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# Global Incidence of Central Serous Chorioretinopathy: A Systematic Review, Meta-analysis, and Forecasting Study

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## ABSTRACT

**Introduction:** Central serous chorioretinopathy (CSC) is a prevalent exudative maculopathy; however, exact details of its incidence and a global estimate of its annual incidence are lacking. It is paramount to understand the details of the incidence of CSC when discussing its societal

and personal impact, the impact of medicine shortages and initiatives for healthcare policies, and organization of retinal service.

**Methods:** In this study, we systematically reviewed the literature on the incidence of CSC and performed meta-analyses to provide an age-stratified estimate of its incidence. By using population statistics from the United Nations Population Division, we were able to estimate the global and country-specific incidence of CSC in 2025 and forecast until 2050.

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**Results:** Seven eligible studies included a total of 324,954 new patients with CSC during their time of investigation. The summary estimate incidence rates per 100,000 person-years were 47.8 (95% confidence interval [CI] 31.7–61.7) for individuals 30–39 years, 71.8 (95% CI 41.7–109.7) for individuals 40–49 years, 58.5 (95% CI 29.9–96.1) for individuals 50–59 years, and 36.2 (95% CI 16.8–62.6) for individuals 60–69 years. We confirmed male sex as a risk factor (odds ratio 2.73,  $P < 0.0001$ ), and found that male individuals were significantly younger than female individuals at onset of CSC (average difference of 3.30 years,  $P < 0.0001$ ). We estimated that in 2025, 1.97 million individuals globally will develop CSC, and that the incidence will increase to 2.03 million individuals in 2030, 2.30 million individuals in 2040, and 2.43 million individuals in 2050. The CSC incidence peaked between 40 and 49 years underscoring the significance in working-age individuals.

**Conclusion:** Numbers presented in this study highlight that CSC is one of the more prevalent maculopathies in our world and underscores the importance of education, research, and health-care planning related to CSC.

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**Keywords:** Central serous chorioretinopathy; Incidence; Forecasting; Systematic review; Meta-analysis

### Key Summary Points

#### *Why carry out this study?*

Central serous chorioretinopathy (CSC) is a prevalent exudative maculopathy; however, exact details of its incidence and a global estimate of its annual incidence are lacking.

It is paramount to understand the details of the incidence of CSC when discussing its societal and personal impact, the impact of medicine shortages and initiatives for health-care policies, and organization of retinal services.

#### *What was learned from the study?*

In this study, we systematically reviewed the literature on the incidence of CSC and performed meta-analyses to provide an age-stratified estimate of its incidence. By using population statistics, we were able to estimate the global and country-specific incidence of CSC in 2025 and forecast until 2050.

In 2025, 1.97 million individuals globally will develop CSC. The incidence will increase to 2.03 million individuals in 2030, 2.30 million individuals in 2040, and 2.43 million individuals in 2050.

## INTRODUCTION

Central serous chorioretinopathy (CSC) is considered to be the fourth most prevalent exudative maculopathy [1, 2], first described by von Graefe in 1866 [3]. CSC primarily affects men between the ages of 30 and 50 years [1]. It is also relatively prevalent in female individuals, and both pediatric cases and cases in adults aged 80+ years have been described [4–6]. Although CSC pathophysiology remains incompletely understood, important risk factors include corticosteroid exposure [7–9],

hypertension [10], and smoking [11]. Clinically, studies have outlined the presence of a thickened choroid with hyperpermeability features on indocyanine green angiography (ICGA) which may be representative of choroidal congestion due to arteriovenous anastomoses [12], strain in venous outflow through the sclera [13], and scleral thickening [14]. Congestion in the choroidal perfusion may lead to an increased fluid pressure from the choroid, through the Bruch's membrane, into the subretinal pigment epithelium (RPE) space. This leads to small serous RPE detachments, which represent a common feature of CSC. When the RPE pumping function no longer can withstand the fluid pressure, leakage through the RPE barrier and decompensation lead to accumulation of subretinal fluid [12, 13]. Accumulation of subretinal fluid is a defining key clinical feature of CSC, although the local damage to the subretinal tissue may also lead to outer retinal atrophy, macular neovascularization, and intraretinal fluid [1, 15]. Although most cases of acute CSC will spontaneously resolve without need for any treatment [1], treatment of chronic CSC is needed to prevent irreversible vision loss [1]. International guidelines and best evidence suggest half-dose photodynamic therapy (PDT) for these cases [1, 16]. The recent global shortage of verteporfin has highlighted the need for continuous research to better understand CSC pathophysiology and underscored the need to develop new therapies [17, 18].

It is paramount to understand the details of the incidence of CSC when discussing its societal and personal impact [19–21], healthcare policies [18], impact of medicine shortage [17, 18], and retinal service organization [1, 22, 23]. Further, when planning for development of drugs and new therapies, the number of patients potentially eligible for therapy is of great significance for several stakeholders [24].

In this study, our aim was to provide the best estimate of the incidence of CSC across individual countries as well as the total global numbers by summarizing available evidence in the field.

## METHODS

### Study Design

This study was a combined systematic review, meta-analysis, and forecasting study. We first systematically searched the scientific literature for studies on the incidence of CSC. On the basis of data from these studies, we conducted meta-analyses on the incidence of CSC across demographic strata. These incidence rates were then applied to demographic stratified population census and forecasting analyses from the United Nations Department of Economic and Social Affairs Population Division. Our protocol was registered in the PROSPERO database (registration nr. CRD42024624111). We followed the recommendations of the Cochrane Handbook [25]. The study was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [26]. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors. Systematic reviews, meta-analyses, and forecasting studies using publicly available data do not require institutional review board approval according to Danish law.

### Eligibility Criteria

Eligible studies must have sampled a population that can be considered representative of the general population. The population must have been examined for the presence of CSC. The outcome of interest is the incidence of CSC defined as new cases of the disease within a defined period of time. Thus, this requires studies to be of an observational cohort design. Both prospective and retrospective study designs were considered eligible. We did not enforce any restrictions on the diagnostic definition or the criteria for CSC. Studies without original data, conference abstracts, or non-peer-reviewed literature were not considered eligible. For practical purposes,

only studies reported in English language were considered eligible for review.

