Prevalence and Incidence of Dry Eye Disease in Asia: A Systematic Review and Meta-Analysis

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Keywords
Dry eye disease · Prevalence · Incidence · Meta-analysis · Asia

Abstract
Background: Dry eye disease (DED) is the most common ocular surface disease, which severely affects the quality of life. An overall estimate of the prevalence, incidence, and risk factors of DED in Asia would help in planning and implementing appropriate public health strategies. Objectives: The present study aimed to study the epidemiology of DED in Asia. Methods: A comprehensive and systematic search was performed using several databases, including PubMed, Cochrane Library, and Web of Science, in January 2021. A random-effects meta-analysis was performed on logit-transformed prevalence and incidence rates to calculate pooled prevalence and incidence estimates. Meta-regression and subgroup analyses were performed to explain the heterogeneity. Results: Among the 6,742 articles identified, 23 were included in the analysis, with a total sample size of 1,488,935 subjects. Twenty studies reported the prevalence of DED in Asia, two studies reported the incidence, and one study reported both prevalence and incidence. The estimated pooled prevalence of DED in any population in Asia was 20.1% (95% confidence interval [Ozdemir et al., Acta Ophthalmol. 2019;97(1):e91–6]: 13.9–28.3%), and the incidence 16.7% (95% CI: 0–34.9%). The prevalence rate of DED in males and females was 16.4% (95% CI: 10.0–25.8%) and 21.7% (95% CI: 14.7–30.8%; p < 0.001), respectively. In general, the prevalence increased with age. The risk factors considered for specific populations were not significant, and the prevalence in the general population, excluding the populations considered at risk, was similar at 20.9% (95% CI: 12.8–32.1%). Conclusions: DED is common in Asian populations and causes a significant disease burden. Its prevalence is higher in females than that in males, and it tends to increase in severity with age. Further research on additional risk factors is needed to adequately explain the epidemiology of DED in Asia. © 2022 The Author(s). Published by S. Karger AG, Basel

Background

Dry eye disease (DED) is the most common ocular surface disease – it is multifactorial and characterized by an unstable tear film, which leads to a variety of symptoms and visual impairment, including ocular surface damage. Millions of people worldwide are affected by DED [1].
Moreover, patients with DED have reduced quality of life pertaining to vision-related tasks and decreased ability to perform work on video terminals, with consequent limitations on the living environment. Additionally, the disease burden of DED has socio-economic repercussions [2].

DED is recognized as a growing public health issue, with an estimated prevalence rate of 5–50% among people over 50 years old [3]. The incidence of DED has also increased in recent years [4]. The epidemiology of DED has been investigated in several regions. The prevalence may differ depending on ethnicity, living environment, lifestyle habits, and the use of different diagnostic criteria. Therefore, it is challenging to compare different studies directly. Asia comprises of more than half of the world’s population, and several studies suggest that the prevalence of DED in this continent is probably higher than in other areas [5–9].

Several epidemiological studies on DED have been conducted in Asian populations in recent years. However, most of these studies included only a limited sample in single countries. Furthermore, there is a lack of information on the total prevalence of DED in Asia. An overall estimate of the prevalence and incidence of DED in Asian populations would help plan and implement appropriate public health strategies. This systematic review and meta-analysis aimed to estimate the prevalence and incidence of DED in Asia.

**Materials and Methods**

**Protocol and Objective**

Our protocol was registered in PROSPERO on CRD42021241529 with the PRISMA online statement (online suppl Table 1; see www.karger.com/doi/10.1159/000525696 for all online suppl. material) [10].

**Search Methods**

Two authors (Y.C. and J.W.) independently searched for articles between December 2020 and January 2021, using the following keywords: “dry eye,” “keratitis sicca,” “prevalence,” “incidence,” “epidemiology,” and “morbidity.” The following databases were used: PubMed, Cochrane Library, Web of Science, Google Scholar, and Embase (January 1990 to December 2020). The language of the studies was restricted to English. Unpublished materials or data from “gray” articles were not searched.

