



Cochrane
Library

Cochrane Database of Systematic Reviews

Topical corticosteroids for dry eye (Protocol)

Liu SH, Gregory D, Hauswirth S, Infantides C, Abraham AG, Saldanha IJ, Li T

Liu S-H, Gregory D, Hauswirth S, Infantides C, Abraham AG, Saldanha IJ, Li T.
Topical corticosteroids for dry eye (Protocol).
Cochrane Database of Systematic Reviews 2021, Issue 9. Art. No.: CD015070.
DOI: [10.1002/14651858.CD015070](https://doi.org/10.1002/14651858.CD015070).

www.cochranelibrary.com

TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
BACKGROUND	2
OBJECTIVES	2
METHODS	3
ACKNOWLEDGEMENTS	5
REFERENCES	6
APPENDICES	8
CONTRIBUTIONS OF AUTHORS	17
DECLARATIONS OF INTEREST	17
SOURCES OF SUPPORT	18

[Intervention Protocol]

Topical corticosteroids for dry eye

Su-Hsun Liu¹, Darren Gregory¹, Scott Hauswirth¹, Cristos Infantides¹, Alison G Abraham², Ian J Saldanha³, Tianjing Li¹

¹Department of Ophthalmology, University of Colorado Denver Anschutz Medical Campus, Aurora, CO, USA. ²Department of Epidemiology, University of Colorado Denver Anschutz Medical Campus, Aurora, CO, USA. ³Center for Evidence Synthesis in Health, Department of Health Services, Policy, and Practice, Brown University School of Public Health, Providence, Rhode Island, USA

Contact address: Su-Hsun Liu, suhsun.liu@cuanschutz.edu.

Editorial group: Cochrane Eyes and Vision Group.

Publication status and date: New, published in Issue 9, 2021.

Citation: Liu S-H, Gregory D, Hauswirth S, Infantides C, Abraham AG, Saldanha IJ, Li T. Topical corticosteroids for dry eye (Protocol). *Cochrane Database of Systematic Reviews* 2021, Issue 9. Art. No.: CD015070. DOI: [10.1002/14651858.CD015070](https://doi.org/10.1002/14651858.CD015070).

Copyright © 2021 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

Objectives

This is a protocol for a Cochrane Review (intervention). The objectives are as follows:

To evaluate the effectiveness and safety of topical corticosteroids compared with placebo, artificial tears, other steroid or non-steroidal therapies, or a combination of therapies for dry eye disease.

BACKGROUND

Description of the condition

Dry eye disease (DED) arises from various etiologic factors leading to tear film instability, ocular surface damage, and neurosensory changes (Bron 2017), causing symptoms such as ocular dryness, burning, itching, pain, and visual impairment (Messmer 2015). Due to a lack of consensus in disease definition before 2017, prevalence estimates of symptomatic DED varied widely between 5% and 50% (Stapleton 2017). In a recent cross-sectional survey on 16 selected towns in Palestine's northern West Bank, Shanti and colleagues reported that 64% of the study population fulfilled the diagnostic criteria for DED (Shanti 2020). Yu and colleagues estimated the average annual healthcare cost for a patient with DED in the USA to be USD 783, and the overall cost of DED to the healthcare system to be USD 3.84 billion (Yu 2011). It is estimated that patients with DED in the UK spent 1.10 million US dollars (2003/2004 prices) seeking ophthalmologic care, with nearly 50% of the cost attributable to prescription drugs (Nichols 2016). Although older age and female sex are consistent risk factors for DED, the pathophysiological mechanisms underlying these correlations remain unclear (Nelson 2017). Besides environmental predispositions (low humidity, high temperature, windy conditions) (Bron 2017), other well-characterized risk factors include prolonged screen viewing, wearing contact lenses, androgen deficiency, medication use, and surgical and cosmetic procedures (Gomes 2017; Stapleton 2017).

To guide clinical management, DED has been categorized historically into aqueous-deficient (due to tear insufficiency) and evaporative (due to increased tear evaporation) subtypes (Messmer 2015). Sjögren syndrome is a major underlying contributor to aqueous-deficient dry eye. Meibomian gland diseases, including meibomian gland dysfunction (MGD) and ocular surface-related causes, can lead to evaporative dry eye (Bron 2017).

Differentiating between aqueous-deficient dry eye and evaporative dry eye is crucial for guiding treatment plans (Bron 2017; Jones 2017). For aqueous-deficient dry eye, treatment options comprise tear supplements, tear stimulants, and, in more severe cases, punctal plugs to preserve tears. Recent systematic reviews have demonstrated the safety and efficacy of artificial tears (Pucker 2016), but not of punctal plugs, Ervin 2017, or autologous serum eye drops (Pan 2017). For evaporative dry eye, cause-specific therapies are available for various meibomian gland diseases, such as lid hygiene and topical antibiotics for anterior blepharitis (Jones 2017); warm compresses for meibomian gland dysfunction (Jones 2017); anti-inflammatory agents, such as topical corticosteroids (steroids) (Jones 2017), cyclosporin A (De Paiva 2019), and rebamipide for ocular surface inflammation (Holland 2019; Kojima 2020).

Description of the intervention

Given their well-established anti-inflammatory effects, topical steroid preparations have been widely accepted as a short-term treatment option for DED. In several trials, one-month use of topical steroid drops has been shown to improve symptoms and clinical signs (Avunduk 2003; Lee 2006; Pflugfelder 2004). The rapid onset of therapeutic effects of topical steroids could make them a useful pre-treatment (or induction) choice before initiating long-term cyclosporin (non-steroidal) treatment (Byun 2012; Sheppard 2014).

How the intervention might work

Accumulating evidence has demonstrated the presence of pro-inflammatory cytokines and T helper cells in the ocular surface regardless of DED etiologies, suggesting that ocular inflammation is a key factor in DED patho-physiology (Bron 2017). Topical steroids have been shown to exert anti-inflammatory actions on multiple targets associated with DED symptoms and signs, including decreasing expression of cytokines, maintaining the integrity of corneal epithelium (De Paiva 2006a; De Paiva 2006b), and restoring tear production in animal models (Lekhanont 2007). In human patients, topical steroids have been shown to reduce pro-inflammatory cytokines in tears (Lekhanont 2007).

Why it is important to do this review

Based on 2013 Medicare data, medications for DED ranked the second highest total costs generated by eye care (Newman-Casey 2018). In England, DED was reportedly a major contributor to prescription costs by general practitioners in the National Health Service (Stephenson 2016). Within the ophthalmic medication group of ocular inflammation medications, prednisolone acetate was the most commonly prescribed ocular anti-inflammatory drug by volume and cost (Newman-Casey 2018). Despite widespread use of topical steroids clinically, significant debates about their role in DED remain. Because of potential risks of ocular hypertension, cataracts, and infections associated with long-term use of topical steroids, published trials comparing the efficacy and safety of topical steroids (versus placebo) in individuals with DED have mostly been of short duration (three to eight weeks) (Jones 2017). Heterogeneity in outcome measures, patient populations, and follow-up durations, albeit short, suggests that the evidence supporting the routine use of topical steroids for DED may not be robust. In large surveys that we conducted, clinicians treating patients with dry eye prioritized the effectiveness of topical anti-inflammatory treatments (such as corticosteroids) as the most important unanswered question (Saldanha 2017), and patients prioritized it as the third-most important question (Saldanha 2018).

A systematic review that critically appraises the currently available data on the effects of topical steroids will provide clinicians, patients, and policymakers with robust and updated research evidence for treating DED. Along with previously published Cochrane Reviews on other local treatments for DED (De Paiva 2019; Downie 2017; Ervin 2017; Pan 2017; Pucker 2016), the current review will inform physicians of the risk-benefit trade-offs for prescribing topical steroids, even for short-term use. The findings of the current review may also highlight evidence gaps and suggest potential directions for future research to address patient-important clinical outcomes.

OBJECTIVES

To evaluate the effectiveness and safety of topical corticosteroids compared with placebo, artificial tears, other steroid or non-steroidal therapies, or a combination of therapies for dry eye disease.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomized controlled trials (RCTs) only. We will exclude within-person studies, where eyes were randomly allocated to the intervention and comparator, given the concern that the effect of topical steroids in one eye may carry over to the other. In addition, we are mostly interested in outcomes at the individual rather than the eye level.

Types of participants

We will include RCTs that enrolled participants with clinically diagnosed DED regardless of etiology or participants who reported dry eye symptoms regardless of severity. However, we will exclude trials of patients with DED secondary to medications or medical procedures, because patients with iatrogenic DED share a distinct profile of risk factors from those with primary DED and may require non-steroid treatments targeting their underlying conditions.

Types of interventions

We will include trials comparing topical steroids with placebo, artificial tears, other steroid or non-steroidal therapy, or a combination of therapies. In particular, we will include trials that examined the following topical steroid preparations.

- Betamethasone
- Clobetasone butyrate
- Dexamethasone
- Difluprednate
- Fluorometholone
- Loteprednol etabonate
- Prednisolone

These topical agents are commonly prescribed to be used twice to four times a day for a duration of two to four weeks; the exact treatment duration may vary depending on the comparator. We will not require a minimum treatment frequency or duration.

Types of outcome measures

Critical outcomes

- Improvement in patient-reported symptoms, quantified by patient questionnaires, such as the Ocular Surface Disease Index or other validated questionnaires ([OSDI](#)).
- Improvement in patient-reported general or vision-related quality of life, measured by patient questionnaires such as the Dry Eye-Related Quality of Life Score ([DEQS](#)).
- Change in visual function, quantified as differences in reading speed using tests such as the short-duration out-loud reading test ([Legge 1989](#)), the 30-minute sustained silent reading test, and the International Reading Speed Texts ([IReST](#)).
- Change in tear film stability (tear film break-up time).

Key time points for these outcomes will be short term (1 to 3 months), intermediate term (3 to < 6 months), or long term (\geq 6 months). For eligible studies that report outcomes at multiple time points within each time window, we will extract outcome data reported at the longest follow-up time point.

Important outcomes

- Change in ocular surface staining (Rose Bengal score/Van Bijsterveld score, fluorescein dye, or lissamine green dye).
- Proportion of participants who showed a decrease in tear osmolarity from baseline, or mean change in tear osmolarity (mOsmol/L).
- Change in aqueous tear production (Schirmer test score or Jones basal secretion test).

We will use the same time points as above for the critical outcomes (1 to 3 months, 3 to < 6 months, and \geq 6 months).

Adverse events

We will collect the proportion of participants with:

- any ocular complication;
- elevated intraocular pressure (\geq 21 mmHg);
- new cataract formation;
- delayed or impaired wound healing.

We will extract data on adverse events reported at the longest time point provided in each included RCT.

Search methods for identification of studies

Electronic searches

We will search the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision Trials Register) (latest issue), Ovid MEDLINE, Ovid MEDLINE E-pub Ahead of Print, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily (January 1946 to present), Embase (January 1947 to present), PubMed (1946 to present), Latin American and Caribbean Health Sciences Literature Database (LILACS) (1982 to present), ClinicalTrials.gov ([www.clinicaltrials.gov](#)), and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) ([www.who.int/ictrp/search/en](#)). We will not use any date or language restrictions in the electronic search for trials.

See: Appendices for details of search strategies for CENTRAL ([Appendix 1](#)), MEDLINE ([Appendix 2](#)), Embase ([Appendix 3](#)), PubMed ([Appendix 4](#)), LILACS ([Appendix 5](#)), ClinicalTrials.gov ([Appendix 6](#)), and the WHO ICTRP ([Appendix 7](#)).

Searching other resources

We will manually search the reference lists of included studies, review articles, and guidelines for additional eligible trials. We will not handsearch conference proceedings or journals as these are included in CENTRAL.

Data collection and analysis

Selection of studies

The Information Specialist will provide separate search results from the electronic databases and the trial registries. The web-based review management software Covidence will automatically identify and remove duplicate references among the imported citations ([Covidence](#)). Two review authors will independently screen the titles and abstracts resulting from the searches using Covidence. Based on the eligibility criteria, the review authors will classify each citation as 'relevant (yes)', 'maybe relevant,' or

'not relevant (no)' for subsequent full-text review. We will then retrieve the full-text articles for the records classified as 'relevant' or 'maybe relevant.' Two review authors will independently assess the full-text copies for eligibility as described in [Criteria for considering studies for this review](#). Any disagreements will be resolved by discussion.

We will correspond with the investigators of potentially eligible studies to request additional information to determine eligibility criteria as needed. If the study authors do not respond within two weeks, we will use the information available from publications and trial registries to determine eligibility. We will list all excluded studies with the reasons for their exclusion in a 'Characteristics of excluded studies' table. Regarding eligible studies identified on trials registers, we will include any such studies in the review irrespective of whether we can identify or access published or unpublished data. In particular, we will classify eligible trials as 'awaiting classification' if the trials are completed but no study results are available, or 'ongoing' if the trials are not completed. Any discrepancies will be discussed by the author team until consensus is reached.

Data extraction and management

Two review authors will independently extract data using an online structured form developed by Cochrane Eyes and Vision ([Covidience](#)). Any discrepancies will be resolved by discussion. We will contact trial investigators or sponsors for missing data. If the trial investigators or sponsors do not respond within two weeks, we will extract relevant data available to us from trials results registers or clinical study reports and other regulatory documents. We will import adjudicated data into Review Manager Web ([RevMan Web 2020](#)).

We will extract the following information from each included study.

- Study-level information: trial setting, countries where participants were recruited, sample size, study duration, and others.
- Participant characteristics: age, sex, comorbidities.
- Outcome data and adverse events: mean, standard deviation or the associated 95% confidence intervals (95% CI) and number of participants for which the outcome was measured for continuous variables; number of events and number of participants for which outcome data were collected for dichotomous variables.

For multi-arm studies, we will use data relevant to our intervention and comparator groups. If two groups contain relevant data, we will combine the groups using the calculator within Review Manager Web.

Assessment of risk of bias in included studies

Two review authors will independently assess the risk of reporting bias using Cochrane's RoB 2 tool for two critical outcomes of each included study ([Higgins 2021](#)): one being symptom-based outcome, and the other visual function or disease severity, depending on the numbers of studies reporting these comparison results. Any disagreements will be resolved by discussion.

We will specifically consider and report on the following domains.

