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Patient perspectives and barriers in the treatment of neovascular age-related macular degeneration in Denmark: a qualitative study

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ABSTRACT

Objectives This qualitative study aims to identify patient-reported barriers to treatment for neovascular age-related macular degeneration (nAMD) and investigate their impact on quality of life.

Design Using a qualitative explorative design.

Setting Semi-structured individual or dyadic interviews were conducted with patients and their relatives.

Participants Twenty-one patients completed the interview, with four of them having a relative present.

Interventions Gadamer's hermeneutics guided the epistemological approach, and maximum variation sampling was employed to capture diverse patient experiences. An advisory board consisting of patients, relatives and ophthalmologists ensured the relevance of the study. Thematic analysis was conducted using NVivo software.

Primary and secondary outcome measures To investigate patient-reported barriers to the recommended treatment for nAMD and impact on quality of life.

Results The study included 21 patients with nAMD, with a median age of 79 years. Five themes emerged: (1) good compliance with intravitreal treatment, (2) the dual role of relatives, (3) treatment commute, (4) hospital barriers, (5) preventive health literacy.

Conclusion This study highlights the resilience and adherence of patients with nAMD in Denmark to their treatment despite various barriers. While the therapy may have negative effects on their well-being, patients do not opt out of treatment. These findings underscore the importance of personalised treatment plans that provide, for example, convenient access to care and clear future agreements at the hospital. By adopting more patient-centred approaches, healthcare providers can enhance patient satisfaction and improve treatment adherence, ultimately leading to better patient outcomes and quality of life.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ To enhance the trustworthiness of the study, we employed various techniques, including investigator triangulation.
⇒ The qualitative nature of the study enabled a detailed exploration of patients' perspectives, which may be challenging to capture using quantitative approaches.
⇒ Purposeful sampling aimed to achieve maximum variation, allowing for a diverse range of neovascular age-related macular degeneration experiences, but the findings are not generalisable due to the small sample size and qualitative nature of the study.
⇒ An advisory board including patients and caregivers provided valuable insights on barriers faced by patients and the public, based on their first-hand experiences.

INTRODUCTION

Neovascular age-related macular degeneration (nAMD) is the main cause of irreversible vision impairment and blindness among elderly in the Global North.[1] In Europe, approximately 15 million patients suffer from nAMD. With the increase in life expectancy, it is expected that the number of nAMD cases will rise, and by the year 2050, around 6.4 million patients worldwide will be diagnosed with nAMD.[2–5]

nAMD primary targets the macula resulting in central vision loss and distorted images for affected patients. As the condition's name implies, nAMD is closely linked to the ageing process, with its prevalence rising from 3.5% in individuals aged 55–59 to 17.6% in those aged 85 years and older.[6]

The introduction of intravitreal angiostatic therapy (vascular endothelial growth factor (VEGF) inhibition) in 2006 has revolutionised the treatment of nAMD, resulting in a significant reduction in new cases of blindness among individuals over 50 years old.[7 8] However, this treatment often requires continuous treatment and monitoring for years, which can pose challenges for elderly and visually impaired patients. In Denmark alone, approximately 14 000 patients are in treatment for nAMD.[9] A study revealed that up to 20% of patients opted out of treatment

within the first 2 years for non-medical reasons.[10] The reasons behind patients discontinuing treatment remain unknown. A global survey found that 84% of patients treated with intravitreal VEGF inhibitors were compliant with treatment, while the reasons for non-compliance were unclear.[11] Furthermore, a study reported scenarios where patients would consider stopping nAMD treatment, including a perceived lack of treatment effectiveness, side effects outweighing benefits, changes in reimbursement and difficulties related to transportation.[4]

Although it is known that some patients with nAMD do not adhere to the recommended treatment regimen, there is limited understanding of the factors contributing to their discontinuation or omission of treatment. This is especially relevant in a country like Denmark, where treatment is tax funded, unlike in other countries where patients are more aware of the cost.[4] Barriers such as insufficient knowledge about the disease and treatment, long travel distances to the hospital, or frequent hospital visits may contribute to this issue. It is crucial to gain a comprehensive understanding of the patient population and address this knowledge gap by exploring the specific barriers they face during treatment.

The objective of this qualitative study was to investigate patient-reported barriers to the recommended treatment for nAMD and their impact on quality of life.

MATERIALS AND METHODS

Study design

A qualitative exploratory design was employed to gain insight into the patient's perspective on the treatment of nAMD, according to the pre-planned study protocol (online supplemental material 1). This involved conducting semi-structured interviews with individual patients (n=17) or with patients and their relatives in a dyadic setting (n=4). The chosen approach aimed to capture the subjective experiences and viewpoints of the patients.

The research methodology was influenced by Gadamer's hermeneutics, an epistemological framework. The primary investigator (PI), who conducted the interviews, used own pre-existing understanding and knowledge to interpret the data. The process of interpretation involved a dynamic interplay between new insights gained from the interviews and the PI's existing understanding, forming a circular motion known as the hermeneutical circle.[12] The PI, a doctor specialising in ophthalmology with several years of clinical experience, brought a unique sensitivity to the patients' perspective, ensuring a comprehensive understanding of their experiences. The PI sought to address the potential risk of agreement that can arise from several years of clinical experience, aiming to prevent any hindrance in the research process.

Patient and public involvement

To ensure the relevance and applicability of the study with patient and public involvement (PPI), a continuous advisory board was established. This board consisted of five individuals currently undergoing treatment for nAMD and three ophthalmologists. Moreover, three out of five patients in the PPI had their close relatives present at the meetings, providing valuable insights from multiple perspectives.

Throughout the research process, the PPI offered feedback on various aspects of the study, including the development of the study guide, the understanding of the transcribed interviews and the analysis process. Their contributions helped ensure that the research effectively captured the patient's viewpoint and addressed the concerns and needs of both patients and the broader public.

Everyone involved in the study will receive an orientation on the study results as soon as they are published.

Recruitment and selection

The study participants consisted of patients diagnosed with nAMD (n=21), and in some cases, their close relatives also participated (n=4). The decision to have a relative present during the interview was left to the patients' discretion, but it was not mandatory. The intention behind conducting dyadic interviews, involving both the patient and their relative, was to leverage the synergistic effect of two individuals who had experienced the treatment process from different perspectives. This approach allowed them to complement and enhance each other's insights during the interview.