**Inclusion and Exclusion Criteria**

We reviewed all studies involving DED in the Asian populations. Specifically, the search strategy was to include a sample of an Asian population with a minimum of 30 individuals. The types of studies included cross-sectional, cohort, and case-control studies and randomized controlled trials. All the studies were conducted in Asia and reported the overall prevalence and/or incidence of DED directly or indirectly. Articles that only considered symptoms, signs, or self-reported history to diagnose DED were excluded. Studies of patients using contact lenses or who developed DED after refractive surgery procedures were also excluded. In case of longitudinal studies, we considered the baseline findings. In addition, when different articles described the same type of research, the study with the largest population was selected. When there was a disagreement regarding the inclusion of articles, consensus was reached by discussing with the senior author (W.Z.).

**Data Extraction and Quality Assessment**

After screening the titles and abstracts, the full text of each selected article was obtained and reviewed. Two authors (Y.C. and J.W.) independently extracted the data for the following variables: first author, publication year, diagnostic criteria, country, region, sample size, study setting, patient age, examination year, and sex ratio. If the two authors disagreed on the results, consensus was achieved by discussing with the senior author (W.Z.). The corresponding authors of the included articles were contacted if any essential data were unavailable. The origin was classified as hospital-based, school-based, or community-based. Studies using specific diagnostic criteria for both symptoms and signs were included. These criteria were divided into four types based on the corresponding sources of classification: Asian regions, including the Asian Dry Eye Society (ADES) [11], the Chinese Society [12], the Japanese Society [13], and the Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) [14]. The geographic region and the income level of the study populations were obtained from World Population Prospects 2019 (https://population.un.org/wpp/).

Since we included several types of studies in our analysis, different quality assessments were conducted accordingly. The Newcastle-Ottawa Scale (NOS) of the bias assessment tool was used to evaluate the methodological quality of case-control and cohort studies. The maximum NOS score is 11; <3 indicates low quality, 4–7 indicates medium quality, and 8–11 indicates high quality [15]. The Agency for Healthcare Research and Quality (AHRQ) scale was used to assess the methodological quality of cross-sectional studies. The maximum score of the scale is 9, with <5 indicating low quality [16]. All low-quality studies were excluded.

**Statistical Analysis**

We performed a meta-analysis and meta-regression analysis for the prevalence of DED. All analyses were performed using R-4.1.3 software (R Core Team, Vienna, Austria; available at https://www.R-project.org/). Pooled prevalence, incidence, and 95% confidence intervals (CIs) were analyzed to estimate the prevalence and incidence of DED in Asia. The heterogeneity between studies was tested using Cochran’s Q statistic (Q-test) and the I² index. The classification of heterogeneity was based on the I² statistic: <25% indicated a low level; 25–50%, a moderate level; and >50%, a high level of heterogeneity [17]. The quantitative estimates for prevalence and incidence from each study were pooled separately using a random-effects logit-transformed statistical model. We also performed a subgroup analysis based on the following categories: age, sex, study setting, diagnostic criteria, region, sample size, income, and population. Meta-regression was performed to search for the source of heterogeneity by year of publication, year of examination, study setting, income, sex ratio, sample size,
diagnostic criteria, and population. A “leave-one-out” sensitivity analysis was also performed to evaluate the results. Begg’s test and Egger’s test were used to estimate the publication bias of the included studies. All analyses were considered statistically significant with a $p$ value <0.05.

**Results**

**Search Results**

The initial search identified 6,742 articles (Fig. 1). All studies that were not published in English were excluded. After eliminating duplicates, the titles and abstracts were screened for potential eligibility. All articles with a non-Asian population or the reported studies conducted outside of Asia were excluded, which resulted in 806 eligible studies. These articles were screened based on the inclusion and exclusion criteria, and subsequently, 124 eligible studies remained. Three articles using the same sample were excluded, and 23 articles were finally included in the review. Among these, the prevalence of DED in the Asian population was reported in 21 studies. Three studies reported the incidences considering periods ranging from 3 months to 8 years [18–20]. One study reported both the prevalence and incidence of DED in Asian populations [18]. The main characteristics of these 23 studies are listed in Table 1.

**Quality of Articles**

The quality assessment of 19 cross-sectional studies was analyzed using the AHRQ criteria. Two case-control studies [38, 40] and three cohort studies [19, 20, 39] were assessed using the NOS criteria (Table 1). All the studies had a quality score of at least 6, and the majority were of medium quality.

