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# Association between dry eye symptoms and suicidal ideation

Sun-Bi Um



The Graduate School

Yonsei University

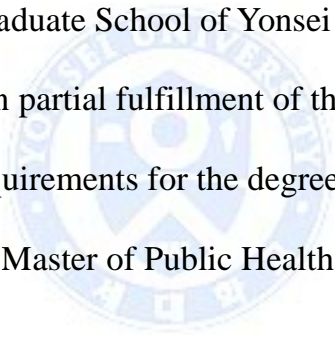
Department of Public Health

# Association between dry eye symptoms and suicidal ideation

A Master's Thesis

Submitted to the Department of Public Health  
and the Graduate School of Yonsei University

in partial fulfillment of the  
requirements for the degree of  
Master of Public Health



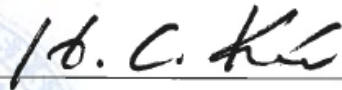
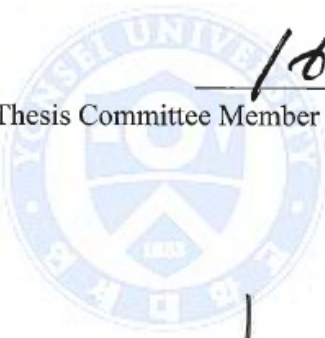
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June 2015

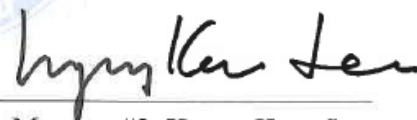
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## **ABSTRACT**

# **Association between dry eye symptoms and suicidal ideation**

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(Directed by Professor Il Suh)

### **INTRODUCTION:**

Several studies have examined the association between dry eye disease (DED) with depression and quality of life. However, very few numbers of studies further examined the association between DED and suicidal ideation targeting a large population. Therefore, this study assessed the associations of DED with

depression and suicidal ideation in the general Korean adult population.

**METHODS:**

Data from 16,453 participants (7,008 men and 9,445 women) aged  $\geq 19$  years included in the fifth Korea National Health and Nutrition Examination Survey (KNHANES), conducted in 2010-2012, were analyzed. DED was defined as a previous diagnosis by an ophthalmologist, as well as dry eye symptom experience. Diagnosis of depression and suicidal ideation were obtained via responses to an interviewer-assisted questionnaire and questions asked in a closed-ended response format. Logistic regression was used to examine the associations between DED, depression, and suicidal ideation.

**RESULTS:**

People with diagnosed DED exhibited a 1.31 (95% confidence interval (CI) 1.11-1.56) times higher odds of having depression and 1.21 (95% CI 1.02-1.43) times higher odds of suicidal ideation than those without DED, after adjusting for sex, age, body mass index, smoking behavior, alcohol consumption, physical activity, major cardiovascular disease, and cancer. Similarly, people experiencing dry eye symptoms were also at higher risk for depression (adjusted odds ratio 1.47; 95% CI 1.28-1.70) and were more likely to think of committing suicide (adjusted odds ratio 1.44; 95% CI 1.24-1.66) than those who did not.

**CONCLUSION:**

Our finding suggests that dry eye symptoms were associated with depression and suicidal ideation in both sexes. For diagnosed DED and suicidal ideation, association was observed in women.



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**Keywords:** Depression, Dry eye, Suicidal ideation

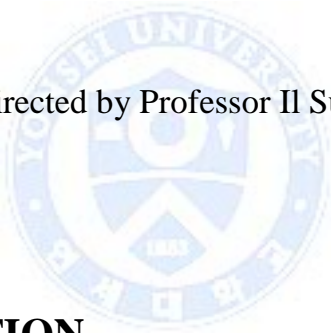
# **Association between dry eye symptoms and suicidal ideation**

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## **I. INTRODUCTION**

### ***1. Background***

Worldwide, one million people die from suicide every year (Public health action for the prevention of suicide 2012), and suicide rates are expected to increase from 1.8% in 1998 to 2.4% in 2020 (Patton et al. 2009). While suicide

may be associated with a number of factors such as psychological, biological, behavioral, physical, socio-cultural, and environmental factors (Ro et al. 2015), untreated mental illness (including depression, bipolar disease, schizophrenia, and others) is the main cause for the vast majority of suicides (Cheatle 2014; Ro et al. 2015; Subramaniam et al. 2014). Nevertheless, while the link between suicide and mental illness is well established, studies have yet to thoroughly investigate whether ocular disease is linked with suicide.

Dry eye disease (DED) is one of the most frequently encountered ocular morbidities worldwide, with an estimated prevalence of 4.3% to 73.5% for either clinically diagnosed or symptom experienced DED (Caffery et al. 1998; Chia et al. 2003; Lee et al. 2002; Lekhanont et al. 2006; Lin et al. 2003; Schaumberg et al. 2009; Schaumberg et al. 2003; Um et al. 2014; Viso, Rodriguez-Ares and Gude 2009) and a comparably higher prevalence in Asian populations than in Western populations (Lee et al. 2002; Lin et al. 2003; Schaumberg et al. 2009; Schaumberg et al. 2003). Vision plays a very important role in almost every task humans perform, at all stages of life and no matter what age. The health of the human eye depends on the flow of tears to provide constant moisture and lubrication to maintain vision and comfort. However, once tear flow is impaired, the human eye can experience symptoms of redness, stinging, burning, or a scratchy sensation, which lead to eye fatigue, visual disturbance, and even impaired quality of life

(QOL) (Le et al. 2012; Lekhanont et al. 2006; Mertzanis et al. 2005; Miljanovic et al. 2007; Nichols, Mitchell and Zadnik 2002; Schiffman et al. 2003). Also, patients with DED frequently report significant disturbances in their psychiatric state, showing symptoms of anxiety and depression (Li et al. 2011; Tounaka et al. 2014; Vehof et al. 2014).

## ***2. Objective***

Many suicidal attempts happen impulsively in moments of crisis, along with a breakdown in one's ability to deal with life stresses, such as chronic pain and illness (Ratcliffe et al. 2008). However, beyond depression, relatively few studies investigated whether prolonged symptoms of DED may possibly cause suicidal thoughts. Therefore, we aimed to examine the associations between DED, depression, and suicidal ideation using a nationally representative data targeting the entire Korean population. We hypothesized that equivalent results would be observed as in previous studies concerning the association between DED and depression, and reports of suicidal ideation would be higher in participants suffering from DED.

## **II. METHODS**

### ***1. Study population***

This study used data from the fifth Korea National Health and Nutrition Examination Survey (KNHANES), which was conducted in 2010-2012. The KNHANES is a nationally representative survey of the non-institutionalized civilian population, and is annually carried out by the Korea Centers for Disease Control and Prevention (KCDC). A complex, stratified, multistage probability sampling design based on region and household was applied in this survey to represent the national population of South Korea. The survey procedures were carried out in accordance of the Declaration of Helsinki, and participants who were willing to participate in the survey were required to sign informed consent forms approved by the Institutional Review Board of the KCDC. The KNHANES was first conducted in 1998 on a triennial basis until 2005, and from 2007, the survey was conducted annually with a variety of health measurements. The survey consists of three parts: a health interview survey, a health examination survey, and a nutrition survey. Survey questionnaires were self-administered or conducted by trained staff members, depending on the section, and examinations were

administered by highly-trained medical personnel. Further details of the survey have been described elsewhere (Kweon et al. 2014).