- Bias arising from the randomization process

- Bias introduced by deviations from intended interventions
- Bias due to missing outcome data
- Bias in outcome measurement
- Bias in selective reporting of outcome data

We will grade each domain as low risk of bias, high risk of bias, or with some concerns as guided by signalling questions in each domain. For each outcome, we will use the same response options as for individual domains to provide an overall assessment on a given study. We will assess each trial as at:

- 'low risk of bias': all domains are judged to be at low risk;
- 'some concerns': one or more domains are judged to be with some concerns, and none are at high risk;
- 'high risk of bias': one or more domains are considered to be at high risk, or if multiple domains are judged to be with some concerns such that we have low confidence in the validity of the reported findings ([Higgins 2021](#)).

Measures of treatment effect

We will calculate mean differences (MD) with 95% CI for continuous outcomes, and risk ratios (RR) with 95% CI for dichotomous outcomes. Where possible, we will check for the skewness of continuous data ([Altman 1996](#)). We will use the standardized mean difference (SMD) for continuous measures obtained by different measurement tools, as is frequently encountered in the reporting of symptoms, quality of life, and functional outcomes.

Unit of analysis issues

Trials may randomize one or both eyes to the intervention or comparator. If individuals were randomly allocated to treatment, but only one eye per person was included in the trial, then there will not be a 'unit of analysis' issue. In such cases, we will document how the eye was selected. If participants were randomly allocated to treatment, but both eyes were included and reported, we will analyze as 'clustered data' (i.e. adjusted for within-person correlation). We will exclude studies that have allocated different eyes to different treatments, as there may be a confounding cross-over effect due to systemic absorption.

Dealing with missing data

We will use imputed data if computed by the trial investigators using an appropriate method, but will not impute missing data ourselves. We will attempt to contact the trial investigators and request clarification or missing information when the trial publication does not include outcome data for all participants that were randomized. If we do not hear back from the trial investigators within two weeks, we will conduct a complete-case analysis, assuming the data were missing completely at random. We will assess whether this assumption is reasonable by collecting data from each included trial on the number of participants excluded or lost to follow-up and the reasons for loss to follow-up by treatment group, if reported.

Assessment of heterogeneity

We will examine the overall characteristics of the studies, in particular the types of participants, types of interventions, and study design, to assess the extent to which the studies may be sufficiently similar to permit a meaningful meta-analysis of study results. We will examine forest plots of study results to visualize

potential consistency in the results of the studies, in particular considering the size and direction of intervention effects. We will calculate the I^2 statistic, which quantifies the percentages the total variability in effect estimates that is due to heterogeneity rather than sampling error (chance) (Higgins 2002). As suggested in Chapter 10 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2021), we will consider the following thresholds for interpreting I^2 values:

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity;
- 50% to 90%: may represent substantial heterogeneity;
- 75% to 100%: considerable heterogeneity.

Assessment of reporting biases

We will assess selective outcome reporting for each included trial by comparing the study outcomes prespecified in the protocol or clinical trial registry (if available) with those reported in the publication. When trial protocols or trial registry records are unavailable or inaccessible, we will compare the outcomes specified in the methods section with those presented in the results section. We will evaluate risk of bias due to non-reporting (missing evidence) for critical outcomes. We will apply the framework for assessing the risk of bias due to missing results to determine the potential risk associated with each relevant outcome, separately. We will prepare a qualitative summary table for documenting outcome syntheses assessed for risk of bias, with the possible judgement for each outcome 'low risk of bias,' 'high risk of bias,' or 'some concerns,' depending upon how likely the synthesized result is judged to be biased due to missing evidence (Page 2021).

Data synthesis

In addition to qualitative synthesis of the included trials, we will combine data using a random-effects model in Review Manager Web if there are two or more trials reporting on the same outcome. If we find evidence suggesting considerable clinical, methodological, or statistical heterogeneity, we will not combine the data in a meta-analysis but instead describe them qualitatively.

Subgroup analysis and investigation of heterogeneity

If there are sufficient trials (> 10), we will conduct subgroup analysis on critical outcomes by men versus women, and by causes of dry eye (Sjögren syndrome, non-Sjögren syndrome, meibomian gland dysfunction).

Sensitivity analysis

We will perform sensitivity analyses for each critical outcome by excluding trials at high risk of bias for that particular outcome and by excluding industry-funded studies.

Summary of findings and assessment of the certainty of the evidence

We will prepare a summary of findings table presenting relative and absolute risks (Schünemann 2019). Two review authors will independently grade the overall certainty of the evidence for each of the following outcomes using the GRADE approach (GRADEpro GDT).

- Improvement in patient-reported symptom scores
- Improvement in patient-reported general or vision-related quality of life scores
- Improvement in tear film stability (tear film break-up time)
- Improvement in ocular surface staining
- Improvement in tear osmolarity
- Ocular adverse event: incident elevated intraocular pressure (IOP) ≥ 21 mmHg
- Ocular adverse event: new cataract formation

We will grade the certainty of the evidence as 'high,' 'moderate,' 'low,' or 'very low' according to (1) risk of bias among included trials; (2) indirectness of evidence; (3) unexplained heterogeneity or inconsistency of results; (4) low precision of results; and (5) risk of publication bias (Schünemann 2013). In the case of a discrepancy between the two review authors, a third review author will adjudicate.

ACKNOWLEDGEMENTS

We thank Lori Rosman, Information Specialist for CEV@US, who created the electronic search strategies.

We also thank Renee Wilson, Assistant Managing Editor for CEV@US, and Anupa Shah, Managing Editor for Cochrane Eyes and Vision, for their support and guidance in the preparation of this review.

We would like to thank two anonymous reviewers for providing insightful comments for the protocol.

This protocol was managed by CEV@US and was signed off for publication by Gianni Virgili.

REFERRENCES

Additional references

Altman 1996

Altman DG, Bland JM. Detecting skewness from summary information. *BMJ* 1996;313(7066):1200.

Avunduk 2003

Avunduk AM, Avunduk MC, Varnell ED, Kaufman HE. The comparison of efficacies of topical corticosteroids and nonsteroidal anti-inflammatory drops on dry eye patients: a clinical and immunocytochemical study. *American Journal Ophthalmology* 2003;136(4):593-602. [DOI: [10.1016/s0002-9394\(03\)00326-x](https://doi.org/10.1016/s0002-9394(03)00326-x)]

Bron 2017

Bron AJ, de Paiva CS, Chauhan SK, Bonini S, Gabison EE, Jain S, et al. TFOS DEWS II pathophysiology report. *Ocular Surface* 2017;15(3):438-510.

Byun 2012

Byun YJ, Kim TI, Kwon SM, Seo KY, Kim SW, Kim EK, et al. Efficacy of combined 0.05% cyclosporine and 1% methylprednisolone treatment for chronic dry eye. *Cornea* 2012;31(5):509e13. [DOI: [10.1097/ICO.0b013e31818c69ef](https://doi.org/10.1097/ICO.0b013e31818c69ef)]

Covidence [Computer program]

Veritas Health Innovation Covidence. Melbourne, Australia: Veritas Health Innovation, accessed 17 August 2021. Available at covidence.org.

Deeks 2021

Deeks JJ, Higgins JPT, Altman DG. Chapter 10: Analysing data and undertaking meta-analyses. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.2 (updated February 2021). Cochrane, 2021. Available from training.cochrane.org/handbook.

De Paiva 2006a

De Paiva CS, Corrales RM, Villarreal AL, Farley WJ, Li DQ, Stern ME, et al. Corticosteroid and doxycycline suppress MMP-9 and inflammatory cytokine expression, MAPK activation in the corneal epithelium in experimental dry eye. *Experimental Eye Research* 2006;83(3):526-35. [DOI: [10.1016/j.exer.2006.02.004](https://doi.org/10.1016/j.exer.2006.02.004)]

De Paiva 2006b

De Paiva SC, Corrales RM, Villarreal AL, Farley W, Li DQ, Stern ME, et al. Apical corneal barrier disruption in experimental murine dry eye is abrogated by methylprednisolone and doxycycline. *Investigative Ophthalmology and Vision Science* 2006;47(7):2847-56. [DOI: [10.1167/iovs.05-1281](https://doi.org/10.1167/iovs.05-1281)]

De Paiva 2019

De Paiva CS, Pflugfelder SC, Ng SM, Akpek EK. Topical cyclosporine A therapy for dry eye syndrome. *Cochrane Database of Systematic Reviews* 2019, Issue 9. Art. No: CD010051. [DOI: [10.1002/14651858.CD010051.pub2](https://doi.org/10.1002/14651858.CD010051.pub2)]

DEQS

Sakane Y, Yamaguchi M, Yokoi N, Uchino M, Dogru M, Oishi T, et al. Development and validation of the Dry Eye-Related Quality-of-Life Score questionnaire. *JAMA Ophthalmology* 2013;131(10):1331-8. [DOI: [10.1001/jamaophthalmol.2013.4503](https://doi.org/10.1001/jamaophthalmol.2013.4503)]

Downie 2017

Downie LE, Ng SM, Lindsley KB, Akpek EK. Omega-3 and omega-6 polyunsaturated fatty acids for dry eye disease. *Cochrane Database of Systematic Reviews* 2019, Issue 12. Art. No: CD011016. [DOI: [10.1002/14651858.CD011016.pub2](https://doi.org/10.1002/14651858.CD011016.pub2)]

Ervin 2017

Ervin AM, Law A, Pucker AD. Punctal occlusion for dry eye syndrome. *Cochrane Database of Systematic Reviews* 2017, Issue 6. Art. No: CD006775. [DOI: [10.1002/14651858.CD006775.pub3](https://doi.org/10.1002/14651858.CD006775.pub3)]

Gomes 2017

Gomes JAP, Azar DT, Baudouin C, Efron N, Hirayama M, Horwath-Winter J, et al. TFOS DEWS II iatrogenic report. *Ocular Surface* 2017;15(3):511-38.

GRADEpro GDT [Computer program]

McMaster University (developed by Evidence Prime, Inc.) GRADEpro Guideline Development Tool. Hamilton (ON): McMaster University (developed by Evidence Prime, Inc.), accessed 17 August 2021. Available from gradepro.org.

Higgins 2002

Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* 2002;21(11):1539-58.

Higgins 2021

Higgins JPT, Savović J, Page MJ, Elbers RG, Sterne JAC. Chapter 8: Assessing risk of bias in a randomized trial. In: Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, Welch V, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.2 (updated February 2021). Cochrane, 2021. Available from training.cochrane.org/handbook.

Holland 2019

Holland EJ, Darvish M, Nichols KK, Jones L, Karpecki PM. Efficacy of topical ophthalmic drugs in the treatment of dry eye disease: a systematic literature review. *Ocular Surface* 2019;17(3):412-23. [DOI: [10.1016/j.jtos.2019.02.012](https://doi.org/10.1016/j.jtos.2019.02.012)]

IReST

Trauzettel-Klosinski S, Dietz K, IReST Study Group. Standardized assessment of reading performance: the New International Reading Speed Texts IReST. *International Ophthalmology and Vision Science* 2012;53:5452-61. [DOI: [10.1167/iovs.11-2824](https://doi.org/10.1167/iovs.11-2824)]

Jones 2017

Jones L, Downie LE, Korb D, Benitez-Del-Castillo JM, Dana R, Deng SX, et al. TFOS DEWS II Management and Therapy Report. *Ocular Surface* 2017;15(3):575-628.

Kojima 2020

Kojima T, Dogru M, Kawashima M, Nakamura S, Tsubota K. Advances in the diagnosis and treatment of dry eye. *Progress in Retinal and Eye Research* 2020 Jan 29 [Epub ahead of print]. [DOI: [10.1016/j.preteyeres.2020.100842](https://doi.org/10.1016/j.preteyeres.2020.100842)]

Lee 2006

Lee HK, Ryu IH, Seo KY, Hong SW, Kim HC, Kim EK. Topical 0.1% prednisolone lowers nerve growth factor expression in keratoconjunctivitis sicca patients. *Ophthalmology* 2006;113:198e205. [DOI: [10.1016/j.ophtha.2005.09.033](https://doi.org/10.1016/j.ophtha.2005.09.033)]

Legge 1989

Legge GE, Ross JA, Luebker A, Lamay J. Psychophysics of reading: VIII. The Minnesota low-vision reading test. *Optometry and Vision Science* 1989;66:843-53.

Lekhanont 2007

Lekhanont K, Leyngold IM, Suwan-Apichon O, Rangsin R, Chuck RS. Comparison of topical dry eye medications for the treatment of keratoconjunctivitis sicca in a botulinum toxin B-induced mouse model. *Cornea* 2007;26(1):84-9. [DOI: [10.1097/ICO.0000240079.24583.a1](https://doi.org/10.1097/ICO.0000240079.24583.a1)]

Messmer 2015

Messmer EM. The pathophysiology, diagnosis, and treatment of dry eye disease. *Deutsches Ärzteblatt International* 2015;112(5):71-81.

Nelson 2017

Nelson JD, Craig JP, Akpek EK, Azar DT, Belmonte C, Bron AJ, et al. TFOS DEWS II Introduction. *Ocular Surface* 2017;15(3):269-75. [DOI: [10.1016/j.jtos.2017.05.005](https://doi.org/10.1016/j.jtos.2017.05.005)]

Newman-Casey 2018

Newman-Casey PA, Woodward MA, Niziol LM, Lee PP, De Lott LB. Brand medications and Medicare Part D: how eye care providers' prescribing patterns influence costs. *Ophthalmology* 2018;125(3):332-9.

Nichols 2016

Nichols KK, Bacharach J, Holland E, Kislan T, Shettle L, Lunascek O, et al. Impact of dry eye disease on work productivity, and patients' satisfaction with over-the-counter dry eye treatments. *Investigative Ophthalmology and Vision Science* 2016;57(7):2975-82. [DOI: [10.1167/iovs.16-19419](https://doi.org/10.1167/iovs.16-19419)]

OSDI

Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. *Archives of Ophthalmology* 2000;118(5):615-21. [DOI: [10.1001/archophth.118.5.615](https://doi.org/10.1001/archophth.118.5.615)]

Page 2021

Page MJ, Higgins JPT, Sterne JAC. Chapter 13: Assessing risk of bias due to missing results in a synthesis. In: Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, Welch V, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.2 (updated February 2021). Cochrane, 2021. Available from training.cochrane.org/handbook.