**Diagnostic Criteria for DED**

We considered the main DED diagnostic criteria that are used in Asian regions, including criteria from the Asian Dry Eye Society [11], the Chinese DED Society [12], and the Japanese DED Society [13]. In addition, the
Table 1. General characteristics of the studies included

| Author (reference) | Prevalence or incidence, % | Origin of data | Study design | Country | Income level | Diagnostic criteria | Sample size | Age, mean or range | Year of examining | Quality scores |
|--------------------|-----------------------------|----------------|--------------|---------|--------------|-------------------|-------------|-------------------|------------------|---------------|
| Li et al. 2021 [21] | 41.4                        | Hospital       | Cross-section | China   | Upper-middle | Chinese Society   | 1,849       | 18–45             | 2015–2016        | 7             |
| Tandon et al. 2020 [22] | 26.2                        | Community      | Cross-section | India   | Lower-middle | TFOS DEWS         | 5,403       | 4,332             | 9,735            | 7             |
| Ma et al. 2018 [23] | 20.0                        | Hospital       | Cross-section | China   | Upper-middle | ADES              | 34          | 46               | 80               | 6             |
| Hua et al. 2014 [24] | 46.5                        | Community      | Cross-section | China   | Upper-middle | Chinese Society   | 1,336       | 926              | 2,262            | 7             |
| Wen et al. 2012 [25] | 60.0                        | Hospital       | Cross-section | China   | Upper-middle | Chinese Society   | 286         | 186              | 472              | 2009–2010      |
| Wang et al. 2019 [26] | 29.0                        | Hospital       | Cross-section | China   | Upper-middle | Chinese Society   | 21          | 17               | 38               | 2018          |
| Arita et al. 2019 [27] | 33.4                        | Community      | Cross-section | Japan   | High         | ADES              | 223         | 133              | 356              | 55.5±22.4      |
| Li et al. 2018 [28] | 10.0                        | School         | Cross-section | China   | Upper-middle | ADES              | 504         | 397              | 901              | 2016          |
| Tandon et al. 2020 [29] | 64.0                        | Community      | Cross-section | Palestine | Lower-middle | TFOS DEWS         | 405         | 364              | 769              | 2010–2016      |
| Zou et al. 2018 [30] | 17.5                        | Community      | Cross-section | China   | Upper-middle | Japanese Society  | 853         | 507              | 1,360            | 2016          |
| Li et al. 2017 [31] | 8.0                         | Hospital       | Cross-section | China   | Upper-middle | Japanese Society  | 3,565       | 3,092            | 6,657            | 2010          |
| Noor et al. 2020 [32] | 22.4                        | Hospital       | Cross-section | Indonesia | Upper-middle | ADES              | 33          | 16               | 49               | 2017          |
| Gong et al. 2017 [33] | 27.8                        | Community      | Cross-section | China   | Upper-middle | Chinese Society   | 714         | 301              | 1,015            | 2013          |
| Hashemi et al. 2014 [34] | 8.7                         | Community      | Cross-section | Iran    | Upper-middle | TFOS DEWS         | 595         | 413              | 1,008            | 2009          |
| Kawashima et al. 2015 [35] | 3.8                         | Community      | Cross-section | Japan   | High         | Japan Society     | 38          | 331              | 369              | 2015          |
| Moon et al. 2016 [36] | 6.6                         | School         | Cross-section | Korea   | High         | TFOS DEWS         | 430         | 486              | 916              | 2015          |
| Uchino et al. 2013 [37] | 11.6                        | Community      | Cross-section | Japan   | High         | Japanese Society  | 187         | 374              | 561              | 2012          |
| Yusufo et al. 2018 [38] | 13.3                        | Hospital       | Cross-section | China   | Upper-middle | TFOS DEWS         | 31          | 29               | 60               | 2014–2015      |
| Shimazaki et al. 2020 [39] | 55.7                        | Hospital       | Cross-section | Japan   | High         | ADES              | 606         | 384              | 990              | 2019          |
| Yan et al. 2020 [40] | 12.5                        | Hospital       | Cohort       | China   | Upper-middle | TFOS DEWS         | 120         | 0               | 120              | 2018–2019      |
| Donthineni et al. 2019 [41] | 14.6                        | Hospital       | Cohort       | India   | Lower-middle | TFOS DEWS         | 694,987     | 763,843          | 1,458,830       | 2010–2018      |
| Huang et al. 2020 [42] | 33.7                        | Community      | Cohort       | China   | Upper-middle | ADES              | 263         | 197              | 460              | 2016–2018      |
| Wang et al. 2019 [43] | 24.4                        | Hospital       | Case-control | China   | Upper-middle | TFOS DEWS         | 76          | 2                | 78               | 2017–2018      |

