The North Carolina Diabetic Retinopathy Telemedicine Network:

Final Program Evaluation

By

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Abstract

Importance: Retinal tele-screening with remote expert interpretation is an emerging strategy for providing diabetic retinopathy (DR) evaluations in the primary care setting and is especially useful in reaching patients living in rural and underserved areas.

Objective: To evaluate the effectiveness of telemedicine in providing retinal screenings to patients with diabetes who participated in the North Carolina Diabetic Retinopathy Telemedicine Network (NCDRTN).

Design: Cross-sectional study conducted from January 2014 to November 2015.

Setting: 5 Area Health Education Center (AHEC) primary care clinics which serve rural and underserved populations in North Carolina.

Participants: 1787 patients with diabetes received retinal screening photographs with remote expert interpretation to determine the presence and severity of DR. Participants included patients aged 18 years or older with Type I or Type II diabetes mellitus who presented to these 5 clinics for their routine diabetes care. Of these patients, 1661 with complete data were included in the statistical analysis.

Main Outcomes and Measures: Identification of patient characteristics associated with DR and ophthalmologist referral as well as percentage increase in DR screening rates at the 5 clinics.

Results: 1661 patients with complete data were included in the analysis. 1323 (79.7%) had no DR, 183 (11.0%) had DR without referral, and 155 (9.3%) had DR with referral. Age and race were not associated with DR, but were associated with referral. Older patients (OR = 1.28) and African American patients (OR = 1.84) or another minority (OR = 2.19) had greater

odds of referral when compared to those who were Caucasian and/or younger by 10 year increments. Patients with higher HgA1c levels (OR = 1.19) and longer duration of diabetes (OR = 1.76) had increased odds of having DR that required referral. Stroke (OR = 1.65) and kidney disease (OR = 1.59) were the comorbid conditions most associated with DR and referral in our study population. The mean reported pre-implementation DR screening rate among the 5 clinics was 25.6% and the post-implementation DR screening rate in active patients was 40.4%.

Conclusions and Relevance: When implemented in the primary care setting, telemedicine is an effective intervention for increasing the reach of DR screening in patients with diabetes who otherwise face access barriers to proper and timely eye care.

Introduction

Diabetic retinopathy (DR) is the most common microvascular complication of diabetes [1] and is the leading cause of new cases of blindness among adults aged 20–74 years in the United States (U.S.). [2] Recent estimates reveal 4.2 million or 28.5% of people with diabetes over age 40 have DR and 655,000 of these individuals have vision-threatening retinal disease. [2] By the year 2050, the prevalence of DR in Type I and Type II diabetic patients aged 40 and older is projected to increase to 16.0 million (from 5.5 million in 2005) and the prevalence of vision-threatening DR is projected to increase to 3.4 million (from 1.2 million in 2005). [3]

Early detection of DR is crucial to prevent the loss of vision. Medical and surgical therapies have dramatically reduced the progression of DR. In fact, timely intervention with laser therapy and anti-VEGF therapy can reduce the risk of severe vision loss by over 90%. [4–12] While national and international DR screening guidelines have been established by organizations such as the American Academy of Ophthalmology (AAO), National Committee for Quality Assurance (NCQA), National Eye Institute (NEI), Centers for Disease Control and Prevention (CDC), and the World Health Organization (WHO), screening rates in the U.S. remain low in the predominant health care paradigm wherein patients with diabetes are referred from primary care providers to ophthalmologists for dilated eye examinations to determine whether DR is present. On average, less than 50% of patients with diabetes meet current annual screening recommendations. [13–17] Socioeconomic and geographic barriers to care, delayed referrals from primary care providers, and lack of patient awareness regarding the importance of annual retinal examinations have been cited as reasons for low screening rates. [18–21] Among minorities, language, cultural, and educational barriers may also contribute to disparities in screening and treatment. [15,17,22] Timely treatment with panretinal and focal laser photocoagulation surgery has been proven in the ETDRS, DRS, and DRVS trials [8–10] to significantly decrease vision loss from diabetes. A recent landmark trial from the Diabetic Retinopathy Clinical Research Network has demonstrated that anti-VEGF therapy can preserve visual acuity to a similar degree as laser therapy for proliferative DR. [12] Thus, the challenge lies first in the early identification of patients at risk of vision loss on a societal scale.

Telemedicine is an emerging strategy for improving DR evaluation through retinal imaging with remote expert interpretation. Introducing this technology at the point of care of the primary physician could substantially reduce many of the above barriers and improve early detection of retinopathy. While other countries such as the United Kingdom and France have demonstrated high rates of DR screening through telemedicine programs, [23–25] large-scale data in the U.S. is sparse and limited primarily to the Veterans Administration (VA) system. While the VA has achieved a high level of efficiency and quality of DR screening for their patients, [26–29] it may be difficult to generalize their findings to practice settings with a diverse patient and payor mix.

In the present study, our goal was to evaluate the effectiveness of telemedicine as an intervention for increasing the reach of DR screening for patients with diabetes who have eye care access barriers in North Carolina. By collecting patient metadata in this diverse clinic population, we also examined factors associated with DR and ophthalmologist referral.

Methods

The North Carolina Diabetic Retinopathy Telemedicine Network (NCDRTN) is an innovative public health initiative that aims to use retinal tele-screening to reduce rates of vision loss from DR by providing efficient, effective retinal evaluation to patients with diabetes who live in some of the most rural and underserved parts of the state. This program was funded by The Duke Endowment and is a collaboration between the University of North Carolina (UNC) Chapel Hill Department of Ophthalmology and 5 Area Health Education Center (AHEC) affiliated primary care clinics across North Carolina: Mountain AHEC (MAHEC) in Asheville, Moses Cone Hospital Internal Medicine (MCH-IM) and Family Medicine (MCH-FM) clinics in Greensboro, East Carolina University (ECU) Department of Family Medicine, and Southern Regional AHEC (SRAHEC) in Fayetteville. The program evaluation associated with this project was approved by the UNC Institutional Review Board.

Patient recruitment. Patients were included in this study if they had Type I or Type II diabetes mellitus, were 18 years of age or older, and received primary care for their diabetes at one of the 5 AHEC clinics. Patients were excluded if they were unable to undergo imaging due to cognitive impairment or if they already had a documented retinal exam within the past 12 months with an eye care provider. Retinal tele-screening was performed in the primary care clinics, which serve large numbers of Medicare and Medicaid recipients, uninsured patients, and racial/ethnic minorities. Staff at each clinic identified and enrolled patients with diabetes who had not received a retinal exam within the past 12 months into the NCDRTN. Patients were identified from clinic rosters on the day of service or were contacted ahead of their scheduled diabetes care visits for enrollment into the program. Clinic electronic medical records (EMR) were also queried to identify and recruit patients who were due for retinal screening. In some instances, clinics used computer monitor advertisements within clinic waiting areas, informational flyers in English and Spanish, and patient education brochures to recruit patients into the program.

Retinal photography & image transfer. Depending on the available resources at each clinic, existing nursing staff, clinic technicians, and/or ancillary personnel were trained as retinal fundus camera operators. Patients underwent retinal fundus photography at the most convenient time during their visit so that their imaging session could be seamlessly integrated into the existing clinic flow. The MAHEC, SRAHEC, MCH-IM, and MCH-FM clinics each used a manual table-top digital nonmydriatic (undilated) fundus camera (VisuCam Pro NM; Carl Zeiss Meditec AG, Jena, Germany), whereas the ECU clinic used a fully automated table-top digital nonmydriatic fundus camera (Centervue DRS; Centervue, Fremont, CA) to capture a single 45° macula-centered retinal photograph in both eyes. In the vast majority of cases, no pupillary dilation was required.

After assessment of image quality, the DICOM (Digital Imaging and Communications in Medicine) images and patient metadata were securely transmitted via the RetinaVue Network (Welch Allyn, Skaneateles, NY), which is a HIPAA-compliant, web-based protocol for secure image transmission. [30] Metadata included standard clinical diabetes metrics as well as social determinants of health as defined under "Data Collection" below. A single retina specialist (SG) at the UNC-Chapel Hill Department of Ophthalmology remotely interpreted the retinal images for the presence of DR and, if present, classified the DR severity according to the International Clinical DR and DME disease severity scales. [31] An electronic report containing the retinal images, the stratified level of DR, a preliminary diagnosis for each eye, and a recommended management plan based upon DR severity was sent electronically to the originating primary care provider within 24 hours for incorporation into the patient's EMR. In general, patients with no DR or mild non-proliferative DR (NPDR) were scheduled for repeat follow-up photographs in 12 months within the NCDRTN. Patients with mild to moderate NPDR were scheduled for repeat follow-up photographs in 6 months. Patients with diabetic macular edema (DME), severe NPDR or proliferative DR (PDR), or ungradable images were scheduled for a referral visit with an ophthalmologist in the patient's local community for additional evaluation and treatment as needed.

Patient education. Prior to NCDRTN implementation, diabetic patients in the AHEC clinics received little to no education regarding DR. Retinal tele-screening in these clinics facilitated the education of patients regarding their diabetes and its effect on their vision. To raise patient and provider awareness of the importance of retinal screening to reduce complications of diabetes, each clinic was provided with educational materials from the National Eye Institute, including flipcharts, posters, YouTube videos, and brochures in both English and Spanish. Each clinic tailored these materials to their own needs and also developed other educational tools for use with their existing diabetes education resources.

Data collection. Along with patient demographics such as age, gender, and race/ethnicity, camera operators also entered data on standard diabetes outcomes (i.e., hemoglobin A1c (HbA1c) and duration of diabetes) and other related conditions (i.e., smoking, hypertension, coronary artery disease, history of stroke and/or myocardial infarction, kidney disease, and family history of glaucoma). Data on social determinants of health, such as residential ZIP code, education level, employment status, and insurance status were also collected. This information was gathered via patient history, patient questionnaire, and/or by abstraction from the patient's EMR at each clinic site. All data were securely transmitted to the retina specialist at the UNC-Chapel Hill Department of Ophthalmology via the RetinaVue Network. Prior to and after NCDRTN implementation, retinal screening rates were collected from each clinic based on the number of patients with diabetes that these clinics serve.

Data analysis. The eyes of 1787 patients were assessed for the presence of DR of various stages of severity (none, mild NPDR, moderate NPDR, severe NPDR, PDR) and for the presence or absence of DME. Of these, six patients below the age of 18 years were excluded. Demographic and clinical variables included several categorical and continuous variables. Race, gender, education level, insurance status, smoking, hypertension, coronary artery disease, stroke, previous myocardial infarction, family history of glaucoma, and kidney disease were categorical variables, whereas age, HbA1c, and duration of diabetes were continuous variables. Importantly, a three-category primary outcome variable for DR and referral at the individual level was determined from exam results for pairs of eyes taking into account that there were some ungradable images. Patients were considered to have no DR if the diagnosis in both eyes was no DR. If either eye had mild or moderate NPDR without DME, then the individual was placed in the DR without referral category; if either eye had severe NPDR, PDR, DME, or an ungradable image, the individual was placed in the DR with referral category.

The goal of the statistical analysis was to identify patient characteristics associated with DR and referral. A complete case analysis was used so that any patients with missing data were deleted from the analysis. Preliminary bivariate analyses were carried out by cross-tabulating categorical variables with the primary outcome and calculating means, standard deviations, and range for continuous variables with respect to the three groups defined by no DR, DR without referral, and DR with referral. Pearson chi-square tests for the categorical variables were computed to test the null hypothesis of no association with the primary outcome. ANOVA was used to assess whether means of the continuous variables varied across the three categories of the primary outcome. Considering the infrequent occurrence of DR, multivariable analysis treated insurance status as a dichotomous variable (insured vs. uninsured), education categories of “some college” and “college degree or more” were combined, and Hispanic and Other race were combined.

