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Published in:
Acta Ophthalmologica

DOI:
10.1111/aos.13842

Publication date:
2019

Document version:
Accepted manuscript

Citation for pulished version (APA):
Hansen, M. H., Munch, I. C., Li, X. Q., Skovgaard, A. M., Olsen, E. M., Larsen, M., & Kessel, L. (2019). Visual acuity and amblyopia prevalence in 11- to 12-year-old Danish children from the Copenhagen Child Cohort 2000. *Acta Ophthalmologica*, *97*(1), 29-35. https://doi.org/10.1111/aos.13842

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Article type : Original Article

Visual acuity and amblyopia prevalence in 11-12-year-old Danish children from the Copenhagen Child Cohort 2000

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Abstract

PURPOSE: To evaluate the prevalence of amblyopia and associated biometric factors in Danish children.

METHODS: Determination of best-corrected visual acuity (BCVA) using ETDRS charts, non-cycloplegic subjective refractioning guided by automated refractometry, axial length and corneal curvature, fundus photography and optical coherence tomography in 1335 children from the population-based Copenhagen Child Cohort 2000 (CCC2000) Eye Study. Birth data were obtained from the Danish Medical Birth Registry.

RESULTS: The mean (± SD) age of children was 11.7 (±0.4) years and 47 % were boys. Amblyopia prevalence was 1.5 (95% CL 0.8-2.2) %. Unilateral amblyopic eyes (BCVA < 80 ETDRS letters (0.8 snellen) and ≥ 2 lines difference between the eyes) was 0.6 (95% CL 0.3-1.0) mm shorter, 1.34 (95% CL 0.30-2.37) D more hyperopic, and had 0.79 (95% CL 0.14-1.44) D more astigmatism compared with fellow eyes. Compared with the right eyes of the non-amblyopic children, unilateral amblyopic eyes were 1.03 (95% CL 0.5-1.6) mm shorter, 2.48 (95% CL 1.11-3.86) D more hyperopic, 1.09 (95% CL 0.43-1.75) D more astigmatic, and had a 47 (95 % CL 13-81) µm thicker subfoveal choroid.

CONCLUSION: Amblyopia was found in 1.5 % of Danish children born 22 years after the inception of the nationwide preschool visual screening program. Amblyopia was associated with anisometropia, astigmatism, a thicker subfoveal choroid, and a history of childhood strabismus.

Keywords: Visual acuity, amblyopia, axial length, corneal curvature, choroidal thickness, children, cohort study

Introduction

Amblyopia is a disorder in development of vision that affects 1-5 % in human populations with no major exceptions (Holmes & Clarke 2006). Amblyopia develops during early childhood and is caused by disturbance in visual development most commonly due to misaligned eyes in strabismus or to a disrupted visual input to one or, more rarely, both eyes, secondary to conditions such as anisometropia, uncorrected severe hyperopia, ptosis, tumors, corneal scars and cataract (Holmes & Clarke 2006). In 1978, Denmark introduced a preschool visual screening program in relation to the systemic general health examination made by general practitioners at 3, 4 and 5 year of age (Danish Health and Medicines Authority 1978). Since the introduction of the program, amblyopia has been reported to have decreased three- to fourfold, from 1.8 - 3.2 % before (Vinding et al. 1991; Hoeg et al. 2015) to 0.4 - 1.07 % after the inception of the program (Jensen & Goldschmidt 1986; Hoeg et al. 2015).

In this study, we examined the prevalence of amblyopia in Denmark 33 years after the inception of the comprehensive national screening program by examining 1335 children aged 11-12 years from the population-based Copenhagen Child Cohort 2000 Study. We also compared biometric characteristics in amblyopic eyes with non-amblyopic fellow eyes and eyes of non-amblyopic children.

Methods

Study population

The Copenhagen Child Cohort 2000 (CCC2000) is a prospective, population-based observational study of children born in the year 2000 in 16 municipalities of the defunct Copenhagen County of Denmark, a largely suburban part of the Greater Copenhagen region (Skovgaard et al. 2005). The CCC2000 was designed and initiated to evaluate mental health and mental development from birth to adulthood. The CCC2000 Eye Study was added to the mental health study in 2011 at the 11-year-follow-up examination of the CCC2000 cohort (Skovgaard et al. 2005; Li et al. 2014). Ascertainment of participants for the CCC2000 Eye Study is illustrated in Figure 1. Of the initial 6,090 children from the CCC2000 birth cohort, 4,847 were eligible at the age of 11 (14 were untraceable, 19 had died, 217 had emigrated and 993 were exempted from public data registry access). Of the 4,847 children, 1,632 attended the CCC2000 11-year follow-up examination and were eligible for inclusion in the Eye Study in which 1,406 (86.2%) participated. Only children with visual acuity measurements from both eyes (n= 1,335) were included in the present analysis. The complete study protocol of the Eye Study has previously been described (Li et al. 2014).