### **Information Sources, Search Strategy, and Study Selection**

We searched 12 scientific literature databases: PubMed, Cochrane Central, EMBASE, Web of Science Core Collection, BIOSIS Citation Index, BIOSIS Previews, Current Contents Connect, Data Citation Index, Derwent Innovations Index, KCI-Korean Journal Database, ProQuest Dissertations and Theses Citation Index, and SciELO Citation Index. Searches were performed on 10 August 2024 by one trained author (Y.S.). Details regarding search phrases used in individual databases are available in Supplementary Material. Records from the literature search were imported to End-Note X9.3.1. for Mac (Clarivate Analytics, Philadelphia, PA, USA) for screening. One author (Y.S.) screened all titles and abstracts to remove obviously irrelevant studies and duplicates. Records which were neither duplicates nor obviously irrelevant were then retrieved in full text for eligibility evaluation. All reference lists were evaluated for potential eligible studies. Eligibility evaluation was made independently by two authors (I.N.F. and A.A-V.) who then discussed discrepancies and consulted a third author (Y.S.) for final decision.

### **Data Extraction, Outcome Measures, and Risk of Bias Within Studies**

Data extraction was performed using pre-designed extraction forms and data was extracted on study characteristics, study population and methods, and study outcomes. The outcome of interest was the incidence of CSC. This outcome was defined as incidence per person (i.e., not incidence per eye). We evaluated risk of bias within studies using the Newcastle–Ottawa Scale for Cohort Studies [27]. Data extraction and risk of bias within study evaluation were performed individually by two authors (I.N.F. and A.A-V.) who then discussed discrepancies and consulted a third author (Y.S.) for final decision.

### **Data Synthesis, Meta-analyses, Risk of Bias Across Studies, and Forecasting Analyses**

Studies were reviewed qualitatively in text and tables. We conducted meta-analyses according to age strata in the general population. Subgroup analyses were performed for the risk of male sex for the incidence of CSC and for the difference in age of CSC onset according to sex. All meta-analyses were conducted using MetaXL v.5.3. (EpiGear International, Sunrise Beach, QLD, Australia) for Microsoft Excel v.2205 (Microsoft, Redmont, WA, USA). The random-effects model was applied to account for heterogeneity across studies. Caution must be exercised in incidence meta-analyses especially in cases when numbers reach extremes (i.e., 0% or 100%) as calculations potentially lead to variance instability and erroneous study weighting [28]. One method to address this issue, which we applied in our analysis, was to transform all incidence numbers using the double arcsine method for analysis and then back-transform numbers for interpretation [28]. We calculated 95% confidence intervals (95% CI) for all summary estimates. Because of the low number of studies eligible for the meta-analyses, we deemed it not possible to perform meaningful heterogeneity analyses, Funnel plot analyses, or sensitivity analyses.

Population statistics and forecasts were acquired from the United Nations Population Division [29], which regularly provides official estimates and projects as prepared by the Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat. We used the 2024 Revision of World Population Prospects edition of the data and employed the medium (i.e., most likely) estimate of the forecasts for future population statistics. Using these data, which can be granulated according to countries and age strata, we calculated the expected incidence of CSC for each age stratum in each country using our meta-analytically calculated age-specific incidence of CSC. These numbers were summarized to provide country-specific incidence of CSC as well as the global incidence of CSC according to years 2025, 2030, 2040, and 2050.

## RESULTS

### Study Selection

The literature search identified 626 records. Of these, 227 records were duplicates and 366 records were deemed obviously irrelevant. The remaining 33 records were all read in full text for eligibility evaluation. All reference lists were reviewed for any further additional eligible

studies. Finally, seven studies were found eligible for the qualitative review and five of these were eligible for the quantitative synthesis (Fig. 1).

### Study Characteristics

The seven eligible studies for review included a total of 324,954 new patients with CSC during their time of investigation [6, 30–35]. Studies were conducted in the USA ( $n=2$ ), Israel ( $n=1$ ),

