Philippine Clinical Practice Guidelines on Contact Dermatitis

August 2023

Disclaimer and Contact Information

This clinical practice guideline (CPG) is intended to be used by specialists and general practitioners who are primary care providers. Although adherence to this guideline is encouraged by the Department of Health (DOH), it should not restrict clinicians from using their clinical judgment and considering patient's values, needs, and preferences while handling individual cases. Clinicians and relevant stakeholders must always exercise sound clinical decision-making as the individual patient's history, current physical status, and responses to treatment may vary.

Payors and policymakers, including hospital administrators and employers, can also utilize this CPG, but nonconformance to this document should not be the sole basis for granting or denying financial assistance or insurance claims. Recommendations from this CPG should not be treated as strict rules to base legal action.

The developers of this CPG are aware of its limitations. Evidence summaries are based on the best available scientific evidence at the time of their formulation. As such, certain aspects of the interventions or diagnostic tests may not be completely addressed by the included studies.

The scope of this clinical practice guideline (CPG) does not cover the entirety of the management of contact dermatitis. This resource offers suggestions or recommendations for interventions in situations where there is variability in clinical practice and controversies surrounding decision-making.

Contact Us

Send us an email at emcgutierrez@yahoo.com for any questions or clarifications on the outputs and process of this practice guideline.

Acknowledgments

This CPG on contact dermatitis would not have been possible without the initiative and financial support from the Department of Health. The DOH neither imposed any condition nor exerted any influence on the procedures and in the final recommendations and output.

The technical proficiency and guidance of the University of the Philippines Manila Institute of Clinical Epidemiology and the leadership of Jose R. Reyes Memorial Medical Center enabled the completion of this national CPG. This CPG received immense support from Dr. Emmanuel F. Montaña Jr., the JRRMMC Medical Center Chief, and Dr. Ma. Flordeliz Abad-Casintahan, the Chairman of the Department of Dermatology at JRRMMC, the National Specialty Center for Dermatology.

The credibility of this CPG is upheld by the Conflict of Interest (COI) Review Committee, which oversaw the assessment and management of potential COIs among all members involved in this guideline development.

The Steering Committee was also indispensable in carrying out the legwork, coordinating among various professional society representatives and committees, and holding *en banc* meetings. The SC was also in charge of overall organization and management and is accountable for the quality of the CPG.

The Evidence Review Experts undertook the extensive technical work in searching and synthesizing the evidence while ensuring objectivity in each stage of the process and presenting the evidence in the panel discussion.

The contribution of consensus panelists from various healthcare sectors renders this guideline invaluable. The panelists devoted their time and energy to sharing their knowledge, experience, and expertise to weigh the scientific evidence, patients' values and preferences, and other relevant issues such as accessibility, feasibility, and equity in the healthcare system of the country.

The guideline developers were also assisted by the following supportive members: the external facilitator who moderated the discussion of the consensus panel members, the technical coordinators who provided expertise in guideline preparation, and technical writer who collated the evidence base and drafted the final CPG manuscript.

This CPG would not have been successfully endorsed for approval without the external review provided by Dr. Hester Gail Lim-Bueser and Dr. Bryan Edgar K. Guevara.

