#### ORIGINAL RESEARCH



## The Impact of the COVID-19 Pandemic on Tele-ophthalmology-Based Retinal Screening

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Received: June 7, 2024 / Accepted: July 19, 2024 / Published online: August 2, 2024  $\circledcirc$  The Author(s) 2024

## ABSTRACT

*Introduction*: This study reports our experiences with systematic retinal screening in Denmark through optometrists with access to teleophthalmological services before, during, and after the COVID-19 pandemic.

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J. Grauslund Department of Ophthalmology, Odense University Hospital, Odense, Denmark *Methods*: We evaluated an optometrist-based retinal screening system with a referral option for tele-ophthalmological service by a consultant ophthalmologist within the time period of August 1, 2018 to September 30, 2023. The optometrist collected patient history, refraction, best-corrected visual acuity, intraocular pressure, basic slit-lamp examination, 4-in-1 visual field

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report, and retinal imaging using color fundus 45° photography. Tele-ophthalmological services were provided by consultant ophthalmologists. Within pre-defined periods of pre-COVID-19, COVID-19, and post-COVID-19, we evaluated the rate of referrals to the tele-ophthalmological service, diagnoses made, and referrals to the public healthcare system.

Results: A total of 1,142,028 unique individuals, which corresponded to 19.1% of the entire population of Denmark, underwent screening by the optometrists; 50,612 (4.4%) of these individuals were referred to the tele-ophthalmological examination by consultant ophthalmologists. A referral for further ophthalmic examination, either at hospital or at an ophthalmic practice, was made for 10,300 individuals (20.4% of those referred for tele-ophthalmology, corresponding to 0.9% of the population screened). The referral rate from the screening to the tele-ophthalmological service increased from before COVID-19 (3.4%) to during COVID-19 (4.3%) and further after COVID-19 (6.4%). This increase coincided with an increasing prevalence of conditions seen in the tele-ophthalmological service.

*Conclusion*: During a period of 5 years, 19.1% of the entire population of Denmark underwent retinal screening. This provided an adjunctive health service during a period of severe strain on the public healthcare system, while limiting the number of excessive referrals to the public healthcare system. Temporal trends illustrated an increased pattern of use of a large-scale tele-ophthalmological system.

**Keywords:** Retinal screening; Tele-ophthalmology; Healthcare organization; COVID-19

## **Key Summary Points**

#### Why carry out this study?

As the COVID-19 pandemic hit Denmark, widespread lockdown and the immense strain on healthcare workers further challenged access to the public eye care system.

This study evaluated an optometrist-based retinal screening system with a referral option for tele-ophthalmological service to understand retinal health, referral patterns, and screening outcomes before, during, and after the COVID-19 pandemic.

#### What was learned from this study?

A total of 1,142,028 unique individuals were screened (19.1% of the entire population of Denmark), and 50,612 (4.4%) of these individuals were referred to the teleophthalmological examination of which 10,300 (20.4% of the individuals referred for tele-ophthalmology, corresponding to 0.9% of the population screened) were referred for further examination either at hospital or at an ophthalmic practice.

Referrals from optometrists to the tele-ophthalmological service increased slightly from before COVID-19 (3.4%) to during COVID-19 (4.3%) and post-COVID-19 (6.4%).

When looking at the referrals from the tele-ophthalmological system to the public healthcare system, we observed an increase in acute and subacute referrals from before COVID-19 (1.2% and 6.4%, respectively) to during COVID-19 (1.8% and 8.4%, respectively) which decreased again after COVID-19 (1.1% and 7.5%, respectively) (p<0.001,  $\chi^2$  test).

Trend analyses showed subtle changes in the prevalence of diagnoses from before COVID-19 to during COVID-19 and after COVID-19.

Such systems allow for a meaningful adjunctive health service to that of the existing public healthcare, all while limiting the number of excessive referrals to the public healthcare system.

## INTRODUCTION

Demographic pressures caused by ageing populations in developed countries put healthcare systems under considerable strain [1, 2]. As increasing age is the strongest risk factor for development of prevalent eye diseases, this phenomenon is expected to put great strain on the eye care system in many countries [3–9]. Denmark's population of over 80-year-olds is expected to double in the next 30 years [10]. The strain on the publicly funded Danish healthcare system is already reaching its limits as the waiting time for eye examination in primary care ophthalmic practice is continuously increasing, alongside much political debate [11].

As the COVID-19 pandemic hit Denmark, widescale lockdown and the immense pressure on healthcare workers added fuel to the fire for limited access to eye care. Meanwhile, an ongoing transformation process among Danish optometrists has led to a shift from offering only basic optical services to providing systemic screening services using fundus imaging, noncontact tonometry, and visual field analysis. These developments echo a broader European trend which is seen most notably in the UK [12, 13]. However, this paradigm shift in service provision has also sparked debates within the eye care sector, raising concerns about the potential increase in false positive referrals that might overshadow the benefits derived from such expanded services [14, 15]. To mitigate this concern, 79 stores of the optician chain store Louis Nielsen (Louis Nielsen A/S, Aalborg, Denmark) collaborated with MitØje, a group of consultant ophthalmologists, to provide a tele-ophthalmology service.

