Understanding Quality of Life in High Digital Device Users who are Treated with Systane Hydration PF

Study Protocol and Statistical Analysis Plan

NCT04837807

November 19th, 2021

Andrew Pucker, O.D.,PhD, Principal Investigator University of Alabama at Birmingham
Birmingham, AL 35294

CONSENT FORM TO BE PART OF A RESEARCH STUDY

Title of Research: Understanding Quality of Life in High Digital Device Users who are Treated with a Preservative Free Artificial Tear

UAB IRB Protocol #: IRB-30007063

Principal Investigator: Andrew D. Pucker, OD, PhD

Sponsor: ALCON RESEARCH, LTD

General Information	You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form.
Purpose	The purpose of the study is to determine the effect of a preservative free artificial tear on dry eye symptoms and visual quality of life in patients who have Digital Eye Strain (DES).
Duration & Visits	You will be in this study for 2 weeks with 3 in person visits with each visit lasting about 1 hour.
Overview of Procedures	This study will include eye tests, surveys, and the use of an over the counter, preservative free artificial tear. You will be randomly placed by chance in either the unit-dose drop group or the multi-dose drop group at the first visit. You will then be switched to the other group at the second visit. Both dispensing methods contain the same artificial tear.
Risks	The risks of this study do not exceed that of a normal eye exam. The use of all eye drops comes with a risk of eye irritation or an allergic reaction; however, allergic reactions with these drops are very rare.
Benefits	You may not benefit directly from this study, but knowledge gained from this study could potentially help future persons suffering from eye discomfort or DES.
Alternatives	The only alternative to this study is to not take part in this study and to continue with your regular eye care.

Purpose of the Research Study

We are asking you to take part in a research study. Although the use of digital devices has greatly improved many aspects of modern life, heavy use of digital devices can lead to the development of a condition known as Digital Eye Strain (DES). DES is a condition where patients experience symptoms such as glare, trouble with focusing, visual blur, fatigue, eye discomfort and dryness as well as an overall lower quality of life. This study plans to determine if symptoms associated DES can be reduced or alleviated with the use of a preservative free artificial tear. This study will also compare two ways to dispense these drops (unit-dose vs. multi-dose). We plan to enroll a total of 30 subjects at the University of Alabama at Birmingham.

Conflict of Interest Disclosure

Dr. Andrew Pucker, the principal investigator for this study, receives consulting fees from companies other than the sponsor, which may affect his financial interests. If you would like more information, please ask Dr. Pucker.

Study Participation & Procedures

If you agree to participate in this study, you will be asked to come in for 3 in person visits over the course of 2 weeks that will last about 1 hour each. You will be asked to complete surveys used to gauge eye comfort and health, and you will be asked complete the below procedures in the listed order. The testing listed below is often included in a typical eye exam.

Study Visit 1

- **Subject History, Eligibility, Informed Consent:** You will be asked to complete a screening survey to verify that you are eligible for the study. We will also fully explain this study to you and let you decide if you would like to participate.
- **Impact of Dry Eye on Daily Life (IDEEL) Questionnaire:** We will ask you to complete a self-administered survey to understand how common daily activities are affected by eye comfort.
- **Visual Acuity:** We will evaluate your ability to read the eye chart.
- **Slit-Lamp Biomicroscope:** We will use a lighted biomicroscope to document your eye health.
- **Randomization:** We will place you by chance in one of the dosage groups. Both dosage options contain the same artificial tears. You will also be educated how to use the eye drops each day.
- **Eye Drop Log:** You will be given a paper daily log to record the time and number of drops used each day and eye comfort throughout the day. We ask that you use the drops at least 4 times per day. You will also be asked to record the duration and type of digital device used each day, and you will be asked to return this log at your next study visit.