Participating Societies, Organizations, Agencies and/or Institutions

UP Manila – National Institutes of Health
Institute of Clinical Epidemiology

Jose R. Reyes Memorial Medical Center Manila

Philippine Dermatological Society

Philippine College of Occupational Medicine

Philippine Academy of Family Physicians

Philippine College of Physicians

Philippine Society of Allergy, Asthma and Immunology

Philippine Alliance of Patient Organization

Philippine Nurses Association

Table of Contents

List of Abbreviations and Acronyms

AAAAI	American Academy of Allergy, Asthma & Immunology
AD	Atopic dermatitis
CD	Contact dermatitis
COI	conflict of interest
CI	confidence interval
CP	Consensus Panel
CPG	Clinical practice guideline
DOH	Department of Health
DLQI	Dermatology Life Quality Index
EASI	Eczema Area and Severity Index
ERE	Evidence Review Experts
EtD	Evidence to Decision
FDA	Food and Drug Administration
GIDA	Geographically isolated and disadvantaged areas
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
HECSI	hand eczema severity index
ICE	Institute of Clinical Epidemiology
JAK	Janus kinase
JRRMMC	Jose R. Reyes Memorial Medical Center
LGU	local government unit
MD	mean difference
MeSH	Medical Subject Headings
NB-UVB	narrowband ultraviolet-B
NGC	National Guideline Clearinghouse
NIH	National Institutes of Health
OR	odds ratio
PAFP	Philippine Academy of Family Physicians
PAPO	Philippine Alliance of Patient Organization
PICO	population, intervention, comparator, outcome
PCOM	Philippine College of Occupational Medicine
PCP	Philippine College of Physicians
PDS	Philippine Dermatological Society
PNA	Philippine Nurses Association
PSAAI	Philippine Society of Allergy, Asthma, and Immunology
PUVA	Psoralen plus ultraviolet-A
QoL	quality of life
RCT	randomized controlled trial
ROAT	repeat open application test
RR	Risk ratio
SC	Steering Committee
TCI	topical calcineurin inhibitors
TCS	topical corticosteroids
UHC	Universal Health Care
UPM	University of the Philippines Manila
VAS	visual analogue scale

List of Tables

List of Figures

List of Boxes

Executive Summary

Contact dermatitis (CD) is categorized into two main subtypes: allergic and irritant. Allergic contact dermatitis ranked fifth and irritant contact dermatitis ninth among all dermatologic consults recorded in 2020 by the Philippine Dermatologic Society. Contact dermatitis imposes not only restricted social participation and decreased overall well-being but also causes an economic burden. It is especially relevant because all individuals are at risk of developing this skin condition. Despite the risk of CD, there has been no established clinical practice guideline that would support healthcare workers in their clinical decision-making in the country.

This CPG on CD aims to provide recommendations on aspects of CD diagnosis and management where significant variability and controversy in clinical practice are observed in the country. It does not aim to address every facet of contact dermatitis care, but it is intended to be used by general physicians and specialists, other healthcare professionals, and policymakers to improve management of CD. Its target beneficiaries are the patients with contact dermatitis and, indirectly, the broader population in the Philippines.

This guideline is based on the current best available evidence (literature search up until April 2023), local resources, infrastructure, and the practice context in the country. Guideline recommendations were developed following a standard methodology for guideline development outlined in the DOH CPG Manual 2018. Distinct working groups were established. Existing clinical studies were comprehensively searched and reviewed to address nine key questions. A multi-sectoral panel of representatives and experts collaborated to develop a set of recommendations that were agreed upon by consensus. The GRADE method was used to determine the direction and strength of each recommendation.

For the nine clinical questions, nine recommendation statements were developed, each of which was accompanied by a corresponding strength of recommendation and certainty of evidence (Table 1). Of these, the majority were based on low to very low certainty of evidence.

1.1. Summary of Recommendations

Table 1. Summary of recommendation statements, strength of recommendation, and certainty of evidence on the management of contact dermatitis

1	We suggest the use of patch testing to diagnose allergic contact dermatitis.	Very Low ⊕◯◯◯	Weak
2	Among patients with suspected allergic contact dermatitis, we recommend the use of ROAT as initial or presumptive test to identify potential contact allergens.	Low ⊕⊕◯◯	Strong
3	Among patients with suspected allergic contact dermatitis, we recommend against the use of home remedies and/or over-the-counter products.	Very Low ⊕◯◯◯	Strong
4	Among patients with contact dermatitis, we recommend the provision of patient education.	Moderate ⊕⊕⊕◯	Strong
5	Among adult patients with contact dermatitis, we recommend the use of emollient/barrier cream as an adjunct to topical corticosteroids.	Low ⊕⊕◯◯	Strong
6	Among adult patients with contact dermatitis, we suggest against the use of topical calcineurin inhibitors over topical corticosteroids as pharmacologic therapy.	Very Low ⊕◯◯◯	Weak
7	We recommend that patients with contact dermatitis who have frequent eruptions, co-existing atopic dermatitis, and those who have severe disease at baseline be referred to a higher level of care.	Low ⊕⊕◯◯	Strong
8	Among patients with chronic recalcitrant contact dermatitis, we suggest the use of narrowband phototherapy as adjunct treatment.	Low ⊕⊕◯◯	Weak
9	Among adults diagnosed with severe or recalcitrant chronic contact dermatitis, we suggest against the use of systemic immunosuppressives (methotrexate, azathioprine, cyclosporin, mycophenolate mofetil, JAK inhibitors) compared to oral corticosteroids and/or oral antihistamines in addition to topical emollients and/or topical corticosteroids.	Low ⊕⊕◯◯	Weak

