Depression, Post-traumatic Stress Disorder, and Dry Eye Syndrome: A Study Utilizing the National United States Veterans Affairs Administrative Database

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• PURPOSE: To study the scope of dry eye syndrome (DES) in veterans on a national level and to evaluate the relationship between psychiatric diagnoses and DES.
• DESIGN: Case-control study.
• METHODS: Setting: Patients were seen in a Veterans Affairs (VA) eye clinic between 2006 and 2011. Patient population: Patients were divided into cases and controls with regard to their dry eye status (cases = ICD-9 code for DES plus dry eye therapy; controls = patients without ICD-9 code plus no therapy). Main outcome measures: The prevalence of DES and the influence of psychiatric diagnoses on the risk of DES.
• RESULTS: A total of 2 454 458 patients were identified as either a dry eye case (n = 462 641) or control (n = 1 991 817). Overall, 19% of male patients and 22% of female patients had a diagnosis of DES, with female sex imparting an increased risk of DES at each decade compared to male sex (odds ratio [OR] 1.22–2.09). Several conditions were found to increase DES risk, including post-traumatic stress disorder (OR 1.92, 95% CI 1.91–1.94) and depression (OR 1.92, 95% CI 1.91–1.94) (analyses adjusted for sex and age). The use of several systemic medications was likewise associated with an increased risk of DES, including antidepressant medications (OR 1.97, 95% CI 1.79–2.17) and antianxiety medication (OR 1.74, 95% CI 1.58–1.91). Multivariate analysis (adjusted for age and sex) revealed that for psychiatric diagnoses, both the use of medication and the diagnosis remained significant risk factors when considered concomitantly, although the magnitude of each association decreased.
• CONCLUSIONS: DES is a disease associated with depression and post-traumatic stress disorder, and is prevalent among male and female veterans receiving eye care services. The association could be driven by underlying disease physiology or medications used to treat psychiatric conditions. Regardless of the causal link, this suggests that individuals with a known psychiatric diagnosis should be questioned about dry eye symptoms and, if applicable, referred to an eye care physician. (Am J Ophthalmol 2012;154:340–346. Published by Elsevier Inc.)

Accepted for publication Feb 3, 2012.

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DRY EYE SYNDROME (DES) IS A PREVALENT CONDITION both in the United States and worldwide, with manifestations that negatively impact physical and mental functioning.[1–7] We felt that it was essential to study the scope of DES specifically in the Veterans Affairs population, as veterans as a group have demographic characteristics, exposures, and medical profiles that are different from previously studied populations.[8–10] Specifically, while previous US populations have focused on mainly female and/or non-Hispanic white populations,[8,10] veterans are a predominantly male population with a diverse racial and ethnic make-up. A recent evaluation of the scope of DES in Miami veterans found a high prevalence of disease in this population, with 12% of male and 22% of female patients carrying a diagnosis of DES.[11] The presence of a psychiatric diagnosis, including depression and post-traumatic stress disorder (PTSD), and the use of psychiatric medication imparted a 2-fold risk of having a DES diagnosis.[11] This study highlighted that DES is present in both male and female patients and suggested that veterans may be uniquely more susceptible to DES given the comorbidities found in this population.[11] A limitation of the study, however, was that it only looked at a demographically select subset of veterans[11] and therefore the generalizability of data onto a national veteran population was uncertain.

The Veterans Affairs (VA) has recently created a centralized data warehouse that contains merged information from several VA clinical and administrative systems. The premise behind its creation was that the incorporation of data from multiple differing data sets throughout the VA into 1 standard database structure would facilitate reporting and data analysis. The goal of this study, therefore, was to use this national data set to study the scope of DES in veterans on a national level and to evaluate the relationship between important comorbidities in veterans and DES, especially the relationship between psychiatric diagnoses and DES.