Study Visit 2

- **Impact of Dry Eye on Daily Life (IDEEL) Questionnaire:** We will ask you to complete a self-administered survey to understand how common daily activities are affected by eye comfort.
- **Visual Acuity:** We will evaluate your ability to read the eye chart.
- **Slit-Lamp Biomicroscope:** We will use a lighted biomicroscope to document your eye health.
- **Drop Survey:** You will be asked to complete an investigator-developed survey to help understand your perception of the eye drops and dosage method.
- **Crossover:** You will be placed in the opposite dosage group, and you will be educated how to use the drops each day.
- **Eye Drop Log:** You will be given a paper daily log to record the time and number of drops used each day and eye comfort throughout the day. We ask that you use the drops at least 4 times per day. You will also be asked to record the duration and type of digital device used each day, and you will be asked to return this log at your next study visit.

Study Visit 3

- **Impact of Dry Eye on Daily Life (IDEEL) Questionnaire:** We will ask you to complete a self-administered survey to understand how common daily activities are affected by eye comfort.
- **Visual Acuity:** We will evaluate your ability to read the eye chart.
- **Slit-Lamp Biomicroscope:** We will use a lighted biomicroscope to document your eye health
- **Drop Survey:** You will be asked to complete an investigator-developed survey to help understand your perception of the eye drops and dosage method.
- **Completion:** The examiner will reveal the contents of the eye drops. You will then be compensated for your time, and you will be released from the study.

Risks and Discomforts

This study does not involve any inherent risks or discomforts, though there is a chance that you may find the drops to sting slightly upon instillation. This is a common and accepted issue with eye drops; however, it is unlikely since these drops are designed to improve eye comfort. If you find any of the eye tests or the drops to be uncomfortable, you will be allowed to stop the study at any time. There is also a risk of breach of confidentiality; however, every reasonable precaution has been taken to avoid this potential risk.

Benefits

You may not benefit directly from taking part in this study. However, knowledge gained from this research will help the medical community better understand if preservative free artificial tears can help reduce or alleviate the symptoms associated with DES.

Alternatives

Your alternative is to not participate in this study.

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

What protected health information may be used and/or given to others?
All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

Who may use and give out this information?
Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Who might get this information?
All individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. “Sponsor” includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:

- the Office for Human Research Protections (OHRP)
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies

- Governmental agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- the University of Alabama at Birmingham - the physicians, nurses and staff working on the research study (whether at UAB or elsewhere); other operating units of UAB, UAB Hospital, UAB Highlands Hospital, as necessary for their operations; the UAB IRB and its staff of *UAB* and its billing agents
- ALCON RESEARCH, LTD

Why will this information be used and/or given to others?
Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

What if I decide not to give permission to use and give out my health information?
By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?
You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?
Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?
If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others. Including others outside of UAB, without your permission.

<u>Voluntary Participation and Withdrawal</u>

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in it. If you decide not to be in the study, you will not lose any benefits you are otherwise owed.

You are free to withdraw from this study at any time. Your choice to leave the study will not affect your relationship with this institution. However, you should return to see the study doctor for safety reasons so you can be taken off the study drug and referred for follow-up care. Contact the study doctor if you want to withdraw from the study.

You may be removed from the study without your consent if the sponsor ends the study, if the study doctor decides it is not in the best interest of your health, or if you are not following the study rules.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no cost to you for taking part in this study.

Payment for Participation

You will be paid $200 via a Greenphire Clincard at the completion of this study to compensate you for the time that you devoted to this study. Ask the study staff about the method of payment that will be used for this study (e.g., check, cash, gift card, direct deposit).

New Findings

You will be told by the study doctor or the study staff if new information becomes available that might affect your choice to stay in the study.

Questions

If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, please contact the study doctor. You may contact Dr. Andrew D. Pucker at (205) 975-9938 or after hours by emailing him at apucker@uab.edu.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

Legal Rights

You are not waiving any of your legal rights by signing this consent form.