A multivariable cumulative logits model analysis was used to identify characteristics of patients associated with DR or referral. Two cumulative logits were defined from the three-category primary outcome. The first logit was the odds of DR (regardless of referral or not) relative to the odds of no DR. The second logit was the odds of referral relative to the odds of no referral (no DR or DR without referral). Initially, a “full” proportional odds model including all the covariates was fitted; this consisted of two logistic regressions where all covariates shared the same value of the regression coefficient across the two logits. An omnibus chi-square score test for the proportional odds assumption was computed. If it was not statistically significant at the 0.05 significance level, stepwise backwards elimination of covariates was conducted to determine a final proportional odds model with a criterion of $p < 0.05$ for a covariate to stay in the model. However, if the score test rejected the null hypothesis of proportional odds for all covariates ($p < 0.05$), the analysis proceeded to two further stages. First, a stepwise forward selection procedure was conducted to identify a best fitting partial proportional odds model whereby a subset of covariates was identified to have distinct values of their regression coefficients in the two logits. Each step in this stage involved conducting a Wald chi-square test for the proportional odds assumption of a single covariate; when $p < 0.05$, the model was expanded to allow separate regression coefficients for the covariate. Inclusion of covariates having unequal slopes proceeded until all remaining single-covariate proportional odds tests had $p > 0.05$. The final stage of model selection involved applying stepwise backwards elimination for the covariates for which the proportional odds was maintained. Finally, multivariable adjusted odds ratios and their 95% confidence intervals were computed for covariates in the final partial proportional odds model. PROC LOGISTIC in SAS 9.4 (Cary, NC) was used for fitting the cumulative logits models; details of these models are provided in the statistical appendix.

Results

A total of 1787 patients with diabetes from 5 AHEC primary care clinics were evaluated for DR within our ocular telehealth network from January 2014 to November 2015. Overall, 2006 retinal photographs were taken as some patients returned for follow-up during the study period. For the purposes of this study, only data from the first visit was used in the analysis.

Prior to program implementation, the 5 clinics were asked to report the total number of patients with diabetes they serve and the associated retinal screening rate for that population. The overall population of patients with diabetes across these 5 sites was reported as 5905 people, and the mean reported screening rate was 25.6%. After program implementation, to determine the effectiveness of the NCDRTN at reaching "active" patients with diabetes within the overall population, the 5 clinics were asked to provide the number of diabetics who had at least one point-of-care HbA1c measurement in the past twelve months. Based on this definition of "active", 4664 people were reported as active patients with diabetes, and the mean reported post-implementation screening rate was 40.4%.

Table 1 provides a detailed summary of patient characteristics for each clinic site. The mean age of patients was 55.4 years. The overall mean HbA1c was 7.8% and overall mean duration of diabetes was 9.2 years. Women made up a larger percentage of the study population when compared to men (62.7% vs. 37.3%). ECU and MCH-IM screened a larger proportion of African American patients (79.3% and 70.4%, respectively), whereas MAHEC screened a mostly Caucasian population (75.7%). Of note, MAHEC also had the lowest percentage of smokers. MCH-IM had higher proportions of coronary artery disease, stroke, kidney disease, and family history of glaucoma than the other sites. MCH-IM and MCH-FM also had a higher percentage of uninsured patients with lower education levels compared to the other sites.

The statistical analysis was based on 1661 patients with complete data, where 1323 (79.7%) had no DR, 183 (11.0%) had DR without referral, and 155 (9.3%) had DR with referral. Half of 155 patients requiring referral were due to an inadequate image, thus making our ungradable image rate 4.6%. Coronary artery disease, hypertension, stroke, kidney disease, age, HbA1c, and diabetes duration were associated with the primary outcome (no DR, DR without referral, and DR with referral) and these relationships were statistically significant (Table 2 and 3). In the initial multivariable proportional odds model, the omnibus chi-square score test rejected the proportional odds assumption ($Q_{S, 15} = 34.8$; $p = 0.004$). In the second stage forward selection procedure, covariate-specific Wald tests sequentially rejected assumptions of proportional odds for age ($Q_{W,1} = 20.1$; $p < 0.001$) and race ($Q_{W,2} = 8.36$; $p = 0.015$). The final partial proportional odds model contained age, race, HbA1c, diabetes duration, stroke, and kidney disease (Table 4). Interestingly, age and race were not associated with having DR, however, they were associated with the decision for referral. In particular, for every 10 year increase in age, patients had 1.28 times the odds of referral compared to younger patients. African Americans had 1.84 times the odds of referral compared to Caucasians, and patients of other races had 2.19 times the odds of referral compared to Caucasians. For every one unit increase of HbA1c, patients had 1.19 times the odds of having DR versus having no DR and receiving referral versus no referral. Also, for every additional 10 years of diabetes duration, patients had 1.76 times the odds of having DR versus no DR and receiving referral versus no referral. Patients with stroke had 1.65 times the odds of having DR versus no DR and receiving referral versus no referral. Those with kidney disease had 1.59 times the odds of having DR versus no DR and receiving referral versus no referral.

Table 5 shows that other diagnoses can also be incidentally diagnosed using retinal tele-screening. In our study, a total of 50 patients had another diagnosis besides DR, including age-related macular degeneration, drusen, glaucoma, or some other ophthalmic condition. Of those who were referred to an ophthalmologist for follow-up care, 60.4% completed the referral visit.

Discussion

Through the implementation of a retinal tele-screening program for DR evaluation in primary care clinics that spanned the state of North Carolina, we have demonstrated that point-of-care retinal screening coupled with remote expert interpretation reduced access barriers and improved DR screening rates in a diverse group of relatively underserved patients with Type I and II diabetes. As expected, our findings showed that higher HbA1c levels and longer diabetes duration were associated with advanced DR that required referral. Stroke and kidney disease were the comorbid conditions that were most significantly associated with DR and referral in our study population. In terms of social determinants of health, our findings are similar to those of recent studies that have demonstrated the effectiveness of telemedicine in reaching underserved populations in both remote and rural areas as well as urban settings across the United States. [19–21,32–35] Specifically, racial and ethnic minorities constituted 64.5% of our network population, women outnumbered men (62.7% vs. 37.3%), and 72.8% of all patients were publicly insured or uninsured. The statewide prevalence of diabetes in minorities in North Carolina is estimated at 41.6%, [36] which suggests that our telemedicine intervention increased access to retinal evaluations in these traditionally underserved groups. Although race itself was not associated with having DR, the decision for referral was associated with being a minority, meaning that not only were a large proportion of these patients accessing our services, but they were also receiving necessary referrals to further ophthalmic care when needed. It has been shown that racial and ethnic differences are associated with low diabetic eye examination rates despite insurance status, [17] which lends further reason to explore the potential of telemedicine in reducing access barriers for these populations.

DR is a critically important public health problem because visual impairment from this disease is detrimental to patients' personal independence, economic productivity and employment, and overall quality of life. Demographic trends also suggest a disproportionate increase in DR in minority and elderly populations. [2,3,37] As the prevalence of diabetes mellitus is projected to increase from 25 million Americans to a staggering 125 million Americans by the year 2050, [38] the number of patients with diabetes requiring annual retinal screening may far exceed the capacity of the eye care providers who currently see less than half of the diabetic patients needing evaluation for DR.

The implementation of ocular telemedicine programs provides an opportunity to build on the relationship of primary care physicians and their patients in several ways. First, telemedicine presents an opportunity to shift the paradigm of diabetic eye care to one in which primary care providers can play a more instrumental role in the prevention, screening, and monitoring of this eye disease. Second, not only does the ocular telemedicine approach increase detection and surveillance rates of individuals with DR, but it also helps identify those individuals who can be managed and monitored by their primary care providers using a retinal camera in the primary care clinic. In our cohort, 80% of patients with diabetes had no DR and needed only annual photographs for surveillance and 20% had some degree of DR. Telemedicine facilitated referrals to the ophthalmologist for only those patients at risk of vision loss and requiring treatment or those who had ungradable images.

Potential economic benefits at every level should not be overlooked. By requiring fewer subspecialist visits through more targeted referrals to ophthalmologists, both the patient and healthcare system incur fewer costs. Primary care clinics benefit economically, since clinics which meet performance measures such as NCQA and Healthcare Effectiveness Data and Information Set (HEDIS) for diabetic care are reimbursed at a higher rate by insurers. [39] Additionally, the technical component of obtaining retinal photographs – which is separately billable from the image interpretation fee in many states – can help to offset the administrative costs for the primary care physician. By identifying patients at risk of vision loss early in the course of disease, ocular telemedicine programs have the potential to decrease costs to the health care system and society by reducing the economic and social burden of low vision and blindness.

Major strengths of our study are that we included a relatively complete set of patient data from 5 different primary care clinics across a geographically diverse state and we also evaluated a number of clinical and socioeconomic determinants of health. Having a single reader assess all retinal images provided consistency in diagnosis. Also, the usefulness of telemedicine as a modality for long-term monitoring in preventive diabetic eye care is seen from our relatively low referral rate (9.3%) because we monitored those with moderate NPDR or lesser degrees of retinopathy within our network.

The findings of this study should be interpreted in the context of the following limitations. Regarding data collection, a wide variation in pre- and post-implementation screening rates highlights the challenge of incorporating retinal screenings in the primary care setting. For example, effective utilization of EMR systems was a challenge throughout the course of our study as each clinic was using a unique EMR system to capture, measure, and track data. Furthermore, a few sites implemented completely new EMR systems during the study period and each site underwent at least one EMR update. Data reporting on screening rates and the number of patients with diabetes served by each clinic varied due to constraints on the ability to query the different EMR systems among the clinics. It is therefore likely that the reported screening rates underreport the number of patients with diabetes that actually meet ADA guidelines for DR screening and treatment in the NCDRTN. Additionally, examining factors associated with DR does not necessarily identify predictors, and increasing DR screening rates does not necessarily improve rates of treatment. However, the identification of patients with retinopathy is a critical first step. Finally, some clinics already have high rates of DR screening and the implementation of a telemedicine network would not significantly influence their detection rates. However, patient satisfaction is likely to improve due to the convenience of point-of-care screening. [40]

There are several avenues for future work in the arena of retinal tele-screening. As demonstrated by multiple international studies, [41–44] future directions for research could include an assessment of patient and provider satisfaction with the convenience of tele-retinal screening programs in primary care settings in the U.S. Also, there has recently been growing interest in the development of low-cost and portable retinal imaging equipment which has spurred a great deal of innovation in the field of ophthalmic imaging. For example, the use of hand-held and smartphone-enabled cameras holds great promise for delivering on the goal of reaching patients in remote and underserved areas, and these intervention methods warrant formal study to establish the efficacy and effectiveness of such imaging techniques. [45]

DR screening via telemedicine in the primary-care setting represents an opportunity for primary care physicians to take a more active role in the prevention of a blinding disease, to better educate patients with diabetes about the importance of retinal examinations, to facilitate appropriate referrals from the primary care provider to the ophthalmologist, and to reinforce and streamline follow-up care with ophthalmologists. Telemedicine screening for DR is a public health imperative with the potential to increase surveillance rates, reduce socioeconomic disparities, increase access to care, and ultimately prevent vision-threatening DR and improve visual outcomes and quality of life for patients with diabetes.

