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Original Article

Geographical disparities in visual acuity at diagnosis among patients with neovascular age-related macular degeneration

Peter Joseph Wartenberg[1, 2] Andrea Nedergaard Jensen[1, 3], Alexander Kai Thomsen[1, 2] & Torben Lykke Sørensen[1, 2]

1) Department of Ophthalmology, Zealand University Hospital, Roskilde, 2) Faculty of Health and Medical Sciences, University of Copenhagen, 3) Department of Public Health, University of Copenhagen, Denmark

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ABSTRACT

INTRODUCTION. Neovascular age-related macular degeneration (nAMD) affects approximately 8% of the global population. While socioeconomic and geographical disparities have been increasingly studied in Denmark, geographical disparity in best corrected visual acuity (BCVA) at the time of diagnosis in nAMD remains understudied. This study aimed to investigate possible geographical disparity in BCVA at the time of diagnosis in nAMD patients in Region Zealand, Denmark.

METHODS. This was a retrospective study using data from the database "Bedre Oftalmologi for Brugere" from 2011 to 2021. BCVA was extracted for patients at the time of diagnosis with nAMD. Patients were grouped geographically by postal code and municipality. Data were analysed using the Kruskal-Wallis test to investigate geographical disparity and stratified by sex.

RESULTS. A total of 4,266 eyes with nAMD were included. Variations in BCVA at the time of nAMD diagnosis were found between geographical regions in Region Zealand at postal code level and at municipality level. Furthermore, we found a disparity between municipalities among males and females. However, no statistically significant disparity between postal codes was found among males or females.

CONCLUSIONS. There was a significant geographical disparity in BCVA at the time of diagnosis in nAMD patients, inviting further investigation to determine the extent and roots of this disparity.

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Age-related macular degeneration (AMD) is an eye disease affecting approximately 8% of individuals aged ≥ 50 years globally, and is the leading cause of irreversible visual impairment and blindness in the Global North [1]. Age is the greatest risk factor for developing AMD, and its incidence triples per decade after the age of 50 years [2]. Thus, prevalence is expected to increase due to ageing populations [3, 4]. AMD is characterised by degenerative changes in the retina, predominantly in the macula, that affect neural, structural and vascular layers [5]. There are no approved treatments for AMD in Denmark before it reaches the late neovascular form (nAMD), though Age-Related Eye Disease Study (AREDS)-2 supplements are recommended in intermediate AMD. nAMD is characterised by the presence of new macular blood vessels, where vascular endothelial growth factor A (VEGF-A) is a key driver [5]. nAMD is treated with repeated intravitreal anti-VEGF injections, which inhibit the development of neovascularisation and leakage that lead to visual impairment.

Best corrected visual acuity (BCVA) at nAMD diagnosis is important for prognosis, as it establishes a maximum

for expected effects of treatment with anti-VEGF antibodies [6]. As a result, early diagnosis and treatment are important for preserving vision [7]. However, studies show that diagnosis is often made after visual acuity has decreased markedly, with one study finding a median BCVA at diagnosis in nAMD patients starting anti-VEGF treatment of 55 Early Treatment of Diabetic Retinopathy Study (ETDRS) letters and another finding a mean BCVA of 57 letters [8, 9].

Inequality in health persists as a challenge in Denmark [10]. This also applies to eye health, with unequal distribution of eye diseases by ethnicity, biological sex, socioeconomic status and age. A recent Danish study reported an association between socioeconomic factors, including education and household income, and a diagnosis of cataract and glaucoma [11]. In addition, studies conducted in the United States found geographical disparity in a range of eye diseases and decreased BCVA [10, 12]. Similarly, a Danish study identified significant disparity in diabetic retinopathy across postal codes in a geographically limited area around Aarhus [13]. Nonetheless, geographical disparities in BCVA among patients with nAMD remain understudied despite their importance in prognosis.

This study aimed to investigate geographical disparities in BCVA at the time of nAMD diagnosis among patients residing in Region Zealand, Denmark, and to examine potential sex differences in diagnostic presentation.

Trial registration: not relevant.

