

**A Feasibility Study of Retinal Screening Using the RetinaVue 100 Hand-Held
(non-mydriatic) Camera in Outpatient Dialysis Centers**

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Short Title: Retinal Screening with RetinaVue 100 in Outpatient Dialysis Centers

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TABLE OF CONTENTS

Table of Contents.....	3
Abbreviations and Definitions of Terms.....	4
Protocol Synopsis.....	5
1 BACKGROUND AND RATIONALE	6
2 STUDY OBJECTIVES	6
3 INVESTIGATIONAL PLAN	7
4 STUDY PROCEDURES.....	7
5 STUDY EVALUATIONS AND MEASUREMENTS.....	8
6 STATISTICAL CONSIDERATIONS.....	8
7 SAFETY MANAGEMENT.....	9
8 DATA COLLECTION AND MANAGEMENT	9
9 RECRUITMENT STRATEGY.....	10
10 CONSENT PROCESS.....	10

ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
ESRD	End-stage renal disease
CSME	Clinically significant macular edema

PROTOCOL SYNOPSIS

Study Title	A Feasibility Study of Retinal Screening Using the RetinaVue 100 Hand-Held (non-mydratic) Camera in Outpatient Dialysis Centers
Funder	WelchAllyn
Clinical Phase	Feasibility
Study Rationale	There are no studies evaluating (diabetic or non-diabetic) retinopathy in the renal dialysis patient population (~300,000 Americans). Approximately 50% of this population has End-stage Renal Disease (ESRD) due to diabetes. Dialysis patients are among the most debilitated patients, and thus, have even more barriers to receiving their recommended annual retinal evaluation. The advent of the RetinaVue hand-held retinal camera holds great promise in this population, as dialysis patients access medical care 3 times a week, for several hours at a time at their dialysis clinic.
Study Objective(s)	<p>Primary</p> <p>To evaluate the usability of the FDA-approved RetinaVue Hand-Held 100 Camera in a population with multiple chronic conditions</p> <p>Secondary</p> <ul style="list-style-type: none"> • To evaluate pre-and-post-screening rates in the diabetic dialysis population. • To determine the proportion of overall retinopathy in a dialysis population • To evaluate participant satisfaction of screening utilizing the FDA-approved RetinaVue 100 hand-held camera
Study Design	This is a feasibility study.
Subject Population	Inclusion Criteria
key criteria for Inclusion and Exclusion:	<ul style="list-style-type: none"> • The subject must currently be seeking treatment for end-stage renal disease (ESRD) at one of the specified dialysis clinics. • The subject must be ≥ 18 years of age. <p>Exclusion Criteria</p> <ul style="list-style-type: none"> • The subject is <18 years of age.
Number Of Subjects	Up to 250 participants
Study Duration	<p>Each subject's participation may last up to 1 year.</p> <p>The entire study is expected to last about 1 year.</p>
Study Phases	(1) Screening for eligibility and obtaining consent, (2) Obtaining retinal images, completion of satisfaction survey, and medical record abstraction (3) For those participants recommended for referral, they will be given the opportunity to follow up with the remote provider.
Screening	
Intervention	
Follow-Up	
Statistical And Analytic Plan	To assess usability of camera utilization, the primary objective, the proportion of inadequate images will be calculated.

1 BACKGROUND AND RATIONALE

1.1 Introduction

There are no studies evaluating (diabetic or non-diabetic) retinopathy in the renal dialysis patient population (~300,000 Americans). Approximately 50% of this population has End-stage Renal Disease (ESRD) due to diabetes. Dialysis patients are among the most debilitated patients, and thus, have even more barriers to receiving their recommended annual retinal evaluation. The advent of the RetinaVue hand-held retinal camera holds great promise in this population, as dialysis patients access medical care 3 times a week, for several hours at a time at their dialysis clinic.

1.2 Non-Clinical and Clinical Study Findings

Potential Benefits:

The potential benefits to subjects from being in this study may include receiving a screening of their eyes, a diagnosis, and potential follow up that they may not have received unless they were in the study.

Risk /Benefit Assessment:

A possible side effect expected would be temporary discomfort in the eye/s due to the camera flash. This is seen infrequently in the clinical setting and should not last more than 2-3 minutes.

