

## ASSOCIATION OF DRY EYES ON SMOKING HABITS: A SYSTEMATIC REVIEW

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### ABSTRACT

**Introduction:** Dry eye disease (DED), dry eye syndrome, and keratoconjunctivitis sicca (KCS) are typical reasons for eye doctor visits. Smoking's effect on DED is yet unknown, and there is conflicting evidence. Several factors contributed to this outcome, including the studies' limited sample sizes, the imbalance of components between cases and controls, and the ambiguous smoking status classification. This article shows a link between smoking and dry eye condition.

**The aim:** This piece of writing provides evidence that demonstrates a connection between smoking and dry eye diseases.

**Methods:** For this systematic review, publications that were published from 2013 to 2023 were taken into account during the search process. This was achieved through the utilization of numerous online reference sources, such as Pubmed and SagePub. The decision was made to exclude review articles, previously published works, and incomplete works.

**Result:** We found 92 articles from PubMed and 107 articles from SagePub, for which title and abstract analysis was carried out. We found 23 relevant articles. We found 11 studies demonstrates a connection between smoking and dry eye diseases.

**Conclusion:** Smoking may not cause DED. The risk of smoking and DED is still debated due to inconsistent findings.

**Keyword:** Dry eye; Keratoconjunctivitis sicca; Pollutant; Risk Factor; Smoking

## INTRODUCTION

Dry eyes, also known as dry eyes disease (DED), dry eye syndrome, and keratoconjunctivitis sicca (KCS), is one of the most common reasons for visiting an eye doctor. Dry eyes, also known as dry eyes disease (DED), dry eye syndrome, and keratoconjunctivitis sicca (KCS) are one of the most common reasons patients come to the eye doctor.<sup>1</sup> Tear Film and Ocular Surface Society Dry Eye Workshop II shows a picture of dry eyes with a multifactorial ocular surface condition characterized by loss of balance in the tear film, and accompanied by ocular symptoms.<sup>2</sup>

The condition may also be accompanied by tear film instability and hyperosmolarity, inflammation and damage to the ocular surface, and neurosensory defects play an etiological role.<sup>2</sup> A 2 to 5 µm thick tear film sits on the surface of the eye and consists of three main parts. The meibomian glands in the eye form a lipid layer which is the top layer. This layer prevents tears from drying too quickly. The lacrimal glands in the orbit and the accessory lacrimal glands (Krause's and Wolfring's glands) in the conjunctiva form the middle aqueous layer.<sup>3,4</sup>

This part is the deepest part of the tear film. Most of the mucus or glycoproteins that make up the basal layer are formed by conjunctival goblet cells. Mucus helps the tear film spread across the corneal epithelium. The development of DED can be caused by a variety of etiologies, and most cases can be caused by more than one etiology, including local ocular influences, systemic disorders, sociodemographic factors, environmental conditions, and iatrogenic causes such as drugs or procedures. Other factors include sociodemographic factors and environmental factors.<sup>4-6</sup>

Exposure to irritants such as chemical fumes, cigarette smoke, pollution, or low humidity are examples of environmental conditions that can contribute to the occurrence of DED.<sup>7</sup> A number of population-based studies have shown that smoking is a modifiable risk factor for various disorders, including vascular disease, lung cancer, and chronic obstructive pulmonary disease (COPD), until finally there is research showing that smoking can be one potential risk factors for DED. Smoking is also a risk factor for the development of DED.<sup>5,8,9</sup>

There is still a lack of knowledge on the influence that smoking has on the development of DED, and there is still information that supports both sides of the issue and contradicts each other. This finding has been linked to a number of different factors, including the small sample sizes of the studies, the imbalance of components that were distributed between the cases and the controls, and the unclear characterisation of smoking status respectively. This piece of writing provides evidence that demonstrates a connection between smoking and dry eye diseases.

## METHODS

The 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) was used as the basis for establishing the criteria governing the methodology of this particular systematic review. This review was developed to analyze papers on the association of "dry eye disease" and "smoking". This study assessed several eligible studies. In order for research to be included in this review, it must meet the following requirements: 1) The article must be fully accessible online; 2) Articles must be written in English; and 3) Articles must be published between 2015 and the time of preparation of this review. Text submissions of the following types will not be accepted under any circumstances: 1) Letters to the editor, 2) articles or publications without a Digital Object Identifier (DOI), and 3) review articles and comparable submissions.

