# EVALUATING DRY EYE SYNDROME: THE CORRELATIONS OF PHENOL RED THREAD TEST, TEAR BREAK UP TIME, AND OCULAR SURFACE DISEASE INDEX $^{\odot}$ QUESTIONNAIRES

by

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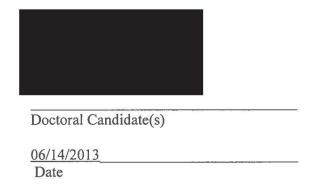
by Cory A Grifka Has been approved May, 2013 APPROVED: , Faculty Advisor ACCEPTED:

Faculty Course Supervisor

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### The Correlation Between Dry Eye Symptoms, Tear Break Up Time, and Aqueous Tear Volume.

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#### **ABSTRACT**

Background: Many tests are commonly used to assess dry eye syndrome. However, their correlation is not always known. As the U.S. population ages, more people will suffer from dry eye symptoms each year. The purpose of this study is to explore the correlations of dry eye symptom surveys with a patient's tear break up time (TBUT) and phenol red thread test (PRTT) results. Methods: The study involved 20 patients. Both males and females were included. Each patient was given an Ocular Surface Disease Index (OSDI<sup>©</sup>) questionnaire with scoring in several categories. Their tear break up time was measured with fluorescein dye and cobalt blue filtered light. Also, the patient's phenol red thread test values were measured. OSDI<sup>©</sup> scores, tear break up time results, and phenol red thread test results were correlated. Results: The study did not find statistically significant correlations among OSDI<sup>©</sup> questionnaires, phenol red thread test values, and tear break up times. However, data trends did show that the patients in the study who had shorter tear break up times tended to have more severe OSDI<sup>©</sup> scores. The relationship between OSDI<sup>©</sup> severity and gender was statistically significant. Females recorded higher OSDI<sup>©</sup> scores. Conclusions: Dry eye disease is a commonly researched topic. Many authors have sought to find correlations among dry eye evaluations. While many studies struggle to find significant correlations among dry eye tests, the value in diagnosing and managing ocular surface disease for patients should not be undervalued.

#### **ACKNOWLEDGEMENTS**

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#### INTRODUCTION

The ocular surface is a delicate interface requiring constant, balanced, healthy coverage by the eye's tear film. The tear film itself, composed of a mucin layer, an aqueous layer, and a lipid layer, must remain in balance in order to avoid the condition known as dry eye syndrome. Many issues may contribute to the formation of dry eye syndrome. Vitamin and mucin deficiencies, decreased aqueous production from inflammation or destruction of lacrimal gland tissue, environmental factors, and variability in meibomian gland function remain prominent causes of the various types of dry eye. Even if each layer is intact and balanced, the upper and lower lids must appose and close correctly in order to maintain a smooth and constant tear film. Also, patients present clinically with varying severity of dry eye syndrome. While the severity of signs commonly correlates with the severity of symptoms, many with a mild clinical picture will report severe symptoms and vice versa.

Currently, millions of people suffer from dry eye on a daily basis. As the U.S. population ages, more people will suffer from its symptoms each year. As a result, today's physicians are faced with the challenge of collecting and analyzing clinical data that may or may not provide a clear insight into the patient's status. Various tests and surveys exist to help guide the physician. However, not all tests and surveys are widely available clinically, and some remain largely too expensive for general ophthalmological practice. Also, many remain purely theoretical. Physicians who routinely diagnose and treat dry eye syndrome may find the practice straight-forward. However, the question still remains of which tests provide the best, repeatable information that helps the physician confidently manage each patient. The purpose of this study is to explore the

correlations of dry eye symptom surveys and a patient's tear break up time (TBUT) and phenol red thread test (PRTT) results. These tests are explored because they are widely used and inexpensive. Also, they provide information that allows the physician to better understand patient symptoms and the state of the aqueous and lipid tear layers.

#### **METHODS**

Twenty patients, both male and female, were examined between the dates of July 2013 and January 2014. Patients were selected based on willingness to contribute to dry eye research, whether or not they had clinically reported complaints of dry eyes. All testing was performed in one examination, and each patient encounter involved the same researcher.