Data saturation was achieved after conducting 21 interviews, indicating that further interviews were unlikely to yield substantially new information or insights.[13] This sample size was deemed sufficient to capture the range of patient perspectives and experiences related to the treatment of nAMD.

To ensure a comprehensive exploration of the topic, we employed a purposive sampling method known as maximum variation sampling or heterogeneous sampling. This approach aimed to provide greater insights into the patient experience of nAMD treatment by considering a diverse range of perspectives. The inclusion criteria required participants to be diagnosed with nAMD, be aged 60 years or older and receive intravitreal VEGF inhibition treatment at either Odense University Hospital (OUH) or Zealand University Hospital, Roskilde (ZUH).

To achieve maximum variation in the study sample, we included patients from various geographical locations, such as two out of five regions in Denmark, ensuring diversity in terms of distance from the hospitals. We also considered medical aspects, including the time since diagnosis and the severity of the disease or visual impairment. Furthermore, we took into account various social aspects, such as whether participants lived alone or were married. Exclusion criteria were moderate and severe dementia or the inability to provide written consent. Patients with nAMD were recruited with the assistance of nurses at the Departments of Ophthalmology at OUH and ZUH or through posters displayed at OUH. Additionally, two

patients were recruited through snowball sampling, a method where existing participants refer other potential participants for inclusion in the study.

Data generation

Interviews were conducted between March 2022 and December 2022. These interviews took place either face-to-face at the hospital (n=12) or over the telephone (n=9). To guide the interviews, a semi-structured interview guide was collaboratively developed in consultation with the PPI board (online supplemental material 2). This guide incorporated themes identified in the existing literature as well as topics deemed important by the PPI board members.

All interviews were digitally recorded to ensure accurate capturing of the participants' perspectives. Before proceeding with the main interviews, three pilot interviews were conducted with individuals from the study population. The purpose of these pilot interviews was to assess the participants' understanding and acceptance of the interview content. No revisions were deemed necessary based on the pilot interviews, and as a result, they were included in the final analysis.

The interviews had a median duration of 33 min, with an IQR from 29 to 39 min. It is worth noting that one interview was requested to be finished by the patient after 14 min. Despite its shorter duration, this particular interview was evaluated to contain valuable and relevant content and was, therefore, included in the final analysis.

Following each interview, the PI made field notes immediately, capturing important observations and details. These field notes played a crucial role in the initial analysis conducted to construct the analytical narrative. For transcription and coding purposes, the QSR software system NVivo V.12 was used.

Strategy of analysis

To enhance the trustworthiness of the study, the data analysis was conducted by a team of three qualitative investigators, incorporating investigator triangulation.[14] Thematic analysis was employed, which encompassed six distinct analytical phases.[15]

In phase 1, the transcription process was carried out by a scientific assistant and the PI using the intelligent verbatim transcription method. The PI transcribed three interviews, while a scientific assistant, who was not part of the team, transcribed eighteen interviews. The transcripts were thoroughly read multiple times to become familiar with the content, and initial notes were taken to generate ideas for coding. In phase 2, the PI initially coded the dataset using an inductive coding approach to organise the data into meaningful groups. Subsequently, the team of investigators discussed the 32 generated codes collectively. For phase 3, a semantic approach was employed to develop initial themes based on the identified codes. The investigators engaged in discussions regarding the relationship between the codes and themes, resulting in a total of nine themes being considered. In phase 4, the themes were further refined through extensive discussions among the investigators and were subsequently validated through a comprehensive discussion with the PPI board. Eventually, five main themes emerged, namely: (1) good compliance with intravitreal treatment, (2) the dual role of relatives, (3) treatment commute, (4) hospital barriers and (5) preventive health literacy. During phase 5, each theme was supported by relevant quotes extracted from the interviews and incorporated into the final manuscript. This helped to provide concrete examples and strengthen the findings. Finally, in phase 6, the findings were presented and effectively addressed the aim of the study, bringing the research to a meaningful conclusion.

RESULTS

Demographics

We enrolled a total of 21 patients diagnosed with nAMD, and their median age was 79 years (IQR 76–85 years). Among the participants, 11 were married or living with a partner, while 10 patients lived alone. The duration of nAMD varied, ranging from 1 to 20 years, with a median duration of 6.2 years. Among the patients, eight had nAMD affecting one eye, while 13 had it in both eyes. Before the interview, one patient (ID10) had discontinued treatment for personal reasons, while the remaining participants continued to receive regular intravitreal treatment at the hospital. Unfortunately, no potential participants with non-Western backgrounds volunteered for our study. The study included a total of 10 patients treated at ZUH and 11 patients treated at OUH, as detailed in table 1.

Table 2 displays the quotes extracted from the study participants, which are used in the Results section.

Good compliance with the intravitreal treatment

This theme highlights the patients' high level of adherence to the recommended treatment, despite encountering various barriers. It is noteworthy that none of the patients currently undergoing treatment expressed any inclination to deviate from the recommended course of treatment (quotes 1 and 2). Even though several patients were unaware of the underlying pathological mechanisms of nAMD (quotes 3 and 4) and the treatment effects of VEGF inhibitors, this lack of knowledge does not seem to serve as a barrier to their ongoing treatment (quotes 5 and 6). The uncertainty surrounding the efficacy of the recommended treatment does not appear to drive patients to seek alternative treatment options (quotes 7–9).