A total of 18,571 participants aged 19 years or older were initially included for analyses. We further excluded 1,097 participants lacking information on age, body mass index (BMI), smoking behavior, alcohol consumption, physical activity, major cardiovascular disease (CVD), cancer, depression diagnosis, menopausal status, and suicidal ideation. Since previous studies indicated that patients taking antidepressants had a higher chance of developing DED (Kim et al. 2011; Moss, Klein and Klein 2008; Schaumberg et al. 2009), we additionally excluded 242 participants who were receiving depression treatments. Lastly, after excluding non-responses on DED questionnaires, 7,008 men and 9,445 women (5,054 of whom were postmenopausal) were analyzed in relation to DED diagnosis, while 6,752 men and 9,155 women (4,919 postmenopausal) were analyzed according to dry eye symptoms (Figure 1). All analyses were performed separately according to the presence of DED diagnosis and dry eye symptoms (not mutually exclusive).



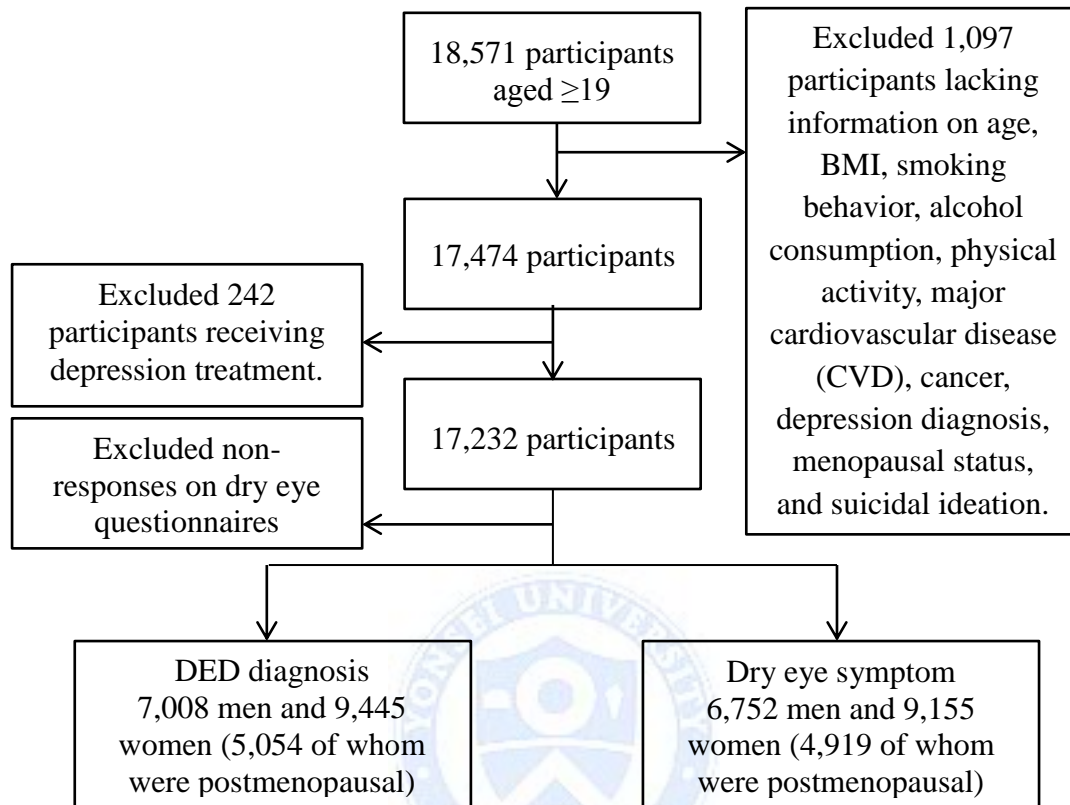


Figure 1. Flowchart of the selection criteria of the final study population

## ***2. Measurements***

### **1) Assessment of dry eye**

Examination for eye diseases was conducted by ophthalmologists designated by the Korean Ophthalmological Society (KOS). In order to ensure accurate examinations, ophthalmologists are educated and trained twice a year by the KCDC and the KOS. In 2010, the KNHANES introduced dry eye questionnaires to evaluate the prevalence of dry eye. Due to the survey design, presence of DED and dry eye symptoms were observed by close ended response questionnaires. Ophthalmologists interviewed each participant on whether they have been diagnosed with DED by an ophthalmologist before, especially emphasizing on “by an ophthalmologist.” To increase accuracy of the data collected, participants were also asked on whether he or she experienced frequent symptoms of dryness of the eye or a sense of irritation. Participants who responded “yes” to the above questionnaires were either assigned to DED diagnosis or dry eye symptoms. Those who answered “no” were classified as a control.

### **2) Assessment of depression and suicidal ideation**

Diagnosis of depression was assessed by interviewing each participant on whether he or she has ever been diagnosed with depression by a psychiatrist

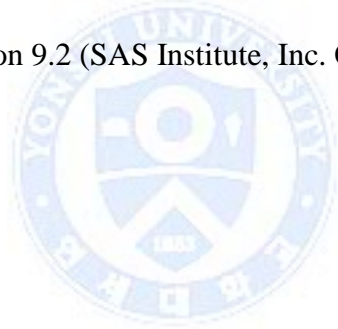
before. To increase accuracy of the data collected, participants were first asked on whether they have been diagnosed with depression so far which was followed with an emphasis on “by a psychiatrist.” Suicidal ideation was assessed by asking participants on whether they thought about committing suicide within the past 12 months.

### **3) Covariates**

Age, BMI, smoking behavior, alcohol consumption, physical activity, major CVD, and cancer were considered as covariates in the present analyses. Age and BMI were analyzed as continuous variables. Smoking behavior was categorized as non-smoking versus former or current smoking (including light and heavy smoking). Alcohol consumption was categorized as non-drinking (never consumed alcohol for the entire life and/or within the past year) versus consumption of once per week or less or of twice per week or more. Physical activity was categorized according to frequency of exercise: none versus at least once per week or more. History of major CVD (myocardial infarction and stroke) and cancer were also obtained.

### *3. Statistical Analysis*

All statistical analyses in this study were conducted using sampling weights assigned to each participant provided by the KNHANES. Student's t-test and chi-square test were used to analyze the general characteristics of the study population according to presence of DED, sex, and menopausal status for women. Serial multiple logistic regression models were used to examine the independent associations between DED, depression, and suicidal ideation. All analyses were performed using SAS version 9.2 (SAS Institute, Inc. Cary, NC).



### **III. RESULTS**

#### ***1. Characteristics of the study population according to the presence of dry eye***

Table 1 lists the characteristics of men according to the presence of dry eye. The two study groups (DED and non-DED) showed significant differences in household income, alcohol consumption, and physical activity ( $P < 0.05$  for each). For mental health components, perceived stress, depression diagnosis, and suicidal ideation did not differ in DED and non-DED men. Concerning those with dry eye symptom, unlike DED diagnosis, significant differences were noted in mental health components: perceived stress, depression diagnosis, and suicidal ideation. Among men experiencing dry eye symptom, 28.7% reported moderate to severe stress, 9.3% had depression, and 12.0% thought about suicide, all which were significantly higher than those with no dry eye symptom.