Topical corticosteroids for dry eye (Protocol)

Copyright © 2021 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Pan 2017

Pan Q, Angelina A, Marrone M, Stark WJ, Akpek EK. Autologous serum eye drops for dry eye. *Cochrane Database of Systematic Reviews* 2017, Issue 2. Art. No: CD009327. [DOI: [10.1002/14651858.CD009327.pub3](https://doi.org/10.1002/14651858.CD009327.pub3)]

Pflugfelder 2004

Pflugfelder SC, Maskin SL, Anderson B, Chodosh J, Holland EJ, de Paiva CS, et al. A randomized, double-masked, placebo-controlled, multicenter comparison of loteprednol etabonate ophthalmic suspension, 0.5%, and placebo for treatment of keratoconjunctivitis sicca in patients with delayed tear clearance. *American Journal Ophthalmology* 2004;138(3):444-57. [DOI: [10.1016/j.ajo.2004.04.052](https://doi.org/10.1016/j.ajo.2004.04.052)]

Pucker 2016

Pucker AD, Ng SM, Nichols JJ. Over the counter (OTC) artificial tear drops for dry eye syndrome. *Cochrane Database of Systematic Reviews* 2016, Issue 2. Art. No: CD009729. [DOI: [10.1002/14651858.CD009729.pub2](https://doi.org/10.1002/14651858.CD009729.pub2)]

RevMan Web 2020 [Computer program]

The Cochrane Collaboration Review Manager Web (RevMan Web). Version 1.22.0. The Cochrane Collaboration, 2020. Available at revman.cochrane.org.

Saldanha 2017

Saldanha IJ, Dickersin K, Huffless ST, Akpek EK. Gaps in current knowledge and priorities for future research in dry eye. *Cornea* 2017;36(12):1584-91. [DOI: [10.1097/ICO.0000000000001350](https://doi.org/10.1097/ICO.0000000000001350)]

Saldanha 2018

Saldanha IJ, Petris R, Han G, Dickersin K, Akpek EK. Research questions and outcomes prioritized by patients with dry eye. *JAMA Ophthalmology* 2018;136(10):1170-9. [DOI: [10.1001/jamaophthalmol.2018.3352](https://doi.org/10.1001/jamaophthalmol.2018.3352)]

Schünemann 2013

Schünemann H, Brozek J, Guyatt G, Oxman A, editor(s). *Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach (updated October 2013)*. GRADE Working Group, 2013. Available from gdt.guidelinedevelopment.org/app/handbook/handbook.html.

Schünemann 2019

Schünemann HJ, Higgins JPT, Vist GE, Glasziou P, Akl EA, Skoetz N, et al. Chapter 14: Completing 'Summary of findings' tables and grading the certainty of the evidence. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch V, editor(s). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.0 (updated July 2019). Cochrane, 2019. Available from training.cochrane.org/handbook/archive/v6.

Shanti 2020

Shanti Y, Shehada R, Bakkar MM, Quaddumi J. Prevalence and associated risk factors of dry eye disease in 16 northern West bank towns in Palestine: a cross-sectional study. *BMC Ophthalmology* 2020;20(26):1-8. [DOI: [10.1186/s12886-019-1290-z](https://doi.org/10.1186/s12886-019-1290-z)]

Sheppard 2014

Sheppard JD, Torkildsen GL, Lonsdale JD, D'Ambrosio FA Jr, McLaurin EB, Eiferman RA, et al, OPUS-1 Study Group. Lifitegrast ophthalmic solution 5.0% for treatment of dry eye disease: results of the OPUS-1 Phase 3 Study. *Clinical Trial* 2014;121(2):475-83. [DOI: [10.1016/j.ophtha.2013.09.015](https://doi.org/10.1016/j.ophtha.2013.09.015)]

Stapleton 2017

Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F, et al. TFOS DEWS II Epidemiology Report. *Ocular Surface* 2017;15(3):334-65.

APPENDICES
Appendix 1. CENTRAL search strategy

```

#1 MeSH descriptor: [Dry Eye Syndromes] explode all trees
#2 (dry near/2 eye*)
#3 (ocular near/2 dry*)
#4 MeSH descriptor: [Tears] explode all trees
#5 tear*
#6 MeSH descriptor: [Xerophthalmia] explode all trees
#7 xerophthalmi*
#8 MeSH descriptor: [Vitamin A Deficiency] explode all trees
#9 ("vitamin A" near/3 deficien*)
#10 ("avitaminosis a" or (retinol near/1 deficien*) or "hypovitaminosis A")
#11 MeSH descriptor: [Keratoconjunctivitis Sicca] explode all trees
#12 (Keratoconjunctiv* or "kerato conjunctivitis")
#13 MeSH descriptor: [Sjogren's Syndrome] explode all trees
#14 ((Sjogren* or Sjoegren*) near/2 (syndrom* or disease*))
#15 (sicca next/1 syndrom*)
#16 MeSH descriptor: [Stevens-Johnson Syndrome] explode all trees
#17 (Steven* and Johnson and (syndrom* or disease*))
#18 MeSH descriptor: [Pemphigoid, Benign Mucous Membrane] explode all trees
#19 (Benign and Muco* and Pemphigoid*)
#20 (Cicatricial near/2 Pemphigoid*)
#21 blepharoconjunctiviti*
#22 MeSH descriptor: [Meibomian Glands] explode all trees
#23 (meibomian or tarsal)
#24 MeSH descriptor: [Lacrimal Apparatus Diseases] explode all trees
#25 (lacrima* or epiphora)
#26 {OR #1-#25}
#27 MeSH descriptor: [Adrenal Cortex Hormones] explode all trees
#28 corticosteroid* OR glucocorticoid* OR mineralocorticoid* OR "adrenal cortex hormone" OR "adrenal cortex hormones" OR "adrenal cortical hormone" OR "adrenal cortical hormones" OR "adrenocortical hormone" OR "adrenocortical hormones" OR adrenocorticosteroid* OR corticoid* OR steroid*
#29 MeSH descriptor: [Betamethasone] explode all trees
#30 Betamethasone* OR adbeon OR becasone OR beprogel OR "beta methason" OR "beta methasone" OR "beta-phos/ac" OR betacortril OR betadexamethasone OR betametasone OR betamethasolone OR betamethason OR betamethasonum OR betamethazone OR betason OR betnasol OR betnelan OR "betnesol v" OR "betnovate a" OR betsolan OR betsolan OR betsopart OR celestan OR celestane OR celeston OR celestone OR celestoderm OR cidoten OR dermobet OR diprolen OR flubenisolone OR methasone OR "nsc 39470" OR nsc39470 OR ophtamesone OR "rg 833" OR rg833 OR rinderon OR "sch 4831" OR sch4831 OR walacort OR "378-44-9"
#31 "clobetasone butyrate" OR "cci 5537" OR cci5537 OR "clobetasone 17 butyrate" OR emovate OR eumovate OR "gr 2 1214" OR "gr 2-1214" OR "gr 21214" OR "gr2-1214" OR kindavate OR "sn 203" OR sn203 OR trimovate OR "25122-57-0"
#32 MeSH descriptor: [Dexamethasone] explode all trees
#33 Dexamethasone* OR adrecort OR adrenocot OR "aeroceb dex" OR "aeroceb-d" OR aflucon OR aflucon OR alfaly OR anaflogistico OR aphtasolon OR arcodexan OR arcodexane OR artrosone OR auxiron OR azium OR bidexol OR "bisu ds" OR calonat OR cebedex OR cetadexon OR colofoam OR corsona OR corsone OR cortastat OR cortidex OR cortidexason OR cortidrona OR cortidrone OR cortisumman OR "dacortina fuerte" OR "dacortine fuerte" OR dalalone OR danasone OR "de-sone la" OR decacortin OR decadeltosona OR decadeltosone OR decaderm OR decadion OR decadran OR decadron OR decadronal OR decadrone OR decaesadril OR decagel OR decaject OR decalix OR decameth OR decamethasone OR decasone OR decaspay OR decasterolone OR decdan OR decilone OR decofluor OR decitancyl OR dekacort OR delladec OR deltafluoren OR deltafluorene OR dergramin OR deronil OR desacort OR desacortone OR desadrene OR

```

desalark OR desameton OR desametone OR desigdron OR "dexa cortisyl" OR "dexa dabrosan" OR "dexa korti" OR "dexa scherosan" OR "dexa scherozon" OR "dexa scherozone" OR "dexa-p" OR "dexacen 4" OR dexachel OR dexamcort OR dexamcortal OR dexamcorten OR dexamcortin OR dexamcortisyl OR dexamabroson OR dexamdecadrol OR dexamadol OR dexamgel OR dexamgen OR dexamhelicacort OR dexamkorti OR dexamalien OR dexamlocal OR dexamme OR dexamecortin OR dexameson OR dexamenesone OR dexametasone OR dexameth OR dexamethason OR dexamethazon OR dexamethazone OR dexamethonium OR dexamonozon OR dexan OR dexe OR dexo OR dexpap OR dextelan OR dextenza OR dextrasone OR dexycu OR dezone OR dibasona OR doxamethasone OR esacortene OR "exs1" OR exadion OR exadiione OR firmalone OR "fluormethyl prednisolone" OR fluormethylprednisolone OR fluormone OR fluorocort OR fluorodelta OR fluoromethylprednisolone OR fortecortin OR gammacorten OR gammacortene OR grosodexon OR grosodexone OR hemady OR hexadecadiol OR hexadecadrol OR hexadiol OR hexadrol OR isnacort OR "isopto dex" OR "isopto maxidex" OR "isopto-dex" OR "isopto-maxidex" OR isoptodex OR isoptomaxidex OR "lokalisom f" OR loverine OR luxazone OR marvidione OR maxidex OR mediamethasone OR megacortin OR mephameson OR mephamesone OR metasolon OR metasolone OR "methazon ion" OR "methazone ion" OR methazonion OR methazonione OR methylfluorprednisolone OR "metisone lafi" OR mexasone OR millicorten OR millicortenol OR "mk 125" OR mk125 OR mymethasone OR neoforderx OR neofordex OR nisomethassona OR novocort OR "nsc 34521" OR nsc34521 OR "oftan-dexa" OR opticorten OR opticortinol OR oradexan OR oradexon OR orgadrone OR ozurdex OR pidexon OR policort OR posurdex OR "predni f tablinen" OR "predni-f" OR "prednisolone f" OR prodexona OR prodexone OR sanamethasone OR santenson OR santeson OR sawasone OR solurex OR spoloven OR sterasone OR thilodexine OR triamcimetil OR vexamet OR visumetazone OR visumethazone OR "50-02-2"

#34 difluprednate* OR "cm 9155" OR cm9155 OR durezol OR epitopic OR myser OR "w 6309" OR w6309 OR "warner 6309" OR ENV905 OR "23674-86-4"

#35 MeSH descriptor: [Fluorometholone] explode all trees

#36 Fluorometholone* OR cortilet OR cortisdin OR delmeson OR delmesone OR efflumidex OR eflone OR flosef OR flauon OR fluforte liquifilm OR flulon OR flumelon OR flumetholone OR flumex OR flumexo OR fluometholone OR fluoph OR "fluor opthal" OR "fluor-op" OR fluorlon OR fluormetholone OR fluoromethalone OR fluoropos OR fml OR fuluson OR isopto flucon OR loticort OR methasite OR oxyline OR "426-13-1"

#37 MeSH descriptor: [Loteprednol Etabonate] explode all trees

#38 Loteprednol* OR alrex OR "cddd 5604" OR cddd5604 OR CEHOAC OR "Chloromethyl 17-ethoxycarbonyloxy-11-hydroxy-3-oxoandrosta-1,4-diene-17-carboxylate" OR "17-ethoxycarbonyloxy-11-hydroxy-3-oxoandrosta-1,4-diene-17-carboxylate, Chloromethyl" OR "Chloromethyl 17 ethoxycarbonyloxy 11 hydroxy 3 oxoandrosta 1,4 diene 17 carboxylate" OR eysuvir OR "hgp 1" OR hgp1 OR invelty OR "kpi 121" OR kpi121 OR "le-mpp" OR lotemax OR loterex OR loterox OR lotesoft OR "p 5604" OR p5604 OR "82034-46-6"

#39 MeSH descriptor: [Prednisolone] explode all trees

#40 Prednisolone* OR adelcort OR antisolon OR antisolone OR aprednislon OR aprednislone OR benisolone OR benisolone OR berisolone OR berisolone OR caberdelta OR capsoid OR "co hydeltra" OR codelcortone OR compresolon OR cortadeltona OR cortadeltone OR cortalone OR cortelinter OR cortisolone OR cotolone OR dacortin OR dacrotin OR decaprednil OR "decortin h" OR decortril OR "dehydro cortex" OR "dehydro hydrocortisone" OR "dehydro hydrocortisone" OR dehydrocortex OR dehydrocortisol OR dehydrocortisole OR dehydrohydrocortison OR dehydrohydrocortisone OR delcortol OR "delta 1 17 hydroxycorticosterone 21 acetate" OR "delta 1 hydrocortisone" OR "delta cortef" OR "delta cortril" OR "delta ef cortelan" OR "delta f" OR "delta hcortol" OR "delta hydrocortisone" OR "delta hydrocortisone" OR "delta ophticor" OR "delta stab" OR "delta-cortef" OR "delta1 dehydrocortisol" OR "delta1 dehydrohydrocortisone" OR "delta1 hydrocortisone" OR deltacortef OR deltacortenolo OR deltacortil OR deltacortoil OR deltacortril OR deltaderm OR deltaglycortril OR deltahycortol OR deltahydrocortison OR deltahydrocortisone OR deltaophticor OR deltasolone OR deltastab OR deltidrosol OR deltisilone OR deltisolone OR deltolasson OR deltolassone OR deltosona OR deltosone OR "depo-predate" OR dermosolon OR dhasolone OR DiAdresonF OR "di adreson f" OR "di adresone f" OR "di-adreson-f" OR "diadreson f" OR "diadresone f" OR dicortol OR domucortone OR encortelone OR encortelone OR encortolon OR equisolon OR "fernisolone-p" OR glistelone OR hefasolon OR "hostacortin h" OR hydeltra OR hydeltrone OR hydrelta OR hydrocortancyl OR hydrocortidelt OR hydrodeltalone OR hydrodeltisone OR hydroretrocortin OR hydroretrocortine OR inflanefran OR insolone OR "keteocort h" OR "key-pred" OR lenisolone OR leocortol OR liquipred OR "lygal kopftinktur n" OR mediasolone OR meprisolone OR meprisolone OR metacortalon OR metacortalone OR metacortandralon OR metacortandralone OR metacortelone OR "meti derm" OR meticortelone OR metiderm OR morlone OR mydraped OR "neo delta" OR nisolon OR nisolone OR "nsc 9120" OR nsc9120 OR opredsonne OR panafcortelone OR panafcortolone OR panafort OR paracortol OR phlogex OR "pre cortisyl" OR preconin OR precortalon OR precortancy OR precortisyl OR "pred-ject-50" OR "predacort 50" OR "predaject-50" OR "predalone 50" OR predartrina OR predartrine OR predate OR "predate-50" OR predeltoline OR predisole OR predisyr OR "predne dome" OR prednecort OR prednedome OR prednelan OR "predni coelin" OR "predni h tablinen" OR "predni-helvacort" OR predniccoelin OR prednicort OR prednicortelone OR "prednifor drops" OR predniment OR predniretard OR prednis OR prednisil OR prednisolon OR prednisolona OR prednivet OR prednorsolon OR prednorsolone OR predonine OR predorgasolona OR predorgasolone OR "pregna 1, 4 diene 11beta, 17alpha, 21 triol 3, 20 dione" OR prelon OR prelonne OR prenilone OR prenin OR prenolone OR preventan OR prezolon OR rubycort OR scherisolona OR scherisolona OR serilone OR solondo OR solone OR solupren OR soluprene OR spiricort OR spolotane OR sterane OR sterolone OR supercortisol OR supercortizol OR taracortelone OR walesolone OR wysolone OR "50-24-8"