N/A, not available; ADES, Asian Dry Eye Society; TFOS DEWS, Ocular Surface Society Dry Eye Workshop.
International Dry Eye Association diagnostic standard was used as the reference [14]. The studies that diagnosed DED using symptoms as well as signs were included. The symptoms were classified into two types: symptom scales and questionnaires. Among the 23 studies, symptom scales were used in 10 studies, the ocular surface disease index (OSDI) in nine studies [22, 23, 26, 29, 32, 34, 36, 39, 40], and the remaining study was performed using the dry eye questionnaire-5 (DEQ-5) [18].

### Prevalence of DED

Among the 23 studies included in this study, 21 reported a prevalence of DED in the Asian population ranging from 3.8 to 64.0%. These studies were conducted in seven countries, with China consisting of the majority of the patients. The remaining studies were from Japan, Korea, India, Indonesia, Palestine, and Iran. Twenty studies in total were from East Asia. All the studies were conducted between 2007 and 2019.

### Table 2. Subgroup analysis of the prevalence of DED in Asia

| Variable                  | Studies, n | N     | Prevalence, % (95% CI) | I², % |
|---------------------------|------------|-------|------------------------|-------|
| **Age**                   |            |       |                        |       |
| <20                       | 4          | 2,211 | 11.9 (4.4–19.4)        | 81.4  |
| 20–29                     | 3          | 8,021 | 7.5 (6.1–8.9)          | 52.9  |
| 30–39                     | 3          | 8,021 | 7.7 (0.3–17.8)         | 0     |
| 40–49                     | 5          | 11,468| 11.5 (7.1–18.0)        | 96.2  |
| 50–59                     | 6          | 18,205| 13.3 (6.6–25.7)        | 97.3  |
| 60–69                     | 4          | 11,179| 22.6 (11.4–40.8)       | 98.1  |
| ≥70                       | 4          | 16,828| 28.9 (6.8–51.1)        | 99.5  |
| **Sex**                   |            |       |                        |       |
| Female                    | 16         | 24,328| 21.7 (14.7–30.8)       | 98.6  |
| Male                      | 15         | 24,208| 16.4 (10.0–25.8)       | 98.6  |
| **Study setting**         |            |       |                        |       |
| Hospital                  | 10         | 10,393| 22.0 (13.4–34.0)       | 99.5  |
| Community                 | 9          | 17,435| 22.1 (12.2–36.7)       | 99.3  |
| School                    | 2          | 1,817 | 8.1 (6.1–10.9)         | 85.7  |
| **Diagnostic criteria**   |            |       |                        |       |
| TFO DEWS                  | 7          | 12,686| 18.4 (9.5–32.7)        | 99.2  |
| Asian criteria            | 5          | 15,013| 25.9 (14.3–42.3)       | 98.9  |
| Chinese criteria          | 5          | 5,636 | 31.4 (16.7–51.1)       | 99.4  |
| Japanese criteria         | 4          | 8,947 | 9.2 (5.4–15.4)         | 97.7  |
| **Region**                |            |       |                        |       |
| East Asia                 | 17         | 18,084| 18.8 (12.5–27.3)       | 99.4  |
| China                     | 12         | 14,892| 20.9 (13.5–30.9)       | 99.5  |
| Japan                     | 4          | 2,276 | 19.4 (6.2–46.7)        | 99.2  |
| Korea                     | 1          | 916   | 6.6 (5.1–8.4)          | N/A   |
| South Asia                | 2          | 10,743| 15.7 (6.9–31.6)        | 99.2  |
| India                     | 1          | 9,735 | 26.2 (25.3–27.1)       | N/A   |
| Iran                      | 1          | 1,008 | 8.7 (7.1–10.6)         | N/A   |
| **Sample size**           |            |       |                        |       |
| <500                      | 9          | 1,622 | 20.9 (12.2–33.3)       | 96.9  |
| 500–1,000                 | 5          | 4,137 | 22.9 (8.3–49.1)        | 99.6  |
| >1,000                    | 7          | 23,886| 17.7 (10.5–28.2)       | 99.7  |
| **Income**                |            |       |                        |       |
| High                      | 5          | 3,192 | 15.8 (5.8–36.6)        | 99.3  |
| Middle                    | 16         | 26,453| 21.7 (14.9–30.5)       | 99.4  |
| **Population**            |            |       |                        |       |
| General                   | 14         | 26,687| 20.9 (12.8–32.1)       | 99.3  |
| Diabetes                  | 3          | 1,478 | 22.3 (8.8–46.2)        | 99.9  |
| VDT user                  | 2          | 930   | 14.1 (4.8–35.0)        | 99.2  |
| Lupus erythematosus       | 1          | 78    | 12.5 (7.7–19.7)        | N/A   |
| Mental illness            | 1          | 472   | 29.0 (16.8–45.2)       | N/A   |