0002-9394/$36.00
doi:10.1016/j.ajo.2012.02.009

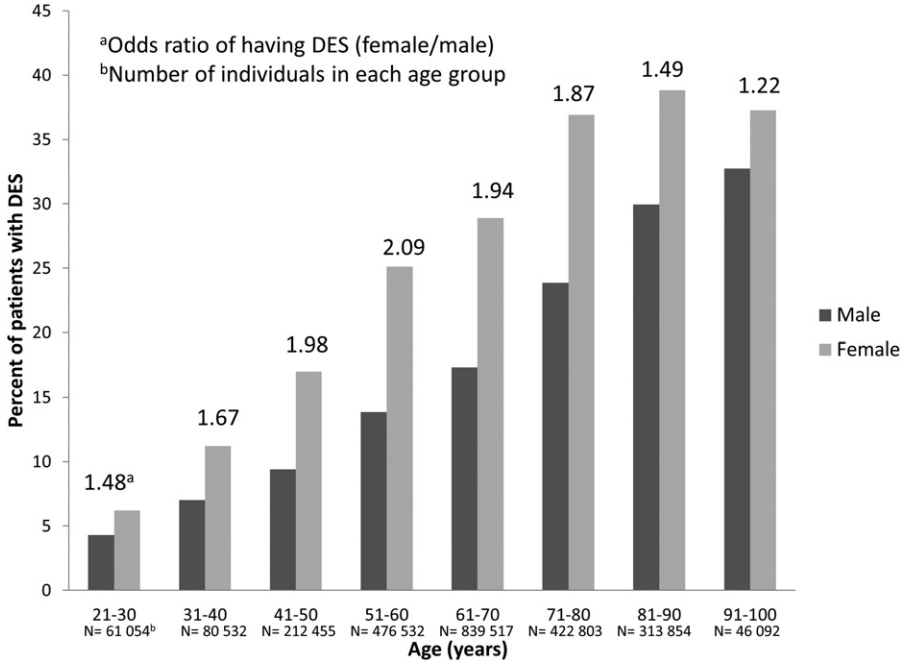

FIGURE 1. Percentage of patients with dry eye syndrome by sex and age in a Veterans Affairs population receiving eye care services.

TABLE 1. Demographic Information for Patients Seen at a Veterans Affairs Medical Center Eye Clinic Over a 5-Year Period

Patient Characteristic	Number[a]	Percent[b]	OR[c]
Race			
White	321 017	20%	—
Black	85 553	21%	1.41 (1.39–1.42)
Asian or Pacific Islander	8386	21%	1.29 (1.26–1.32)
American Indian or Alaskan	2739	20%	1.28 (1.22–1.33)
Ethnicity			
Hispanic	4254	30%	1.66 (1.60–1.72)
Not Hispanic	413 441	20%	—

[a]Number of patients with dry eye syndrome (present if ICD-9 code 375.15 and received some form of dry eye therapy).
[b]Percent in group with dry eye syndrome.
[c]Odds ratio (OR) adjusted for sex and age. An OR greater than 1 represents an increased likelihood of dry eye syndrome.

METHODS

• **STUDY POPULATION:** All patients seen in a VA eye clinic between July 5, 2006 and July 4, 2011 were included in this retrospective analysis. As the data included patients from 365 VA eye clinics in all Veterans Integrated Service Networks (VISNs), it captured all veterans that were seen in a US VA eye clinic during the study period. Patients seen in VA clinics consist of ex-military personnel but do not include or represent all former military personnel. Patients seen in other Veterans Affairs outpatient clinics during this time period were not included as a preliminary analysis revealed that non–eye care professionals did not use the ICD-9 code for DES. Patients were divided into cases and controls with regard to their dry eye status. Cases included patients with an International Classification of Disease code (ICD-9) for DES (375.15) who received some form of dry eye therapy (n = 462 641); controls included patients who received eye clinic care but who did not have an ICD-9 code for DES and did not receive any form of dry eye therapy (n = 1 991 817). Dry eye therapies included: any type of artificial tear, gel, or ointment; topical cyclosporine 0.05% (Restasis); or punctal plugging procedure (Current Procedural Terminology [CPT] codes 68760 and 68761). Patients were excluded from the risk factor analysis if they had discordant dry eye information (eg, an ICD-9 diagnosis but no dry eye therapy or no ICD-9 diagnosis but with dry eye therapy).