Methods

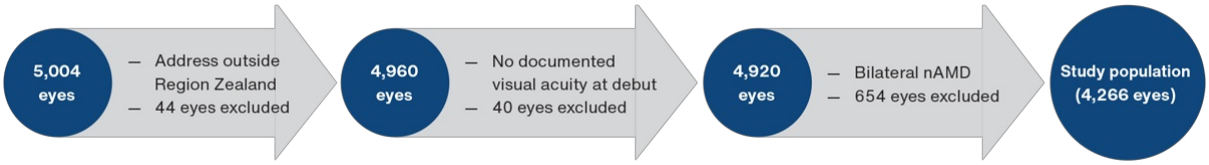
Study design and setting

This retrospective study was conducted in Region Zealand, Denmark. Region Zealand serves approximately 840,000 inhabitants and has 17 municipalities, which are further divided into 129 postal codes. There are two public ophthalmology departments in the region that administer intravitreal anti-VEGF treatments. After referral from practising ophthalmologists or other hospital departments, further diagnostic procedures are generally initiated within two weeks, including the final diagnosis of nAMD. Clinical and demographic data were retrieved from the clinical database “Bedre Oftalmologi for Brugere” (BOB), which stores data from the ophthalmology departments in Region Zealand. Patient information included their care pathways, BCVA and treatments.

Study population

Individuals residing in Region Zealand who were diagnosed with nAMD (International Classification of Diseases, tenth version (ICD-10) diagnosis code DH353J) during a ten-year period from 11 January 2011 to 4 August 2021, were included. BCVA was obtained using an ETDRS chart. In total, 4,096 eyes with a diagnosis of nAMD were scored using an ETDRS chart and a minority of the eyes (n = 170) were scored using a Snellen chart. These were converted to ETDRS using a conversion table [12]. Data for each patient included BCVA at diagnosis in the affected eye, sex, municipality and postal code. In the initial data extraction, 5,004 eyes diagnosed with nAMD were registered in BOB. The exclusion criteria were: 1) residence outside of Region Zealand, 2) missing BCVA data and 3) the better eye in patients with bilateral nAMD (to best determine disease progression before diagnosis) (**Figure 1**).

FIGURE 1 Flow chart of the in- and exclusion of the patient population.



nAMD = neovascular age-related macular degeneration.

Geographical differences

Comparisons of municipalities in the region were conducted to examine disparities. To detect geographical disparity at the most precise geographical level, differences between postal codes in Region Zealand were examined. Due to varying population sizes across the postal codes, we grouped bordering postal codes within the same municipality in an effort to increase the statistical strength of the analysis (Appendix 1).

Best corrected visual acuity

Median BCVA was categorised into four groups (ETDRS letters): ≥ 70 letters, 60-69 letters (70 in the better eye: threshold for obtaining or keeping a driver's license, 36-59 letters (visually impaired), 0-35 letters (socially blind).

Statistical analysis

All analyses were performed using R (version 2024.04.0+735). Descriptive statistics were used to describe patient characteristics by frequencies with percentage, mean with SD and median with IQR where appropriate. Kruskal-Wallis tests were conducted to assess differences in patients' BCVA at diagnosis by place of residence. Additionally, post-hoc pairwise tests were conducted using the Benjamini-Hochberg correction. $p < 0.05$ was considered statistically significant.

Results

A total of 4,266 eyes were included. For patient characteristics, please see **Table 1**.

TABLE 1 A summary of patient characteristics, including the number and proportion of the study population.

All eyes, n (%)	
Female	2,699 (63.3)
Male	1,567 (36.7)
Total	4,266
BCVA according to Early Treatment of Diabetic Retinopathy Study	
0-35, n (%)	642 (15.0)
36-59, n (%)	1,454 (34.0)
60-69, n (%)	979 (22.9)
≥ 70, n (%)	1,191 (27.9)
Median BCVA	60.0

BCVA = best corrected visual acuity.

Geographical disparity

Among municipalities, a difference in BCVA at diagnosis was observed ($p < 0.001$), which was subsequently confirmed by post-hoc pairwise tests (Appendix 2). Additionally, differences in BCVA at diagnosis were observed between postal codes ($p = 0.0019$), though these were not confirmed by post-hoc tests. When analysing each sex separately, differences were identified among males ($p = 0.017$) and females ($p = 0.049$) at the municipality level, though these were not confirmed by post-hoc tests. No differences were found among males or females at the postal code level.

