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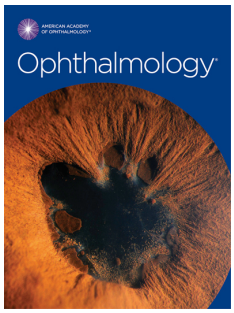

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Running head: Association of Dry Eye Severity with Work Productivity

Key words: Dry eye disease, economic impact, work productivity

This article contains additional online-only material. The following should appear (available at www.aaojournal.org): Credit Roster.

Abbreviations

DREAM is Dry Eye Assessment and Management

DED is dry eye disease

OSDI is Ocular Surface Disease Index

GEE is generalized estimating equations

TBUT is tear break-up time

WPAI is Work Productivity and Activity Impairment

ABSTRACT

Purpose: To evaluate the association of dry eye disease (DED) severity with work productivity and activity impairment.

Design: Longitudinal observational study within a randomized clinical trial.

Participants: People with moderate to severe dry eye disease who enrolled in the multicenter Dry Eye Assessment and Management (DREAM) study.

Methods: Participants completed the Work Productivity and Activity Impairment questionnaire at 0, 6, and 12 months and were assessed in parallel for symptoms and signs (conjunctival and corneal staining, tear break-up time, and Schirmer test) of DED. Associations of work productivity and activity impairment with symptom and signs were evaluated with linear regression models using generalized estimating equations and controlling for demographics and comorbidities.

Main Outcome Measures: Work productivity (employment, absenteeism, presenteeism, overall work impairment) and activity impairment.

Results: Among 535 participants at baseline, 279 (52%) were employed and mean activity impairment was 24.5%. Among those employed, the mean score was 2% for absenteeism, 18% for presenteeism, and 19.6% for overall work impairment. Higher Ocular Surface Disease Index (OSDI) symptom scores were associated with greater absenteeism, presenteeism and activity impairment. Overall work impairment and activity impairment were greater by 4.3% and 4.8%, respectively, per 10 units difference in OSDI score ($p<0.001$). Longitudinal increases (worsening) in OSDI scores were associated with increasing impairment in work and non-work related activity: 2.0% and 3.1% per 10 units in OSDI, respectively ($p<0.01$). Worse corneal staining and tear break-up time were associated with higher overall work impairment and activity level ($p\leq0.04$). However, longitudinal changes in these two signs were not associated with changes in work productivity or activity impairment.

Conclusions: Worse symptoms of DED are associated with decreased work productivity and activity level, both cross-sectionally (inter-individually) and longitudinally within person (intra-individually). Corneal staining and tear break-up time are associated with inter-individual differences but not intra-individual changes in work productivity and activity impairment.

INTRODUCTION

Dry eye disease (DED) is a multifactorial condition characterized by inflammation of the ocular surface and alteration in the quality and/or quantity of tears.[1] The nature of DED symptoms and their intensity vary widely among patients, and may include constant eye irritation, dryness, stinging sensation, ocular fatigue and vision impairment. DED is highly prevalent in the global adult population, with risk that increases with age and female gender.[2] Based on a survey of 75,000 participants, DED affects 6.8% of the adult U.S population, including 2.7% of young adults (18-34 years old).[3] The few studies that examined the burden of DED from an economic perspective suggest that the bulk of its cost lies in decreased work productivity.[4-8] Increasing Ocular Surface Disease Index (OSDI), a measure of DED severity through self-reported symptoms, has been shown to correlate with decreasing productivity (mean estimates ranged from 1.6% to 53.4% reductions, for mild and severe DED respectively) and with a decline in non-work-related activities.[7] This literature is generally based on surveys of symptoms at a single time-point, mostly with no concurrent assessment of pathophysiological signs. Moreover, the cross-sectional design of all studies focused on this topic does not permit gleaning information on the possible association between changes in DED severity over time within individuals and changes in their level of productivity/activity. DED, because of its pervasive impact on everyday life and high prevalence across a wide age-range, including the working age population, is a major public health problem with economic implications that, while believed to be considerable, are still largely unknown. The Dry Eye Assessment and Management (DREAM) study prospectively monitored DED patients over the course of one year, performing eye evaluations at 6 months intervals and concurrently assessing severity of symptoms, quality of life, use of healthcare resources, and effects on work productivity.[9] These data enable a more rigorous evaluation of the relationship between DED and the ability of individuals to carry out their work and to function in their daily lives.