A search for studies to be included in the systematic review was carried out from December 24<sup>th</sup>, 2023 using the PubMed and SagePub databases by entering the words: "dry eye disease" dan "smoking". Where ("*dry eye syndromes*"[MeSH Terms] OR ("*dry*"[All Fields] AND "*eye*"[All Fields] AND "*syndromes*"[All Fields]) OR "*dry eye syndromes*"[All Fields] OR ("*dry*"[All Fields] AND "*eye*"[All Fields] AND "*disease*"[All Fields]) OR "*dry eye disease*"[All Fields]) AND ("*smoke*"[MeSH Terms] OR "*smoke*"[All Fields] OR "*smoke s*"[All Fields] OR "*smoked*"[All Fields] OR "*smokes*"[All Fields] OR "*smoking*"[MeSH Terms] OR "*smoking*"[All Fields] OR "*smokings*"[All Fields] OR "*smoking s*"[All Fields]) used as search keywords.

The study authors changed the criteria for what should be included in the study and what should not be included in the study after completing a literature search and reading the titles and abstracts of previously published studies. In the process of preparing a systematic review, consideration is only given to studies that successfully meet each requirement. The included studies were reviewed to gather information about each individual study in the form of title, author, publication date, study location of origin, research study design, and research variables.

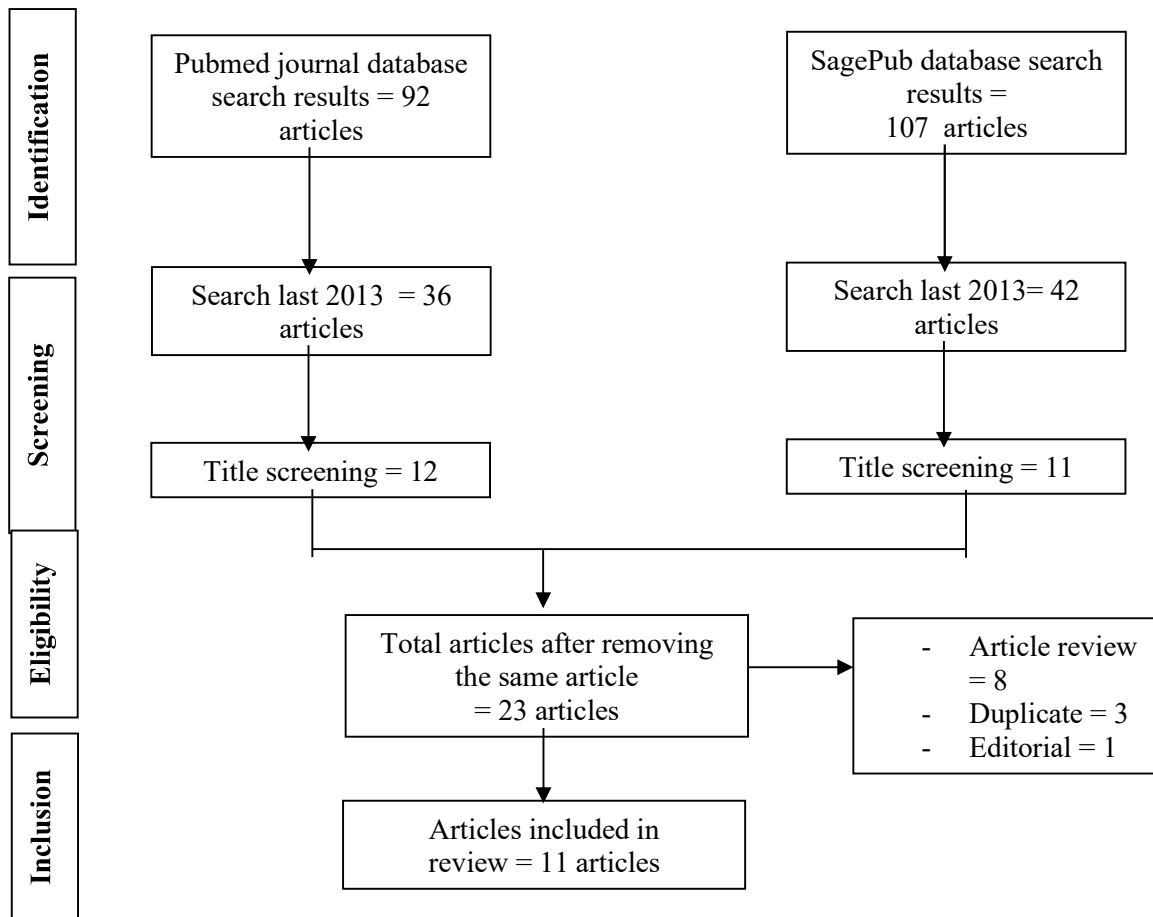


Figure 1. Article search flowchart

In order for you to examine and take into consideration this information, it is presented to you in a particular way. In order to establish whether research were qualified for consideration, the authors carried out an independent examination of a selection of studies that were discovered in the titles and abstracts of papers. Following that, the complete texts of the studies that are eligible for inclusion in the systematic review will be studied in order to determine which studies are suitable for inclusion in the review as the final inclusion for the purpose of the review.