• **DATA COLLECTION:** All data were extracted from the Corporate Data Warehouse (CDW) by an expert programmer (A.L.F.) and automatically converted into an SPSS format. The Veterans Administration's Corporate Data Warehouse is a national repository comprising data from several Veterans Health Administration (VHA) clinical and administrative systems. The CDW operates within the VA Office of Information & Technology Field Operations Business Intelligence Service Line. CDW data are stored in a relational database. Multiple VA data sources are merged so that cohorts are definable by attributes such as ICD-9 codes and CPT codes from both inpatient and

TABLE 2. Medical Conditions as Defined by ICD-9 Code in Patients Seen at a Veterans Affairs Medical Center Eye Clinic Over a 5-Year Period

Medical Condition	Number[a]	Percent[b]	OR[c]
Vascular			
Diabetes mellitus:			
yes	215 844	20%	1.06 (1.06–1.07)
no	246 797	18%	—
Hypertension:			
yes	380 918	22%	1.82 (1.80–1.83)
no	81 723	11%	—
Lipid metabolism disorder:			
yes	358 630	22%	1.56 (1.55–1.57)
no	104 011	13%	—
Ischemic heart disease:			
yes	192 333	26%	1.55 (1.54–1.56)
no	270 308	16%	—
Cerebral vascular disease:			
yes	100 966	29%	1.61 (1.60–1.63)
no	361 675	17%	—
Psychiatric			
Psychiatric illness:			
yes	210 960	24%	1.88 (1.87–1.90)
no	251 681	16%	—
PTSD:			
yes	105 239	24%	1.92 (1.91–1.94)
No	357 402	18%	1.00
Depression:			
yes	126 831	24%	1.92 (1.91–1.94)
no	335 810	18%	—
Alcohol dependence:			
yes	52 316	19%	1.33 (1.31–1.34)
no	410 325	19%	—
Drug dependence:			
yes	157 542	19%	1.33 (1.32–1.34)
no	305 099	19%	—
Autoimmune & arthritis			
Autoimmune disease[d]:			
yes	110 700	31%	2.18 (2.17–2.20)
no	351 941	17%	—
Nonautoimmune arthritis:			
yes	281 148	27%	2.28 (2.26–2.29)
no	181 493	13%	—
Gout:			
yes	52 532	27%	1.48 (1.46–1.50)
no	410 109	18%	—
Thyroid disease:			
yes	23 812	31%	1.81 (1.78–1.83)
no	438 829	19%	1.00
Prostate			
Benign prostatic hyperplasia:			
yes	178 091	28%	1.74 (1.73–1.75)
no	284 550	16%	—
Prostate cancer:			
yes	47 479	27%	1.21 (1.19–1.22)
no	415 162	18%	—

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TABLE 2. Medical Conditions as Defined by ICD-9 Code in Patients Seen at a Veterans Affairs Medical Center Eye Clinic Over a 5-Year Period *(Continued)*

Medical Condition	Number[a]	Percent[b]	OR[c]
Miscellaneous			
Sleep apnea:			
yes	27 798	33%	2.46 (2.43–2.50)
no	434 843	18%	—
Rosacea:			
yes	21 097	37%	2.29 (2.25–2.34)
no	441 544	18%	—
HIV:			
yes	3009	19%	1.41 (1.35–1.47)
no	459 632	19%	1.00
Chemotherapy:			
yes	9452	30%	1.54 (1.50–1.58)
no	453 189	19%	—
Ocular			
Glaucoma:			
yes	164 171	28%	1.84 (1.83–1.85)
no	298 470	16%	—

HIV= human immunodeficiency virus; PTSD = post-traumatic stress disorder.

[a]Number of patients with dry eye syndrome (present if ICD-9 code 375.15 and received some form of dry eye therapy).

[b]Percent in group with dry eye syndrome.

[c]Odds ratio (OR) adjusted for sex and age. An OR greater than 1 represents an increased likelihood of dry eye syndrome.

[d]Autoimmune diseases include: Behcet syndrome, sarcoidosis, systemic lupus erythomatosis, rheumatoid arthritis, Wegener granulomatosis, vasculitis, vitiligo, psoriasis, ankylosing spondylitis, inflammatory bowel disease, Reiter syndrome, autoimmune hepatitis, and collagen vascular diseases.

outpatient encounters or from abnormal values of vital signs like blood pressure, weight, and height, within a target time period. These data sets are kept current by frequent updates with new data from the source databases so timely data are available for research.