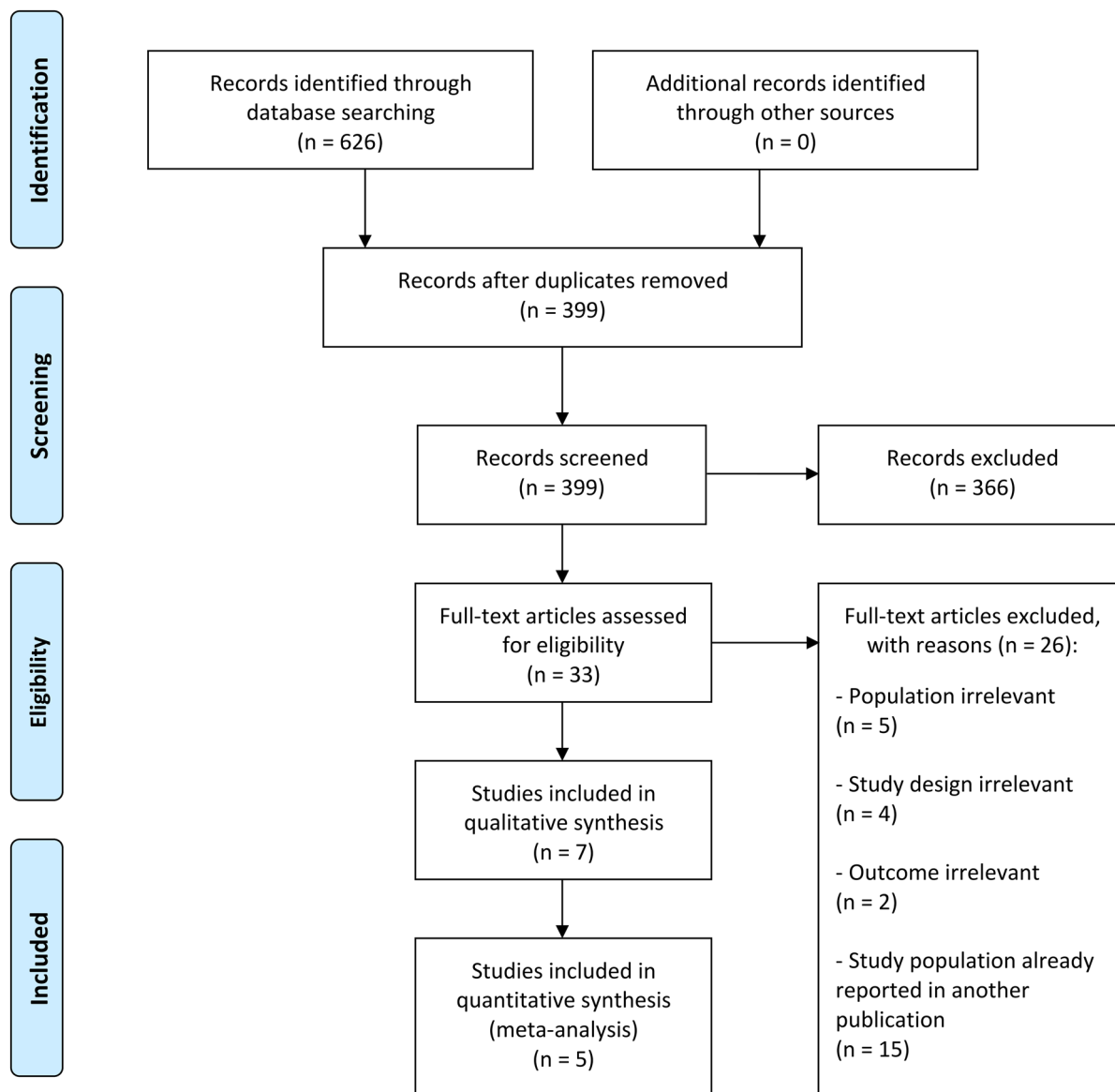


Fig. 1 Study selection process as illustrated using the PRISMA flow diagram

Japan ( $n=1$ ), Russia ( $n=1$ ), South Korea ( $n=1$ ), and Taiwan ( $n=1$ ). All studies were retrospective in nature and were designed as a cohort study, although the authors defined their study otherwise in two studies [30, 35]. Four studies were population-based studies and three were clinic-based studies. The majority of incident CSC cases were male across all studies. Mean age at time of diagnosis ranged between 39 and 55 years and there was a trend of male individuals being diagnosed at a slightly younger age than female individuals. Detailed study and population characteristics are summarized in Table 1.

### Results of Individual Studies

Kitzmann et al. used medical records of all patients in Olmsted County, Minnesota from the period 1980–2002 through the Rochester Epidemiology Project to present the first large-scale epidemiological estimate of the incidence of CSC [6]. Annual incidence rates remained stable throughout the study period and were 9.5 per 100,000/year in male individuals and 1.6 per 100,000/year in female individuals [6]. Female individuals had a median age category of 40–44 years at time of diagnosis, which was older than the male individuals who had a median age category 35–39 years [6]. Tsai et al. extracted data for 2001–2006 from the National Health Insurance Database system in Taiwan, which is a mandatory health insurance registration system [34]. Annual incidence rates were 27 per 100,000/year in male individuals and 11 per 100,000/year in female individuals, and throughout the study period incidence rates were subject to an increase [34]. Incidence rates peaked in male individuals in the age category 35–39 years, whereas in female individuals two peaks were observed in the age categories 25–29 years and 55–59 years [34]. Pan et al. used insurance claims data for 2007–2016 from the IBM MarketScan database, which is a healthcare database for patients with employer-provided health insurance in the USA [33]. Annual incidence rate increased slightly during the study period from 16.9 to 20.7 per 100,000/year [33]. Incidence rates were higher in male individuals

than in female individuals, and the incidence rates peaked at slightly earlier age in male individuals than in female individuals [33]. This study did not present stratified data on incidence according to demography but reported that obstructive sleep apnea was a significant risk factor of CSC [33]. Agliullin et al. collaborated with eye clinics in Kazan, Russia and the Russian Federal State Statistics Service to describe the incidence of CSC in Kazan between 2009 and 2018 [30]. The incidence in male individuals rose from 3.2 to 14.8 per 100,000/year during the study period, whereas the incidence in female individuals remained largely unchanged from 8.0 to 7.7 per 100,000/year [30]. Female individuals had a median age of 55 years at time of diagnosis, which was significantly older than the male individuals who had a median age of 45 years [30]. Kido et al. conducted a nationwide population-based cohort study based on the health insurance claims database of the Japan Ministry of Health, Labor, and Welfare from the period 2011–2018 [31]. Annual incidence rates remained stable throughout the study period and were 54.2 per 100,000/year in male individuals and 15.7 per 100,000/year in female individuals [31]. Female individuals had a mean age of 54.7 years at time of diagnosis, which was significantly older than the male individuals who had a mean age of 50.5 years [31]. This study also reported that 13.2% of the study cohort later received any major treatment defined as PDT (at  $110 \pm 95$  days from diagnosis), laser photocoagulation (at  $60 \pm 82$  days from diagnosis), or anti-vascular endothelial growth factor injection (at  $96 \pm 92$  days from diagnosis) [31]. Lee and Bae extracted data from the Korean Health Insurance Review and Assessment Service which registers interaction with healthcare system nationwide, and extracted data for 2015–2019 [32]. Annual incidence rates were 19.6 per 100,000/year in male individuals and 8.9 per 100,000/year in female individuals, and throughout the study period incidence rates were subject to an increase in both male and female individuals [32]. Female individuals had median age category of 50–59 years at time of diagnosis, which was older than the male individuals who had a median age category 40–49 years [32]. This study also found that