#41 {OR #27-#40}

#42 #26 AND #41 in Trials

Appendix 2. MEDLINE (Ovid) search strategy

1 Randomized Controlled Trial.pt.

- 2 Controlled Clinical Trial.pt.
3 (randomized or randomised).ab,ti.
4 placebo.ab,ti.
5 drug therapy.fs.
6 randomly.ab,ti.
7 trial.ab,ti.
8 groups.ab,ti.
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10 exp animals/ not humans.sh.
11 9 not 10
12 exp dry eye syndromes/
13 (dry adj2 eye*).tw.
14 (ocular adj2 dry*).tw.
15 exp tears/
16 tear*.tw.
17 exp xerophthalmia/
18 xerophthalmi*.tw.
19 exp vitamin A deficiency/
20 (vitamin A adj3 deficien*).tw.
21 (avitaminosis a or retinol deficien* or hypovitaminosis A).tw.
22 exp keratoconjunctivitis sicca/
23 (Keratoconjunctiv* or kerato conjunctivitis).tw.
24 exp Keratoconjunctivitis/
25 limit 24 to yr="1966 - 1985"
26 exp Sjogren's syndrome/
27 ((Sjogren* or Sjoegren*) adj2 (syndrom* or disease*)).tw.
28 sicca syndrom*.tw.
29 exp Stevens Johnson syndrome/
30 (Steven* and Johnson and (syndrom* or disease*)).tw.
31 exp Pemphigoid, Benign Mucous Membrane/
32 Benign Muco* Pemphigoid*.tw.
33 (Cicatricial adj2 Pemphigoid*).tw.
34 blepharoconjunctivit\$.tw.
35 exp meibomian glands/
36 (meibomian or tarsal).tw.
37 exp lacrimal apparatus diseases/
38 (lacrima* or epiphora).tw.
39 or/12-23,25-38
40 exp Adrenal Cortex Hormones/
41 (corticosteroid* or glucocorticoid* or mineralocorticoid* or "adrenal cortex hormone" or "adrenal cortex hormones" or "adrenal cortical hormone" or "adrenal cortical hormones" or "adrenocortical hormone" or "adrenocortical hormones" or adrenocorticosteroid* or corticoid* or steroid*).tw.
42 exp Betamethasone/
43 (Betamethasone* or adbeon or becasone or beprogel or "beta methason" or "beta methasone" or "beta-phos/ac" or betacortril or betadexamethasone or betametasone or betamethasolone or betamethason or betamethazone or betason or betnasol or betnelan or "betnesol v" or "betnovate a" or betsolan or betsolon or betsoptar or celestan or celeston or celestona or celestone or celestoderm or cidoten or dermobet or diprolen or flubenisolone or methasone or "nsc 39470" or nsc39470 or ophtamesone or "rg 833" or rg833 or rinderon or "sch 4831" or sch4831 or walacort or "378-44-9").tw,rn.
44 ("clobetasone butyrate" or "cci 5537" or cci5537 or "clobetasone 17 butyrate" or emovate or eumovate or "gr 2 1214" or "gr 2-1214" or "gr 21214" or "gr2-1214" or kindavate or "sn 203" or sn203 or trimovate or "25122-57-0").tw,rn.
45 exp Dexamethasone/
46 (Dexamethasone* or adrecort or adrenocot or "aeroceb dex" or "aeroceb-d" or aflucon or aflucon or alfaly or anaflogistico or aphtasolon or arcodexan or arcodexane or artrosone or auxiron or azium or bidexol or "bisu ds" or calonat or cebedex or cetadexon or colofoam or corsona or corsone or cortastat or cortidex or cortidexason or cortidrona or cortidrone or cortisumman or "dacortina fuerte" or "dacortine fuerte" or dalalone or danasone or "de-sone la" or decacortin or decadeltosona or decadeltosone or decaderm or decadion or decadran or decadron or decadronal or decadronale or decaesadril or decagel or decaject or decalix or decameth or decamethasone or decasone or decaspary or decasterolone or decdan or decilone or decofluor or dectancyl or dekacort or delladec or deltafluoren or deltafluorene or dergramin or deronil or desacort or desacortone or desadrene or desalark or desameton or desametone or desigdrone or "dexa cortisyl" or "dexa dabrosan" or "dexa korti" or "dexa scherosan" or "dexa scherozon" or "dexa scherozone" or "dexa-p" or "dexacen 4" or dexachel or dexacort or dexacortal or dexacorten or dexacortin or dexacortisyl or dexadabroson or dexadecadrol or dexadrol or dexagel or dexagen or dexahelvacort or dexakorti or dexalien or dexalocal or dexame or dexamecortin or dexameson or dexamesone or dexametason or dexametasone or dexameth or dexamethason or dexamethazon or dexamethazone or dexamethonium or dexamonozon

or dexan or dexane or dexano or dexpot or dexaschereson or dexascherozon or dexascherozone or dexasone or dexasone or dexinoral or dexionil or dexamethsone or dexona or dexone or dexpak or dextelan or dextenza or dextrasone or dexycu or dezone or dibasona or doxamethasone or esacortene or "ex s1" or exadion or exadione or firmalone or "fluormethyl prednisolone" or fluormethylprednisolon or fluormethylprednisolone or fluormone or fluorocort or fluorodelta or fluoromethylprednisolone or fortecortin or gammacorten or gammacortene or grosdexon or grosdexone or hemady or hexadecadiol or hexadecadrol or hexadiol or hexadrol or isnacort or "isopto dex" or "isopto maxidex" or "isopto-dex" or "isopto-maxidex" or isoptodex or isoptomaxidex or "lokaison f" or loverine or luxazone or marvidione or maxidex or medihamethasone or megacortin or mephameson or mephamesone or metasalon or metasolone or "methazon ion" or "methazone ion" or methazonion or methazonione or methylfluorprednisolone or "metisone lafi" or mexasone or millicorten or millicortenol or "mk 125" or mk125 or mymethasone or neoforderx or nefordex or nisomethasona or novocort or "nsc 34521" or nsc34521 or "oftan-dexa" or opticorten or opticortinol or oradexan or oradexon or oradexone or orgadrone or ozurdex or pidexon or policort or posurdex or "predni f tablinen" or "predni-f" or "prednisolone f" or prodexona or prodexone or sanamethasone or santenson or santeson or sawasone or solurex or spoloven or sterasone or thilodexine or triamcimetil or vexamet or visumetazone or visumethazone or "50-02-2").tw,rn.

47 (difluprednate* or "cm 9155" or cm9155 or durezol or epitopic or myser or "w 6309" or w6309 or "warner 6309" or ENV905 or "23674-86-4").tw,rn.

48 exp Fluorometholone/

49 (Fluorometholone* or cortilet or cortisdin or delmeson or delmesone or efflumidex or eflone or flosef or fluaton or flucon or fluforte liquifilm or flulon or flumelon or flumetholone or flumex or flumexo or fluometholone or fluoph or "fluoro opthal" or "fluorop" or fluorlon or fluormetholone or fluoromethalone or fluoropos or fml or fuluson or isopto flucon or loticort or methasite or oxyline or "426-13-1").tw,rn.

50 exp Loteprednol Etabonate/

51 (Loteprednol* or alrex or "cddd 5604" or cddd5604 or CEHOAC or "Chloromethyl 17-ethoxycarbonyloxy-11-hydroxy-3-oxoandrosta-1,4-diene-17-carboxylate" or "17-ethoxycarbonyloxy-11-hydroxy-3-oxoandrosta-1,4-diene-17-carboxylate, Chloromethyl" or "Chloromethyl 17 ethoxycarbonyloxy 11 hydroxy 3 oxoandrosta 1,4 diene 17 carboxylate" or eysuvis or "hgp 1" or hgp1 or inveltys or "kpi 121" or kpi121 or "le-mpp" or lotemax or loterex or loterox or lotesoft or "p 5604" or p5604 or "82034-46-6").tw,rn.

52 exp Prednisolone/

53 (Prednisolone* or adelcort or antisolon or antisolone or aprednislon or aprednisone or benisolon or benisolone or berisolone or berisolone or caberdelta or capsoid or "co hydeltra" or codelcortone or compresolon or cortadeltona or cortadelton or cortalone or cortelinter or cortisolone or cotolone or dacortin or dacrotin or decaprednil or "decortin h" or decortril or "dehydro cortex" or "dehydro hydrocortisone" or "dehydro hydrocortisone" or dehydrocortex or dehydrocortisol or dehydrocortisole or dehydrohydrocortison or dehydrohydrocortisone or delcortol or "delta 1 17 hydroxycorticosterone 21 acetate" or "delta 1 hydrocortisone" or "delta cortef" or "delta cortil" or "delta ef cortelan" or "delta f" or "delta hycortol" or "delta hydrocortisone" or "delta hydrocortisone" or "delta ophticor" or "delta stab" or "delta-cortef" or "delta1 dehydrocortisol" or "delta1 dehydrohydrocortisone" or "delta1 hydrocortisone" or deltacortef or deltacortenolo or deltacortil or deltacortoil or deltacortril or deltaderm or deltahydrocortil or deltahycortol or deltahydrocortison or deltahydrocortisone or deltaophticor or deltasolone or deltastab or deltidrosol or deltilone or deltilisolone or deltolasson or deltolassone or deltosona or deltosone or "depo-predate" or dermosolon or dhasolone or DiAdresonF or "di adreson f" or "di adresone f" or "di-adreson-f" or "diadreson f" or "diadresone f" or dicortol or domucortone or encortelon or encortelone or encortolon or equisolon or "fernisolone-p" or glistelone or hefasolon or "hostacortin h" or hydeltra or hydeltrone or hydrelta or hydrocortancyl or hydrocortidelt or hydrodeltalone or hydrodeltisone or hydroretrocortin or hydroretrocortine or inflanefran or insolone or "ketecort h" or "key-pred" or lenisolone or leocortol or liquipred or "lygal koptfinktur n" or mediasolone or meprisolone or meprisolone or metacortalon or metacortalone or metacortandralon or metacortandralone or metacortelone or "meti derm" or meticortelone or metiderm or morlone or mydraped or "neo delta" or nisolon or nisolone or "nsc 9120" or nsc9120 or opredson or panafcortelone or panafcortolone or panafort or paracortol or phlogex or "pre cortisy" or preconin or precortalon or precortancyl or precortisyl or "pred-ject-50" or "predacort 50" or "predaject-50" or "predalone 50" or predartrina or predartrina or predartrine or predartrine or "predate-50" or predeltilone or predisole or predisyr or "predne dome" or prednecort or prednedome or prednelan or "predni coelin" or "predni h tablinen" or "predni-helvacort" or prednicoelin or prednicort or prednicortelone or "prednifor drops" or predniment or predniretard or prednis or prednisil or prednisolone or prednisolona or prednivet or prednorsolon or prednorsolone or prednonine or predorgasolona or predorgasolone or "pregna 1, 4 diene 11beta, 17alpha, 21 triol 3, 20 diene" or prelon or prelon or prenilone or prenilone or prenilone or preventan or prezolon or rubycort or scherisolon or scherisolona or serilone or solondo or solone or solupren or soluprene or spiricort or spolotane or sterane or sterolone or supercortisol or supercortizol or taracortelone or walesolone or wylsolone or "50-24-8").tw,rn.

54 or/40-53

55 39 and 54

56 11 and 55

The search filter for trials at the beginning of the MEDLINE strategy is from the published paper by Glanville et al (Glanville 2006).