The data used for this analysis were extracted from the CDW Encounters tables. The source of CDW Encounters is the National Patient Care Database, or NPCD. NPCD provides a single flat file to CDW on each business day that contains the most recent inserts and updates. CDW Encounters is normally current to within a couple of days. This extraction included demographic information (date of birth, sex, race, ethnicity), medical diagnosis information (extracted based on ICD-9 codes), use of systemic therapy (extracted based on pharmacy codes), and procedures (extracted based on CPT codes).

• **MAIN OUTCOME MEASURES:** The main outcome measure was prevalence of DES and its associated risk factors.

• **STATISTICAL ANALYSIS:** All statistical analyses were performed using SPSS 18.0 (SPSS Inc, Chicago, Illinois, USA) statistical package. Continuous variables were compared between the groups using the Student t test and categorical variables were compared using the χ^2 test. Multivariate logistic regression analysis (using the presence of DES as the dependent variable) was used to evaluate the effect of various risk factors on DES. All multivariate analyses were adjusted for sex and age.

RESULTS

• **DRY EYE SYNDROME PREVALENCE:** During the studied period, 3 133 262 patients were seen in a VA eye clinic. After excluding discordant cases (n = 120 061 with an ICD-9 code for DES but no DES therapy; n = 558 743 with DES therapy but no ICD-9 code for DES), a total of 2 454 458 patients were identified as being either a dry eye case (n = 462 641) or control (n = 1 991 817). The period prevalence for these patients was 19% (n = 462 641/2 454 458).

• **RISK FACTOR ANALYSIS OF DEMOGRAPHIC CHARACTERISTICS:** Overall, 19% of male patients and 22% of female patients had a diagnosis of DES, with female sex imparting an increased risk of DES at every age group (odds ratio [OR] 1.22–2.09) (Figure). The mean age of our population was 64.2 years (SD 14.26). The Figure depicts the percentage of patients with DES by decade of age and sex; the overall risk of DES increased by 1.42 for each increasing decade (95% confidence interval [CI] 1.42–1.42). The Veterans Affairs administrative database did not have complete information on self-identified race and ethnicity (this information was available for 86% of

TABLE 3. Systemic Medications as Defined by Pharmacy Codes in Patients Seen at a Veterans Affairs Medical Center Eye Clinic Over a 5-Year Period

Systemic Medication	Number[a]	Percent[b]	OR[c]
Antihistamines:			
yes	170 120	30%	2.37 (2.35–2.38)
no	292 521	16%	—
Antianxiety medication:			
yes	153 294	27%	2.02 (2.01–2.03)
no	309 347	16%	—
Antidepression medication:			
yes	249 709	24%	2.06 (2.05–2.08)
no	212 932	15%	—
Beta blockers:			
yes	250 346	25%	1.65 (1.64–1.66)
no	212 295	15%	—
Anti–BPH medications:			
yes	199 501	29%	2.01 (2.00–2.03)
no	263 140	15%	—
Calcium channel blockers:			
yes	202 175	26%	1.66 (1.65–1.67)
no	260 466	16%	1.00
Cholesterol–lowering medication:			
yes	337 639	23%	1.66 (1.65–1.67)
no	125 002	13%	—
Diuretic:			
yes	125 748	30%	1.75 (1.73–1.76)
no	336 893	17%	—
ACE inhibitor:			
yes	279 436	23%	1.54 (1.53–1.55)
no	183 205	15%	—
Angiotensin receptor antagonist:			
yes	68 880	28%	1.51 (1.50–1.53)
no	393 761	18%	—

ACE = angiotensin-converting enzyme; BPH = benign prostatic hyperplasia.

[a]Number of patients with dry eye syndrome (present if ICD-9 code 375.15 and received some form of dry eye therapy).

[b]Percent in group with dry eye syndrome.

[c]Odds ratio (OR) adjusted for sex and age. An OR greater than 1 represents an increased likelihood of dry eye syndrome.

patients). With this limitation, identification as being nonwhite increased the risk of DES, with the OR for blacks, Asians or Pacific Islanders, and American Indians being 1.41, 1.29, and 1.28, respectively, compared to whites (Table 1). While Hispanics comprised only a small percentage of the total veteran population (0.7%), Hispanics had a 1.69-fold higher risk of DES than their non-Hispanic counterparts (risk adjusted for age and sex).