**Table 1** Study characteristics

References	Design	Country	Study population	Diagnosis of CSC	Data granularity
Agliullin et al. (2021) [30]	Retrospective clinic-based cohort study	Russia	Population in Kazan during 2009–2018, who received medical care in eye clinics in Kazan. In total, 831 new patients with CSC were identified. Overall mean age was not reported and 50.4% were male. Median age was 45 years in male individuals, 55 years in female individuals	N/A	Stratified by sex
Kido et al. (2022) [31]	Retrospective population-based cohort study	Japan	Data from the nationwide health insurance claims database of the Japan Ministry of Health, Labor, and Welfare from the period 2011–2018. In total, 247,930 new patients with CSC were identified. Overall mean age was not reported and 75.9% were male. Mean age was 50.4 ± 12.5 years in male individuals and 54.7 ± 13.5 years in female individuals	Identification of cases was based on database registration according to diagnosis codes. Diagnostic definitions were not described	Stratified by age and sex

Table 1 continued

References	Design	Country	Study population	Diagnosis of CSC	Data granularity
Kitzmann et al. (2008) [6]	Retrospective population-based cohort study	USA	Data from medical records of all patients in Olmsted County, Minnesota from the period 1980–2002. In total, 74 new patients with CSC were identified. Overall mean age was 41 (range 29–56) years and 85.1% were male	CSC was defined as a localized neurosensory retinal detachment associated with focal leak(s) at the level of the RPE by FA without other possible cause for the exudation	Stratified by age and sex
Lee and Bae (2022) [32]	Retrospective population-based cohort study	South Korea	Data from the nationwide Korean Health Insurance Review and Assessment Service from the period 2013–2019. In total, 36,053 new patients with CSC were identified. Overall mean age was not reported and 77.9% were male. Mean age was $48 \pm 9$ years in male individuals and $51 \pm 10$ years in female individuals	Identification of cases was based on database registration according to diagnosis codes. Diagnostic definitions were not described	Stratified by age and sex

Table 1 continued

References	Design	Country	Study population	Diagnosis of CSC	Data granularity
Pan et al. (2020) [33]	Retrospective clinic-based cohort study	USA	Data from the IBM MarketScan database, which is one of the largest healthcare databases available for patients with employer-provided health insurance in the USA. Data were extracted for the period 2007–2016. In total, 39,254 new patients with CSC were identified. Overall mean age and sex distribution was not reported	Identification of cases was based on database registration according to diagnosis codes. Diagnostic definitions were not described	Stratified by age and sex
Tsai et al. (2013) [34]	Retrospective population-based cohort study	Taiwan	Data from the nationwide National Health Insurance in Taiwan from 2001 to 2006. In total, 786 new patients with CSC were identified. Overall mean age was 39.3 ± 10.5 years and 63.6% were male	Identification of cases was based on database registration according to diagnosis codes. Diagnostic definitions were not described	Stratified by age and sex
Yahalomi et al. (2024) [35]	Retrospective clinic-based cohort study	Israel	Data from 2018 to 2021 from the only regional hospital which delivers care for CSC in an area in Israel. In total, 35 new patients with CSC were identified. Overall mean age was 44.7 ± 10.1 years and 82.8% were male	CSC was diagnosed based on macular OCT. Ultra-widefield FA was performed for differential diagnostics. Diagnostic definitions were not described	Stratified by sex

CSC central serous chorioretinopathy, FA fluorescein angiography, N/A not available, OCT optical coherence tomography, RPE retinal pigment epithelium, USA United States of America

eyes with CSC were at higher risk of later obtaining a diagnosis of exudative age-related macular degeneration [32]. Yahalomi et al. reported incidence of CSC for the period 2018–2021 based on medical records from a defined area of Southwestern Israel [35]. The incidence was reported to be 0.2 per 100,000/year but with a significant increase recorded during the COVID-19 pandemic at which time the incidence was 0.5 per 100,000/year [35]. The authors reported a mean visual acuity at presentation of 0.20–0.43 logMAR, time from initial presentation to hospital administration of 22–34 days, mean central macular thickness at presentation of 478–502  $\mu\text{m}$ , and a mean disease remission of 4.1–6.2 months, without any significant differences between these parameters and whether or not CSC occurred during the COVID-19 pandemic [35].

### Risk of Bias Within Studies

One risk of bias present across all studies was the retrospective study design which challenged the adequacy of the follow-up. In three studies,

we assessed that it would be difficult to demonstrate, on the basis of the study description, if the outcome of interest was not present at the start of study at least in certain cases. In the evaluation of comparability, we noted if incidence rates were presented both stratified according to age and sex, as both are important demographic factors that are known to play a role in CSC. Comparability was excellent for five studies. The overall quality score across studies was high and ranged between 6 and 8 (Table 2).

### Meta-analyses

Although Kitzmann et al. provided incidence rates of CSC according to age, optical coherence tomography (OCT)-based diagnosis of CSC was deemed unlikely, at least for the majority of the patients, because of the study period of 1980–2002 [6]. For the primary outcome meta-analyses, three other studies did not present incidence rates of CSC according to age [30, 33, 35]. For the subgroup analyses, certain data from Agliullin et al. and Pan et al.

**Table 2** Risk of bias within individual studies

References	Selection				Comparability	Outcome			Quality score
	#1	#2	#3	#4		#1	#2	#3	
Agliullin et al. (2021) [30]	★	★	★	–	★	★	★	–	7/9
Kido et al. (2022) [31]	★	★	★	★	★★	★	★	–	8/9
Kitzmann et al. (2008) [6]	★	★	★	★	★★	★	★	–	8/9
Lee and Bae (2022) [32]	★	★	★	★	★★	★	★	–	8/9
Pan et al. (2020) [33]	★	★	★	–	★	★	★	–	6/9
Tsai et al. (2013) [34]	★	★	★	★	★★	★	★	–	8/9
Yahalomi et al. (2024) [35]	★	★	★	–	★	★	★	–	6/9

The Newcastle–Ottawa Quality Assessment Scale for Cohort Studies evaluates categories within three domains: Selection, Comparability, and Outcome. Categories within Selection are (#1) representativeness of the exposed cohort, (#2) selection of the non-exposed cohort, (#3) ascertainment of exposure, and (#4) demonstration that outcome of interest was not present at start of study. For Comparability, only one category is evaluated in (#1) comparability of cohorts based on the design or analysis. Categories within Outcome are (#1) assessment of outcome, (#2) was follow-up long enough for outcomes to occur, and (#3) adequacy of follow-up of cohorts. The quality score is a summary of number of stars across all categories within each study

were eligible [30, 33]. Thus, various aspects of the quantitative synthesis are based on data from five studies [30–34].