In this study, we present our experiences in providing systematic retinal screening in Denmark through optometrists with access to teleophthalmological services before, during, and after the COVID-19 pandemic.

## METHODS

#### Study Design

This is a cross-sectional study of referrals from high street optician stores to the tele-ophthalmological service from August 1, 2018 to September 30, 2023. We evaluated diagnoses before, during, and after the COVID-19 pandemic to understand the impact of the pandemic on the referral patterns. All aspects of this study followed the tenets of the Declaration of Helsinki. All patients provided mandatory consent to data processing and company policies prior to data sharing. All data storage and data management aspects complied with the standards of European Union General Data Protection Regulation. All data extracted were fully anonymous, and as the study is classified as quality assessment, neither ethics approval nor any permission for the use of the data is needed according to the Danish Data Protection Agency. Data was extracted from Louis Nielsen A/S and MitØje Aps and was accessible to the author Danson V. Muttuvelu.

## Organization of the Tele-ophthalmological Service

The details of the organization of this service are detailed in a previous study [13]. Briefly, eye health screening was provided as a routine service across 79 high street optician stores of Louis Nielsen A/S. This routine service was subject to a fee (245 DKK per June 2024), which was waived upon purchase of glasses or contact lenses, at times of sales promotions, or at the discretion of the optometrist. Optometrists collected patient history, refraction, best-corrected visual acuity, intraocular pressure (IOP), optometrist slit-lamp examination, 4-in-1 visual field report, and retinal imaging using color fundus 45° photography. The onsite optometrist reviewed these examinations. In case of abnormalities or suspicion of disease as evaluated by the optometrist, results and images were submitted through the tele-ophthalmological system for evaluation by at least one experienced ophthalmologist. Thus, referrals were not made solely on the basis of vision complaints. Three different priority classes were employed: acute cases leading to immediate phone call-based consultation with immediate action by the ophthalmologist; subacute cases leading to image review same day; non-acute cases leading to image review within 72 h. In cases when the ophthalmologist

confirmed the presence of an abnormality or a disease which the patient was not already aware of, the patient was either booked for a follow-up/ observation of the retina utilizing the facilities at the local optician store or referred for treatment through the national eye care system. All diagnoses were based on International Classification of Diseases, 10th Revision (ICD-10) categories.

Selection of cases for tele-ophthalmology and priority of cases were systematized through flowcharts and systematic training of optometrists. All participating ophthalmologists were experienced consultants registered in the Danish Patient Safety Authority's specialists register. The ophthalmologists followed internal guidelines and were subject to internal training to streamline referral patterns. All acute sight-threatening cases were immediately referred to a hospital department of ophthalmology or neurology. All subacute patients and patients assigned to ordinary waiting lists were referred to a general ophthalmologist by electronic referral letter prepared by an ophthalmologist, including the objective findings from the retinal screening and a tentative diagnosis.

#### Devices for Screening and Data Sharing Platform

The IOP was measured by either rebound tonometry (iCare, Helsinki, Finland) or noncontact tonometry (Nidek Tonoref II/III, Aichi, Japan). Visual fields were measured using an Octopus 900 system (Haag-Streit, Bern, Switzerland). Color fundus photography was obtained by Centervue DRS (iCare, Helsinki, Finland). The referral platform was based on cloud-based imaging software provided by Optoflow (KIDE Clinical Systems, Espoo, Finland; Topcon Healthcare, Tokyo, Japan). Data registration and patient referral was performed using electronic software systems by EG Healthcare A/S (Ballerup, Denmark) and through the online national referral platform DNHF, which links referral systems in the Danish primary and hospital healthcare.

#### **COVID-19 Pandemics in Denmark**

The timeline of the COVID-19 pandemic, global events, events in Denmark, political decisions,

periods of national lockdown, etc. are all documented by the Statens Serum Institut (Copenhagen, Denmark), which is the national public surveillance institute under the Danish Ministry of Health [16]. A detailed timeline is published in Danish [16], from which we extracted major Danish policy changes and major events and translated into English to contextualize this study (Table 1). For this study, we defined the pre-COVID-19 period as August 1, 2018 to March 10, 2020; COVID-19 period as March 11, 2020 to January 31, 2022; and post-COVID-19 period as February 1, 2022 until September 30, 2023.