CI, confidence interval; N/A, not available; VDT, computer and visual-display terminals.
**Fig. 2.** Forest plot of the prevalence of DED in Asia. CI, confidence interval.

**Fig. 3.** Forest plot of the prevalence of DED in different income levels. CI, confidence interval.
In any Asian population, we estimated that 20.1% of the individuals suffer from DED (95% CI: 13.9–28.3%; Fig. 2). Two studies were conducted only in children aged 6–15 years [26, 36], while two others included only older subjects (≥50 years) [32, 38]. The prevalence of DED generally increased with age (Table 2). The highest reported prevalence was 28.9% (95% CI: 6.8–51.1%) in persons ≥70 years of age [22, 23, 31], and the lowest was 7.5% (95% CI: 6.1–8.9%) in young adults (20–29 years) [27, 31, 34]. In high-income countries [18, 27, 35–37], the prevalence was 15.8% (95% CI: 5.8–36.6%), similar to that in upper-middle-income countries (19.1%, 95% CI: 13.1–27.0%; Fig. 3). In East Asia, the prevalence was 18.8% (95% CI: 12.5–27.3%), whereas in South Asia 15.7% (95% CI: 6.9–31.6%). We observed a significantly lower reported prevalence in school-based populations (8.1%). In contrast, the prevalence in hospital-based individuals (22.0%) was similar to the community-based individuals (22.1%) (Fig. 4). With regards to studies in specific populations, 3 considered diabetic patients [23, 26, 30], and two focused on computer and visual-display terminal (VDT) users [35, 37]. The pooled estimate from 14 studies performed in the general population was 20.9% (95% CI: 12.8–32.1%), which was similar to that in the whole population.

The meta-regression model quantified the impact of age, sex ratio, time range, income, and diagnostic criteria on the prevalence reported. The results showed that the sex ratio and diagnostic criteria were statistically significant determinants of prevalence (p < 0.05), whereas age, time range, and income were not significantly associated.

The proportion of studies wherein the number of females was predominant was 31.7%, while males formed the majority in 10.3% of the studies.

Diagnostic criteria can be divided into four categories, based on different sources of classification. The prevalence of DED based on diagnostic criteria from the TFOS DEWS was 18.4% (95% CI: 9.5–32.7%) [21–23, 25, 27–30], while that in studies using the ADES criteria was 25.9% (95% CI: 14.3–42.3%) [18, 24, 32, 36]. The estimate prevalence in studies using criteria from China [26, 37–40] and Japan [31, 33–35] were 31.4% (95% CI: 16.7–51.1%) and 9.2% (95% CI: 5.4–15.4%), respectively.
A sensitivity analysis was also conducted in these studies (Fig. 5). We observed that none of the studies would have influenced the heterogeneity of the results.

Incidence of DED

Among the 23 studies, three studies examined 1,460,280 subjects in total and reported an incidence of DED ranging from 1.46% to 33.7% [18–20]. The studies were conducted for a duration between 4 months and 8 years in China, Japan, and India. The largest population was from an Indian study conducted on 1,458,830 participants [19]. The pooled estimate for the incidence of DED was 16.7% ($I^2 = 99.4\%, 95\%\ CI: 0–34.9\%$; Fig. 6). One study from China reported an incidence estimate of 33.7% in diabetic individuals [20], which was significantly higher than that in the other two studies on the general population [18, 19].