As part of the eye exam, drops may be put in the eyes to dilate the pupils. The drops may blur vision and make the subject sensitive to light. The drops will wear off over several hours. There is a small risk of an allergic reaction to the drops. There is also a small risk that the drops could cause the eye pressure to rise. If this happens, it will be treated, but there is a small risk of losing vision from the pressure rise. Due to the blurring effect on vision and possible light sensitivity, we will recommend that the subject not drive until the blurring effects of the drops have worn off. If necessary, the subject should have someone with them who can drive for them after the exam.

There may be uncommon or previously unknown risks.

2 STUDY OBJECTIVE

Primary Objective:

- To evaluate the usability of the FDA-approved RetinaVue Hand-Held 100 Camera in a population with multiple chronic conditions

Secondary Objective

- To determine rates of overall retinopathy in a dialysis population
- To evaluate participant satisfaction of screening utilizing the FDA-approved RetinaVue 100 hand-held camera

3 INVESTIGATIONAL PLAN

3.1 Study Design

This is a feasibility study to evaluate the usability of the FDA-approved RetinaVue 100 and contribute to knowledge about integrating telehealth into medical services.

3.2 Study Duration, Enrollment and Number of Subjects

The study team anticipates the study duration to be about 1 year.

This study will recruit participants from four UNC outpatient dialysis clinics in the following locations: Carrboro, Siler City, Pittsboro, and Mebane, North Carolina.

The study proposes enrolling up to 250 subjects across all four study sites.

3.3 Study Population

Inclusion Criteria

- The subject must currently be seeking treatment for end-stage renal disease (ESRD) at one of the specified dialysis clinics.
- The subject must be ≥ 18 years of age.

Exclusion Criteria

- The subject is <18 years of age.

4 STUDY PROCEDURES (what will be done)

- Determine last documented retinal examination (electronic medical record)
- Determine cause of End-stage Renal Disease (ESRD) and vintage, I.e. how long patient has been on dialysis (paper chart)
- Determine patient demographics (electronic medical record)
 - DOS, DOB (age)
 - Gender, race
 - Medical history (coronary artery disease, stroke, hypertension, if diabetes -duration)
 - Medical labs (HbA1c, cholesterol, blood pressure)
 - Smoking history
 - Social determinants of health (education level, insurance status, etc).
- Check bilateral visual acuity with near card.
- Obtain bilateral retinal photographs with or without dilation.
- Complete the Usability survey.
- Complete the Participant Satisfaction survey.
- Upload patient images and metadata.
- Through the study PI, a board-certified ophthalmologist, interpret patient retinal images and return of diagnosis and management plan to dialysis unit including a wellness report to be given to individual subjects.
- Analyze data with biostatistician consultant
- Timeline. Quarter 1 (May –August 2016): Retinal image and metadata acquisition, clinic 1 and 2; Quarter 2 (September 2016-November 2016): retinal image and metadata acquisition clinic 3 and 4; Quarter 3 (December 2016-February 2017): data analysis; Quarter 4 (March 2017-May 2017): manuscript and presentation preparations.
- Subject results will be entered into the medical record. If something of note is found in a subject's

retinal scan, then staff at the dialysis clinic will provide follow up for any abnormalities found as part of clinical care.

5 STUDY EVALUATIONS AND MEASUREMENTS

The following variables will be abstracted from medical records:

- Last documented retinal examination, cause of End-stage Renal Disease (ESRD) and vintage, I.e. how long patient has been on dialysis, DOS, DOB (age), gender, race, medical history (coronary artery disease, stroke, hypertension, if diabetes -duration), medical labs (HbA1c, cholesterol, blood pressure), smoking history, social determinants of health (education level, insurance status, etc).

Obtaining retinal images

- Nonmydriatic fundus images of both eyes were obtained from participants using the WelchAllyn RetinaVue™ 100 Imager. For those subjects with pupils smaller than 3 mm in either eye, a low dose dilation drop of 0.5% tropicamide will be administered to enlarge the pupil and assist in image capture. The images will be electronically sent via a HIPAA compliant portal to an offsite, board-certified ophthalmologist for remote interpretation. Following interpretation, a report will be generated that details any clinical findings and referral recommendations, which will then be distributed to individual subjects and uploaded to their electronic medical record. For those participants recommended for referral, they will be given the opportunity to follow up with the remote provider.