**RESULT**

Carreira, et al (2023)<sup>10</sup> showed smokers exhibited greater rates of dry eye (100% vs 0%,  $p < 0.001$ ), meibomian gland dysfunction (MGD), and lower CET readings than controls ( $p < 0.05$ ). After therapy, the SFA subgroup showed improvements in TBUT, CFS, and LLT ( $64.02 \pm 1.87$  nm vs  $49.56 \pm 4.33$  nm,  $p = 0.05$ ), but not the SH subgroup, and became comparable to controls. After therapy, smokers had lower dry eye prevalence (0% vs 12.82% vs 16.26%,  $p > 0.05$ ). No improvement in meibomian gland morphology or CET was seen following therapy ( $p < 0.05$ ).

Chatterjee, et al completed a survey of 2,378 individuals, of which 1397 (58.7%) were men and 981 (41.3%) were women. The crude and age-adjusted prevalence of each positive symptom was 6.5% and 6.8%, respectively (95% CI = 5.8-7.0%). Red eyes were the most common symptom (2.8%), followed by burning sensation (1.8%), foreign body sensation (1.7%), dry eyes (1.2%), gummy eyes (1.2 %), and crusts on eyelashes (0.8%). Associated risk factors are female genital mutilation, digital screen use, smoking, and exposure to air conditioning.<sup>11</sup>

Table 1. Literature included in this study

Author	Origin	Method	Sample	Result
Carreira, 2023 <sup>10</sup>	Portugal	Randomized Controlled Trial	Seventy-eight eyes	Smoking is linked to the development of dry eye, meibomian gland dysfunction (MGD), and thinning of the corneal epithelium. These conditions can only be partially reversed by using lubricating eye drops, ideally

				those containing saturated fatty acids (SFA).
<b>Chatterjee, 2021<sup>11</sup></b>	India	Cross sectional	2.378	The prevalence of DED symptoms in this urban Indian population is lower than the prevalence reported in most other population-based studies conducted in countries other than India, and also lower than the prevalence found in other hospital-based studies conducted in India. in India. As a result, the frequency of DED in India is lower than existing estimates or is distributed in a non-uniform manner.
<b>Vehof, 2021<sup>12</sup></b>	Netherland	Cross sectional	79.866	This study of dry eye verifies, but also disputes, some of the risk variables found in previous epidemiological studies. In addition, many additional risk factors were found that fall into a variety of different etiological categories. It is disconcerting to see that young adults have a disproportionate prevalence of dry eye complaints; this discovery requires additional research.
<b>Tandon, 2020<sup>7</sup></b>	India	Cross sectional	9.735	People under 40 years of age have a high prevalence of DED. Extrinsic factors (geographical location, sun exposure, smoking, and indoor smoke) and intrinsic factors (age, gender, hypertension, diabetes, and body mass index) play a role in its prevalence.
<b>Inomata, 2020<sup>13</sup></b>	Japan	Cross sectional	4.454	This study identifies and categorizes individuals who have dry eye associated with contact lenses as well as risk variables associated with dry eye. Collection of information about subjective symptoms of dry eye caused by contact lenses can be used for prospective prevention of the development of dry eye caused by contact lenses.
<b>Arita, 2019<sup>14</sup></b>	Japan	Cross sectional	356	This population has a high prevalence of MGD and ED. The pathophysiology of MGD is different from ED, despite the fact that both conditions share similar symptoms that affect the eyes.
<b>Tank, 2019<sup>15</sup></b>	India	Cross sectional	80	There is a significant correlation between dry eye test abnormalities and

				smoking, increased smoking burden, and type of smoking.
<b>Titiyal, 2018<sup>16</sup></b>	India	Cross sectional	15.625	In North India, the prevalence of DED is 32%, and the age range 21-40 years is the most commonly affected age. VDT use, smoking, and wearing contact lenses are all associated with an increased risk of developing DED.
<b>Castro, 2018<sup>17</sup></b>	Brazil	Cross sectional	3.107	The percentage of smokers who experienced dry eyes in this study was less than 8%.
<b>Man, 2017<sup>18</sup></b>	Singapore	Cross sectional	1.682	Over six years, one in twenty Malay adults was diagnosed with SDED. There are differences between men and women in the factors that contribute to the incidence of SDED. In future research and activities aimed at improving public health, differences in these gender-specific risk variables should be taken into account.
<b>Acar, 2017<sup>19</sup></b>	Turkey	Cross sectional	63	Smoking behavior appears to have a deleterious impact on the dry eye characteristics.