#### Ocular Surface Disease Index<sup>©</sup> (OSDI<sup>©</sup>) Questionnaire

After receiving consent, each patient was then presented with an OSDI<sup>©</sup> questionnaire. The questionnaire was explained, and the patient was prompted to accurately account their recent dry eye symptoms. Three sections appeared on the OSDI<sup>©</sup> questionnaire. Section one contained five questions which related to dry eye symptoms in the last week. The section stated, "Have you experienced any of the following during the last week?" Symptoms included sensitivity to light, grittiness, painful and sore eyes, blurred vision, and poor vision. Patients rated each symptom on a scale of zero to four. Zero corresponded with "none of the time." One corresponded with "some of the time." Two corresponded with "half of the time." Three corresponded with "most of the time." Four corresponded with "all of the time." "Not applicable" was an available answer if the

patient felt the question did not apply to them. Severity was ranked on the same scale throughout all sections.

Section two contained four questions which related to quality of life. The section stated, "Have problems with your eyes limited you in performing any of the following during the last week?" Quality of life measures included reading, driving at night, working on a computer or bank machine, and watching television.

Section three contained three questions that also related to symptoms. The section stated, "Have your eyes felt uncomfortable in any of the following situations during the last week?" Situations included windy conditions, places or areas with low humidity, and areas that were air conditioned. Following completion of the questionnaire, patient responses and total number of questions answered were totaled. The OSDI<sup>©</sup> value was then calculated as seen in **Figure 1** below.

$$OSDI^{\circ} score = \underbrace{(sum \ of \ scores) \ x \ 25}_{(number \ of \ questions \ answered)}$$

Figure 1. Calculation of OSDI<sup>©</sup> score.

After calculation of each patient's OSDI<sup>©</sup> score, they were categorized into one of four groups. An OSDI<sup>©</sup> score of zero to twelve equaled normal severity. Thirteen to twenty two equaled mild severity. Twenty three to thirty two equaled moderate severity. Thirty three to one hundred was considered severe. OSDI<sup>©</sup> scores were rounded to the nearest whole number.

#### Phenol Red Thread Test

Following administration of the OSDI<sup>©</sup> questionnaire, each patient's tear volume was tested using a Zone-Quick phenol red thread test (Menicon America, San Mateo, CA, USA). Zone-Quick cotton thread is treated with a pH indicator called phenol red. As the thread absorbs tears in the conjunctival sac, it begins to turn from yellow to red. Each test contains two sterilized threads.

The lip of the thread was placed on the lower lid approximately one third of the distance from the lateral canthus with the eye open in primary position. The thread avoided the cornea. Following 15 seconds of contact with the eye, the thread was removed, and the length of wetting was measured using the Zone-Quick packaging scale. Measurements were made to the nearest millimeter (mm). The test was performed on both of the patient's eyes, and in each case, results were averaged to a final value.

#### Tear Break Up Time

Tear break up time was measured last to avoid errors in phenol red thread test measurements. Using BioGlo fluorescein sodium ophthalmic strips (HUB Pharmaceuticals LLC, Rancho Cucamonga, CA, USA), each patient's tear break up time was calculated in both eyes. Sterile saline was used to wet each BioGlo strip, and fluorescein was instilled by lightly touching the inferior palpebral conjunctiva. Using a slit lamp and diffuse cobalt blue light, each patient was instructed to blink normally and then hold their eyes open for as long as possible. Tear break up time was recorded when the first evidence of fluorescein breakup was found. Measurements were made to the nearest second (sec). The test was performed on both of the patient's eyes, and in each case, results were averaged to a final value.

#### **RESULTS**

#### Correlation Between OSDI® Severity and Gender

Using a T-test to compare OSDI<sup>©</sup> severity between males and females, the value differences were found to be statistically significant. In the study, females had statistically significant higher OSDI<sup>©</sup> severity. **Figure 2** shows the group statistics for gender breakdown. **Figure 3** shows the gender based T-test results.

