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The Association Between Dry Eye Disease and Depression and Anxiety in a Large Population-Based Study

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• PURPOSE: To investigate the association between dry eye disease and each of depression and anxiety.

• DESIGN: Retrospective, case-control study.

• METHODS: <u>SETTING</u>: University of North Carolina outpatient clinics. <u>STUDY POPULATION</u>: All patients over the age of 18 years seen between July 2008 and June 2013 were included in the analysis. <u>OBSERVATION PROCE-DURE</u>: Cases were defined according to ICD-9 diagnosis codes for dry eye disease, anxiety, and depression. <u>OUTCOME MEASURE</u>: Separate odds ratios were calculated for dry eye disease and each of anxiety and depression. Similar odds ratios were also calculated between dry eye disease and rheumatoid arthritis, a systemic disease with a known association with dry eye, as a way of validating our approach.

• RESULTS: A total of 460 611 patients were screened; 7207 patients with dry eye were included, while 20 004 patients with anxiety and 30 100 patients with depression were included. The adjusted odds ratio for dry eye disease and anxiety was 2.8 (95% confidence interval [CI] 2.6–3.0). For dry eye disease and depression, the odds ratio was 2.9 (95% CI 2.7–3.1).

• CONCLUSIONS: We identified a statistically significant association between dry eye disease and each of depression and anxiety. Such an association has implications for ophthalmologists in the management and treatment of dry eye disease. (Am J Ophthalmol 2015;159: 470–474. © 2015 by Elsevier Inc. All rights reserved.)

RY EYE DISEASE IS A MULTIFACTORIAL CHRONIC disease with variable prevalence. The International Dry Eye Workshop (DEWS) researchers have discussed extensively the inherent difficulty in defining its prevalence and demography.¹ Dry eye disease remains a largely symptomatic diagnosis, without a single defining diagnostic test.¹ Despite these difficulties, several

population-based studies have reported the prevalence of dry eye, with quoted prevalence rates ranging from 5.5% to 33.7%. Other researchers argue that the true prevalence is considerably higher.^{2–12} Nevertheless, there is little question that dry eye remains a common and complex problem for health care providers. In addition, dry eye is associated with other ocular and systemic illnesses. Sjogren syndrome, for example, is an autoimmune disease that has as part of its diagnostic criteria the presence of dry eye. Rheumatoid arthritis and dry eye are related to each other as well.^{13,14} Studies have found an association between dry eye and diabetes mellitus,^{1,15} though other studies have not shown this link.¹⁶

More recently, several population-based studies have investigated a possible association between dry eye and depression. Wen and associates observed an increased frequency of dry eye disease in 472 psychiatric patients being treated for a variety of psychiatric illnesses, including depression and anxiety.¹⁷ Likewise, Galor and associates demonstrated an association between dry eye disease and post-traumatic stress disorder as well as depression in a veterans population.¹⁸ Finally, a recent study from the Beijing Eye Study identified an association between dry eye disease and depression symptoms in an elderly population in Beijing.¹⁹ However, all current data available on this association have focused on a small population²⁰ or on an agespecific population such as the elderly.^{19,21}

The purpose of this study was to investigate the association between dry eye disease and both depression and anxiety in a large adult population in the United States. To our knowledge, this is the largest population in which these associations have been studied to date. In addition to depression, we analyzed the association between dry eye and another disease with an already known association, rheumatoid arthritis, to validate our analytical approach.

METHODS

WE PERFORMED A RETROSPECTIVE CASE-COHORT STUDY BY performing a chart review using the Carolina Data Warehouse of all patients seen in the outpatient setting at the University of North Carolina between July 1, 2008 and June 30, 2013. The study design was prospectively approved by the University of North Carolina Institutional

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TABLE 1. Association Between Dry Eye Disease and

 Depression and Anxiety: Aggregated Data From the Carolina

 Data Warehouse (Cases Defined Using ICD 9 Diagnosis

 Codes for Each Disease Entity and Further Divided by Age)

| Sex | Age Group | Total | With Dry Eye | With Anxiety | With Depression | With Rheumatoid Arthritis |
|--------|--------------|--------|-----------------|-----------------|--------------------|------------------------------|
| Female | 18–35 | 96 847 | 493 | 3779 | 5373 | 243 |
| | 36–50 | 71 791 | 847 | 3942 | 5893 | 662 |
| | 51–65 | 64 966 | 1646 | 3861 | 6103 | 1096 |
| | >65 | 53 799 | 1958 | 2560 | 4123 | 933 |
| Male | 18–35 | 43 832 | 204 | 2007 | 2331 | 65 |
| | 36–50 | 41 859 | 439 | 1847 | 2564 | 155 |
| | 51–65 | 47 762 | 670 | 1838 | 3128 | 358 |
| | >65 | 39 755 | 950 | 993 | 1887 | 326 |
| | | | | | | |