Table 2 shows the characteristics of women according to the presence of dry eye. DED diagnosed and non-DED women showed significant differences in smoking behavior, perceived stress, and depression ( $P < 0.05$  for each). Though, no difference was observed in suicidal ideation. Regarding dry eye symptom,

significant differences were observed in perceived stress, depression, and suicidal ideation, just as in men. Compared with women with no dry eye symptom, 35.7% of women with dry eye symptom reported moderate to severe stress, 23.2% were diagnosed with depression, and 22.0% thought about suicide. The results remained consistent even after stratifying women according to menopausal status (Table 3-1 and Table 3-2).



Table 1. Characteristics in men according to the presence of dry eye

Variables	DED diagnosis		P-value	Dry eye symptom		P-value
	No (n=6631)	Yes (n=377)		No (n=5978)	Yes (n=774)	
Age (years)	44.2±15.4	46.2±15.9	0.195	44.2±15.4	45.5±16.2	0.084
Body mass index (kg/m <sup>2</sup> )	24.1±3.3	24.2±3.0	0.348	24.1±3.4	23.8±3.0	0.906
Waist circumference (cm)	84.1±9.2	84.6±8.9	0.309	84.2±9.3	83.6±8.6	0.793
Mean SBP (mmHg)	120.8±15.2	118.1±13.9	0.327	120.8±15.2	119.4±14.3	0.539
Mean DBP (mmHg)	79.3±10.8	77.1±8.8	0.801	79.3±10.8	78.6±10.3	0.780
Glucose (mg/dL)	98.2±22.1	98.5±21.4	0.849	98.1±21.8	98.0±21.0	0.661
Total cholesterol (mg/dL)	187.3±36.1	186.6±31.2	0.990	187.4±36.1	186.7±33.1	0.363
HDL cholesterol (mg/dL)	49.7±11.8	51.6±12.6	0.264	49.7±11.7	51.4±11.9	0.123
Household income level						
Lowest	1179 (13.6)	59 (11.5)	0.019	1044 (13.6)	146 (13.8)	0.424
Low	1733 (27.3)	95 (22.5)		1545 (26.9)	214 (28.1)	
High	1868 (30.5)	100 (28.3)		1704 (30.9)	196 (27.2)	
Highest	1851 (28.6)	123 (37.8)		1685 (28.7)	218 (30.9)	
Alcohol consumption						
None	1077 (12.8)	79 (18.0)	0.016	979 (13.3)	138 (12.2)	0.428
≤1/week	3007 (48.8)	187 (51.6)		2713 (48.4)	364 (51.5)	
≥2/week	2547 (38.3)	111 (30.4)		2286 (38.3)	272 (36.3)	
Smoking behavior						
None	1219 (20.2)	78 (22.2)	0.070	1111 (13.3)	139 (20.1)	0.353
Former	2681 (33.4)	186 (39.1)		2416 (48.4)	356 (36.9)	
Current	2731 (46.4)	113 (38.7)		2451 (38.3)	279 (43.0)	
Physical activity						
Never	3966 (57.6)	204 (49.9)	0.024	3558 (57.5)	460 (55.0)	0.324
≥1 days/week	2665 (42.4)	173 (50.1)		2420 (42.5)	314 (45.0)	
Major CVD						
None	6461 (98.4)	363 (97.9)	0.340	5823 (98.4)	748 (98.1)	0.498
≥1	170 (1.6)	14 (2.1)		155 (1.6)	26 (1.9)	
Cancer						
None	6573 (99.5)	372 (99.1)	0.241	5927 (99.5)	762 (99.2)	0.159
≥1	58 (0.5)	5 (0.9)		51 (0.5)	12 (0.8)	
Perceived stress						
No and mild	5111 (75.6)	289 (73.5)	0.486	4638 (76.0)	569 (71.3)	0.028
Moderate to severe	1520 (24.4)	88 (26.5)		1340 (24.0)	205 (28.7)	
Depression diagnosis						
No	6187 (93.6)	343 (91.6)	0.185	5593 (93.9)	697 (90.7)	0.003
Yes	444 (6.4)	34 (8.4)		385 (6.1)	77 (9.3)	
Suicidal ideation						
No	5979 (90.7)	339 (89.7)	0.588	5409 (91.0)	675 (88.0)	0.037
Yes	652 (9.3)	38 (10.3)		569 (9.0)	99 (12.0)	

Data were expressed as numbers and percentages (categorical) or mean ± standard deviation (continuous).

Values were estimated with considering sampling weights.

DED: Dry eye disease; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; CVD: Cardiovascular disease.

Table 2. Characteristics in women according to the presence of dry eye

Variables	DED diagnosis		P-value	Dry eye symptom		P-value
	No (n=8126)	Yes (n=1319)		No (n=7114)	Yes (n=2041)	
Age (years)	46.2±16.6	46.1±16.0	0.735	46.3±16.5	46.2±16.5	0.537
Body mass index (kg/m <sup>2</sup> )	23.3±3.7	23.0±3.6	0.378	23.3±3.7	23.1±3.7	0.302
Waist circumference(cm)	78.1±10.3	77.6±9.7	0.493	78.2±10.2	77.6±10.2	0.059
Mean SBP (mmHg)	116.0±17.9	115.4±16.6	0.509	116.1±17.6	115.5±18.0	0.725
Mean DBP (mmHg)	73.6±9.9	73.5±9.3	0.245	73.7±9.8	73.4±9.9	0.902
Glucose (mg/dL)	94.8±20.3	94.6±17.7	0.400	94.7±19.8	95.2±20.7	0.346
Total cholesterol (mg/dL)	188.6±36.2	188.3±36.6	0.503	188.5±36.2	188.9±36.5	0.613
HDL cholesterol (mg/dL)	55.9±12.7	56.1±12.0	0.513	55.5±12.6	56.5±12.4	0.300
Household income level						
Lowest	1708 (18.1)	255 (17.7)	0.791	1482 (18.1)	413 (17.5)	0.755
Low	2073 (27.4)	336 (26.0)		1823 (27.5)	518 (26.6)	
High	2155 (28.0)	359 (28.2)		1900 (28.0)	544 (28.0)	
Highest	2190 (26.6)	369 (28.0)		1909 (26.4)	566 (27.9)	
Alcohol consumption						
None	3024 (32.3)	503 (32.8)	0.673	2666 (33.1)	775 (31.5)	0.227
≤1/week	4391 (57.7)	725 (58.3)		3826 (56.9)	1109 (59.4)	
≥2/week	711 (9.9)	91 (8.9)		622 (10.0)	157 (9.1)	
Smoking behavior						
None	7223 (86.1)	1209 (89.3)	0.010	6320 (86.1)	1851 (87.7)	0.216
Former	439 (6.5)	65 (6.4)		385 (6.5)	100 (6.4)	
Current	464 (7.4)	45 (4.4)		409 (7.4)	90 (5.9)	
Physical activity						
Never	5561 (68.5)	916 (68.4)	0.963	4889 (68.9)	1389 (67.2)	0.280
≥1 days/week	2565 (31.5)	403 (31.6)		2225 (31.1)	652 (32.8)	
Major CVD						
None	111 (1.0)	1304 (99.1)	0.631	7021 (99.1)	2015 (99.0)	0.763
≥1	8015 (99.0)	15 (0.9)		93 (0.9)	26 (1.0)	
Cancer						
None	8005 (98.7)	1293 (98.2)	0.207	7009 (98.7)	2001 (98.2)	0.121
≥1	121 (1.3)	26 (1.8)		105 (1.3)	40 (1.8)	
Menopausal status						
Premenopausal	3825 (57.2)	566 (54.8)	0.238	3346 (57.0)	890 (54.7)	0.153
Postmenopausal	4301 (42.8)	753 (45.2)		3768 (43.0)	1151 (45.3)	
Perceived stress						
No and mild	5887 (71.0)	900 (66.1)	0.002	5202 (71.9)	1369 (64.3)	<.0001
Moderate to severe	2239 (29.0)	419 (33.9)		1912 (28.1)	672 (35.7)	
Depression diagnosis						
No	6588 (81.8)	1020 (77.8)	0.008	5806 (82.5)	1571 (76.8)	<.0001
Yes	1538 (18.2)	299 (22.2)		1308 (17.5)	470 (23.2)	
Suicidal ideation						
No	6744 (82.7)	1072 (80.4)	0.097	5956 (83.4)	1610 (78.0)	<.0001
Yes	1382 (17.3)	247 (19.6)		1158 (16.6)	431 (22.0)	