	Group Statistics							
Gende	er	N	N Mean		Std. Error Mean			
00001/61	Male	6	11.1111	10.26275	4.18975			
OSDI Value	Female	14	34.2758	21.84442	5.83817			
PRTT OD (mm)	Male	6	22.00	7.616	3.109			
	Female	14	27.07	8.426	2.252			
PRTT OS (mm)	Male	6	22.17	6.646	2.713			
PKTT OS (IIIII)	Female	14	27.64	8.635	2.308			
Average PRTT	Male	6	22.083	6.4375	2.6281			
Value (mm)	Female	14	27.357	8.3030	2.2191			
TBUT OD (sec)	Male	6	7.17	3.251	1.327			
TBOT OD (sec)	Female	14	6.86	2.538	.678			
TBUT OS (sec)	Male	6	7.00	2.530	1.033			
IBOTOS (Sec)	Female	14	6.50	2.378	.635			
Average TBUT	Male	6	7.083	2.8003	1.1432			
(sec)	Female	14	6.679	2.4068	.6432			

Figure 2. Group statistics for OSDI<sup>©</sup>, phenol red thread test, and tear break up time values..

		In	depende	nt Samp	les Test					
		Levene's T Equality of V		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2~	Mean	Std. Error	95% Confide of the Dif	
						tailed)	Difference	Difference	Low er	Upper
	Equal variances assumed	2.026	.172	-2.455	18	.024	-23.16468	9.43506	-42.98702	-3.34235
OSDI Value	Equal variances not assumed			-3.224	17.660	.005	-23.16468	7.18597	-38.28272	-8.04664
PRTT OD (mm)	Equal variances assumed	.047	.830	-1.266	18	.222	-5.071	4.005	-13.487	3.344
	Equal variances not assumed			-1.321	10.510	.215	-5.071	3.839	-13.569	3.426
PRTT OS (mm)	Equal variances assumed	.678	.421	-1.380	18	.184	-5.476	3.968	-13.812	2.859
	Equal variances not assumed			-1.537	12.363	.149	-5.476	3.562	-13.212	2.259
Average PRTT	Equal variances assumed	.430	.520	-1.380	18	.184	-5.2738	3.8204	-13.3002	2.7526
(mm)	Equal variances not assumed			-1.533	12.272	.151	-5.2738	3.4397	-12.7498	2.2022
	Equal variances assumed	1.485	.239	.230	18	.820	.310	1.344	-2.514	3.133
TBUT OD (sec)	Equal variances not assumed			.208	7.750	.841	.310	1.490	-3.147	3.766
	Equal variances assumed	0.000	1.000	.423	18	.677	.500	1.181	-1.982	2.982
TBUT OS (sec)	Equal variances not assumed			.412	9.006	.690	.500	1.213	-2.243	3.243
Average TBUT	Equal variances assumed	.511	.484	.329	18	.746	.4048	1.2307	-2.1809	2.9904
(sec)	Equal variances not assumed			.309	8.345	.765	.4048	1.3118	-2.5985	3.4080

**Figure 3.** Gender based T-test results: Results show a statistically significant difference in OSDI<sup>©</sup> values between males and females.

#### Correlation Between OSDI<sup>©</sup> Severity and Phenol Red Thread Test Values

Using a Levene's test, a one-way ANOVA test, and pairwise comparisons, the correlation between OSDI<sup>©</sup> severity and the phenol red thread test was calculated. The results can be seen in **Figure 4**, **Figure 5**, **Figure 6**, **Figure 7**, and **Figure 8**. Data analysis did not show a statistically significant correlation between OSDI<sup>©</sup> severity and phenol red thread tests. Possible reasons for lack of statistical significance are included in the discussion and conclusion.

Descriptive Statistics									
Dependent Variable: Average PRTT (mm)									
OSDI Group Mean Deviation									
Normal	24.583	5.5174	6						
Mild	29.000	3.6056	3						
Moderate	20.800	6.0270	5						
Severe	29.500	11.4018	6						
Total	25.775	8.0139	20						

Figure 4. Descriptive statistics using average phenol red thread test value as the dependent variable.

Levene's Test of Equality of Error Variances <sup>a</sup>							
Dependent Variable: Average PRTT (mm)							
F	df1	df2	Sig.				
4.166	3	16	.023				

Figure 5. Levene's test of equality of error variances using average phenol red thread test value as the dependent variable: The test shows that equal variances may not be assumed.