Signatures

Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

_____

Signature of Participant Date

_____

Signature of Person Obtaining Consent Date

Understanding Quality of Life in High Digital Device Users who are Treated with Systane Hydration PF

Principal Investigator:
Andrew D. Pucker, OD, PhD, FAAO[1]

Co-Investigators:
Chris Lievens, OD, MS, FNAP, FAAO[2]
Gerald McGwin, Jr., MS, PhD[1]
Quentin X. Franklin, BS[1]
Gregory S. Wolfe, OD, MPH, FNAP, FAAO[2,3]

University of Alabama at Birmingham[1]
School of Optometry
1716 University Blvd
Birmingham, AL 35233
apucker@uab.edu
(920) 579-2900

Southern College of Optometry[2]
Memphis, TN

Center for Eye and Health Outcomes[3]
Memphis, TN

I. INTRODUCTION & RATIONALE

Extensive computer use is no longer an employment-specific challenge. Use of digital devices in work, home, and leisure settings is now the norm, and it is now socially expected.[1] While the introduction of high-powered computers and digital devices have greatly improved many aspects of modern life, the pervasive use of digital devices has caused some patients to develop a condition known as Digital Eye Strain (DES). DES has been reported to be as high as 93% the population depending upon how the condition is defined, and its severity has been found to increase with increased digital device time.[1, 2] DES is a condition where patients experience symptoms such as glare, accommodative dysfunction, defocus, fatigue, discomfort, and dryness from digital device use,[2] and these dry eye symptoms may also result in decreased quality of life.[3] While dryness symptoms in DES are likely multifactorial (e.g., contact lens use, systemic disease status), much of the dryness symptoms in DES are probably due to tear film evaporation secondary to having a reduced number of blinks per minute while using digital devices.[2] Since much of the ocular symptoms associated with DES stem from excessive tear evaporation, artificial tears have become an accepted DES treatment.[2]

Systane Hydration PF is a recently released preservative-free artificial tear that is able to supplement the ocular surface's moisture while simultaneously soothing the eye. Systane Hydration PF has HydroBoost technology, which is thought to enhance the drop's effectiveness by incorporating ingredients that increase drop retention. While Systane Hydration PF should in theory improve the symptoms and subsequently the quality of life of patients who have DES, this clinical application has yet to be tested. This drop furthermore is available in both unit-dose and multi-dose options; however, it is unclear if patient perceive a difference between the two dispensing methods. Therefore, the primary purpose of this study is to recruit patients who have DES and to treat them with Systane Hydration PF and determine how regular use of this drop impacts a patient's ocular surface symptoms and overall quality of life. This study will secondarily compare the two dispensing methods to determine if patients prefer one method over the other.

II. SPECIFIC AIM

Aim: Determine the effect of Systane Hydration PF on dry eye symptoms and visual quality of life in subjects who have Digital Eye Strain (DES).

Hypothesis 1: Systane Hydration PF will significantly improve IDEEL Work scores in heavy digital device users (≥ 8 hours of wear/day).

Hypothesis 2: Subjects will report higher ease of use satisfaction when using multi-dose Systane Hydration PF compared to unit-dose Systane Hydration PF.

III. STUDY DESIGN

Subjects

This two-week, three-visit study will be conducted at the University of Alabama at Birmingham (Birmingham, AL, USA). A total of 30 subjects will be recruited since this is a descriptive study. Subjects will be recruited from each site via clinic records, email, and fliers. Adult (>18 years) patients who answer yes to the following two questions and use digital devices (e.g., computers, tablets, or smart phones) ≥8 hours/day will be recruited:

"Are your eyes dry, irritated, or itchy or do they burn while using a digital screen, like a computer or smartphone? **Yes** or No

"Eye fatigue is the physical discomfort of your eyes after spending periods of time throughout the day in front of a digital screen, like a computer or smartphone."[4] Do you have eye fatigue based upon the this definition? **Yes** or No

Subjects will also be required to have a Work Impact of Dry Eye on Daily Life (IDEEL) score ≤80 to ensure that they have clinically meaningful symptoms,[5] and they will be required to have an Ocular Surface Disease Index (OSDI) score between 13 and 32 (inclusive) to ensure that they have mild to moderate dry eye symptoms.[6, 7] Subjects will be excluded if they had worn contact lenses in the past week or during the course of the study, have known systemic health conditions that are thought to alter tear film physiology (e.g., Sjögren's syndrome), have a history of ocular surgery within the past 12 months, have a history of severe ocular trauma, active ocular infection or inflammation, are currently using isotretinoin-derivatives or ocular medications, are currently using a dry eye treatment other than artificial tears, are currently using more than 4 drops of artificial tears per day in each eye, or if they are pregnant or breast feeding.[8] If subjects are currently using artificial tears, they will be required to refrain from using them for at least 24 hours before their baseline visit, and they will only be allowed to use Systane Hydration during the study.

