

Supplemental Online Content

McCann P, Abraham AG, Mukhopadhyay A, et al. Prevalence and incidence of dry eye and meibomian gland dysfunction in the United States: a systematic review and meta-analysis. *JAMA Ophthalmol*. Published online October 27, 2022. doi:10.1001/jamaophthalmol.2022.4394

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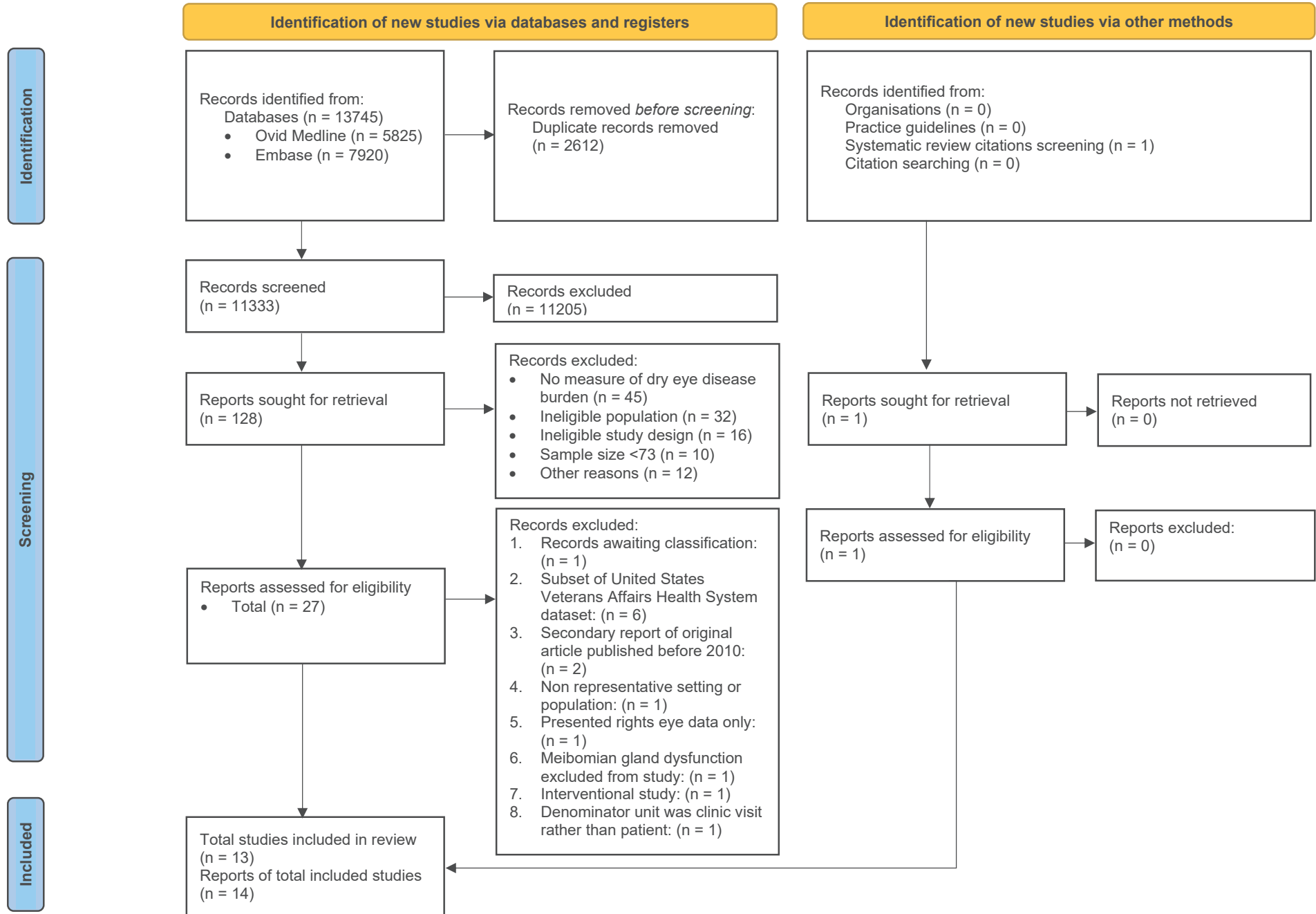
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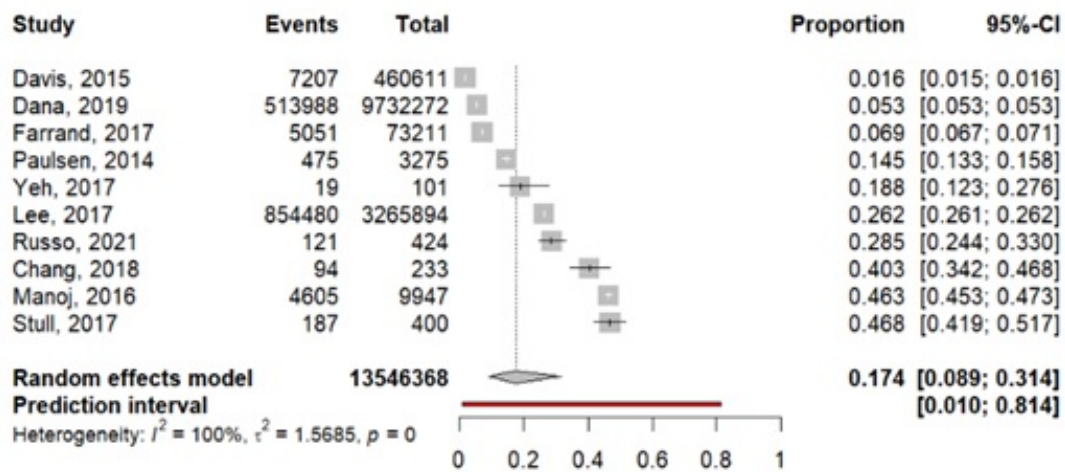
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This supplemental material has been provided by the authors to give readers additional information about their work.