Tests of Between-Subjects Effects								
Dependent Variable:	Average PRT	Γ(mm)						
Source	Type III Sum of Squares	df	Mean Square	F	Sig.			
Corrected Model	246.729 <sup>a</sup>	3	82.243	1.352	.293			
Intercept	12452.016	1	12452.016	204.654	.000			
OSDI SEVERITY 2	246.729	3	82.243	1.352	.293			
Error	973.508	16	60.844					
Total	14507.250	20	or	aat hokulaa shaabiin miiq ar asuuri Juliyaa hujiin isan kaabaadiin bii 💽 ra				
Corrected Total	1220.238	19	Si i prophosuli signi sani, metavito krahvanji bi quomingli ti detti razbiorniji. Si	and a second POPPER transaction on the control of t				

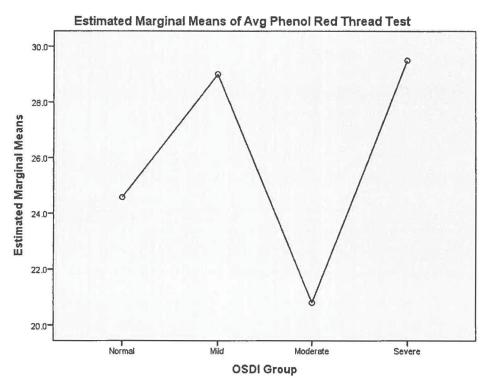
a. R Squared = .202 (Adjusted R Squared = .053)

Figure 6. One-way ANOVA analysis of OSDI<sup>©</sup> severity and phenol red thread test values: Analysis shows no statistically significant difference among the OSDI<sup>©</sup> groups.

		Pairwise (	Comparisons			
Dependent Variable	e: Average Pl	RTT (mm)				
		Mean			(00000) P/65 (BCO)-00000	dence Interval fference
(I) OSDI Group		Difference (I-J)	Std. Error	Sig.ª	Lower Bound	Upper Bound
Normal	Mild	-4.417	5.516	.435	-16.109	7.276
	Moderate	3.783	4.723	.435	-6.230	13.796
	Severe	-4.917	4.503	.291	-14.464	4.630
Mild	Nomal	4.417	5.516	.435	-7.276	16.109
	Moderate	8.200	5.697	.169	-3.876	20.276
	Severe	500	5.516	.929	-12.193	11.193
Moderate	Normal	-3.783	4.723	.435	-13.796	6.230
	Mild	-8.200	5.697	.169	-20.276	3.876
	Severe	-8.700	4.723	.084	-18.713	1.313
Severe	Normal	4.917	4.503	.291	-4.630	14.464
	Mild	.500	5.516	.929	-11.193	12.193
	Moderate	8.700	4.723	.084	-1.313	18.713

Figure 7. Pairwise comparison values showing no statistically significant difference among OSDI<sup>©</sup> severity groups.

a. Adjustment for multiple comparisons: Least Significant Difference (equivalent to no



**Figure 8.** Estimated marginal means of average phenol red thread test values (mm): Analysis showed no statistically significant difference among the OSDI<sup>©</sup> severity groups.

#### Correlation Between OSDI® Severity and Tear Break Up Time

Using a Levene's test, a one-way ANOVA test, and pairwise comparisons, the correlation between OSDI<sup>©</sup> severity and tear break up time was calculated. The results can be seen in Figure 9, Figure 10, Figure 11, Figure 12, and Figure 13. Data analysis did not show a statistically significant correlation between OSDI<sup>©</sup> severity and tear break up time. Possible reasons for lack of statistical significance are included in the discussion and conclusion. However, when observing the overall trend in data, it can be seen that in this study, the patients' OSDI<sup>©</sup> severities and tear break up time values did correlate, just not in a statistically significant manner.

Des	criptive Stati	istics	
Dependent Variable:	Average TB	UT (sec)	
OSDI Group	Mean	Std. Deviation	N
Normal	7.917	2.4170	6
Mild	8.500	2.1794	3
Moderate	6.100	2.5100	5
Severe	5.417	2.0595	6
Total	6.800	2.4623	20

Figure 9. Descriptive statistics using average tear break up time as the dependent variable.

Levene's Test of Equality of Error Variances <sup>a</sup> Dependent Variable: Average TBUT (sec)							
.377	3	16	.771				

Figure 10. Levene's test of equality of error variances using average tear break up time as the dependent variable: The test shows that equal variances may be assumed.