All subjects and their parents or legal guardians gave their signed informed consent prior to examinations. The protocol was in accordance with the Declaration of Helsinki and declared by the local medical ethics committee to fall outside the realm of their jurisdiction because of its non-invasive nature (jr.nr. H-3-2011-028).

[FIGURE 1]

Procedures

Past medical history and information about current medication use were obtained from the parents. Birth weight and gestational age were obtained from the Danish Medical Birth Registry (Knudsen & Olsen 1998).

Best-corrected visual acuity (BCVA) was determined using ETDRS charts (4-meter original series; Precision-Vision, La Salle, IL, USA) in both eyes after subjective refractioning guided by automated refractometry (Retinomax K-plus; Right MFG Co., Ltd., Tokyo, Japan). BCVA was defined as the maximum number of letters the participant was able to read with as little negative correction as possible. For the subjective refractioning, participants were encouraged to read as many letters as possible with one eye at a time. Hereafter positive lens power (+0.5 diopters (D)) was added continuously until a loss of at least 3 letters occurred, followed by the adding of -0.25 D lenses until there was no more gain of letters. Both automated and subjective fractioning were performed under non-mydriatic conditions.

Axial length and corneal curvature were obtained using an interferometric device (IOL-Master, version 3.01.0294; Carl Zeiss Meditec, La Jolla, CA, USA). Axial length was calculated based on an average of at least 5 scans and the corneal curvature as the average of 3 scans that each consisted of five individual measurements. Fundus photographs were captured using a non-mydriatic camera (Topcon TRC-NW7SF, Topcon Medical Systems, Oakland, NJ, USA). Optical coherence tomography (OCT) included macular scans in high resolution with and without enhanced-depth imaging (Heidelberg Spectralis; Heidelberg Engineering, Heidelberg, Germany).

Choroidal thickness was measured by an experienced operator (XQL) using the manufacturer's software (Heidelberg Eye Explorer, version 1.6.1.0; Heidelberg Engineering) as previously described (Li et al. 2011; Li et al. 2014). Retinal thickness was measured using the software-generated, fovea-centered thickness map providing the average and minimal thickness of the center field (1000 µm in diameter).

Definition of visual impairment and amblyopia

Normal vision was defined as BCVA ≥ 80 letters (corresponding to ≤ 0.1 logMAR or ≥ 20/25 (0.8) Snellen) in both eyes, suboptimal vision as BCVA between 60 and 80 letters (0.1< logMAR < 0.5 or 20/25 (0.8)> Snellen > 20/60 (0.3)) in one or both eyes, low vision as BCVA ≤ 60 letters (≥ 0.5 logMAR or ≤ 20/60 (0.3) Snellen) in the better seeing eye, and legal blindness as BCVA ≤ 35 letters (≥ 1.0 logMAR or ≤ 20/200 (0.1) Snellen) in the better seeing eye.

Amblyopia was defined as having a difference of at least 10 ETDRS letters between the two eyes and a BCVA < 80 letters (> 0.1 logMAR, < 20/25 (0.8) Snellen) in the worse seeing eye. Bilateral amblyopia was defined as bilateral axial length < 21 millimeters in combination with bilateral suboptimal vision (< 80 letters). One child was included as amblyopic even though she only had a 9-letter-difference between eyes

and BCVA in the best-seeing eye better than 80 ETDRS letters. She was included because her right eye only saw 75 ETDRS letters and had an abnormally short axial length (19.45 mm).

Clinically significant anisometropia was defined as either an interocular axial length difference ≥ 1 mm (axial anisometropia) or a difference of the spherical equivalent refraction larger than 2 D (refractive anisiometropia). Corneal astigmatism was defined using negative cylinder measurements calculated from the IOL Master's keratometry results. Thus, clinically significant astigmatism was defined as a difference between the steepest and the flattest meridian (K1 and K2) greater than 1 D. Anisoastigmatism was defined as a difference in astigmatism between the two eyes ≥ 1 D, independent of the axes of astigmatism. Astigmatism was categorized by the K1 axis as with-the-rule when either below 30° or above 150°, oblique when either 30° to 60° or 120° to 150° and against-the-rule when between 60° and 120°.

