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Prevalence of neovascular age-related macular degeneration and geographic atrophy in Denmark

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ABSTRACT

INTRODUCTION: In Denmark, age-related macular degeneration (AMD) is the most common cause of blindness. To better understand current and future challenges, we estimated and projected the annual number of patients with neovascular AMD and geographic atrophy in Denmark from 2016 to 2060.

METHODS: Detailed age- and gender-stratified prevalence estimates of neovascular AMD and geographic atrophy in a Scandinavian population were identified and applied to age- and gender-stratified population numbers provided by Statistics Denmark. Prevalence estimates were calculated for each year from 2016 to 2060. Future forecasts were provided by Statistics Denmark and based on calculations by the Danish Institute for Economic Modelling and Forecasting.

RESULTS: We estimated that there are currently ~30,000 patients with neovascular AMD and ~21,000 patients with geographic atrophy in Denmark. The majority of these patients are persons aged ≥ 85 years. For neovascular AMD, the number of patients will grow to ~33,000 in 2020, ~58,000 in 2040 and ~72,000 in 2060. For geographic atrophy, the number of patients will grow to ~23,000 in 2020, ~41,000 in 2040, and ~50,000 in 2060.

CONCLUSIONS: We expect a steady growth in the prevalence of neovascular AMD and geographic atrophy in Denmark due to an ageing population. These numbers emphasise the importance of disease prevention, careful planning of health service activities and continuing research.

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TRIAL REGISTRATION: not relevant.

Age-related macular degeneration (AMD) is a degenerative disease of the central retina [1]. In Denmark, one out of three persons above 60 years of age have early signs of the disease defined as the presence of small deposits of cellular debris under the retina (drusen) [2]. Drusen formation is linked to an inefficiency of the retina and its supporting epithelium to handle the constant exposure to reactive oxygen species [1]. This is the result of an age-related decline in cellular function [3], genetic composition [1] and environmental exposure [1]. Overall, ageing is the single most important factor for the development of early AMD and for progression

to the late stages of the disease [1], which comprises two substantially different phenotypes (**Figure 1**).

One phenotype – neovascular AMD – is characterised by formation of new vessels in the choroid (capillaries under the retina) which protrude through Bruch's membrane (basal membrane of the retina) and into the retina [1]. This neovascularisation is caused by a complex immunological interplay wherein secretion of vascular endothelial growth factor (VEGF) is the most important driving force [4, 5], which can be counteracted clinically by intravitreal injections with VEGF inhibitors [6, 7]. If left untreated or if the treatment is unresponsive, fibrosis starts developing, which marks the end-stage of neovascular AMD where vision is lost permanently [1].

Another phenotype of late AMD – geographic atrophy – is characterised by a neurodegenerative process wherein retinal nerve cells and supporting tissue undergo cellular death in clearly demarcated areas [1]. There is currently no approved medical treatment; however, this might change in near future since phase 2-results of a monoclonal antibody targeted complement factor D, Lampalizumab (Genentech, CA, USA), was recently published with results suggesting a 20% reduction in lesion area progression [8].

Both neovascular AMD and geographic atrophy significantly impact the quality of life of the patients [7, 9]. Patients develop rapid visual loss upon progression to neovascular AMD [1]. Patients typically complain of sudden worsening of central vision that is described as straight lines becoming wavy (metamorphopsia), blurred vision or an area with no vision (scotoma). The visual loss is typically slower in patients with geographic atrophy [1], and the visual experience can be characterised as blurred vision that gradually takes the form of a scotoma. Visual rehabilitation does exist and is focused on using the remaining vision to sustain visual function as much as possible. In Denmark, this task is performed by dedicated institutes around the country (in Danish: "synscentraler").

Diagnosis, treatment and rehabilitation of AMD proves a significant challenge in the publicly funded Danish healthcare system. The large number of patients underlines the need for careful design of health the ser-

ORIGINAL ARTICLE

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vices [10, 11] and constitutes a significant economic burden as VEGF inhibitors generated costs of approximately 400 m DKK in 2016 in Denmark alone according to the Danish Health Data Authority.