	Tests of Between-Subjects Effects								
Dependent Variable:	Average TBL	JT (sec)							
Source	Type III Sum of Squares	df	Mean Square	F	Sig.				
Corrected Model	30.083 <sup>a</sup>	3	10.028	1.885	.173				
Intercept	900.313	1	900.313	169.238	.000				
OSDISEVERITY2	30.083	3	10.028	1.885	.173				
Error	85.117	16	5.320	per Pauling I who are also the control per 2 are 1 to 2 persons (supply 1911 C.).	Na maranga jaraha (gasiN, gargas) (Nil Jara (1995) (1995)				
Total	1040.000	20							
Corrected Total	115.200	19	( A Albertina - Land Albertina - Albertina	and the state of t	comment of grand and a Profile of the State				

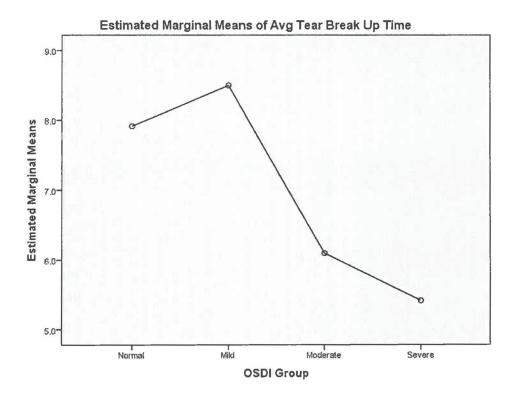
**Figure 11.** One-way ANOVA analysis of  $OSDI^{\mathbb{O}}$  severity and tear break up time: Analysis shows no statistically significant difference among the  $OSDI^{\mathbb{O}}$  severity groups.

		Pairwise C	omparisons			
Dependent Variab	le: Average T	BUT (sec)	- United			
(I) OSDI Group		Mean Difference (I-J)	Std. Error	Sig.ª	95% Cor Interval for I Lower Bound	
Normal	Mild	583	1.631	.725	-4.041	2.874
	Moderate	1.817	1.397	.212	-1.144	4.777
	Severe	2.500	1.332	.079	323	5.323
Mild	Normal	.583	1.631	.725	-2.874	4.041
	Moderate	2.400	1.684	.173	-1.171	5.971
	Severe	3.083	1.631	.077	374	6.541
Moderate	Normal	-1.817	1.397	.212	-4.777	1.144
	Mild	-2.400	1.684	.173	-5.971	1.171
	Severe	.683	1.397	.631	-2.277	3.644
Severe	Normal	-2.500	1.332	.079	-5.323	.323
	Mild	-3.083	1.631	.077	-6.541	.374
	Moderate	683	1.397	.631	-3.644	2.277

Figure 12. Pairwise comparison values showing no statistically significant difference among OSDI<sup>©</sup> severity groups.

Based on estimated marginal means

a. Adjustment for multiple comparisons: Least Significant Difference (equivalent to no adjustments).



**Figure 13.** Estimated marginal means of average tear break up time (sec): Analysis showed no statistically significant difference among the OSDI<sup>©</sup> severity groups.

## Correlations Among OSDI<sup>©</sup> Severities, Phenol Red Thread Test Values, and Tear Break Up Times

Using Box's test, a MANOVA test, and pairwise comparisons, the correlations among OSDI<sup>©</sup> severities, phenol red thread test values, and tear break up times were analyzed. The results can be seen in **Figure 14**, **Figure 15**, **Figure 16**, and **Figure 17**. Data analysis did not show a statistically significant correlation among the three tests simultaneously. Possible reasons for lack of statistical significance are included in the discussion and conclusion.

OSDI Group		Mean	Std. Deviation	N	
Average PRTT Values (mm)	Normal	24.583	5.5174	6	
	Mild	29.000	3.6056	3	
	Moderate	20.800	6.0270	5	
	Severe	29.500	11.4018	6	
	Total	25.775	8.0139	20	
Average TBUT (sec)	Normal	7.917	2.4170	6	
	Mild	8.500	2.1794	3	
	Moderate	6.100	2.5100	5	
	Severe	5.417	2.0595	6	
	Total	6.800	2.4623	20	

Figure 14. Descriptive statistics of average phenol red thread test values and average tear break up times.