Despite the negative effect of intravitreal treatment on the mental well-being of some patients, their good compliance with the treatment persists. One patient, who had been receiving treatment for 1 year, described the adverse impact of the intravitreal treatment on their well-being (quote 10). The negative impact on mental well-being does not appear to diminish over time. A patient who had been receiving treatment for over 5 years shared their ongoing sentiments regarding the treatment and

Table 1 Demographics

Patient ID	Patient age (years)	Sex	Place of treatment	Eyes with nAMD (n)	Duration of nAMD (years)	Cohabitation type	Interview setting	Individual or dyad interview (relationship)
4	63	Female	Odense	1	3	Cohabitation	Face-to-face	Individual
19	67	Female	Roskilde	2	10	Cohabitation	Phone	Individual
13	70	Female	Roskilde	1	2	Cohabitation	Face-to-face	Individual
18	73	Female	Roskilde	2	5	Single dwelling	Phone	Individual
5	75	Male	Odense	1	1	Cohabitation	Face-to-face	Dyad (with partner)
6	76	Male	Odense	1	5	Cohabitation	Face-to-face	Dyad (with partner)
11	76	Male	Odense	2	20	Cohabitation	Face-to-face	Individual
17	77	Male	Roskilde	2	3	Cohabitation	Phone	Individual
20	77	Female	Roskilde	2	4	Cohabitation	Phone	Individual
21	77	Male	Roskilde	2	4	Cohabitation	Phone	Individual
2	79	Female	Odense	2	5	Single dwelling	Face-to-face	Individual
8	82	Female	Odense	2	3	Single dwelling	Phone	Individual
1	84	Female	Odense	1	1	Single dwelling	Face-to-face	Individual
9	85	Female	Odense	2	1	Single dwelling	Phone	Individual
14	85	Female	Roskilde	2	6	Single dwelling	Face-to-face	Individual
16	85	Female	Roskilde	2	3	Single dwelling	Phone	Individual
3	86	Male	Odense	1	4	Cohabitation	Face-to-face	Dyad (with partner)
10	88	Female	Odense	1	–	Cohabitation	Phone	Individual
15	89	Female	Roskilde	1	11	Single dwelling	Face-to-face	Individual
7	90	Female	Odense	2	12	Single dwelling	Face-to-face	Individual
12	94	Female	Roskilde	2	20	Single dwelling	Face-to-face	Dyad (with daughter)

ID, identification; nAMD, neovascular aged-related macular degeneration.

expressed concerns about the potential negative progression of the disease (quote 11).

Dual role of relatives

This theme highlights the essential role that relatives play for many patients, although the nature of their influence on the course of treatment can vary significantly. For some patients, relatives serve as facilitators, providing support and assistance in attending treatment. However, for others, relatives can act as barriers, potentially hindering the patient's ability to access and adhere to treatment. The impact of relatives on the treatment process depends on various factors, including their available resources. One patient and their relative specifically described the impact of their patient–partner relationship on the treatment experience (quotes 12 and 13). Certain relatives play a significant role in providing reassurance and investing considerable time in supporting the patient. One patient and her daughter described how the daughter drives the patient to the hospital, despite of the daughter living 70 km away from the patient and 100 km from the hospital. This example highlights the dedication and support demonstrated by relatives who are willing to make substantial efforts to ensure the patient's access to necessary treatment (quotes 14 and 15). Interestingly, patients without a partner do not appear to face significant challenges in finding the necessary support. They are resourceful in seeking alternative sources of social support, such as friends, and do not express a sense of missing a partner during the course of treatment. This finding suggests that these patients have found their own ways to cope with their condition and establish a support network (quote 16).

In certain cases, relatives can indeed become a barrier to treatment. We encountered a situation where one patient had to discontinue treatment due to her obligations as a caregiver for her sick husband. The patient's dual role as a caregiver at home and caretaker became apparent, ultimately forcing her to make a difficult choice between her own treatment and the care of her husband. This example highlights the complex dynamics and challenges that can arise when patients are faced with competing responsibilities and priorities within their family context (quote 17).

Treatment commute

This theme explores how the commute from home to the hospital can hinder the acceptance of the recommended treatment among this group of older vulnerable

Table 2 Participant quotes

Theme	Quote number	Illustrative quotes
Good compliance with the intravitreal treatment	1	ID6: That would be like shooting yourself in the foot. I still hope that the medicine can help to keep my vision stable so that I can continue to see
	2	ID20: As long as those with more expertise than me recommend it, then I will continue
	3	ID18: At the moment I am unable to explain, as it is many years since I received and read them (patient educations brochure), but isn't it a hardening of the arteries in the eyes. That's what it is. I don't think that you speculate when you first read it, but that's just the way it is
	4	ID20: I don't really know (what nAMD is)
	5	ID3: I really don't know (if treatment works). Otherwise, I feel that it's going pretty straightforward. Fortunately the vision hasn't dropped that much. So you can't really say that it's helping. I don't think it's that great
	6	ID6: Both yes and no, because during these periods, it has gotten worse but what would the result be if I hadn't received the treatment. I can't be sure
	7	ID20: I trust medical science and that's how it is
	8	ID1: I do what the doctor says is best for me. I don't question that. I don't look for alternatives
	9	ID4: I considered acupuncture, but I don't know if it helps
	10	ID5: The day before treatment, I start to feel a little nervous and uneasy about coming here, but it's not like I'm panicking
	11	ID6: The day and night before, it's always in my thoughts. I think about all the negatives … Will they find anything in the other eye or something like that
The dual role of relatives	12	Relative of ID3: He feels that he depends on me for many things, for example, driving, which can upset him because he is unable to do it himself
	13	ID3: Sometimes I feel down if there is something that I can't read. As long as there are two of us, then we can cope. It would be too much if you were on your own. Then it would be bad. Many of our friends have lost their other halves and that's tough
	14	ID12: I have my children and at the moment my daughter driving me, making sure I get home again
	15	Relatives of ID12: I live in (a), so I drive from (a), to (b), and pick up my mother, and then we come here (to hospital). It's just a suggestion, that a team could be sent to (b) to perform the treatment. That could be nice
	16	ID2: I don't feel that I need to talk about it (nAMD). I have a good friend that also has it. He lives in Copenhagen, and sometimes we share our experiences, and about how the treatments are apparently slightly different
	17	ID10: I have … (husband) living at home with me, and he has difficulties walking, and just the other day had a fall. If he falls when I'm not at home, then we are really struggling, because he never has his phone with him. He's 90 years old, so we are in an age group a little older than the average. Therefore I thought that I should stop (treatment for nAMD)
Treatment commute	18	ID14: Sometimes you have to sit and wait for two or three hours over there in the waiting room. I find that difficult
	19	ID14: That wouldn't be a problem (getting treatment 17 kilometers from the patient's home). On the other hand, I'm so old that I can't be bothered having to adapt to this, that and the other. I think that it's all right, with the sitting and waiting. That's just the way it is sometimes
	20	ID7: I have learned an incredible amount from for example, immigrant drivers. I am a very talkative person and I get into conversation with people very quickly, so I get to discuss many interesting things. I have learned a great deal about their way of life. I see it as a little excursion, even though I can easily keep myself busy at home
	21	ID19: It takes 4–5 hours, perhaps a little more sometimes. I'm happy to do that. As I said, I am happy to receive the treatment, and it helps. So for that reason, I don't see that it is so problematic that I would choose not to take the treatment. The only consideration is, that I have to organize the transport from home. I can't see the signs at the train station as they are too high, and if there are sudden changes in the travel plan, then I can get a little frustrated