Tandon, et al (2020)<sup>7</sup> conducted study involving 9,735 people. The prevalence of DED was 26.2%, higher in the plains (41.3%) compared to hills (24.0%) and coastal areas (9.9%) ( $p < 0.001$ ) and increased with age ( $p < 0.001$ ), female gender ( $p < 0.001$ ), smoking ( $p < 0.001$ ), indoor smoke ( $p < 0.001$ ), diabetes ( $p = 0.02$ ), hypertension ( $p < 0.001$ ), occupation with dominant outdoor activities ( $p = 0.013$ ) and increased sun exposure. Multi-logistic regression showed a positive association with smoking (odds ratio [OR] = 1.2; 95% confidence interval [CI] = 1.03-1.3).

Titiyal, et al (2018)<sup>16</sup> conducted a study where 32% of their research participants experienced DED. They showed that 552 patients underwent objective evaluation; of these, 81.3% (449/552) experienced severe DED. The correlation between hours of visual display terminal (VDT) use and DED was statistically significant ( $P < 0.001$ ), and 89.98% of patients with VDT use for four or more hours experienced severe dry eyes. Smoking and wearing contact lenses increased the risk of developing severe DED ( $P < 0.001$ ).

Arita, et al (2019)<sup>14</sup> conducted research on 356 residents of Takushima Island. The prevalence of MGD and ED was 32.9% and 33.4%, respectively, with a coexistence rate of 12.9%. The prevalence of MGD was associated with male gender (OR = 2.42), age (OR per decade = 1.53), and oral intake of lipid-lowering agents (OR = 3.22). The prevalence of ED was associated with female gender (OR = 3.36), contact lens wear (OR = 2.84), conjunctiva (OR = 2.57), and eyelid margin abnormalities (OR = 3.16). This study did not show a link between smoking and dry eyes.

Inomata, et al<sup>13</sup> conducted research on 4,454 people. About a quarter (1058/4454) of participants smoked. Regarding the medical history survey, the majority of participants (61.67%) did not show hypertension, diabetes, systemic disease, or history of mental illness. Hay fever was present in approximately half of the participants (2249/4454, 50.49%). Smoking can cause dry eyes with OR = 2.07 (95% CI = 1.49-2.88). T-distributed Stochastic Neighbor Embedding analysis visualized and grouped 14 groups based on subjective symptoms of contact lens-related dry eye.

Castro, et al (2018)<sup>17</sup> showed that the overall prevalence of DED was 12.8%. Previous diagnosis of DED was reported in 10.2% and severe symptoms in 4.9%. Logistic regression analysis confirmed several significant risk factors, such as female gender (OR = 1.74; 95% CI = 1.12-1.93), age  $\geq 60$  years (OR = 2.00; 95% CI = 1.44-2.77), history of ocular surgery (OR = 1.84; 95% CI = 1.30-2.60), contact lens wear (OR = 1.93; 95% CI: 1.36-2.73), cancer treatment (OR = 3.03; 95% CI = 1.36-6.59), computer use  $> 6$  h/day (OR = 1.77; 95% CI = 1.36-2.31), users of antidepressants (OR = 1.61; 95% CI = 1.12-2.31) and anti-allergists (OR = 2.11; 95% CI = 1.54-2.89). This study did not show a link between smoking and dry eyes.

Many independent risk factors are associated with DED, for example female gender, contact lens use, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, eye surgery including cataract and laser refractive surgery, keratoconus, osteoarthritis, connective tissue diseases, atherosclerosis, Graves' disease, autistic disorders, depression,

fatigue, Crohn's disease, sarcoid, lichen planus, rosacea, liver cirrhosis, sleep apnea, sinusitis, current smoking, high blood pressure, and BMI. Dry eyes are not related to cholesterol or glucose levels.<sup>12</sup>

Man, et al (2017)<sup>18</sup> followed up for six years. A total of 86 of 1682 participants experienced DED corresponding to an age-standardized 6-year incidence of 5.1% (95% CI = 4.1-6.4%). Glaucoma and poor self-assessed health were independently associated with incident DED in men (P = 0.003 and 0.03, respectively), whereas contact lens use (P = 0.002), history of thyroid disease (P = 0.03), and cataract surgery (P = 0.02) were predictive of incident DED in women. This study did not show a link between smoking and dry eyes.

