# Telemedicine for Age-Related Macular Degeneration

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## Abstract

***Background:*** *As the leading cause of vision loss in the United States, age-related macular degeneration (AMD) would seem to be amenable to interventions that increase access to screening and management services for patients. AMD poses several unique challenges for telemedicine, however. The disease lacks clinical consensus on the effectiveness and cost-effectiveness of screening the general population, and more complex imaging modalities may be required than for what has traditionally been used for diabetic retinopathy telehealth systems.*

***Methods:*** *The current literature was reviewed to find clinical trials and expert consensus documents on the state-of-the-art of telemedicine for AMD.*

***Results:*** *A range of feasibility studies have reported success with telemedicine strategies for AMD. Several investigators have reported experience with AMD screening and remote-monitoring systems as well as artificial intelligence applications.*

***Conclusions:*** *There are currently no large-scale telemedicine programs for either screening or managing AMD, but new approaches to screening and managing the condition may allow for expansion of high-quality convenient care for an increasing patient population.*

**Keywords:** *telemedicine, teleophthalmology, ophthalmology*

## Introduction

Age-related macular degeneration (AMD) is the leading cause of vision loss in the United States.[1] As such, the disease presents an appropriate target for ocular telehealth interventions. Unlike diabetic retinopathy (DR), there is no consensus about the utility of population screening for AMD.[2] Some groups have found value by adding screening for AMD to existing DR screening programs,[3,4] but others have not found screening programs for AMD to be cost-effective.[5] Several groups have investigated the feasibility and validity of telehealth programs for AMD. Owing to the uncertainty of the role of screening for AMD, several groups have explored other telehealth paradigms for this disease.

## Clinical Feasibility

Although the clinical and research gold standard for DR diagnosis is seven-field Early Treatment Diabetic Retinopathy Study stereoscopic fundus photography, the "gold standard" for the diagnosis of AMD remains clinical examination and fluorescein angiography with or without optical coherence tomography (OCT). Therefore, several groups have sought to validate the use of fundus photographs for the diagnosis of AMD through the detection of characteristic lesions of AMD (drusen, hyperpigmentation, choroidal neovascular membrane [CNVM], and geographic atrophy [GA]). Specifically as it relates to the presence of CNVM, a retrospective analysis of stereoscopic images of 127 fellow eyes from the Macular Photocoagulation Study correctly identified all 30 eyes that developed CNVM as defined by fluorescein angiogram.[6]

To determine the accuracy of diagnosing AMD with monoscopic images alone, Scholl et al. at Moorfields Eye Hospital compared digitized color, mydriatic monoscopic images with stereoscopic 35 mm slides, and found an agreement of 83–93% for the presence or absence of intermediate drusen depending on the macular subfield examined.[7] Furthermore, they found agreement of 94–96% for GA and 94–98% for CNVM.

Pirbhai et al. conducted a prospective comparison of mydriatic monoscopic color fundus photographs with conventional clinical evaluation and fluorescein angiography.[8] In this study, the diagnoses rendered on the basis of the monoscopic images were 89.2% sensitive and 85.7% specific. Clinical recommendations based on the monoscopic images corresponded to the gold standard clinical examination 80.3% of the time. The kappa statistic is frequently used to test interrater reliability and can range from −1.0 to 1.0. In this study, the kappa was 0.59, which the authors concluded was evidence of good agreement.[8]

In another study, Duchin et al.[9] compared nonmydriatic fundus images with a conventional clinical dilated fundus examination with a retina specialist. In 94 eyes of 47 patients,[9] they found sensitivity for referable AMD (Age-Related Eye Disease Study [AREDS] grading level 3 or greater) to be 84–88% and specificity of 81% between their two expert graders. Of note, the authors used their existing telemedicine infrastructure for DR screening.

## Clinical Experience

To expand upon feasibility studies, several groups have implemented ocular telehealth programs for AMD. In a randomized controlled trial, participants referred for possible or established neovascular AMD were randomly assigned to either conventional clinical examination or image acquisition and remote interpretation at an ocular telehealth site.[10] Data collected included best-corrected visual acuity, intraocular pressure, color fundus photographs (mydriatic status not specified in publication, but clarified as dilated by senior article author, Dr. Thomas Sheidow, pers. comm., February 9, 2018), and OCT.

These data were transmitted to retina specialists at a tertiary referral site. They found no delay in presentation for care in the telescreening group, but did note increased interval between detection and reinitiation of therapy in participants with established AMD. They did not detect any adverse outcomes in terms of visual acuity attributable to this delay in this small study.