Box's Test of Equality of Covariance Matrices <sup>a</sup>				
Box's M	9.774			
F	.786			
df1	9			
df2	617.561			
Sig.	.630			

Figure 15. Box's test of equality of covariance showing equal covariances.

Multivariate Tests <sup>a</sup>						
Effect		Value	F	Hypothesis df	Error df	Sig.
Intercept	Pillai's Trace	.949	140.738 <sup>b</sup>	2.000	15.000	.000
	Wilks' Lambda	.051	140.738 <sup>b</sup>	2.000	15.000	.000
	Hotelling's Trace	18.765	140.738 <sup>b</sup>	2.000	15.000	.000
	Roy's Largest Root	18.765	140.738 <sup>b</sup>	2.000	15.000	.000
OSDISEVERITY2	Pillai's Trace	.483	1.699	6.000	32.000	.153
	Wilks' Lambda	.571	1.616 <sup>b</sup>	6.000	30.000	.177
	Hotelling's Trace	.656	1.530	6.000	28.000	.205
	Roy's Largest Root	.439	2.341°	3.000	16.000	.112

a. Design: Intercept + OSDISEVERITY2

Figure 16. MANOVA multivariate test analysis shows no statistically significant difference among the OSDI<sup>©</sup> groups, phenol red thread test values, and tear break up time.

Tests of Between-Subjects Effects						
Source		Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	Average PRTT (mm)	246.729 <sup>8</sup>	3	82.243	1.352	.293
	Average TBUT (sec)	30.083 <sup>b</sup>	3	10.028	1.885	.173
Intercept	Average PRTT (mm)	12452.016	1	12452.016	204.654	.000
	Average TBUT (sec)	900.313	1	900.313	169.238	.000
OSDISEVERITY 2	Average PRTT (mm)	246.729	3	82.243	1.352	.293
	Average TBUT (sec)	30.083	3	10.028	1.885	.173
Error	Average PRTT (mm)	973.508	16	60.844		
	Average TBUT (sec)	85.117	16	5.320		
Total	Average PRTT (mm)	14507.250	20			
	Average TBUT (sec)	1040.000	20	Committee of the second se	ar commenter and the same and a same and	
Corrected Total	Average PRTT (mm)	1220.238	19	par naj ca Pract Aff supplemental meta mej er auch period 🕻 er a		
	Average TBUT (sec)	115.200	19		The experimental and the second section of the ex-	

a. R Squared = .202 (Adjusted R Squared = .053)

Figure 17. Tests of between-subjects effects analysis shows no statistically significant difference among the OSDI<sup>©</sup> groups, phenol red thread test values, and tear break up time.

b. Exact statistic

c. The statistic is an upper bound on F that yields a lower bound on the significance level.

b. R Squared = .261 (Adjusted R Squared = .123)

#### **DISCUSSION**

The results of the study did not show a statistically significant correlation between OSDI<sup>©</sup> severity and either phenol red thread test values or tear break up time. Also, through MANOVA analysis, there was no statistically significant correlation among all three tests simultaneously. However, the difference in OSDI<sup>©</sup> severity between males and females was found to be statistically significant. This statistically significant correlation was also discovered in a 2013 study by Schaumberg et al.<sup>1</sup>

As discussed, some variables may have contributed to the study's findings.

Research would have benefited from a larger sample size. In addition, the ANOVA calculations would have been more accurate if the sample size for each OSDI® severity category was the same. Other factors also influenced the results of the study. If it is believed that a patient has dry eye syndrome, the physician must decipher between two major common causes. These major causes include aqueous deficient dry eye and lipid deficient dry eye. Through examination results, the patients in this study who reported OSDI® complaints suffered mainly from lipid deficient dry eye. This factor played a role in the calculation of OSDI® severity versus phenol red thread test correlations. It also explains why when observing the overall trend in data, OSDI® severity and tear break up time values clearly correlated, although not in a statistically significant way. To better study these correlations in the future, different populations of patients should be identified who have either aqueous deficient dry eye or lipid deficient dry eye. Then, these populations should be studied separately to examine their OSDI® score, phenol red thread test, and tear break up time correlations.