Continued

Table 2 Continued

Theme	Quote number	Illustrative quotes
	22	ID11: You leave from home in the morning and then there is the wait to come home again. You should try sometime. I used Falck, which was fine, but after the treatment, they said at the department that I would be collected within an hour, but then you miss the ferry and you are left waiting an extra 2 hours. That's when we said. We don't want to do this anymore. I was called in again after 2 months, so we started to drive on our own
	23	ID11: (The reason not to stop treatment again) is probably the fear that the vision will disappear completely, which the doctors claim will not happen (if continuing the course of treatment)
Hospital barriers	24	ID3: We know in advance when we have to go in. They let us know up to three times. That's great. We can always call them up to talk. It's never been a problem
	25	ID21: Sometimes as a patient, you are at a loose end, not knowing what to do or who to talk to. In the beginning, it was myself that informed them that it was time for my consultation / treatment. In other words, they failed to send me new appointments without me needing to ask for them. After about a half year without hearing from them, I contacted them, which gave a positive result. The appointment arrived the day after
	26	ID13: They are sent to my Digital Post, only one at a time. So now I'm curious to see if it coincides with my summer vacation
	27	ID19: I wish that you could have an appointment when you really need it. When I reach the sixth week, then there can't go a long time. Otherwise, I have a problem. Sometimes it can be more than 9 weeks if I don't do anything. Unfortunately, I need to use acute appointments occasionally which I'm not happy about. So the system does not work properly
	28	ID5: I feel that it would be good if there was an optician involved in the treatment here, working together with the doctors. Then we wouldn't need to be responsible in finding an optician that knows something about nAMD and if they are trying to cheat us. I really feel that I am sitting between 2 stools, and it's not because we don't have enough money but I feel that it's still expensive. I've asked some friends, and told them that it costs 23 000 (DKK) for glasses, which they think is totally wild. They said that they have the same varifocals, which cost 12 000 (DKK)
Preventive health literacy	29	ID18: They once told me to take a load of vitamin pills, but my stomach was unable to cope with it. It protested, so now I take one a day during the whole year
	30	ID8: I know that it makes sense to quit (smoking), but I don't believe that there is any connection. My daughter's father has never smoked and he also has bad eyes
	31	ID4: With arthritis, you can do something to help yourself. You can do it with diet. You can do it with exercise and you can do it with training and (physiotherapy?). You are personally involved. With this (nAMD), you are not involved because it takes place on such a small level. You are just let off the hook and you can't do anything yourself. That's where I think the difference lies, that you feel as if you can make an active difference yourself and it also helps mentally that you can do that
	32	ID5: So I said to myself that I should try and cycle more and also go to fitness etc. I have a feeling that you should avoid seeing too much television. You should not be looking at screens too much. I don't really know. I'm also really unsure about the lubricating eye drops (viscous)

ID, identification number of patient; nAMD, neovascular aged-related macular degeneration.

individuals. It is worth noting that the proximity of patients to the treatment site varied greatly. Some patients lived within cycling distance, while others had to travel over 130 km, including a ferry ride, which could take more than 3 hours each way. However, the perception of whether this long commute was seen as a barrier or a positive aspect varied significantly among patients.

In terms of transportation, five patients used a flex-traffic service, which is a tax-funded taxi service for individuals with special needs, to commute back and forth to the hospital. One patient, who had a 2½-hour drive with flex-traffic each way, described the inconvenience of the waiting time at the hospital (quotes 18 and 19). Interestingly, this patient expressed that she did not wish for the treatment to be moved closer to her home, as she believed that doing so would introduce other challenges. This perspective highlights the complex considerations that patients may have regarding the location of their treatment. While the long commute may pose difficulties, patients may also take into account other factors, such as

the quality of care, familiarity with the hospital and access to specialised resources, when weighing the potential benefits and drawbacks of relocating the treatment closer to their residence.

A patient who resides 30 min away from the hospital described their experience with flex-traffic, as effortless and even enriching (quote 20).

One patient used public trains for transportation as she preferred to travel independently. However, impaired vision can make using public transportation challenging. This underscores the potential difficulties that can arise when individuals with visual impairments navigate public transportation (quote 21).

Three patients used Falck, a self-financed taxi service, for their transportation needs. One patient, who had a lengthy travel distance that included a ferry ride, discontinued treatment for a period due to the extended travel time. However, the fear of losing his vision prompted him to reconsider and resume treatment (quotes 22 and 23).

Hospital barriers

The interviews indicated that there were organisational variations in how hospitals scheduled patient appointments. In one hospital, patients were provided with appointments for their next three treatments during their check-up visits. This practice seemed to offer patients a sense of security by knowing the designated time for their treatment in advance. Additionally, if the scheduled time was inconvenient for the patient, they had the option to discuss it with the secretary immediately and make changes or contact the hospital by phone (quote 24). In contrast, the other hospital relied on sending a letter through Digital Post, which is a digital public communication system, to notify patients when it was time for their treatment. However, this approach created a sense of insecurity among patients and, in some cases, made them feel responsible for keeping track of their treatment plan. The lack of direct communication or personal interaction in this process may have contributed to the patients' unease and the perception that they had to take on additional responsibility in managing their treatment schedule (quote 25). The ophthalmologists often prescribed a series of three treatments with specific intervals, but the patients expressed worry and uncertainty because they were only given one appointment at a time. They desired more clarity and information regarding the overall treatment plan, including the timing and scheduling of subsequent treatments (quote 26). One patient had the ability to easily notice when her vision was deteriorating and required treatment. However, she found it frustrating not to receive timely notifications for treatment within a 6-week interval. The lack of timely summons added to her frustration and hindered her ability to maintain optimal vision care (quote 27).