Three studies were eligible for meta-analyses of the incidence rates of CSC stratified according to age with the following age strata: 30–39 years, 40–49 years, 50–59 years, and 60–69 years (Table 3) [31, 32, 34]. The summary estimate incidence rates were 47.8 (95% CI 31.7–61.7) per 100,000 person-years for individuals 30–39 years, 71.8 (95% CI 41.7–109.7) per 100,000 person-years for individuals 40–49 years, 58.5 (95% CI 29.9–96.1) per 100,000 person-years for individuals 50–59 years, and

36.2 (95% CI 16.8–62.6) per 100,000 person-years for individuals 60–69 years.

Four studies were eligible for the subgroup analysis for male sex as a risk factor [31–34]. The summary estimate of male sex as a risk factor for incident CSC was statistically significant at odds ratio 2.73 (95% CI 2.28–3.28;  $P < 0.0001$ ) (Table 4).

Four studies were eligible for the subgroup analysis of age difference between male and female individuals in incident CSC [30–32, 34]. The summary estimate of the age difference at incident CSC was statistically significant at  $-3.30$  years (95% CI  $-4.77$  to  $-1.84$  years;

**Table 3** Meta-analyses of the age-specific incidence of central serous chorioretinopathy

References	Incidence per 100,000 person-years	95% CI	Weight (%)
30–39 years			
Kido et al. (2022) [31]	57.0	55.5–58.5	34.5
Lee and Bae (2022) [32]	74.6	70.1–79.2	34.1
Tsai et al. (2013) [34]	20.4	14.7–27.0	31.4
Pooled estimate	47.8	31.7–61.7	100.0
40–49 years			
Kido et al. (2022) [31]	91.4	89.7–93.2	33.8
Lee and Bae (2022) [32]	127.9	122.5–133.5	33.6
Tsai et al. (2013) [34]	22.6	16.7–29.4	32.6
Pooled estimate	71.8	41.7–109.7	100.0
50–59 years			
Kido et al. (2022) [31]	63.6	62.1–65.2	34.2
Lee and Bae (2022) [32]	110.5	105.5–115.6	34.1
Tsai et al. (2013) [34]	21.5	13.1–31.9	31.8
Pooled estimate	58.5	29.9–96.1	100.0
60–69 years			
Kido et al. (2022) [31]	38.9	37.8–40.0	34.6
Lee and Bae (2022) [32]	71.6	66.8–76.6	34.3
Tsai et al. (2013) [34]	12.0	5.6–20.7	31.1
Pooled estimate	36.2	16.8–62.6	100.0

95% CI 95% confidence interval

**Table 4** Meta-analysis of male sex as a risk factor for incident central serous chorioretinopathy

References	Odds ratio	95% CI	Weight (%)
Kido et al. (2022) [31]	3.45	3.37–3.55	25.9
Lee and Bae (2022) [32]	3.47	3.38–3.57	25.9
Pan et al. (2020) [33]	2.44	2.33–2.54	25.7
Tsai et al. (2013) [34]	1.80	1.56–2.08	22.5
Pooled estimate	2.73	2.28–3.28	100.0

95% CI 95% confidence interval

$P < 0.0001$ ), i.e., male individuals were significantly younger than female individuals at onset of CSC (Table 5).

### Estimated Global Incidence of Central Serous Chorioretinopathy

Estimated incidence of CSC was calculated for all countries, for subregions, and globally and are presented in Table 6. We estimate that in 2025, 1.97 million individuals globally will develop CSC, and that the incidence will increase to 2.03 million individuals in 2030, 2.30 million individuals in 2040, and 2.43 million individuals in 2050. Eastern Asia is estimated to

be the subregion with the highest number of new patients with CSC in 2025; however, incidence rate in Eastern Asia is expected to decline towards 2050 and be surpassed by Southern Asia.

## DISCUSSION

In this study, we systematically reviewed studies on the incidence of CSC, performed meta-analyses to estimate the incidence of CSC within specific age strata, and estimated current and future numbers of patients with newly onset CSC for each country and on a global scale. We find that the incidence of CSC peaks in the age range of 40–49 years (71.8 per 100,000/year). We confirm male sex as a risk factor at an odds ratio of 2.73 and find that CSC in male individuals occurs on average 3.3 years before it does in female individuals. In 2025, we estimate that globally, 1.97 million individuals will develop CSC—a number we expect will gradually increase to 2.43 million individuals in 2050. Our forecasting analyses highlight interesting trends of country-specific increasing and decreasing incidence of CSC because of country-specific expected population changes.

Definition of CSC has changed and arguably improved throughout time. In 1978, one study described four cases of CSC treated with non-steroidal anti-inflammatory drugs [36]. However, in the 1978 study, CSC was also defined as cystoid macular edema that can occur after eye

**Table 5** Meta-analysis of the age difference between male and female individuals at incident central serous chorioretinopathy

References	Mean difference, years	95% CI, years	Weight (%)
Agliullin et al. (2021) [30]	– 10.00	– 12.02 to – 7.98	19.0
Kido et al. (2022) [31]	– 4.20	– 4.32 to – 4.08	29.7
Lee and Bae (2022) [32]	– 3.00	– 3.27 to – 2.73	29.4
Tsai et al. (2013) [34]	+ 3.30	+ 1.70 to + 4.90	21.9
Pooled estimate	– 3.30	– 4.77 to – 1.84	100.0

Comparison is made against female individuals, i.e., negative values indicate lower age at time of diagnosis in male individuals and positive values indicate higher age at time of diagnosis in male individuals