TABLE 4. Multivariate Logistic Regression Analysis Evaluating the Relationship Between Psychiatric Diagnoses/Medications and Dry Eye Syndrome in Patients Seen at a Veterans Affairs Medical Center Eye Clinic Over a 5-Year Period

Prognostic Factors	OR[a]	95% CI	OR[b]	95% CI
Diagnosis of depression	1.21	1.20–1.22	1.11	1.10–1.12
Diagnosis of post-traumatic stress disorder	1.32	1.31–1.34	1.26	1.25–1.28
Antidepression medications	1.54	1.53–1.56	1.25	1.24–1.26
Antianxiety medications	1.55	1.54–1.56	1.25	1.24–1.26

CI = confidence interval.

[a]Odds ratio (OR) adjusted for sex and age. Model includes 4 listed variables as well as sex and age.

[b]Odds ratio (OR) adjusted for sex and age. Model includes all medical diagnoses and systemic medications along with sex and age. All variables remained significant at the $P < .0005$ level except for drug dependence and angiotensin-converting enzyme inhibitor use, which were not significant in the model ($P > .05$).

• **RISK FACTOR ANALYSIS OF MEDICAL CONDITIONS:** Systemic diagnoses were identified in the administrative database using ICD-9 codes. After adjusting for sex and age, several medical conditions were found to increase DES risk in our population (Table 2). The magnitude of increased risk was highest in patients with sleep apnea (OR 2.46), rosacea (OR 2.29), nonautoimmune arthritis (OR 2.28), depression (OR 1.92), and PTSD (OR 1.92). The overall period prevalence of depression in our population was 22% and in those with the diagnosis 24% had DES, compared to 18% without depression. The overall prevalence of PTSD in our population was 18% and in those with the diagnosis 24% had DES, compared to 18% without PTSD. Combining both groups, the positive predictive value of a psychiatric disorder (PTSD and/or depression) on DES ranged from 6% in the 21-to-30 age group to 44% in the 81-to-90 age group, reflecting the increasing prevalence of DES with increasing age. In a forward stepwise regression model considering age, sex, and all medical diagnoses, the presence of depression (OR 1.34, 95% CI 1.33–1.35) and PTSD (OR 1.43, 95% CI 1.42–1.45) remained significant predictors of DES risk.

• **RISK FACTOR ANALYSIS OF SYSTEMIC MEDICATIONS:** The use of several systemic medications was likewise associated with an increased risk of DES (Table 3). The highest increased risk was found in patients using antihistamines (OR 2.37), with 30% of users having DES compared to 16% of non-users. Other medications associated with increased DES risk were antidepressant medications (OR 2.06), antianxiety medications (OR 2.02), and anti–benign prostatic hyperplasia medications (OR 2.01). Multivariate logistic regression analysis examining the

relationship between medical diagnoses and use of relevant systemic medications revealed that for psychiatric diagnoses, both the use of medication and the diagnosis remained significant risk factors, although the magnitude of each association decreased when both factors were analyzed concomitantly (Table 4).

DISCUSSION

THE GOAL OF THIS STUDY WAS TO USE THE NATIONAL VA administrative database to evaluate the scope of DES in veterans on a national level and to examine whether comorbidities identified in a Miami VA population remained important in predicting DES risk on a national level. Specifically, given the higher burden of depression and PTSD in veterans, we were interested in studying the impact of a psychiatric diagnosis and medication use on DES. We found that a significant proportion of veterans in our retrospective study had DES, with men having an overall prevalence of 19%. In arriving at this prevalence, we calculated a period prevalence that combined existing DES cases with incident cases during the 5-year study period as we could not determine the exact timing of DES onset from the medical record. Our calculated period prevalence may therefore be an overestimation of the true point prevalence at any given time point. Our prevalence estimate is higher than the one found in the Miami VA population, where men had an overall prevalence of 12%.[11] Potential explanations for this finding could be unmeasured environmental differences (eg, higher humidity in the Miami area providing a protective effect) or differences in physician coding in Miami compared to a national arena. The national estimate is also much higher than that found by Schaumberg and associates in a prospective study of men from the Physicians Health Study, where DES prevalence ranged from 3.9% (50- to 54-year-olds) to 7.7% (80-year-olds and above).[9]

