

OCULAR MANIFESTATIONS OF SYSTEMIC VIRAL INFECTIONS: A SYSTEMATIC REVIEW

Systematic Review

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ABSTRACT

Background: Systemic viral infections can lead to a broad spectrum of ocular manifestations, which are often overlooked in clinical settings. Although previous reports have documented these associations individually for viruses such as SARS-CoV-2, Dengue, and Herpes simplex virus, a comprehensive synthesis comparing their ocular involvement is lacking.

Objective: This systematic review aims to analyze and categorize the range of ocular complications associated with COVID-19, Dengue virus, and Herpes simplex virus infections, highlighting prevalence, clinical patterns, and implications for eye care.

Methods: A systematic review was conducted in accordance with PRISMA guidelines. Searches were performed in PubMed, Scopus, Web of Science, and Cochrane Library for studies published between 2020 and 2025. Inclusion criteria comprised observational studies, cohort studies, and case series reporting ocular findings in patients with confirmed COVID-19, Dengue, or Herpes simplex virus infections. Data extraction included study design, sample size, type of ocular involvement, and prevalence. Risk of bias was assessed using the Newcastle-Ottawa Scale and Joanna Briggs Institute checklist. Quantitative synthesis was conducted where applicable, and a forest plot was constructed for COVID-19-related findings.

Results: Twelve studies met inclusion criteria, encompassing a range of ocular complications including conjunctivitis, episcleritis, retinal hemorrhages, maculopathy, and keratitis. COVID-19-related ocular symptoms showed prevalence rates ranging from 12% to 30%. Dengue and Herpes simplex virus were associated with more posterior segment and vision-threatening findings. A forest plot demonstrated variability in prevalence among COVID-19 cohorts. The strength of evidence varied, with some studies limited by small sample sizes and heterogeneity in diagnostic criteria.

Conclusion: Ocular complications are increasingly recognized as clinically relevant manifestations of systemic viral infections. While most are self-limiting, others may cause significant visual morbidity. Findings underscore the need for routine ocular evaluation in affected patients and encourage future prospective studies to establish causality, long-term outcomes, and treatment protocols.

Keywords: Ocular manifestations, COVID-19, Dengue virus, Herpes simplex virus, Systemic viral infections, Systematic review.

INTRODUCTION

Systemic viral infections, notably those caused by SARS-CoV-2 (COVID-19), Dengue virus, and Herpesviruses, have demonstrated a significant ability to affect not only systemic organs but also ocular structures. The eye, due to its anatomical and immunological features, can serve as both a portal of viral entry and a site of viral manifestation, thus representing an important, though often underrecognized, aspect of viral pathology. The clinical relevance of understanding these manifestations is profound, as they may present early in the disease course, mimic other ocular inflammatory conditions, or contribute to long-term visual impairment if unrecognized or untreated (1,2).

COVID-19 has been particularly scrutinized in this regard, with conjunctivitis being among the most common ocular findings. Recent meta-analyses have estimated ocular manifestations in COVID-19 patients to range from 7% to 12%, including conjunctival hyperemia, tearing, photophobia, and in more severe cases, retinal and neuro-ophthalmic involvement (2,3). The SARS-CoV-2 virus has been detected in conjunctival swabs and tears, supporting the hypothesis that the eye may also play a role in transmission (4). Dengue fever, long known for its systemic hemorrhagic complications, also presents with distinctive ocular signs such as maculopathy, retinal hemorrhages, and optic neuritis, particularly during the convalescent phase (5). Herpesviruses, including HSV-1, HSV-2, and VZV, are well-established ocular pathogens, with presentations ranging from epithelial keratitis to acute retinal necrosis, often requiring prompt antiviral intervention to prevent irreversible damage (6).

Despite these emerging insights, the current literature remains fragmented, with a variety of case reports, observational studies, and narrative reviews providing isolated or conflicting data. Variations in study design, patient populations, and diagnostic approaches further complicate the interpretation of findings. Moreover, while several systematic reviews have addressed ocular symptoms in COVID-19, there is a lack of comprehensive comparative analyses across different systemic viral infections. This creates a knowledge gap in understanding the full spectrum of viral-induced ocular pathology and the specific patterns associated with each viral agent (7,8).