eFigure 1 PRISMA Search Flow Diagram





eFigure 2 Forest Plot of dry eye prevalence including all studies

eTable 1. MEDLINE and Embase search strategies

MEDLINE (via Ovid MEDLINE® ALL)	
1	exp Dry Eye Syndromes/
2	exp Keratoconjunctivitis Sicca/
3	exp Xerophthalmia/
4	exp Meibomian Glands/
5	(dry* adj3 eye*).tw,kf.
6	((keratoconjunctivitis or kerato-conjunctivitis) adj1 sicca).tw,kf.
7	xerophthalmi*.tw,kf.
8	meibomian gland dysfunction.tw,kf.
9	exp Sjogren's Syndrome/
10	((Sjogren* or Sjoegren*) adj1 (syndrom* or disease*)).tw,kf.
11	(9 or 10) and (exp Eye/ or eye*.mp. or ocular*.mp. or ophthalm*.mp.)
12	or/1-8,11
13	exp Epidemiology/
14	exp Epidemiologic Methods/
15	epidemiology.fs.
16	burden of disease.tw,kf.
17	DALY*.tw,kf.
18	death rate*.tw,kf.
19	Disability Adjusted Life Years.tw,kf.
20	disease burden.tw,kf.
21	endemic*.tw,kf.
22	epidemic*.tw,kf.
23	epidemiolog*.tw,kf.
24	frequency.tw,kf.
25	incidence*.tw,kf.
26	morbidities.tw,kf.
27	morbidity.tw,kf.
28	occurrence.tw,kf.
29	outbreak*.tw,kf.
30	prevalence.tw,kf.
31	surveillance.tw,kf.