1. Introduction

1.1. Background

Contact dermatitis is categorized into two main subtypes: allergic and irritant.[1] Allergic contact dermatitis ranked fifth and irritant contact dermatitis ninth among all dermatologic consults recorded in 2020 by the Philippine Dermatologic Society. Contact dermatitis imposes not only restricted social participation and decreased overall well-being but also causes an economic burden[2]. It is especially important because all individuals are at risk of developing contact dermatitis[1]. Despite the burden of CD[1], there is no established Philippine clinical practice guideline that would support healthcare workers in their clinical decision-making and institutions in capacity building and policy-making.

This CPG primarily aims to assist healthcare providers in in the primary care setting in accurately diagnosing and effectively managing patients suspected of CD or with CD. A clinical practice guideline is one way to help clinicians decide on the best management options with the aim of reducing variations in practice, managing healthcare costs, and helping promote allocation of resources, among other goals.[3]

This guideline on CD may be used to strengthen the national initiatives to provide sectoral strategy and planning that adheres to the requirements of the Universal Health Care Act.[4] Various academic and medical institutions may also utilize the guideline in teaching evidence-based practices on contact dermatitis. It may also assist the national health insurance programs to expand the inclusions of essential health benefit packages for patients with skin conditions.

1.2. Objectives

The overall objective of this guideline is to present evidence-based recommendations for the diagnosis and treatment of contact dermatitis with health issues in the local context.

1.3. Scope and Purpose

This CPG provides evidence-based recommendations on the diagnosis and treatment of patients with contact dermatitis.

1.4. Target Population

These guideline questions and recommendations target health outcomes of all patients with contact dermatitis, both adults and children. Some questions are specific to adults who are suspected to have contact dermatitis or who have a specific CD type or status (i.e., irritant or allergic; chronic, recurrent, or recalcitrant).

1.5. Intended Users

The recommendations contained herein are intended to help in the decision-making of the following stakeholders: barangay health workers, general practitioners, dermatologists, internists, family medicine specialists, occupational medicine specialists, medical and allied healthcare students, trainees, patients, and policymakers.

1.6. Key Clinical Issues and Questions

Table 2. Prioritized clinical questions on contact dermatitis

No.	Clinical Questions
1	Should we use patch testing to diagnose allergic contact dermatitis?
2	Should we use a repeat open application test (ROAT) as an alternative test for patients suspected of allergic contact dermatitis?
3	Should patients with suspected contact dermatitis use home remedies and/or over-the-counter topical products to alleviate their symptoms?
4	Among patients with contact dermatitis, should we recommend patient and/or family education versus none to improve outcomes?
5	Among adult patients with contact dermatitis, should we use topical corticosteroids and emollients, barrier creams, as compared to topical corticosteroids alone to improve outcomes?
6	Among individuals with contact dermatitis, should topical calcineurin inhibitors be used versus topical corticosteroids?
7	Among adults with chronic, recurrent, or recalcitrant contact dermatitis, should we refer to a higher level of care?
8	Should we use other modalities such as phototherapy as adjunct treatment among patients with chronic recalcitrant contact dermatitis?
9	Among adults diagnosed with severe or recalcitrant chronic contact dermatitis, should we use systemic immunosuppressives (azathioprine, methotrexate, cyclosporine, mycophenolate mofetil, or janus kinase inhibitors) instead of oral corticosteroids and/or oral antihistamines in addition to topical corticosteroids and/or emollients?

