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Effectiveness of interventions for dry eye: a protocol for an overview of systematic reviews

Paul McCann ,[1] Zanna Kruoch,[2] Riaz Qureshi,[1] Tianjing Li[1]

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[1]Department of Ophthalmology, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, USA
[2]Cedar Springs Eye Clinic, College of Optometry, University of Houston, Houston, Texas, USA

Correspondence to
Dr Paul McCann;
paul.mccann@cuanschutz.edu

ABSTRACT

Introduction Dry eye is a leading cause of ocular morbidity and economic and societal burden for patients and healthcare systems. There are several treatment options available for dry eye and high-quality systematic reviews synthesise the evidence for their effectiveness and potential harms.

Methods and analysis We will search the Cochrane Eyes and Vision US satellite (CEV@US) database of eyes and vision systematic reviews for systematic reviews on interventions for dry eye. CEV@US conducted an initial search of PubMed and Embase to populate the CEV@US database of eyes and vision systematic reviews in 2007, which was updated most recently in August 2021. We will search the database for systematic reviews published since 1 January 2016 because systematic reviews more than 5 years are unlikely to be up to date. We will consider Cochrane and non-Cochrane systematic reviews eligible for inclusion. Two authors will independently screen articles. We will include studies that evaluate interventions for dry eye and/or meibomian gland dysfunction with no restriction on types of participants or review language. We will select reliable systematic reviews (ie, those meeting pre-established methodological criteria) for inclusion, assessed by one investigator and verified by a second investigator. We will extract ratings of the certainty of evidence from within each review. We will report the degree of overlap for systematic reviews that answer similar questions and include overlapping primary studies. We will present results of the overview in alignment with guidelines in the Cochrane Handbook of Systematic Reviews of Interventions (Online Chapter 5: Overviews of Reviews), the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement, and an overview of reviews quality and transparency checklist. The anticipated start and completion dates for this overview are 1 May 2021 and 30 April 2022, respectively.

Ethics and dissemination This overview will not require the approval of an Ethics Committee because it will use published studies. We will publish results in a peer-reviewed journal.

PROSPERO registration number CRD42021279880.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ To our knowledge, this is the only overview of reviews of interventions for dry eye.
⇒ We will search for relevant reviews in the 'Cochrane Eyes and Vision US satellite database of eyes and vision systematic reviews' which is compiled using robust search methods and eligibility criteria.
⇒ We will include only reliable systematic reviews (ie, those meeting an established set of methodologic criteria) in the overview.
⇒ We will explore systematic review evidence for both benefits and harms of interventions for dry eye.
⇒ We will explore degrees of systematic review overlap for any included reviews which answer similar questions and report reasons for any discrepant conclusions across overlapping reviews.

INTRODUCTION

Dry eye disease (DED) is defined by the Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop II (DEWS-II) as 'a multifactorial disease of the ocular surface characterised by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.'[1] As there is no gold standard diagnostic test for DED,[1] we use the term 'dry eye' to describe various presentations of ocular discomfort and visual disturbance caused by tear film abnormalities.

Dry eye is a common clinical manifestation and is a leading cause for eye clinic attendances.[2 3] Dry eye is estimated to be prevalent in 5%–50% of worldwide populations depending on disease definition and other contextual factors.[4] In the USA, per capita total expenditures for dry eye medications increased from US$310.8 million in 2007 and 2008 to US$1.79 billion by 2015 and 2016, making dry eye medication expenditure highest among all ophthalmic medication classes.[5] Furthermore, out-of-pocket expenditure is highest for dry eye medications increasing from US$122.51 million in 2007 and 2008 to US$194.0 million in 2015 and 2016.[5] Dry eye expenditure has been shown to be similar across national

healthcare settings.[6–8] Despite these expenditures, there remains controversy regarding the clinical effectiveness of newer and costlier treatments for dry eye.[9]

Dry eye can be categorised as an aqueous deficient, evaporative or mixed mechanism disease.[1] Aqueous deficient disease is primarily due to reduced lacrimal gland secretion and evaporative disease is predominantly due to abnormalities in the Tear Film Lipid Layer (TFLL).[10] The TFLL is composed of lipids and phospholipids which originate from the meibomian glands and other lipid-secreting glands.[11 12] Meibomian gland dysfunction (MGD), the major cause of abnormalities in the meibomian glands, leads to disruption of the quality and volume of the TFLL. MGD is recognised as a leading cause of DED.[13] Improved understanding of the aetiology and pathophysiology of dry eye has led to the introduction of multiple treatment modalities to manage various aspects of the condition.[14]