Participant satisfaction survey

- Participants will be asked to complete a brief participant satisfaction survey, which asks questions regarding their satisfaction with their exam experience. The survey utilizes a five-point Likert scale with responses ranging from strongly agree (1) to strongly disagree (5). The survey also allows for participants to provide qualitative observations about their experience. The survey asks about satisfaction of time to complete exam, comfort during the exam, comfort after the exam, first eye recovery after the camera flash, second eye recovery after the camera flash, and satisfaction with overall experience.

6 STATISTICAL CONSIDERATION

6.1 Statistical Methods

Descriptive analyses will be used to assess demographic and medical history variables, camera usability, overall retinopathy, and participant satisfaction data. To assess usability of camera utilization, the proportion of inadequate images will be calculated. For participant satisfaction data, a response rate will be calculated followed by an overall mean score and standard deviation, and proportions for each of the six survey components. To assess overall retinopathy, a three-category outcome variable for retinopathy and referral at the individual level will be determined: (1) No retinopathy, (2) retinopathy without referral, and (3) retinopathy with referral. The following definitions will be determined (results for pairs of eyes will take into account that there may be some unreadable images): If the diagnosis in both eyes is no retinopathy then the individual has no retinopathy; otherwise, if either eye is considered severe, has proliferative diabetic retinopathy, clinically significant macular edema (CSME), or an inadequate image, the individual will be put into the retinopathy with referral category; likewise, if either eye is

mild/minimal or moderate retinopathy without CSME, then the individual will be placed into the retinopathy non-referral category.

6.2 Sample Size and Power

The study aims to recruit and collect data from all individuals currently receiving treatment at the specified dialysis clinics. As such, the proposed sample (N=250) reflects the number of patients actively seeking treatment at those sites. Furthermore, this is a feasibility study and therefore 250 subjects is sufficient for the study team to determine the usability of the camera and to determine the prevalence of retinal disease in the dialysis population. In such a study, a power calculation is not indicated.

7 SAFETY MANAGEMENT

This study presents no more than minimal risk to participants and as such, the study team does not anticipate any obvious safety concerns. However, the study team and/or a representative for WelchAllyn, Inc. will periodically monitor the data for the study duration.

As defined by UNC's IRB, unanticipated problems involving risks to study subjects refers to any incident, experience, or outcome that:

Is unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied; Is related or possibly related to a subject's participation in the research; and suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.

Any events that meet the criteria for "Unanticipated Problems," as defined by UNC's IRB will be reported by the study staff using the IRB's web-based reporting system.

Though the likelihood of adverse events and other UPs for this trial is low, the study team plans to review data on a weekly or biweekly basis in order to determine whether there are safety concerns or other unexpected problems occurring. In the event that safety concerns or other problems arise, the study team will meet to create a plan to remedy any issues.

8 DATA COLLECTION AND MANAGEMENT

Obtained study data will be recorded in an Excel spreadsheet which will be made available to study staff. Subsequent data management will be the responsibility of the study staff for quality control assurance and integrity of data and will occur concurrently with data collection. In addition, a representative of the funding source will occasionally monitor the data.

The research study staff will use patient records, both paper and electronic format, and will conduct this research according to the UNC established conditions for the collection of medical and personal information as part of doing this research study. All information obtained in this study that can be identified with subject name will remain confidential as far as possible. No names will be revealed in any reports or publications resulting from this study without consent of the subject. The members of the research team, monitors, and any country, state or federal regulatory agencies or the Institutional Review Board may access the data.

When the study has been terminated with the UNC IRB, hardcopy files which may include identifiable data will be stored onsite within the Research Manager's office for a period of 4 years or until has been

requested to be destroyed by the PI, whichever comes first. All protocol and/or identifiable data, when it can be destroyed, will be placed in a secured, university issued, confidential recycling bin for shredding.

9 RECRUITMENT STRATEGY

Subjects will be identified at dialysis centers as those subjects currently seeking treatment. All subjects listed as being a patient of the dialysis unit will be approached by a member of the study team while in clinic.

10 CONSENT PROCESS

Before recruitment and enrollment onto this study, potential subjects will be approached about the study by study personnel and given the informed consent document for review. A study team member will review the consent document with the subject and/or their representative allowing ample time for questions, answers and clarifications. After a thorough review, with all parties satisfied about the research trial, subjects wishing to participate will be asked to sign and date the Informed Consent document. Once the subject signs and dates the informed consent along with the individual obtaining consent, the appropriate copies will be distributed to the study files, and a copy given to the subject for their own records.