In a national veteran population, the presence of a psychiatric diagnosis including depression and PTSD and the use of psychiatric medication were predictors of DES. Our studies are the first to suggest the psychiatric conditions themselves, and not only their treatments, are involved in the pathophysiology of DES. The biological plausibility comes from recent studies that demonstrated serotonin in human tears[12] and serotonin receptors in human conjunctivae,[13,14] coupled with the dysregulation of neuropeptides in patients with depression and PTSD.[15] Antidepressants have been previously shown to increase the risk of DES[8,16,17] and are thought to mediate their effect through the anticholinergic pathway. It is important to note, however, that while we hypothesize that psychiatric diagnoses and treatment lead to DES, this study does not allow us to determine directionality. It is also possible that the pathophysiology is one where DES symptoms impact one's emotional state to a degree that contributes to the development of a psychiatric illness. Future studies will be needed to explore the direction and relationship of the noted associations.

Regarding other DES risk factors found in our study, there is biological plausibility for an association between sleep apnea and DES, including irritation from a continuous positive airflow pressure machine[18] and the common association of sleep apnea with floppy eyelid syndrome.[19] Likewise, there is a well-established association between rosacea,[20,21] glaucoma medication use,[22,23] and dry eye syndrome. Previous studies have also shown that patients with arthritis are at higher risk for DES.[8,17,24]

As with all retrospective reports, our study has limitations that need to be considered when interpreting the study results. This study relied on ICD-9 codes and medication use to define and exclude DES. In this manner, it is possible that patients with DES but without a documented diagnosis were excluded from the case group or included in the control group. Given the retrospective nature of the study, the eye examination that led to the diagnosis of DES was also variable and it was therefore not possible to further subcategorize patients into mild and severe disease. Our study cases, therefore, include a heterogeneous mix of diagnoses, which could have influenced the strength and direction of associations in our analysis. Furthermore, several variables that could have affected DES risk were not evaluated in this study, including ocular comorbidities (eg, previous cataract surgery, pterygium) and environmental factors. Finally, several therapies that can be used to treat DES as well as other ocular surface disorders (eg, topical corticosteroids, bandage contact lenses) were not included as dry eye therapies. This was done as we hoped that patients whose symptoms required more aggressive therapy would be captured by artificial tear use and that the exclusion of these nonspecific medications would minimize the inclusion of non-DES-related ocular surface entities into the DES case group. With these limitations in mind, this study confirms that DES is common in both male and female veterans, although it is important to bear in mind that patients seen in VA clinics do not include or represent all former military personnel. Furthermore, the treatment of a psychiatric disorder increases the risk of having a DES diagnosis. The study highlights the need for future research regarding the mechanisms by which depression and post-traumatic stress disorder may impact the health of the ocular surface. In the meantime, primary care physicians should consider asking patients with known psychiatric diagnoses about dry eye symptoms and refer symptomatic cases to an eye care provider for further evaluation.

ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF Interest. Publication of this article was supported by a grant from the Veterans Affairs Medical Center, Washington, D.C. (Dr Galor), and with unrestricted funds from Research to Prevent Blindness, New York, New York. Financial disclosures: A.G.: Veterans Affairs career development award; V.L.P.: consultancy, Alcon; lecture fees, Alcon; research grant (RO1 EY018624) from Alcon and Bank of America; D.L.:grants NEI R21 EY019096, R01OH00315, CDC 66442T, 1U58DP002652-01, James and Esther 1KG07-33979, Bankhead Coley 1BG06-341963; H.F.: NIH 1R18AE000049-01 and Merit review grants (VA, CSP-465, and CSP-G002). Involved in conception and design (A.G.); analysis and interpretation (A.G., W.F., D.J.L., H.F.); writing the article (A.G.); critical revision (A.G., W.F., D.J.L., H.F., A.L.F., V.L.P., K.L.Z.); final approval (A.G., W.F., D.J.L., H.F., A.L.F., V.L.P., K.L.Z.); data collection (A.L.F.), statistical expertise (A.G., W.F., D.J.L., H.F.); and literature search (A.G.). The Miami Veterans Affairs Institutional Review Board reviewed and approved the retrospective examination of patient records for this study, which was conducted in accordance with the principles of the Declaration of Helsinki.