#### **Data Analysis and Statistics**

Summary data were reported for the entire study period on demographics, ICD-10 diagnosis, referral priority, and region (according to the European Union Nomenclature of Territorial Units for Statistics (NUTS) level 2). The three periods (pre-COVID-19, during COVID-19, post-COVID-19) were then compared. Since age was a normally distributed continuous variable, comparisons were made using the one-way analysis of variance (ANOVA) for age. Other variables were categorical and hence the  $\chi^2$  test was used. To better understand changes in the diagnostic cases between the three periods, we also performed another analysis in which the period pre-COVID-19 was used as the reference and the odds ratio (OR) was calculated for during and post-COVID-19. Statistical significance was defined as p values below 0.05. For the temporal trend analysis of diagnoses, multiple testing of 24 diagnoses required Bonferroni adjustment. For this analysis, statistical significance was defined as *p* values below 0.002.

## RESULTS

### **Study Population**

Throughout the study period, 1,142,028 unique individuals underwent screening. This corresponded to 19.1% of Denmark's entire population (5,952,575 as of September 2023). Age was

Table 1	Brief timeline of COVID-19 events in Denmark	
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Year 2020	
February 26	First Danish case of COVID-19
March 6	Ban on events > 1000 individuals and recommendation of social distancing
March 11	Nationwide lockdown for 2 weeks for all non-essential institutions and shops, and assembly ban for > 100 individuals
March 18	Ban on social gatherings for > 10 individuals and temporary closure of shops and shopping centers until April 13, 2020
April 21	Introduction of nationwide large-scale COVID-19 testing strategy
April 14–May 27	Gradual opening of institutions, shops, shopping centers, and outdoors activities
June 8	Ban on social gatherings changes from > 10 individuals to > 50 individuals
October 23	Ban on social gatherings changes from > 50 individuals to > 10 individuals
December 17–25	Closure of all shops, shopping centers, restaurants, non-essential public institutions until February 28, 2021
December 27	Start of vaccination against COVID-19
Year 2021	
January 5	Ban on social gatherings changes from > 10 individuals to > 5 individuals
March 1	Gradual opening of institutions, shops, shopping centers, and outdoors activities
March 18	Ban on social gatherings changes from > 5 individuals to > 10 individuals
May 4	Ban on social gatherings changes from > 10 individuals to > 25 individuals
May 28	Introduction of the Danish Corona-Passport app (a negative recent COVID-test or COVID vac- cination can be shown through the Corona-Passport app and is a requirement for certain public activities)
June–December	Gradual increase in percentage of vaccinated and gradual regulation of assembly rules
Year 2022	
February	All COVID-19 restrictions are removed

Detailed timeline of events is available in Danish from Statens Serum Institut which is the national public surveillance institute under the Danish Ministry of Health [16]

50.9±18.8 years, and 637,276 (55.8%) were female. According to our definitions of the COVID-19 pandemic timeline in Denmark, data were stratified into screening pre-COVID-19 (n=521,317; 870/day; age 52.0±19.2 years; 56.5% female), COVID-19 (n=345,626; 728/day; age 51.0±19.4 years; 55.3% female), and post-COVID-19 (n=275,085; 780/day; 48.7±18.8 years; 55.1% female). All these individuals were unique customers, and repeated visits from already included customers were not included in these analyses (the total numbers of visits including any repeated visits were 521,317, 511,000, and 567,000 for pre-COVID-19, COVID-19, and post-COVID-19, respectively). A total of 50,612 individuals (4.4%) were referred from the optometrists to the tele-ophthalmological examination for assessment of the images by a consultant ophthalmologist. The rates of referral from optometrists to the tele-ophthalmological service throughout pre-COVID-19, COVID-19, and post-COVID-19 were respectively 3.4% (n=17,914), 4.3% (n=15,014), and 6.4% (n=17,684); there was a small but statistically significant increase in the rate of referrals over time (p<0.0001,  $\chi^2$  test).

# Diagnoses Identified and Consequences of Tele-ophthalmological Examination

Among those referred for tele-ophthalmological examination (n = 50,612), their age was 55.1±17.1 years, and 26,195 (51.8%) were female. The age difference between those screened and those referred was 4.2 years (95% confidence interval (95% CI) 4.0-4.4 years, p < 0.0001, independent samples t test); hence, those referred for tele-ophthalmological examination were on average slightly older. Individuals of male biological sex were slightly more likely to be referred for tele-ophthalmological examination (OR 1.19, 95% CI 1.16-1.20, p < 0.0001). Data on NUTS level 2 region was available for 49,414 individuals (97.6%), which showed that most referrals for tele-ophthalmological examinations came from Central Denmark Region (28.8%), which is the second most populous administrative region/NUTS2 level region of Denmark. Overall, glaucoma/ ocular hypertension (OHT) (cases with either glaucoma, ocular hypertension, or individuals screened for glaucoma for various reasons, e.g., family history, high intraocular pressure, or optic nerve head suggestive of glaucoma) was the most prevalent diagnosis (n=10,173,20.1%). Detailed diagnoses of the 50,612 individuals screened for tele-ophthalmological examination are summarized in Table 2. Any referral for further ophthalmic examination, either in hospital or in a private ophthalmology practice, was made for 10,300 individuals (20.4%). Of these, 677 cases were acute referrals, most prevalently due to optic disc swelling (n=217, 32.1%) of the acute referrals); and 3726 cases were subacute referrals, most prevalently due to wet age-related macular degeneration (AMD) (n=628, 16.9% of the subacute referrals).