Appendix 3. Embase.com search strategy

- #1 'randomized controlled trial'/exp
- #2 'randomization'/exp
- #3 'double blind procedure'/exp
- #4 'single blind procedure'/exp

```

#5 random*:ab,ti
#6 #1 OR #2 OR #3 OR #4 OR #5
#7 'animal'/exp OR 'animal experiment'/exp
#8 'human'/exp
#9 #7 AND #8
#10 #7 NOT #9
#11 #6 NOT #10
#12 'clinical trial'/exp
#13 (clin* NEAR/3 trial*):ab,ti
#14 ((singl* OR doubl* OR trebl* OR tripl*) NEAR/3 (blind* OR mask*)):ab,ti
#15 'placebo'/exp
#16 placebo*:ab,ti
#17 random*:ab,ti
#18 'experimental design'/exp
#19 'crossover procedure'/exp
#20 'control group'/exp
#21 'latin square design'/exp
#22 #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21
#23 #22 NOT #10
#24 #23 NOT #11
#25 'comparative study'/exp
#26 'evaluation'/exp
#27 'prospective study'/:exp
#28 control*:ab,ti OR prospectiv*:ab,ti OR volunteer*:ab,ti
#29 #25 OR #26 OR #27 OR #28
#30 #29 NOT #10
#31 #30 NOT (#11 OR #23)
#32 #11 OR #24 OR #31
#33 'dry eye'/exp
#34 (dry NEAR/2 eye*):ab,ti,kw
#35 (ocular NEAR/2 dry*):ab,ti,kw
#36 'lacrimal fluid'/exp
#37 tear*:ab,ti,kw
#38 'xerophthalmia'/exp
#39 xerophthalmi*:ab,ti,kw
#40 'retinol deficiency'/exp
#41 ('vitamin a' NEAR/3 deficien*):ab,ti,kw
#42 'avitaminosis a':ab,ti,kw OR (retinol NEAR/1 deficien*):ab,ti,kw OR 'hypovitaminosis a':ab,ti,kw
#43 'keratoconjunctivitis sicca'/exp
#44 keratoconjunctiv*:ab,ti,kw OR 'kerato conjunctivitis':ab,ti,kw
#45 'sjoegren syndrome'/exp
#46 ((sjogren* OR sjoegren*) NEAR/2 (syndrom* OR disease*)):ab,ti,kw
#47 (sicca NEXT/1 syndrom*):ab,ti,kw
#48 'stevens johnson syndrome'/exp
#49 steven*:ab,ti,kw AND johnson:ab,ti,kw AND (syndrom*:ab,ti,kw OR disease*:ab,ti,kw)
#50 'mucous membrane pemphigoid'/exp
#51 benign AND muco* AND pemphigoid*:ab,ti,kw
#52 (cicatricial NEAR/2 pemphigoid*):ab,ti,kw
#53 blepharoconjunctiviti*:ab,ti,kw
#54 'meibomian gland'/exp
#55 meibomian:ab,ti,kw OR tarsal:ab,ti,kw
#56 'lacrimal gland disease'/exp
#57 lacrima*:ab,ti,kw OR epiphora:ab,ti,kw
#58 #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50
OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57
#59 'corticosteroid'/exp
#60 corticosteroid*:ab,ti,kw,tn OR glucocorticoid*:ab,ti,kw,tn OR mineralocorticoid*:ab,ti,kw,tn OR 'adrenal cortex hormone':ab,ti,kw,tn
OR 'adrenal cortex hormones':ab,ti,kw,tn OR 'adrenal cortical hormone':ab,ti,kw,tn OR 'adrenal cortical hormones':ab,ti,kw,tn
OR 'adrenocortical hormone':ab,ti,kw,tn OR 'adrenocortical hormones':ab,ti,kw,tn OR adrenocorticosteroid*:ab,ti,kw,tn OR
corticoid*:ab,ti,kw,tn OR steroid*:ab,ti,kw,tn
#61 'betamethasone'/exp

```

#62 betamethasone*:ab,ti,kw,tn,rn OR adbeon:ab,ti,kw,tn,rn OR becasone:ab,ti,kw,tn,rn OR beprogel:ab,ti,kw,tn,rn OR 'beta methason':ab,ti,kw,tn,rn OR 'beta methasone':ab,ti,kw,tn,rn OR 'beta-phos/ac':ab,ti,kw,tn,rn OR betacortril:ab,ti,kw,tn,rn OR betadexamethasone:ab,ti,kw,tn,rn OR betametasone:ab,ti,kw,tn,rn OR betamethasolone:ab,ti,kw,tn,rn OR betamethason:ab,ti,kw,tn,rn OR betamethasonum:ab,ti,kw,tn,rn OR betamethazone:ab,ti,kw,tn,rn OR betason:ab,ti,kw,tn,rn OR betnasol:ab,ti,kw,tn,rn OR betnelan:ab,ti,kw,tn,rn OR 'betnesol v':ab,ti,kw,tn,rn OR 'betnovate a':ab,ti,kw,tn,rn OR betsolan:ab,ti,kw,tn,rn OR betsolon:ab,ti,kw,tn,rn OR betsopart:ab,ti,kw,tn,rn OR celestan:ab,ti,kw,tn,rn OR celestene:ab,ti,kw,tn,rn OR celeston:ab,ti,kw,tn,rn OR celestona:ab,ti,kw,tn,rn OR celestone:ab,ti,kw,tn,rn OR celestoderm:ab,ti,kw,tn,rn OR cidoten:ab,ti,kw,tn,rn OR dermobet:ab,ti,kw,tn,rn OR diprolen:ab,ti,kw,tn,rn OR flubenisolone:ab,ti,kw,tn,rn OR methasone:ab,ti,kw,tn,rn OR 'nsc 39470':ab,ti,kw,tn,rn OR nsc39470:ab,ti,kw,tn,rn OR ophtamesone:ab,ti,kw,tn,rn OR 'rg 833':ab,ti,kw,tn,rn OR rg833:ab,ti,kw,tn,rn OR rinderon:ab,ti,kw,tn,rn OR 'sch 4831':ab,ti,kw,tn,rn OR sch4831:ab,ti,kw,tn,rn OR walacort:ab,ti,kw,tn,rn OR '378-44-9':ab,ti,kw,tn,rn

#63 'clobetasone butyrate'/exp

#64 'clobetasone butyrate':ab,ti,kw,tn,rn OR 'cci 5537':ab,ti,kw,tn,rn OR cci5537:ab,ti,kw,tn,rn OR 'clobetasone 17 butyrate':ab,ti,kw,tn,rn OR emovate:ab,ti,kw,tn,rn OR eumovate:ab,ti,kw,tn,rn OR 'gr 2 1214':ab,ti,kw,tn,rn OR 'gr 2-1214':ab,ti,kw,tn,rn OR 'gr 21214':ab,ti,kw,tn,rn OR 'gr2-1214':ab,ti,kw,tn,rn OR kindavate:ab,ti,kw,tn,rn OR 'sn 203':ab,ti,kw,tn,rn OR sn203:ab,ti,kw,tn,rn OR trimovate:ab,ti,kw,tn,rn OR '25122-57-0':ab,ti,kw,tn,rn

#65 'dexamethasone'/exp

#66 dexamethasone*:ab,ti,kw,tn,rn OR adrecort:ab,ti,kw,tn,rn OR adrenocot:ab,ti,kw,tn,rn OR 'aeroceb dex':ab,ti,kw,tn,rn OR 'aeroceb-d':ab,ti,kw,tn,rn OR aflucoson:ab,ti,kw,tn,rn OR afluosone:ab,ti,kw,tn,rn OR alfalyl:ab,ti,kw,tn,rn OR anaflogistico:ab,ti,kw,tn,rn OR aphtasolon:ab,ti,kw,tn,rn OR arcodexan:ab,ti,kw,tn,rn OR arcodexane:ab,ti,kw,tn,rn OR artrosone:ab,ti,kw,tn,rn OR auxiron:ab,ti,kw,tn,rn OR azium:ab,ti,kw,tn,rn OR bidexol:ab,ti,kw,tn,rn OR 'bisu ds':ab,ti,kw,tn,rn OR calonat:ab,ti,kw,tn,rn OR cebedex:ab,ti,kw,tn,rn OR cetadexon:ab,ti,kw,tn,rn OR colofoam:ab,ti,kw,tn,rn OR corsona:ab,ti,kw,tn,rn OR corsone:ab,ti,kw,tn,rn OR cortastat:ab,ti,kw,tn,rn OR cortidex:ab,ti,kw,tn,rn OR cortidexason:ab,ti,kw,tn,rn OR cortidrona:ab,ti,kw,tn,rn OR cortidrone:ab,ti,kw,tn,rn OR cortisumman:ab,ti,kw,tn,rn OR 'dacortina fuerte':ab,ti,kw,tn,rn OR 'dacortine fuerte':ab,ti,kw,tn,rn OR dalalone:ab,ti,kw,tn,rn OR danasone:ab,ti,kw,tn,rn OR 'de-sone la':ab,ti,kw,tn,rn OR decacortin:ab,ti,kw,tn,rn OR decadeltosona:ab,ti,kw,tn,rn OR decadeltosone:ab,ti,kw,tn,rn OR decaderm:ab,ti,kw,tn,rn OR decadion:ab,ti,kw,tn,rn OR decadran:ab,ti,kw,tn,rn OR decadron:ab,ti,kw,tn,rn OR decadronal:ab,ti,kw,tn,rn OR decadrone:ab,ti,kw,tn,rn OR decaesadril:ab,ti,kw,tn,rn OR decagel:ab,ti,kw,tn,rn OR decaject:ab,ti,kw,tn,rn OR decalix:ab,ti,kw,tn,rn OR decameth:ab,ti,kw,tn,rn OR decamethasone:ab,ti,kw,tn,rn OR decasone:ab,ti,kw,tn,rn OR decaspRAY:ab,ti,kw,tn,rn OR decasterolone:ab,ti,kw,tn,rn OR decdan:ab,ti,kw,tn,rn OR decilone:ab,ti,kw,tn,rn OR decofluor:ab,ti,kw,tn,rn OR dictancyl:ab,ti,kw,tn,rn OR dekacort:ab,ti,kw,tn,rn OR delladec:ab,ti,kw,tn,rn OR deltafluoren:ab,ti,kw,tn,rn OR deltafluorene:ab,ti,kw,tn,rn OR dergramin:ab,ti,kw,tn,rn OR deronil:ab,ti,kw,tn,rn OR desacort:ab,ti,kw,tn,rn OR desacortone:ab,ti,kw,tn,rn OR desadrene:ab,ti,kw,tn,rn OR desalark:ab,ti,kw,tn,rn OR desameton:ab,ti,kw,tn,rn OR desametone:ab,ti,kw,tn,rn OR desigdron:ab,ti,kw,tn,rn OR 'dexa cortisyl':ab,ti,kw,tn,rn OR 'dexa dabrosan':ab,ti,kw,tn,rn OR 'dexa korti':ab,ti,kw,tn,rn OR 'dexa scherosan':ab,ti,kw,tn,rn OR 'dexa scherozon':ab,ti,kw,tn,rn OR 'dexa scherozone':ab,ti,kw,tn,rn OR 'dexa-p':ab,ti,kw,tn,rn OR 'dexacen 4':ab,ti,kw,tn,rn OR dexachel:ab,ti,kw,tn,rn OR dexacort:ab,ti,kw,tn,rn OR dexacortal:ab,ti,kw,tn,rn OR dexacorten:ab,ti,kw,tn,rn OR dexacortin:ab,ti,kw,tn,rn OR dexacortisyl:ab,ti,kw,tn,rn OR dexadabroson:ab,ti,kw,tn,rn OR dexadecadrol:ab,ti,kw,tn,rn OR dexadrol:ab,ti,kw,tn,rn OR dexagel:ab,ti,kw,tn,rn OR dexagen:ab,ti,kw,tn,rn OR dexahelvacort:ab,ti,kw,tn,rn OR dexakorti:ab,ti,kw,tn,rn OR dexalien:ab,ti,kw,tn,rn OR dexalocal:ab,ti,kw,tn,rn OR dexam:ab,ti,kw,tn,rn OR dexamecortin:ab,ti,kw,tn,rn OR dexameson:ab,ti,kw,tn,rn OR dexamesone:ab,ti,kw,tn,rn OR dexametason:ab,ti,kw,tn,rn OR dexametasone:ab,ti,kw,tn,rn OR dexameth:ab,ti,kw,tn,rn OR dexamethason:ab,ti,kw,tn,rn OR dexamethazon:ab,ti,kw,tn,rn OR dexamethazone:ab,ti,kw,tn,rn OR dexamethonium:ab,ti,kw,tn,rn OR dexamonomozon:ab,ti,kw,tn,rn OR dexan:ab,ti,kw,tn,rn OR dexane:ab,ti,kw,tn,rn OR dexano:ab,ti,kw,tn,rn OR dexapot:ab,ti,kw,tn,rn OR dexaschereson:ab,ti,kw,tn,rn OR dexascherozon:ab,ti,kw,tn,rn OR dexascherozone:ab,ti,kw,tn,rn OR dexason:ab,ti,kw,tn,rn OR dexasone:ab,ti,kw,tn,rn OR dexinoral:ab,ti,kw,tn,rn OR dexionil:ab,ti,kw,tn,rn OR dexmethylsone:ab,ti,kw,tn,rn OR dexona:ab,ti,kw,tn,rn OR dexone:ab,ti,kw,tn,rn OR dexpak:ab,ti,kw,tn,rn OR dextelan:ab,ti,kw,tn,rn OR dextenza:ab,ti,kw,tn,rn OR dextralone:ab,ti,kw,tn,rn OR dexycu:ab,ti,kw,tn,rn OR dezone:ab,ti,kw,tn,rn OR dibasona:ab,ti,kw,tn,rn OR doxamethasone:ab,ti,kw,tn,rn OR esacortene:ab,ti,kw,tn,rn OR 'ex s1':ab,ti,kw,tn,rn OR exadion:ab,ti,kw,tn,rn OR exadione:ab,ti,kw,tn,rn OR firmalone:ab,ti,kw,tn,rn OR 'fluormethyl prednisolone':ab,ti,kw,tn,rn OR 'fluormethylprednisolone':ab,ti,kw,tn,rn OR fluorocort:ab,ti,kw,tn,rn OR fluorodelta:ab,ti,kw,tn,rn OR 'fluoromethylprednisolone':ab,ti,kw,tn,rn OR fortecortin:ab,ti,kw,tn,rn OR gammacorten:ab,ti,kw,tn,rn OR gammacortene:ab,ti,kw,tn,rn OR grosodexon:ab,ti,kw,tn,rn OR grosodexone:ab,ti,kw,tn,rn OR hemady:ab,ti,kw,tn,rn OR hexadecadiol:ab,ti,kw,tn,rn OR hexadecadrol:ab,ti,kw,tn,rn OR hexadiol:ab,ti,kw,tn,rn OR hexadrol:ab,ti,kw,tn,rn OR isnacort:ab,ti,kw,tn,rn OR 'isopto dex':ab,ti,kw,tn,rn OR 'isopto maxidex':ab,ti,kw,tn,rn OR 'isopto-dex':ab,ti,kw,tn,rn OR 'isopto-maxidex':ab,ti,kw,tn,rn OR isoptodex:ab,ti,kw,tn,rn OR isoptomaxidex:ab,ti,kw,tn,rn OR 'lokalison f':ab,ti,kw,tn,rn OR loverine:ab,ti,kw,tn,rn OR luxazone:ab,ti,kw,tn,rn OR marvidione:ab,ti,kw,tn,rn OR maxidex:ab,ti,kw,tn,rn OR medihamethasone:ab,ti,kw,tn,rn OR megacortin:ab,ti,kw,tn,rn OR mephameson:ab,ti,kw,tn,rn OR mephamesone:ab,ti,kw,tn,rn OR metasolon:ab,ti,kw,tn,rn OR metasolone:ab,ti,kw,tn,rn OR 'methazon ion':ab,ti,kw,tn,rn OR 'methazone ion':ab,ti,kw,tn,rn OR methazonion:ab,ti,kw,tn,rn OR methazonione:ab,ti,kw,tn,rn OR methylfluorprednisolone:ab,ti,kw,tn,rn OR 'metisone lafi':ab,ti,kw,tn,rn OR mexasone:ab,ti,kw,tn,rn OR millicorten:ab,ti,kw,tn,rn OR millicortenol:ab,ti,kw,tn,rn OR 'mk 125':ab,ti,kw,tn,rn OR mk125:ab,ti,kw,tn,rn OR mymethasone:ab,ti,kw,tn,rn OR neforderx:ab,ti,kw,tn,rn OR nefordex:ab,ti,kw,tn,rn OR nisomethasona:ab,ti,kw,tn,rn OR novocort:ab,ti,kw,tn,rn OR 'nsc 34521':ab,ti,kw,tn,rn OR nsc34521:ab,ti,kw,tn,rn OR 'oftan-dexa':ab,ti,kw,tn,rn OR opticorten:ab,ti,kw,tn,rn OR opticortinol:ab,ti,kw,tn,rn OR oradexan:ab,ti,kw,tn,rn OR oradexon:ab,ti,kw,tn,rn OR oradexone:ab,ti,kw,tn,rn OR orgadrone:ab,ti,kw,tn,rn OR ozurdex:ab,ti,kw,tn,rn OR pidexon:ab,ti,kw,tn,rn OR policort:ab,ti,kw,tn,rn OR posurdex:ab,ti,kw,tn,rn OR 'predni f tablinen':ab,ti,kw,tn,rn OR 'predni-f':ab,ti,kw,tn,rn OR 'prednisolone f':ab,ti,kw,tn,rn OR prodexona:ab,ti,kw,tn,rn OR prodexone:ab,ti,kw,tn,rn OR