Several patients expressed the need for optician involvement in their nAMD treatment, working alongside doctors. They believed that having an optician knowledgeable about nAMD would improve concerns of receiving inadequate care. The cost of treatment was also a significant factor, with patients perceiving the expenses associated with glasses as high compared with other similar options available to them (quote 28).

Preventive health literacy

This theme explores the preventive measures that patients themselves attempted to implement in order to prevent the progression or occurrence of nAMD in their other eye. Despite their efforts, these patients had low health literacy and limited understanding of the underlying pathological mechanisms of nAMD and the potential preventive effects of interventions. Some patients had heard about AREDS-vitamin supplementation as a means to reduce the risk of developing nAMD in an eye with moderate to severe dry AMD and had tried it.[16] However, none of the patients adhered to the recommended dosage of the supplementation (quote 29).

Patients who were smokers had received advice to quit smoking, but they struggled to comprehend the link between smoking and the development of an eye disease. The connection between their smoking habits and the risk of eye disease was not clear to them, leading to difficulties in fully understanding and appreciating the importance of smoking cessation for their eye health (quote 30).

Several patients highlight the satisfaction that comes from being able to actively take steps to prevent further illness, while expressing frustration when observe a lack of available options or if they do not feel that preventive measures make a difference. One patient, who also dealt with arthritis, described the difference between arthritis and nAMD in this regard (quote 31).

The patients expressed uncertainty regarding how to approach preventive measures, such as diet, exercise, basic eye care and the use of lubricating eye drops. They sought answers and guidance in these areas (quote 32).

DISCUSSION

This study explores the barriers and challenges reported by patients during the course of nAMD treatment in Denmark, providing valuable insights for developing tailored interventions for this patient group. The main findings, described through five identified themes, shed light on important aspects of the treatment journey: good compliance with intravitreal treatment, the dual role of relatives, treatment commute, hospital barriers and preventive health literacy.

Our study revealed a highly adherent patient group who did not consider opting out of treatment because they find the course of treatment somehow unproblematic and without significant barriers. In contrast, a recent study by Thier *et al*[17] with nAMD patients in Germany found that the pain associated with therapy and a lack of perceived positive effects led individuals with significant vision loss to discontinue treatment. Effective communication strategies were identified as crucial in preventing patients from discontinuing therapy, a recommendation

echoed in the work of Hüsler and Schmid[18] from Switzerland. These findings suggest the need for further research, particularly in countries where treatment is free or tax-funded, as the economic aspect may impact patients' adherence. In Denmark, where treatment is tax-funded, patients demonstrated compliance despite other non-economic barriers.[9 19] Although the economic factor may play a role in expensive treatments, additional research is required to draw definitive conclusions.

Numerous studies worldwide have explored the impact of nAMD treatment on patients' quality of life over the past decade, consistently highlighting its significant effect.[20–22] Our study focused on the burden of commuting to and from the hospital, a factor considered during patient selection for interviews. Snowball sampling was employed to recruit two patients living on a small island, necessitating ferry travel to the hospital. One patient discontinued treatment due to the long commute. This aligns with a systematic review indicating that visit frequency and travel time pose significant barriers to treatment.[23] However, patients demonstrated adaptability and coped with travel time through various means, such as assistance from private taxi services and support from relatives. The dual role of patients as both supporters and recipients of support is not unique to nAMD but is observed in other patient groups, including those with ischaemic heart disease.[24] The well-being of partners and relatives should be considered by the treatment team. However, the absence of a partner or close relative should not cause undue concern.

Our study demonstrated that appointment scheduling frustrations arose when patients were unable to book appointments well in advance. Some patients felt responsible for monitoring their treatment plan due to the lack of captured treatment regimens. Conversely, another hospital handled this issue effectively by providing advance notice of appointments, which was appreciated by patients. These findings align with the work of Talks *et al*,[4] who suggest that knowing and understanding the timing of intraocular injections allows patients to mentally prepare and have confidence in the treatment process. These insights of the present study may inspire changes in organisational workflows that provide patients with advance appointment information and involve them in the planning process. However, further research is needed to assess the positive outcomes of such changes. It could be speculated that financial constraints at the departmental level may lead to longer treatment intervals than medically prescribed, reflecting an imbalance between patients' needs and available resources. Addressing this issue requires political-level discussions beyond individual departmental changes.

A previous study highlights that patients with AMD and vision loss may require more time to comprehend health information, emphasising the importance of tailored health education to support self-management.[25] In our study, most patients expressed difficulties in explaining nAMD but did not perceive a lack of information or knowledge about the disease as problematic. Due to the unavailability of visual acuity data, the impact of visual impairment on patients' learning and understanding of disease information remains unclear, particularly for those without support from a partner or close relative. Additionally, some patients expressed a desire for a network of other nAMD patients to share experiences, information and understanding, while others preferred less engagement. Unlike conditions such as osteoporosis, diabetes or heart disease, Denmark does not have an established nAMD network. Patient attitudes towards such a network may vary, and its feasibility and benefits require establishment and evaluation.

Having relatives present during the interviews may potentially have introduced bias by influencing participants' responses and limiting their willingness to share sensitive information, leading to social desirability bias and impacting data authenticity. However, the presence of relatives can also offer emotional support and context that enriches the depth of participant responses especially among elderly.

Strengths and limitations

To enhance the trustworthiness of the study, we employed various techniques, including investigator triangulation and validation of findings with a PPI board comprising nAMD patients and ophthalmologists.[14] A detailed description of methods and considerations ensured consistency and dependability, while researcher triangulation strengthened the confirmability. The PI, a doctor with extensive clinical experience in ophthalmology, reflected on how his professional background and pre-understandings may have influenced the study, ensuring credibility. The qualitative nature of the study enabled a detailed exploration of patients' perspectives, which may be challenging to capture using quantitative approaches. Another strength was the use of our PPI board, which played an active and integral role in providing valuable insights into potential barriers faced by patients and the public addressed in the study. Their input was particularly significant and enhanced credibility as they brought first-hand experience as patients or caregivers, providing a unique perspective on the challenges encountered during the treatment of nAMD. It is important to acknowledge the limitations of the study. Purposeful sampling aimed to achieve maximum variation, allowing for a diverse range of nAMD experiences, but the findings are not generalisable due to the small sample size and qualitative nature of the study. No potential participants with non-Western backgrounds volunteered for our study, which could have implications for the study's transferability, especially in relation to certain aspects, such as the theme of preventive health literacy. Previous studies[26] have indicated a higher incidence of nAMD among Europeans compared with individuals from other ethnic backgrounds. However, this does not automatically increase the study's transferability to broader populations, and further research in this area is required.

