. Although many
201 epidemiological studies have been conducted in Europe,^{2, 20-24} there have been few attempts to
202 harmonize these studies in order to provide estimations of the prevalence of visual impairment
203 throughout the continent. In 2011, the EUREYE study suggested that the prevalence of visual
204 impairment and blindness may be higher in Southern Europe than in Northern Europe (with the
205 exception of Tallinn, Estonia, demonstrating prevalence rates as high as in Southern Europe) and that
206 European women may be more affected than European men.² However, this study was performed in 6

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

221 The European Eye Epidemiology (E³) consortium is a collaborative initiative between 41
222 epidemiological studies across Europe to share and meta-analyze epidemiological data on ocular
223 health.²⁷ The aim of the present study was to provide more precise estimates of the prevalence of non-
224 refractive visual impairment in older Europeans and to assess potential temporal trends and
225 geographical variations.

226

227 **POPULATIONS AND METHODS**

228 **Studies and participants**

229 To date, E³ comprises data from 41 studies with a range of ophthalmic data on approximately 170,000
230 individuals from population-based and other studies (case-control, cases only, randomized trials).²⁷

231 The present study was based on the fourteen E³ population-based studies that collected best-
232 corrected visual acuity (BCVA) data (n=70,723). Studies in the E³ consortium were eligible for
233 inclusion in this analysis if they were population-based, and had available data on BCVA, together with
234 sex, age at measurement, and year of measurement.

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

242

243 **Demographic and outcome variables**

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

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

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

259

260

261

262 **Statistical analysis**

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

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

278 Finally, in order to estimate the numbers of people affected by visual impairment and blindness, we
279 applied the age- and period-specific prevalence rates to the population of European high-income
280 countries, as defined by the GBD (Andorra, Austria, Belgium, Cyprus, Denmark, Finland, France,
281 Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain,
282 Sweden, Switzerland, United Kingdom).²⁵ Population estimates were obtained from Eurostat. To
283 obtain the estimates of numbers of people affected by visual impairment and blindness for the year
284 2000, we applied prevalence estimates of visual impairment and blindness for the 1991-2006 period to
285 the Eurostat estimates of population for year 2000. Similarly, for the year 2010, we applied visual
286 impairment and blindness prevalence estimates for the 2007-2012 period to the Eurostat population
287 estimates for year 2010.

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

290

291 **RESULTS**

292 Fourteen studies were included in the statistical analysis (Table 1). They were conducted between
293 1991 and 2012 and included 70,723 participants. Age-specific prevalence estimates of the different
294 visual endpoints in the participating studies are presented in Figure 1. The prevalence of non-
295 refractive visual impairment strongly increased with age in all studies. For non-refractive blindness,
296 increasing prevalence with age was not so obvious in some studies, but this was mainly due to low
297 number of affected subjects, particularly in the older age groups. A significant inter-study variability in
298 age-specific prevalence estimates was observed, again especially in the older age groups.

299 In Table 2, we estimated age-standardized prevalence rates of visual endpoints according to several
300 factors (sex, period of eye examination, and geographical area). Prevalence of all visual endpoints
301 tended to be somewhat higher in women, but the confidence intervals were largely overlapping with
302 those of men. Age-standardized prevalence rates of all visual endpoints were much lower in the most
303 recent time period (2007-2012) in comparison to the older studies (1991-2006). Indeed, the
304 prevalence of non-refractive visual impairment (WHO standard) decreased from 2.22% to 0.83%
305 ($p=0.02$). As shown in Figure 2, the differences were more pronounced in the older participants, and
306 particularly striking in individuals aged 85 years or more: prevalence of non-refractive visual
307 impairment (WHO standard) was 15.69 % before 2006 and less than 4.39% after 2006. Similarly, in
308 this age group, prevalence of non-refractive blindness was about 3.26% before 2006 and 0.82% after
309 2006. By contrast, we observed no clear difference of prevalence of visual impairment and blindness
310 between Northern, Western and Southern Europe (for instance, for non-refractive visual impairment
311 1.64 %, 1.55 % and 1.53 %, respectively, $p=0.40$).

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

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

325

326 **DISCUSSION**

327 This study, which summarizes published and unpublished data from 14 studies performed in Europe
328 from 1991 to 2012, provides evidence for a major decrease in the prevalence of non-refractive visual
329 impairment and blindness in older Europeans in recent years. The age-standardized prevalence of
330 non-refractive visual impairment in people aged 55 years or older decreased from 2.22% in 1991-
331 2006, to 0.83% in 2007-2012. It tended to be higher in women than men in 1991-2006 (2.67% versus
332 1.88%), but not in 2007-2012 (0.87% versus 0.88%). No differences were observed according to
333 geographical area. The projected numbers of affected older inhabitants in European high-income
334 countries decreased from 2.5 million affected subjects in 2000 to 1.2 million in 2010.