**Table 2** Details of those referred for tele-ophthalmological examination (N = 50,612)

Characteristics	Data	
Age, mean ± SD, years	55.1±17.1	
Biological sex, $N(\%)$		
Female	26,195	
	(51.8%)	
Male	24,417	
	(48.2%)	
Diagnosis, $N(\%)$		
Cataract	752 (1.5%)	
CSC	184(0.4%)	
Chorioretinal scar	384 (0.8%)	
Choroidal melanoma suspected	72 (0.1%)	
Choroidal naevus	7511 (14.8%)	
Diabetic retinopathy	264 (0.5%)	
Dry AMD	5645 (11.2%)	
Epiretinal membrane	2149 (4.2%)	
Glaucoma/OHT <sup>a</sup>	10,173	
	(20.1%)	
Hypertensive retinopathy	327 (0.6%)	
Macular edema	79 (0.2%)	
Macular hole	230 (0.5%)	
Optic disc atrophy	48 (0.1%)	
Optic disc drusen	405 (0.8%)	
Optic disc swelling	376 0.7%)	
Other disorders of the disc	1128 (2.2%)	
Posterior uveitis	31 (0.1%)	
Retinal artery occlusion	81 (0.2%)	
Retinal detachment	44(0.1%)	
Retinal hemorrhage	1784 (3.5%)	
Retinal vein occlusion	737 (1.5%)	
Retinopathy unspecified	7465 (14.7%)	
Wet AMD	811 (1.6%)	
Other diagnoses <sup>b</sup>	249 (0.5%)	

Table 2 continued

Characteristics	Data	
Normal examination	9683 (19.1%)	
Referral priority (if any), $N(\%)$		
Acute	677 (1.3%)	
Subacute	3726 (7.4%)	
Normal waiting	5897 (11.7%)	
Total (any referral)	10,300 (20.4%)	
Geographic region, $N(\%)$		
Capital Region of Denmark	10,881 (21.5%)	
Central Denmark Region	14,586 (28.8%)	
North Denmark Region	7948 (15.7%)	
Region Zealand	8296 (16.4%)	
Region of Southern Denmark	7703 (15.2%)	

*AMD* age-related macular degeneration, *CSC* central serous chorioretinopathy, *N* numbers, *OHT* ocular hypertension, *SD* standard deviation

<sup>a</sup>This category is a sum of cases with either glaucoma, ocular hypertension, or individuals screened for glaucoma for various reasons (family history, high intraocular pressure, or optic nerve head suggestive of glaucoma)

<sup>b</sup>Other diagnoses were either categorized as "unspecific disorder in the eye" or named with a specific diagnosis (anterior uveitis, cholesterol embolism, macular scarring, myopic degeneration, and vitreous opacities)

#### Temporal Trends of Diagnoses and the Impact of COVID-19 Pandemic

Among those referred for tele-ophthalmological examination, we observed subtle but statistically significant changes in the demographics throughout the three study periods (Table 3). Age increased ( $54.4\pm17.2$  years,  $55.1\pm16.9$  years, and  $55.9\pm17.0$  years for pre-COVID-19, COVID-19, and post-COVID-19, respectively; p < 0.001, one-way analysis of variance). Male biological sex constituted an increasing proportion (47.5%, 48.6%, and 48.8% for pre-COVID-19,

COVID-19, and post-COVID-19, respectively; p = 0.031,  $\chi^2$  test). The geographical composition of those referred for tele-ophthalmological examination also underwent noteworthy changes. From pre-COVID-19 to COVID-19, an increasing proportion of individuals from the Central Denmark Region and Region Zealand were evaluated, which afterwards normalized to pre-COVID-19 levels. We observed a pattern of an increase in acute and subacute referrals from before COVID-19 (1.2% and 6.4%, respectively) to during COVID-19 (1.8% and 8.4%, respectively) which decreased again after COVID-19 (1.1% and 7.5%, respectively) (p < 0.001,  $\chi^2$  test).