[FIGURE 2]

Statistics

The SAS® 9.4 statistical software package was used for all statistical analyses. We used Student's t-tests for the comparison of corneal curvature and subfoveal choroidal thickness between amblyopic eyes and the right eyes of non-amblyopic children. Due to unequal sample variance, the Welch–Satterthwaite equation was used for the comparison of BCVA, spherical equivalent, axial length, astigmatism and foveal retinal thickness between amblyopic eyes and non-amblyopic children's right eyes and gestational age and birth weight between amblyopic and non-amblyopic children. The comparisons of the amblyopic eyes with the fellow eyes were performed using paired Student's t-tests. A mixed model using the unstructured covariance structure was used to adjust for axial length in the paired analysis of choroidal thickness.

We used Fischer's exact test to compare the axis distribution and the frequencies of anisometropia and anisoastigmatism between the amblyopic and non-amblyopic children.

Only unilaterally amblyopic children were included in the biometric analysis. All children were included when determining the prevalence of amblyopia and when analyzing birth weight and gestational age. The spherical equivalent was calculated by adding half of the cylinder to the spherical refraction.

Results

[TABLE 1]

The study included 1335 children (47 % boys, 53 % girls) with a mean (±SD) age of 11.7 (±0.4) years, range 10.6 to 12.8 years, with no differences between amblyopic and non-amblyopic children (Table 1). The majority of children (97.7%) had normal vision (BCVA≥ 80 letters in both eyes), with the mean BCVA in the cohort being 89 ETDRS letters (range 50-100 letters in right eyes and 50-97 letters in left eyes; Figure 2). Thirty-one (2.3%) of the children had suboptimal vision (BCVA between 60 and 80 letters in one or both eyes), but no child had low vision (BCVA ≤ 60 letters in the better-seeing eye) or was legally blind.

Twenty children (1.5 % (95% CL 0.8-2.2)) had amblyopia, 8 boys and 12 girls (Table 2). Eight of the children were amblyopic in the right eye, 11 in the left eye and one child had bilateral amblyopia (Table 2). Mean BCVA in the unilateral amblyopic eyes was 66 (range 50 to 79 letters) ETDRS letters which in average was 23 ETDRS letters less ($p<0.0001$) than both the fellow eyes and the right eyes of non-amblyopic children (Table 3). In order to compare our results to prior Danish and Swedish studies (Table 4) more strict definitions of amblyopia were used as well (≤ 70 ETDRS letters and < 70 ETDRS letters), giving a prevalence of 1.0 % (95 % CL 0.45-1.5) and 0.9 % (95 % CL 0.39-1.4) respectively.

A history of childhood strabismus was reported in 35 % (n=7) of children with amblyopia. Clinically significant anisometropia were present in 37 % (n=7) of the unilateral amblyopic children compared to 0.4 % (n=5) of the non-amblyopic children (Table 1). Anisoastigmatism ≥ 1 D were present in 27.8 % (n=5) of the unilateral amblyopic children and 0.5 % (n=6) of the non-amblyopic children (Table 1).

[TABLE 2]

The mean axial length of amblyopic eyes was 22.2 (±1.1) mm or 0.6 mm (95 % CL 0.3-1.0, $p=0.0022$) shorter than in fellow eyes and 1.0 mm (95 % CL 0.5-1.6, $p=0.0008$) shorter than in right eyes of non-amblyopic children (Table 3). All 6 children with an interocular axial length difference ≥ 1 mm (axial anisometropia) were amblyopic (Table 1).

The mean corneal curvature of amblyopic eyes was 43.1 (±1.6) D and the mean magnitude of astigmatism was 1.88 (±1.3) D (Table 3). There were no significant abnormalities of the mean corneal curvature in amblyopic eyes, neither when compared to fellow eyes nor when compared to right eyes in non-amblyopic children (Table 3). Mean astigmatic error in amblyopic eyes was 0.79 D (95 % CL 0.14-1.44, $p<0.020$) higher than in the fellow eyes and 1.09 D (95 % CL 0.43-1.75, $p<0.0028$) higher than right eyes in non-amblyopic children (Table 3).

The axis distributions of both eyes of the amblyopic children were 95 % with-the-rule, 0 % oblique and 5 % against-the-rule. There were no significant differences compared with the right eyes of non-amblyopic children (p=0.61) (Table 3).

Amblyopic eyes had a mean spherical equivalence of 2.57 (±2.9) D which on average was 1.34 D (95 % CL 0.30-2.37, p=0.014) higher than in fellow eyes and 2.48 D (95 % CL 1.11-3.86, p=0.0013) higher than in right eyes of the non-amblyopic children (Table 3).

Mean subfoveal choroidal thickness in amblyopic eyes was 436 (±89) µm, which was 77 µm (95 % CL 42-112, p<0.0001) thicker than in right eyes of non-amblyopic children (Table 3). The difference remained significant after adjusting for axial length (47 µm 95 % CL 13-81, p=0.0074) (Table 3). When comparing the amblyopic eyes with their fellow eyes, the mean subfoveal choroid was 47 µm (95 % CL 14-80, p=0.0081) thicker in the amblyopic eyes than in the fellow eyes in the crude analysis, but this difference was not significant after adjusting for differences in axial length (p=0.36) (Table 3).