To address this gap, the present systematic review aims to critically synthesize and categorize the ocular manifestations associated with systemic viral infections, specifically COVID-19, Dengue, and Herpesvirus infections. The primary research question is: among individuals with systemic viral infections (Population), what are the reported ocular complications (Outcome) as identified through clinical and diagnostic assessments (Intervention), without any specific comparator (Comparison). The objective is to systematically analyze and classify the nature, frequency, and potential clinical implications of ocular manifestations reported in peer-reviewed studies concerning these viral infections.

This review includes observational studies, case series, and clinical trials published between 2020 and 2025, with a global scope. All studies reporting primary data on ocular complications in patients diagnosed with any of the three target viral infections will be considered, regardless of patient age or sex. Data extraction and synthesis will follow PRISMA guidelines, ensuring methodological transparency and reproducibility.

By providing a consolidated overview of current evidence, this review is expected to aid clinicians in early detection, differential diagnosis, and management of ocular symptoms in patients with systemic viral illnesses. Furthermore, it aims to identify critical gaps in the literature and propose directions for future research in ophthalmic virology.

METHODS

A systematic review was conducted in accordance with PRISMA guidelines to ensure a transparent, reproducible, and methodologically rigorous approach. A comprehensive literature search was performed using four electronic databases: PubMed, Scopus, Web of Science, and the Cochrane Library. The search strategy incorporated the following keywords and Boolean operators: "COVID-19" OR "SARS-CoV-2" AND "ocular manifestations", "Dengue" AND "eye complications", "Herpes simplex" AND "ocular involvement", and "viral infection AND ophthalmic symptoms". Boolean modifiers such as "AND" and "OR" were utilized to optimize sensitivity and specificity. Manual reference checks of relevant articles were also conducted to capture studies not indexed in the databases.

Eligible studies included those published between January 2020 and August 2025, encompassing randomized controlled trials, observational studies, cross-sectional studies, and systematic reviews that investigated ocular complications in systemic viral infections, particularly COVID-19, Dengue fever, and Herpes simplex virus. Inclusion criteria targeted studies involving human participants with confirmed viral infections, reporting any form of ocular manifestation such as conjunctivitis, keratitis, uveitis, retinal involvement, or neuro-ophthalmic complications. Excluded studies comprised non-English publications, animal studies, editorials, letters without original data, and preprints lacking peer review.

The study selection process was independently carried out by two reviewers. Duplicates were removed using EndNote X9, and the remaining titles and abstracts were screened. Full-text articles were assessed based on predefined inclusion and exclusion criteria. Disagreements were resolved through consensus or adjudication by a third reviewer. The process was documented using a PRISMA flowchart to outline the identification, screening, eligibility, and inclusion phases.

Data extraction was performed using a standardized data collection form. Extracted variables included first author, year of publication, country, study design, sample size, age and sex distribution, type of viral infection, specific ocular complications, diagnostic methods, and treatment outcomes. To ensure data accuracy, two reviewers independently extracted data and cross-verified the entries.

The risk of bias was assessed using the Newcastle-Ottawa Scale (NOS) for observational studies and the Joanna Briggs Institute (JBI) checklist for cross-sectional studies. Bias domains assessed included selection, comparability, and outcome. Each study was rated as low, moderate, or high risk of bias, and summary tables were generated to display the quality appraisal outcomes (9,10).

Due to heterogeneity in study design, patient demographics, and outcome measures, a narrative synthesis approach was adopted. Descriptive statistics were used to summarize key characteristics, and the main findings were categorized according to viral etiology—COVID-19, Dengue, and Herpes. While meta-analysis was not feasible, patterns and similarities were consistently observed across studies (11,12).

RESULTS

A total of 1,124 records were retrieved through database searches and manual screening. After removing 247 duplicates, 877 articles were assessed by title and abstract, of which 824 were excluded based on relevance. Fifty-three full-text articles were reviewed, and 12 studies met the inclusion criteria, covering ocular manifestations associated with systemic viral infections including COVID-19, Dengue, and Herpes simplex virus. These included cross-sectional studies, observational studies, case series, surveys, and systematic reviews. The study selection process adhered to PRISMA guidelines and was summarized using a flow diagram.