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Table 1. Patient Characteristics (No. (%)) by NCDRTN Site (N = 1661)

Characteristic	ECU (N = 435)	MAHEC (N = 313)	MCH-FM (N = 327)	MCH-IM (N = 270)	SRAHEC (N = 316)	Total (N = 1661)
Age, mean (SD), y	54.1 (12.2)	58.7 (13.1)	54.4 (12.1)	55.9 (11.0)	54.1 (14.2)	55.4 (12.7)
Gender						
Female	277 (63.7)	187 (59.7)	214 (65.4)	170 (63.0)	193 (61.1)	1041 (62.7)
Male	158 (36.3)	126 (40.3)	113 (34.6)	100 (37.0)	123 (38.9)	620 (37.3)
Race / Ethnicity						
African American	345 (79.3)	53 (16.9)	192 (58.7)	190 (70.4)	141 (44.6)	921 (55.4)
Caucasian	77 (17.7)	237 (75.7)	85 (26.0)	52 (19.3)	138 (43.7)	589 (35.4)
Hispanic	8 (1.8)	18 (5.8)	34 (10.4)	16 (5.9)	20 (6.3)	96 (5.8)
Other	5 (1.2)	5 (1.6)	16 (4.9)	12 (4.4)	17 (5.4)	55 (3.3)
Diabetes Duration, mean (SD), y	9.3 (8.5)	8.3 (7.9)	8.2 (7.2)	10.3 (8.3)	9.7 (8.8)	9.2 (8.2)
HbA1c, mean (SD), %	7.9 (2.5)	7.2 (1.9)	7.9 (2.5)	8.0 (2.5)	7.9 (2.4)	7.8 (2.4)
Smoking						
Yes	119 (27.4)	46 (14.7)	126 (38.5)	76 (28.2)	67 (21.2)	434 (26.1)
No	316 (72.6)	267 (85.3)	201 (61.5)	194 (71.9)	249 (78.8)	1227 (73.9)
Insurance						
Medicare	176 (40.5)	157 (50.2)	87 (26.6)	97 (35.9)	118 (37.3)	635 (38.2)
Medicaid	115 (26.4)	41 (13.1)	44 (13.5)	34 (12.6)	59 (18.7)	293 (17.6)
Private	120 (27.6)	103 (32.9)	47 (14.4)	45 (16.7)	136 (43.0)	451 (27.1)
Uninsured	24 (5.5)	12 (3.8)	149 (45.6)	94 (34.8)	3 (1.0)	282 (17.0)
Education						
Less than High School	87 (20.0)	43 (13.7)	115 (35.2)	97 (35.9)	60 (19.0)	402 (24.2)
High School degree	222 (51.0)	217 (69.3)	119 (36.4)	107 (39.6)	130 (41.1)	795 (47.9)
Some College	85 (19.5)	27 (8.6)	66 (20.2)	55 (20.4)	79 (25.0)	312 (18.8)
College degree or more	41 (9.4)	26 (8.3)	27 (8.3)	11 (4.1)	47 (14.9)	152 (9.2)
Coronary artery disease						

Yes	59 (13.6)	30 (9.6)	28 (8.6)	69 (25.6)	44 (13.9)	230 (13.8)
No	376 (86.4)	283 (90.4)	299 (91.4)	201 (74.4)	272 (86.1)	1431 (86.1)
Hypertension						
Yes	357 (82.1)	198 (63.3)	229 (70.0)	224 (83.0)	236 (74.7)	1244 (74.9)
No	78 (17.9)	115 (36.7)	98 (30.0)	46 (17.0)	80 (25.3)	417 (25.1)
Stroke						
Yes	42 (9.7)	15 (4.8)	15 (4.6)	36 (13.3)	30 (9.5)	138 (8.3)
No	393 (90.3)	298 (95.2)	312 (95.4)	234 (86.7)	286 (90.5)	1523 (91.7)
Previous MI						
Yes	44 (10.1)	27 (8.6)	19 (5.8)	34 (12.6)	35 (11.1)	159 (9.6)
No	391 (89.9)	286 (91.4)	308 (94.2)	236 (87.4)	281 (88.9)	1502 (90.4)
Kidney Disease						
Yes	53 (12.2)	31 (9.9)	14 (4.3)	47 (17.4)	23 (7.3)	168 (10.1)
No	382 (87.8)	282 (90.1)	313 (95.7)	223 (82.6)	293 (92.7)	1493 (89.9)
Family Hx of Glaucoma						
Yes	15 (3.5)	4 (1.3)	7 (2.1)	23 (8.5)	12 (3.8)	61 (3.7)
No	420 (96.6)	309 (98.7)	320 (97.9)	247 (91.5)	304 (96.2)	1600 (96.3)

Table 2. Characteristics of Individuals: Frequencies (%) of Categorical Variables (N = 1661)

Characteristic	No DR (N = 1323, 79.7%)	DR without Referral (N = 183, 11.0%)	DR with Referral (N = 155, 9.3%)	p value*
Gender				0.96
Female	831 (79.8)	113 (10.9)	97 (9.3)	
Male	492 (79.4)	70 (11.3)	58 (9.4)	
Race / Ethnicity				0.070
African American	713 (77.4)	107 (11.6)	101 (11.0)	
Caucasian	486 (82.5)	64 (10.9)	39 (6.6)	
Hispanic	76 (79.2)	9 (9.4)	11 (11.5)	
Other	48 (87.3)	3 (5.5)	4 (7.3)	
Smoking				0.34
Yes	338 (77.9)	56 (12.9)	40 (9.2)	
No	985 (80.3)	127 (10.4)	115 (9.4)	
Insurance				0.19
Medicare	512 (80.6)	59 (9.3)	64 (10.1)	
Medicaid	229 (78.2)	39 (13.3)	25 (8.5)	
Private	368 (81.6)	44 (9.8)	39 (8.7)	
Uninsured	214 (75.9)	41 (14.5)	27 (9.6)	
Education				0.14
Less than High School	309 (76.9)	53 (13.2)	40 (10.0)	
High School degree	637 (80.1)	76 (9.6)	82 (10.3)	
Some College	253 (81.1)	40 (12.8)	19 (6.1)	
College degree or more	124 (81.6)	14 (9.2)	14 (9.2)	
Coronary artery disease				0.009
Yes	166 (72.2)	33 (14.4)	31 (13.5)	
No	1157 (80.9)	150 (10.5)	124 (8.7)	
Hypertension				0.041
Yes	981 (78.9)	134 (10.8)	129 (10.4)	
No	342 (82.0)	49 (11.8)	26 (6.2)	

Stroke				0.008
Yes	97 (70.3)	19 (13.8)	22 (15.9)	
No	1226 (80.5)	164 (10.8)	133 (8.7)	
Previous MI				0.11
Yes	117 (73.6)	21 (13.2)	21 (13.2)	
No	1206 (80.3)	162 (10.8)	134 (8.9)	
Kidney Disease				0.005
Yes	118 (70.2)	25 (14.9)	25 (14.9)	
No	1205 (80.7)	158 (10.6)	130 (8.7)	
Family Hx of Glaucoma				0.053
Yes	45 (73.8)	5 (8.2)	11 (18.0)	
No	1278 (79.9)	178 (11.1)	144 (9.0)	

*Pearson chi-squared test; **816 patients had missing employment

Table 3. Characteristics of Continuous Variables by Main Categories (N = 1661)

Variable	**No DR (N = 1323)**		**DR without Referral (N = 183)**		**DR with Referral (N = 155)**		**ANOVA**
	Mean (s.d.)	**Min-Max**	**Mean (s.d.)**	**Min-Max**	**Mean (s.d.)**	**Min-Max**	**p-value**
Age	55.3 (12.7)	18.7-93.9	53.3 (12.1)	21.2-85.2	58.0 (12.6)	27.4 – 87.2	.003
HbA1c	7.5 (2.3)	4.0 – 17.0	8.7 (2.5)	4.0-14.0	8.6 (2.6)	5.0 – 16.0	<.001
Diabetes Duration	8.2 (7.7)	0-54.0	12.8 (9.0)	0–51.0	13.2 (9.2)	0-43.0	<.001

Table 4. Odds Ratios (95% Confidence Intervals) from Partial Proportional Odds Model

Variable	Odds ratio of DR versus no DR	Odds ratio of referral versus no referral
Age (10 year units)	0.99 (0.90, 1.10)	1.28 (1.11, 1.48)
African American (vs. Caucasian)	1.21 (0.92, 1.59)	1.84 (1.24, 2.73)
Other (vs. Caucasian)	1.22 (0.75, 1.98)	2.19 (1.16, 4.11)
HbA1c*	1.19 (1.13,1.25)	1.19 (1.13,1.25)
Diabetes Duration* (10 year units)	1.76 (1.53, 2.02)	1.76 (1.53, 2.02)
Stroke*	1.65 (1.10, 2.48)	1.65 (1.10, 2.48)
Kidney Disease*	1.59 (1.10, 2.31)	1.59 (1.10, 2.31)

*Common odds ratio estimate and 95% CI under the proportional odds assumption

Table 5. Frequencies of Other Diagnoses (N = 50)

Diagnosis	One eye only	Both eyes	Total Patients
AMD Grade 1; Dry	0	4	4
AMD Grade 2; Drusen; Degenerative	0	6	6
AMD Grade 3; Degeneration; Retinal; Secondary Pigmentary	1	3	4
AMD Grade 4; Chorioretinal scar; Posterior Pole	0	1	1
Drusen; Hereditary (extramacular drusen)	3	4	7
Glaucoma: Optic nerve cupping	4	11	15
Other diagnosis	8	4	12
Total	17	33	50

GIS-Mapping of Diabetic Retinopathy in North Carolina

Abstract

Importance: Minimal information exists on the use of geographic information systems (GIS) mapping for visualizing access barriers to eye care for patients with diabetes.

Objective: To use GIS-mapping techniques to visualize the locations and travel times of patients participating in the North Carolina Diabetic Retinopathy Telemedicine Network (NCDRTN) relative to 5 primary care clinics and to ophthalmologists and primary care providers across the state.

Design: Cross-sectional study conducted from January 2014 to November 2015.

Setting: 5 Area Health Education Center (AHEC) primary care clinics which serve rural and underserved populations in North Carolina.

Participants: 1787 patients with diabetes received retinal screening photographs with remote expert interpretation to determine the presence and severity of diabetic retinopathy (DR). Participants included patients aged 18 years or older with Type I or Type II diabetes mellitus who presented to these 5 clinics for their routine diabetes care.

Main Outcomes and Measures: Development of qualitative maps illustrating the density of patients with diabetes and their distribution around the 5 NCDRTN sites by ZIP code and the density of ophthalmologists and primary care providers by ZIP code relative to United States (U.S.) Census Urban Areas. A travel time map was also created using road network analysis to determine all areas that can be reached by car in a user-specified amount of time.

Results: Whereas the clinics located in Greensboro, Asheville, and Fayetteville screened patients from more immediate surrounding areas, the Greenville site had the widest distribution of ZIP codes, suggesting that patients travel from greater distances to reach this facility. Primary

care providers were spread somewhat uniformly across the state, whereas ophthalmologists were concentrated around urban centers. Also, the number and type of surface roads surrounding the clinics determined the distance and time patients must travel to receive care.

Conclusions and Relevance: GIS-mapping is a useful technique for visualizing geographic access barriers to eye care for patients with diabetes and may help to identify underserved areas that would benefit from the expansion of retinal screening programs via telemedicine.

Introduction

Diabetic retinopathy (DR) – a condition in which high blood glucose levels damage the blood vessels of the retina – is the most common microvascular complication of diabetes [1] and is the leading cause of new cases of blindness among working-age Americans. [2] Recent estimates reveal 4.2 million or 28.5% of people with diabetes over age 40 have DR and 655,000 of these individuals have vision-threatening retinal disease. [2] By the year 2050, the prevalence of DR in Type I and Type II diabetic patients aged 40 and older is projected to increase to 16.0 million (from 5.5 million in 2005) and the prevalence of vision-threatening DR is projected to increase to 3.4 million (from 1.2 million in 2005). [3]

North Carolina has been identified as one of the nation's top ten "diabetes hot spots," where the burden of diabetes will be greatest in the next 10 years. By 2025, the number of people with diabetes in North Carolina is projected to increase to almost 1.9 million at a cost to the state of $17.9 billion. [4] In 2012, the prevalence of diabetes among North Carolinians was 10.4%, [5] which was higher than the national average of 9.3%. [6] Of these patients with diabetes, about 20% are already diagnosed with DR, and the other 80% are at risk for developing DR. [7]

Given that patients with early stages of DR are often asymptomatic at the time that vision-saving laser treatment should be given, early detection and timely referral to an ophthalmologist are imperative to preventing vision loss. However, in our current eye care paradigm, less than 50% [8–11] of patients with diabetes meet the current screening guidelines [12–14] that recommend annual retinal exams by an ophthalmologist. Health care access barriers resulting from socioeconomic, geographic, transportation, education, language, and cultural challenges compromise the quality and effectiveness of DR treatment, thus placing patients with diabetes at unnecessary risk for this blinding disease.