The mean foveal retinal thickness in the amblyopic eyes was 235 (±35) µm (Table 3). There was no difference in retinal thickness between amblyopic eyes and fellow eyes or right eyes of non-amblyopic children.

The mean birth weight and mean gestational age of the amblyopic children was 3461 (±86) g and 39 weeks (± 3 weeks and 3 days) respectively (Table 1). There were no significant differences between the amblyopic and non-amblyopic children, neither in birth weight nor gestational age (Table 1).

[TABLE 3]

Discussion

We investigated the prevalence of amblyopia and the associated biometric risk factors in 1335 Danish children from a population-based birth cohort and found that 1.5 % (n=20) of the children were amblyopic. Unilaterally amblyopic eyes tended to be shorter, more hyperopic, more astigmatic and to have a thicker subfoveal choroid compared to fellow eyes and right eyes in non-amblyopic children.

Amblyopia prevalence is difficult to compare between different studies because of variation in the definition of amblyopia. In this report, we have compared various amblyopia criteria. Using a criterion of unilateral reduction of vision ≤ 20/40 (≤ 70 ETDRS letters) we found an amblyopia prevalence of 1.0 %. This

is comparable to a previous finding of 1.1 % from 1986 based on a survey of 8,769 schoolchildren (2^{th} -5^{th} grade ≈ 8-11 years old) (Jensen & Goldschmidt 1986) using the same criterion. A more recent study using a threshold of BCVA < 20/40 (<70 ETDRS letters) found a prevalence of 1.4 % in a study of 3,826 Danish adults (Hoeg et al. 2015). Their population, however, included participants from both before and after the initiation of the preschool vision screening. While the prevalence among the non-screened was 1.8 %, that of the screened participants was 0.4 % (2/454) which did not differ significantly from the 0.9 % (12/1335) found in our population using the same criterion. The most recent published Danish study examining 445 children aged 4.5 to 7 years in year 2015-2016 and defining amblyopia as at least 2 lines of difference in BCVA between the eyes and/or BCVA worse than 0.3 logMAR (< 70 ETDRS letters or < 0.5 Snellen) (Sandfeld et al. 2018) found a prevalence of 2.7 % (n=12). This was slightly higher, but still comparable to our observation (1.4 %, n=19), which could be due to the young age of the children who have not completed the full screening program yet. In addition, the study did not report whether or not the children already were in amblyopia treatment. Similar prevalences of amblyopia have been reported from screened populations in Sweden, where a study of children aged 10 years, born in 1982 (n=3,126) found a prevalence of 0.9 % using a threshold of BCVA ≤ 20/40 (≤ 70 ETDRS letters) and 1.7 % with a threshold of ≤20/28 (≈ < 80 ETDRS letters) (Kvarnstrom et al. 1998). Another Swedish study of 12-13-years old children born in 1985 (n=1,046) found a prevalence of 1.1% with a visual acuity cutoff at ≤20/40 (≤ 70 ETDRS letters) (Ohlsson et al. 2001). In summary, our observations do not suggest that the prevalence of amblyopia in Denmark is changing or that it differs from that in Sweden which also has a national pre-school vision screening.

[Table 4]

Amblyopia was highly associated with strabismus and anisometropia as has previously been shown (Robaei et al. 2006; Friedman et al. 2009; Chia et al. 2010). The anisometropia seemed mainly to be due to shorter axial lengths rather than an abnormally flat corneal curvature. Corneal astigmatism > 1 D however, was highly associated with amblyopia.

The subfoveal choroid was thicker in amblyopic eyes compared to non-amblyopic eyes even after adjusting for axial length. This finding is in agreement with a meta-analysis of choroidal thickness in 449 amblyopic patients from Turkey, China and Japan (Liu et al. 2017) who found that after adjusting for axial length amblyopic eyes were 58 µm ($p<0.001$) and 56 µm ($p=0.003$) thicker than the fellow eyes and control eyes, respectively. Our results support that when comparing amblyopic and non-amplyopic children, amblyopia is associated with having a thick choroid, independent of axial length.

There was no significant difference in foveal retinal thickness between amblyopic eyes and non-amblyoipc eyes. This is in contrast to a recent meta-analysis of unilateral amblyopia, which reported significantly thicker foveae in amblyopic eyes compared with non-amblyopic eyes. The study included 265 eyes in either group and the standardized mean difference was 0.22 (95% CI 0.05-0.39) µm with a mean central thickness ranging from 146 to 239 µm (Li et al. 2015).