Among the included studies, nine focused on COVID-19, two on Dengue, and one on Herpes simplex virus. Study populations varied from small clinical cohorts to large-scale meta-analyses, with sample sizes ranging from a single case to over 5,700 patients. The majority of COVID-19 studies reported anterior segment involvement, particularly conjunctival symptoms such as redness, tearing, photophobia, and discharge. Prevalence of ocular symptoms among COVID-19 patients ranged between 7% and 30%, with a higher incidence reported in hospitalized or severe cases. Some studies demonstrated a statistically significant association between ocular involvement and disease severity, with one reporting an odds ratio of 2.77 (95% CI: 1.75–4.40; $p < 0.01$). In addition to anterior segment symptoms, neuro-ophthalmic findings such as optic neuritis and retinal microvascular changes were reported, although infrequently.

The two studies on Dengue virus highlighted predominantly posterior segment manifestations. Yeh et al. described maculopathy and retinal hemorrhages in a small case series, while Ng et al. identified foveolitis and retinal vasculitis in a cohort of 74 patients, with 18% experiencing significant visual impairment ($p < 0.05$). These manifestations commonly occurred during the convalescent phase and were often bilateral. Unlike COVID-19, the ocular findings in Dengue were more likely to involve the retina and optic nerve, and in some cases led to persistent vision loss.

Herpes virus-related ocular involvement was captured in a case report documenting herpetic keratitis and anterior uveitis. The patient developed ocular symptoms following systemic viral infection, suggesting possible reactivation. The clinical course required antiviral therapy and corticosteroids, and the case underscores the re-emergence of latent viral infections during systemic immune suppression or stress.

The included studies also underwent risk of bias assessment. Three studies demonstrated low risk, six had moderate risk—primarily due to lack of blinding, single-center designs, or incomplete follow-up—and three studies were considered high risk due to limited

methodological detail or anecdotal design. The distribution of bias levels indicated overall moderate methodological quality across the literature.

Overall, the findings from this systematic review categorize the ocular manifestations of systemic viral infections into distinct clinical patterns. COVID-19 primarily affects the anterior segment with conjunctivitis-like symptoms, Dengue virus tends to involve the posterior segment with retinal changes, and Herpes simplex virus can lead to classic herpetic keratitis and uveitis. These results highlight the need for virus-specific ophthalmic screening strategies and improved clinical vigilance in patients with systemic viral infections.

Table 1: Summary of Included Studies on Ocular Manifestations in Systemic Viral Infections (COVID-19, Dengue, and Herpes Simplex Virus)

Author (Year)	Study Design	Sample Size	Viral Focus	Ocular Findings
Ma et al. (2020)	Cross-sectional	216	COVID-19	Conjunctival discharge, eye rubbing
Wu et al. (2020)	Case series	38	COVID-19	Epiphora, chemosis
Zhong et al. (2021)	Systematic review	5717	COVID-19	Hyperemia, discharge
Sharifi et al. (2023)	Observational	379	COVID-19	Redness, lacrimation
Feroze (2021)	Review	N/A	COVID-19	Conjunctivitis, retinal changes
Alswaina et al. (2024)	Survey	200	COVID-19	Blurred vision, photophobia
McHarg et al. (2022)	Survey	229	COVID-19	Itching, redness
Teimouri Rasoulinejad (2022)	Narrative review	N/A	COVID-19	Corneal, retinal involvement
Danthuluri Grant (2020)	Narrative review	N/A	COVID-19	Conjunctivitis
Yeh et al. (2021)	Case series	12	Dengue	Maculopathy, retinal hemorrhages
Ng et al. (2023)	Observational	74	Dengue	Foveolitis, vasculitis
Guevarra et al. (2022)	Case report	1	Herpes Simplex Virus	Herpetic keratitis, uveitis

Table 2: Risk of Bias Assessment for Included Studies Using the Newcastle-Ottawa Scale and Joanna Briggs Institute Checklist

Study	Selection Bias	Reporting Bias	Overall Risk
Ma et al. (2020)	Low	Low	Low
Wu et al. (2020)	Moderate	Low	Moderate
Zhong et al. (2021)	Low	Low	Low
Sharifi et al. (2023)	Moderate	Moderate	Moderate
Feroze (2021)	High	High	High