The North Carolina Diabetic Retinopathy Telemedicine Network (NCDRTN) is an innovative screening program that was developed to address the growing burden of DR in the state. This program aims to reduce eye care access barriers and improve DR evaluation by using the emerging strategy of telemedicine to bring retinal exams to the point-of-care of the primary physician. The screening network allows primary physicians to remotely capture, send, and receive retinal images between the University of North Carolina (UNC) Chapel Hill Department of Ophthalmology and 5 Area Health Education Center (AHEC) affiliated primary care clinics across North Carolina: Mountain AHEC (MAHEC) in Asheville, Moses Cone Hospital Internal Medicine (MCH-IM) and Family Medicine (MCH-FM) clinics in Greensboro, East Carolina University (ECU) Department of Family Medicine in Greenville, and Southern Regional AHEC (SRAHEC) in Fayetteville. From January 2014 to November 2015, our program has provided 2006 eye screenings to a total of 1787 patients with diabetes across North Carolina. The results of the larger NCDRTN program evaluation are reported separately.

Recent studies have demonstrated the effectiveness of telemedicine in reaching underserved populations in both remote and rural areas as well as urban settings across the United States. [15–21] Although geographic and transportation challenges have been cited as reasons for which patients with diabetes face access barriers to eye care, visual data analyses of such barriers is scant. The purpose of the present study is to use geographic information systems (GIS) mapping techniques to visualize the location of patients participating in the NCDRTN relative to our program sites and to ophthalmologists and primary care providers across the state. Understanding and visualizing patient and physician location data may allow for better identification of areas of need, where access barriers may be preventing patients with diabetes from receiving proper eye care. Such mapping may also help to inform the future expansion of the retinal tele-screening program to other underserved parts of North Carolina.

Methods

Data collection. Patient ZIP code data were collected along with medical and socioeconomic data at the time of retinal imaging in the primary care provider's office. This information was collected via patient history, patient questionnaire, and/or by abstraction from patients' medical records. A total of 1787 patients with either Type I or Type II diabetes mellitus were included in the dataset, with 361 (20.2%) having any level of DR and 1426 (79.8%) having no DR in either eye. For the purposes of this study, only patients with DR were mapped since they may require further ophthalmologic care or more frequent follow-up within the NCDRTN.

Medical practice ZIP code data for licensed, active ophthalmologists and primary care providers were obtained directly from the North Carolina Medical Board (Raleigh, NC). Of a total of 36,189 active physicians registered with the North Carolina Medical Board, 571 ophthalmologists and 7182 primary care providers were included in this study as of December 2015. For purposes of this analysis, primary care providers were defined as physicians with an active North Carolina medical license who self-classified as practicing in the following primary areas: Internal medicine, family medicine, endocrinology, geriatric medicine, adolescent medicine, pediatrics, pediatric endocrinology, general practice, general preventive medicine, and public health & general. Similarly, ophthalmologists were defined as physicians with an active North Carolina medical license who self-classified their primary area of practice within ophthalmology.

Data aggregation. All maps were generated in ArcGIS software (ArcGIS 10.2.1; Esri). To protect the privacy of patients, precise locations were obscured and discrete points for patients and physicians (i.e., ophthalmologists and primary care providers) were aggregated to a coarser unit of geography via the use of associated ZIP code data. This methodology also allowed for easier interpretation of the maps, especially in the case of visualizing physician locations.

Patients and physicians were separately aggregated to their corresponding ZIP codes to derive a count of the number of patients and physicians per ZIP code, respectively. To facilitate a wider variety of visualization options, both patients and physicians were aggregated to centroids of ZIP codes.

To aggregate patients and physicians to ZIP codes, tabular patient and physician datasets were summarized to derive a count of the number of occurrences of each 5-digit ZIP code where a patient lives or a physician works. Frequencies of the 5-digit ZIP codes for each table were calculated using Pivot Tables in Excel. Patients who had some level of DR diagnosed in either eye were used to calculate ZIP code frequency since these patients would require the most stringent follow-up or referral to an ophthalmologist. The inverse of this selection was also made (i.e. patients with no DR diagnosis), and ZIP code frequency was calculated. For physicians, ZIP code frequencies were calculated after selection of the relevant specialties listed above.

Creation of density maps. Frequency tables were then joined to ZIP code Shapefiles, a common format for spatial data within GIS, to allow for displaying the density of patients or physicians at the ZIP code level. To join the data, tabular joins were done in ArcMap: The patient ZIP code frequency tables were joined to a Shapefile of ZIP code polygons and a

Shapefile of ZIP code points, using the ZIP code field as a common ID. This same process was carried out for primary care providers and ophthalmologists.

Once joined, new files for the joins listed above were created, resulting in ZIP code point and polygon files that show the number of patients and the number of physicians within each ZIP code. These count data were then used to display the ZIP codes in three different density maps:

1. A graduated color (choropleth) map showing the number of patients per ZIP code, where light colors indicate low values and dark colors indicate high values.
2. Two dot density maps showing a stylized distribution of physicians within each ZIP code polygon. In these maps, points were randomly scattered within the boundaries of each ZIP code polygon, with each point corresponding to a user-defined number of individuals. Given the large number of primary care providers in the dataset, a 1-to-3 dot density was selected (compared to a 1-to-1 density for ophthalmologists) in order to render the maps more readable.

Creation of travel time map. The travel time map was created in ArcMap using tools in the Network Analysis toolbox. "Service areas" – or polygons representing all of the areas that can be reached by car in a user-specified amount of time by traversing the real-world road network – were created around each of the 5 NCDRTN primary care clinics. Three different service areas were created: 20 minutes, 40 minutes, and 60 minutes.

Results

The 5 primary care clinics included in the NCDRTN were chosen to participate in our telemedicine study because of the primarily rural and underserved patient populations they serve.

Figure 1 illustrates the density of patients with diabetes and their distribution around the 5 NCDRTN sites by ZIP code. The Greenville clinic site had the widest distribution of darkly-shaded ZIP codes, suggesting that more patients are traveling from outlying areas in the eastern part of the state to seek medical care at this facility. The Greensboro, Asheville, and Fayetteville sites had a more concentrated distribution of ZIP codes, with most patients deriving from areas closer to the clinic sites and a comparatively smaller number of patients traveling from further away.

Figures 2 and 3 demonstrate the density of licensed primary care providers and ophthalmologists throughout the state, respectively. The density of these physicians has been plotted by ZIP code relative to U.S. Census Urban Areas that contain ≥ 50,000 people. Given that each black dot in Figure 2 represents 3 primary care providers, this map demonstrates that these primary care doctors make up a fifth of all physicians in the state (7182 primary care providers of 36,189 total physicians). These doctors also have a denser coverage of both rural and urban parts of the state when compared to ophthalmologists, who are mostly concentrated in the urban centers.

The travel time map allows for visualization of potential access barriers that patients may face as a result of the number and type of surface roads available in their geographic area. As shown in Figure 4, the 20 minute service area represents all areas that can be reached within 20 minutes of travel time. The 40 minute service area represents all areas that can be reached within 40 minutes of travel time; this area is displayed as a ring around the 20 minute area, thus representing the areas that can be reached in 20-40 minutes of driving. Likewise, the 60 minute service area represents all areas that can be reached within 60 minutes of travel time; this area is displayed as a ring around the 40 minute area, thus representing the areas that can be reached in 40-60 minutes of driving.

The city of Greensboro has an extensive network of interstate roads passing through or around the city, which better connects patients with the more developed and resource-rich metropolitan areas of the North Carolina Piedmont region. The metropolitan areas of the Triad (Greensboro, Winston-Salem, and High Point) and the Triangle (Chapel Hill, Durham, and Raleigh) contain a number of well-known health care facilities and hospital centers that offer patients in the Greensboro area with ample opportunities for seeking quality care. In contrast, Greenville and Fayetteville are smaller cities with larger surrounding rural areas. They contain a sparser network of small roads with lower travel speeds, which limit patient access to the few health care facilities in these two regions. Those living in the greater Asheville area face an additional and unique access barrier since they must contend with mountainous terrain in order to travel to the urban portions of Asheville. Since patients here must use small mountain roads with low travel speeds to access health care facilities within the city of Asheville, their perceived distance to health clinics may be inflated when compared to those patients who can easily access interstate roads for quicker travel. As such, this travel time barrier may influence the frequency and likelihood with which patients living in rural mountain areas seek health care. Figure 4 thus illustrates how travel time along road networks may influence uptake of health care services. This map shows that the spread of travel activity is influenced by how easily people can travel along interstate corridors, which effectively extend the distance that a person is able to travel in a given amount of time. For example, although patients living in mountainous regions of western North Carolina may be close to the MAHEC NCDRTN site based on mileage, their effective travel time is considerably lengthened by the circuitous nature of mountain roads in this area.

However, patients traveling along I-40 through the Asheville city center would be able to travel much further in the same amount of time.

Discussion

In the first study of its kind, we have demonstrated that GIS-mapping is a useful technique for visualizing geographic access barriers to eye care for patients with diabetes. By mapping the statewide distribution of providers serving the primary care needs of diabetic patients alongside ophthalmologists in North Carolina relative to the ZIP codes from which patients travel to reach our 5 NCDRTN sites, we have shown that patient accessibility to these doctors is influenced by the geography and road networks that connect them. This knowledge will help inform the future expansion of the NCDRTN program as we are able to identify opportunities for strategic collaborations between primary care providers and ophthalmologists across the state.

To date, there has been minimal published literature on the use of GIS-mapping for evaluating geographic access barriers such as distance and travel-time to health care facilities in the United States. A few studies have used spatial analysis to determine how distance to hospitals and specialist care affects timely health care delivery, [22–26] and at least two studies have used spatial analysis to identify areas of high diabetes prevalence so that public health programs can be targeted to places where patient uptake of preventive care services is more likely. [27,28] All of these studies demonstrate that GIS-mapping is a useful tool for studying how geographic access barriers influence health service delivery and resource allocation.

As the prevalence of diabetes is projected to increase from 25 million Americans to a staggering 125 million Americans by the year 2050, [29] the number of patients with diabetes requiring annual retinal screening will far exceed the capacity of the eye care providers who currently see less than half of the diabetic patients needing evaluation for DR. Coupled with an aging population, various access barriers to care, and growing shortages in primary care physicians nationwide, [30] the current paradigm for diabetic eye care will not be able to meet patients' needs without employing innovative strategies for health care delivery. Our study shows that telemedicine holds great potential for reducing travel-times and geographic barriers to care by allowing physicians to connect over large distances with patients in some of the most rural and underserved areas. However, large-scale and cost-effective implementation of sustainable telemedicine systems will require the strategic allocation of health care resources. GIS-mapping is a helpful tool for informing the scale-up of such systems as areas can easily be identified where investments in telemedicine programs would be most worthwhile. By using publicly available census data, other demographic variables, and socioeconomic determinants of health in conjunction with patient medical records, this type of data visualization can help inform strategic planning for the expansion of broader public health care services. Predictive modeling can also help to identify catchment areas where disease burden is likely to worsen over time and where the need for expanded health care services will be greatest.

A major strength of our study is that it includes patient data from an innovative eye screening program that spans 5 different primary care clinics across a geographically diverse state. These clinics provide health care to patients in both rural and urban areas across the mountains, piedmont, and coastal regions of North Carolina. Given the variety of geographic areas included in this study, the number and quality of road networks in these areas also play an important role in the access barriers that patients face to receiving quality health care.

Although our study included a total of 1787 patients with diabetes, only 361 (20.2%) had any level of DR. Given the small sample size of patients with disease, we were not able to visualize whether those facing more geographic barriers to health care also experience higher rates of DR. Additionally, we used coarse, 5-digit ZIP code level data to map to ZIP code centroids in order to protect patient privacy. However, more detailed 9-digit ZIP code level data and individual address information may have provided a more accurate visualization of the exact distance that patients are travelling to reach our primary care clinic sites.