Temporal trends of diagnoses and their prevalence per 100,000 individuals screening throughout the entire program at the three timepoints (pre-COVID-19, during COVID-19, and post-COVID-19) are summarized in Table 4. We observed a statistically significant increase in the prevalences of cataract, central serous chorioretinopathy, choroidal naevi, diabetic retinopathy, dry AMD, epiretinal membrane, glaucoma/OHT, macular hole, optic disc swelling, retinal detachment, retinal hemorrhage, retinal vein occlusion, retinopathy unspecified, and wet AMD. Diagnoses of other disorders of the disc were less prevalent during than before COVID-19. After the pandemic, these diagnoses reverted to pre-COVID-19 levels. The other diagnoses were not subject to statistically significant changes throughout the study period.

## DISCUSSION

In this study, we report the experiences of high street optician stores which facilitated widescale high-volume screening before, during, and after COVID-19 pandemic in Denmark. Although the COVID-19 pandemic led to statistically significant changes, it must be underscored that overall changes were subtle. On the basis of more than 1.1 million unique individuals who underwent retinal screening (corresponding to 19.1% of Denmark's entire population), we found that the need for referral for tele-ophthalmological service was at 4.4%. The need for further referral for ophthalmological consultation was

Characteristics	Before COVID-19 ( <i>n</i> = 17,914)	During COVID-19 ( <i>n</i> = 15,014)	After COVID-19 ( <i>n</i> = 17,684)	<i>p</i> value
Age, mean ± SD, years	$54.4 \pm 17.2$	55.1±16.9	55.9±17.0	< 0.001
Biological sex, $N(\%)$				0.031
Female	9412 (52.5%)	7722 (51.4%)	9061 (51.2%)	
Male	8502 (47.5%)	7292 (48.6%)	8623 (48.8%)	
Geographic region, $N(\%)$				< 0.001
Capital Region of Denmark	4314 (24.1%)	3043 (20.3%)	3524 (19.9%)	
Central Denmark Region	5034 (28.1%)	4580 (30.5%)	4972 (28.1%)	
North Denmark Region	3110 (17.4%)	2354 (15.7%)	2484 (14.0%)	
Region Zealand	2654 (14.8%)	2545 (17.0%)	3097 (17.5%)	
Region of Southern Denmark	2363 (13.2%)	2145 (14.3%)	3195 (18.1%)	

 Table 3 Demographic changes of those referred for tele-ophthalmological examination before, during, and after the COVID-19 pandemic

Age is compared using one-way ANOVA. The other variables were categorical and were compared using the  $\chi^2$  test N numbers, SD standard deviation

20.4% of the 4.4%, i.e., 0.9% of those screened in high street optician stores. Experiences from the organization of our screening system have widescale implications. A publicly funded healthcare system does not have economic incentives to examine a large number of false positives referred from a large-scale screening system [14]. Instead, a large number of false positives can potentially worsen outcomes for those with a disease because the increased demand for ophthalmic examination can be expected to increase waiting times of the existing healthcare providers [14]. Therefore, introduction of optometrist-facilitated screening initiatives has been subject to debate in Denmark [14]. We show that our organization reduces the number of potential referrals from optometrists to the public health system from 4.4% to 0.9% (a factor of five) of individuals screened. This is a very large and necessary reduction if such screening initiatives are to be introduced in countries with publicly funded healthcare systems.

The referral rate to the tele-ophthalmological service increased during COVID-19. Considering widespread information campaigns with social distancing, information on infection hygiene, and the immense strain on healthcare workers, we speculate that an important proportion of those in need of an eye check were unable to obtain such services through the public health system and were instead taken care of by high street optician stores. This highlights two important points. First, in times of strain on publicly financed ophthalmic health services, an optometrist-based retinal screening service in collaboration with tele-ophthalmological support may provide important and meaningful assistance. This can be observed in the increase in acute referrals (immediate referrals to a hospital department of ophthalmology or neurology) from 1.2% before COVID-19 to 1.8% during COVID-19 which decreased again to 1.1% after COVID-19. Second, there is also a real and relevant need for individuals to seek eye examinations without significant symptoms, and this demand is often underappreciated in a publicly funded healthcare system, which needs to prioritize those with disease. This is especially important during times of extra strain on the system, such as the case in COVID-19 pandemic. For these healthy individuals, seeking a screening service facilitated by high street optician stores may be a relevant approach; however, a teleophthalmological referral system in that context