METHODS

Detailed descriptions of the study procedures have been published previously.[9, 10] Individuals with moderate to severe DED were enrolled in the DREAM clinical trial from October 2014 through July 2016, at 27 clinical centers in the United States.[9] Because there was no difference in changes in symptoms and signs of DED between the supplemented and control groups in the DREAM study,[10] we combined the groups for the analyses in this report. The study participants were adult individuals 18 years or older, who had had moderate to severe ocular symptoms related to DED for at least 6 months. Each participant had a visit at baseline and two follow ups, at 6 and 12 months, during which he/she was asked to complete a number of questionnaires and to undergo a battery of tests to assess the signs of DED. The institutional review board associated with each center approved the protocol and consent form. All participants provided written informed consent. The study conformed to the tenets of the Declaration of Helsinki.

Questionnaires used for this study included the Ocular Surface Disease Index (OSDI) and the Work Productivity and Activity Impairment (WPAI). The OSDI questionnaire measures the severity of DED symptoms and consists of 12 questions grouped into three sections: ocular symptoms, vision-related function, and environmental factors.[11] The OSDI is based on a recall period of 7 days and yields scores ranging from 0 (no symptoms) to 100 (worst). The WPAI questionnaire is a validated survey tool that consists of 6 questions assessing the impact of health problems on work performance and on regular daily activities outside of work.[12] For respondents who are employed, the WPAI summarizes information related to the loss of productivity during working hours, due to health reasons, expressed as a percentage reduction of the total work time. For all respondents, employed and unemployed, it provides information about the degree of impairment in the performance of regular activities due to health reasons. The WPAI survey uses a 7 days recall period and presents the level of impairment as a

percentage, from 0% (no limitations) to 100% (activity completely prevented by health problems).

Data on medical care received by participants included self-reported visits with any healthcare provider (1 month recall period) and hospitalizations in the previous 6 months. Care by an ophthalmologist was not analyzed after baseline because patients received their care for dry eye disease by their DREAM clinician according to protocol guidelines.

Signs of DED in each eye were measured at each of the 3 study visits, and the worse value of sign between the two eyes was used for data analysis. Conjunctival staining with lissamine green dye was assessed on the nasal and temporal conjunctiva with total scores ranging from 0 (no staining) to 6 (worst). Corneal staining with fluorescein dye was assessed in 5 sectors of the cornea with total scores ranging from 0 (no staining) to 15 (worst). Tear break-up time (TBUT) after blinking was measured in seconds with higher scores indicating better tear film stability. Wetting of Schirmer test strips 5 minutes after insertion with anesthesia was measured in mm with higher values indicating better tear production.

Statistical Analysis

Comparisons of baseline characteristics between age groups were made using chi-square tests for categorical characteristics, and analysis of variance for continuous characteristics. Comparisons of OSDI scores between people with or without visits to medical providers were made using linear regression with the generalized estimating equations (GEE) approach to control for the correlated nature of the data longitudinally collected from individuals.[13] Differences in mean changes in WPAI measures from baseline to 12 months were evaluated using paired t-tests. Changes in employment from baseline to 12 months were expressed as a risk difference and estimated using binomial regression of employment by time, adjusted by categorical age and using the GEE approach.

Estimates of the associations of scores on the OSDI or signs with each WPAI measure, and of the associations of changes of scores on the OSDI or signs from baseline with corresponding changes of each WPAI measure, were calculated by linear regression with GEE, using all study visits, and adjusting for categorical age, sex, time, cardiovascular disease (angina, history of myocardial infarction or past cardiac surgery), and current depression status. Risk differences for OSDI or signs with the proportion of people employed were calculated by binomial regression with GEE, adjusting for the same variables, and risk differences for changes in OSDI or signs with changes in employment were calculated by binomial regression with GEE, adjusting for baseline employment and categorical age. The models for change in employment were adjusted only for age because of failure of the regression algorithm to converge when the full set of covariates were included. All analyses were performed using SAS 9.4 (Cary, NC).