Future research should involve larger sample sizes of patients with diabetes to study the strength of the correlation between the quality of road networks, geography, and access barriers to health care as well as to study how standard clinical diabetes metrics and other socioeconomic determinants of health correlate with effective health care delivery.

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Figure 1. Diabetic Patients in NCDRTN per ZIP Code

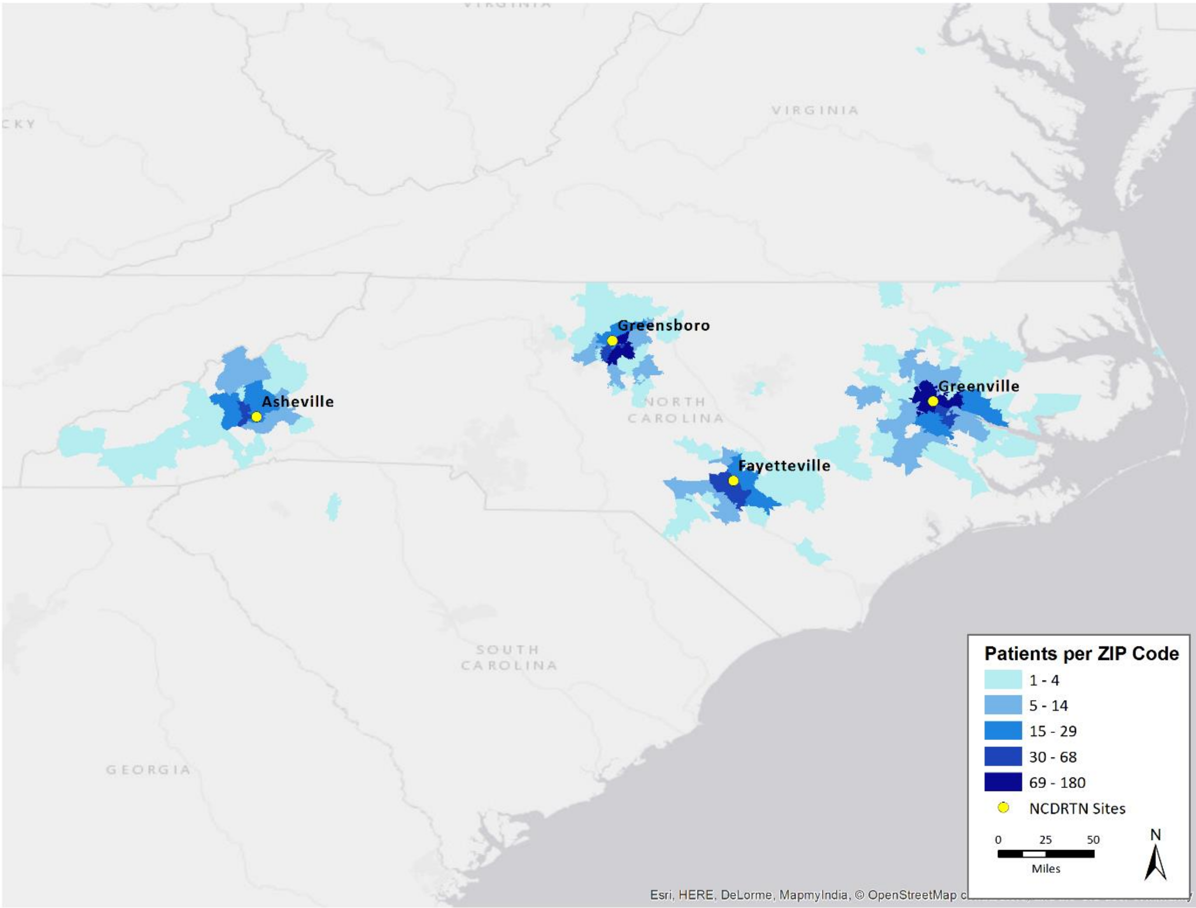


Figure 2. Density of Primary Care Providers in North Carolina

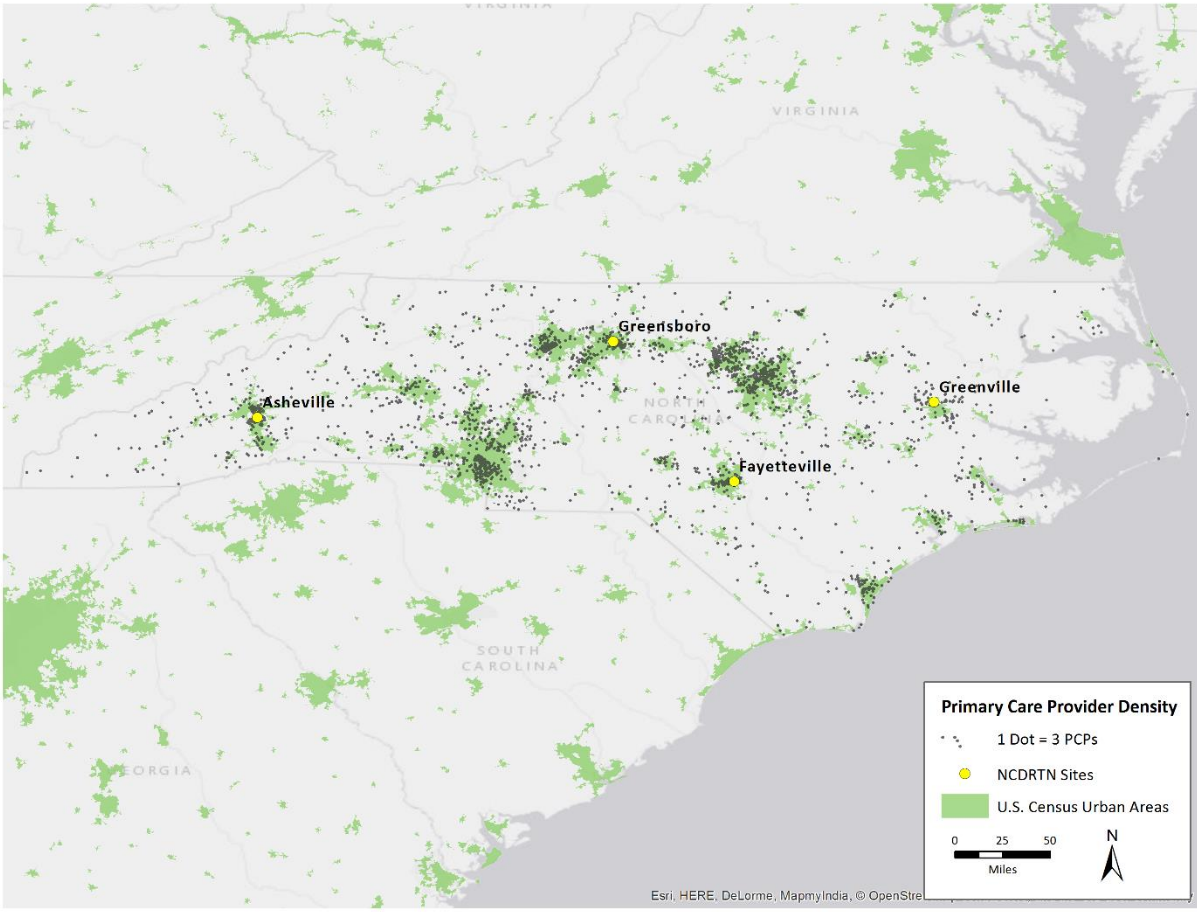


Figure 3. Density of Ophthalmologists in North Carolina

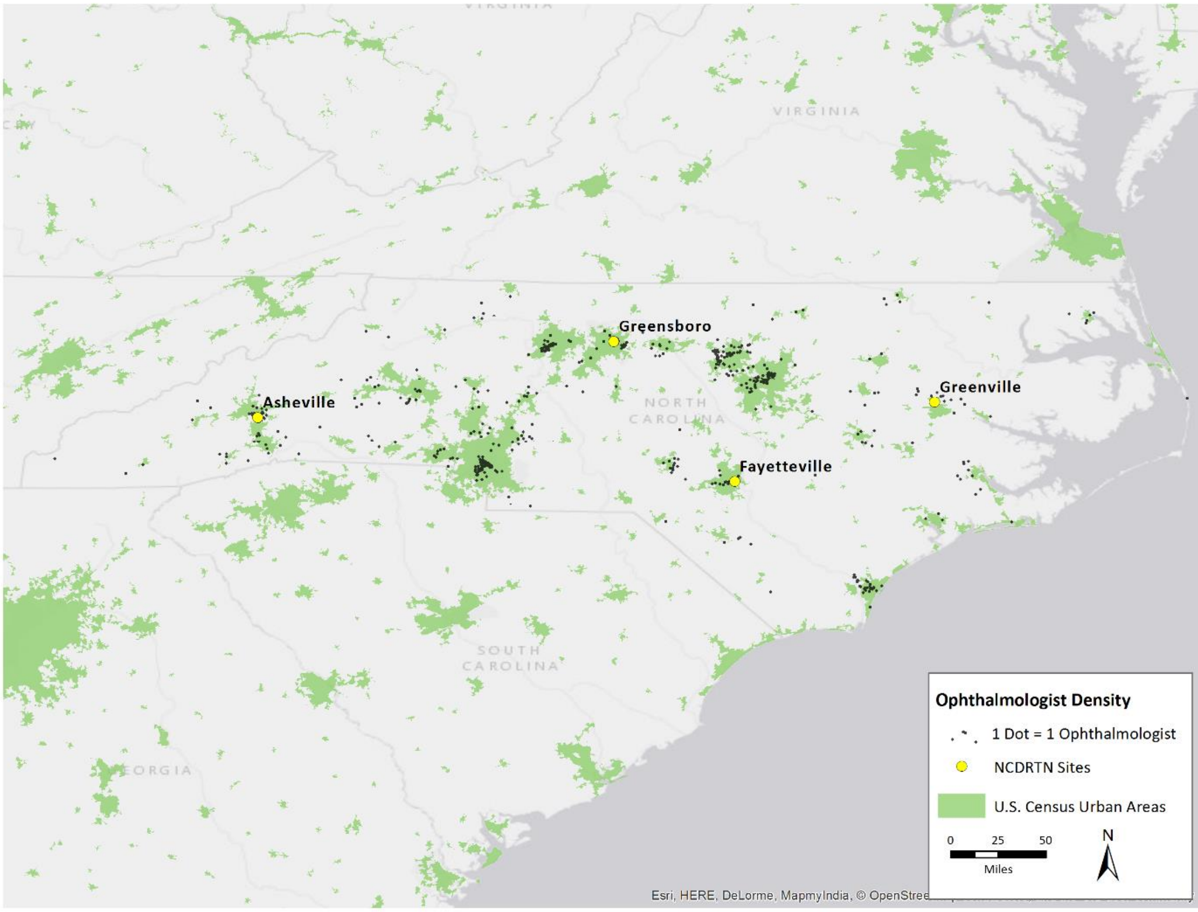
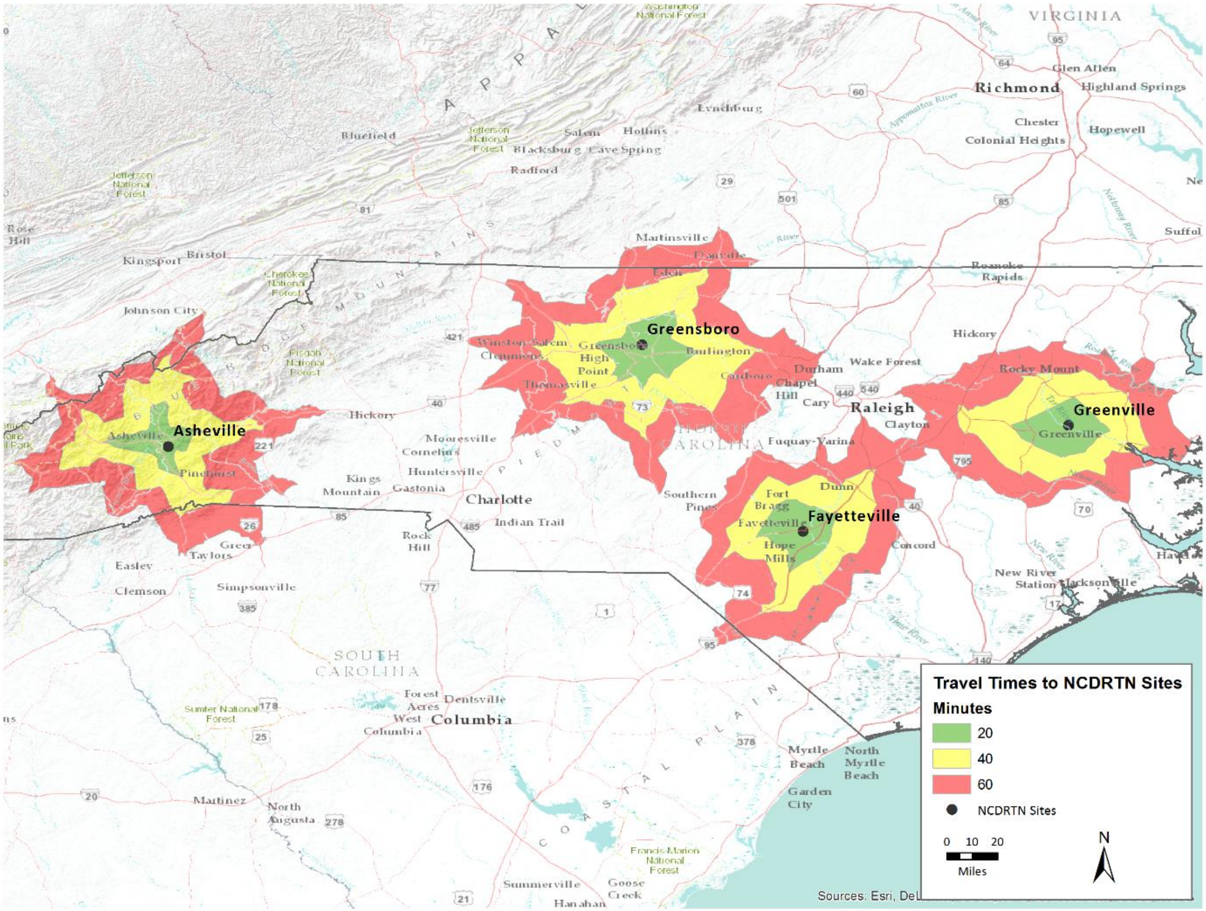