Diagnosis	Before COVID-19	During COVID-19	After COVID-19	<i>p</i> value
Cataract	276 (53)	248 (72)	228 (83)	< 0.0001*
CSC	52 (10)	57 (16)	75 (27)	< 0.0001*
Chorioretinal scar	125 (24)	109 (32)	150 (55)	< 0.0001*
Choroidal melanoma suspected	21 (4)	34 (10)	17 (6)	0.0038
Choroidal naevus	2062 (396)	2347 (679)	3102 (1128)	< 0.0001*
Diabetic retinopathy	102 (20)	60 (17)	102 (37)	< 0.0001*
Dry AMD	2058 (395)	1531 (443)	2056 (747)	< 0.0001*
Epiretinal membrane	605 (116)	651 (188)	893 (325)	< 0.0001*
Glaucoma/OHTª	4041 (775)	2838 (821)	3294 (1197)	< 0.0001*
Hypertensive retinopathy	140 (27)	94 (27)	93 (34)	0.18
Macular edema	25 (5)	26 (8)	28 (10)	0.020
Macular hole	63 (12)	85 (25)	82 (30)	< 0.0001*
Optic disc atrophy	23 (4)	7 (2)	18 (7)	0.023
Optic disc drusen	187 (36)	101 (29)	117 (43)	0.021
Optic disc swelling	113 (22)	119 (34)	144 (52)	< 0.0001*
Other disorders of the disc	576 (110)	254 (73)	298 (108)	< 0.0001*
Posterior uveitis	12 (2)	10 (3)	9 (3)	0.71
Retinal artery occlusion	35 (7)	24 (7)	22 (8)	0.80
Retinal detachment	11 (2)	11 (3)	22 (8)	0.0002*
Retinal hemorrhage	462 (89)	569 (165)	753 (274)	< 0.0001*
Retinal vein occlusion	216 (41)	256 (74)	265 (96)	< 0.0001*
Retinopathy unspecified	3171 (608)	2157 (624)	2137 (777)	< 0.0001*
Wet AMD	245 (47)	266 (77)	300 (109)	< 0.0001*
Other diagnoses <sup>b</sup>	93 (18)	76 (22)	80 (29)	0.0054

Table 4 Temporal trends of diagnoses throughout study periods

Data are provided as number of cases, and numbers in parentheses state the diagnosis prevalence per 100,000 individuals screened during the study period

AMD age-related macular degeneration, CSC central serous chorioretinopathy, OHT ocular hypertension

\*Statistical significance at P < 0.002 according to Bonferroni adjustment for multiple testing

<sup>a</sup>This category is a sum of cases with either glaucoma, ocular hypertension, or individuals screened for glaucoma for various reasons (family history, high intraocular pressure, or optic nerve head suggestive of glaucoma)

<sup>b</sup>Other diagnoses were either categorized as "unspecific disorder in the eye" or named with a specific diagnosis (anterior uveitis, cholesterol embolism, macular scarring, myopic degeneration, and vitreous opacities) may be crucial to avoid a large number of false positives. To put these considerations into perspective, of 1,142,028 unique individuals who underwent screening in this study, the optometrist evaluated no need for further referral for 1,091,416 individuals (95.6%) but suggested a need for an ophthalmologist for the remaining 50,612 individuals; however, through the teleophthalmological system, 40,312 of these individuals could avoid referrals to the public health system and thus allow for better use of publicly financed healthcare.

Geographical differences in referral patterns were observed during COVID-19. In Denmark, there is a geographical uneven distribution of ophthalmologists, which leads to variations in the waiting time for non-acute appointments in publicly funded ophthalmic practices. In particular, the Central Denmark Region is significantly underserved in terms of publicly funded ophthalmic practices [17]. During COVID-19, we observed that a greater proportion of individuals referred to tele-ophthalmological examinations were from this underserved geographical region [17]. Thus, we speculate on the basis of our data that the screening system also functioned as a support system to the existing healthcare when the pandemic-associated strain on the health system led to excessive waiting time for those with a disease. In other words, this organization was able to help not only healthy individuals who requested an eye examination but also those with symptoms in need of help.

Temporal trends showed subtle but interesting changes in the prevalence of diagnoses. It is important to acknowledge the limitations of our data extraction and database to understand the accuracy of data. For every single patient, one action diagnosis is obtained. Thus, data are simplified to the most severe/action needing diagnosis when considering individuals with multiple diagnoses in one eye or different diagnoses in each eye. This approach will theoretically underestimate more benign conditions. In that regard, we found that prevalent conditions that require an urgent referral or action (optic disc swelling, retinal detachment, retinal vein occlusion, and wet AMD) were subject to an increase in prevalence during the study periods, whereas more rare conditions that also do require an urgent referral or action (suspected choroidal melanoma, hypertensive retinopathy, posterior uveitis, and retinal artery occlusion) were not subject to any statistically significant temporal changes. We speculate that for the prevalent conditions, the COVID-19 pandemicrelated strain on the public health system may have led to an increasing utilization of the optometrist-based retinal screening system. After the COVID-19 pandemic, an increasing awareness of optometrist-based retinal screening has helped to sustain its broad use. Apart from widescale advertisements by the high street optician stores, it is also our anecdotal experience that family medicine physicians recommend optometrists to their patients when it seems impossible to reach an ophthalmologist. Thus, there is an increasing notion in Danish society that high street optician stores can play a meaningful role in the initial triage/screening of the eyes. It should be noted that when considering changes in the prevalence of conditions in the tele-ophthalmological system, demographic changes [3–9] or changes in the prevalence of diseases for other reasons may also play an important role. One example is that we observed an increase in individuals with retinal hemorrhages during COVID-19, which persisted after COVID-19. While we do not fully understand the reason for this observation, it is noteworthy that a number of cases with retinal hemorrhages have been related to COVID-19 infection or after vaccination against COVID-19 [18-21].