Best corrected visual acuity at diagnosis among municipalities

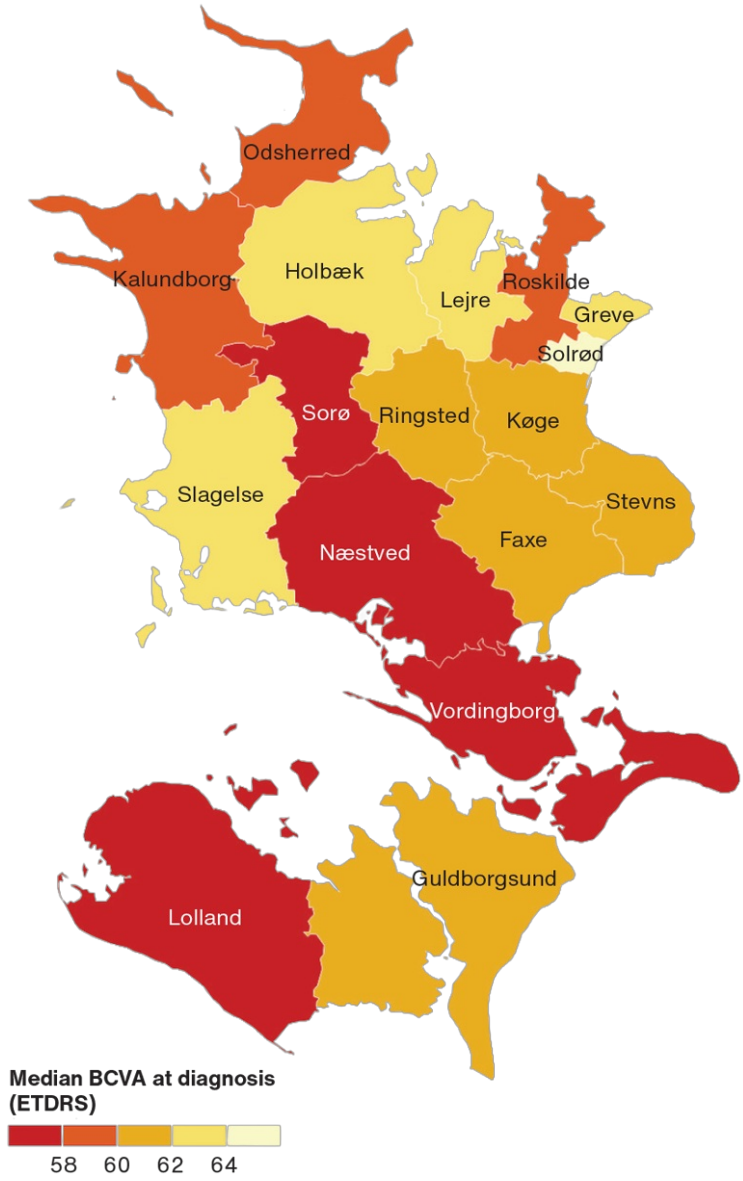
For the entire study population, the municipalities of Lolland and Næstved had the lowest BCVA at diagnosis (median of 56 letters), whereas Solrød Municipality had the highest BCVA at diagnosis, at 66 (median letters). Sex stratification showed similar results, with Solrød Municipality having the highest BCVA at diagnosis (males: 68 letters, and females: 65.5 letters). For females, Næstved Municipality had the lowest BCVA at diagnosis (56 letters), whereas for males, Vordingborg Municipality had the lowest BCVA at diagnosis (53 letters) (Appendix 3).

Best corrected visual acuity at diagnosis among postal codes

When assessing differences in BCVA at diagnosis at the postal code level, Guldborgsund (Group 2) had the lowest median BCVA at diagnosis (52 letters), and postal codes 4040 in Roskilde and Holbæk (Group 3) had the highest BCVA at diagnosis, both at 67 letters. Among females, the lowest median BCVA was observed in a postal code in Odsherred (4540: 49.5 letters), whereas the highest value was observed in a postal code in Roskilde (4040: 69.0). Among males, the lowest median BCVA was found in a grouping in Næstved Municipality (Group 1: 47 letters)

and the highest values were observed in a postal code in Lejre (4320) and Solrød (2680), both at 68.0 letters (**Figure 2**).

FIGURE 2 Best corrected visual acuity at diagnosis of neovascular age-related macular degeneration by municipality in Region Zealand



BCVA = best corrected visual acuity; ETDRS = Early Treatment of Diabetic Retinopathy Study.

Notably, none of the groups from Lolland, Næstved or Vordingborg municipalities had a median BCVA at diagnosis of > 60 letters, indicating these areas had the lowest BCVA at diagnosis in Region Zealand (Appendix 4).