Figure 4. Driving Time to NCDRTN Sites



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APPENDIX A: Systematic Literature Review

Abstract

Purpose: This review is a synthesis of published articles examining the effectiveness of telemedicine in reducing access barriers to diabetic retinopathy (DR) screening in primary care settings.

Methods: A systematic review of relevant qualitative and quantitative studies was conducted. PubMed, Web of Science, and EMBASE databases were searched using relevant keywords and MeSH terms for English language articles published from January 2006 – January 2016. Articles were selected and analyzed based on the following criteria: Study design, technology and imaging techniques utilized, setting (location, population), diabetic patient demographics and proportion screened, DR classification, and proportion of patients requiring referral to an eye care provider. International studies and technical papers were excluded. Data were abstracted by a single author (PDJ).

Results: Six studies met the search criteria. Only one study was a randomized controlled trial demonstrating that telemedicine is highly effective for DR screening when compared to traditional surveillance. All six studies showed that telemedicine increases retinal screening rates in the primary care setting. Three studies demonstrated the telemedicine intervention within community-based health centers and outpatient clinics, and all six studies included underserved populations and ethnic minorities. No studies evaluated the effect of screening on treatment.

Conclusion: When utilized in the primary care setting, telemedicine is an effective intervention for increasing DR screening rates in patients with diabetes who otherwise face

access barriers to proper and timely eye care. However, more rigorous research is needed before large-scale dissemination and implementation of this screening strategy can take place.

Introduction

Diabetic retinopathy (DR) – a condition in which the retinal microvasculature is damaged through ischemia, neovascularization, hemorrhage, and edema – is the most common microvascular complication of diabetes [1] and is the leading cause of new cases of blindness among adults aged 20–74 years in the United States (U.S.). [2] Recent estimates reveal 4.2 million or 28.5% of people with diabetes over age 40 have DR and 655,000 of those with DR have advanced retinal disease that could lead to vision loss. [2] From 1997 to 2011, diabetic adults aged 18 years or older who reported difficulty seeing despite glasses or contact lenses grew from 2.7 million to 4.0 million. [3] By the year 2050, the prevalence of DR in Type I and Type II diabetic patients aged 40 and older is projected to increase to 16.0 million (from 5.5 million in 2005) and the prevalence of vision-threatening DR is projected to increase to 3.4 million (from 1.2 million in 2005).[4]

DR is often asymptomatic at the time treatment is required. Early screening and detection of retinal disease is therefore crucial to prevent the loss of vision. Current screening guidelines by the American Diabetes Association (ADA) recommend an initial dilated eye exam by an ophthalmologist within 3-5 years of diabetes onset in adults and children older than 10 years of age. [5] Additionally, an initial dilated exam by an ophthalmologist is imperative at the time Type II diabetes is diagnosed, since this disease can manifest before patients become aware of symptoms, and because almost 20% of people with Type II diabetes already have DR at the time of diagnosis. Subsequent exams should occur yearly or more frequently in progressive DR. [6,7]

Medical and surgical therapies have been shown to dramatically reduce the progression of DR. Timely treatment with panretinal and focal laser photocoagulation surgery has been shown in the ETDRS, DRS, and DRVS trials to reduce the risk of severe vision loss by over 90%. [8–14] More recently, anti-VEGF therapy has also been shown to preserve visual acuity to a similar degree as laser therapy for proliferative DR. [15] However, despite recommendations, public awareness campaigns, and national and international DR screening guidelines established by leading eye care organizations and public health agencies, screening rates in the U.S. remain low. Even with the inclusion of DR as a primary Healthcare Effectiveness Data and Information Set (HEDIS) compliance metric for the management of diabetic patients, on average, less than 50% of patients with diabetes meet current screening recommendations. [16–19]

Barriers to receiving eye care harm efforts to raise DR screening rates to recommended levels and also compromise the quality and effectiveness of DR management and treatment. As a consequence, patients with visual impairment from DR experience a loss of personal independence, loss of economic productivity and employment, and diminished quality of life. [2,20] Socioeconomic and geographic barriers to care, delayed referrals from primary care providers, and lack of patient awareness regarding the importance of annual retinal exams have been cited as reasons for low screening rates. Amid minorities, language and cultural barriers may also contribute to disparities in screening and treatment and low adherence to screening has been attributed to poor patient education. [17,19,21,22]

An emerging strategy for increasing compliance with DR screening recommendations, improving early detection of DR, and circumventing access barriers to eye care is the use of telemedicine for digital retinal imaging with remote expert interpretation. Introducing retinal cameras at the level of the primary care provider could substantially reduce the access barriers that patients must otherwise overcome to obtain specialist eye care.

The main objective of this systematic review is to compile and analyze existing evidence on DR screening programs utilizing telemedicine in primary care settings. The literature search was guided by the following focused PICO (population, intervention, comparator, outcome) question: For diabetics who receive health care at a primary care center, how effective is DR screening utilizing digital retinal photography with remote interpretation at decreasing access barriers to eye care when compared to referral for a clinical exam by an eye care provider? For this review, effectiveness of the intervention is defined by the ability of ocular telemedicine to increase DR screening rates in a study population of diabetics who face access barriers to eye care. Referrals to eye care providers are also included.

Methods

To answer the PICO question, a PubMed search was performed on January 21, 2016 using the following Medical Subject Headings (MeSH) phrases: Diabetic retinopathy AND telemedicine AND (delivery of health care OR underserved OR minority groups OR minority OR minorities OR health services accessibility OR access OR medically underserved areas) AND (program evaluation OR evaluation OR effectiveness OR implementation).

Limits were placed to include only English language articles published in the last 10 years (January 2016 – January 2006). No search limits were used for study design. Articles were excluded if the title or abstract emphasized other interventions such as optical coherence tomography, or if they were technical papers on imaging and automated software analysis, predictive modeling, or cost-effectiveness. International studies and technology assessments seeking to validate the accuracy of a specific telemedicine software were excluded. Web of Science and EMBASE were also searched using the same strategy, and abstracts were reviewed to determine relevance. Hand searches of citations in the included articles were performed to identify other relevant studies. After reading the full text of the included articles, data were abstracted by a single author (PDJ) and the following information was summarized in Table 1: Study design, technology and imaging techniques utilized, setting (location, population), patient demographics and proportion screened, DR classification and proportion of patients requiring referral to an eye care provider, and other comments. The studies are arranged from highest to lowest by order of relevance.

Results

The PubMed search strategy returned 65 articles, Web of Science returned 18 articles, and EMBASE returned 52 articles. Six articles were identified as meeting search criteria. Only one study was a randomized controlled trial that explored the comparative effectiveness of telemedicine versus traditional surveillance for DR screening. Three studies took place in the setting of community-based health centers and outpatient clinics. All six studies included underserved populations and ethnic minorities, with two articles drawing a large number of patients from Native American reservations and communities. Also, all six studies addressed the effect of telemedicine on screening rates for the diabetic population. Although referral rates were addressed in every article, none of them evaluated the effect of screening on treatment.

Mansberger, et al.: Tribal Vision Project [23,24]

Mansberger, et al. is the most relevant study in this review, as it is the only long-term randomized controlled trial that investigates the comparative effectiveness of telemedicine versus traditional surveillance for obtaining a DR screening examination. This 5-year study was conducted at two primary care clinics that serve a large proportion of American Indian / Native Alaskan patients with diabetes. Five hundred sixty-seven patients were recruited from two clinics and randomized into either the telemedicine arm or the traditional surveillance arm. The telemedicine group received a larger proportion of DR screening exams (94.0%) when compared to the traditional surveillance group (56.0%) within one year of enrollment into the study. In comparison to the traditional surveillance group, a larger proportion of patients in the telemedicine group obtained a DR screening exam in the ≤ 6 month time bin (94.6% vs. 43.9%) and the > 6 – 18 month time bin (53.0% vs. 33.2%). However, patients in the traditional surveillance group were offered telemedicine screening after being enrolled in the study for 2 years, and this modification in the intervention increased uptake of DR screening in this group. Even with some attrition in both groups over time, subsequent time bins showed that the difference in uptake between the telemedicine and traditional surveillance groups had changed as follows: > 18 – 30 months (44.3% vs. 39.5%), > 30 – 42 months (45.0% vs. 46.4%), and > 42 – 54 months (51.1% vs. 56.0%). Also, although a small group of patients chose to continue traditional surveillance despite being offered telemedicine, this gap eventually narrowed so that most patients (89.0%) were opting for DR screenings via telemedicine by > 42 – 54 months.

No details were given on concealment of allocation, so it is unknown whether patients in the telemedicine arm were aware that their clinic's primary care providers were consulting with an ophthalmologist via the internet rather than assessing fundus images and providing ocular diagnoses and recommendation plans on their own. This detail becomes important when considering that these patients may not have been aware that they were receiving a specialist level of care in their primary care provider's office.

Selection bias in this study was minimal since the telemedicine and traditional surveillance groups were similar in baseline demographic and medical characteristics (i.e., p values across various parameters were not significant).

To confirm whether patients in the telemedicine and traditional surveillance arms were receiving their recommended DR screening exams, the study investigators captured exam data directly from patients' medical records in the primary care office or via data entry forms that were faxed or mailed back to the primary care offices from outside eye care providers. Thus, there was minimal measurement bias in this study because the same criteria were used for data reporting among both groups, and research staff were vigilant about contacting providers for missing data. Also, two study investigators graded all fundus images using a standard protocol.