Limitations of this study should be acknowledged. Individuals visiting high street optician stores are more likely to have any refractive errors or an eye disease, which introduces a selection bias. Moreover, individuals are more likely to seek an eye health check if they have symptoms or complaints. Another important limitation is that all diagnoses are based on tele-ophthalmological evaluation without access to more advanced examinations such as optical coherence tomography (OCT) or retinal angiography. In routine clinic, we can tailor our questions to the patient, and explore patient history in detail. Similarly, we can tailor our slit-lamp examination according to our suspicions. In a tele-ophthalmology-based system, patient history and slit-lamp examination

are based on brief text snippets written by the optometrist in the high street optician store. Thus, the diagnostic precision should be seen in light of these limitations. Further, we do not have access to the final diagnoses after potential referral to the public health system, nor do we have any insight into potential false negatives among those screened by optometrists but never referred to tele-ophthalmological examination. The rate of false negatives was not investigated in this study, but remains an important topic, also from a medicolegal perspective. One Spanish study evaluated diagnostic accuracy of optometrist-based screening using fundus photography as compared to an examination by an ophthalmologist, and the consequences of OCT to the optometrist-based screening system [22]. On the basis of 1334 eyes, the authors reported a sensitivity of 98% (95% CI 97-99%) and a specificity of 38% (95% CI 94-97%) when only using fundus photography [22]. Thus, the optometrists were excellent at ruling out a disease, but only 38% of those presumed with disease had actually a disease. Adding OCT to the study led to an unchanged excellent level of sensitivity of 96% (95% CI 94-97%), and an improved level of specificity of 53% (95% CI 49-57%) [22]. We therefore expect false negatives to be a rare issue, but nevertheless they remain an important issue to consider. Adding OCT may provide value in lowering the number of false positives from optometrist-based screening; however, a recent report suggests that a tele-ophthalmology-based intermediary, at least in Denmark, is a more cost-effective strategy [23]. However, adding OCT in the optometrist-based screening may provide a better quality of the screening service regardless, while also considering the evaluation by the consultant ophthalmologists at the teleophthalmology part of the service.

Our findings illustrate important opportunities and challenges for tele-ophthalmologybased eye health screening in Denmark. It should be noted, however, that these circumstances may not be easily generalizable outside of Denmark with different healthcare systems, population demographics, pandemic responses, and legislation.

## CONCLUSION

This study reported important experiences of how high street opticians facilitated widespread high-volume screening before, during, and after the COVID-19 pandemic in Denmark. During a study period of 5 years, our system performed retinal screening for one in five individuals in Denmark. We highlight diagnoses, implications, and possibilities for a supportive role of a basic eye screening service for the public health system. We recommend further studies to examine the health and societal benefits of such widescale national screening systems.

## ACKNOWLEDGEMENTS

We thank the participants of the study.

*Authorship.* All authors adhered to the ICMJE guidelines for authorship.

Author Contributions. Conceptualization: Marie L.R. Rasmussen, Yousif Subhi, Danson V. Muttuvelu, methodology: Marie L.R. Rasmussen, Yousif Subhi, Danson V. Muttuvelu; analysis and interpretation: Marie L.R. Rasmussen, Lasse J. Cehofski, Julie Davies, Carsten Faber, Mads K. Falk, Jakob Grauslund, Michael S. Hansen, Pearse A. Keane, Sundaram Natarajan, Tunde Peto, Yousif Subhi, Charles C. Wykoff, Danson V. Muttuvelu; writing—original draft preparation: Marie L.R. Rasmussen, Yousif Subhi, Danson V. Muttuvelu; writing—review and editing: Marie L.R. Rasmussen, Lasse J. Cehofski, Julie Davies, Carsten Faber, Mads K. Falk, Jakob Grauslund, Michael S. Hansen, Pearse A. Keane, Sundaram Natarajan, Tunde Peto, Yousif Subhi, Charles C. Wykoff, Danson V. Muttuvelu; supervision: Danson V. Muttuvelu. All authors (Marie L.R. Rasmussen, Lasse J. Cehofski, Julie Davies, Carsten Faber, Mads K. Falk, Jakob Grauslund, Michael S. Hansen, Pearse A. Keane, Sundaram Natarajan, Tunde Peto, Yousif Subhi, Charles C. Wykoff, Danson V. Muttuvelu) read and approved the final manuscript.