Data were expressed as numbers and percentages (categorical) or mean ± standard deviation (continuous).

Values were estimated with considering sampling weights.

DED: Dry eye disease; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; CVD: Cardiovascular disease.



Table 3-1. Characteristics in premenopausal women according to the presence of dry eye

Variables	DED diagnosis		P-value	Dry eye symptom		P-value
	No (n=3825)	Yes (n=566)		No (n=3346)	Yes (n=890)	
Age (years)	35.6±9.3	35.3±9.5	0.217	35.8±9.3	34.8±9.5	0.129
Body mass index (kg/m <sup>2</sup> )	22.6±3.7	22.1±3.5	0.938	22.7±3.6	22.1±3.6	0.134
Waist circumference (cm)	75.1±9.5	74.0±8.7	0.272	75.2±9.5	73.9±9.0	0.074
Mean SBP (mmHg)	109.1±13.2	108.4±12.3	0.430	109.5±13.1	107.5±12.7	0.329
Mean DBP (mmHg)	72.1±9.4	71.9±9.0	0.136	72.4±9.3	71.2±9.1	0.935
Glucose (mg/dL)	91.3±16.7	90.6±12.7	0.559	91.3±15.8	91.2±18.6	0.063
Total cholesterol (mg/dL)	179.7±32.8	179.1±31.5	0.062	179.8±33.1	179.0±31.5	0.011
HDL cholesterol (mg/dL)	57.2±12.4	57.6±11.3	0.161	56.9±12.1	57.7±12.5	0.787
Household income level						
Lowest	243 (8.3)	39 (8.9)	0.172	222 (8.4)	48 (7.8)	0.539
Low	974 (28.0)	145 (26.3)		852 (28.2)	226 (26.4)	
High	1297 (32.9)	167 (28.7)		1137 (32.7)	287 (31.8)	
Highest	1311 (30.8)	215 (36.2)		1135 (30.7)	329 (34.0)	
Alcohol consumption						
None	750 (18.8)	111 (19.5)	0.640	679 (20.0)	161 (16.4)	0.059
≤1/week	2605 (68.5)	401 (69.4)		2260 (67.3)	629 (71.8)	
≥2/week	470 (12.7)	54 (11.0)		407 (12.7)	100 (11.7)	
Smoking behavior						
None	3274 (83.1)	498 (86.8)	0.018	2867 (83.2)	769 (84.5)	0.047
Former	264 (7.7)	41 (8.2)		221 (7.4)	70 (9.0)	
Current	287 (9.2)	27 (5.0)		258 (9.3)	51 (6.5)	
Physical activity						
Never	2479 (66.2)	366 (62.6)	0.153	2179 (66.6)	570 (63.4)	0.130
≥1 days/week	1346 (33.8)	200 (37.4)		1167 (33.4)	320 (36.6)	
Major CVD						
None	3819 (99.9)	566 (100.0)	N/A	3341 (99.9)	889 (99.9)	0.754
≥1	6 (0.1)	0 (0.0)		5 (0.1)	1 (0.1)	
Cancer						
None	3799 (99.4)	562 (99.2)	0.605	3325 (99.4)	881 (99.2)	0.521
≥1	26 (0.6)	4 (0.8)		21 (0.6)	9 (0.8)	
Perceived stress						
No and mild	2657 (68.3)	347 (60.9)		2350 (69.6)	544 (59.3)	<.0001
Moderate to severe	1168 (31.7)	219 (39.1)	0.002	996 (30.4)	346 (40.7)	
Depression diagnosis						
No	3239 (84.1)	464 (81.2)		2851 (84.9)	724 (79.8)	0.004
Yes	586 (15.9)	102 (18.8)	0.153	495 (15.1)	166 (20.2)	
Suicidal ideation						
No	3287 (84.7)	473 (81.8)	0.131	2898 (85.4)	725 (79.5)	0.000
Yes	538 (15.3)	93 (18.2)		448 (14.6)	165 (20.5)	

Data were expressed as numbers and percentages (categorical) or mean ± standard deviation (continuous).

Values were estimated with considering sampling weights.

DED: Dry eye disease; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; CVD: Cardiovascular disease; N/A: Not applicable.

Table 3-2. Characteristics in postmenopausal women according to the presence of dry eye

Variables	DED diagnosis		P-value	Dry eye symptom		P-value
	No (n=4301)	Yes (n=753)		No (n=3768)	Yes (n=1151)	
Age (years)	60.4±13.1	59.3±11.9	0.028	60.3±13.2	59.9±12.1	0.934
Body mass index (kg/m <sup>2</sup> )	24.3±3.6	24.1±3.4	0.388	24.2±3.6	24.3±3.5	0.983
Waist circumference (cm)	82.1±9.9	82.1±9.0	0.822	82.1±9.8	82.1±9.7	0.356
Mean SBP (mmHg)	125.2±19.1	123.9±17.1	0.953	124.81±18.9	125.1±18.8	0.675
Mean DBP (mmHg)	75.7±10.3	75.4±9.3	0.888	75.5±10.2	75.9±10.1	0.195
Glucose (mg/dL)	99.7±23.5	99.7±21.6	0.255	99.4±23.5	100.4±22.2	0.036
Total cholesterol (mg/dL)	201.0±37.1	200.1±39.2	0.228	200.6±37.0	201.5±38.4	0.053
HDL cholesterol (mg/dL)	53.9±12.9	54.2±12.7	0.924	53.5±13.0	55.1±12.0	0.046
Household income level						
Lowest	1465 (31.0)	216 (28.5)	0.012	1260 (31.0)	365 (29.2)	0.767
Low	1099 (26.6)	191 (25.7)		971 (26.5)	292 (26.8)	
High	858 (21.3)	192 (27.8)		763 (21.9)	257 (23.5)	
Highest	879 (21.0)	154 (18.1)		774 (20.7)	237 (20.5)	
Alcohol consumption						
None	2274 (50.4)	392 (49.0)	0.865	1987 (50.5)	614 (49.6)	0.787
≤1/week	1786 (43.4)	324 (44.7)		1566 (43.1)	480 (44.5)	
≥2/week	241 (6.2)	37 (6.4)		215 (6.4)	57 (5.9)	
Smoking behavior						
None	3949 (90.0)	711 (92.3)	0.407	3453 (89.9)	1082 (91.5)	0.183
Former	175 (4.9)	24 (4.1)		164 (5.2)	30 (3.3)	
Current	177 (5.1)	18 (3.7)		151 (4.9)	39 (5.2)	
Physical activity						
Never	3082 (71.5)	550 (75.5)	0.063	2710 (71.8)	819 (71.9)	0.975
≥1 days/week	1219 (28.5)	203 (24.5)		1058 (28.2)	332 (28.1)	
Major CVD						
None	4196 (97.9)	738 (98.1)	0.698	3680 (98.0)	1126 (97.9)	0.825
≥1	105 (2.1)	15 (1.9)		88 (2.0)	25 (2.1)	
Cancer						
None	4206 (97.8)	731 (97.1)	0.287	3684 (97.9)	1120 (97.1)	0.193
≥1	95 (2.2)	22 (2.9)		84 (2.1)	31 (2.9)	
Perceived stress						
No and mild	3230 (74.6)	553 (72.5)	0.313	2852 (75.1)	825 (70.5)	0.012
Moderate to severe	1071 (25.4)	200 (27.5)		916 (24.9)	326 (29.5)	
Depression diagnosis						
No	3349 (78.6)	556 (73.7)	0.019	2955 (79.3)	847 (73.1)	0.001
Yes	952 (21.4)	197 (26.3)		813 (20.7)	304 (26.9)	
Suicidal ideation						
No	3457 (80.1)	599 (78.8)	0.464	3058 (80.7)	885 (76.1)	0.006
Yes	844 (19.9)	154 (21.2)		710 (19.3)	266 (23.9)	