32 survival rate*.tw,kf.
33 years lived with disability.tw,kf.
34 years of life lost.tw,kf.
35 YLD*.tw,kf.
36 YLL*.tw,kf.
37 or/13-36
38 12 and 37
39 38 NOT (exp animals/ NOT exp humans/)
40 limit 39 to yr="2010 -Current"

Embase (via Elsevier)

#1 'dry eye'/exp
#2 'dry eye syndrome'/exp
#3 'evaporative dry eye disease'/exp
#4 'keratoconjunctivitis sicca'/exp
#5 'xerophthalmia'/exp
#6 'meibomian gland'/exp
#7 (dry* NEAR/3 eye*):ab,ti,kw
#8 ((keratoconjunctivitis or kerato-conjunctivitis) NEAR/1 sicca):ab,ti,kw
#9 xerophthalmi*:ab,ti,kw
#10 'meibomian gland dysfunction':ab,ti,kw
#11 'Sjogren syndrome'/exp
#12 ((Sjogren* or Sjogren*) NEAR/1 (syndrom* or disease*)):ab,ti,kw
#13 (#11 OR #12) AND ('eye'/exp OR eye* OR ocular* OR ophthalm*)
#14 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #13
#15 'epidemiology'/exp
#16 epidemiology:lnk
#17 'burden of disease':ab,ti,kw
#18 DALY*:ab,ti,kw
#19 'death rate*':ab,ti,kw
#20 'Disability Adjusted Life Years':ab,ti,kw
#21 'disease burden':ab,ti,kw
#22 endemic*:ab,ti,kw
#23 epidemic*:ab,ti,kw

#24 epidemiolog*:ab,ti,kw
#25 frequency:ab,ti,kw
#26 incidence*:ab,ti,kw
#27 morbidities:ab,ti,kw
#28 morbidity:ab,ti,kw
#29 occurrence:ab,ti,kw
#30 outbreak*:ab,ti,kw
#31 prevalence:ab,ti,kw
#32 surveillance:ab,ti,kw
#33 'survival rate*':ab,ti,kw
#34 'years lived with disability':ab,ti,kw
#35 'years of life lost':ab,ti,kw
#36 YLD*:ab,ti,kw
#37 YLL*:ab,ti,kw
#38 #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR
#26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37
#39 #14 AND #38
#40 #39 NOT ([animals]/lim NOT [humans]/lim)
#41 #40 AND [2010-2021]/py

eTable 2. Excluded full texts

Author, year	Citation	Reason for exclusion
Schachter, 2014	Investigative Ophthalmology & Visual Science 2014;55: 49	Contacted author via email: Awaiting classification
Dermer, 2018	Clinical ophthalmology (Auckland, N.Z.) 2018;12: 2471-2481	Subset of United States Veterans Affairs Health System dataset
Pouyeh, 2012	American Journal of Ophthalmology 2012;153: 1061-1066.e3	Subset of United States Veterans Affairs Health System dataset
Brown, 2013	Investigative Ophthalmology & Visual Science 2013;54: 5310	Original dry eye prevalence published in 1997
van Landingham, 2014	British Journal of Ophthalmology 2014;98: 639 LP - 644	Original dry eye prevalence published in 1997
Sridhar, 2018	Seminars in ophthalmology 2018;33: 185-190	Non representative setting or population
Murakami, 2015	Investigative Ophthalmology & Visual Science 2015;56: 2508	Presented data for rights eyes only
Gupta, 2018	Cornea 2018;37: 426-430	Meibomian gland dysfunction excluded from study
Ziemanski, 2018	American Journal of Ophthalmology 2018;189: 29-40	Interventional study
Stagg, 2014	Investigative Ophthalmology & Visual Science 2014;55: 5572	Denominator unit was clinic visit rather than patient
Modi, 2014	Investigative ophthalmology & visual science 2014;55: 650-653	Subset of United States Veterans Affairs Health System dataset
Galor, 2013	Investigative Ophthalmology & Visual Science 2013;54: 1426-1433	Subset of United States Veterans Affairs Health System dataset, MGD not defined and MGD prevalence not explicitly reported
Galor, 2011	American journal of ophthalmology 2011;152: 377-384.e2	Subset of United States Veterans Affairs Health System dataset
Galor, 2014	Ophthalmology 2014;121: 972-973.e1	Subset of United States Veterans Affairs Health System dataset