*Funding.* No funding or sponsorship was received for this study or publication of this article. The Rapid Service Fee was funded by the authors.

**Data Availability.** The datasets generated during and/or analyzed during the current study are not publicly available as public access to individual data points was not part of the consent given by the participants in study.

#### Declarations

Conflict of Interest. Marie L.R. Rasmussen declares: speaker fee from Santen; advisory board member from Santen. Lasse J. Cehofski declares: advisory board member for AbbVie, Novartis, and Roche; speaker fees from AbbVie and Bayer; travel grants from AbbVie and Roche. Jakob Grauslund declares: advisory board member or speaker fees from Novartis, Bayer, Apellis, Novo Nordisk, and Roche. Michael S. Hansen declares: speakers fee from Roche. Pearse A. Keane declares: speakers fee from Heidelberg Engineering, Topcon, Allergan, and Bayer; consultancy for Google, DeepMind, Roche, Novartis, Apellis, and BitFount; equity ownership in Big Picture Medical. Yousif Subhi declares: speaker fees from Bayer and Roche. Yousif Subhi is an Editorial Board member of Ophthalmology and Therapy. Yousif Subhi was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions. Charles C. Wykoff declares: consultant for 4DMT, AbbVie, Adverum Biotechnologies, Aerie, AGTC, Alcon, Alimera, Allergan, Allgenesis, Alnylam, Annexon Biosciences, Apellis, Arrowhead, Ascidian, Bausch+Lomb, Bayer, Bionic Vision Technologies, Boehringer Ingelheim, Cholgene, Clearside Biomedical, Curacle, Eyebiotech, EyePoint Pharmaceuticals, Foresite, Frontera Therapeutics, Genentech, Gyroscope Therapeutics, IACTA, IVERIC bio, Janssen, Kato Pharma, Kiora, Kodiak Sciences, Kriva Therapeutics, Merck, Nanoscope, Neurotech, NGM Biopharmaceuticals, Notal Vision, Novartis, OccuRx, Ocular Therapeutix, Ocuphire, Ocu-Terra, OliX, ONL, Opthea, Oxular, Palatin Technologies, Perceive Bio, Perfuse, PolyPhotonix,

Ray, RecensMedical, Regeneron, REGENXBIO, Resonance, Roche, Sandoz, Sanofi, SciNeuro Pharmaceuticals, Stealth Biotherapeutics, Surrozen, Suzhou Raymon, Takeda, Thea, Therini, TissueGen, Valo, and Verana Health; research funding from 4DMT, Adverum Biotechnologies, AffaMed Therapeutics, Aldeyra, Alexion, Alimera, Alkahest, Allergan, Allgenesis, Amgen, Annexin Pharmaceuticals, Annexon Biosciences, Apellis, AsclepiX Therapeutics, Bayer, Boehringer Ingelheim, Chengdu Kanghong, Clearside Biomedical, Curacle, Eyebiotech, EyePoint Pharmaceuticals, Gemini, Genentech, GlaxoSmithKline, Graybug Vision, Gyroscope Therapeutics, IONIS, iRENIX, IVERIC bio, Janssen, Kodiak Sciences, LMRI, McMaster University, Nanoscope, Neurotech, NGM Biopharmaceuticals, Novartis, Ocular Therapeutix, Ocuphire, OcuTerra, OliX, Ophthotech, Opthea, Oxurion, Oxular, Oyster Point Pharma, Perceive Bio, RecensMedical, Regeneron, REGENXBIO, Rezolute, Roche, Sam Chun Dang Pharm, Sandoz, Senju Pharmaceutical, Shanghai Henlius Biotech, Taiwan Liposome Company, Unity Biotechnology, Verily Life Sciences, and Xbrane Biopharma; on advisory board of Aerie, Kato Pharma; Board member of ASRS. Vit-Buckle Society: stock options for ONL. PolyPhotonix, RecensMedical, TissueGen, Visgenx, Vitranu. Danson V. Muttuvelu declares: consultancy fee from Alcon. MicroSurgical Technology, and Johnson & Johnson. Julie Davies, Carsten Faber, Mads K. Falk, Sundaram Natarajan, and Tunde Peto declare that they have no competing interests.

*Ethical Approval.* All aspects of this study followed the tenets of the Declaration of Helsinki. All patients provided mandatory consent to data processing and company policies prior to data sharing. All data storage and data management aspects comply with the standards of the European Union General Data Protection Regulation. All data extracted were fully anonymous, and as the study is classified as quality assessment, neither ethics approval nor any permission for the use of the data is needed according to The Danish Data Protection Agency. Data was extracted from Louis Nielsen A/S and MitØje Aps and was accessible to the author Danson V. Muttuvelu.

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