Data were expressed as numbers and percentages (categorical) or mean ± standard deviation (continuous).

Values were estimated with considering sampling weights.

DED: Dry eye disease; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; CVD: Cardiovascular disease.

## ***2. Association between dry eye and depression***

Figure 2 portrays the odds ratio (OR) and 95% confidence interval (CI) of depression when adjusted for age, BMI, smoking behavior, alcohol consumption, physical activity, major CVD, and cancer. Regardless of sex, participants diagnosed with DED exhibited an increased risk of depression with an odds ratio (OR) of 1.31 (95% confidence interval (CI) 1.11-1.56; P=0.002), compared to non-DED. After stratifying by sex and menopausal status in women, the risk of having depression remained higher for DED diagnosed women (OR 1.31; 95% CI 1.09-1.57; P=0.004) when compared to their respective non-DED counterparts. Postmenopausal women also revealed higher OR of 1.32 (95% CI 1.05-1.66; 0.018) for depression compared to undiagnosed postmenopausal women. Though in DED diagnosed men (OR 1.29; 95% CI 0.82-2.03, P=0.270) and premenopausal women (OR 1.31; 95% CI 0.99-1.74, P=0.058) the values were not significant.

Similar patterns were observed for participants experiencing dry eye symptoms. Overall, participants with dry eye symptoms showed a 1.47 times higher (95% CI 1.28-1.70; P<.0001) risk for depression than those without symptoms. As above, men and women with dry eye symptoms also revealed higher ORs of 1.54 (95% CI 1.13-2.12; P=0.007) and 1.44 (95% CI 1.22-1.68; P<.0001) for depression in

comparison to their respective counterparts. Even after stratifying women into menopausal status, premenopausal (OR 1.50; 95% CI 1.18-1.92, P=0.001) and postmenopausal (OR 1.41; 95% CI 1.15-1.73, P=0.001) women both had higher risks of depression compared to those who never experienced dry eye symptoms. The results remained consistent when unadjusted for potential confounders (Table 4).



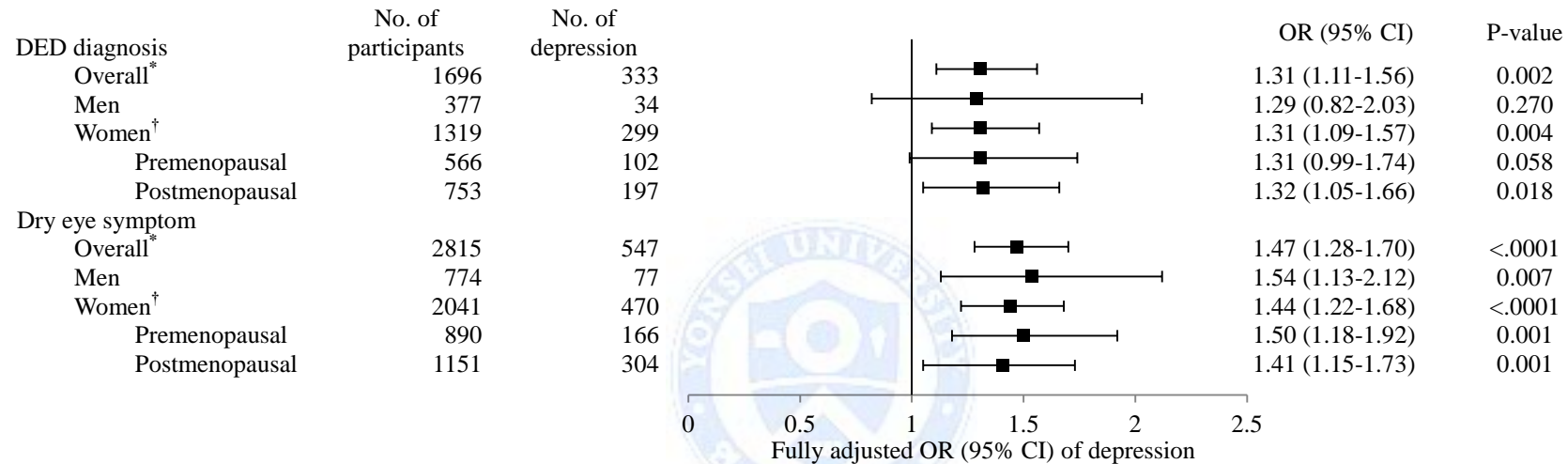


Figure 2. Odds ratios and 95% confidence intervals of depression diagnosis according to diagnosed dry eye disease (DED) and symptom experienced. Odds ratio and confidence intervals were estimated with considering sampling weights. Reference group are those who has never been diagnosed with DED and never experienced symptoms of dry eye. Adjusted for age, BMI, smoking behavior, alcohol consumption, physical activity, major CVD, and cancer. \*additionally adjusted for sex, †additionally adjusted for menopausal status. Abbreviations: DED: Dry eye disease; OR: Odds ratio; CI: Confidence interval.