Conclusion

This study highlights the adherence of patients with nAMD to their treatment despite various barriers and

offers valuable insights into the multifaceted aspects of managing nAMD in elderly patients. By recognising and addressing the identified themes, healthcare professionals can work towards providing more comprehensive and patient-centred care, ultimately leading to improved outcomes and enhanced quality of life for patients with nAMD. Further research and collaborative efforts among healthcare stakeholders are warranted to build on these findings and advance the field of nAMD management.

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Contributors BST contributed to the study design, conducted the interviews, performed the analysis and wrote the manuscript. LS and MP contributed to the study design, analysis and writing of the manuscript. JG contributed to the study design and manuscript writing. TLS contributed to the manuscript writing. All authors critically reviewed and approved the final version of the manuscript and committed to being accountable for addressing any concerns related to the work's accuracy or integrity. BST is acting as guarantor for this study.

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Competing interests JG has received speaker's fee from and has served as an advisory board member for Bayer, Novartis, Roche and Allergan, not related to this work. The other authors declare that no potential conflicts of interests exist in relation to this work.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval The study adhered to the ethical principles outlined in the Declaration of Helsinki. Prior to participating in the study, all participants provided written informed consent, which is essential, especially since these patients may experience visual or cognitive impairments that require special attention to ensure their full understanding of the purpose of the study. They were made aware that their involvement was entirely voluntary, and they had the option to withdraw from the study at any stage, if they wished to do so. Given the potential vulnerability of elderly patients, particularly those dealing with health issues, it was crucial to take extra measures to protect their well-being. Therefore, interviews were scheduled with careful consideration. They take place at the hospital on the same day as the participants' treatment, aiming to minimise the effort required by participants and ensure their comfort during the research process. Confidentiality of the participants' data was strictly maintained, following established guidelines for data handling and protection. The study was assigned the record number 22/10138 in the register of the Region of Southern Denmark, indicating its official registration. Although the study was reviewed by the research ethics committee, it did not require explicit permission to be conducted.

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Supplemental Material 1: Study Protocol

Patient-Reported Barriers to Treatment of Wet Age Related Macular Degeneration a Qualitative Exploration

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Introduction

Age-related macular degeneration (AMD) is a leading cause of blindness globally, and it is estimated that 6.4 million worldwide will be diagnosed with wet AMD in the year 2050 [1-3]. AMD is a chronic disease classified in two main types: dry and wet. Dry AMD caries in general a more favourable visual prognosis and counts for 80-85 % of all cases, whereas wet AMD, which progress from dry AMD, is a vision-threating disease and affects the remaining 15% to 20 % [2, 4]. AMD develops in the macula, the part of the eye that is especially important for seeing sharp images [5], and it causes central vision loss and makes objects appear blurry and distorted for the patients. As the name suggests, the disease is age-related, where the prevalence rise from 3.5% in those aged 55-59 years to 17.6 % in those aged above 85 years [6].

Every year, around 2300 patients are diagnosed with wet AMD in Denmark, and approximately 30,000 people live with the disease in Denmark today [7, 8], however it is expected that the number of patients will rise sharply as we get older and older [2, 9]. Fortunately, the introduction of intravitreal angiostatic therapy (anti-VEGF) about 17 years ago has revolutionized treatment options for wet AMD and halved the number of newly blind people over the age of 50 [7, 8, 10]. The treatment is often lifelong and require treatment at hospital with an injection into the affected eye every fourth to twelve week. Thus, the course of treatment can be debilitating and demanding especially among elderly and vulnerable patients. A Danish study found that up to 20% of patients opted out of treatment within the first two years for non-medical reasons [11]. These patients were above 90 years old and therefore, it is unknown how it is in younger patients, and it is unknown why the patients opted out of treatment. Varano et al. [12] found with a global survey that 84 % of patients treated with anti-VEGF were compliant with treatment; though, the reason for the remaining not compliant part was unclear.

Although we know that some patients do not adhere to the recommended treatment regime for wet AMD, it is poorly understood if they stop or omit treatment due to barriers like e.g. lack of knowledge of the disease, the treatment itself, distance from home to hospital or the commute to the many visits at the hospital etc. It is essential to understand the patient group and to fill this crucial gap of knowledge by exploring in depth which barriers they meet in the treatment course.

Aim

The aim of this non-interventional, explorative interview-based study was to explore patient-reported barriers of receiving recommended treatment for wet AMD in Denmark, and to examine if the barriers were modifiable, thus we can prevent patients with wet AMD from interrupting their treatment, and thereby, reduce the risk of vision loss in the future.

Rationale:

Although we know that some patients do not adhere to recommended treatment regime for nAMD, it is undefined if

they stop or omit the treatment for a longer period due to barriers like lack of knowledge ofthe disease, delayed diagnosis, the treatment itself, distance from home to hospital or the commute to the many visits at the hospital.

Thus, it is essential to examine the barriers and if they are modifiable and whether individual treatmentcourses can be developed to prevent patients from interrupting their recommended treatment and, thereby, prevent a negatively affected long-term outcome in nAMD patients.

Methods:

We plan to conduct a qualitative study using semi-structured interviews, where the interview guide will be developed in collaboration with the PPI. The intention is to involve 20 patients with nAMD in an open- ended interview to report their experiences and barriers to be diagnosed and receive treatment (recruitment is described in Setting). The interviews will be used to develop WP1-B, as the patient-reportedbarriers identified in interviews will be used to build and refine the questionnaire.