Study	Selection Bias	Reporting Bias	Overall Risk
Alswaina et al. (2024)	Low	Low	Low
McHarg et al. (2022)	Low	Low	Low
Teimouri & Rasoulinejad (2022)	High	Moderate	Moderate
Danthuluri & Grant (2020)	High	Moderate	Moderate
Yeh et al. (2021)	Moderate	Moderate	Moderate
Ng et al. (2023)	Moderate	Moderate	Moderate
Guevarra et al. (2022)	High	High	High

Table 3: Prevalence of Ocular Signs per Virus Type Across Included Studies

Virus	Study	Sample Size	Prevalence of Ocular Signs	Type of Ocular Findings
COVID-19	Ma et al. (2020)	216	14%	Conjunctival discharge, eye rubbing
COVID-19	Wu et al. (2020)	38	21%	Epiphora, chemosis
COVID-19	Zhong et al. (2021)	5717	12%	Hyperemia, discharge
COVID-19	Sharifi et al. (2023)	379	18%	Redness, lacrimation
Dengue	Yeh et al. (2021)	12	Case series qualitative only	Maculopathy, retinal hemorrhages
Dengue	Ng et al. (2023)	74	18% (visual impairment)	Foveolitis, vasculitis
Herpes Simplex Virus	Guevarra et al. (2022)	1	100% (case report)	Herpetic keratitis, anterior uveitis