Table 4. Association between dry eye and depression in the overall participants and stratified by sex

	No. of participants	No. of depression	Odds ratio (95% Confidence Intervals) for depression			
			Unadjusted	P-value	Adjusted <sup>‡</sup>	P-value
<b>Overall*</b>						
DED diagnosis						
No	14757	1982	1.00		1.00	
Yes	1696	333	1.68 (1.43-1.98)	<.0001	1.31 (1.11-1.56)	0.002
Dry eye symptom						
No	13092	1693	1.00		1.00	
Yes	2815	547	1.77 (1.54-2.03)	<.0001	1.47 (1.28-1.70)	<.0001
<b>Men</b>						
DED diagnosis						
No	6631	444	1.00		1.00	
Yes	377	34	1.35 (0.87-2.10)	0.186	1.29 (0.82-2.03)	0.270
Dry eye symptom						
No	5978	385	1.00		1.00	
Yes	774	77	1.59 (1.16-2.17)	0.004	1.54 (1.13-2.12)	0.007
<b>Women<sup>†</sup></b>						
DED diagnosis						
No	8126	1538	1.00		1.00	
Yes	1319	299	1.28 (1.07-1.53)	0.008	1.31 (1.09-1.57)	0.004
Dry eye symptom						
No	7114	1308	1.00		1.00	
Yes	2041	470	1.43 (1.22-1.67)	<.0001	1.44 (1.22-1.68)	<.0001
<b>Premenopausal women</b>						
DED diagnosis						
No	3825	586	1.00		1.00	
Yes	566	102	1.23 (0.93-1.63)	0.154	1.31 (0.99-1.74)	0.058
Dry eye symptom						
No	3346	495	1.00		1.00	
Yes	890	166	1.41 (1.16-1.73)	0.001	1.50 (1.18-1.92)	0.001
<b>Postmenopausal women</b>						
DED diagnosis						
No	4301	952	1.00		1.00	
Yes	753	197	1.31 (1.04-1.64)	0.020	1.32 (1.05-1.66)	0.018
Dry eye symptom						
No	3768	813	1.00		1.00	
Yes	1151	304	1.43 (1.12-1.81)	0.004	1.41 (1.15-1.73)	0.001

Odds ratio and confidence intervals were estimated with considering sampling weights.

\*additionally adjusted for sex; <sup>†</sup>additionally adjusted for menopausal status.

<sup>‡</sup>Adjusted for age, body mass index, smoking behavior, alcohol consumption, physical activity, major CVD, and cancer.

### ***3. Association between dry eye and suicidal ideation***

Figure 3 shows the OR and 95% CI of suicidal ideation when fully adjusted for potential confounders. Overall, participants diagnosed with DED revealed a 1.21 times higher (95% CI 1.02-1.43; P=0.031) risk for suicidal ideation than non-DED participants. When stratified by sex, women (OR 1.22; 95% CI 1.02-1.46; P=0.033) with known DED were also more likely to think of suicide than those without DED, however in men (OR 1.14; 95% CI 0.74-1.76; P=0.552) a significant association did not exist. In premenopausal women, the significance remained by showing an OR of 1.32 (95% CI 1.01-1.73; P=0.041) for suicidal ideation, yet in postmenopausal women (OR 1.16; 95% CI 0.93-1.45; P=0.198) the significance disappeared.

Participants with subjective dry eye symptoms revealed a 1.44 times higher (95% CI 1.24-1.66; P<.0001) risk for suicidal ideation compared to their symptomless counterparts. Compared to men and women with no dry eye symptoms, men with symptoms were at 1.36 times higher (95% CI 1.02-1.82; P=0.039) risk for suicidal ideation, while women were at 1.46 times higher (95% CI 1.23-1.71; P<.0001) risk for suicidal ideation, respectively. When stratified by menopausal status in women, premenopausal (OR 1.55; 95% CI 1.23-1.96; P=0.000) and postmenopausal women (OR 1.35; 95% CI 1.11-1.64; P=0.002) both showed

significant associations with suicidal ideation by revealing higher ORs. The results remained consistent when unadjusted for potential confounders, though the significance disappeared in women and premenopausal women (Table 5).





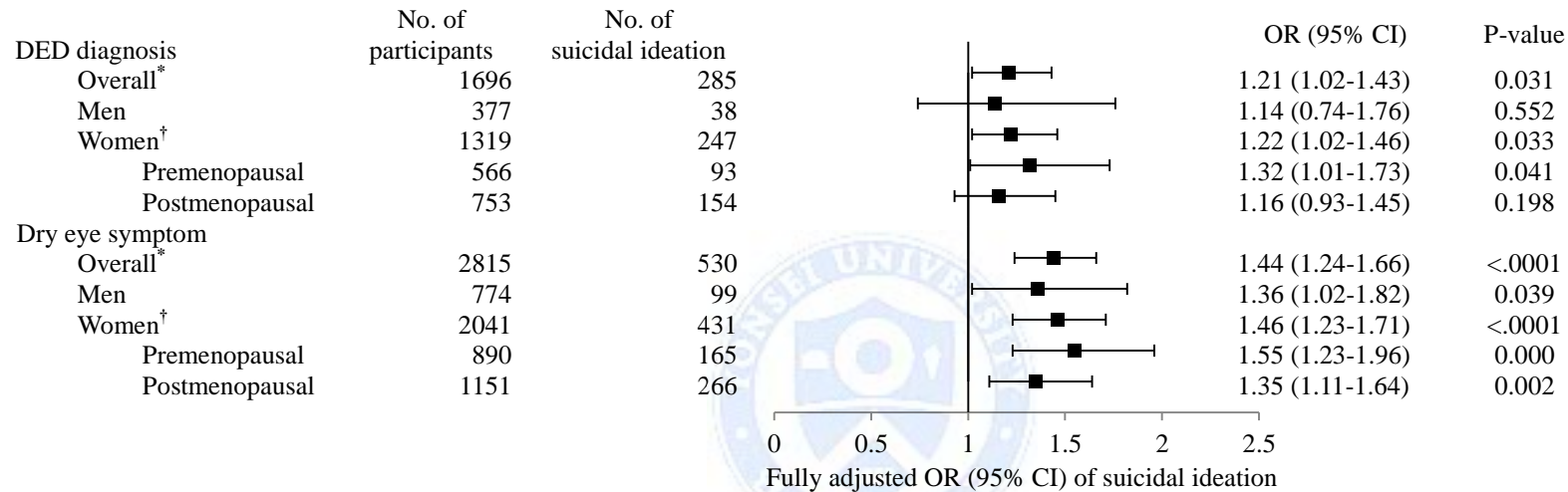


Figure 3. Odds ratios and 95% confidence intervals of suicidal ideation according to diagnosed dry eye disease (DED) and symptom experienced. Odds ratio and confidence intervals were estimated with considering sampling weights. Reference group are those who has never been diagnosed with DED and never experienced symptoms of dry eye. Adjusted for age, BMI, smoking behavior, alcohol consumption, physical activity, major CVD, and cancer. \*additionally adjusted for sex, †additionally adjusted for menopausal status. Abbreviations: DED: Dry eye disease; OR: Odds ratio; CI: Confidence interval.