335 In a meta-analysis of population-based studies from high-income countries (including United States,
336 Australia, and Europe) performed in the 1990's, the prevalence rates for non-refractive visual
337 impairment according to US standards (BCVA<20/40) were very similar to our estimates, varying
338 from 0.56% in subjects aged 55 to 59 years to 23.73 % in subjects 80 years or older¹⁶ (in comparison
339 with 0.72 % in subjects aged 55-64 years to 28.95% in those age 85 years or more for the 1991-2006
340 period in the present study). In the National Health and Nutrition Examination Study (NHANES), the
341 prevalence of non-refractive visual impairment (BCVA<20/40) in non-Hispanic whites aged 60 years
342 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
343 2006-2008.¹⁹ We observed a similar estimate in 1991-2006 (4.68 %, 95 % CI:2.68%-6.68%) for the

344 period 1991-2006, with largely overlapping confidence intervals, but a lower estimate in 2007-2012
345 (2.86%, 95% CI: 1.52%-4.20%).¹⁹ This difference might be due to different temporal trends in Europe
346 and the United States (with stability or even increase in the United States, contrasting with decrease
347 in Europe) or to the fact that the decrease in prevalence of non-refractive visual impairment has
348 happened after 2008, and thus was not observed in NHANES. To our knowledge, there are no
349 available estimates of the prevalence of visual impairment in the United States after 2008. However,
350 the GBD meta-analysis is also in favor of a decreasing prevalence of visual impairment in Northern
351 America (from 3.5% in 1990 to 2.5% in 2010 for presenting visual acuity (PVA)<20/60).²⁶

352 The results of the GBD meta-analysis are not directly comparable to the present study, since they
353 were based on presenting visual acuity (PVA), thus including visual impairment due to refractive
354 errors. However, the temporal trends were similar to our study. Indeed, in the GBD study, the
355 prevalence of visual impairment and blindness (PVA<20/60 and PVA<20/400, respectively) decreased
356 worldwide from 1990 to 2010.²⁵ This was in particular the case in European high-income countries,
357 with a prevalence of visual impairment in subjects aged 50 years or more estimated at 6.2% (95%
358 confidence interval (CI): 4.3%- 9.5%) in 1990 and 3.9% (95% CI: 2.8%- 6.6%) in 2010.²⁶ Since they
359 estimated that 47% of visual impairment was due to refractive errors at both time points, their
360 estimates appear somewhat higher than ours (2.22% and 0.83% for non-refractive visual impairment
361 and blindness, respectively).

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

369 probably due to improvement in ophthalmological care over the last 20 years, with an easier access
370 to eye care professionals in most European countries and a better reimbursement of medical
371 expenses. In particular, surgical procedures for cataract surgery, and intraocular lenses, have
372 improved over the last 20 years, increasing its availability, safety, and results in terms of visual acuity.
373 Indeed, the proportion of visual impairment due to cataract has been reported to decrease in the last
374 20 years, worldwide, and in particular in industrialized countries.¹⁴ Moreover, new ocular therapies
375 have been developed in this period, including intravitreal injections of anti-vascular endothelial
376 growth factor (VEGF) agents for exudative macular diseases (neovascular AMD, diabetic macular
377 edema, and macular edema due to retinal vein occlusion), which were introduced in 2006.³⁰⁻³² These
378 therapies have led to major improvements in the visual prognosis of these diseases, and most
379 probably contribute to a decrease in the overall prevalence of visual impairment.^{34,35} For instance, a
380 decrease of 50 % of the incidence of blindness due to AMD has been reported in Denmark, mainly
381 after the introduction of intravitreal therapies for AMD in 2006.³³

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

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

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

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

408 The E3 consortium has provided a large data set to meta-analyze temporal trends for prevalence of
409 visual impairment across Europe. One of the strengths is that this meta-analysis was built not only on
410 published data, but also on unpublished data, which have not been included in previous estimates.

411 The size of the dataset is much larger than in previous meta-analyses of European subjects, in
412 particular for the most recent time period (2007-2012). For instance, the GBD meta-analysis included
413 only 2 European studies conducted in this time period, both performed in Spain and totaling 1600
414 participants, while for the same time period, the present-meta-analysis included 6 studies from 7
415 European countries, totaling more than 36,000 participants. The estimates were also derived from
416 raw data provided by each study following standardized procedures, in particular in the definition of
417 the different visual endpoints.

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

425 Representativeness of the population samples is probably also heterogeneous among studies. In
426 order to assess whether the lower prevalence rates observed in the most recent studies might be
427 due to a lower representativeness of those studies, we performed analyses limited to the 3 most
428 representative studies of the 2007-2012 period (Rotterdam III, Tromsø 6th, and Coimbra Eye Study).
429 Prevalence of non-refractive visual impairment was similar in this subgroup (1.17%, 95% CI: 0.66% -
430 1.67%) as in the main analysis for the 2007-2012 period (0.83%, 95% CI: 0.38%-1.28%), and lower
431 than in the studies performed in 1991-2006 (2.22%, 95% CI: 1.34%-3.10%).

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

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

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

451

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

457

458 **Author contributions:**

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

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557 Figures legends:

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

562

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

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