In Denmark, an ongoing demographic shift is expected to significantly increase the number of elderly people. In this paper, our aim was to estimate the Danish prevalence of subtypes of late AMD – neovascular AMD and geographic atrophy – and their projected prevalence until 2060 to provide a basis for discussions, decisions and planning.

METHODS

Population numbers for Denmark and projections until 2060

Statistics Denmark is the central authority on societal statistics in Denmark. Every year, Statistics Denmark compiles data on current population, immigration, emigration, livebirths and deaths, which are then provided to the Danish Institute for Economic Modelling and Forecasting (DREAM), which is an independent semi-governmental institution that provides analyses and forecasting relating to the Danish economy [12]. Statistics Denmark and DREAM model the data based on assumptions regarding migration, fertility and mortality [12]. The assumptions are based on historical experience [12]. Based on the final model, one population projection is made available to the public, which may be further stratified by different variables such as age and gender [13]. Its assumptions on population primo and population increase (calculated from immigration, emigration, livebirths, and deaths) are also available to the public [12].

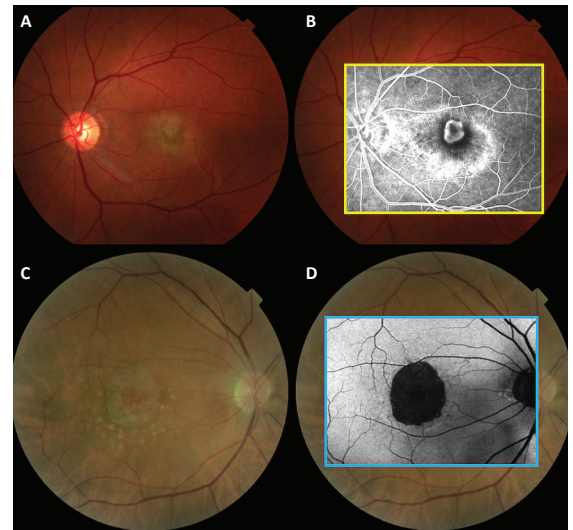
TABLE 1

Population of elderly people in Denmark in 2016 and estimated number of patients with neovascular age-related macular degeneration (AMD) using the prevalence estimates of the Age Gene/Environment Susceptibility Reykjavik Study.

Age group, yrs	Total population, n	Neovascular AMD		Geographic atrophy	
		%	n	%	n
<i>Females</i>					
66-69	141,834	0.6	851	0.3	426
70-74	151,845	1.3	1,974	0.7	1,063
75-79	104,872	3.1	3,251	1.9	1,993
80-84	72,159	6.0	4,330	5.8	4,185
≥ 85	79,025	11.3	8,930	6.4	5,058
<i>Males</i>					
66-69	136,122	0.5	681	0.0	0
70-74	140,598	0.6	844	0.2	281
75-79	89,001	1.5	1,335	1.9	1,691
80-84	53,210	6.3	3,352	4.4	2,341
≥ 85	39,364	11.4	4,487	9.0	3,543
Total	1,008,030	3.0	30,034	2.0	20,580

FIGURE 1

A. Retinal photograph of a left eye with neovascular age-related macular degeneration. B. Retinal angiography is used for a detailed examination, diagnosis and activity measurement of the choroidal neovascularisation. Shown here in a locational-matched yellow-framed image, early-phase fluorescein-based retinal angiography clearly reveals the neovascular activity. C. Retinal photograph of a right eye with geographic atrophy. D. Retinal auto-fluorescence is used for a detailed examination, diagnosis and activity measurement of the geographic atrophy. Shown here in a locational-matched blue-framed image, lack of auto-fluorescence confirms degeneration of the retinal pigment epithelium-photoreceptor complex.