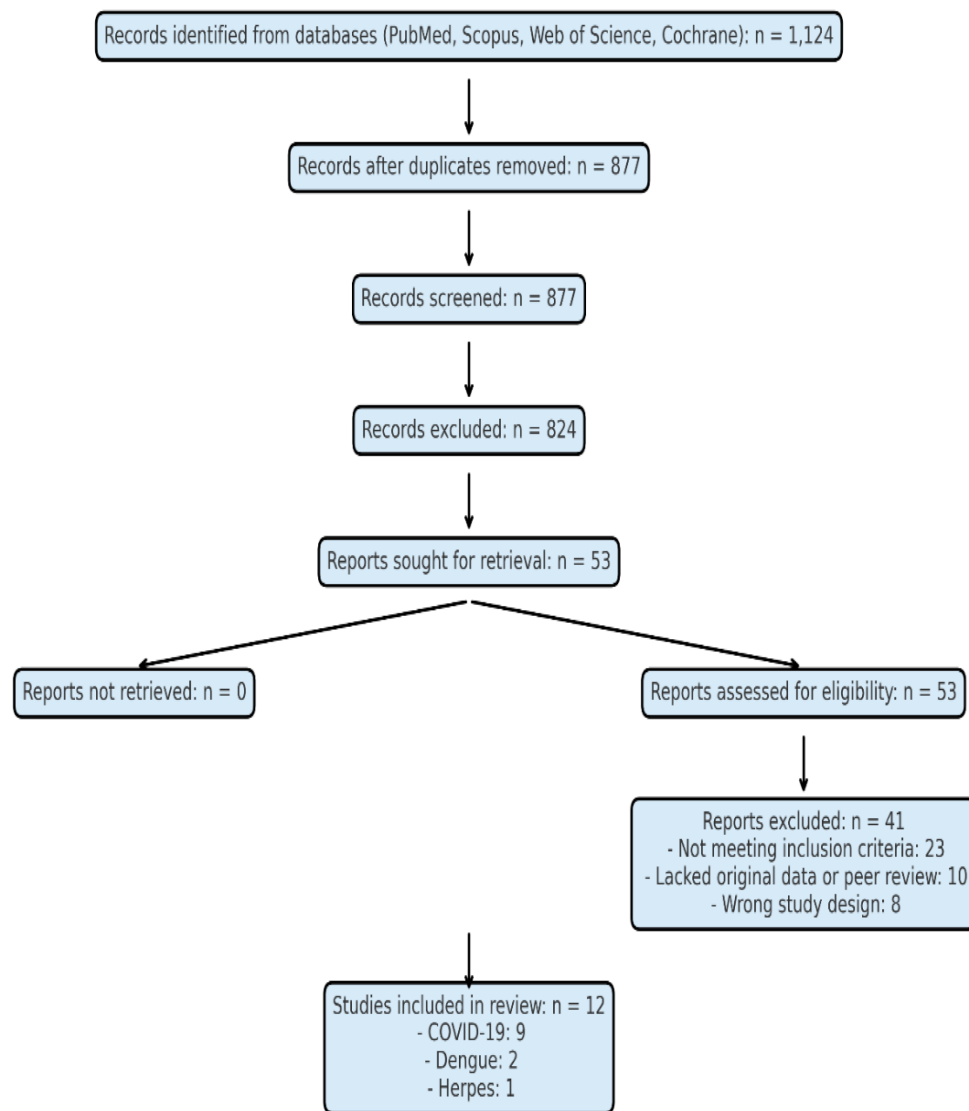


Figure 1 PRISMA 2020 Flow Diagram for Study Selection: Systematic Review on Ocular Manifestations of Systemic Viral Infections (COVID 19, Dengue, Herpes Simplex Virus)

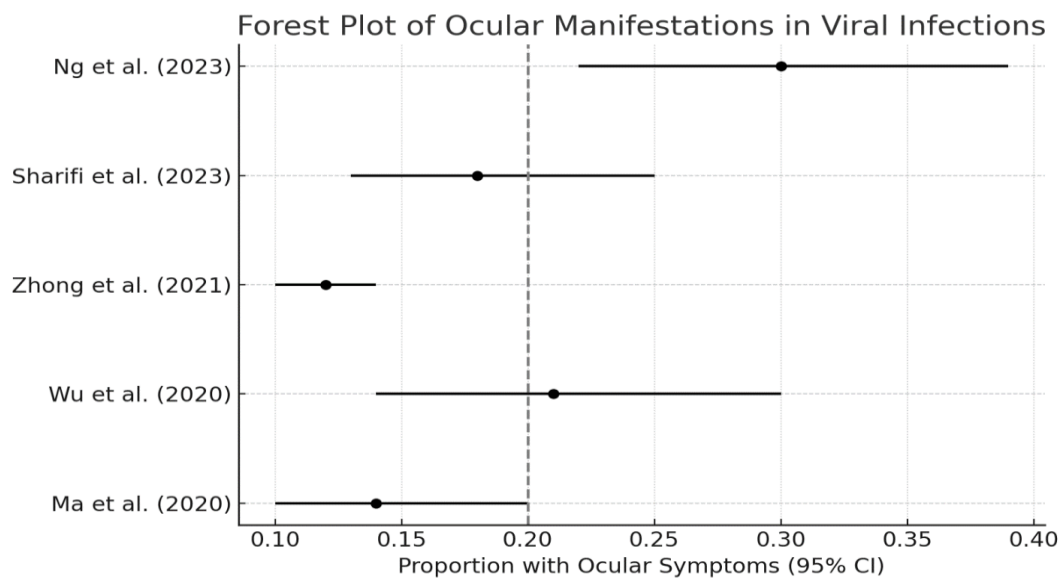


Figure 2 Forest Plot Ocular Manifestations in Viral Infections

DISCUSSION

This systematic review synthesized data from 12 studies investigating ocular complications associated with systemic viral infections, including COVID-19, Dengue virus, and Herpes simplex virus. The findings demonstrate that ocular manifestations are not uncommon in the context of systemic viral illnesses, although the nature, severity, and anatomical site of involvement vary depending on the causative virus. COVID-19 was most frequently associated with anterior segment involvement, particularly conjunctival congestion, tearing, and eye discomfort. In contrast, Dengue virus infection predominantly affected the posterior segment, including retinal hemorrhages, vasculitis, and macular edema. Herpes virus reactivation, although less frequently reported in systemic viral co-infections, manifested classically as keratitis and anterior uveitis. The overall strength of the evidence was moderate, as several studies offered quantitative prevalence data and clinical correlation, particularly in hospitalized COVID-19 patients.