Publication Bias

The funnel plot, Egger’s test, and Begg’s test were performed to analyze the publication bias. Although the asymmetrical shape of the funnel plot suggested a potential publication bias (Fig. 7), the Begg’s test ($p = 0.507$) and Egger’s test ($p = 0.522$) showed no bias. Based on these results, we found no significant evidence of publication bias on the prevalence of DED in Asia. The effect of publication bias on the incidence of DED was not analyzed since the number of studies was small.

Discussion

This systematic review and meta-analysis was conducted to estimate the prevalence and incidence of DED in Asia. To the best of our knowledge, our study is the first to determine an overall DED epidemiology estimate in this continent. Asia is the most overpopulated region in the world and comprises more than half of the world’s total population. Our findings are of significant value for epidemiology and clinical research on DED in Asia and worldwide.

Several previous systematic reviews have reported estimates of DED globally and in Asian regions [3, 37, 41, 42]. The DEWS committee reported that in Southeast Asia, the prevalence ranged from 20.0 to 52.4% [3], which was consistent with our results (22.5%) for the same region, and was within the range above. The Women’s Health Study Questionnaire study reported that the prevalence was 21.6% in Asian women [3], which was also similar to our estimates in the female population. In Asia,
systematic reviews of DED prevalence have been conducted in China. In Chinese individuals aged between 5 and 89 years, the prevalence of DED based on symptoms and signs was estimated as 13.55% [43]. Our study showed a prevalence of 20.9% in China, which was higher than previous results. The reasons for this difference may vary. Among the studies included in our analysis, 14 studies were published after 2016, while the previous reviews were conducted on studies published mostly between 2010 and 2016 [43]. We considered several diagnostic criteria for studies based on the Chinese population. Previous systematic reviews reported only the prevalence and not the incidence of DED in this population. Our study separated the two different concepts, avoiding the possibility of prevalence underestimation.

Previous studies showed that the prevalence of DED in Asian populations is higher than that for other ethnicities [3, 5]. The recent prevalence reported in America was 6.8% in 75,000 adults [44]. The 2016 estimate of prevalence from a Canadian study was 22.0%, which was based on the diagnostic criteria of a DEQ-5 score >6/22 [45]. Several studies in other regions currently used only symptoms to diagnose DED [9, 46, 47], which was in contrast to our inclusion criteria. Therefore, those studies may have overestimated the results; nonetheless, the prevalence of DED in Asia in our study was significantly higher than that reported in the other regions. Contrasting the reported prevalence of DED diagnosed using both symptoms and clinical signs in a meta-analysis in Africa was 50.8%, which was higher than our estimate [48].

Furthermore, several ocular surface diseases may present with symptoms, including DED; thus, its prevalence might be overestimated due to the lack of specificity in diagnosing this disease based on symptoms alone. We included studies with different diagnostic criteria, including both symptoms and signs. This review is the first to divide the studies into several categories, based on different dry eye diagnostic criteria. As there is no standard for diagnosis, the prevalence that was estimated using the criteria of the China Dry Eye Society was higher than that estimated using other criteria. However, the prevalence was significantly lower using the diagnostic criteria from the Japan Dry Eye Society. The studies using diagnostic criteria from the TFOS DEWS showed a 18.4% prevalence (95% CI: 9.5–32.7%), and the estimate with ADES criteria was 25.9% (95% CI: 14.3–42.3%). Comparing the criteria between TFOS DEWS and ADES, the most relevant difference was their standard for breakup time. The ADES diagnostic criteria define the breakup time threshold as ≤5 s, whereas TFO DEWS considers it ≤10 s. According to the Japanese criteria, DED diagnosis requires...
the presence of symptoms and two signs, including abnormal tear film and positive ocular surface staining, while other criteria require only symptoms and at least one sign. This difference might have contributed to the low prevalence estimation in using the Japanese criteria. Therefore, it is difficult to compare DED estimates directly from different studies, owing to the varying diagnostic standards. Hence, our analysis allowed for more accurate comparisons.