Prevalence estimates of neovascular age-related macular degeneration and geographic atrophy

Several studies have characterised the prevalence of AMD in Nordic countries. The Copenhagen City Eye Study was a population-based investigation of visual acuity and eye diseases conducted in a subsample of participants from the Copenhagen City Heart Study [14]. Here, the investigators looked at various aspects of late AMD, but the prevalence of neovascular AMD and geographic atrophy were not published as age- and gender-stratified prevalence data [14]. The Tromsø Eye study included a subgroup from the 6th Tromsø Study, where 2,539 participants aged 65-87 years had fundus photographs taken [15]. This study determined the prevalence and characteristics of different subtypes of AMD, including geographic atrophy and neovascular AMD [15]. In a larger study, the population-based cohort Age Gene/Environment Susceptibility (AGES) Reykjavik Study recruited 5,330 individuals aged 66-91 years [16]. Since this latter study was the largest with available detailed age- and gender-stratified characterisation of the prevalence of neovascular AMD and geographic atrophy in a Nordic Caucasian population [16], we decided to use its estimates for the present study.

Data analysis

For each year from 2016 to 2060, we used the age- and gender-stratified population counts and estimates from Statistics Denmark [13] and estimated the age- and gender-specific numbers of patients with neovascular AMD and geographic atrophy using the prevalence estimates from the AGES study [16]. All calculations were made in Excel 2013 (Microsoft, Redmont, WA, USA) and figures were prepared in Prism 7 (GraphPad Software, La Jolla, CA, USA).

Trial registration: not relevant.

RESULTS

Population numbers are presented in **Table 1** together with prevalence estimates. We estimate that there are currently ~30,000 patients with neovascular AMD and ~21,000 patients with geographic atrophy in Denmark. The majority of these patients are aged ≥ 85 years.

The estimated numbers of patients with neovascular AMD are presented in **Figure 2**. We expect a steady growth in prevalence, mainly due to an increase in the group of people aged ≥ 85 years. This will lead to the following forecast of patients with neovascular AMD: ~33,000 in year 2020, ~48,000 in year 2030, ~58,000 in year 2040, ~68,000 in year 2050 and ~72,000 in year 2060.

The estimated number of patients with geographic atrophy are presented in **Figure 3**. We expect a steady growth in the prevalence of geographic atrophy due to an increase in the group of people aged ≥ 85 years. This leads to the following forecast of patients with geographic atrophy: ~23,000 in year 2020, ~34,000 in year 2030, ~41,000 in year 2040, ~48,000 in year 2050 and ~50,000 in year 2060.

DISCUSSION

We find that the expected number of patients with any late AMD in Danes aged ≥ 65 years is approximately 51,000, which we project will increase to approximately 122,000 patients in 2060. This increase is mainly the result of an increase in the number of people aged ≥ 85 years.

Ageing is the most important risk factor for progression from early AMD to late AMD [1]. Other important risk factors are family history and lifestyle factors such as physical inactivity, obesity and cigarette smoking [1]. The Age-Related Eye Disease Studies (AREDS) investigated the effects of various antioxidant vitamins and minerals in patients with early AMD in a randomised controlled manner. Based on the positive findings from the latest AREDS2 study, the following oral supplement is recommended per day: vitamin C (500 mg), vitamin E (400 IU), zinc (80 mg), copper (2 mg), lutein (10 mg) and zeaxanthin (2 mg) [17]. Beyond this treatment, studies

suggest that the strongest effect of risk reduction is obtainable through smoking cessation and increased physical activity [1, 2]. Smoking increases the risk of progression by 30% and smoking cessation may lower the risk to that of non-smokers [1, 2]. Being moderately or highly physically active can decrease the risk of progression by 30-50% when compared with physically inactive people [2].

FIGURE 2

Projected number of patients with neovascular age-related macular degeneration in Denmark, 2016-2060.