Although selection and measurement bias were minimal, there may have been important sources of confounding that the authors did not adjust for in this study. For example, social determinants of health such as education level and socioeconomic and insurance status could have played an important role in influencing whether patients sought DR screening from outside eye care providers in the traditional surveillance group. These potential confounders could compromise the internal validity of this study. Choosing the study population from two clinics in Oregon and Kansas that serve a large number of patients from a specific ethnic group could have compromised the external validity of this study because this patient group may face health care access barriers that are not generalizable to the larger population surrounding these clinics or to other geographic areas of the U.S.

A potential limitation of this study may be that the authors did not collect data on patient insurance status, which could have affected whether patients in the traditional arm visited an ophthalmologist for DR screening exams. The fact that patients in the traditional arm obtained more DR screening exams after being offered the telemedicine option may imply that telemedicine effectively eliminated a potential access barrier that was otherwise keeping these patients from seeking diabetic eye care.

Chin, et al.: California Native American Indian Reservations / UC Davis Medical Center [25]

In a retrospective cross-sectional study over a period of nearly five years, Chin et al. examined patients from nine remote, rural medical clinics and one urban academic medical center who had received nonmydriatic retinal screening for a history of nonadherence to annual retinal exams. There was minimal selection bias in this study as all patients with diabetes were included regardless of whether they had any other dilated fundus exams in the past year. Patients seen at the rural sites were younger and more likely to be American Indian and Alaskan Native compared to the population at the urban center. Also, there was minimal measurement bias since all clinics used the same imaging protocol and all images were reviewed by a single ophthalmologist.

Although it seems reasonable to assume that rural patients might have higher prevalence of DR because of limited access to specialist care, this study showed the opposite to be true; there was a significant difference in prevalence of DR between rural (12.6%) and urban (29.6%) patient populations who received retinal tele-screening ($p < 0.001$). Despite this difference, HbA1c levels within 3 months of imaging were comparable for rural versus urban patients (8.3 ± 2.1% vs. 8.3 ± 2.2%), suggesting that these two populations were similar in their glycemic control. However, comparability of HgbA1c levels may be biased, as only 16.7% of rural patients' HgbA1c levels were reported through the EyePACS telemedicine software, whereas 96.9% of urban patients' HgbA1c levels were accessible through the electronic medical records system at the academic center. Data was not collected on other potential confounders, such as socioeconomic factors, compliance with diabetes care, and insurance status, which could have contributed to these findings.

The racial and ethnic diversity of the combined rural and urban study populations was a strength of this study. Of note, patients from rural sites were primarily Native American, so the results from the rural sites may not be generalizable to rural populations elsewhere in the U.S. Further, Native Americans have the highest age-adjusted rate of diagnosed diabetes when compared to other ethnicities,[26] but as shown in Table 1 below, they had a considerably lower prevalence of DR (12.1%) when compared to all other ethnicities in this study. While there may be a variety of reasons for this outcome, such as differences in age, access barriers, education level, insurance coverage, or socioeconomic status, the significance of this finding is compelling: This study demonstrates that telemedicine is an effective strategy for reaching the underserved regardless of geographic location, race, ethnicity, or diabetes status; patients in rural settings who have limited access to eye care providers are just as likely to benefit from tele-screening as those in urban settings who may be non-adherent with retinal exams because of lack of awareness or other factors.

Owsley, et al.: Innovative Network for Sight (INSIGHT) [27]

Owsley, et al. conducted a cross-sectional study across three urban outpatient clinics and one urban pharmacy clinic to determine the rate and types of DR that could be identified using telemedicine. Overall, there were more females recruited from all four sites than males and the majority of study participants were ethnic minorities (88.0%). The mean age at first diabetes diagnosis for patients at all sites was 44.5 years. Of note, the majority of patients at the

University of Alabama site were African-American, whereas those at the University of Miami site were Hispanic, Haitian, or Cuban. The Wake Forest outpatient clinic and the pharmacy clinic at Thomas Jefferson University saw a majority of white patients.

Study participants at the various sites were similar in age, ethnicity, and the age at first diagnosis of diabetes. Since a patient questionnaire was used to collect data on patient age at diabetes diagnosis, HgbA1c level, and date of most recent dilated eye exam, there could have been some recall bias associated with this data collection technique unless this information was verified in patients' medical records.

Only English-speaking participants were invited by physicians and staff to participate at each site except the University of Miami, which recruited both English- and Spanish-speaking patients. In addition to having physicians and staff refer patients, the University of Miami also used flyers in English, Spanish, and Creole for recruitment. Considering that patients who respond to flyers may have higher health literacy, this recruitment technique could have introduced some selection bias into the study. Measurement bias was minimized because all images from all sites were sent to a central location where they were reviewed by a group of trained graders who were all using the same protocol.

Participants at the pharmacy location in Philadelphia were more likely to be white, have health insurance, and to know their HgbA1c level. The DR prevalence at this site was also lower than all other sites (15.8% vs. >23.0%), thus suggesting there may be some compliance bias present since those patients who visit the pharmacy may also be more compliant with their diabetes care. Further, patients at the pharmacy site were more likely to have health insurance when compared to the other sites (79.2% vs. 34.6%), which could confound the study results because these patients may be more likely to seek health care in general.

The findings of this study are generalizable to the broader U.S. population because the clinics spanned four different geographic sites and several major ethnic minorities were represented. However, the external validity may be compromised by the fact that all four clinics were affiliated with major academic centers, thus limiting generalizability to other rural and private clinics in these geographic locations or to non-English-speaking ethnic minorities.

Velez, et al.: Project I See in NC [28]

Velez, et al. was a particularly relevant study for this Master's paper as it specifically targeted Medicaid and uninsured patients who receive diabetes care through two Community Care of North Carolina (CCNC) Networks which span a total of 35 clinic sites in the northwest and southern parts of the state. A total of 1688 patients were included in this study, and the majority of patients were uninsured (59.1%).

Patient demographics between the two CCNC networks were comparable, showing the authors tried to obtain a representative sample of participants by recruiting from two networks that encompass 12 counties and cover both urban and rural communities in North Carolina. Primary care offices, public health departments, hospital-based outpatient clinics, and free clinics for the uninsured were included in these networks.

All images in this study were reviewed and initially graded by a physician who was not an ophthalmologist. Images that were determined to have abnormal findings were triaged to a second grader, who was a certified retinal angiographer. This methodology could have introduced measurement bias into the study if the first grader incorrectly marked an image as normal when it was actually abnormal since that would mean the second grader would not have reviewed the image. Measurement of inter- and intra-grader variability would have helped to determine whether this grading method introduced significant bias into the study.

The Northwest Community Care Network had more patients who did not know what type of diabetes they had when compared to the Access III Lower Cape Fear Network (26.5% vs. 1.1%). The authors note that language barriers among the larger Hispanic population in the Northwest Community Care Network versus interviewer bias from a nurse who probed patients for detailed information in the Lower Cape Fear Network may have contributed to this difference between networks.

The authors collected data on other variables (see "Comments" in Table 1 below) which may be potential confounders, but they did not control for these variables in the analysis, so it is unknown how they might have influenced the results of the study. However, the study findings are generalizable to larger populations of patients with diabetes as several ethnic groups in both urban and rural settings were represented. In particular, the study findings are generalizable to those on public insurance and those who are uninsured, but they may not be generalizable to those with private insurance.

Olayiwola, et al.: Community Health Center, Inc. [29]

The most interesting part of the retrospective, descriptive study by Olayiwola, et al. was that it took place in a large federally qualified health center (FQHC) in Connecticut that serves a high-risk population of minority patients who are mostly uninsured or publicly insured. Over a period of one year, 568 patients with complete demographic and clinical data were screened for DR via telemedicine. There were more women than men in the study (53.3% vs. 46.7%), and 62.3% of the study population were Medicare or Medicaid recipients while 23.9% were uninsured. Participants were mostly Hispanics (41.9%), Whites (32.2%), and African-Americans (12.7%). Selection and measurement bias in this study were minimized because the investigators took a representative sample of underserved patients from the FQHC and all images from all sites were sent to a central location for review by a group of ophthalmologists.

Although the authors collected clinical data on HgbA1c, duration of diabetes, and other comorbid conditions, they only provided descriptive statistics on these measures. They did not explore other social determinants of health such as transportation barriers, education level, or employment status that could act as potential confounders within the study; these variables would play a significant role in diabetes care compliance in this FQHC population and would influence patient adherence to physician recommendations such as DR screening. Although the overall prevalence of DR was low in this study population (25.5%), it is not possible to draw further conclusions without having more information and a more rigorous statistical analysis available.

Findings of this study can be generalized to ethnic minorities and underserved populations that frequently obtain care at an FQHC, but the results may not be generalizable to others in the U.S. who have insurance and other means for obtaining health care.

One of the strengths of this article was that the authors provided a detailed outline of their methodology for program implementation, which is useful when considering the operational scale-up of such a telemedicine screening program.

Discussion

Overall, the evidence summarized in this literature review demonstrates that DR screening rates in underserved populations can be significantly improved by implementing retinal tele-screening programs in the primary care setting. Although studies to date have been of good quality, major limitations still exist. For example, sample sizes of patients with DR within larger study populations of patients with diabetes are still too small to adequately determine the effectiveness of telemedicine screening on subsequent DR treatment and long-term follow-up. There is also a dearth of evidence on how social determinants of health influence diabetic eye care compliance. Although this systematic review was fairly thorough, it was not a comprehensive review of all the available literature on this topic. Since limits were placed for only English language articles on studies conducted in the U.S. in the past 10 years, it is possible that international studies addressing the topic of this review and the limitations of the current literature were not included.

Although retinal tele-screening has been successful in delivering eye care to some of the most underserved patients, evidence for large-scale implementation of this intervention is still insufficient because ocular telemedicine has not yet been studied in a systematic manner. Many diabetic eye care programs provide diabetes care via telemedicine assuming that this methodology works; however, rigorous studies to prove the power of this strategy in reducing the burden of suffering of DR are still lacking. To date, most studies have mainly focused on proof of concept. To truly determine the efficacy and effectiveness of telemedicine for community-based diabetes care, more research is needed through rigorous large cohort studies, randomized controlled trials, and systematic reviews. Exploring community-level interventions and using community-based participatory research methods to evaluate the role and outcomes of telemedicine interventions is also necessary. Quasi experimental studies with pre- and post-test methodology could also be used to understand the effectiveness of ocular telemedicine in improving DR outcomes.

Additionally, broader challenges within the American health care system need to be addressed before telemedicine models can be scaled-up and replicated on a national level. For example, health policies around patient privacy, data security and information exchange, interstate physician licensure, and reimbursement have yet to be fully adapted to this new way of delivering care. Until these issues are addressed, widespread adoption will continue to be a challenge. As such, better evidence is needed through implementation science, feasibility, and cost-effectiveness studies. Such information will be helpful for securing buy-in from key stakeholders such as state and local governments, hospitals, and grassroots community partners who would be essential in fostering the public-private partnerships necessary for further dissemination and implementation.