2. CPG Development Methodology

2.1. Guideline Preparation

The development of this CPG on contact dermatitis adhered to the methodology detailed in the Department of Health *Manual for Clinical Practice Guideline Development*.[3] The DOH chose JRRMMC, a public tertiary hospital, to spearhead the guideline development and to form the CPG Task Force headed by the Steering Committee (SC). The UPM-NIH guided the CPG Task Force in the CPG development process.

The SC is composed of dermatologists, internists, an allergologist, an occupational health physician, and a methodologist. The SC invited institutions and organizations that are stakeholders in the care of contact dermatitis patients to nominate representatives to form the Consensus Panel (CP). The SC also set up the technical working group (TWG), which was comprised of the technical coordinators (TC), the evidence review experts (ERE), and the technical facilitator. The SC identified the clinical issues to be covered by the CPG and, in coordination with the TWG and the CP, finalized the research (PICO) questions from the identified clinical issues. (See Appendix 8.1)

An external COI review committee was formed to assess each Task Force member's potential conflict of interest and provide management of identified COI throughout the process. The details of managing COI can be read in the Management of Conflicts of Interest.

The EREs, guided by the technical coordinators, were tasked with performing a systematic literature search, reviewing the existing CPGs, appraising and synthesizing relevant evidence, drafting evidence-based recommendations, determining the certainty of evidence using GRADE, and presenting their findings to the Steering Committee.

The EREs presented the evidence and draft recommendations during the three *en banc* meetings of the CP, which were held online via Zoom. The CP, on the other hand, was assigned the task of choosing the critical and important outcomes. The CP members were also given an evidence summary for each clinical question to review and were tasked with answering the evidence-to-decision framework survey, which facilitated the CP *en banc* meeting discussions. With the help of the technical facilitator, the CP finalized the statements and the strength of the recommendations. The detailed process of formulating the final recommendations is discussed in Section 2.3.

Composition of the Consensus Panel

The Consensus Panel is a multisectoral group of content experts and key stakeholders in the care of patients with CD. The online *en banc* meetings were attended by this diverse group of stakeholders, including a patient representative, a dermatologist, an internist, an allergologist, a primary care physician, an occupational health physician, and a nurse.

2.2. Evidence Synthesis

Search Methods and Strategies

The EREs performed a comprehensive search of studies in different online databases, such as MEDLINE via PubMed, Google Scholar, Cochrane Library, *ClinicalTrials.gov*, medRxiv, and HERDIN PLUS. They used keywords in free text and MeSH terms depending on the guideline questions.

They looked for systematic reviews and meta-analyses of randomized controlled trials for questions in management. If there were no meta-analyses, RCTs or observational studies were searched and appraised. No language or period filters were used.

The date of the last search ranges from January 15, 2023 to April 6, 2023. The full search strategy with keywords and dates of last search for each question can be found in Appendix 8.3. The PRISMA flow diagram per question is also shown in Appendix 8.4.

Inclusion and Exclusion Criteria

Published literature in the last 15 years (2007 onwards) was one of the inclusion criteria. If available, guidelines that reported systematic literature searches and explicit links between individual recommendations and supporting evidence were considered. Randomized controlled trials from meta-analyses were also included. If no RCTs were found, observational studies were considered.

Depending on the question, the inclusion criteria were studies on adult patients suspected of having CD, those with CD, or those with recalcitrant chronic CD. The outcomes investigated in using diagnostic tests and treatment were clinical improvement, frequency of outpatient consults, improvement in quality of life, prevention of recurrences or hospitalization, and adverse events.

Studies were excluded if the topic was beyond contact dermatitis and involved only special populations such as pediatric, geriatric, immunocompromised, pregnant, and lactating patients. Studies were excluded if there was no intervention, no comparator of interest, or no available full-text article.

Study Quality Assessment

Each study included for questions on management was appraised using the Cochrane Risk of Bias Assessment Tool version 1[5]. This tool was used to examine the trials' randomization process, allocation concealment, blinding of participants and study personnel, outcome reporting, selective reporting, and other biases. The QUADAS-2 tool[6], on the other hand, was utilized to appraise diagnostic accuracy studies based on four domains: patient selection, index test, reference standard, and flow of patients through the study and timing of the index tests and reference standard. Applicability was included in the tool and assessed based on the same domains.