Table 5. Association between dry eye and suicidal ideation in the overall participants and stratified by sex

	No. of participants	No. of suicidal ideation	Odds ratio (95% Confidence Intervals) for suicidal ideation			
			Unadjusted	P-value	Adjusted <sup>‡</sup>	P-value
<b>Overall*</b>						
DED diagnosis						
No	14757	2034	1.00		1.00	
Yes	1696	285	1.38 (1.16-1.64)	0.000	1.21 (1.02-1.43)	0.031
Dry eye symptom						
No	13092	1727	1.00		1.00	
Yes	2815	530	1.60 (1.38-1.85)	<.0001	1.44 (1.24-1.66)	<.0001
<b>Men</b>						
DED diagnosis						
No	6631	652	1.00		1.00	
Yes	377	38	1.13 (0.73-1.73)	0.589	1.14 (0.74-1.76)	0.552
Dry eye symptom						
No	5978	569	1.00		1.00	
Yes	774	99	1.37 (1.02-1.84)	0.037	1.36 (1.02-1.82)	0.039
<b>Women<sup>†</sup></b>						
DED diagnosis						
No	8126	1382	1.00		1.00	
Yes	1319	247	1.17 (0.97-1.39)	0.097	1.22 (1.02-1.46)	0.033
Dry eye symptom						
No	7114	1158	1.00		1.00	
Yes	2041	431	1.42 (1.21-1.67)	<.0001	1.46 (1.23-1.71)	<.0001
<b>Premenopausal women</b>						
DED diagnosis						
No	3825	538	1.00		1.00	
Yes	566	93	1.23 (0.94-1.61)	0.132	1.32 (1.01-1.73)	0.041
Dry eye symptom						
No	3346	448	1.00		1.00	
Yes	890	165	1.51 (1.20-1.90)	0.001	1.55 (1.23-1.96)	0.000
<b>Postmenopausal women</b>						
DED diagnosis						
No	4301	844	1.00		1.00	
Yes	753	154	1.09 (0.87-1.35)	0.465	1.16 (0.93-1.45)	0.198
Dry eye symptom						
No	3768	710	1.00		1.00	
Yes	1151	266	1.32 (1.08-1.60)	0.006	1.35 (1.11-1.64)	0.002

Odds ratio and confidence intervals were estimated with considering sampling weights.

\*Additionally adjusted for sex; <sup>†</sup> additionally adjusted for menopausal status.

<sup>‡</sup> Adjusted for age, body mass index, smoking behavior, alcohol consumption, physical activity, major CVD, and cancer.

## IV. DISCUSSION

In the general Korean population, we found that frequent experiences of dry eye symptoms were significantly associated with depression and suicidal ideation. For the association between previously diagnosed DED and suicidal ideation, significance was observed only in the overall participants and women. According to previous studies (Chia et al. 2003; Moss, Klein and Klein 2000; Oden et al. 1998), women often reported to have higher prevalence of DED than men, therefore we assume that our results were associated in DED diagnosed women. The suicide rate in South Korea has remained the highest among the Organization for Economic Cooperation and Development (OECD) countries for 10 consecutive years since 2002 (OECD Health Data 2012 2012). With an average suicide rate of 12.1 for every 100,000 people for all of OECD nations, South Korea shows a much higher rate of 28.1 (in 2012) (OECD Health Data 2012 2012). Therefore, the high rate of suicide in South Korea and a high prevalence of DED, which has been noted in Asian populations, make South Korea a suitable country in which to analyze the association between dry eye and suicidal ideation.

Our study showed results on the relationship between DED and depression consistent with those in previous studies, although, relatively few studies

examined the relationship between DED and suicidal ideation. One case-control study attempted to determine whether DED patients experience more symptoms of anxiety and depression than a control group. Agreeable with our results, DED patients showed higher scores, corresponding to more frequent symptoms, for anxiety and depression (Li et al. 2011). As well, the Beijing Eye study determined that definite depression was more prevalent in older patients with DED than those without (Labbe et al. 2013). Depression is the most common cause of suicidal ideation and suicide attempts. Epidemiological studies have revealed that major depressive disorders are strong predictors of suicide attempts than other psychiatric disorders, including anxiety, agitation, and poor behavioral control (Nock et al. 2013; Nock et al. 2010); 60% of those who die from suicide suffer from depressive disorder (Oquendo and Mann 2008). Depression can also affect an individual indirectly by mediation through suicidal ideation. For example, impaired health behavior and low physical health status can cause suicidal ideation by mediation through depressive symptoms (Ro et al. 2015). In light of the results of our study, we suggest that depression may lead to suicidal thoughts indirectly by acting as mediation between DED and suicidal ideation.

Prolonged disruptive symptoms of DED can lead to chronic pain, which in turn may cause feelings of depression and suicidal thoughts. Patients with chronic pain often develop complications of physical dysfunction and altered psychological

state, which negatively impact a person's everyday living and quality of life (Fine 2011; Ohayon and Schatzberg 2003). In a parallel manner, persistent symptoms of DED may induce depressive moods. A previous study demonstrated that presence of ocular surface symptoms decreased performance of daily activities, the capacity to work, and emotional well-being (Pouyeh et al. 2012). Other studies have shown that people who experience chronic pain are more likely to develop depression than those who do not and that suicidal ideation is highly co-morbid (Racine, Choiniere and Nielson 2014; Ratcliffe et al. 2008; Tang and Crane 2006). Also, patients suffering from chronic illness and pain are reportedly at an increased risk of suicidal ideation and suicide attempt, even after adjusting for mental disorders (Ratcliffe et al. 2008). Accordingly, the chronic impact of dry eye symptoms on various aspects of life may lead to the development of depression, and as the severity of symptoms worsens, suicide might arise as an alternative choice to escape unbearable pain.

Our results showed that dry eye symptoms were more strongly associated with suicidal ideation than diagnosed DED. The total number of participants with dry eye symptoms almost doubled the number of participants with previous DED diagnosis. Thus, the greater sample size may have increased the statistical power. Also, dry eye symptoms experienced group partially include participants who answered "yes" for previously diagnosed DED meaning that both groups are not

mutually exclusive. A total of 1,415 participants overlapped for DED diagnosis and symptoms regardless of sex. As several DED diagnosed participants would have likely already been receiving ophthalmic treatments to alleviate their pain, yet participants who were undiagnosed but deals with continuous dry eye related symptoms could potentially drive themselves into depression and suicidal thoughts. Therefore, according to the results, by the nature of the data analyzed, dry eye symptoms may have more explanatory power than DED diagnosis in relation to suicidal ideation.

Previous studies have demonstrated that QOL and vision-related QOL in DED patients are significantly low; moreover, decreased QOL are linked with suicidal ideation and attempts at suicide (Kim and Kwon 2012; Pompili et al. 2009). Previously, DED patients enrolled in the Women's Health Study and the Physician's Health Study were surveyed on limitations in daily activities (impact on reading, driving, computer use, performing professional activities, and watching TV) in order to evaluate the impact of DED on vision-related QOL. After controlling potential covariates, DED patients demonstrated problems in reading, carrying out professional work, using a computer, watching TV, and driving during the day and night (Miljanovic et al. 2007). Another study assessed general QOL in DED patients using the Short Form 36 Health Survey, a survey for measuring a patient's overall wellbeing, not specific to dry eyes (Mertzanis et

al. 2005). Their results indicated that DED negatively impacts everyday life by disrupting daily activities, even causing great deteriorations in mental health (Mertzanis et al. 2005). The study also demonstrated that a patient's ability to take adaptive steps to overcome DED becomes insufficient as the severity of DED symptoms increases and that patient with mild DED are potentially able to make lifestyle changes for overcoming the adverse effects of DED symptoms (Mertzanis et al. 2005). In a utility assessment study using time-trade-off method, patients with DED responded that living 10 years with severe DED are comparable to living 1.6 years without DED (Schiffman et al. 2003). Although we were not able to detect the severity of DED, studies have indicated that DED greatly reduces QOL and that a reduced QOL is associated with suicidal ideation and attempt (Kim and Kwon 2012; Pompili et al. 2009). Accordingly, in addition to depression, lower QOL caused by DED may mediate suicidal ideation or attempts at suicide.