The present cohort-based population study is the largest study of its kind in Denmark based on a huge amount of data obtained with advanced ophthalmological examinations. Despite these strengths there are some limitations as well. As amblyopia is a rare condition, a study with a case-control design can be more powerful for detection of associated risk factor for amblyopia. Our study being a population-based cohort study is superior, however, for estimating the prevalence of amblyopia and we were nonetheless able to detect strong biometric associations with amblyopia that were comparable to important prior studies. However, no conclusions on causality could be made due to the cross-sectional design. Another limitation is that we refrained from cycloplegic refractioning to avoid ascertainment bias, the assumption being that placing higher demands on the participants would reduce the recruitment of the most vulnerable children and families also for future examinations of the cohort. Consequently, we may have overestimated the amount of negative spherical power when performing subjective refraction. To compensate for the lack of cycloplegic refraction, we took care to measure optimal BCVA with as little negative correction as possible and by adding axial length measurement and keratometry when assessing anisometropia and astigmatism.

In conclusion, we found a prevalence of amblyopia of 1.5 % in 1,335 children from the Copenhagen area born 33 years after the introduction of national preschool vision screening. Amblyopia was associated with history of childhood strabismus, anisometropia, astigmatism and thicker subfoveal choroid. The frequency of amblyopia was comparable to studies made two and three decades ago suggesting that the efficacy of screening for and intervention against amblyopia in Denmark has reached a plateau.

Acknowledgment

Supported by a grant from the Bagenkop-Nielsen Foundation.

Disclosures: None.

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Table 1. Characteristics of the study population stratified by the presence of amblyopia.

	Amblyopic children (n=20)	Non-amblyopic children (n=1315)	p-values
Age, years	11.7 (±0.4)	11.7 (±0.4)	0.96
Gender [% male]	40 % (95% CL 16-64)	48 % (95% CL 45-50)	0.50
Reduced VA <80 ETDRS letters			
Right eye	45 % (95% CL 21-69)	0.3 % (95% CL 0.006-0.6)	**<0.0001**
Left eye	60 % (95% CL 36-84)	0.6 % (95% CL 0.02-1.0)	**<0.0001**
Anisometropia*			
Axial (≥ 1 mm)	32 % (95% CL 9-55)	0 %	**<0.0001**
Refractive(> 2 D)	32 % (95% CL 9-55)	0.4 % (95% CL 0.05-0.7)	**<0.0001**
Total	37 % (95% CL 13-61)	0.4 % (95% CL 0.05-0.7)	**<0.0001**
Anisioastigmatism ≥ 1 D*	28 % (95% CL 5-51)	0.5 % (95% CL 0.1-0.9)	**<0.0001**
Gestational age [weeks, days]	39w0d (±3w3d)	39w6d ±1w5d	0.28
Birth weight [g]	3461 (±849)	3546 (±587)	0.66

*only unilateral amblyopic children included.

Table 2. Characteristics of the 20 amblyopic children out of 1335 in 11-12-year old population-based study cohort.