Data Synthesis

Each evidence summary presented to the panel prior to and during the *en banc* meetings contains search strategies, characteristics of included studies, an appraisal of the studies, and a summary of findings. Relevant outcomes for every guideline question, if available, were presented with outcome measures and single or pooled effect estimates with confidence intervals. RevMan version 5.4 was used for the data synthesis.

2.3. Formulating Recommendations

Certainty of Evidence and Strength of Recommendations

The EREs drafted the recommendation statement(s) based on the included studies that served as evidence. The GRADE approach was utilized to determine the certainty of the evidence, taking into account various factors such as the risk of bias, indirectness, inconsistency, imprecision, and other pertinent considerations (i.e., large effect, dose-response gradient, plausible confounding factors).[7] The certainty of evidence can be high, moderate, low, or very low. If the certainty of evidence varied for different critical outcomes, the overall certainty was based on the lowest grade. Table 2.1 presents the interpretation for each certainty.

Table 3. Definition of the four levels of evidence

Certainty of Evidence	Definition[8]	Implication
High	The group is very confident that the true effect lies close to the estimate of the effect.	Further research is very unlikely to change our confidence in the effect estimate.
Moderate	The group is moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.	Further research is likely to have an important impact on our confidence in the effect estimate and may change the estimate.
Low	Confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the true effect.	Further research is very likely to have an important impact on our confidence in the effect estimate and is likely to change the estimate.
Very Low	The group has very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of the effect.	Any effect estimate is very uncertain.

The strength of recommendation was contingent upon the decision of the panel subsequent to the deliberation of evidence of benefit and harm along with other pivotal factors in the decision-making process, such as patients' views and preferences, resource availability, accessibility, feasibility, and costs.

Rating of Outcomes

The Consensus Panel prioritized the critical and important outcomes in evaluating the evidence for each guideline question. Prior to the en banc meeting, the CP members were asked to rate the outcomes numerically on a scale of 1 to 9 per question (7 to 9: critical; 4 to 6: important; 1 to : of limited importance).

Patients' Views and Preferences

This guideline guaranteed that patients' views and preferences were considered in all the recommendations through the involvement of a patient representative from the Philippine Alliance of Patient Organization, who participated in all *en banc* meetings for the deliberation of the recommendations. When available, relevant studies on patient views, values, and preferences on the topic were also presented during the CP *en banc* meetings.

Evidence to Decision Framework

The Evidence to Decision (EtD) framework[9] was utilized to help the CP members analyze and weigh the benefits and harms. It also aided them in identifying the resource implications, discussing patients' values and preferences, and taking into account the costs, accessibility, feasibility, and equity issues in the formulation of the recommendations. Appendices 8.8 and 8.9 show a summary of information on costs and available literature on cost-effectiveness, patients' preferences, and local issues with regard to the tests and interventions for each clinical question presented to the panel during the survey and meetings.

The EREs were responsible for finding and presenting studies on stakeholders' values and acceptability, feasibility, and cost-effectiveness studies to aid the CP members in determining potential resource implications. These studies, if available, were included in the EtD and sent to the voting members along with the evidence summary for review prior to the *en banc* meeting. The CP members were asked to complete an online survey containing the domains of the EtD framework before the meeting. The Technical Coordinator presented the collated responses from the survey during the deliberation of the recommendations. The EtD framework provided a structure for the CP members during the online discussion and the transparent judgment of the voting members towards the recommendation.

Consensus Process

The CP members were given an orientation on the 2nd of May to discuss the consensus process prior to the en banc meetings (12th, 23rd, 30th of May, 2023). A quorum could only be achieved if all seven voting members were present during the meetings.

Following the presentation of the evidence summary, the drafted recommendation, and the collated EtD responses from the survey, the technical facilitator led a discussion with the panel to address any queries or concerns regarding the evidence presented and the issues for consideration in the drafting of the recommendations before the voting process.