95% CI 95% confidence interval

**Table 6** Estimated current and future annual incidence of central serous chorioretinopathy

Area	2025	2030	2040	2050
World	1,970,679	2,034,002	2,301,062	2,433,846
Eastern Africa	70,707	84,713	119,632	159,463
Burundi	1746	2087	3344	4149
Comoros	143	165	217	260
Djibouti	238	271	324	363
Eritrea	530	626	823	1101
Ethiopia	19,634	23,098	31,729	43,104
Kenya	8818	10,191	14,111	17,181
Madagascar	4846	5838	7682	10,342
Malawi	2817	3536	5521	7255
Mauritius	361	373	364	350
Mayotte	49	59	88	108
Mozambique	4414	5302	7651	10,843
Réunion	244	229	229	202
Rwanda	2137	2502	3764	4549
Seychelles	37	40	43	44
Somalia	2304	2853	4092	5958
South Sudan	1809	2211	2903	3243
Uganda	6273	7697	11,212	16,579
United Republic of Tanzania	9266	11,336	16,083	22,124
Zambia	2966	3710	5433	7178
Zimbabwe	2075	2589	4021	4530
Middle Africa	28,602	33,348	46,985	65,969
Angola	5224	6048	8698	11,921
Cameroon	4187	4965	7080	9375
Central African Republic	555	638	946	1459
Chad	2570	3105	4252	6119
Congo	1003	1164	1560	1961
Democratic Republic of the Congo	14,245	16,513	23,198	33,667
Equatorial Guinea	336	369	511	592
Gabon	445	505	682	808
Sao Tome and Principe	36	43	58	67

Table 6 continued

Area	2025	2030	2040	2050
Northern Africa	55,470	61,577	76,865	88,252
Algeria	10,631	11,612	14,269	14,871
Egypt	23,414	26,000	33,317	38,788
Libya	1713	1997	2275	2324
Morocco	8977	9632	11,117	11,603
Sudan	7446	8869	12,032	16,768
Tunisia	3141	3300	3640	3689
Western Sahara	147	168	216	210
Southern Africa	15,602	16,799	20,875	23,070
Botswana	461	525	669	888
Eswatini	209	233	310	358
Lesotho	368	402	594	706
Namibia	517	607	777	1047
South Africa	14,047	15,032	18,526	20,072
Western Africa	65,408	76,619	105,311	134,216
Benin	2103	2447	3355	4474
Burkina Faso	3220	3864	5571	7323
Cabo Verde	117	124	160	176
Côte d'Ivoire	4687	5447	7861	9562
Gambia	416	468	651	899
Ghana	5993	6859	8982	10,743
Guinea	2101	2425	3312	4623
Guinea-Bissau	332	398	547	704
Liberia	831	977	1357	1702
Mali	2938	3599	5303	7123
Mauritania	731	855	1200	1645
Niger	3269	3973	5849	8469
Nigeria	33,007	38,462	52,004	64,783
Saint Helena	2	1	1	1
Senegal	2819	3406	4739	6357
Sierra Leone	1340	1574	2121	2740
Togo	1501	1741	2297	2892

Table 6 continued

Area	2025	2030	2040	2050
Central Asia	18,010	18,894	22,767	26,517
Kazakhstan	4837	4846	5726	5992
Kyrgyzstan	1524	1602	1938	2320
Tajikistan	1954	2129	2761	3570
Turkmenistan	1718	1871	2092	2692
Uzbekistan	7976	8446	10,249	11,943
Eastern Asia	538,253	495,086	490,475	438,368
China	466,473	424,819	429,483	384,274
China, Hong Kong SAR	2419	2326	2141	1805
China, Macao SAR	230	219	240	222
China, Taiwan Province of China	7284	7254	6537	5527
Dem. People's Republic of Korea	8220	7703	7185	7467
Japan	35,449	35,072	29,574	24,759
Mongolia	785	812	985	1065
Republic of Korea	17,393	16,880	14,330	13,249
Southern Asia	448,526	494,819	603,780	670,603
Afghanistan	5589	6903	9767	14,223
Bangladesh	34,712	39,046	50,204	56,059
Bhutan	185	205	266	282
India	331,696	364,614	434,813	476,294
Iran (Islamic Republic of)	23,448	25,060	32,329	29,807
Maldives	135	145	203	216
Nepal	5839	6491	7916	9355
Pakistan	41,198	46,289	61,813	77,838
Sri Lanka	5723	6065	6469	6529
Southeastern Asia	172,190	182,682	203,626	213,499
Brunei Darussalam	124	135	150	153
Cambodia	3617	3788	5041	5425
Indonesia	70,491	75,980	82,908	86,351
Lao People's Democratic Republic	1538	1728	2196	2605
Malaysia	8469	9432	11,960	12,994
Myanmar	13,292	14,170	15,620	16,287

Table 6 continued

Area	2025	2030	2040	2050
Philippines	24,417	27,018	32,374	38,005
Singapore	1643	1759	1884	2080
Thailand	21,835	21,477	19,944	18,501
Timor-Leste	239	262	366	466
Vietnam	26,524	26,933	31,184	30,631
Western Asia	66,534	74,725	89,482	102,764
Armenia	788	741	807	734
Azerbaijan	2805	2737	3221	3229
Bahrain	431	463	529	571
Cyprus	390	402	477	439
Georgia	1009	978	1040	1013
Iraq	7883	9349	12,153	15,923
Israel	2018	2202	2540	2823
Jordan	2349	2621	3308	3882
Kuwait	1414	1510	1656	1734
Lebanon	1345	1401	1575	1713
Oman	1170	1341	1659	1916
Qatar	843	880	993	1017
Saudi Arabia	7788	8500	10,849	11,493
State of Palestine	880	1007	1401	1878
Syrian Arab Republic	4557	5804	7541	9022
Türkiye	22,062	24,640	26,206	27,538
United Arab Emirates	2919	3100	3217	4032
Yemen	5884	7049	10,310	13,806
Eastern Europe	81,127	78,833	83,090	68,995
Belarus	2648	2481	2606	2193
Bulgaria	2003	1937	1791	1409
Czechia	3061	3194	2930	2451
Hungary	2839	2935	2562	2294
Poland	10,625	10,881	11,370	9442
Republic of Moldova	820	740	781	649
Romania	5762	5508	5012	4124