Acar, et al (2017) showed the mean ocular surface disease index (OSDI) scores, Schirmer test results, and tear break-up-time (TBUT) levels in chronic smokers were 35.85±24.01 points, 14.25 ± 5.94 mm, and 5.17 ± 2.85 s, respectively. Non-smokers exhibited these values at 15.20 ± 12.93 points, 15.48 ± 7.01 mm, and 10.03±3.44 s. Statistically significant disparities were observed in impression cytology grades, OSDI scores, and TBUT levels between non-smokers and chronic smokers.

## DISCUSSION

Dry eyes are one of the most common eye conditions, which can have a negative impact on a person's quality of life. Dry eyes can prevent a person from being active, and can affect the results of surgical treatments including corneal transplantation, cataract extraction, and refractive lens exchange.<sup>1,5</sup> Dry eye can be diagnosed and its severity assessed using a variety of objective tests that have been developed over the years. This examination has low repeatability, considerable interobserver variability, and weak correlation with patient symptoms and quality of life.<sup>20</sup>

Many independent risk factors are associated with dry eyes, such as female gender, contact lens use, fibromyalgia, chronic fatigue syndrome, eye surgery including cataract and laser refractive surgery, keratoconus, osteoarthritis, connective tissue diseases, atherosclerosis, Graves' disease, autistic disorders, depression, 'burnout', Crohn's disease, sarcoid, lichen plan It was found that current smokers had less dry eye than former smokers, despite the fact that current and former smokers had higher blood pressure. pressure and high body mass index.<sup>12</sup>

Cigarette smoke is a mixture of hundreds of harmful substances distributed in particles and gas phases. Smoking habits worry public health and the environment. Tar and nicotine make up most of the particulate phase, while carbon monoxide, carbon dioxide, and nitric oxide are the main components of the gas phase. In addition, cigarette smoke contains heavy metals such as nickel, cadmium, aluminum, lead, and mercury, as well as nitrosamines, polycyclic aromatic hydrocarbons, a broad spectrum of pro-oxidant compounds, and various other pro-oxidant compounds. Volatile components of cigarette smoke are able to cross the blood-lung barrier and enter the bloodstream.<sup>21,22</sup>

The incidence of decreased corneal sensation was found to be considerably higher among smokers compared to non-smokers, and this finding is consistent with previous research. A substantially higher prevalence of abnormal dry eye tests (reduced TBUT, Schirmer's 2 test, tear meniscus height, and corneal sensations) was observed in cigarette smokers compared to bidi smokers.<sup>15</sup> However, study discovered that bidis contained a higher concentration of nicotine than cigarettes. They hypothesized that ocular surface injury could be attributed to other toxins, given that cigarette smoke is known to contain a multitude of toxins apart from nicotine.<sup>21</sup>

Harmful substances in cigarettes access cellular and biochemical transport systems and cause harmful effects on various organs throughout the body, including the eyes. Multiple studies have provided evidence that smoking is associated with an increased risk of various eye conditions, including diabetic retinopathy, age-related macular degeneration, age-related cataracts, and glaucoma.<sup>21</sup> It has been hypothesized that the association between smoking and DED is due to a number of physiological pathways. Free radicals and toxins produced by cigarette smoke are believed to disrupt the normal function of eye cells.<sup>23</sup>

These substances can increase the incidence of ischemia, hypoxia, and the risk of microinfarction in the ocular capillaries which in turn can prevent the flow of important nutrients for normal eye physiology. The lipid, aqueous, and mucin components of the tear film help distribute them evenly over the corneal surface and maintain its homeostatic balance, allowing it to lubricate, nourish, and protect the ocular surface.<sup>23,24</sup> Cigarette smoke causes lipid peroxidation of the outer lipid layer of the precorneal tear film, causing instability, decreased lipid layer thickness, and rapid evaporation of the tear film, contributing to dry eye symptoms.<sup>25</sup> However, data on the association between smoking and dry eyes are inconsistent.

## CONCLUSION

Smoking may not cause DED. The risk of smoking and DED is still debated due to inconsistent findings.

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