Surveys and Clinical Tests

This will be a prospective, investigator-masked clinical trial, which will be registered with ClinicalTrials.gov. Subjects who meet all study criteria will be enrolled into the study. The contents of the drops will be concealed from the subjects. Clinical measurement will be obtained from both eyes of each subject and testing will be performed in the below order. Testing order was designed to sequentially administered the least invasive to most invasive test. This methodology will ensure that a previous procedure will have a minimal effect on all subsequent assessments.[9] Subject will be asked to bring their spectacles to the study visit and to adhere to the contact lens exclusion factors described above throughout the study.

Visit 1

1. Subject History, Eligibility, Informed Consent: Subjects will be asked to complete a screening survey at the first study visit to verify that they are eligible for the study. All relevant ocular, systemic, and surgical history will be gathered via a questionnaire developed by the investigators. This questionnaire will also ask about digital device usage and eye comfort while using digital devices. The subjects will complete the OSDI questionnaire, and they will be required to have a score between 13 and 32 (inclusive). The subject will be asked to complete the Work IDEEL, and they will be required to have a score ≤80. Non-eligible subjects will be dismissed at this time or rescheduled depending upon the reason for ineligibility. Eligible subjects will be enrolled, consented, and requested to sign a privacy document.

2. Impact of Dry Eye on Daily Life (IDEEL) questionnaire: The full Impact on Daily Life segment of the IDEEL questionnaire will be self-administered electronically to understand how quality of life and common daily activities are affected by eye comfort (e.g., computer work, near work).[10]

3. Visual Acuity: The subject's visual acuity will be measured with a Bailey-Lovie high-contrast (logMAR) chart or equivalent. If the patient is unable to read the 20/40 letters (0.3 logMAR), the investigator will pinhole over the patient's unaided or presenting refractive error correction to determine the subject's visual potential.

4. Slit-Lamp Biomicroscopy: The investigator will use a slit-lamp biomicroscope to document normal and/or remarkable findings of the anterior eye structures: eyelashes (blepharitis), eyelids, conjunctiva, and cornea. Eyelids will be graded based upon a grading scale that was developed by the investigators.

5. Subject Randomization: The examiner will use an electronic randomization system to place the subject in the Systane Hydration Multi-Dose group or the Systane Hydration Unit-Dose group. Subjects will be required to use their allocated drop two to four times per day in each eye.

6. Subject Compliance: Subjects will be given a daily log to record the time and number of drops used each day; these data will be used to determine drop compliance for each dispensing method. They will also be asked to record the duration and type of digital device use each day.

Visit 2

1. Testing: Subjects will be asked to repeat the IDEEL and clinical tests described above at this visit. The compliance log will likewise be collected at this visit and a new one will be given.

2. Drop Application Satisfaction Survey: An investigator developed survey will be created based upon the glaucoma literature to understand patient satisfaction related to applying Systane Hydration via the Unit-Dose and Multi-Dose options.

3. Subject Crossover: Subjects will be switched to the opposite treatment group. No washout period will be needed because all subjects will be using Systane Hydration; they will just be applying the drop via the alterative dispensing method for the second week of the study. Subjects will be required to use their allocated drop two to four times per day in each eye.

Visit 3

1. Testing: Subjects will be asked to repeat the IDEEL and clinical tests described above at this visit. The compliance log will likewise be collected at this visit.