Table 6 continued

Area	2025	2030	2040	2050
Russian Federation	40,336	38,515	42,661	35,107
Slovakia	1583	1635	1597	1360
Ukraine	11,452	11,006	11,780	9967
Northern Europe	30,114	29,599	30,293	30,597
Denmark	1681	1646	1536	1616
Estonia	380	362	378	311
Faroe Islands	15	14	15	15
Finland	1483	1445	1488	1431
Guernsey	19	18	17	16
Iceland	105	109	118	125
Ireland	1410	1536	1603	1453
Isle of Man	25	24	21	20
Jersey	32	31	30	27
Latvia	540	494	497	412
Lithuania	843	778	715	701
Norway	1582	1558	1583	1575
Sweden	2896	2824	2962	3003
UK	19,104	18,761	19,330	19,891
Southern Europe	46,089	45,207	39,307	33,312
Albania	770	714	673	739
Andorra	28	29	26	23
Bosnia and Herzegovina	911	918	816	647
Croatia	1109	1076	997	871
Gibraltar	11	11	12	13
Greece	2964	2930	2580	2102
Holy See	0	0	0	0
Italy	18,569	17,647	14,743	12,644
Kosovo (under UNSC res. 1244)	430	446	481	468
Malta	152	159	176	170
Montenegro	171	167	161	141
North Macedonia	521	506	479	436
Portugal	3050	3057	2649	2283

Table 6 continued

Area	2025	2030	2040	2050
San Marino	11	11	9	8
Serbia	1908	1866	1745	1527
Slovenia	617	612	579	487
Spain	14,866	15,056	13,181	10,755
Western Europe	57,050	53,341	51,849	49,264
Austria	2777	2571	2458	2344
Belgium	3289	3197	3162	3062
France	17,794	17,327	17,046	15,977
Germany	25,058	22,448	21,486	20,165
Liechtenstein	12	12	11	11
Luxembourg	202	207	217	221
Monaco	9	8	8	8
Netherlands	5241	4998	4898	5066
Switzerland	2667	2573	2564	2412
Caribbean	11,341	11,365	11,889	12,448
Anguilla	4	4	5	4
Antigua and Barbuda	27	27	28	27
Aruba	33	31	29	26
Bahamas	114	115	117	122
Barbados	81	78	75	72
Bonaire, Sint Eustatius and Saba	10	10	10	10
British Virgin Islands	12	13	14	12
Cayman Islands	25	26	29	28
Cuba	3660	3249	2834	2628
Curaçao	54	53	49	57
Dominica	19	18	19	20
Dominican Republic	2579	2764	3101	3445
Grenada	30	29	36	35
Guadeloupe	110	95	81	64
Haiti	2240	2511	3142	3700
Jamaica	752	783	833	845
Martinique	105	85	71	56

Table 6 continued

Area	2025	2030	2040	2050
Montserrat	1	1	1	1
Puerto Rico	914	894	790	732
Saint Barthélemy	3	3	3	3
Saint Kitts and Nevis	13	13	14	14
Saint Lucia	51	53	54	57
Saint Martin (French part)	7	6	5	3
Saint Vincent and the Grenadines	27	26	25	25
Sint Maarten (Dutch part)	15	14	14	14
Trinidad and Tobago	417	425	476	417
Turks and Caicos Islands	14	15	16	14
United States Virgin Islands	24	21	19	17
Central America	41,648	45,487	52,564	58,545
Belize	90	103	128	153
Costa Rica	1351	1409	1582	1613
El Salvador	1385	1544	1614	2003
Guatemala	3226	3805	5134	6466
Honduras	2023	2421	3140	3789
Mexico	31,071	33,417	37,627	40,739
Nicaragua	1418	1619	2009	2327
Panama	1084	1169	1331	1456
South America	109,907	117,530	129,570	133,339
Argentina	10,934	11,987	13,266	14,116
Bolivia (Plurinational State of)	2486	2796	3440	4063
Brazil	55,765	59,268	63,958	62,839
Chile	5552	5730	6071	6367
Colombia	13,640	14,645	16,294	17,813
Ecuador	4122	4571	5422	6016
Falkland Islands (Malvinas)	1	1	1	1
French Guiana	66	69	88	93
Guyana	181	193	192	245
Paraguay	1471	1585	1952	2281
Peru	8016	8754	10,183	10,994

Table 6 continued

Area	2025	2030	2040	2050
Suriname	150	156	174	189
Uruguay	878	917	917	961
Venezuela (Bolivarian Republic of)	6646	6858	7612	7363
Bermuda	20	19	17	14
Northern America	102,759	101,672	109,432	110,244
Canada	10,968	11,074	11,792	12,544
Greenland	16	14	14	15
Saint Pierre and Miquelon	2	2	1	1
USA	91,753	90,563	97,607	97,670
Australia/New Zealand	8603	8652	9486	9937
Australia	7176	7259	8018	8423
New Zealand	1426	1394	1468	1514
Melanesia	2463	2783	3499	4151
Fiji	206	216	250	264
New Caledonia	80	82	88	86
Papua New Guinea	1982	2259	2855	3421
Solomon Islands	138	166	222	271
Vanuatu	58	61	84	109
Micronesia	116	115	121	136
Guam	42	40	39	45
Kiribati	25	27	33	42
Marshall Islands	7	6	6	3
Micronesia (Fed, States of)	21	22	24	30
Nauru	2	2	3	3
Northern Mariana Islands	14	12	11	8
Palau	6	5	5	4
Polynesia	159	156	165	157
American Samoa	11	11	10	8
Cook Islands	4	3	3	2
French Polynesia	79	79	86	76
Niue	0	0	0	0
Samoa	40	39	41	48

Table 6 continued

Area	2025	2030	2040	2050
Tokelau	1	1	1	1
Tonga	19	18	19	18
Tuvalu	2	2	2	2
Wallis and Futuna Islands	3	3	3	2

surgery [36, 37], which is a significantly different definition of CSC from that in modern times. The introduction of routine clinical OCT-based macular examination has improved the ability to clearly identify subretinal fluid even in subtle cases but also improved the distinction of various retinal diseases. Therefore, we speculate that cases of retinal disease diagnosed as CSC years ago may not always align with our understanding of CSC today. Further, clinical investigators have put a substantial effort into understanding CSC and distinguishing it from other causes of subretinal fluid, which has been facilitated by improvements in ophthalmic imaging modalities and clinical research [38]. One recent example includes the checkpoint inhibitor-induced adverse effect of subretinal fluid development, which may be due to RPE surface expression of the programmed death ligand-1 (PD-L1) that is also a target for checkpoint inhibition therapy [39]. However, in the 2010s, these cases were sometimes described as CSC despite being an entirely different disease [40]. Therefore, using previous studies to extrapolate incidence rates into today also introduces an important bias as our definition of what constitutes CSC changes and the diagnostic tools available improve over time [41].