REFERENCES

1. The epidemiology of dry eye disease: report of the Epidemiology Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf 2007;5(2):93–107.
2. Brewitt H, Sistani F. Dry eye disease: the scale of the problem. Surv Ophthalmol 2001;45(Suppl 2):S199–202.
3. Schaumberg DA, Sullivan DA, Dana MR. Epidemiology of dry eye syndrome. Adv Exp Med Biol 2002;506(Pt B):989–998.
4. Mertzanis P, Abetz L, Rajagopalan K, et al. The relative burden of dry eye in patients' lives: comparisons to a U.S. normative sample. Invest Ophthalmol Vis Sci 2005;46(1):46–50.
5. Miljanovic B, Dana R, Sullivan DA, et al. Impact of dry eye syndrome on vision-related quality of life. Am J Ophthalmol 2007;143(3):409–415.
6. Schiffman RM, Walt JG, Jacobsen G, et al. Utility assessment among patients with dry eye disease. Ophthalmology 2003;110(7):1412–1419.
7. Rajagopalan K, Abetz L, Mertzanis P, et al. Comparing the discriminative validity of two generic and one disease-specific health-related quality of life measures in a sample of patients with dry eye. Value Health 2005;8(2):168–174.
8. Moss SE, Klein R, Klein BE. Prevalence of and risk factors for dry eye syndrome. Arch Ophthalmol 2000;118(9):1264–1268.
9. Schaumberg DA, Dana R, Buring JE, et al. Prevalence of dry eye disease among US men: estimates from the Physicians' Health Studies. Arch Ophthalmol 2009;127(6):763–768.
10. Schaumberg DA, Sullivan DA, Buring JE, et al. Prevalence of dry eye syndrome among US women. Am J Ophthalmol 2003;136(2):318–326.
11. Galor A, Feuer W, Lee DJ, et al. Prevalence and risk factors of dry eye syndrome in a United States veterans affairs population. Am J Ophthalmol 2011;152(3):377–384.e2.
12. Martin XD, Brennan MC. Serotonin in human tears. Eur J Ophthalmol 1994;4(3):159–165.
13. Sharif NA, Senchyna M. Serotonin receptor subtype mRNA expression in human ocular tissues, determined by RT-PCR. Mol Vis 2006;12:1040–1047.
14. Turner HC, Alvarez LJ, Candia OA, et al. Characterization of serotonergic receptors in rabbit, porcine and human conjunctivae. Curr Eye Res 2003;27(4):205–215.
15. Werner FM, Covenas R. Classical neurotransmitters and neuropeptides involved in major depression: a review. Int J Neurosci 2010;120(7):455–470.
16. Moss SE, Klein R, Klein BE. Long-term incidence of dry eye in an older population. Optom Vis Sci 2008;85(8):668–674.
17. Chia EM, Mitchell P, Rochtchina E, et al. Prevalence and associations of dry eye syndrome in an older population: the Blue Mountains Eye Study. Clin Experiment Ophthalmol 2003;31(3):229–232.
18. Harrison W, Pence N, Kovacich S. Anterior segment complications secondary to continuous positive airway pressure machine treatment in patients with obstructive sleep apnea. Optometry 2007;78(7):352–355.
19. Fowler AM, Dutton JJ. Floppy eyelid syndrome as a subset of lax eyelid conditions: relationships and clinical relevance (an ASOPRS thesis). Ophthal Plast Reconstr Surg 2010;26(3):195–204.
20. Apostol S, Filip M, Dragne C, et al. Dry eye syndrome. Etiological and therapeutic aspects. Oftalmologia 2003;59(4):28–31.
21. Gudmundsen KJ, O'Donnell BF, Powell FC. Schirmer testing for dry eyes in patients with rosacea. J Am Acad Dermatol 1992;26(2 Pt 1):211–214.
22. Fechtner RD, Godfrey DG, Budenz D, et al. Prevalence of ocular surface complaints in patients with glaucoma using topical intraocular pressure-lowering medications. Cornea 2010;29(6):618–621.
23. Leung EW, Medeiros FA, Weinreb RN. Prevalence of ocular surface disease in glaucoma patients. J Glaucoma 2008;17(5):350–355.
24. McCarty CA, Bansal AK, Livingston PM, et al. The epidemiology of dry eye in Melbourne, Australia. Ophthalmology 1998;105(6):1114–1119.

Biosketch

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Biosketch

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