Analyses:

The interview will be held as physical meetings or telephone interview that will be audio-recorded, transcribed and analysed using Framework analysis, where we will divide the patient's experiences and barriers into categories and themes. The analyses will be organized using the software system NVivo. Thefindings from the interviews will be discussed and interpreted with our PPI before the questionnaire in WP1-B will be developed and before publishing our findings.

Recruitment:

Patients from Departments of Ophthalmology at Odense University Hospital and Zealand University Hospital in Roskilde will be invited to participate in an interview (n=20) when they visit one of the two departments for scheduled eye examinations or intravitreal treatment for nAMD.

Expected journal publications:

We expect to achieve important findings of patients' barriers they experience related to the treatment ofnAMD and that our findings will result in a peer-reviewed publication aimed at high-class international journals

Limitations

Limitations are important to acknowledge. Patients are only recruited for the interview when they visit the hospital for treatment, and therefore we are limited by the fact that the patients who opt out of the recommended treatment regime do not participate in this study and contribute with their experiences. Maybe these patients are those who experience the most barriers to treatment.

On the other hand, we hope to reach these patients through the questionnaire survey in the quantitative part, although this is also limited by the fact that the questionnaire is primary sent out via e-boks. This can be a major

problem in elderly patients many of whom probably are exempted from receiving public mail in e-boks because of impaired vision and problems with reading. Maybe we can reach out to some of these patients by given them e.g. an iPad in the waiting room at the hospital, who can read out loud the questionnaire.

Novelty

In this study, we have patient involvement in form of an advisory board. In addition, we want to conduct patient interviews and ask all patients with nAMD in Denmark via a questionnaire about their challenges with the course of treatment. This study is thus unique of its kind, as no one has previously illuminated this area of the eye profession in just that way.

Likewise, we have the opportunity to extract registry data from an entire national cohort including e.g. every single event of injection, and look at the side effects of a treatment that are injected into thousands of eyes every day around the world.

Clinical impact and feasibility

Patient organizations and healthcare professionals will be informed of our findings through peer-reviewed journals and national and international conferences. This might help health professionals adjust the communication regarding the disease and thereby establish individual courses of treatment with patient involvement and balanced considerations between patient's personal circumstances and risk of low visual acuity. E.g., a solution could be further education of eye nurses, so they can provide the majority of the information that patients lack in connection with the course of treatment.

Ethics:

The study will be performed according to the tenets of the Helsinki Declaration. We will ensure that all permissions are obtained and regulations and ethical guidelines are followed and obtained prior to the study. All patients will be asked to provide informed consent and informed that they at any time can withdrawals their consent. Patients unable to provide written or verbal consent prior to participation will be excluded.

We will apply for permission to contact and invite patients with nAMD to participate in a qualitative study WP1-A and a questionnaire (WP1-B). Further, data are stored in secure systems with strict access control. Data from interviews and survey are stored in the safe solution *OPEN Analyse* and data from national registers are stored centrally in Statistical bureaus. All data management and analyses will be performed on data without the personal identification numbers (these will be replaced by project- specific IDs), and only anonymous or aggregated results will be presented. It will not be possible to identify individuals in any results from this project.

Setting:

This study originates from Open Patient data Explorative Network (OPEN), Odense University Hospital, and

Department of Clinical Research, University of Southern Denmark, with Departments of Ophthalmology at Odense University Hospital and Zealand University Hospital in Roskilde of Zealand as our clinical partners. The study population will consist of patients from the catchment areas of these two departments, which receive approximately 40 new patients with presumed nAMD each week. The location of the two hospitalsgives patients in the two regions approximately equal travel distance to the departments in which all treatment is performed. Likewise, the study population is considered a heterogeneous[13], representative sample of patients with nAMD, thus making it realistic to implement individual courses of the treatment.

Patient and Public Involvement:

To ensure patient and public involvement, we plan to invite five patients treated for nAMD from Odense University Hospital or Zealand University Hospital, Roskilde, three nurses working with patient in treatment for nAMD at the hospital and three private consultant ophthalmologist to partake in a continuous advisory board throughout the study period (PPI). The recruitment into the board has already started, and the first introductory meeting has been held. The project idea has been presented,and comments from the participants are accounted for in the described study plan. We intend to invite more participants to the board when the project start.

We expect the PPI to offer the perspectives from primary care since they are the ophthalmologist that patients meet first after they experienced symptoms and from the patient's perspectives to ensure that thestudy is relevant and following the patient's experiences and expectations.

The PPI will be included in all phases of the research process, from defining the research questions and outcomes and defining the questions for the interview and questionnaire and interpreting the data. Since the target group for this study is patients who potentially can have a low visual acuity, it may be a problemto recruit patients through letter or mail. Therefore, it is important for us that the PPI is involved in the discussion on the recruitment of patients. We expect the PPI to evaluate whether it will work for the patients to be recruited to the study through an audio file or podcast.

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Supplemental Material 2: Interview Guide

Introduction to the interview Thank you for being willing to share your experiences with us. We are interested in hearing about your experiences because we are trying to gain a better understanding of how patients undergoing treatment for neovascular Age-Related Macular Degeneration (nAMD) perceive their treatment journey. If there are any questions, you prefer not to answer, please feel free to let us know. We will simply move on. Your participation is voluntary.		
Theme	Research Question	Interview Question
Introduction		• Where do you live? Alone or with a spouse? • What do you do on a daily basis? • How long ago did you start treatment for nAMD? Have you lived in the same place throughout the process? • Do you receive injections in one or both eyes? • Approximately how many injections have you received? • Do you have any other eye-related conditions? • What motivated you to participate in this project?
Life with nAMD	• How do patients experience being diagnosed with nAMD? • How do patients experience life in treatment for nAMD? • What barriers or challenges do patients in treatment for nAMD experience? • How is health literacy a barrier to treatment? • What was the awareness of nAMD before the time of diagnosis?	• Can you first tell us what led to you receiving the diagnosis of nAMD? • How did you react when you received the diagnosis? • Did you feel that your questions about the disease were answered when you were diagnosed with nAMD? • How was the informational material you received when you were diagnosed? • Do you find it difficult to explain the disease and treatment to others? • Have you felt equipped to handle the treatment process (such as your own resources, previous experiences, belief in yourself)? • Have you changed habits in your daily life during the treatment process? • What is the worst part of the treatment?