Discussion

This was the first study to investigate geographical disparities in BCVA at the time of nAMD diagnosis among

patients residing in Region Zealand. Our findings highlight that there are geographical disparities in BCVA at the time of nAMD diagnosis. This was observed across postal codes and municipalities in Region Zealand. These findings bring insights into inequality in eye health in Denmark.

When examining each sex individually, a significant difference in BCVA at diagnosis was identified at the municipality level for both sexes. Conversely, at postal code level, no sex differences were observed. However, post-hoc tests showed a high risk of false positives in the municipality tests. This lack of significant findings may be due to several factors, including variation in group sizes and heterogeneity within groups. The considerable variation in group sizes within postal codes, including small population groups, decreases statistical power due to greater heterogeneity, highlighting the challenges of analysing smaller subgroups.

Interestingly, we found that patients from Lolland, Næstved and Vordingborg municipalities presented with the lowest BCVA at diagnosis, which may be attributable to various factors. Despite Denmark's universal healthcare system providing free access to most healthcare services, including general practitioners and practising ophthalmologists, disparities still exist in health-seeking behaviour. This includes challenges in reaching healthcare facilities, transportation issues, and other logistical barriers identified as delaying diagnosis. Furthermore, low health literacy resulting in delayed response to symptoms has been found to delay diagnosis in nAMD, and a Danish mixed-method study highlighted the need for patient education to improve healthcare-seeking behaviour among these patients [14]. This inequality in access to and utilisation of healthcare services could contribute to variations in treatment outcomes. Moreover, the municipalities of Lolland and Guldborgsund are noted for shorter life expectancies, which may reflect broader challenges in healthcare access and a more comorbid population [15]. These areas, however, have a high concentration of practising ophthalmologists, which could contribute to Guldborgsund's higher BCVA at diagnosis compared with the two other municipalities with poor social determinants of health. Statistical extracts from Statistics Denmark show that Lolland Municipality has the greatest proportion of residents whose highest completed education is either primary school or vocational training, and the lowest disposable family income in Region Zealand (Appendix 5, 6). Similarly, Vordingborg and Næstved municipalities are in the lower half of the region in terms of disposable income. This finding echoes the findings of other studies that have identified socioeconomic inequality in the utilisation of eye health services [16]. Conversely, we found that patients from municipalities with higher disposable income and higher levels of education, including Lejre, Solrød and Greve, showed the highest median BCVA at diagnosis. This is particularly concerning as more individuals in these areas may end up with significantly reduced vision, highlighting the need for targeted interventions and support in these communities [17].

Strengths and limitations

Strengths of this study include the large patient population. The BOB database enhances the reliability of the results, which are entered into the same system and do not require data acquisition from patient journals. Our study has limitations, including potential heterogeneity in BCVA measurements and data entry in the BOB system. Moreover, we only had access to data up to 2021; thus, the results do not necessarily reflect the current situation in Region Zealand. Nonetheless, they provide valuable insights into geographical disparities to consider in future studies, where temporal analysis would be ideal in further investigation. The study period overlapped with the COVID-19 pandemic, including periods of nationwide societal lockdown and public health restrictions, during which healthcare utilisation declined. Following the lifting of restrictions, a compensatory increase in activity was observed [18]. Furthermore, heterogeneity among practising ophthalmologists may potentially have contributed to variations in referrals. Small sample sizes in postal code populations have also limited the ability to stratify by age.

Research implications

The significant geographical differences observed may be attributed to multiple factors, including patient health literacy, access to eye specialists, waiting times and chronic disease management. Nonetheless, further research into this matter is warranted. This study focused only on areas within Region Zealand, resulting in a limited study population. To gain a more comprehensive understanding of the disparity in BCVA at nAMD diagnosis, future research should study whether geographical differences apply across all regions. This expanded approach could offer a broader view of geographical disparities, potentially leading to improved detection of nAMD patients and increased attention to areas where residents have lower BCVA at diagnosis, enabling a targeted detection strategy.

Conclusions

Geographical disparity in BCVA at nAMD diagnosis was observed across municipalities in Region Zealand; however, this pattern was not clearly evident after stratification by sex. Further investigation is needed to develop a more nuanced understanding.

AI declaration: ChatGPT ver. 3.5 was utilised for aid in coding. We, the authors, acknowledge our responsibility for the accuracy and originality of the final work, including the critical evaluation of any AI-generated content.

Correspondence *Torben Lykke Sørensen.* E-mail: tlso@regionsjaelland.dk

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