MGD – Meibomian gland dysfunction

eTable 3. Risk of bias assessments for prevalence and incidence studies

3a. Risk of bias assessments for prevalence studies

Risk of bias domains	Paulsen, 2014	Davis, 2015	Manoj, 2016	Stull, 2017	Yeh, 2017	Farrand, 2017	Lee, 2017	Chang, 2018	Dana, 2019	Russo, 2021	Alghamdi, 2016
Representativeness of target population to national population	N	N	N	N	N	Y	N	N	Y	N	N
Representativeness of sampling frame to target population	Y	N	N	N	N	Y	Y	N	Y	N	Y
Sampling: random or census	N	Y	N	N	N	Y	Y	N	Y	Y	N
Minimal non-response bias	Y	Y	N	Y	N	N	Y	Y	Y	Y	N
Data collected directly from participants	Y	N	Y	N	Y	Y	N	Y	N	N	Y
Acceptable case definition	Y	N	Y	N	Y	Y	N	Y	N	N	Y
Valid and reliable instrument	N	N	Y	N	Y	Y	N	Y	N	N	Y
Same mode of data collection for all participants	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
Prevalence period appropriate	Y	N	N	Y	Y	N	Y	Y	Y	Y	Y
Numerator(s) and denominator(s) appropriate	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
Overall risk of bias	L	H	H	H	H	M	M	M	M	H	H
Y - yes; N - no; NA - not applicable; U - unclear; L - low; M - moderate; H - high											

3b. Risk of bias assessments for incidence studies

Risk of bias domains	Chi, 2012*	Dana, 2019*
Exposed and unexposed groups recruited from the same population	Y	Y
Ascertainment of exposure	N	Y
Strategies to deal with confounders stated	NA	Y
Participants free of the outcome at the start of the study	Y	Y
Valid and reliable measurement of outcome	N	Y
Sufficient follow up time	Y	Y
Follow up complete or incomplete follow up described and explored	U	U
Appropriate statistical analysis	U	Y
Overall appraisal	H	M
Y - yes; N - no; NA - not applicable; U - unclear; L - low; M - moderate; H - high		

eTable 4. Stratified associations with dry eye and meibomian gland dysfunction

Study, Year of publication	Age	Sex	Race / ethnicity	Medical comorbidities	Medication use	US region	Year of estimate	Dry eye disease severity
Paulsen, 2014	21-49 years: 14.1% ≥50 years: 15.2% 21-34 years: 12.8% 35-44 years: 14% 45-54 years: 13.9% 55-64 years: 15.5% 65-84 years: 18.9%	Males: 10.5% Females: 17.9%						
Manoj, 2016		Males: 44.2% ¹ Females: 47.4% ¹		Post cataract surgery: 21.1% ² Post refractive surgery: 9.0% ²	Glaucoma medication: 6.0% ²			Tear hyperosmolarity ¹ : 46.3% ²

								Osmolarity ≥ 316 mOsm/L: 29% ²
Alghamadi, 2016		Males: 92.3% ³ Females: 7.7% ³	White: 55.0% ³ Black: 41.1% ³ Hispanic: 28.7% ³ Non-Hispanic: 71.3% ³	Current smoking: 35.7% ³ Hypertension: 72.1% ³ Hypercholesterolemia: 65.1% ³ Diabetes: 29.5% ³ Posttraumatic stress disorder: 24.8% ³ Depression: 53.5% ³ Arthritis: 47.3% ³ Sleep apnea: 20.9% ³ Benign prostatic hyperplasia: 19.4% ³	Antidepressants: 40.3% ³ Antianxiolytics: 38.0% ³ Antihistamine: 14.7% ³ Nonsteroidal antiinflammatory agents: 34.1% ³			