2. Drop Application Satisfaction Survey: An investigator developed survey will be created based upon the glaucoma literature to understand patient satisfaction related to applying Systane Hydration via the Unit-Dose and Multi-Dose options.

3. Study Completion: The examiner will reveal the study details to the subjects (Systane Hydration PF). The subject will be compensated for their time, and they will be released from the study at this time.

Data Management & Analysis

Surveys and all data will be collected via a secured web service (REDCap) at the time of the study visit. Gerald McGwin, Jr, MS, PhD, Professor and Vice Chairman in the Department of Epidemiology at the University of Alabama at Birmingham, will perform the statistical analyses. All data will be analyzed with SAS Version 9.4 (SAS; Cary, NC, USA). ANOVA, T-tests, and chi-square tests will be used when comparing variables. If the assumptions of these tests cannot be met suitable alternative statistical tests (e.g., Wilcoxon Rank Sum Test, Fisher's Exact Test) will be used instead. The questionnaire data will furthermore be presented in a table that will describe the frequency by which each subject indicated each questionnaire response.

Training of Study Personnel

Prior to enrolling any subjects all clinical examiners will participate in a meeting run by Dr. Pucker. This full investigator meeting will ensure that all study investigators are performing the procedures in the same manner.

Data from each investigator's first subject will also be monitored for quality control before sites are allowed to enroll additional subjects.

IV. Study Timeline

	2021	2021	2021	2021	2021
	Mar	Apr	May	Jun	Jul
Activity					
Contracting	■	■			
IRB Preparation	■	■			
Data Collection			■	■	
Data Analysis				■	■
Final Study Report					■

V. Publication Plans

An abstract evaluating the effects of Systane Hydration PF on ocular comfort and quality of life will be submitted to the Global Specialty Lens Symposium 2022. A summary of this work will be submitted as a manuscript to *Contact Lens & Anterior Eye*.

VI. Conclusions

This project will provide some of the first data related to the quality of life of patients who have DES who are heavy digital device users. It will likewise provide insights into to the usefulness of Systane Hydration PF in patients who have DES, and it will provide some of the first guidance related to dosing methods of dry eye treatments. Ultimately, after completion of this study, clinicians will have a better understanding of the symptomatology surrounding DES and how Systane Hydration PF affects these symptoms.

VII. References

1. Sheppard AL, Wolffsohn JS. Digital eye strain: prevalence, measurement and amelioration. *BMJ Open Ophthalmol* 2018;3:e000146.
2. Coles-Brennan C, Sulley A, Young G. Management of digital eye strain. *Clin Exp Optom* 2019;102:18-29.
3. Paulsen AJ, Cruickshanks KJ, Fischer ME, et al. Dry eye in the beaver dam offspring study: prevalence, risk factors, and health-related quality of life. *Am J Ophthalmol* 2014;157:799-806.
4. Meyer D, Rickert M, Kollbaum P. Ocular symptoms associated with digital device use in contact lens and non-contact lens groups. *Contact lens & anterior eye : the journal of the British Contact Lens Association* 2021;44:42-50.
5. Pouyeh B, Viteri E, Feuer W, et al. Impact of ocular surface symptoms on quality of life in a United States veterans affairs population. *Am J Ophthalmol* 2012;153:1061-1066 e1063.
6. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. *Arch Ophthalmol* 2000;118:615-621.
7. Dougherty BE, Nichols JJ, Nichols KK. Rasch analysis of the Ocular Surface Disease Index (OSDI). *Investigative ophthalmology & visual science* 2011;52:8630-8635.
8. Sullivan BD, Crews LA, Sonmez B, et al. Clinical utility of objective tests for dry eye disease: variability over time and implications for clinical trials and disease management. *Cornea* 2012;31:1000-1008.
9. Bron AJ, Evans VE, Smith JA. Grading of corneal and conjunctival staining in the context of other dry eye tests. *Cornea* 2003;22:640-650.
10. Fairchild CJ, Chalmers RL, Begley CG. Clinically important difference in dry eye: change in IDEEL-symptom bother. *Optom Vis Sci* 2008;85:699-707.