From clinical experience, we also observe that there are asymptomatic patients who obtain a diagnosis of CSC because of an eye examination for another reason. There may be a substantial number of cases with CSC which are never diagnosed. This means that studies based on claims and nationwide diagnosis/treatment registries are at risk of underestimating the true incidence of CSC. Large-scale studies using OCT-based screening may allow estimation of incidence of CSC while also including the asymptomatic cases [42].

Previously, speculation has been made into differences in the prevalence and incidence of CSC across ethnicities [43]. It is speculated that the incidence is higher in Asian individuals than in White individuals, which are again higher than in Black individuals [43]. Very few well-designed studies have dealt with this topic, and findings are not convincing of any strong differences across ethnicities [44, 45]. At least among Black individuals, evidence suggests that CSC may have been underestimated in previous studies [46]. However, if a true difference does exist across ethnicities, that introduces an uncertainty around the estimates calculated in our study which assumes that the incidence is the same across ethnicities. Several factors could explain potential regional differences. Pachy-choroid spectrum diseases seem to be more prevalent in Asian individuals than in White individuals [47–49]. Access to eye-care services differs across regions [50]. Screening practices with routine OCT scans of asymptomatic individuals in certain areas potentially increases the number of identified cases [51]. Also, regional differences in risk factors of CSC (i.e., psychological stress, tobacco smoking, obstructive sleep apnea, corticosteroid exposure) could also influence incidence rates across populations.

Limitations of our systematic review and meta-analysis should be kept in mind when interpreting its results. First, studies available for the age-specific incidence of CSC were all large registry-based studies with limited insight into the diagnostic processes that led to the diagnosis of CSC. Therefore, our estimates can only be as good as these studies. To our best knowledge, no studies have explored the internal validity of the Japanese Health Insurance Claims Database, the Korean Health Insurance Review and Assessment Service Database, or the Taiwan

National Health Insurance Database, for the diagnosis of CSC. Second, our estimates disregard incidence rates in individuals <30 years and >70 years. Although rare, these cases certainly do exist [4–6], and our calculations may therefore slightly underestimate the total incidence rates across all ages. Finally, our population estimates are based on the most likely scenario as predicted by the United Nations Population Division [29]. If this scenario does not hold true, neither does our estimate.

## CONCLUSIONS

We here provide a systematic review and meta-analysis of incidence of CSC and provide the first global incidence calculation for the disease. Numbers presented in this study highlight that CSC is one of the more prevalent maculopathies in our world and underscore the importance of education, research, and healthcare planning related to CSC. Various sources of bias demand careful interpretation of the numbers presented in this study.

**Author Contribution.** Ida Ny Frederiksen, Andreas Arnold-Vangsted, Rodrigo Anguita, Lars Christian Boberg-Ans, Lasse Jørgensen Cehofski, Elon H.C. van Dijk, Nathalie Skovgaard Eriksen, Lorenzo Ferro Desideri, Jakob Grauslund, Josef Huemer, Claudio Iovino, Steffen Emil Künzel, Marie Ørskov, Laurenz J. B. Pauleikhoff, Marie Louise Roed Rasmussen, and Yousif Subhi contributed to the study conception and design. Material preparation, data collection and analysis were performed by Ida Ny Frederiksen, Andreas Arnold-Vangsted, and Yousif Subhi. Ida Ny Frederiksen, Andreas Arnold-Vangsted, Rodrigo Anguita, Lars Christian Boberg-Ans, Lasse Jørgensen Cehofski, Elon H.C. van Dijk, Nathalie Skovgaard Eriksen, Lorenzo Ferro Desideri, Jakob Grauslund, Josef Huemer, Claudio Iovino, Steffen Emil Künzel, Marie Ørskov, Laurenz J. B. Pauleikhoff, Marie Louise Roed Rasmussen, and Yousif Subhi contributed to the interpretation of the results. The first draft of the manuscript was written by Ida Ny Frederiksen and all authors commented on previous versions

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## Declarations

**Conflict of Interest.** Ida Ny Frederiksen, Andreas Arnold-Vangsted, Rodrigo Anguita, Lars Christian Boberg-Ans, Lasse Jørgensen Cehofski, Elon H.C. van Dijk, Nathalie Skovgaard Eriksen, Lorenzo Ferro Desideri, Josef Huemer, Claudio Iovino, Steffen Emil Künzel, Marie Ørskov, Laurenz J. B. Pauleikhoff, and Marie Louise Roed Rasmussen declare that they have no competing interests. Jakob Grauslund declares to have received speakers fee from Allergan, Bayer, Novartis, and Roche, and to have served as an advisory board member for Allergan, Apellis, Bayer, Novartis, and Roche, not related to this work. Yousif Subhi declares to have received speakers fee from Bayer and Roche, to have served as an advisory board member for Astellas,

and to be the inventor of a patent related to biomarkers for polypoidal choroidal vasculopathy (WO2020007612A1), not related to this work. Yousif Subhi is Section Editor of *Ophthalmology and Therapy*. Yousif Subhi was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions.

**Ethical Approval.** This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors. Systematic reviews, meta-analyses, and forecasting studies using publicly available data do not require institutional review board approval according to Danish law.

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