RESULTS

Study Population

The study population consisted of 535 adult (≥ 18 years old) individuals, with symptomatic moderate-to-severe dry eye. The baseline characteristics of the study population, are shown in **Table 1**. Participants had a mean age of 58 years and 81% were women. Three quarters of the study population were Whites, 12% were Blacks and 14% consisted of a mix of other races and people who did not identify themselves as belonging to one racial group. The most prevalent condition among study participants was current depression (16%), followed by diabetes (12%) and rheumatoid arthritis (9%). As for the OSDI score the severity of DED disease, did not increase with age. Mean DED sign scores significantly worsened with older age according to all four key signs of DED (conjunctival staining, corneal staining, TBUT and Schirmer's test). Half of the study population (52.2%) was actively employed. On average this subset of working participants reported a reduction of nearly 20% in their overall productivity

due to health reasons, with no significant differences between age groups. In the whole study population, with and without active employment, the average level of impairment on performing regular activities due to health reasons, was nearly 25%. The mean number of visits to an eye specialist reported at baseline (before randomization in the trial), was similar between men and women and similar across age categories (data not shown).

Relationship between healthcare utilization and severity of DED

To understand the types of providers who are more frequently involved in the care of patients with DED, we analyzed patients who had at least one visit to a health care provider in the previous month compared to those who had none, for potential differences in their mean OSDI score (**Table 2**). Some healthcare-provider visits were positively associated with an increase of mean OSDI: allergist, dentist, diabetes/endocrinologist, ophthalmologist, optometrist and rheumatologist. Finally, there were a total of 19 hospitalizations of 18 people over the course of the study, as assessed by 6 months recall at the 6 and 12 month visits.

Relationship of severity of DED with changes in productivity and regular activities

Among 486 people who completed the surveys at both baseline and 12 months, 15 (3%) gained employment and 30 (6%) lost employment for an age-adjusted net risk difference of -3.0% (95% CI -5.5% to -0.4%, p=0.02). Mean activity impairment decreased by 2.2% (n=488, SD 27.4, 95% CI -4.7 to 0.2, p=0.07), and among those who were employed, absenteeism increased by 0.2% (n=201, SD=8.9, 95% CI -1.0 to 1.4, p=0.73), presenteeism decreased by 5.0% (n=217, SD=22.5, 95% CI -8.0 to -2.0, p=0.001), and overall work impairment decreased by 4.3% (n=201, SD=22.9, 95% CI -7.5 to -1.1, p=0.008). However, there was marked variation among individuals with respect to the change in these parameters. We analyzed whether DED severity could explain some of this variability, adjusting for demographics and other potential factors, such as cardiovascular disease, depression, rheumatoid arthritis and diabetes, which

might themselves impact work performance and non-work-related activities. As shown in Table 3, employment status was not associated with either OSDI score, or any of the clinical indexes of DED that were evaluated (**Table 3**). However, with the sole exception of conjunctival staining, all DED metrics were associated with decreased work performance and with some level of impairment in carrying out regular activities. Decreased productivity may arise both from absenteeism and from impaired performance during working hours (presenteeism). OSDI score was the only DED metric associated with an increase, albeit modest, of absenteeism. The productivity loss due to absenteeism, however, was substantially less than the loss due to presenteeism, about a tenth, given the same increase in OSDI. Worse TBUT and corneal staining correlated both with increases in presenteeism and with impairment of regular activities, whereas worse Schirmer's test results were associated with increased impairment in regular activities, but not with a reduction in work productivity. Finally, we proceeded to examine whether changes in DED severity overtime, within individuals, would correlate with their changes in productivity and level of activity (**Table 4**). Results from assessment of the clinical signs were no longer significant predictors, whereas a 10 units increase in OSDI score was associated with a 2.0% increase in overall work impairment ($p = 0.006$) and a 3.1% increase in activity impairment ($p<0.001$).