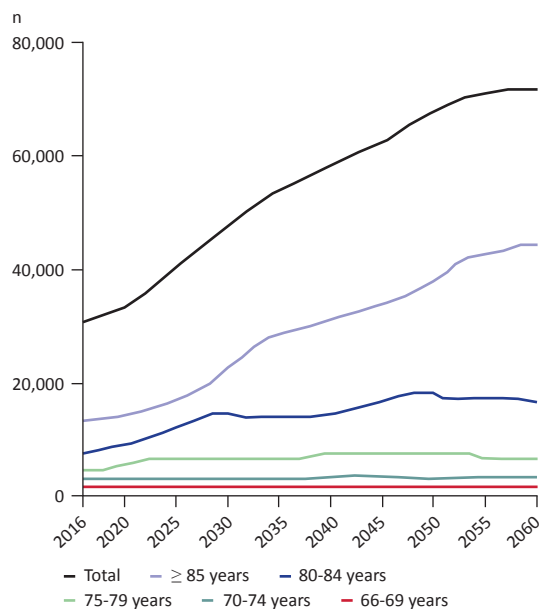
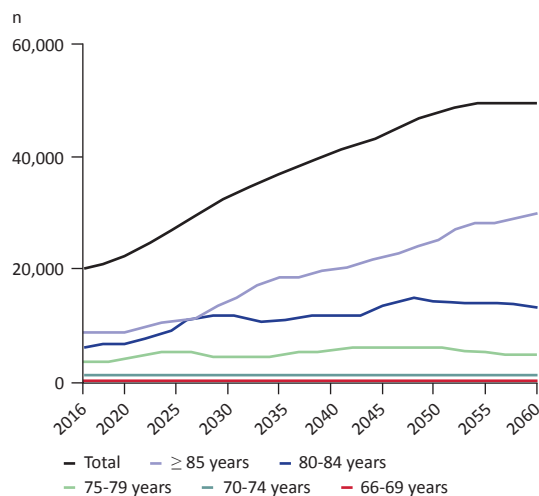


FIGURE 3

Projected number of patients with geographic atrophy in Denmark, 2016-2060.



Lindekleiv & Erke estimated the number of patients with late AMD in Scandinavia in 2013 without distinguishing the subtypes of neovascular AMD and geographic atrophy [18]. Their estimate of approximately 47,000 patients with any late AMD in Denmark in 2013 are in line with the findings of our study. The Danish Council for the Use of Expensive Hospital Medicines in Denmark (Rådet for Anvendelse af Dyr Sygehusmedicin) estimated that the number of patients with neovascular AMD who are in treatment was 13,000-14,000 in their recommendations published in December 2016 [19]. It is expected that one out of every three will discontinue treatment after a year and that some patients present with untreatable eyes [19]. Høeg et al mapped the epidemiology of adult visual impairment in Denmark and found that 50% of visually impaired patients with neovascular AMD were in treatment with VEGF inhibitors [20]. These numbers confirm that the total number of patients with neovascular AMD in Denmark may be around 30,000, which is in line with the results reported in the present paper. Taken together, these numbers demonstrate that AMD is a relatively common disease in Denmark and that we expect an increase in the demand of retinal services. Research is needed into how best to organise such services, and even small improvements towards a higher efficiency (speed of treatment and letting nurses perform injections) or a lower risk of complications (use of operating rooms and protocols for preparations) are welcome to facilitate the necessary adaptation to the increasing demand [10, 11].

Important study limitations should be highlighted. First, prevalence estimates are based on a representative Scandinavian population (the Icelandic population), which can only be considered an approximation. Second, population projections are based on qualified guesses and likely models on important demographic variables: life expectancy, immigration, emigration, livebirths and deaths. The future number of patients thus depends on the model's ability to predict correctly. Third, future developments in risk reduction of progression to neovascular AMD or geographic atrophy may decrease the prevalence of these late stages of the disease.

CONCLUSIONS

We estimate the number of patients with neovascular AMD to be approximately 30,000 and the number of patients with geographic atrophy to be approximately 21,000. We expect a steady growth in these numbers in the future, mainly due to an increase in the group of persons aged ≥ 85 years. In year 2060, we expect the number of patients with any late AMD to be approximately 122,000. Attention should be given to disease prevention, careful planning of health services and continuing research.

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CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

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