DED is a multifactorial disease, and our study also confirmed this characteristic. Female sex and older age, as suggested by previous research, were significant risk factors for DED. Our results confirmed that the prevalence of DED increased with age, while the school-based studies reported a lower estimate than that in the other groups [28, 36]. However, this feature was not significant in populations under 20 years of age. Nonetheless, compared to previous studies on the prevalence of DED, these data strengthened the clinical impression of an expanding younger population of patients with this disease. In addition, four studies included in our study reported the prevalence in subjects under 20 years of age [26–28, 36]. The total population size in this age-group was 1,024, which significantly lower than that of other groups. Although the studies were conducted in three countries, they were published more than 6 years earlier. This may lead to an inevitable unequal distribution of age.

Our research also confirmed that sex was an influential factor for the prevalence of DED. In Asia, the prevalence was 16.4% (95% CI: 10.0–25.8%) in males and 21.7% (95% CI: 14.7–30.8%) in females and was significantly higher in females ($p < 0.001$). Compared to the general population, we found a higher prevalence in subjects with diabetes, which was consistent with previous studies [5, 49]. In contrast, the estimate for VDT users was lower than previously reported, although the difference was not significant [50]. In addition to the lack of a relevant number of studies and populations, we found that two VDT studies were conducted in Japan and used Japanese diagnostic criteria. Conversely, all studies on diabetic patients were Chinese, and one study was performed on children aged 6–15 years. In addition, a previous global epidemiology study reported that the local socio-economic factors may influence the presence of DED in different areas [3]. However, we found that the prevalence in high-income countries was 15.8% (95% CI: 5.8–36.6%) in Asia, compared to 21.7% (95% CI: 14.9–30.5%; $p > 0.05$) in middle-income countries. The studies on high-income populations were conducted in Japan and Korea. A significant difference in prevalence was found between the regions with varying socio-economic factors. The studies reporting the relationship between DED and social economy were few in number; therefore, it was difficult to examine this possible association. Further research on DED prevalence in specific at-risk populations needs to be conducted, which should consider the effects of different lifestyles and environments.

Despite the strengths mentioned above, this study had several limitations. First, the studies of prevalence we examined were only from seven countries, namely China, Japan, Korea, Iran, Palestine, India, and Indonesia. They were mainly conducted in East Asia and South Asia. Hence, there may be a lack of representation of the whole continent, with no studies from Central or North Asia. We might have overestimated or underestimated the results; however, we had no reference points because there were no previous comparisons between the prevalence of DED in different regions of Asia. The limited research has affected our capacity to conduct a regional analysis. In addition, we found only three studies reporting the incidence. The results from China, India, and Japan may not represent the entire Asian incidence of DED since two of these countries are the most heavily populated nations in Asia. Further studies on DED in different regions are warranted. Second, we only included articles in English, possibly excluding other studies intended for the local populations in their native language. The sample size should also be increased to obtain representative results. Third, heterogeneity was detected in the included studies, and the results should be interpreted with caution.

**Conclusion**

In conclusion, our systematic review and meta-analysis summarizes the epidemiology of DED in Asia over the last 30 years. DED is common in Asia and poses a serious personal and social burden. Multiple diagnostic criteria have led to different rates of diagnosis in various populations, and DED diagnosis requires standardization. While DED is more common in older adults and females, we must also consider the prevalence of DED in young subjects. With the global aging trend, the prevalence and burden of DED are also likely to increase. More epidemiological studies, especially on the prevalence of DED and high-risk groups, are required to precisely estimate the burden of DED across Asia and globally.
Epidemiology of Dry Eye Disease in Asia

Statement of Ethics
All analyses were based on previously published studies; thus, no ethical approval and patient consent were required.

Conflict of Interest Statement
All the authors declare that they have no conflicts of interest regarding the publication of this article.

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Author Contributions
Youran Cai and Jiaxin Zhou designed the study; Jintao Wei and Youran Cai searched the articles and extracted data; Youran Cai, Jintao Wei, and Jiaxin Zhou performed the analysis; Wenjin Zou revised the essay. All the authors critically reviewed the manuscript and approved the final version.

Data Availability Statement
All data generated or analyzed during this study and supporting the conclusions of this article are included within the article. Further inquiries can be directed to the corresponding author.

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Epidemiology of Dry Eye Disease in Asia

Ophthalmic Res 2022;65:647–658

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