Proven risk factors of DED may be relevant to suicide. Osaka study found that lower levels of physical activity and sedentary behavior were associated with DED (Hyon et al. 2014). Low physical activity was also linked with suicidal ideation. Another study noted a correlation between low physical activity and suicidal ideation, even absence of regular walking increased suicidal ideation (Foulks et al. 2015). Interestingly, diabetes (Hay et al. 1998), long working hours

(Oden et al. 1998), smoking (Vehof et al. 2014; Viso, Rodriguez-Ares and Gude 2009), air pollution (Um et al. 2014), etc. have all been identified as risk factors of both DED and suicide (Chung et al. 2014; Kim et al. 2015; Lucas et al. 2013; Yoon et al. 2015).

Although our results showed that participants with DED were more likely to experience depression and suicidal ideation, previous studies have indicated that patients with depression are susceptible to DED. Consistent results on the relationship between DED and the use of antidepressants have been reported in the literature (Moss, Klein and Klein 2008; Schaumberg et al. 2009). A cross-sectional study of psychiatric patients noted a higher prevalence of DED among patients with depression and/or anxiety disorders (Wen et al. 2012). The study further analyzed predictors for DED and observed associations between duration of psychiatric disease and use of antidepressant medications (Wen et al. 2012). Another study found that approximately 37% of participants who experienced symptoms of DED were taking antidepressants (Chia et al. 2003). In our study, however, we excluded participants receiving depression treatments in order to assess the direct relationships between DED, depression, and suicidal ideation.

Our study has several limitations that need to be considered when interpreting the results thereof. First, due to the cross-sectional study design, a causal relationship between DED and depression and suicidal ideation would be



impossible to identify. Second, previous diagnoses of DED and dry eye symptoms experienced were assessed via interviews rather than using objective measurements. Unfortunately, KNHANES was not designed to diagnose DED. However, a survey conducted by the Korean Corneal Disease Study Group stated that 79% of corneal subspecialists use the diagnostic methodologies of the International Dry Eye Workshop and 21% use the Dysfunctional Tear Syndrome Study Group guidelines to diagnose DED (Hyon et al. 2014). This statement provides evidence that participants who were diagnosed with DED were at least examined under internationally accepted criteria. Also, the questionnaires from one of the most frequently used short series of DED proposed by Schaumberg were equivalent to the questions surveyed in the KNHANES, yet Schaumberg's questions were able to detect the frequency of symptoms (Foulks et al. 2015). Studies demonstrated that asking two symptoms, dryness and irritation, were equivalent to asking up to 16 symptoms of DED (Oden et al. 1998). Recent report has also established the significance of using short questionnaires for determining the presence of DED in large epidemiological studies where objective examinations may not be practical (Gulati et al. 2006). Third, the diagnosis of depression and suicidal ideation were interviewed using a single questionnaire which may likely be underestimated (L 2009). Although we used a nationally representative data with a large sample size, the validity and reliability of

psychometric measures in the KNHANES was not explicitly ascertained, therefore these cannot be guaranteed. Above all, due to the study design, multiple-choice self-report inventories to measure individual levels of depression were not provided, thus there were no other options. Albeit, to increase accuracy of the data collection, participants were asked on whether they have been diagnosed with depression before by emphasizing on “by a psychiatrist.” Despite these limitations, this study used a complex, stratified, multistage probability sampling design based on region and household representing the entire Korean population. The population is a relatively homogeneous society with an absolute majority of Korean ethnicity (Han et al. 2011), therefore the results may be more consistent than other large population based studies with diverse ethnicities.

## V. CONCLUSION

In conclusion, dry eye symptoms were associated with higher risks of depression and suicidal ideation for the overall participants and for both sexes. For DED diagnosis, women showed an association with suicidal ideation. Our results suggest that DED should be viewed not only as an eye disorder, but also as a condition that affects mental health. Ophthalmologists may provide better treatment to patients with DED by evaluating their psychiatric status. However, further study is required to verify the prospective causal effect of DED on depression and suicidal ideation in a large population-based sample.

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## ABSTRACT (KOREAN)

### ‘안구건조 증상과 자살생각과의 관련성’

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엄선비

#### 연구배경 및 목적:

몇몇 연구에 의하면 안구건조증은 우울증 혹은 삶의 질과의 관련성이 있다고 보고하였다. 그러나 안구건조증과 자살생각과의 관련성을 많은 인구를 대상으로 분석한 연구는 매우 드물다. 본 연구는 일반 한국 성인 인구를

대상으로 안구건조증과 우울증 그리고 자살 생각과의 관련성을 평가하고자 하였다.

#### **연구 방법:**

본 연구는 2010년부터 2012년까지 실시한 제5기 국민건강영양조사의 자료를 이용하여 19세 이상인 성인 인구 16,453명 (남자: 7,008명, 폐경전여성: 4,391명, 폐경후여성: 5,054명)을 대상으로 분석하였다. 안구건조증은 의사에게 진단을 받은 적이 있는지와 대상자가 안구의 건조 또는 자극감을 느낀적이 있는지에 대한 여부로 증상이 가끔 또는 때때로 있는 경우는 제외하였으며 두 문항은 안과 전문의가 판정하였다. 우울증과 자살생각은 대상자가 이전에 의사로부터 우울증 진단을 받은 적이 있는지에 대한 여부와 최근 1년 동안 죽고 싶다는 생각을 해본 적이 있는지를 기입하도록 하였다. 안구건조증과 우울증 그리고 자살생각과의 독립적인 연관성은 로지스틱 회귀분석으로 평가하였다.

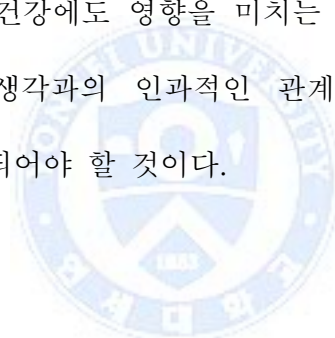
#### **연구 결과:**

잠재적 혼란변수인 나이, 신체질량지수, 흡연여부, 음주여부, 중등도 신체활동 여부, 순환기질환 진단여부와 암 진단여부를 보정한 후에도 안구건조증을 진단 받은 경우 자살생각을 할 오즈비가 전체대상자에서는 1.21배 (95% CI 1.02-1.43)와 여자에서는 1.22배 (95% CI 1.02-1.46)로 통계적으로 유의하게 증가하였으나 남자에서는 관련성이 없었다. 안구건조 증상경험은

혼란변수를 보정한 후 자살생각을 할 오즈비가 전체대상자에서는 1.44배 (95% CI 1.24-1.66), 남자에서는 1.36배 (95% CI 1.02-1.86)와 여자에서는 1.46배 (95% CI 1.23-1.71)로 모두 통계적으로 유의한 관련성을 보였다.

**고찰:**

본 연구에서는 한국 성인 인구에서 안구건조 증상이 우울증 그리고 자살생각과 높은 상관성을 보였으며 남녀 각각에서도 같은 결과가 도출되었다. 안구건조증을 진단 받은 경우 전체대상자와 여자에서만 관련성을 보였다. 이는 안구건조증이 정신 건강에도 영향을 미치는 질환이라는 것을 제안한다. 추후 안구건조증과 자살생각과의 인과적인 관계에 대한 평가를 위해서는 전향적인 연구가 뒷받침 되어야 할 것이다.



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**핵심단어:** 안구건조, 우울증, 자살생각