#### Other Studies Exploring Dry Eye Syndrome Analysis

The challenge and diverse nature of dry eye syndrome has led to numerous other studies exploring its prevalence, analysis, and treatment. Dry eye syndrome is very common in today's population. A 2013 study by Hashemi et al showed the prevalence of dry eye syndrome to be 8.7%. Abnormal Schirmer scores were found in 17.8% of the population, and abnormal TBUT measurements were found in 34.2% of the population. An average of 18.3% of the population had symptoms according to OSDI® scores. This study showed how common this chronic disease is, as well as how varied symptoms versus clinical signs can be.<sup>2</sup>

So, the dilemma continues as to which tests clinicians should use to better evaluate patients. A 2009 study by Moore et al explored which dry eye tests correlated with each other as reliable indicators of dry eye syndrome. It found that statistically, only measures of meibomian gland dysfunction, reduced TBUT, and their use of McMonnie's dry eye questionnaire to be correlated. They suggested that these tests be used to evaluate dry eye syndrome. This study did not involve the OSDI<sup>©</sup> survey currently in question.<sup>3</sup> It should be noted, however, that similar to the Moore et al study, the tests that best correlated in this paper's research included symptom surveys and tear break up time.

Studies by Cuevas et al, Nichols et al, and various others have shown a lack of association between dry eye symptoms and signs. Senchyna and Wax also demonstrated that clinical dry eye measurements, as well as symptoms and signs, did not correlate well. These studies align with the results found when exploring OSDI severity, phenol red threat test results, and tear break up time. Senchyna and Wax also

demonstrated that the phenol red thread test was nearly the most accurate in evaluating tear production, second only to fluorophotometry.<sup>6</sup>

A journal article review of current dry eye research reveals that the ophthalmologic world is teeming with continued research into dry eye syndrome.

Numerous studies show the difficulty in associating dry eye symptoms, signs, and clinical assessments. Research has even shown differences in male to female symptoms and signs. However, it should be noted that expensive clinical equipment and tests are not needed to accurately manage patients with dry eye syndrome. Questionnaires can divulge symptoms that the patient did not think to mention in their history. Tear break up time with fluorescein is an accurate indicator of the state of the tear film's lipid layer. Phenol red thread test, as mentioned above, is second only to fluorophotometry in the accurate evaluation of tear production. Using these tests, an experienced clinician can identify types of dry eye syndrome and treat accordingly.

#### Importance of Dry Eye Syndrome Management

The correct management of dry eye disease is important for a patient's well being. However, a 2013 study by Uchino et al showed that dry eye disease also has the ability to cause an economic impact. The study showed that dry eye disease significantly impacted workplace productivity in populations who frequently used video display terminals. Productivity measures showed up to a 4.82% loss in those with definitive dry eye disease, which could cost companies an estimated \$6,160 annually per employee.

Economic effects and patient symptoms aside, ocular surface disease can have a significant impact on a patient's quality of life. This is an unfortunate effect if the patient is left unmanaged. A 2010 study by Friedman showed that using quality of life measures

before and after dry eye treatment helped to better benefit the patient population. Van Landingham et al demonstrated that while dry eye did not impair reading speed, it was associated with self-reported reading difficulty and the avoidance of newsprint in elderly populations. A 2013 study by Deschamps et al even showed that dry eye disease had a negative impact on driving performance and quality of life through its degradation of optical quality. Patients had significant decreases in response time compared to their age and gender-matched controls.

#### CONCLUSIONS

The study did not find statistically significant correlations among OSDI<sup>©</sup> questionnaires, phenol red thread test values, and tear break up time. However, data trends do show that the patients in the study who had shorter tear break up times tended to have more severe OSDI<sup>©</sup> scores. Also, correlations between OSDI<sup>©</sup> severity and gender were statistically significant, thus confirming research by Schaumberg et al. More research is needed to further establish the significance of dry eye test correlation. Larger sample sizes, as well as patient samples who are split into aqueous deficient versus lipid deficient groups, would further research in a positive direction. However, as mentioned, simple and inexpensive tests paired with physician experience can accurately and repeatable provide adequate information to diagnose and treat patients.