Dry eye treatments aim to restore tear film homeostasis. Each intervention targets the disease via different mechanisms and the ideal choice of therapy is dependent on the predominant underlying aetiology. The TFOS DEWS-II report[14] categorises dry eye therapies into several broad conceptual categories: (1) treatments for tear insufficiency; (2) treatment for lid abnormalities; (3) anti-inflammatory treatments; (4) dietary modifications; (5) local environmental modifications; (6) surgical approaches and (7) complementary and alternative therapies (online supplemental table 1).

The TFOS DEWS II report described a staged treatment algorithm which was adapted to form the American Academy of Ophthalmology (AAO) 2018 dry eye Preferred Practice Pattern (PPP).[14] Three of the recommended treatments were informed by Cochrane reviews available at that time.[15–17] However, since 2018, Cochrane Eyes and Vision (CEV) published three additional Cochrane reviews on other dry eye interventions included in the staged treatment algorithm.[18–20] The Cochrane review for topical cyclosporine A, a treatment recommended for refractory dry eye by the UK National Institute for Health and Care Excellence,[21] is to be updated, and a further Cochrane review on topical corticosteroid treatment is in development.[22]

Several other interventions in the 2018 dry eye AAO PPP staged treatment algorithm do not have cited evidence from systematic reviews. We know these interventions are not evaluated in Cochrane reviews, however, the CEV US satellite (CEV@US) maintains a database of eyes and vision systematic reviews which contains numerous non-Cochrane reviews that may provide evidence for these interventions.[23]

Objectives

The objective of this overview is to summarise and evaluate the current body of reliable systematic reviews which report evidence on benefits and harms of interventions for dry eye.

METHODS AND ANALYSIS

Protocol and registration

We developed methods for this overview based on guidance for conducting overviews of reviews in the Cochrane Handbook of Systematic Reviews of Interventions.[24] The anticipated start and completion dates for this overview are 1 May 2021 and 30 April 2022, respectively. This review does not require approval by an ethics Committee because it will use published studies. We will conduct and report the overview in alignment with guidelines in the Cochrane Handbook of Systematic Reviews of Interventions (Online Chapter 5: Overviews of Reviews),[24] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement,[25] and a checklist developed by Li *et al*.[26] If published before the conduct of the overview we will report the overview in alignment with Preferred Reporting Items for Overviews of Reviews (PRIOR).[27] This protocol is reported in accordance with PRISMA-Protocols 2015 statement (see online supplemental table 2).

Patient and public involvement

No patient involved.

Types of review

We will include Cochrane and non-Cochrane systematic reviews from the 'CEV@US database of eyes and vision systematic reviews' that evaluate interventions for dry eye and/or MGD.[23] Systematic reviews in the 'CEV@US database of eyes and vision systematic reviews' are defined as full-text reports that either labelled themselves as a systematic review or meta-analysis anywhere in the text or that met the definition of a systematic review or a meta-analysis, when these terms were not used, as defined by the Institute of Medicine (now called the National Academy of Medicine).

To investigate beneficial clinical effectiveness, we will consider systematic reviews of randomised controlled trials (RCTs) and to investigate harms we will consider systematic reviews of randomised and non-randomised studies. Systematic reviews that evaluate interventions for dry eye due to underlying causes (eg, Sjögren's syndrome) will be included in the overview. We will only include systematic reviews that meet our minimum criteria for reliability (see below for assessment of reliability of reviews). We will exclude studies published before 1 January 2016 because systematic reviews published more than 5 years ago are unlikely to be up to date.[28 29]

Types of participants

We will include studies with participants who have dry eye or MGD as defined by the review authors. We will not apply exclusion criteria based on age or other subpopulations (eg, post-cataract surgery). We will exclude participants with blepharitis, allergic (seasonal, perennial allergic, atopic and vernal) keratoconjunctivitis and infectious keratoconjunctivitis.

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Types of interventions

Interventions for dry eye that have been evaluated in Cochrane and non-Cochrane systematic reviews of RCTs will be considered eligible for inclusion in this overview. We will compare interventions with no treatment, placebo, standard of care, other active treatment or as reported in the systematic reviews.