DISCUSSION

This is the first longitudinal study that evaluates the association between severity and progression of DED and its societal impact in terms of employment, decreased work productivity and, more generally, activity impairment. Our results demonstrate a significant association between increasing DED severity and decreased work productivity and, importantly, indicate that DED severity is a significant explanatory factor not only for differences in work productivity among individuals, but also for changes in productivity overtime, within individuals.

Within the larger context of its public health implication, DED, due to the high prevalence and the widespread age range of the affected population, raises important concerns with respect to the economic burden it imposes on our society.[14] DED lacks a gold standard diagnostic test and metrics based on self-reported symptoms have been widely used in the literature to measure its severity and characterize how it affects patients' daily lives.[15] The OSDI in particular has proven to be a reliable and valid instrument for the measurement of DED symptom severity.[11] A significant association between higher OSDI scores and impaired work productivity while on the job (presenteeism) has been reported by a number of studies, based on self- reported symptoms obtained from surveys administered online.[5-8] Patient reported symptoms, however, might be influenced by strong participant characteristics, including the individual perception of pain, coping style, psychological stress, models of behavior derived from the social environment, as well as chronic comorbidities, such as cardiovascular disease, arthritis and depression, which might themselves confound the association of DED and productivity.[16] Our study provides stronger evidence of the specificity of the association between DED and decreased productivity by incorporating multiple types of ophthalmologic examination (cornea staining, conjunctival staining, Schirmer test and TBUT) alongside OSDI measures, and by controlling for concomitant diseases that are known risk factors for reduced work productivity.[17]

Among the diagnostic tests evaluated, conjunctival staining was the only one that was not associated with activity impairment or work productivity. Moreover, the Schirmer test, as compared to corneal staining and TBUT, had a markedly weaker association with general activity impairment, and its association with work productivity was not significant, possibly due to the reduced sample size from the exclusion of people not employed. The low concordance observed among the results of different clinical tests, might be a consequence of the heterogeneous nature of this disease and the different pathophysiologic pathways underlying DED, and further underscores the importance of complementary metrics that evaluate signs and

symptoms of DED, consistent with the revised definition of DED from the TFOS DEWS-II.[2] The strongest effect on work productivity was found with OSDI, which was also the only DED metric associated with absenteeism, albeit to a lesser extent than with presenteeism. An OSDI score from 0 to 12 is generally interpreted as normal. On average, the OSDI of our patient population, selected with inclusion criteria of moderate to severe DED, was approximately 44. While clinical signs of DED were associated with work productivity only in cross-sectional analysis, OSDI score maintained a significant association also under a longitudinal analysis of the data, controlling for demographics and comorbidities. In particular, an increase of ten units in OSDI was associated with about 2% decrease in productivity. Effective treatments that relieve DED symptoms, therefore, not only would improve patients' quality of life, but might also induce increases in their productivity. For example, a treatment that on average decreases the OSDI of our study population from 44 to normal range (0- 12), might have increased its productivity approximately by 6%, assuming that productivity gains are accrued only when outside the normal OSDI range.

Although the goal of this study was not to estimate the direct cost of DED, it is worth noting the association between increasing DED severity and an increasing number of visits with a number of health care providers, besides ophthalmologists. Such an increase is probably not caused by DED directly, nor by increasing age, which in our cohort was not correlated with higher OSDI. It may instead be the indirect effect of other diseases associated with DED, such as people with Sjogren syndrome having a higher number of visits to a dentist or a rheumatologist. Potentially, a systemic link exists between the progression of DED and other comorbidities, whereby DED tends to be more severe in patients with concomitant conditions. This suggest that part of the indirect cost on society of other common chronic conditions, such as diabetes, might be, to some degree, mediated by DED.