Farrand, 2017	18-49 years: 3.4% ⁴ ≥50 years: 11.3% ⁴	Males: 4.5% ¹ Females: 8.8% ¹				Northeast: 6.69% 95%CI 6.14, 7.24 Midwest: 6.40% 95%CI 5.98, 6.82 South: 7.04% 95%CI 6.66, 7.41 West: 6.78% 95%CI 6.30, 7.25	Mild: 50% Moderate: 42% Severe: 8%
Yeh, 2017							SPEED ≥9: 18.8% ² SPEED ≥6: 42.6% ²
Yalamanchi li, 2018	50-59 years: 7.72% 80-89 years: 13.71%		Asian: 10.20% 95%CI 7.58, 13.59 Caucasian: 13.20% 95%CI 12.60, 13.83 African American: 5.56% 95%CI 4.87, 6.34				

Chang, 2018								DEQ5 ≥6: 40.3% ² DEQ5 ≥12: 10.3% ²
Dana, 2019	2008: 0.15 ^{5,6} 2009: 0.17 ^{5,6} 2010: 0.18 ^{5,6} 2011: 0.20 ^{5,6} 2012: 0.26 ^{5,6} 2008: 0.42 ^{5,7} 2009: 0.46 ^{5,7} 2010: 0.51 ^{5,7} 2011: 0.56 ^{5,7} 2012: 0.65 ^{5,7} 2008: 1.03 ^{5,8} 2009: 1.15 ^{5,8} 2010: 1.28 ^{5,8} 2011: 1.40 ^{5,8} 2012: 1.62 ^{5,8}	Males: 2.96% ^{2,5} Females: 7.78% ^{2,5} 2005: 0.33 ^{5,9} 2006: 0.42 ^{5,9} 2007: 0.51 ^{5,9} 2008: 0.62 ^{5,9} 2009: 0.75 ^{5,9} 2010: 0.94 ^{5,9} 2011: 1.14 ^{5,9} 2012: 1.55 ^{5,9} 2005: 1.36 ^{5,10} 2006: 1.66 ^{5,10} 2007: 1.97 ^{5,10} 2008: 2.30 ^{5,10} 2009: 2.67 ^{5,10} 2010: 3.16 ^{5,10}					2005: 0.83 ⁵ 2006: 1.03 ⁵ 2007: 1.23 ⁵ 2008: 1.44 ⁵ 2009: 1.69 ⁵ 2010: 2.03 ⁵ 2011: 2.38 ⁵ 2012: 3.02 ⁵	

		2011: 3.65 ^{5,10} 2012: 4.52 ^{5,10}						
1 - Proportion of sex group 2 - Proportion of all participants 3 - Proportion of participants with meibum quality score ≥ 2 4 - Self-reported diagnosis AND symptoms 5 - Overall DED prevalence 6 - 18-39 years 7 - 40-49 years 8 - ≥ 50 years 9 - Males 10 - Females								

eTable 5. Univariable model associations with dry eye and meibomian gland dysfunction

Study, Year of publication	Age	Sex	Race / ethnicity	Medical comorbidities	Medication use
Davis, 2015				Diabetes mellitus: OR 2.25	
Lee, 2017		Female: OR 1.25 95%CI 1.24, 1.27 ^{1,2}	Black: OR 1.05 95%CI 1.04, 1.05 ^{1,3}	Migraine: OR 1.31 95%CI 1.30, 1.32 ² Rheumatoid arthritis: OR 1.93 95%CI 1.90, 1.96 ² Diabetic neuropathy: OR 1.72 95%CI 1.71, 1.73 ² Anxiety: OR 1.31 95%CI 1.30, 1.32 ² Depression: OR 1.36 95%CI 1.35, 1.37 ² Posttraumatic stress disorder: OR 1.27 95%CI 1.26, 1.28 ²	Analgesics: OR 2.07 95%CI 2.05, 2.08 ² Antidepressant: OR 1.53 95%CI 1.52, 1.54 ² Anxiolytic: OR 1.44 95%CI 1.43, 1.45 ²
Farrand, 2017			White: 7.03% 95%CI 6.79, 7.27 ⁴ African American: 6.29% 95%CI 5.49, 7.09 ⁴ Hispanic: 6.23% 95%CI 5.50, 6.96 ⁴ Asian: 4.25% 95%CI 3.57, 4.93 ⁴ Other: 8.74% 95%CI 7.33, 10.16 ⁴		