sanamethasone:ab,ti,kw,tn,rn OR santenson:ab,ti,kw,tn,rn OR santeson:ab,ti,kw,tn,rn OR sawasone:ab,ti,kw,tn,rn OR solurex:ab,ti,kw,tn,rn OR spoloven:ab,ti,kw,tn,rn OR sterasone:ab,ti,kw,tn,rn OR thilodexine:ab,ti,kw,tn,rn OR triamcimetil:ab,ti,kw,tn,rn OR vexamet:ab,ti,kw,tn,rn OR visumetazone:ab,ti,kw,tn,rn OR visumethazone:ab,ti,kw,tn,rn OR '50-02-2':ab,ti,kw,tn,rn #67 'difluprednate'/exp
 #68 difluprednate*:ab,ti,kw,tn,rn OR 'cm 9155':ab,ti,kw,tn,rn OR cm9155:ab,ti,kw,tn,rn OR durezol:ab,ti,kw,tn,rn OR epitopic:ab,ti,kw,tn,rn OR myser:ab,ti,kw,tn,rn OR 'w 6309':ab,ti,kw,tn,rn OR w6309:ab,ti,kw,tn,rn OR 'warner 6309':ab,ti,kw,tn,rn OR env905:ab,ti,kw,tn,rn OR '23674-86-4':ab,ti,kw,tn,rn #69 'fluorometholone'/exp
 #70 ((fluorometholone*:ab,ti,kw,tn,rn OR cortilet:ab,ti,kw,tn,rn OR cortisdin:ab,ti,kw,tn,rn OR delmeson:ab,ti,kw,tn,rn OR delmesone:ab,ti,kw,tn,rn OR efflumidex:ab,ti,kw,tn,rn OR eflone:ab,ti,kw,tn,rn OR flosef:ab,ti,kw,tn,rn OR fluaton:ab,ti,kw,tn,rn OR flucon:ab,ti,kw,tn,rn OR fluforte:ab,ti,kw,tn,rn) AND liquifilm:ab,ti,kw,tn,rn OR flulon:ab,ti,kw,tn,rn OR flumelon:ab,ti,kw,tn,rn OR flumetholon:ab,ti,kw,tn,rn OR flumetholone:ab,ti,kw,tn,rn OR flumex:ab,ti,kw,tn,rn OR flumexo:ab,ti,kw,tn,rn OR fluometholone:ab,ti,kw,tn,rn OR fluoph:ab,ti,kw,tn,rn OR 'fluoro opthal':ab,ti,kw,tn,rn OR 'fluor-op':ab,ti,kw,tn,rn OR fluorlon:ab,ti,kw,tn,rn OR fluormetholon:ab,ti,kw,tn,rn OR fluoromethalone:ab,ti,kw,tn,rn OR fluoropos:ab,ti,kw,tn,rn OR fml:ab,ti,kw,tn,rn OR fuluson:ab,ti,kw,tn,rn OR isopto:ab,ti,kw,tn,rn) AND flucon:ab,ti,kw,tn,rn OR loticort:ab,ti,kw,tn,rn OR methasite:ab,ti,kw,tn,rn OR oxyline:ab,ti,kw,tn,rn OR '426-13-1':ab,ti,kw,tn,rn #71 'loteprednol etabonate'/exp
 #72 loteprednol*:ab,ti,kw,tn,rn OR alrex:ab,ti,kw,tn,rn OR 'cddd 5604':ab,ti,kw,tn,rn OR cddd5604:ab,ti,kw,tn,rn OR cehoac:ab,ti,kw,tn,rn OR 'chloromethyl 17-ethoxycarbonyloxy-11-hydroxy-3-oxoandrosta-1,4-diene-17-carboxylate':ab,ti,kw,tn,rn OR '17-ethoxycarbonyloxy-11-hydroxy-3-oxoandrosta-1,4-diene-17-carboxylate, chloromethyl':ab,ti,kw,tn,rn OR 'chloromethyl 17 ethoxycarbonyloxy 11 hydroxy 3 oxoandrosta 1,4 diene 17 carboxylate':ab,ti,kw,tn,rn OR eysuvis:ab,ti,kw,tn,rn OR 'hgp 1':ab,ti,kw,tn,rn OR hgp1:ab,ti,kw,tn,rn OR inveltys:ab,ti,kw,tn,rn OR 'kpi 121':ab,ti,kw,tn,rn OR kpi121:ab,ti,kw,tn,rn OR 'le-mpp':ab,ti,kw,tn,rn OR lotemax:ab,ti,kw,tn,rn OR loterex:ab,ti,kw,tn,rn OR loterox:ab,ti,kw,tn,rn OR lotesoft:ab,ti,kw,tn,rn OR 'p 5604':ab,ti,kw,tn,rn OR p5604:ab,ti,kw,tn,rn OR '82034-46-6':ab,ti,kw,tn,rn #73 'prednisolone'/exp
 #74 prednisolone*:ab,ti,kw,tn,rn OR adelcort:ab,ti,kw,tn,rn OR antisolon:ab,ti,kw,tn,rn OR antisolone:ab,ti,kw,tn,rn OR aprednislon:ab,ti,kw,tn,rn OR aprednislone:ab,ti,kw,tn,rn OR benisolon:ab,ti,kw,tn,rn OR benisolone:ab,ti,kw,tn,rn OR berisolon:ab,ti,kw,tn,rn OR berisolone:ab,ti,kw,tn,rn OR caberdeleta:ab,ti,kw,tn,rn OR capsoid:ab,ti,kw,tn,rn OR 'co hydeltra':ab,ti,kw,tn,rn OR codelcortone:ab,ti,kw,tn,rn OR compresolon:ab,ti,kw,tn,rn OR cortadeltona:ab,ti,kw,tn,rn OR cortadeltone:ab,ti,kw,tn,rn OR cortalone:ab,ti,kw,tn,rn OR cortelinter:ab,ti,kw,tn,rn OR cortisolone:ab,ti,kw,tn,rn OR cotolone:ab,ti,kw,tn,rn OR dacortin:ab,ti,kw,tn,rn OR dacrotin:ab,ti,kw,tn,rn OR decaprednil:ab,ti,kw,tn,rn OR 'decortin h':ab,ti,kw,tn,rn OR decortril:ab,ti,kw,tn,rn OR 'dehydro cortex':ab,ti,kw,tn,rn OR 'dehydro hydrocortisone':ab,ti,kw,tn,rn OR dehydrocortex:ab,ti,kw,tn,rn OR dehydrocortisol:ab,ti,kw,tn,rn OR dehydrocortisole:ab,ti,kw,tn,rn OR dehydrohydrocortison:ab,ti,kw,tn,rn OR dehydrohydrocortisone:ab,ti,kw,tn,rn OR delcortol:ab,ti,kw,tn,rn OR 'delta 1 17 hydroxycorticosterone 21 acetate':ab,ti,kw,tn,rn OR 'delta 1 hydrocortisone':ab,ti,kw,tn,rn OR 'delta cortef':ab,ti,kw,tn,rn OR 'delta cortril':ab,ti,kw,tn,rn OR 'delta ef cortelan':ab,ti,kw,tn,rn OR 'delta f':ab,ti,kw,tn,rn OR 'delta hcortol':ab,ti,kw,tn,rn OR 'delta hydrocortisone':ab,ti,kw,tn,rn OR 'delta ophticor':ab,ti,kw,tn,rn OR 'delta stab':ab,ti,kw,tn,rn OR 'delta-cortef':ab,ti,kw,tn,rn OR 'delta1 dehydrocortisol':ab,ti,kw,tn,rn OR 'delta1 dehydrohydrocortisone':ab,ti,kw,tn,rn OR 'delta1 hydrocortisone':ab,ti,kw,tn,rn OR deltacortef:ab,ti,kw,tn,rn OR deltacortenolo:ab,ti,kw,tn,rn OR deltacortil:ab,ti,kw,tn,rn OR deltacortoil:ab,ti,kw,tn,rn OR deltacortril:ab,ti,kw,tn,rn OR deltaderm:ab,ti,kw,tn,rn OR deltaglycortil:ab,ti,kw,tn,rn OR deltahycortol:ab,ti,kw,tn,rn OR deltahydrocortison:ab,ti,kw,tn,rn OR deltahydrocortisone:ab,ti,kw,tn,rn OR deltaophthicor:ab,ti,kw,tn,rn OR deltasolone:ab,ti,kw,tn,rn OR deltastab:ab,ti,kw,tn,rn OR deltidrosol:ab,ti,kw,tn,rn OR deltisilone:ab,ti,kw,tn,rn OR deltisolon:ab,ti,kw,tn,rn OR deltisolone:ab,ti,kw,tn,rn OR deltolasson:ab,ti,kw,tn,rn OR deltolassone:ab,ti,kw,tn,rn OR deltosona:ab,ti,kw,tn,rn OR deltosone:ab,ti,kw,tn,rn OR 'depo-predate':ab,ti,kw,tn,rn OR dermosolon:ab,ti,kw,tn,rn OR dhasolone:ab,ti,kw,tn,rn OR diadresonf:ab,ti,kw,tn,rn OR 'di adreson f':ab,ti,kw,tn,rn OR 'di adresone f':ab,ti,kw,tn,rn OR 'di-adreson-f':ab,ti,kw,tn,rn OR 'diadreson f':ab,ti,kw,tn,rn OR 'diadresone f':ab,ti,kw,tn,rn OR dicortol:ab,ti,kw,tn,rn OR domucortone:ab,ti,kw,tn,rn OR encortelon:ab,ti,kw,tn,rn OR encortelone:ab,ti,kw,tn,rn OR encortolon:ab,ti,kw,tn,rn OR equisolon:ab,ti,kw,tn,rn OR 'fernisolone-p':ab,ti,kw,tn,rn OR glistelone:ab,ti,kw,tn,rn OR hefasolon:ab,ti,kw,tn,rn OR 'hostacortin h':ab,ti,kw,tn,rn OR hydeltra:ab,ti,kw,tn,rn OR hydeltrene:ab,ti,kw,tn,rn OR hydrelta:ab,ti,kw,tn,rn OR hydrocortancyl:ab,ti,kw,tn,rn OR hydrocortidelt:ab,ti,kw,tn,rn OR hydrodeltalone:ab,ti,kw,tn,rn OR hydrodeltisone:ab,ti,kw,tn,rn OR hydroretrocortin:ab,ti,kw,tn,rn OR hydroretrocortine:ab,ti,kw,tn,rn OR inflanefran:ab,ti,kw,tn,rn OR insolone:ab,ti,kw,tn,rn OR 'keteocort h':ab,ti,kw,tn,rn OR 'key-pred':ab,ti,kw,tn,rn OR lenisolone:ab,ti,kw,tn,rn OR leocortol:ab,ti,kw,tn,rn OR liquipred:ab,ti,kw,tn,rn OR 'lygal kopftinktur n':ab,ti,kw,tn,rn OR mediasolone:ab,ti,kw,tn,rn OR meprisolone:ab,ti,kw,tn,rn OR meprisolone:ab,ti,kw,tn,rn OR metacortalon:ab,ti,kw,tn,rn OR metacortalone:ab,ti,kw,tn,rn OR metacortandralon:ab,ti,kw,tn,rn OR metacortandralone:ab,ti,kw,tn,rn OR metacortelone:ab,ti,kw,tn,rn OR 'meti dermat':ab,ti,kw,tn,rn OR meticortelone:ab,ti,kw,tn,rn OR metiderm:ab,ti,kw,tn,rn OR morlone:ab,ti,kw,tn,rn OR mydrapred:ab,ti,kw,tn,rn OR 'neo delta':ab,ti,kw,tn,rn OR nisolone:ab,ti,kw,tn,rn OR nisolone:ab,ti,kw,tn,rn OR 'nsc 9120':ab,ti,kw,tn,rn OR nsc9120:ab,ti,kw,tn,rn OR opredson:ab,ti,kw,tn,rn OR panafcortelone:ab,ti,kw,tn,rn OR panafcortolone:ab,ti,kw,tn,rn OR panafort:ab,ti,kw,tn,rn OR paracortol:ab,ti,kw,tn,rn OR phlogex:ab,ti,kw,tn,rn OR 'pre cortisyl':ab,ti,kw,tn,rn OR preconin:ab,ti,kw,tn,rn OR precortalon:ab,ti,kw,tn,rn OR precortancyl:ab,ti,kw,tn,rn OR precortisyl:ab,ti,kw,tn,rn OR 'pred-ject-50':ab,ti,kw,tn,rn OR 'predacort 50':ab,ti,kw,tn,rn OR 'predaject-50':ab,ti,kw,tn,rn OR 'predalone 50':ab,ti,kw,tn,rn OR predartrina:ab,ti,kw,tn,rn OR predartrine:ab,ti,kw,tn,rn OR predate:ab,ti,kw,tn,rn OR 'predate-50':ab,ti,kw,tn,rn OR predeltilone:ab,ti,kw,tn,rn OR predisole:ab,ti,kw,tn,rn OR predisyr:ab,ti,kw,tn,rn OR 'predne dome':ab,ti,kw,tn,rn OR prednecort:ab,ti,kw,tn,rn OR prednedome:ab,ti,kw,tn,rn OR prednelan:ab,ti,kw,tn,rn OR 'predni coelin':ab,ti,kw,tn,rn OR 'predni h tablinen':ab,ti,kw,tn,rn OR 'predni-helvacort':ab,ti,kw,tn,rn OR prednicoelin:ab,ti,kw,tn,rn