Table 1. Summary of Selected Studies

Study	Technology / Imaging Technique	Setting	Patient Demographics and % Screened	DR / Referrals to Eye Care Providers	Comments
Mansberger, et al. [23,24] RCT study 567 diabetics randomized from August 1, 2006 – September 31, 2009 and followed up to 5 years	Nonmydriatic Nidek NM-1000 camera; Devers Eye Institute developed its own telemedicine platform ***<u>Telemedicine arm:</u>*** Captured 6 undilated, 45° photos OU using modified Diabetic Retinopathy Study protocol: Stereo pair centered on optic disc, stereo pair centered on macula, one superotemporal image, one inferotemporal image Images read by 2 experienced Devers Eye Institute investigators using an international classification scale and the Proliferative Diabetic Retinopathy study	567 total patients screened from Yellowhawk Tribal Health Center, Pendleton, OR and Hunter Health Clinic, Wichita, KS → 296 randomized to telemedicine arm; 271 randomized to traditional surveillance arm using random number generator ***<u>Traditional arm:</u>*** Patients received usual primary care (e.g., HbA1c testing) and were told to arrange a visit with a community eye care provider within 1 year ***<u>5 time bins for study participation:</u>*** 1.) ≤ 6 mos (-6 mos to +6 mos after enrollment) 2.) > 6 – 18 mos 3.) > 18 – 30 mos 4.) > 30 – 42 mos 5.) > 42 – 54 mos	52% (295/567) females 48% (272/567) males With primary, secondary, tertiary ethnicities combined: 72.5% (411/567) non-White and 50.3% American Indian/ Alaska Native 75.6% (429/567) obtained DR screening exam → 94% (278/296) in telemedicine arm; 56% (151/271) in traditional arm 24.3% (138/567) did not obtain DR screening exam	***<u>Telemedicine arm:</u>*** 278/429 patients w/ DR exams 72.3% no DR 13.7% mild NPDR 2.9% moderate NPDR 0.0% severe NPDR 1.8% PDR 9.4% ungradable 20.5% referred ***<u>Traditional arm:</u>*** 151/429 patients w/ DR exams 70.2% no DR 13.9% mild NPDR 7.9% moderate NPDR 2.0% severe NPDR 3.3% PDR 2.6% ungradable 24.5% referred ***<u>DR prevalence by ethnicity:</u>*** 650 eyes = no DR <u>159 eyes = with DR</u> → 40.3% White 20.8% American Indian / Alaskan Native 25.8% African-American 10.7% Hispanic / Latino 2.5% Asian / other	Collected data on age, gender, primary / secondary / tertiary ethnicity, systolic and diastolic blood pressure, HgbA1c, duration of diabetes Difference in baseline demographic and medical characteristics was not statistically significant between arms Used highest stage of DR between two eyes to define DR prevalence and stage Criteria for referral = 1.) Moderate NPDR or worse 2.) Presence of clinically significant macular edema (CSME) 3.) Unable-to-determine result from either eye Telemedicine screening was offered to patients in traditional arm after 2 years of study enrollment

Study	Technology / Imaging Technique	Setting	Patient Demographics and % Screened	DR / Referrals to Eye Care Providers	Comments
Chin, et al. [25] Retrospective cross-sectional study from July 2006 – May 2011	***Rural clinics:*** Nonmydriatic Topcon TRC-NW6S with Nikon D80 camera back; EyePACS telemedicine platform ***Urban clinic:*** Nonmydriatic Nidek AFC-210 camera; ANKA telemedicine software Both clinics captured a single, undilated, nonstereoscopic 45°, 10-megapixel image of optic disc and macula OU All images from rural and urban clinics read by single retinal specialist at University of California Davis Eye Center	872 patients from 9 rural clinics in California Native American Indian Reservations 517 patients from 1 urban family medicine clinic at Univ. of California Davis Medical Center, Sacramento, CA	***Rural clinics:*** 59.2% female 40.8% male 60.1% Native American and/or Alaskan 3.0% White non-Hispanic 0.2% Asian 0.1% Black 0.1% Native Hawaiian and other Pacific Islander 0.1% Hispanic or Latino 36.4% unspecified ***Urban clinic:*** 55.5% female 44.5% male 27.3% White non-Hispanic 21.9% Black 19.3% Hispanic or Latino 17.0% Asian 2.9% Native Hawaiian and other Pacific Islander 1.4% Native American and/or Alaskan 10.3% unspecified	***Rural clinics:*** 73.3% (639/872) with no DR; 12.6% (110/872) with some level of DR 17.6% ungradable images ***Urban clinic:*** 56.1% (290/517) with no DR; 29.6% (153/517) with some level of DR 14.3% ungradable images ***DR prevalence by ethnicity:*** 12.1% Native American and/or Alaskan 25.8% White non-Hispanic 30.7% Black 26.7% Hispanic or Latino 34.4% Asian 31.3% Native Hawaiian and other Pacific Islander 15.7% unspecified ***Referrals:*** All patients with detectable DR were examined by an eye care provider within weeks to months of tele-screening	Collected data on age, gender, ethnicity, HgbA1c, fundus abnormalities other than DR Table 1 in paper: Participants in urban center tended to be older than those at rural sites ($p < 0.001$) Table 1 in paper: Participants in rural sites were more likely to be American Indian / Alaska Native ($p < 0.001$)

Study	Technology / Imaging Technique	Setting	Patient Demographics and % Screened	DR / Referrals to Eye Care Providers	Comments
Owsley, et al. [27] Cross-sectional study Univ. of Alabama – Birmingham: January 26 – July 24, 2012 Univ. of Miami: March 2, 2012 – April 11, 2013 Johns Hopkins / Wake Forest – Winston-Salem, NC: May 5, 2013 – November 14, 2014 Thomas Jefferson Univ. – Philadelphia, PA: December 5, 2011 – March 29, 2013	Nonmydriatic Nidek AFC-230 camera; Wills Eye Hospital telemedicine platform Clinics captured 3 photos OU: Anterior segment, nasal fundus, and temporal fundus Images read by trained graders at Wills Eye Hospital telemedicine reading center using National Health Service's DR grading classification system	1894 total patients screened from 4 clinics ***<u>3 outpatient clinics:</u>*** Univ. of Alabama, Birmingham – Internal Medicine safety net clinic Univ. of Miami – FQHC serving uninsured / underinsured Johns Hopkins / Wake Forest Univ. – outpatient clinic serving low-income people in downtown Winston-Salem, NC ***<u>1 urban outpatient pharmacy:</u>*** Thomas Jefferson Univ. – outpatient pharmacy in Philadelphia, PA	63.1% (1191/1894) females; 36.9% (696/1894) males ***<u>Birmingham:</u>*** 31.7% (600/1894) diabetics screened 29.5% insured 84.3% African American 14.5% White ***<u>Miami:</u>*** 32.1% (608/1894) diabetics screened 22.6% insured 41.1% Hispanic 33.9% African American 11.5% Haitian 11.0% Cuban ***<u>Winston-Salem:</u>*** 9.5% (180/1894) diabetics screened 51.7% insured 68.9% African American 21.1% White ***<u>Philadelphia:</u>*** 26.7% (506/1894) diabetics screened 79.2% insured 68.2% African American 18.8% White	21.7% of all patients with any level of DR in either eye; 94.1% of these had background DR 22.2% – 23.7% background DR in Birmingham, Miami, Winston-Salem vs. 14.4% in Philadelphia 0% – 11.4% preproliferative and proliferative DR across all sites 9.3% maculopathy across all sites Overall DR prevalence similar for whites vs. combined ethnic/racial minorities (22.6% vs. 21.6%)	Used patient questionnaire to collect data on patient demographics, age at DM diagnosis, HgA1c level, date of most recent dilated eye exam, smoking status, and health insurance status Also looked at rate of other ocular findings

Study	Technology / Imaging Technique	Setting	Patient Demographics and % Screened	DR / Referrals to Eye Care Providers	Comments
Velez, et al. [28] Descriptive, cross-sectional study October 2005 – September 2007	Unspecified camera type; Wake Forest School of Medicine telemedicine platform Two 45° photos OU: One centered on optic nerve and macula, one of superotemporal vascular arcade Images read by 2 trained graders (a physician and a certified retinal angiographer); a consulting ophthalmologist was available for challenging images	1688 total patients screened from 2 Community Care of North Carolina (CCNC) Networks → 1030 from Northwest Community Care Network (12 sites) and 658 from Access III of Lower Cape Fear Network (23 sites)	***Access III of Lower Cape Fear Network:*** 69% (456/658) females; 31% (202/658) males 50% African-American 44% White 5% Hispanic 1% Other 40% Medicaid 2% Medicare 58% Uninsured ***Northwest Community Care Network:*** 64% (655/1030) females; 36% (375/1030) males 40% African-American 49% White 10% Hispanic 1% Other 40% Medicaid 0% Medicare 60% Uninsured	***Access III of Lower Cape Fear Network:*** 83.7% no DR 9.3% mild NPDR 5.8% moderate to severe NPDR 0.9% PDR 0.3% ungradable ***Northwest Community Care Network:*** 87.5% no DR 8.0% mild NPDR 3.4% moderate to severe NPDR 1% PDR 0.1% ungradable ***Referrals:*** 12% of total patients referred 5% required urgent referral for vision-threatening retinopathy All patients with moderate to severe NPDR or PDR were referred	Patients' pupils were dilated for retinal imaging using 1% tropicamide eye drops → no adverse reactions reported Used patient questionnaire to collect data on age, sex, race, previous history of dilated eye exam, duration of diabetes, self-reported vision changes in the previous year, knowledge of comorbid conditions, and awareness of any existing retinopathy

Study	Technology / Imaging Technique	Setting	Patient Demographics and % Screened	DR / Referrals to Eye Care Providers	Comments
Olayiwola, et al. [29] Retrospective descriptive study Patients screened from July 2009 – June 2010	2 nonmydriatic Canon CR-1 cameras rotated between multiple sites; EyePACS telemedicine platform Clinics captured 8 images OU: 2 external, 6 retinal Images read by ophthalmologists at Yale Eye Center / Dept. of Ophthalmology using EyePACS Retinopathy Grading System	611 total patients screened (568 with complete demographic and clinical data) at multiple Community Health Center, Inc. primary care / FQHC sites Cameras were rotated between sites on a weekly basis	46.7% (265/568) males; 53.3% (303/568) females 12.7% (72/568) Black 3.2% (18/568) Asian 32.2% (183/568) White 41.9% (238/568) Hispanic / Latino 0.5% (3/568) Native American / American Indian 3.5% (20/568) Other 6.0% (34/568) Unspecified 23.9% (136/568) Uninsured 62.3% (354/568) Publicly insured	74.5% (423/568) no DR 25.5% (145/568) with some level of DR → 12.3% (70/568) mild NPDR 6.9% (39/568) moderate NPDR 3.7% (21/568) severe NPDR 2.6% (15/568) PDR 13% (75/568) required referral	Collected data on age, gender, ethnicity, insurance status, duration of diabetes, HgbA1c, insulin therapy, hypertension, systolic and diastolic blood pressure, hyperlipidemia, coronary artery disease, chronic kidney disease

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APPENDIX B: The Partial Proportional Odds Regression Model

We propose the cumulative logistic regression model for the three groups: No DR, DR without referral and DR with referral. Let their respective probabilities be defined as:

$$P(Y=1) = P(\text{No Diabetic Retinopathy})=\pi_1$$

$$P(Y=2) = P(\text{Diabetic Retinopathy without Referral})=\pi_2$$

$$P(Y=3) = P(\text{Diabetic Retinopathy with Referral}) =\pi_3$$

with $\pi_1 + \pi_2 + \pi_3 =1$. The groups are ordered in the sense that DR with referral is the most severe and no DR is the least severe. Define the cumulative logits:

$$L_1=\log [\pi_1/(\pi_2+\pi_3)] \text{ and}$$

$$L_2=\log [(\pi_1+\pi_2)/\pi_3].$$

Specifically, L_1 is log odds of no DR versus having a DR diagnosis, whereas the second logit is the log odds of no referral versus referral. The cumulative logits model specifies that these logits depend upon covariates. In particular, the final partial proportional odds model (Table 3) is:

$$L_1=\alpha_1+\beta_{11}*\text{Age}+\beta_{21}*\text{Caucasian}+\beta_{31}*(\text{Other Race}) + \beta_4*\text{hgba1c}+ \beta_5*(\text{Diabetes Duration}) +$$
$$\beta_6*\text{Stroke} + \beta_7*\text{Kidney Disease}$$

$$L_2=\alpha_2+\beta_{12}*\text{Age}+\beta_{22}*\text{Caucasian}+\beta_{32}*(\text{Other Race}) + \beta_4*\text{hgba1c}+ \beta_5*(\text{Diabetes Duration}) +$$
$$\beta_6*\text{Stroke} + \beta_7*\text{Kidney Disease}$$

This model specifies proportional odds for HbA1c, diabetes duration, and kidney disease as evident by the common log odds ratio parameters in the two logits, which are $\beta_{4,}$ β_5, and β_6, respectively. On the other hand, age and race have distinct regression coefficients in the two logits.