Types of outcomes

We will report results for each outcome in the format described by the primary review. We expect to report dichotomous or ordinal categorical outcomes as proportions. We expect to report continuous outcomes as change from baseline and/or measurement values at designated follow-up time ranges (box 1). We will extract each outcome at time points within each of the following time ranges, less than 1 month, 1 –3 months, 3–6 months and beyond 6 months. When we have multiple outcome measurements within a time window, we will choose the one measured at the longest follow-up time point. For example, if one outcome in a review is reported at 2 months and at 3 months, we will present the 3-month outcome. We will also document important outcome measurements from other time points that are reported within each time window. When there are meta-analyses, we will extract estimates of effect and 95% CIs for each outcome and pooled estimates of effect and precision.

We acknowledge that outcomes may not be available from every review or available within some of these prespecified time ranges. We also acknowledge that relevant outcomes other than those been prespecified in this protocol may be available in systematic reviews. We will justify any deviation from the protocol regarding reporting of outcomes or time windows not prespecified in the protocol.

We will not use specific outcomes as eligibility criteria for the search strategy in this overview. We have selected outcomes based on those reported in the Cochrane suite of dry eye reviews,[15–20] TFOS DEWS-II Diagnostic Methodology Report[30] and a study by Saldanha *et al*,[31] which identified and ranked research outcomes important to patients with dry eye.

Search methods for identification of reviews

CEV@US conducted an initial search of PubMed, the Cochrane Library and Embase for systematic reviews related to vision research and eye care in 2007.[23] The search has been updated seven times since, most recently on 3 August 2021. The search was designed to be comprehensive with the assistance of information specialists from Johns Hopkins University who work with CEV. All records in the CEV@US database of eyes and vision systematic reviews have been allocated tags which label the condition (eg, dry eye) and review type (eg, intervention, prognostic etc.)

We will search the 'CEV@US database of eyes and vision systematic reviews' for Cochrane and non-Cochrane reviews.[23] We will search the following terms in the titles

Box 1 Critical and additional outcomes

Critical outcomes

Dry eye-specific patient-reported outcome measures (eg, Ocular Surface Disease Index; Standard Patient Evaluation of Eye Dryness; patient-reported symptom severity and/or frequency):

⇒ Report changes in questionnaire scores and/or patient-reported symptom severity and/or frequency scores or report measurement values at the designated time ranges.

⇒ Report proportion of participants with improved self-reported visual symptoms at the designated time ranges.

Additional outcomes

Tear film stability:

⇒ Non-invasive tear break-up time (NITBUT)

⇒⇒Report changes from baseline in NITBUT or report measurement values at the designated time ranges.

⇒⇒Report proportion with a cut-off measurement indicative of dry eye as reported in the review at the designated time ranges.

⇒ Fluorescein tear break-up time (TBUT)

⇒⇒Report changes from baseline in TBUT or report measurement values at the designated time ranges.

⇒⇒Report proportion with a cut-off measurement indicative of dry eye as reported in the review at the designated time ranges.

Tear osmolarity:

⇒ Change in tear osmolarity

⇒⇒Report changes from baseline in tear osmolarity or report measurement values at the designated time ranges.

⇒⇒Report proportion with hyperosmolarity (≥309 mOsm/L) and/or proportion with an increase or decrease in tear osmolarity value at the designated time ranges.

⇒ Change in interocular differences in tear osmolarity

⇒⇒Report changes from baseline in tear osmolarity interocular differences or report interocular difference values at the designated time ranges.

⇒⇒Report proportion with difference of >8 mOsm/L and/or proportion with an increase or decrease in interocular difference at the designated time ranges.

Ocular surface dye staining:

⇒ Report changes from baseline in fluorescein, rose bengal or lissamine green staining scores based on validated clinical scales or report clinical scale values at the designated time ranges.

⇒ Report proportion with a result indicative of dry eye as reported in the review at the designated time ranges.

Aqueous production:

⇒ Report changes from baseline in aqueous volume as measured by Schirmer I or Schirmer II or report measurement values at the designated time ranges.

⇒ Report proportion with a result indicative of dry eye as reported in the review at the designated time ranges.

Best-corrected visual acuity (BCVA) with the Snellen chart or its equivalent:

⇒ Report changes from baseline in BCVA or report BCVA at the designated time ranges.

⇒ Report proportion of participants with one or more lines of improvement from baseline at the designated time ranges.