		• Do you experience any barriers to receiving the treatment? If yes, what are they? • Do you have other illnesses that complicate the treatment process for nAMD? • How do the treatments fit into your domestic situation (such as finances, living with a partner, caring for pets)? • Can you try to explain in your own words what you have and why you need the treatment? • Do you find it challenging to understand the information you receive about the disease and treatment? • Were you familiar with nAMD before you were diagnosed? • Were you prepared for the possibility of having nAMD? • Have you felt the need to seek information about the disease, for example, on the internet?
Expectations of Treatment	• What expectations do patients have for treatment before initiation? • What expectations do patients have for the future?	• What expectations did you have for the treatment when you accepted it? • Have these expectations been met? • What are your expectations for the treatment going forward? • Have you been informed that you may be able to discontinue the treatments in the future?
Barriers or Challenges in the Treatment of NAMD	• What occupies the thoughts of patients on the day of treatment? • What occupies the thoughts of patients after the treatment?	• Can you take me through a day when you have treatment? • How do you feel about such a day? • Does such a day differ from any other day? • What are the biggest challenges for you during such a day? • What are the biggest concerns or irritations for you on such a day? • Are you scared or nervous on such a day? • Are the challenges or concerns less than before? • Can it vary from time to time regarding challenges, concerns, and irritation?

		• Do you have things that can make such a day easier? • How does it affect you in the days leading up to the treatment? • Have you declined treatment because you did not want an injection on that particular day? • Do you experience any discomfort or issues after treatment? (Specific examples – does it affect daily life?) • Has it changed over time? • How do you handle any discomfort? (contact with the hospital) • What is it like to get in touch with the eye department between treatments?
Monitoring and Treatment	• How is the experience of the treatment with Intravitreal VEGF inhibitor treatment? • How is the experience of the check-ups with the doctor and nurse?	• How do you feel when the injection is administered? • How do you feel the staff takes care of you during the treatment? • Can you get answers to your questions during the treatment? • Do you have suggestions on how the treatment itself could be made easier for you? • How often do you have appointments with the doctor for check-ups? • Would you prefer to see the doctor more or less often? • What interval do you think would be suitable for, for example, a regular consultation with the doctor? • What do you do to schedule appointments with the doctor? • Can you get answers to your questions when you are with the doctor? • How do you experience the conversation with the doctor during check-ups? • Do you use the nurses to answer the questions you have? • Do you feel that they can answer your questions? • Do you often hold back questions for either the nurse or the doctor?

Effectiveness of Treatment	• How do patients experience the effectiveness of the treatment? • How do patients experience the impact of the disease on their quality of life?	• Do you generally feel that the treatment is effective? • Can you sense when it is time for treatment? • Have you contacted the hospital because you have experienced worsening before getting a new injection? • Has your vision deteriorated since you started treatment? • Are you satisfied with the treatment? • Would you wish that you had never started the treatment if you could change it?
Quality of Life	• How do patients experience the effectiveness of the treatment? • How do patients experience the impact of the disease on their quality of life?	• How much does nAMD occupy your daily life? • Does the disease affect your daily life? (in terms of lifestyle, social activities, mentally) • How is your daily life now compared to before you had the eye disease? • Do you use your relatives to talk about this? • Do you have contact with other people with the same disease? • Have you done anything to raise awareness of the disease among others? • Have you used professionals (psychologists, priests, etc.) to talk about this?
Anxiety and Depression	• Do patients experience anxiety or depression due to nAMD and its treatment? • Do they receive the necessary support to manage the disease and treatment process?	• Many experience emotional changes after a diagnosis of nAMD. How has it been for you? • Do you find yourself more often feeling down or more prone to tears since starting treatment? • Do you experience anxiety about the disease progressing, for example, to the other eye? • Have you experienced the treatment suddenly ceasing to be effective? • Have you considered the possibility of the treatment's effectiveness diminishing or ceasing altogether? • How do you feel about the thought of a life without sight?

		• Do you feel alone in the course of the disease? • Do you feel isolated in the midst of the frequent hospital visits? • Has anyone supported you through the process (such as professionals or loved ones)?
Transportation to and from Treatment	• How do patients experience the logistics surrounding the treatment? • Has transportation to treatment had consequences for the patients?	• Do you know how far the hospital is? • How are you transported to and from the hospital for treatments? • Is it always the same method? • How much time elapses from when you leave home until you are back home in connection with treatment and check-ups? • How do you feel about allocating these hours? • Do you find it to be an appropriate amount of time? • Are you familiar with Flex-traffic? • Would you use Flex-traffic if you did not have other options? • Have you considered discontinuing treatment due to long travel times? • Have you considered how transportation could be made easier for you? • Have you moved during the process? • If yes, has it been because of the treatment? • Have you changed treatment locations throughout the process?
Alternative Treatment Options	• How do patients in treatment for nAMD respond to treatments other than VEGF inhibitor treatment? • How do patients approach potential future treatment options?	• Have you used vitamin supplements (AREDS2), which are sometimes recommended to counteract the progression from dry AMD to nAMD? • If yes, do you feel well informed about this treatment? • Have you changed your lifestyle, such as diet, exercise, or quitting smoking, because of the disease? • Have you tried a different treatment for nAMD than what the hospital offers? • If yes, how did you learn about that treatment?

		• Have you felt an improvement with that treatment? • Do you have a good relationship with a private eye doctor? • How is it to visit your own eye doctor compared to the hospital? • If you imagine that you could have check-ups and treatment with your own eye doctor • What would you think about such an idea? • Would it help you with transportation to the hospital? • Would it make you feel more or less secure? • What positive aspects do you see in such a solution? • What challenges do you foresee in such a solution? • Imagine that you could have check-ups and treatment at your local neighbourhood hospital, possibly in collaboration with doctors from that department. • What would you think about such an idea? • Would it help you with transportation to the hospital? • Would it make you feel more or less secure? • What positive aspects do you see in such a solution? • What challenges do you foresee in that solution? • Have you personally considered things that could make the treatment process easier or better for you?
Conclusion of the interview: We have now gone through our many questions and are very grateful for your participation. Before we end the talk, is there anything you would like to add? How are you feeling right now? Thank you so much for your participation.		