Sex	Eye	BCVA [letters]	AL [mm]	K1 [D]	K2 [D]	K1-K2 [D]	Axis [degrees]	SER [D]	Gestational age	Birth weight [g]	Childhood strabismus
Right eye amblyopia											
Female	OD	75	22.0	41.2	42.3	-1.1	174°	+1.625	39w 4d	3600	
	OS	88	22.4	41.5	42.4	-0.9	2°	+1.875			
Female	OD	66	23.3	41.8	45.1	-3.3	16°	+1.375	42w 1d	4500	
	OS	89	22.8	42.9	43.2	-0.3	6°	+1.625			
Male	OD	50	21.1	46.6	47.5	-0.9	158°	+7.00	41w 0d	4012	
	OS	91	23.5	42.4	43.3	-0.9	5°	+0.00			
Female	OD	75	19.5	43.7	45.1	-1.4	98°	+7.75	37w 4d	3110	
	OS	84	19.5	43.7	45.4	-1.7	75°	+8.00			
Female	OD	65	23.7	42.4	43.4	-1.1	170°	-0.125	38w 0d	3350	Yes
	OS	87	24.1	42.6	43.0	-0.4	5°	-0.875			
Male	OD	65	22.7	42.8	43.4	-0.6	171°	+0.75	34w 6d	2400	
	OS	90	23.4	43.1	43.9	-0.8	0°	+0.75			
Male	OD	60	21.4	42.2	44.0	-1.8	7°	+1.625	39w 5d	3950	
	OS	86	22.5	42.5	43.4	-0.9	6°	-0.125			
Female	OD	77	22.9	43.1	43.9	-0.8	23°	-0.25	36w 6d	2800	Yes
	OS	92	22.8	43.2	44.0	-0.8	165°	-0.50			
Left eye amblyopia											
Male	OD	85	23.1	39.2	40.6	-1.4	174°	+3.875	38w 1d	2650	Yes
	OS	65	21.5	38.7	41.3	-2.6	2°	+7.25			
Male	OD	85	21.3	42.6	45.1	-2.5	0°	+4.50	38w 6d	4250	
	OS	75	20.8	42.8	45.4	-2.6	11°	+5.25			
Female	OD	88	22.5	42.1	43.2	-1.1	2°	-0.25	41w 4d	4500	
	OS	52	22.4	42.3	43.5	-1.2	176°	+0.50			
Male	OD	87	22.3	42.1	43.3	-1.2	6°	+2.625	38w 3d	3050	
	OS	75	21.9	41.9	43.4	-1.5	176°	+3.625			
Female	OD	90	23.1	40.9	41.9	-1.0	6°	+0.50	39w 4d	3600	
	OS	55	22.2	38.6	44.4	-5.8	174°	+2.875			
Female	OD	90	23.9	42.7	43.1	-0.4	10°	+0.125	40w 3d	3110	
	OS	50	21.9	42.1	43.3	-1.2	20°	+5.625			
Male	OD	89	22.9	44.1	44.8	-0.7	0°	+0.50	42w 0d	3500	Yes
	OS	60	21.9	44.0	44.6	-0.6	21°	+2.75			
Male	OD	97	23.0	43.4	45.1	-1.7	8°	+0.625	41w 0d	3430	Yes
	OS	61	22.0	42.7	46.4	-3.7	179°	+3.00			
Female	OD	90	23.7	41.6	42.0	-0.4	172°	-0.125	41w 3d	3850	Yes
	OS	72	24.3	40.8	42.2	-1.4	163°	-2.00			
Female	OD	87	23.9	40.0	42.5	-2.5	170°	+0.25	37w 6d	2650	
	OS	68	23.3	40.4	42.5	-2.1	15°	+0.75			
Female	OD	93	22.7	.	.	.	.	+0.00	42w 4d	4000	
	OS	79	22.3	.	.	.	.	-0.625			
Bilateral amblyopia											

Female	OD	70	20.4	42.2	44.5	-2.3	10°	+5.00	27w 0d	999	Yes (OD)
	OS	79	20.3	42.3	44.2	-1.9	9°	+4.375			

AL = axial length, K1 = flattest corneal meridian, K2 = steepest corneal meridian, Axis of K1 meridian, SER = spherical equivalent refraction.

Table 3. Best-corrected visual acuity and ocular biometry in unilaterally amblyopic (n=19) and in non-amblyopic children (n=1315) aged 11-12 years.

	Unilaterally amblyopic children N=19			**Non-amblyopic children N=1315**	
	Amblyopic eyes	Mean difference (95% CL of mean)	**Fellow eyes**	**Right eyes**	Compared to amblyopic eyes (95% CL of mean)
ETDRS letters [no.]	66±9	-23 (-28; -18) **p < 0.0001**	89 ±3	89 ±3	-23 (-28; -19) **p < 0.0001**
Spherical equivalent refraction [D]	2.57 ±2.9	1.34 (0.30; 2.37) **p = 0.014**	1.23 ±2.2	0.08 ±0.8	2.48 (1.11; 3.86) **p = 0.0013**
Axial length [mm]	22.2 ±1.1	-0.6 (-1.0; -0.3) **p = 0.0022**	22.8 ±1.0	23.2 ±0.8	-1.0 (-1.6; -0.5) **p = 0.0008**
Mean corneal curvature [D]	43.1 ±1.6	0.26 (-0.24; 0.76) p = 0.29	42.8 ±1.2	43.2 ±1.4	-0.19 (-0.83; 0.44) p = 0.55
Axis distributions of k1					
With-the-rule	94 %		94 %	91 %	
Oblique	0 %	p=1.0	0 %	5 %	p=0.61
Against-the-rule	6 %		6 %	4 %	
K1-K2 [D]	-1.88 ±1.3	-0.79 (-1.44; -0.14) **p = 0.020**	-1.09 ±0.6	-0.79 ±0.4	-1.09 (-1.75; -0.43) **p = 0.0028**
Foveal retinal thickness [µm]	235 ±35	0.4 (-3; 4) p = 0.82	235 ±34	222 ±16	13 (-5; 31) p = 0.14
Subfoveal choroidal thickness [µm]	436 ±89	47 (14; 80) **p = 0.0081**	389 ±86	359 ±78	77 (42; 112) **p < 0.0001**
Adjusted for axial length		13 (-16; 42) p = 0.36			47 (13; 81) **P = 0.0074**

Values are mean ± standard deviation.

Table 4. Amblyopia prevalence compared with prior Danish and Swedish studies.