Our findings must be interpreted in the context of some potential limitations of this study. First, the study population consisted of participants in the DREAM trial; therefore, the generalizability of our findings is bound by the trial's eligibility criteria.[10] Some of these criteria relevant to work and activity impairment are moderate to severe symptoms, age 18 or older, no current contact lens wear, ability to attend 3 examination sessions over the course of 1 year. However, the external validity of the results is enhanced by the multicenter design comprising 27 centers across the U.S. Second, the lack of patients without DED does not permit the comparison of the work and activity impairment values to a baseline reference. However, while we cannot address the differences between people with DED versus people without DED, we do address the impact of increasing severity of DED, something that most other studies do not address. Finally, other comorbidities and personal life circumstances that may affect impairment were not accounted for in the analysis.

In conclusion, greater severity of dry eye symptoms as measured by the OSDI is associated with lower worker productivity and activity both cross-sectionally and longitudinally. These results further strengthen the evidence that DED symptoms have a negative economic impact and that efforts to reduce symptoms would bring economic benefits.

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TABLE 1: Baseline characteristics							
				Age (years)			
		Total	Range	<45	45-64	65+	p-value
DEMOGRAPHICS *(n = 535)*							
Age (years)	mean (SD)	58.0 (13.2)	18.0 - 87.0	34.6 (7.2)	56.5 (5.3)	71.5 (5.3)	<0.001
	N (%)			81 (100%)	283 (100%)	171 (100%)	
Sex	Female	434 (81%)		59 (73%)	232 (82%)	143 (84%)	0.11
	Male	101 (19%)		22 (27%)	51 (18%)	28 (16%)	
Race	White	398 (74%)		57 (70%)	201 (71%)	140 (82%)	0.02
	Black	64 (12%)		7 (9%)	41 (14%)	16 (9%)	
	Other/Multiple/No answer	73 (14%)		17 (21%)	41 (14%)	15 (9%)	
COMORBIDITIES *(n=535)*							
Diabetes		62 (12%)		5 (6%)	33 (12%)	24 (14%)	0.19
Rheumatoid arthritis		49 (9%)		7 (9%)	28 (10%)	14 (8%)	0.82
CVD		28 (5%)		2 (2%)	13 (5%)	13 (8%)	0.18
Depression		87 (16%)		9 (11%)	36 (20%)	42 (15%)	0.16
EYES HEALTH *(n=535)*							
OSDI score (higher is worse)		42.1 (15.5)	20.8 - 81.3	43.1 (16.1)	42.4 (15.4)	41.0 (15.4)	0.50
Conjunctival staining score (higher is worse)		3.3 (1.5)	0.0 - 6.0	3.0 (1.4)	3.5 (1.5)	3.2 (1.5)	0.02
Corneal staining score (higher is worse)		4.4 (3.1)	0.0 - 15.0	3.1 (2.5)	4.4 (3.2)	4.9 (3.1)	<0.001
Tear break-up time (sec.) (higher is better)		2.7 (1.4)	0.0 - 11.0	3.0 (1.6)	2.6 (1.2)	2.7 (1.5)	0.04
Schirmer test (mm) (higher is better)		8.2 (6.3)	0.0 - 36.0	10.1 (7.6)	8.0 (6.6)	7.6 (4.8)	0.01
PRODUCTIVITY							
All Participants (n =535)							
Employment		279 (52%)		56 (69%)	179 (63%)	44 (26%)	<0.001
Activity impairment		24.5 (26.7)	0.0 - 100.0	26.3 (26.1)	24.8 (27.3)	23.2 (26.0)	0.67
Employed Participants (n =274)							
Absenteeism		2.0 (7.9)	0.0 - 66.7	3.8 (11.6)	1.5 (6.4)	1.9 (7.5)	0.20
Presenteeism		18.0 (21.6)	0.0 - 100.0	21.8 (23.4)	18.1 (21.1)	12.6 (20.5)	0.11
Overall Work Impairment		19.6 (22.5)	0.0 - 100.0	25.1 (24.4)	19.1 (21.6)	14.5 (22.8)	0.07