⇒ Report proportion of participants with 20/20 BCVA or better at the designated time ranges.

⇒ Report proportion of participants with 20/40 BCVA or better at the designated time ranges.

Conjunctival goblet cell density:

Continued

Box 1 Continued

⇒ Report changes from baseline of goblet cell density or report goblet cell density at the designated time ranges.
⇒ Report proportion with change in clinical grade at the designated time ranges.

Impression cytology:
⇒ Report changes from baseline in grades of epithelial metaplasia or report grades of epithelial metaplasia at the designated time ranges.
⇒ Report proportion with change in clinical grade at the designated time ranges.

Matrix metalloproteinase-9 (MMP-9):
⇒ Report proportion with MMP-9 (eg, InflammaDry) measurement of >40 ng/mL at the designated time ranges.

Meibomian gland dysfunction:
⇒ Report changes in lipid layer thickness, measured using tear film interferometry or report lipid layer thickness at the designated time ranges.
⇒ Report changes from baseline in eyelid irregularity, measured using a validated method or report eyelid irregularity at the designated time ranges.
⇒ Report changes from baseline in degree of eyelid telangiectasia, measured using a validated method or report degree of eyelid telangiectasia at the designated time ranges.
⇒ Report changes from baseline in degree of meibomian gland orifice plugging, measured using a validated method or report degree of meibomian gland orifice plugging at the designated time ranges.
⇒ Report changes from baseline in meibomian gland drop-out (%), measured using meibography or report meibomian gland drop-out (%) at the designated time ranges.

Artificial tear use:
⇒ Report changes from baseline in frequency of utilisation as reported by systematic reviews or report frequency of utilisation at the designated time ranges.

Non-specific patient-reported outcomes (eg, health-related quality of life; vision-related quality of life; visual function questionnaires; patient-reported treatment preferences, acceptability and effectiveness)
⇒ Report changes from baseline or measurements at the designated time ranges.

Adverse outcomes:
⇒ Report proportion of individuals who experienced and/or frequency of adverse outcomes (eg, ocular burning or stinging; ocular discomfort; ocular pain; ocular foreign body sensation; intervention-specific complications,eg, spontaneous punctal plug extrusion, bacterial and viral infection) at the designated time ranges and/or at the study endpoints.
⇒ We will also collect and report other adverse outcomes—other specific harms, non-specific harms ('any harm'), surrogate for harm (drop-out due to harm)—that we find whether they were prespecified or not.

and abstracts of the 'CEV@US database of eyes and vision systematic reviews': "dry eye", "dry eye disease", "dry eye syndrome", "ocular surface disease", "meibomian gland dysfunction", "meibomian gland disease", "dysfunctional tear syndrome", "Sjögren's disease", "Sjögren's syndrome", "xerophthalmia", "sicca" and "keratoconjunctivitis sicca." Our search of the CEV@US database is included as online supplemental box 1. We will also screen all systematic reviews in 'CEV@US database of eyes and vision systematic reviews' that are 'tagged' with "condition: dry eye" and "review type: Intervention reviews" for relevant reviews. We will limit our search to reviews published since 1 January 2016.

Data collection and analysis

Selection of reviews

We will remove duplicate records and import the search results into Covidence, a web-based review management software.[32] Two investigators will independently evaluate each systematic review title and abstract for dry eye related interventions and the prespecified definition of a 'systematic review'. Investigators will classify each record as 'yes' (relevant), 'maybe' (possibly relevant) and 'no' (not relevant) for further full-text screening. We will retrieve the full-text reviews for records considered 'relevant' or 'possibly relevant'. Then, two investigators will independently screen the full text reviews for eligibility and classify reviews as 'to be included' or 'to be excluded'. We will report reasons for exclusion of full texts in an 'Excluded Reviews' table. A PRISMA statement flow diagram will be used to summarise study selection.

When an updated systematic review is published, we will include only the most recent publication. When possible, we will obtain prepublication versions of new or updated Cochrane systematic reviews, which can then be assessed for inclusion in the overview. If a conference abstract and journal publication of a systematic review are published, we will include only the full journal publication. We will resolve by consensus any disagreements between investigators regarding decisions to include reviews. If consensus cannot be reached, we will perform adjudication by a third investigator.