Authors	Amblyopia definition	Prevalence	Prevalence in our study	p-values
Hoeg et al. 2015 (n=454)	BCVA < 20/40 Snellen (<70 ETDRS letters) and ≥ 2 lines difference	0.4 % (n=2)	0.9 % (n=12)	0.54[a]
Jensen & Goldschmidt 1986 (n=8769)	Unilateral reduction of BCVA ≤ 20/40 Snellen (≤ 70 ETDRS letters)	1.1 % (n=94)	1.0 % (n=13)	0.74[b]
Ohlsson et al. 2001 (n=1046)	BCVA ≤20/40 Snellen (≤ 70 ETDRS letters) and ≥ 2 lines difference	1.1% (n=11)	1.0 % (n=13)	0.83[b]
Kvarnstrom et al. 1998 (n=3126)	BCVA ≤ 20/40 Snellen (≤ 70 ETDRS letters)	0.9 % (n=28)	1.0 % (n=13)	0.80[b]
	BCVA ≤20/28 Snellen (≈ < 80 ETDRS letters)	1.7 % (n=53)	1.5 % (n=20)	0.63[b]
Sandfeld et al. 2018 (n=445)	BCVA < 20/40 Snellen (<70 ETDRS letters) and/or ≥ 2 lines difference	2.7 % (n=12)	1.4 % (n=19)	0.075[b]

[a]Fishers exact test, [b]χ^2-test.