TABLE 2: OSDI score by provider see in the last month						
	0 visits		>0 visits			
Provider	**OSDI mean (SD)**	**n**	**OSDI mean (SD)**	**n**	**Difference (95% CI)**	**p**
Primary Care Physician	35.2 (18.2)	1082	34.9 (19.2)	421	-0.4 (-2.6, 1.9)	0.75
Internal Medicine Physician	35.2 (18.5)	1456	33.9 (18.4)	47	-1.3 (-7.0, 4.4)	0.66
Acupuncturist	34.9 (18.4)	1477	45.6 (22.1)	26	10.6 (-0.5, 21.7)	0.06
Alllergist	**35.0 (18.4)**	**1478**	**43.5 (19.6)**	**25**	**8.5 (1.3, 15.7)**	**0.02**
Cardiologist	35.1 (18.5)	1459	36.5 (18.6)	44	1.4 (-4.4, 7.2)	0.63
Chiropractor	34.9 (18.4)	1427	39.7 (19.8)	76	4.8 (-0.8, 10.3)	0.09
Dentist	**34.6 (18.2)**	**1264**	**37.9 (19.5)**	**239**	**3.3 (0.5, 6.2)**	**0.02**
Dermatologist	35.2 (18.5)	1430	33.2 (18.7)	73	-2.0 (-6.9, 3.0)	0.43
Diabetes/Endocrinologist	**34.9 (18.4)**	**1467**	**42.7 (20.0)**	**36**	**7.7 (0.6, 14.9)**	**0.03**
Gastroenterologist	35.2 (18.5)	1450	32.6 (17.6)	53	-2.6 (-7.1, 1.8)	0.24
Gynecologist	35.0 (18.4)	1442	39.3 (20.2)	61	4.4 (-1.1, 9.9)	0.12
Neurologist	35.1 (18.4)	1463	37.7 (20.2)	40	2.7 (-5.1, 10.4)	0.50
Oncologist	35.1 (18.4)	1473	36.4 (23.1)	30	1.3 (-8.8, 11.4)	0.80
Ophthalmologist	**34.7 (18.4)**	**1412**	**41.2 (18.9)**	**91**	**6.4 (2.3, 10.6)**	**<0.01**
Optometrist	**35.0 (18.5)**	**1459**	**40.4 (18.6)**	**44**	**5.4 (-0.0, 10.9)**	**0.05**
Physical therapist	35.2 (18.5)	1438	34.1 (17.9)	65	-1.0 (-6.0, 3.9)	0.68
Podiatrist	35.0 (18.4)	1460	40.7 (20.5)	43	5.8 (-1.0, 12.5)	0.09
Psychiatrist	35.0 (18.5)	1454	37.8 (17.3)	49	2.7 (-3.9, 9.3)	0.42
Psychologist	35.1 (18.5)	1458	37.5 (16.0)	45	2.4 (-3.2, 8.1)	0.40
Rheumatologist	**34.8 (18.3)**	**1426**	**40.8 (20.6)**	**77**	**6.0 (0.3, 11.6)**	**0.04**
Other	34.9 (18.4)	1343	36.8 (18.9)	160	1.9 (-1.3, 5.0)	0.24
Only providers with >24 visits are included						

TABLE 3 Association of symptom and sign scores with work productivity and activity impairment