OR prednicort:ab,ti,kw,tn,rn OR prednicortelone:ab,ti,kw,tn,rn OR 'prednifor drops':ab,ti,kw,tn,rn OR predniment:ab,ti,kw,tn,rn
 OR predniretard:ab,ti,kw,tn,rn OR prednis:ab,ti,kw,tn,rn OR prednisil:ab,ti,kw,tn,rn OR prednisolon:ab,ti,kw,tn,rn OR
 prednisolona:ab,ti,kw,tn,rn OR prednivet:ab,ti,kw,tn,rn OR prednorsolon:ab,ti,kw,tn,rn OR prednorsolone:ab,ti,kw,tn,rn OR
 prednonine:ab,ti,kw,tn,rn OR predorgasolona:ab,ti,kw,tn,rn OR predorgasolone:ab,ti,kw,tn,rn OR 'pregna 1, 4 diene 11beta, 17alpha, 21
 triol 3, 20 dione':ab,ti,kw,tn,rn OR prelon:ab,ti,kw,tn,rn OR prelone:ab,ti,kw,tn,rn OR premilone:ab,ti,kw,tn,rn OR prenin:ab,ti,kw,tn,rn
 OR prenolone:ab,ti,kw,tn,rn OR preventan:ab,ti,kw,tn,rn OR prezolon:ab,ti,kw,tn,rn OR rubycort:ab,ti,kw,tn,rn OR scherisolona:ab,ti,kw,tn,rn
 OR scherisolona:ab,ti,kw,tn,rn OR serilone:ab,ti,kw,tn,rn OR solondo:ab,ti,kw,tn,rn OR solone:ab,ti,kw,tn,rn OR solupren:ab,ti,kw,tn,rn
 OR soluprene:ab,ti,kw,tn,rn OR spiricort:ab,ti,kw,tn,rn OR spolotane:ab,ti,kw,tn,rn OR sterane:ab,ti,kw,tn,rn OR sterolone:ab,ti,kw,tn,rn
 OR supercortisol:ab,ti,kw,tn,rn OR supercortizol:ab,ti,kw,tn,rn OR taracortelone:ab,ti,kw,tn,rn OR walesolone:ab,ti,kw,tn,rn OR
 wysolone:ab,ti,kw,tn,rn OR '50-24-8':ab,ti,kw,tn,rn
 #75 #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74
 #76 #58 AND #75
 #77 #32 AND #76

Appendix 4. PubMed search strategy

#1 ((randomized controlled trial[pt]) OR (controlled clinical trial[pt]) OR (randomised[tiab] OR randomized[tiab])) OR (placebo[tiab]) OR
 (drug therapy[sh]) OR (randomly[tiab]) OR (trial[tiab]) OR (groups[tiab])) NOT (animals[mh] NOT humans[mh])
 #2 dry[tw] AND (eye[tw] OR eyes[tw] OR eyelid*[tw]) NOT Medline[sb]
 #3 (ocular[tw] AND dry[tw]) NOT Medline[sb]
 #4 tear*[tw] NOT Medline[sb]
 #5 xerophthalmi*[tw] NOT Medline[sb]
 #6 ("vitamin A"[tw] AND deficien*[tw]) NOT Medline[sb]
 #7 ("avitaminosis a"[tw] OR retinol deficien*[tw] OR "hypovitaminosis A"[tw]) NOT Medline[sb]
 #8 (Keratoconjunctiv*[tw] OR "kerato conjunctivitis"[tw]) NOT Medline[sb]
 #9 ((Sjogren*[tw] OR Sjoegren*[tw]) AND (syndrom*[tw] OR disease[tw] OR diseases[tw])) NOT Medline[sb]
 #10 sicca syndrom*[tw] NOT Medline[sb]
 #11 (Steven*[tw] AND Johnson[tw] AND (syndrom*[tw] OR disease[tw] OR diseases[tw])) NOT Medline[sb]
 #12 (Cicatricial [tw] AND Pemphigoid*[tw]) NOT Medline[sb]
 #13 Blepharoconjunctiviti*[tw] NOT Medline[sb]
 #14 (meibomian[tw] OR tarsal[tw]) NOT Medline[sb]
 #15 (lacrima*[tw] OR epiphora[tw]) NOT Medline[sb]
 #16 #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15
 #17 corticosteroid*[tw] OR glucocorticoid*[tw] OR mineralocorticoid*[tw] OR "adrenal cortex hormone"[tw] OR "adrenal cortex
 hormones"[tw] OR "adrenal cortical hormone"[tw] OR "adrenal cortical hormones"[tw] OR "adrenocortical hormone"[tw] OR
 "adrenocortical hormones"[tw] OR adrenocorticosteroid*[tw] OR corticoid*[tw] OR steroid*[tw]
 #18 Betamethasone*[tw] OR adbeon[tw] OR becasone[tw] OR beprogel[tw] OR "beta methason"[tw] OR "beta methasone"[tw] OR
 "beta-phos/ac"[tw] OR betacortril[tw] OR betadexamethasone[tw] OR betamethasone[tw] OR betamethasolone[tw] OR betamethasone[tw] OR
 betamethasonum[tw] OR betamethasone[tw] OR betason[tw] OR betnasol[tw] OR betnelan[tw] OR "betnesol v"[tw] OR "betnovate a"[tw]
 OR betsolan[tw] OR betsolon[tw] OR betsopart[tw] OR celestan[tw] OR celestene[tw] OR celeston[tw] OR celestona[tw] OR celestone[tw]
 OR celestoderm[tw] OR cidoten[tw] OR dermobet[tw] OR diprolen[tw] OR flubenisolone[tw] OR methasone[tw] OR "nsc 39470"[tw] OR
 nsc39470[tw] OR ophtamesone[tw] OR "rg 833"[tw] OR rg833[tw] OR rinderon[tw] OR "sch 4831"[tw] OR sch4831[tw] OR walacort[tw] OR
 "378-44-9"[tw]
 #19 "clobetasone butyrate"[tw] OR "cci 5537"[tw] OR cci5537[tw] OR "clobetasone 17 butyrate"[tw] OR emovate[tw] OR eumovate[tw] OR
 "gr 2 1214"[tw] OR "gr 2-1214"[tw] OR "gr 21214"[tw] OR "gr2-1214"[tw] OR kindavate[tw] OR "sn 203"[tw] OR sn203[tw] OR trimovate[tw]
 OR "25122-57-0"[tw]
 #20 Dexamethasone*[tw] OR adrecort[tw] OR adrenocot[tw] OR "aeroceb dex"[tw] OR "aeroceb-d"[tw] OR afluconos[tw] OR
 afluconose[tw] OR alfalyf[tw] OR anafllogistico[tw] OR aphtasolon[tw] OR arcodexan[tw] OR arcodexane[tw] OR artrosone[tw] OR
 auxiron[tw] OR azium[tw] OR bidexol[tw] OR "bisu ds"[tw] OR calonat[tw] OR cebedex[tw] OR cetadexon[tw] OR colofoam[tw]
 OR corsona[tw] OR corsone[tw] OR cortastat[tw] OR cortidex[tw] OR cortidexason[tw] OR cortidrona[tw] OR cortidrone[tw] OR
 cortisumman[tw] OR "dacortina fuerte"[tw] OR "dacortine fuerte"[tw] OR dalalone[tw] OR danasone[tw] OR "de-sone la"[tw] OR
 decacortin[tw] OR decadeltosona[tw] OR decadeltosone[tw] OR decaderm[tw] OR decadion[tw] OR decadran[tw] OR decadron[tw]
 OR decadronal[tw] OR decadrone[tw] OR decaesadril[tw] OR decagel[tw] OR decaject[tw] OR decalix[tw] OR decameth[tw] OR
 decamethasone[tw] OR decasone[tw] OR decaspray[tw] OR decasterolone[tw] OR decdan[tw] OR decilone[tw] OR decofluor[tw]
 OR decitancyl[tw] OR dekacort[tw] OR delladec[tw] OR deltafluoren[tw] OR deltafluorene[tw] OR dergramin[tw] OR deronil[tw] OR
 desacort[tw] OR desacortone[tw] OR desadrene[tw] OR desalark[tw] OR desameton[tw] OR desametone[tw] OR desigdrone[tw] OR
 "dexa cortisyl"[tw] OR "dexa dabrosan"[tw] OR "dexa korti"[tw] OR "dexa scherosan"[tw] OR "dexa scherozon"[tw] OR "dexa scherozone"[tw]
 OR "dexa-p"[tw] OR "dexacen 4"[tw] OR dexachel[tw] OR dexacort[tw] OR dexcortal[tw] OR dexcorten[tw] OR dexcorticin[tw] OR
 dexacortisyl[tw] OR dexadabroson[tw] OR dexadecadrol[tw] OR dexadrol[tw] OR dexagel[tw] OR dexagen[tw] OR dexahelvacort[tw]
 OR dexakorti[tw] OR dexalien[tw] OR dexualocal[tw] OR dexame[tw] OR dexametcortin[tw] OR dexameson[tw] OR dexamesone[tw] OR
 dexametason[tw] OR dexametasone[tw] OR dexameth[tw] OR dexamethason[tw] OR dexamethazon[tw] OR dexamethazone[tw] OR
 dexamethonium[tw] OR dexamonozon[tw] OR dexan[tw] OR dexane[tw] OR dexano[tw] OR dexpapot[tw] OR dexascheroson[tw] OR