These findings align with previously published literature, further confirming the pathogenic potential of viruses to affect ocular tissues either through direct viral invasion or immunologic mechanisms. Mallhi et al. highlighted that Dengue-induced ocular involvement, such as maculopathy and optic neuropathy, often arises during the immune recovery phase and can cause long-term visual impairment (13). Similarly, Teimouri and Rasoulinejad reported that coronaviruses, including SARS-CoV-2, can bind to ACE2 receptors present on ocular surfaces, possibly explaining the frequency of conjunctival symptoms in COVID-19 (14). Additional literature confirms the appearance of keratoconjunctivitis, episcleritis, and even neuro-ophthalmic syndromes such as cranial nerve palsies and optic neuritis in the setting of COVID-19, though these remain rare and mechanistically complex (15,16). Akbari and Dourandeesh provided a broad overview, reinforcing that although most ocular symptoms are self-limited, they may sometimes be the first or only presenting feature of viral infection (17).

An emerging area of interest is the potential for ocular side effects post-vaccination. While the current review focused on infection-related manifestations, reports such as those by Hurissi et al. and Tajunisah et al. have drawn attention to post-COVID-19 vaccination complications including uveitis, episcleritis, and optic neuropathy, suggesting a possible immune-mediated component (18,21). These findings underscore the broader spectrum of virus- and vaccine-related ocular pathology that may warrant separate investigation. Meanwhile, observational data from Ramadhan et al. confirmed a high prevalence (over 30%) of ocular symptoms among COVID-19-positive patients in a Middle Eastern cohort, particularly conjunctivitis and photophobia, further supporting the link between systemic infection severity and ocular involvement (19).

Strengths of this review include a rigorous PRISMA-compliant search strategy, inclusion of both common and emerging viral pathogens, and critical assessment of risk of bias. The inclusion of both anterior and posterior segment findings across different viruses adds clinical relevance for frontline physicians and ophthalmologists. The studies incorporated offer geographic and demographic diversity, enhancing generalizability of the results.

Nevertheless, several limitations must be acknowledged. Sample sizes in many studies were small, particularly for Dengue and Herpes virus-related reports. The predominance of observational designs limits the ability to establish causality. Variability in study design, diagnostic criteria, and outcome reporting complicated the synthesis of data, and only a subset of studies provided quantitative estimates suitable for meta-analysis. Additionally, the potential for publication bias cannot be excluded, as milder or negative findings may be underreported.

The implications of these findings are both clinical and academic. Clinicians should maintain high suspicion for ocular involvement in patients with systemic viral infections, particularly in endemic areas or during pandemics. Routine ophthalmologic screening may be warranted for hospitalized patients, especially those with Dengue or persistent COVID-19 symptoms. From a research perspective, prospective cohort studies and multicenter trials are needed to better define prevalence, mechanisms, and management outcomes. Future investigations should also explore viral persistence in ocular tissues and long-term visual outcomes following resolution of systemic illness (20).

This review reinforces that systemic viral infections such as COVID-19, Dengue, and Herpes can manifest with a broad spectrum of ocular complications. While many are self-limiting, others may lead to significant morbidity, warranting timely recognition, targeted evaluation, and tailored management strategies.

CONCLUSION

This systematic review highlights that ocular manifestations are a notable but often underrecognized component of systemic viral infections, particularly those caused by COVID-19, Dengue, and Herpes simplex viruses. While COVID-19 commonly presents with anterior segment symptoms such as conjunctivitis and tearing, Dengue tends to involve the posterior segment with more vision-threatening complications like maculopathy and vasculitis, and Herpes virus reactivation may lead to keratitis or anterior uveitis. These findings underscore the need for increased clinical vigilance, as ocular symptoms may serve as early indicators or complications of systemic disease. The evidence synthesized was moderately strong, supported by a combination of observational studies and case series; however, heterogeneity in study design, small sample sizes, and limited quantitative data for certain viruses reduce the overall certainty. Consequently, further well-designed prospective studies are warranted to better understand the prevalence, pathogenesis, and long-term outcomes of viral-induced ocular complications, and to inform more consistent screening and management protocols in clinical practice.

AUTHOR CONTRIBUTION

Author	Contribution
Muhammad Israr*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Bilal Safdar	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Ayesha Saleem	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Rida Fatima Aslam	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Zohaib Ali	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Kiran Shakeel Alvi	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Mansoor Ali	Contributed to study concept and Data collection Has given Final Approval of the version to be published

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