Yeh, 2017	p = 0.246 ⁵	p = 0.384 ⁵	Asian: OR 1.47, p = 0.59 ^{6,7}		Allergy medication: OR 6.03 ⁶ p = 0.16
Chang, 2018	Insufficient data	Female: OR 1.42 95%CI 0.80, 2.52 ⁸ Female: OR 1.91 95%CI 0.69, 5.43 ⁹	Black: OR 0.83 95%CI 0.42, 1.65 ^{3,8} Black: OR 0.57 95%CI 0.16, 2.00 ^{3,9}	Diabetes: OR 1.31 95%CI 1.30, 1.32 ⁸ Hypertension: OR 1.93 95%CI 1.90, 1.96 ⁸ Thyroid disease: OR 1.72 95%CI 1.71, 1.73 ⁸ Refractive surgery: OR 1.27 95%CI 1.26, 1.28 ⁸ Diabetes: OR 3.98 95%CI 1.14, 13.86 ⁹ Hypertension: OR 1.27 95%CI 0.44, 3.61 ⁹ Thyroid disease: OR 1.99 95%CI 0.53, 7.49 ⁹ Refractive surgery: OR 2.28 95%CI 0.46, 11.44 ⁹	Anxiolytic: OR 1.73 95%CI 0.64, 4.67 ⁸ Antidepressant: OR 1.75 95%CI 0.61, 5.01 ⁸ Antihistamine: OR 1.83 95%CI 0.85, 3.96 ⁸ Analgesics: OR 1.70 95%CI 0.78, 3.70 ⁸ Glaucoma medication: OR 0.49 95%CI 0.05, 4.76 ⁸ Anxiolytic: OR 1.17 95%CI 0.25, 5.48 ⁹ Antidepressant: OR 1.37 95%CI 0.29, 6.47 ⁹ Antihistamine: OR 3.33 95%CI 1.25, 8.88 ⁹ Analgesics: OR 1.01 95%CI 0.28, 3.61 ⁹
<p>1 - Reference: male 2 - No dry eye vs tear film dysfunction 3 - Reference: white 4 - Proportion of race with dry eye 5 - Meiboscore = 3 6 - No MG atrophy vs meiboscore = 3 7 - Reference: Non-Asian 8 - No symptoms vs DEQ-5 ≥6 9 - No symptoms vs DEQ-5 ≥12</p>					

eTable 6. Multivariable model associations with dry eye and meibomian gland dysfunction

Study, Year of publication	Age	Sex	Race / ethnicity	US region
Paulsen, 2014	OR 1.01 95%CI 1.00, 1.02 ¹	Female: OR 1.45 95%CI 1.14, 1.85 ²		
Farrand, 2017	35-44 years: OR 1.29 95%CI 1.14, 1.47 ³ 45-54 years: OR 1.95 95%CI 1.74, 2.20 ³ 55-64 years: OR 3.34 95%CI 2.98, 3.74 ³ 65-74 years: OR 3.74 95%CI 3.30, 4.23 ³ ≥75 years: OR 4.95 95%CI 4.26, 5.74 ³	Female: OR 2.00 95%CI 1.88, 2.13 ²	African American: OR 0.96 95%CI 0.86, 1.06 ⁴ Hispanic: OR 1.34 95%CI 1.19, 1.51 ⁴ Asian: OR 1.08 95%CI 0.91, 1.27 ⁴ Other: OR 1.44 95%CI 1.22, 1.69 ⁴	Midwest: OR 1.02 95%CI 0.93, 1.12 ⁵ South: OR 1.14 95%CI 1.05, 1.24 ⁵ West: OR 1.08 95%CI 0.98, 1.18 ⁵
<p>1 - Per increase in age group (21-34, 35-44, 45-54, 55-64, 65-84) 2 - Reference: male 3 - Self-reported diagnosis AND symptoms 4 - Reference: white 5 - Reference: Northeast</p>				