Another *in situ* study was performed by De Bats et al. in Lyon, France.[11] In this study, 1,022 individuals were screened for known presence of AMD and absence of comorbidity that would preclude AMD management, of whom 683 were eligible and interested in participating. Nonmydriatic color photographs were then taken at two community health examination centers and then transmitted for grading by an ophthalmologist. Images were gradable in 80% of the 1,363 images acquired, and AMD was diagnosed in 178 eyes. There was no gold standard assessment of participants in this study.

As in DR, retinopathy of prematurity, and other retinal conditions, there is growing interest in the use of artificial intelligence (AI) systems for image processing and interpretation.[12] Such systems may allow for more rapid/instantaneous grading of images with similar accuracy to expert human grading. Investigators have used a variety of public and private data sets including the Singapore Integrated Diabetic Retinopathy Screening Programme[13] and the AREDS[14,15] to train deep learning algorithms to identify features of AMD on color fundus photographs. Other groups have likewise used deep learning approaches to identify AMD on OCT images.[16,17] At the time of this writing, no AI system is Food and Drug Administration (FDA) approved for AMD.

## Remote Monitoring

Several groups have looked to other telehealth paradigms beyond store-and-forward remote screening/detection, such as remote monitoring. Andonegui et al. sought to determine whether ancillary testing performed without a live examination could allow clinicians to reach a similar assessment and plan to that diagnostic decisions based on a live examination.[18] In this study, 201 participants with exudative AMD who had received a minimum of three prior ranibizumab injections initially had a live examination with spectral domain-optical coherence tomography (SD-OCT), fundus photography, and visual acuity measurements. Antivascular endothelial growth factor (VEGF) retreatment decisions were made based on this live examination and recorded.

At least 4 weeks later, the ancillary data were anonymized and randomly distributed to the same two retina physicians who had seen them previously. A retreatment decision was then rendered and recorded based on this "remotely acquired" clinical data simulating a telehealth encounter. The same treatment decision was reached in 90% of cases, with 8% of patients receiving "false positive" (i.e., the remote decision was to retreat, but the live decision was to defer), and 1% receiving a "false negative" (i.e., the remote decision was to defer, but the live decision was to treat).

Moving further away from remote image acquisition and transmission, Azzolini et al. sought to determine whether an e-health decision support tool could help general ophthalmologists follow AMD patients without referral.[19] General ophthalmologists could enter in patient age, visual acuity, Amsler grid results, presence of macular hemorrhage, and fellow eye status. A risk score for active exudation is calculated, and the general provider can directly schedule with a retinal provider in instances of high risk. A comparison of consecutive patients undergoing usual care was also established.

During the study period, 360 patients with known AMD were examined within the network. Of these, 310 were judged high risk of disease progression, and referred for a live examination. Of these, 276 received intravitreal anti-VEGF therapy. There was less of a delay before initiating therapy in the "network" as compared with the usual care patients, and all providers judged the system to be "good" or "very good." The validation of risk score is listed as "unpublished data" and the 50 patients with low risk scores were not examined in this study.

Another approach at remote monitoring using a consumer device was explored in the AREDS 2 study.[20] In this study, participants with nonexudative AMD at high risk for developing choroidal neovascularization (CNV) were randomized to either use the ForeseeHome device daily at home or to standard-of-care symptom monitoring. The device tests macular visual field using hyperacuity techniques, and sent an alert to investigators if a substantial change was noted. During a prespecified interim analysis, a statistically significant smaller decline in visual acuity was noted at the time of diagnosis of active CNV in the ForseeHome group as compared with standard-of-care monitoring. For this reason, early termination for efficacy was recommended. After FDA approval of the device, a cost-effectiveness analysis from a federal government perspective found that home telemonitoring of patients at high risk for CNV was cost-effective compared with biannual in-person examination.[21]

## Conclusions

Across a range of studies, then, numerous different ocular telehealth strategies have been tested for AMD. Because of the lack of well-defined high-risk population, merely extending existing DR screening pathways to screen for AMD is not currently in use, nor recommended. Ocular telehealth for AMD is likely to require expansion of the remote screening tool kit of a network-connected nonmydriatic fundus camera to include technologies such as OCT and possibly OCT angiography. As new strategies are tested in high-quality studies, and as the population ages, and the burden of AMD increases, there will likely be opportunities for remote monitoring, either through teleconsultation with general medical providers, or optometric or general ophthalmologic providers, or through consumer-facing home monitoring. Indeed, finding solutions to the challenges of remote detection and management of AMD may allow for the generalization of ocular telehealth methods to a number of different conditions, and may help usher the field away from a disease-specific paradigm.

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No competing financial interests exist.

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