Assessment of reliability of reviews

We will assess the reliability of reviews using an adapted form used in previous studies.[33–37] Data items for the form are derived from the Critical Appraisal Skills Programme, the Assessment of Multiple Systematic Reviews and the PRISMA. This is consistent with the proposal that methodological assessment of systematic reviews within overviews should address quality of the methods and quality of the reporting.[38 39]

We will assess the reliability of reviews using an adapted form used in previous studies.[33–37] Data items for the form are derived from the Critical Appraisal Skills Programme, the Assessment of Multiple Systematic Reviews and the PRISMA. We will classify a systematic review as potentially reliable if it meets the following methodological criteria: (1) the review defined eligibility criteria for selection of individual studies, (2) the review conducted a comprehensive literature search for eligible studies, (3) the review assessed the risk of bias of the individual included studies using any method, (4) the review used appropriate methods for meta-analyses (criterion only assessed if meta-analysis was performed) and (5) we observed concordance between the review's findings and conclusions (table 1). If one or more of the criteria in table 1 are not met, we will consider the systematic review

Table 1 Criteria for assessing the reliability of systematic reviews

Criterion	Definition applied to systematic review reports
Defined eligibility criteria	Described inclusion or exclusion criteria, or both, for eligible studies.
Conducted comprehensive literature search	Review authors (1) described an electronic search of 2 or more bibliographic databases; (2) used a search strategy comprising a mixture of controlled vocabulary and keywords; and (3) reported using at least 1 other method of searching, such as searching of conference abstracts, identifying ongoing trials, complemented electronic searching by handsearch methods (eg, checking reference lists) and contacting included study authors or experts.
Assessed risk of bias of included studies	Used any method (eg, scales, checklists or domain-based evaluation) designed to assess methodological rigour of included studies.
Used appropriate methods for meta-analysis	Used quantitative methods that (1) were appropriate for the study design analysed (eg, maintained the randomised nature of trials, used adjusted estimates from observational studies) and (2) correctly computed the weight for included studies.
Observed concordance between review findings and conclusions	Authors' reported conclusions were consistent with findings, provided a balanced consideration of benefits and harms, and did not favour a specific intervention if evidence was lacking.

as unreliable, and we will exclude it from the overview. We will report reasons for unreliability in the 'Unreliable Reviews' table. One investigator will conduct a reliability assessment followed by verification of the reliability assessment by a second author. Any discrepancies or disagreements will be resolved by consensus and if they cannot be resolved then a third author will adjudicate. Single extraction with verification has been shown to be as accurate as double-independent data abstraction.[40]

Managing overlapping systematic reviews

We will include all relevant reliable Cochrane and non-Cochrane systematic reviews in the overview irrespective of degree of overlap using the full inclusion technique.[41] We will calculate the degree of overlap between all pairs of reviews and carefully examine those which have a high degree of overlap (>25%). We will not conduct any quantitative synthesis, and will draw conclusions carefully, taking the overlap into consideration. We will assess and document the extent of the primary study overlap between overlapping reviews by calculating the 'corrected covered area' (CCA).[42] CCA values will be interpreted as follows: 0–10 (slight), 11–15 (moderate), 16–25 (high) and >25 (very high). We will explore degrees of overlap using a citation matrix and represent them using network diagrams. If reviews that answer a similar question report discordant results or conclusions, we will explore the reasons for the discrepancies according to the guide by Jadad *et al*.[43]

Risk of bias of primary studies and strength of evidence

We will extract and report existing risk of bias assessments for the primary studies contained within each included systematic review. We will not repeat or update the risk of bias assessments that have already been conducted by systematic review authors. We will extract existing Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessments as reported in each review. If other measures of certainty of evidence were used, we will report the tool used and record the result for each relevant trial. We will not perform GRADE assessments for reviews because GRADE implementation is highly subjective and context dependent.[44 45] Our method can serve as a prompt for the overview readers to perform their own GRADE assessments when evaluating the evidence which can be tailored to their own purposes (eg, guideline development).