	Employment 535 patients 1495 observations		Absenteeism 299 patients 713 observations		Presenteeism 305 patients 752 observations		Overall work impairment 299 patients 713 observations		Activity impairment 535 patients 1503 observations	
	Risk difference (95% CI)	**p-value**	**Mean change (%) (95% CI)**	**p-value**	**Mean change (%) (95% CI)**	**p-value**	**Mean change (%) (95% CI)**	**p-value**	**Mean change (%) (95% CI)**	**p-value**
OSDI score (per 10, higher is worse)	-1.51% (-3.15%, 0.13%)	0.07	0.40 (0.05, 0.76)	0.03	4.01 (2.83, 5.19)	<0.001	4.28 (3.05, 5.51)	<0.001	4.76 (3.79, 5.73)	<0.001
Conjunctival staining score (higher is worse)	-1.33% (-3.58%, 0.92%)	0.25	-0.08 (-0.44, 0.28)	0.67	0.10 (-1.05, 1.26)	0.86	0.26 (-0.96, 1.48)	0.68	0.16 (-0.97, 1.30)	0.78
Corneal staining score (higher is worse)	-1.00% (-2.14%, 0.14%)	0.24	-0.06 (-0.24, 0.13)	0.56	0.70 (0.02, 1.37)	0.04	0.75 (0.04, 1.46)	0.04	0.80 (0.21, 1.39)	0.008
Tear break-up time (seconds) (higher is better)	0.72% (-0.88%, 2.32%)	0.38	-0.17 (-0.46, 0.12)	0.26	-1.55 (-2.27, -0.82)	<0.001	-1.56 (-2.39, -0.74)	<0.001	-1.13 (-2.02, -0.24)	0.01
Schirmer test (mm) (higher is better)	0.28% (-0.25%, 0.81%)	0.30	0.00 (-0.10, 0.10)	0.97	-0.16 (-0.44, 0.13)	0.28	-0.16 (-0.47, 0.15)	0.31	-0.29 (-0.54, -0.03)	0.03

Models were adjusted for age (categorical), sex, race, arthritis, diabetes, cardiovascular disease, depression, and month
The Schirmer test was missing from 8 observations (3 for absenteeism, presenteeism, and overall work impairment)

TABLE 4 Association of change (Δ) in symptom and sign scores with change in work productivity and activity impairment

	ΔEmployment 498 patients 959 observations		ΔAbsenteeism 223 patients 397 observations		ΔPreseenteism 237 patients 435 observations		ΔOverall work impairment 223 patients 397 observations		ΔActivity impairment 499 patients 968 observations	
	Risk difference (95% CI)	**p-value**	**Mean change (%) (95% CI)**	**p-value**	**Mean change (%) (95% CI)**	**p-value**	**Mean change (%) (95% CI)**	**p-value**	**Mean change (%) (95% CI)**	**p-value**
ΔOSDI score (per 10, increase is worse)	0.08% (-0.88%, 1.03%)	0.88	0.32 (-0.17, 0.82)	0.20	2.18 (0.88, 3.49)	0.001	2.00 (0.58, 3.41)	0.006	3.07 (1.94, 4.20)	<0.001
ΔConjunctival staining score (increase is worse)	-0.12% (-1.47%, 1.24%)	0.87	-0.26 (-0.71, 0.19)	0.25	-0.10 (-1.74, 1.55)	0.91	0.02 (-1.74, 1.78)	0.98	0.09 (-1.47, 1.66)	0.91
ΔCorneal staining score (increase is worse)	-0.14% (-0.86%, 0.57%)	0.69	-0.05 (-0.38, 0.27)	0.75	0.31 (-0.62, 1.24)	0.51	0.18 (-0.78, 1.14)	0.71	-0.71 (-1.58, 0.15)	0.11
ΔTear break-up time (seconds) (increase is better)	-0.37% (-1.24%, 0.50%)	0.41	-0.13 (-0.44, 0.19)	0.42	-0.76 (-1.84, 0.32)	0.17	-0.48 (-1.55, 0.59)	0.38	-0.93 (-1.92, 0.06)	0.07
ΔSchirmer test (mm) (increase is better)	0.07% (-0.26%, 0.40%)	0.52	0.05 (-0.16, 0.27)	0.63	0.36 (-0.10, 0.83)	0.12	0.32 (-0.21, 0.85)	0.23	0.17 (-0.23, 0.57)	0.39

Models were adjusted for age (categorical), sex, race, arthritis, diabetes, cardiovascular disease, depression, and month
The models for change in employment were adjusted for age only because of failure to converge when the full set of covariates were included
The Schirmer test was missing from 8 observations (2 for absenteeism, presenteeism, and overall work impairment)

Precis

Worse symptoms of dry eye disease are associated with decreased work productivity and activity level, both cross-sectionally and longitudinally within person.