dexascherazon[tw] OR dexascherzone[tw] OR dexason[tw] OR dexasone[tw] OR dexinoral[tw] OR dexioni[tw] OR dexamethsone[tw] OR dexona[tw] OR dexone[tw] OR dexpak[tw] OR dextelan[tw] OR dextenza[tw] OR dextrasone[tw] OR dexycu[tw] OR dezone[tw] OR dibasona[tw] OR doxamethasone[tw] OR esacortene[tw] OR "ex s1"[tw] OR exadion[tw] OR exadione[tw] OR firmalone[tw] OR "fluormethyl prednisolone"[tw] OR fluormethylprednisolon[tw] OR fluormethylprednisolone[tw] OR fluormone[tw] OR fluorocort[tw] OR fluorodelta[tw] OR fluoromethylprednisolone[tw] OR fortecortin[tw] OR gammacorten[tw] OR gammacortene[tw] OR grosodexon[tw] OR grosodexone[tw] OR hemady[tw] OR hexadecadiol[tw] OR hexadecadrol[tw] OR hexadiol[tw] OR hexadrol[tw] OR isnacort[tw] OR "isopto dex"[tw] OR "isopto maxidex"[tw] OR "isopto-dex"[tw] OR "isopto-maxidex"[tw] OR isoptodex[tw] OR isoptomaxidex[tw] OR "lokalison f"[tw] OR loverine[tw] OR luxazone[tw] OR marvidione[tw] OR maxidex[tw] OR mediamethasone[tw] OR megacortin[tw] OR mephameson[tw] OR mephamesone[tw] OR metasolon[tw] OR metasolone[tw] OR "methazon ion"[tw] OR "methazone ion"[tw] OR methazonion[tw] OR methazonione[tw] OR methylfluorprednisolone[tw] OR "metisone lafi"[tw] OR mexasone[tw] OR millicorten[tw] OR millicortenol[tw] OR "mk 125"[tw] OR mk125[tw] OR mymethasone[tw] OR neoforderx[tw] OR neofordex[tw] OR nisomethasona[tw] OR novocort[tw] OR "nsc 34521"[tw] OR nsc34521[tw] OR "oftan-dexa"[tw] OR opticorten[tw] OR opticortinol[tw] OR oradexan[tw] OR oradexon[tw] OR oradexone[tw] OR orgadrone[tw] OR ozurdex[tw] OR pidexon[tw] OR policort[tw] OR posurdex[tw] OR "predni f tablinen"[tw] OR "predni-f"[tw] OR "prednisolone f"[tw] OR prodexona[tw] OR prodexone[tw] OR sanamethasone[tw] OR santenson[tw] OR santeson[tw] OR sawasone[tw] OR solurex[tw] OR spoloven[tw] OR sterasone[tw] OR thilodexine[tw] OR triamcimetil[tw] OR vexamet[tw] OR visumetazone[tw] OR visumethazone[tw] OR "50-02-2"[tw]
 #21 difluprednate*[tw] OR "cm 9155"[tw] OR cm9155[tw] OR durezol[tw] OR epitopic[tw] OR myser[tw] OR "w 6309"[tw] OR w6309[tw] OR "warner 6309"[tw] OR ENV905[tw] OR "23674-86-4"[tw]
 #22 Fluorometholone[tw]* OR cortilet[tw] OR cortisdin[tw] OR delmeson[tw] OR delmesone[tw] OR efflumidex[tw] OR eflone[tw] OR flosef[tw] OR fluaton[tw] OR flucon[tw] OR "fluforte liquifilm"[tw] OR flulon[tw] OR flumelon[tw] OR flumetholon[tw] OR flumetholone[tw] OR flumex[tw] OR flumexo[tw] OR fluometholone[tw] OR fluoph[tw] OR "fluoro opthal"[tw] OR "fluor-op"[tw] OR fluorlon[tw] OR fluormetholon[tw] OR fluoromethalone[tw] OR fluoropos[tw] OR fml[tw] OR fuluson[tw] OR "isopto flucon"[tw] OR loticort[tw] OR methasite[tw] OR oxyalone[tw] OR "426-13-1"[tw]
 #23 Loteprednol*[tw] OR alrex[tw] OR "cddd 5604"[tw] OR cddd5604[tw] OR CEHOAC[tw] OR "Chloromethyl 17-ethoxycarbonyloxy-11-hydroxy-3-oxoandrosta-1,4-diene-17-carboxylate"[tw] OR "17-ethoxycarbonyloxy-11-hydroxy-3-oxoandrosta-1,4-diene-17-carboxylate, Chloromethyl"[tw] OR "Chloromethyl 17 ethoxycarbonyloxy 11 hydroxy 3 oxoandrosta 1,4 diene 17 carboxylate"[tw] OR eysuvis[tw] OR "hgp 1"[tw] OR hgp1[tw] OR inveltys[tw] OR "kpi 121"[tw] OR kpi121[tw] OR "le-mpp"[tw] OR lotemax[tw] OR loterex[tw] OR loterox[tw] OR lotesoft[tw] OR "p 5604"[tw] OR p5604[tw] OR "82034-46-6"[tw]
 #24 Prednisolone*[tw] OR adelcort[tw] OR antisolon[tw] OR antisolone[tw] OR aprednislon[tw] OR aprednislone[tw] OR benisolon[tw] OR benisolone[tw] OR berisolon[tw] OR berisolone[tw] OR caberdelta[tw] OR capsoid[tw] OR "co hydeltra"[tw] OR codelcortone[tw] OR compresolon[tw] OR cortadeltona[tw] OR cortadeltone[tw] OR cortalone[tw] OR cortelinter[tw] OR cortisolone[tw] OR cotolone[tw] OR dacortin[tw] OR dacrotin[tw] OR decaprednil[tw] OR "decortin h"[tw] OR decortril[tw] OR "dehydro cortex"[tw] OR "dehydro hydrocortisone"[tw] OR "dehydro hydrocortisone"[tw] OR dehydrocortex[tw] OR dehydrocortisol[tw] OR dehydrocortisole[tw] OR dehydrohydrocortison[tw] OR dehydrohydrocortisone[tw] OR delcortol[tw] OR "delta 1 17 hydroxycorticosterone 21 acetate"[tw] OR "delta 1 hydrocortisone"[tw] OR "delta cortef"[tw] OR "delta cortil"[tw] OR "delta ef cortelan"[tw] OR "delta f"[tw] OR "delta hycortol"[tw] OR "delta hydrocortisone"[tw] OR "delta hydrocortisone"[tw] OR "delta ophthicor"[tw] OR "delta stab"[tw] OR "delta-cortef"[tw] OR "delta1 dehydrocortisol"[tw] OR "delta1 dehydrohydrocortisone"[tw] OR "delta1 hydrocortisone"[tw] OR deltacortef[tw] OR deltacortenolo[tw] OR deltacortil[tw] OR deltacortoil[tw] OR deltacortril[tw] OR deltaderm[tw] OR deltaglycortril[tw] OR deltahycortol[tw] OR deltahydrocortison[tw] OR deltahydrocortisone[tw] OR deltaoptyticor[tw] OR deltasolone[tw] OR deltastab[tw] OR deltidrosol[tw] OR deltisilon[tw] OR deltisolon[tw] OR deltisolone[tw] OR deltolasson[tw] OR deltolassone[tw] OR deltosona[tw] OR deltosone[tw] OR "depo-predate"[tw] OR dermosolon[tw] OR dhasolone[tw] OR DiAdresonF[tw] OR "di adreson f"[tw] OR "di adresone f"[tw] OR "di-adreson-f"[tw] OR "diadreson f"[tw] OR "diadresone f"[tw] OR dicortol[tw] OR domucortone[tw] OR encortelon[tw] OR encortelone[tw] OR encortolon[tw] OR equisolon[tw] OR "fernisolone-p"[tw] OR glistelone[tw] OR hefasolon[tw] OR "hostacortin h"[tw] OR hydeltra[tw] OR hydetrone[tw] OR hydrelta[tw] OR hydrocortancyl[tw] OR hydrocortidelt[tw] OR hydrodeltalone[tw] OR hydrodeltisone[tw] OR hydroretrocortin[tw] OR hydroretrocortine[tw] OR inflanefran[tw] OR insolone[tw] OR "keteocort h"[tw] OR "key-pred"[tw] OR lenisolone[tw] OR leocortol[tw] OR liquipred[tw] OR "lygal koftinktur n"[tw] OR mediasolone[tw] OR meprisolon[tw] OR meprisolone[tw] OR metacortalon[tw] OR metacortalone[tw] OR metacortandralon[tw] OR metacortandralone[tw] OR metacortelone[tw] OR "meti derm"[tw] OR meticortelone[tw] OR metiderm[tw] OR morlone[tw] OR mydrapred[tw] OR "neo delta"[tw] OR nisolon[tw] OR nisolone[tw] OR "nsc 9120"[tw] OR nsc9120[tw] OR opredson[tw] OR panafcortelone[tw] OR panafcortolone[tw] OR panafort[tw] OR paracortol[tw] OR phlogex[tw] OR "pre cortisy"[tw] OR preconin[tw] OR precortalon[tw] OR precortancyl[tw] OR precortisy[tw] OR "pred-ject-50"[tw] OR "predacort 50"[tw] OR "predaject-50"[tw] OR "predalone 50"[tw] OR predartrina[tw] OR predartrine[tw] OR predate[tw] OR "predate-50"[tw] OR predeltilone[tw] OR predisole[tw] OR predisyrtw] OR "predne dome"[tw] OR prednecort[tw] OR prednedome[tw] OR prednelan[tw] OR "predni coelin"[tw] OR "predni h tablinen"[tw] OR "predni-helvacort"[tw] OR prednicoelin[tw] OR prednicort[tw] OR prednicortelone[tw] OR "prednifor drops"[tw] OR predniment[tw] OR predniretard[tw] OR prednis[tw] OR prednisil[tw] OR prednisolon[tw] OR prednisolona[tw] OR prednivet[tw] OR prednorsolon[tw] OR prednorsolone[tw] OR predonine[tw] OR predorgasolona[tw] OR predorgasolone[tw] OR "pregna 1, 4 diene 11beta, 17alpha, 21 triol 3, 20 dione"[tw] OR prelon[tw] OR prelon[tw] OR prenilone[tw] OR prenilone[tw] OR prenolone[tw] OR preventan[tw] OR prezolon[tw] OR rubycort[tw] OR scherisolon[tw] OR scherisolona[tw] OR serilone[tw] OR solondo[tw] OR solone[tw] OR solopren[tw] OR soloprene[tw] OR spiricort[tw] OR spolotane[tw] OR sterane[tw] OR sterolone[tw] OR supercortisol[tw] OR supercortizol[tw] OR taracortelone[tw] OR walesolone[tw] OR wysolone[tw] OR "50-24-8"[tw]
 #25 #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24
 #26 #1 AND #16 AND #25

Appendix 5. LILACS search strategy

("Dry Eye" OR "Síndromes de Ojo Seco" OR "Síndromes do Olho Seco" OR MH:C11.496.260\$ OR Tear\$ OR Lágrimas OR MH:A12.200.882\$ OR Xerophthalmia OR Xeroftalmia OR MH:C11.187.810\$ OR MH:C11.496.260.892\$ OR "Vitamin A Deficiency" OR "Deficiencia de Vitamina A" OR MH:C18.654.521.500.133.628\$ OR MH:SP6.016.052.063.109\$ OR "avitaminosis a" OR "retinol deficiency" OR "hypovitaminosis A" OR Keratoconjunctivitis OR "kerato conjunctivitis" OR Queratoconjunctivitis OR Ceratoconjuntivite OR MH:C11.187.183.394\$ OR MH:C11.204.564.585\$ OR MH:C11.496.260.394\$ OR "Sjogren's Syndrome" OR "Síndrome de Sjögren" OR MH:C05.550.114.154.774\$ OR MH:C05.799.114.774\$ OR MH:C07.465.815.929.669\$ OR MH:C11.496.260.719\$ OR MH:C17.300.775.099.774\$ OR MH:C20.111.199.774\$ OR "sicca syndrome" OR "Stevens Johnson Syndrome" OR "Síndrome de Stevens Johnson" OR MH:C07.465.864.500\$ OR MH:C17.800.229.400.683\$ OR MH:C17.800.865.475.683\$ OR "Pemphigoid Benign Mucous Membrane" OR "Penfigoide Benigno de la Membrana Mucosa" OR "Penfigoide Mucomembranoso Benigno" OR "Cicatricial Pemphigoid" OR MH:C11.187.482\$ OR MH:C17.800.865.670\$ OR blepharconjunctivit\$ OR "Meibomian Glands" OR "Glândulas Tarsales" OR "Glândulas Tarsais" OR MH:A09.371.337.614 OR MH:A10.336.827.600 OR "Lacrimal Apparatus Diseases" OR "Enfermedades del Aparato Lagrimal" OR "Doenças do Aparelho Lacrimal" OR MH:C11.496\$ OR lacrima\$ or epiphora) AND (corticosteroid\$ OR glucocorticoid\$ OR mineralocorticoid\$ OR "adrenal cortex hormone" OR "adrenal cortical hormone" OR "adrenocortical hormone" OR adrenocorticosteroid\$ OR corticoid\$ OR steroid\$ OR MH:D06.472.040\$ OR Betamethason\$ OR Betametason\$ OR MH:4.210.500.745.432.769.199\$ OR MH:D04.210.500.908.093\$ OR "Clobetasone butyrate" OR Dexamethason\$ OR Dexametason\$ OR MH:D04.210.500.745.432.769.344\$ OR MH:D04.210.500.908.431\$ OR "Loteprednol etabonate" OR MH:D04.210.500.054.079.129.284\$ OR "Etabonato de Loteprednol" OR Prednisolon\$ OR MH:D04.210.500.745.432.769.795\$)

Appendix 6. ClinicalTrials.gov search strategy

(dry eye OR Keratoconjunctivitis) AND (corticosteroid OR glucocorticoid OR mineralocorticoid OR adrenal cortex hormones OR adrenal cortical hormones OR adrenocortical hormones OR adrenocorticosteroid OR corticoid OR steroids OR betamethasone OR clobetasone butyrate OR dexamethasone OR difluprednate OR fluorometholone OR loteprednol etabonate OR prednisolone)

Appendix 7. WHO ICTRP search strategy

dry eye AND corticosteroid OR dry eye AND glucocorticoid OR dry eye AND mineralocorticoid OR dry eye AND adrenal cortex hormones OR dry eye AND adrenal cortical hormones OR dry eye AND adrenocortical hormones OR dry eye AND adrenocorticosteroid OR dry eye AND corticoid OR dry eye AND steroids OR dry eye AND betamethasone OR dry eye AND clobetasone butyrate OR dry eye AND dexamethasone OR dry eye AND difluprednate OR dry eye AND fluorometholone OR dry eye AND loteprednol etabonate OR dry eye AND prednisolone

Keratoconjunctivitis AND corticosteroid OR Keratoconjunctivitis AND glucocorticoid OR Keratoconjunctivitis AND mineralocorticoid OR Keratoconjunctivitis AND adrenal cortex hormones OR Keratoconjunctivitis AND adrenal cortical hormones OR Keratoconjunctivitis AND adrenocortical hormones OR Keratoconjunctivitis AND adrenocorticosteroid OR Keratoconjunctivitis AND corticoid OR Keratoconjunctivitis AND steroids OR Keratoconjunctivitis AND betamethasone OR Keratoconjunctivitis AND clobetasone butyrate OR Keratoconjunctivitis AND dexamethasone OR Keratoconjunctivitis AND difluprednate OR Keratoconjunctivitis AND fluorometholone OR Keratoconjunctivitis AND loteprednol etabonate OR Keratoconjunctivitis AND prednisolone

CONTRIBUTIONS OF AUTHORS

SL, AA, IS, TL: Background, Objectives, and Methods drafting and revision.

DG, SH, CI: Background drafting and Methods review.

TL: overall supervision of the protocol preparation and revision.

All authors have reviewed and approved the final version of the protocol.

DECLARATIONS OF INTEREST

- Su-Hsun Liu:** reports a grant from the National Eye Institute, National Institutes of Health, USA; payment to institution.
- Darren Gregory:** reports working as an Ophthalmologist at the University of Colorado Eye Center. Their clinical work focuses on the treatment of dry eyes, which sometimes involves the use of topical corticosteroid medications.
- Scott Hauswirth:** reports grants and contracts for paid investigator from TearSolutions and Sylentis (contract pending - study not yet underway as of 23 February 2021); paid to institution. Payments for presentations from Kala Pharmaceuticals, Dompe, Sun Pharmaceuticals, Takeda, and Avedro; personal payment. Support for INTREPID meeting (indirect) from Alcon/Novartis; personal payment. Stock shares in Oyster Point (paid for and owned individually, not as compensation), TearRestore (compensation for design and medical advisory work), and Horizon Pharma (paid for and owned individually, not as compensation); personal payment. Consulting fees for study design and analysis from Ocular Therapeutix (pending); personal payment. Advisory Board payments from Dompe, NuSight Medical, Kala Pharmaceuticals, Sun Pharmaceuticals, EyePoint Medical, EyeVance Pharma, Horizon Pharma, Avedro/Glaukos, Quidel, and Sight Sciences; personal payment. Writing assistance from Takeda (medical writer for review paper); personal payment. SH reports publishing opinions on topical immunomodulation in dry eye in the OSDocs Facebook group (moderator/co-

administrator role) and published "When Dry Eye Compromises Corneal Integrity" in *Review of Optometry*, Nov 2017 (contract pending - study not yet underway as of 23 February 2021). They report working as an Optometrist at the University of Colorado.

- **Cristos Ifantides:** reports being an inventor with intellectual property assigned to their university. The design relates to dry eye but does not relate to corticosteroid use for dry eye. It is a design for a new form of eyeglasses that can theoretically help with dry eye (patent application filed, University of Colorado), paid to institution. Ownership of stock in Pfizer. Their partner works for AbbVie, who makes medications related to dry eye. She does not work in the eye care space. CI reports working as a clinician at Denver Health and University of Colorado, where they are an attending physician.
- **Alison G Abraham:** declared that she has no conflicts of interest.
- **Ian J Saldanha:** reports grants and contracts, Cochrane Eyes and Vision, from National Eye Institute, National Institutes of Health, USA; payment to institution. Travel reimbursement for making a talk on outcomes related to dry eye in 2018 from Johns Hopkins Wilmer Eye Institute; personal payment.
- **Tianjing Li:** reports a grant from the National Eye Institute, National Institutes of Health, USA; payment to institution.

SOURCES OF SUPPORT

Internal sources

- No sources of support provided

External sources

- Public Health Agency, UK

The HSC Research and Development (R&D) Division of the Public Health Agency funds the Cochrane Eyes and Vision editorial base at Queen's University Belfast.

- National Eye Institute, National Institutes of Health, USA

Cochrane Eyes and Vision US Project, supported by grant UG1EY020522 (PI: Tianjing Li, MD, MHS, PhD)

- Queen's University Belfast, UK

The work of Gianni Virgili, Co-ordinating Editor for Cochrane Eyes and Vision, is funded by the Centre for Public Health, Queen's University of Belfast, Northern Ireland.