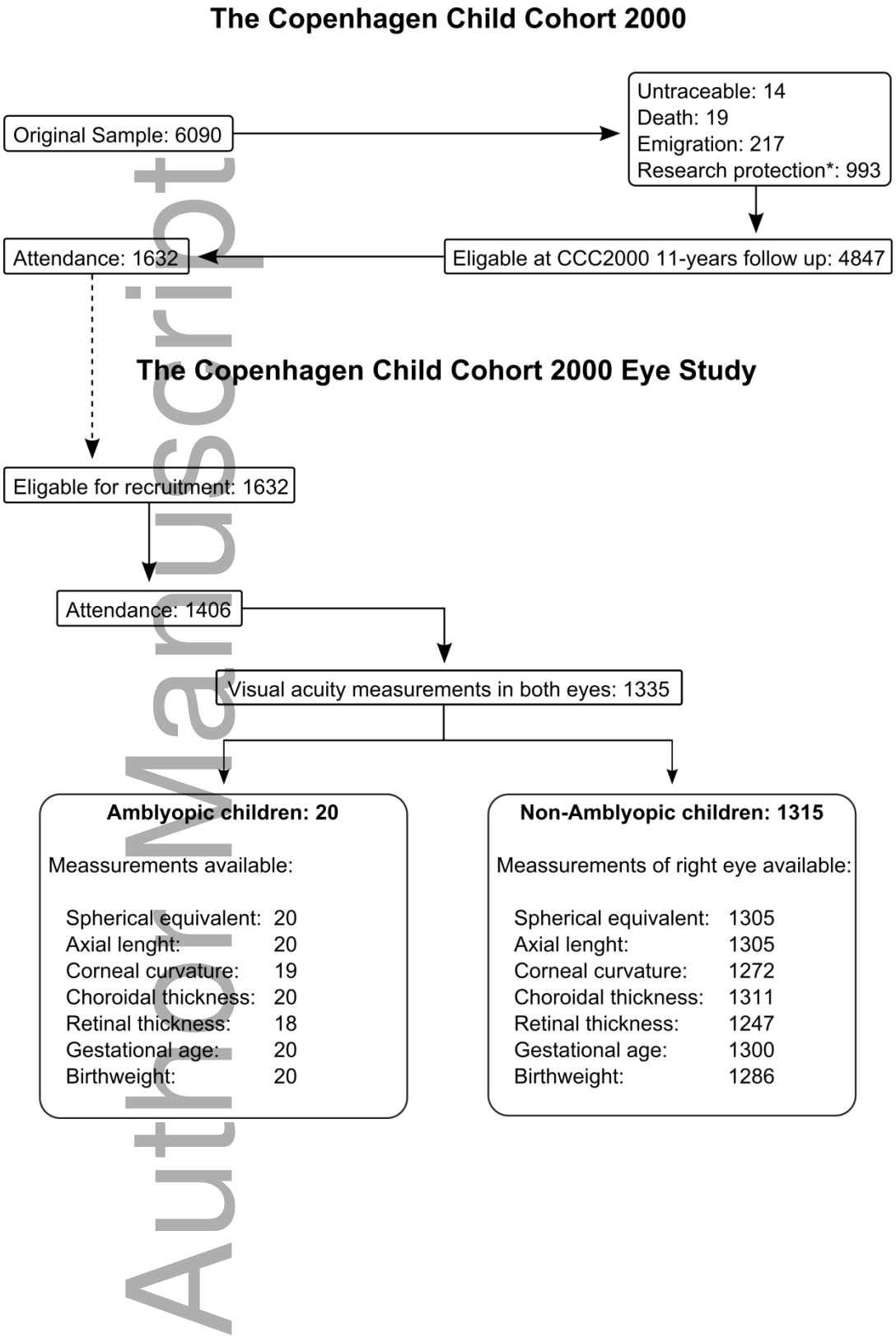

Figure 1. Ascertainment of participants. Research protection (*) refers to a procedure in force until the 1st April 2014 whereby citizens could opt for a general exemption from being invited to participate in research projects through the national civil registry.

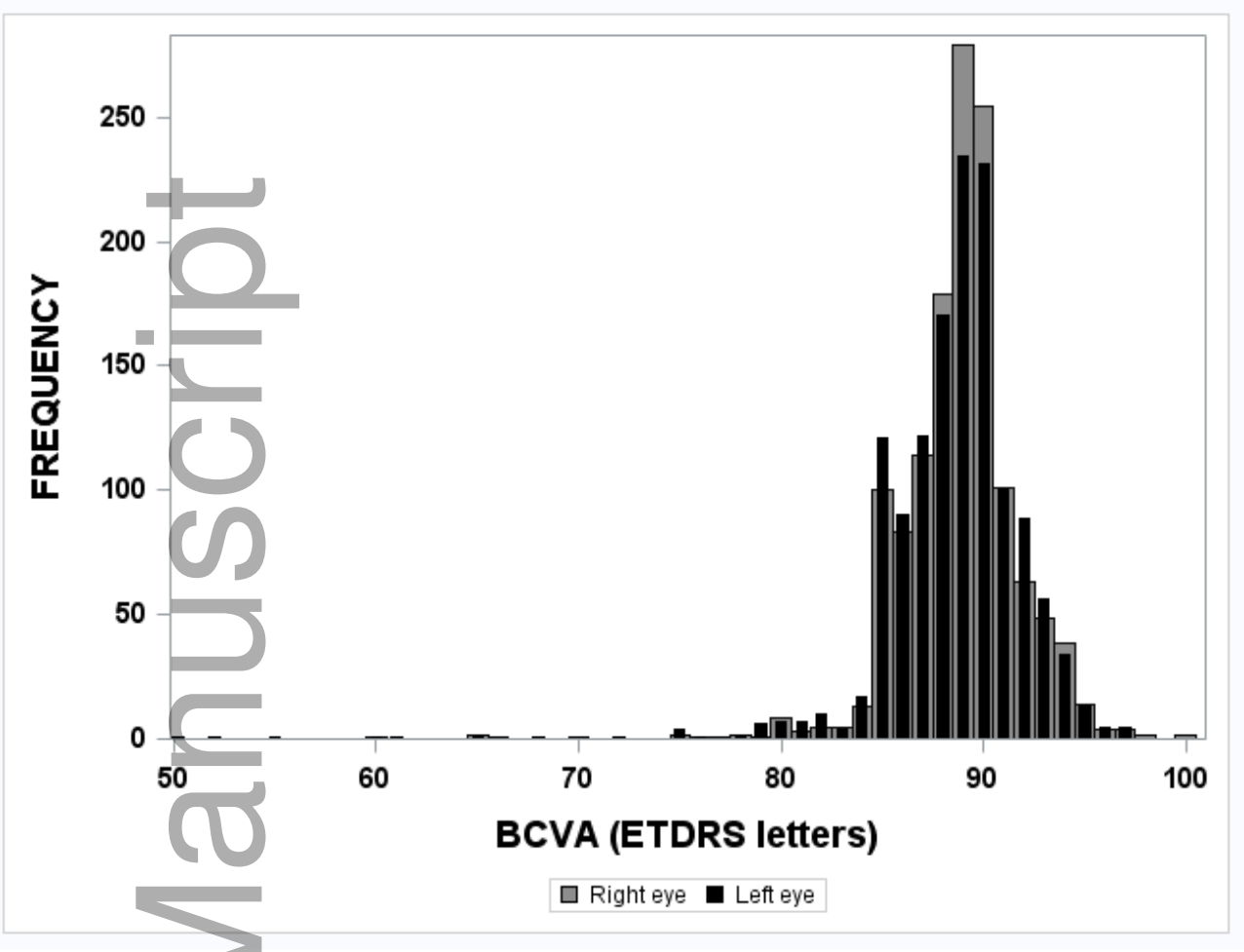

Figure 2. Best-corrected visual acuity distribution in right and left eyes in study population.