Data synthesis

Descriptive characteristics of included systematic reviews

One investigator will extract information about the descriptive characteristics of each systematic review into a data collection form using a platform such as the Systematic Review Data Repository Plus.[32] An independent investigator will verify the information for accuracy.[46] We will report the following information in a 'Characteristics of included reviews' table: basic information about systematic reviews (eg, title, authors, year of publication, date last assessed as up to date, number of studies and participants included in the systematic review), systematic review's search strategies (eg, number of databases searched, names of databases searched, date of last search update), systematic review's population(s), systematic review's interventions (eg, type of intervention), systematic review's comparators (eg, type of comparator), systematic review's approach to reporting publication bias for the overview critical outcome (eg, presence or absence of publication bias assessment, method of assessment, publication bias result), systematic review's approach to harms (eg, prespecified all harms assessed, assessed both prespecified and non-prespecified harms, did not prespecify any harms) and primary and secondary outcomes (as specified in Methods section of the systematic reviews). We will also report additional information (eg, additional comments, systematic review limitations and methodological quality/risk of bias notes).

Summary of quantitative outcome data

For benefit outcomes, we will extract the results only from syntheses (both qualitative and quantitative) of RCTs and exclude data that comes from non-randomised sources. A focus on RCTs for benefit outcomes is supported by Cochrane and mitigates the potential influence of confounding factors when synthesising multiple types of evidence.[47] For harms, we will extract all reported harms and associated estimates of effect from the reviews, regardless of study design. Guidelines for review methods recommend using non-randomised sources of evidence for a thorough harms assessment because there are often limitations to the assessment and reporting of harms in trial publications.[47–49]

We will present the results of all included systematic reviews as they are reported, except for the terms used for harms which we will classify according to standardised language (Medical Dictionary for Regulatory Activities) to ensure comparability across reviews. We will report all prespecified outcomes irrespective of statistical significance of the findings. We will not reanalyse outcome data for any reviews or subpopulations. We will report narrative summaries and corresponding tables of the data contained within each included systematic review. We will present effect estimates, 95% CIs and measures of heterogeneity if studies pooled data in meta-analyses. We will present the results from each systematic review in turn rather than each outcome measure in turn across systematic reviews to avoid inviting readers to make their own informal indirect comparisons.[24] We will stratify reporting of results by subgroup when deemed appropriate. For example, for individuals under 18 years old or for subpopulations defined by other exposures (eg, postcataract surgery). We will present results to align with guidelines in the Online Chapter 5 (Overviews of Reviews) in the Cochrane Handbook of Systematic Reviews of Interventions and the PRISMA statement.

DISCUSSION

This protocol prospectively outlines our approach to conducting an overview of systematic reviews and meta-analyses of interventions for dry eye. The results of this overview are envisioned to be used by physicians and guideline developers in clinical decision-making processes and development of clinical guidelines. The overview may also aid researchers and funding bodies by benchmarking quality of dry eye review conduct and reporting, and by highlighting gaps in evidence and future research needs.

High-quality systematic reviews are used by guideline developers to inform clinically relevant recommendations, as part of clinical guidelines, to support decision making, reduce clinical practice variation, improve health outcomes and optimise resource allocation. When making recommendations, decision-makers can become overwhelmed by the volume of systematic reviews and this is compounded by the pace of their publication, the variability in their quality and the potential for overlapping reviews, which address similar research questions, to report discordant conclusions.

This overview of reviews will provide a summary of the breadth of systematic review evidence for dry eye interventions without the need for decision makers to assimilate the results of multiple systematic reviews. This overview will search for relevant and contemporaneous systematic reviews, enable assessment of the rigour of the conduct and reporting of the systematic reviews, and provide the opportunity to explore review overlap and the reasons for discrepancies in conclusions across overlapping reviews.

Potential limitations of our overview include that we will not re-extract data from any primary studies, and we will rely on the accuracy of data extraction by the systematic review authors. In addition, we will not reassess risk of bias or evidence certainty conducted by the systematic review authors and, when reporting them, we will rely on the accuracy of the assessments by the review authors. Another potential limitation is that the included reviews may not capture all existing primary studies and we will not search for primary studies. Finally, this overview will not search for or evaluate systematic reviews on the cost-effectiveness for dry eye interventions and this may be a future area of work. Despite these limitations, this overview will serve as a broad synthesis of reliable evidence regarding the wide range of treatments available for dry eye and, to our knowledge, it is the only overview of reviews to address this research question.

Ethics and dissemination

This overview does not require the approval of an Ethics Committee because it will use previously published studies. We will publish our results in a peer-reviewed journal and present at relevant conferences.

Contributors PM: Design, drafting, final submission. ZK: Concept, design, drafting. RQ: Design, drafting. TL: Concept, design, drafting, final submission, guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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ORCID iD
Paul McCann http://orcid.org/0000-0002-6950-4288

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