The chronic nature of dry eye syndrome, coupled with the fact that more people suffer from the disease each year, makes dry eye a frequently researched topic. Every month, new articles are published exploring test correlations and the value in diagnosing and treating dry eye syndrome. Previous studies have shown that tear break up time and

phenol red thread tests are accurate ways of diagnosing dry eye syndrome. However, until more research is published establishing clinical test correlations to patient symptoms, physicians should use whichever tests they feel necessary to best form a clinical diagnosis in suspected dry eye patients. Some may find simple tests exploring aqueous volume and lipid uniformity to be a solid and cost effective way to manage patients. Others may use more sophisticated methods such as tear osmolarity and fluorophotometry to provide more comprehensive clinical pictures. While little may be certain in today's research of dry eye, it can be said that the ophthalmological advancements and ongoing research serve to establish an excellent prognosis for future treatment of ocular surface disease.

#### REFERENCES

- Schaumberg DA, Uchino M, Christen WG, Semba RD, Buring JE, Li JZ. Patient reported differences in dry eye disease between men and women: impact, management, and patient satisfaction. *PLoS ONE* [Internet]. 2013 Sep 30 [cited 2014 Feb 10];8(9):1-11. doi: 10.1371/journal.pone.0076121
- Hashemi H, Khabazkhoob M, Kheirkhah A, Emamian MH, Mehravaran S, Shariati M, Fotouhi A. Prevalence of dry eye syndrome in an adult population. *Clin Exp Ophthalmol* [Internet]. 2013 Jul 15 [cited 2014 Feb 1];1:1-7. doi: 10.1111/ceo.12183
- Moore JE, Graham JE, Goodall EA, Dartt DA, Leccisotti A, McGilligan VE, Moore TCB. Concordance between common dry eye diagnostic tests. *Brit J Ophthalmol* [Internet]. 2008 Sep 9 [cited 2014 Feb 1];93:66-72. doi: 10.1136/bjo.2007.131722
- 4. Cuevas M, Gonzalez-Garcia MJ, Castellanos E, Quispaya R, Parra P, Fernandez I, Calonge M. Correlations among symptoms, signs, and clinical tests in evaporative-type dry eye disease caused by meibomian gland dysfunction. *Curr Eye Res* [Internet]. 2012 Apr 3 [cited 2014 Feb 10];37(10):855-63. doi: 10.3109/02713683.2012.683508
- 5. Nichols KK, Nichols JJ, Mitchell GL. The lack of association between signs and symptoms in patients with dry eye disease. *Cornea* [Internet]. 2004 Apr 20 [cited

- 2014 Feb 10];23(8):762-70. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15502475
- Senchyna M, Wax MB. Quantitative assessment of tear production: a review of methods and utility in dry eye drug discovery. *J Ocul Biol Dis Infor* [Internet].
   2008 Mar [cited 2014 Feb 10];1(1):1-6. doi: 10.1007/s12177-008-9006-2
- Uchino M, Uchino Y, Dogru M, Kawashima M, Yokoi N, Komuro A, Sonomura Y, Kato H, Kinoshita S, Schaumberg DA, Tsubota K. Dry eye disease and work productivity loss in visual display users: the Osaka study. *Am J Ophthalmol* [Internet]. 2013 Nov 1 [cited 2014 Feb10];157(2):294-300. doi: 10.1016/j.ajo.2013.10.014
- Friedman NJ. Impact of dry eye disease and treatment on quality of life. Curr
   Opin Ophthalmol [Internet]. 2010 [cited 2014 Feb 10];21:310-16. doi:
   10.1097/ICU.0b013e32833a8c15
- Van Landingham SW, West SK, Akpek EK, Munoz B, Ramulu PY. Impact of dry
  eye on reading in a population based sample of the elderly: the Salisbury Eye
  Evaluation. *Brit J Ophthalmol* [Internet]. 2013 Oct 11 [cited 2014 Feb 10];0:1-6.
  doi: 10.1136/bjophthalmol-2013-303518
- 10. Deschamps N, Ricaud X, Rabut G, Labbe A, Baudouin C, Denoyer A. The impact of dry eye disease on visual performance while driving. *Am J Ophthalmol* [Internet]. 2013 [cited 2014 Feb 10];156:184-9. doi: 10.1016/j.ajo.2013.02.019