Review Board. The Carolina Data Warehouse is a repository of clinical, research, and administrative data captured from the electronic health records of all patients who have entered into the University of North Carolina Health Care System since July 1, 2004. Our study population included any patient over the age of 18 years at the time of data extraction with any data in the Carolina Data Warehouse. Cases were defined according to ICD-9 codes as follows: dry eye disease (ICD-9 code 375.15), anxiety (ICD-9 code 300, 300.00, 300.01, 300.02), depression (311, 296.2x, 296.3x), or rheumatoid arthritis (ICD-9 code 714.0). Patients for whom age could not be determined were excluded.

Using the diagnostic codes outlined above, odds ratios were separately estimated between dry eye and each of the other diseases. We were primarily interested in the associations between the diagnosis of dry eye disease and each of depression and anxiety.

We used separate logistic regression models to estimate associational odds ratios, each adjusted for age group and sex, along with 95% confidence intervals. For purposes of de-identification, data were extracted from the Carolina Data Warehouse and aggregated by sex and age group, with age groups predefined as 18–35 years, 36–50 years, 51–65 years, and older than 65 years. These age groups were defined prior to the data analysis. To explore the potential for differential associations across age groups, we fit additional models that included disease-by-age-group interactions. We report 95% confidence intervals for the associations within each of these age groups along with a test of the interaction term for comparing associations across age groups.

RESULTS

A TOTAL OF 460 611 PATIENTS WERE INCLUDED IN THE analysis; the clinic payer mix was estimated to be 50% Medicare, 25% private insurance, 15% Medicaid, and 10% uninsured. Of the 460 611 patients, there were 7207

TABLE 2. Estimated Prevalence of Dry Eye in Patients With or Without Each of Depression and Anxiety

| | With Dry Eye | Without Dry Eye | Total | |
|--------------------|--------------|-----------------|---------|--|
| With anxiety | 823 (4.0%) | 20 004 (96.0%) | 20 827 | |
| Without anxiety | 6384 (1.5%) | 433 400 (98.5%) | 439 784 | |
| With depression | 1302 (4.2%) | 30 100 (95.8%) | 31 402 | |
| Without depression | 5905 (1.4%) | 423 304 (98.6%) | 429 209 | |
| Total | 7207 | 453 404 | 460 611 | |
| | | | | |

patients with dry eye, 20 004 patients with anxiety, and 30 100 patients with depression. Seventy-six patient records were excluded because age could not be determined. Table 1 summarizes the aggregated data. Table 2 presents the prevalence of dry eye in patients with each of depression and anxiety, respectively.

The estimated odds ratio between dry eye disease and anxiety was 2.8, with a 95% confidence interval of (2.6, 3.0) (See Table 3). The estimated odds ratio between dry eye disease and depression was 2.9, with a 95% confidence interval of (2.7, 3.1). The estimated odds ratio between dry eye disease and rheumatoid arthritis was 3.2, with a 95% confidence interval of (2.8, 3.7). We found evidence that these associations differed across age groups (Table 4). Notably, there was a greater association with dry eye and rheumatoid arthritis in the youngest age group compared to the older age groups.

DISCUSSION

THE PURPOSE OF THIS STUDY WAS TO ANALYZE THE ASSOCIation between dry eye disease and each of depression and anxiety. As discussed previously, other studies of these associations had focused on a specific population, such as an elderly population in Beijing or a Veterans Affairs population.^{17,18} Our study, however, included over 7000 patients with dry eye across all age groups, which we argue represents a larger and more diverse population than previously studied.

We identified statistically significant associations between dry eye disease and each of depression and anxiety. Such an association is of importance to the eye care provider, who may serve as the entrance to medical care for patients. For example, in the case of diabetes mellitus, patients who have been previously undiagnosed with the disorder may present initially to the eye care provider owing to a decrease in vision. Given our findings, we believe this may be the case for patients with depression and anxiety as well, who may present to seek medical care first with symptoms of dry eye. Perhaps there is a role for the eye care provider to initiate screening measures in dry eye patients for these comorbidities. To our Download English Version:

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