Three rounds of voting were allowed until consensus (75% of total votes, or 6 votes) was reached on the direction and wording of the recommendation statement (i.e., for or against

the intervention). Once consensus was reached, the group discussed and voted on the strength of recommendation. Similarly, voting was allowed for up to three rounds. The CP arrived at consensus on all recommendations for all nine questions, except for one that required a Delphi approach for consensus.

2.4. External Review

A group of independent reviewers examined the manuscript. Two experts in content and research methodology from PDS engaged in contact dermatitis management were invited by the Steering Committee to compose the External Review Panel.

They deliberated on the content and checked the technical aspects of the CPG recommendations using the Appraisal of Guidelines Research & Evaluation-Recommendation Excellence (AGREE-REX) checklist.

The AGREE-REX is a valid and reliable tool to evaluate the quality of guideline recommendations that consists of three theoretical domains and nine items. The overall score was determined by calculating the scores of individual reviewers using the 7-point scale (ranging from 1=strongly disagree to 7=strongly agree) for each of the nine items.[10] The total obtained score was computed by adding the scores of all nine items. To convert the total obtained score into a percentage of the maximum possible scale, the following formula was applied[10]:

$$Overall\ score = \frac{Obtained\ score - Minimum\ possible\ score}{Maximum\ possible\ score - Minimum\ possible\ score}$$

wherein,
Maximum possible score = 7 (highest quality) x 9 items x 2 appraisers = 126
Minimum possible score = 1 (lowest quality) x 9 items x 2 appraisers = 18

This CPG received an overall score of **85.2%.** Refer to the following table for the individual scores.

Table 4. Individual reviewer's scores on the domains and items of the AGREE-REX for this CPG on CD

Domains	Items	Appraiser 1	Appraiser 2	Total Domain Score
1. Clinical Applicability	1. Evidence	6	6	36
	2. Applicability to Target Users	6	6	
	3. Applicability to Patients/Populations	6	6	
2. Values and Preferences	4. Values and Preferences of Target User	7	7	50
	5. Values and Preferences of Patients/Populations	6	6	
	6. Values and Preferences of Policy/Decision-Makers	6	6	
	7. Values and Preferences of Guideline Developers	6	6	
3. Implementability	8. Purpose	6	6	

Domains	Items	Appraiser 1	Appraiser 2	Total Domain Score
	9. Local Application and Adoption	6	6	24
	Total Obtained Score			110

The external reviewers both recommend these guideline recommendations for use in the appropriate context and local context. This CPG will be submitted to the Secretary of Health for final approval as a DOH-endorsed CPG or "National CPG".

2.5. Editorial Independence

Funding Source

This CPG on contact dermatitis received financial support from the Department of Health. The DOH neither imposed any conditions nor exerted any influence on the procedures and final recommendations and output.

Management of Conflicts of Interest

Prior to the start of guideline or the formulation of consensus statements, all task force members (including the task force chair, steering committee members, technical coordinator, evidence reviewers, technical writer, and potential consensus panelists) were required to submit a complete disclosure.[11] These included financial, intellectual, or other personal interests that could be perceived by others to influence their judgment on issues addressed by this CPG. The members were also entrusted with disclosing immediate family members' potential COIs. The panelists' disclosures and contributions to the field were reviewed both individually and collectively to create a balanced panel.

The scope of disclosure included a 4-year period. All Task Force members were asked and reminded to avoid any new financial conflicts for a year after the completion of the guideline recommendations.[11]

The Conflict of Interest Review Committee (COIRC) evaluated the COIs of the Task Force members throughout the entire process of developing the guideline. Conflicts that relate directly to the disease, diagnostic techniques, intervention, or management were said to be *primary*; those that do not relate directly were characterized as *secondary*.

The algorithm for COI management is shown in Figure 1. In general, those relationships and activities that are (1) intellectual in nature and lacking direct and indirect financial benefit or (2) unrelated to the content area and focus of the PICO question or recommendation with a company that has no products in that specific topic area are allowed. Where intellectual conflicts exist, relationships should be disclosed to the group of panelists throughout the development process and included in the final publication.

Based on the disclosures, the specific terms of management were set forth by the COIRC for each Task Force member and limited participation in this way: (1) broadcast conflict (manageable with minor constraints), (2) cannot vote (manageable with major constraints), and (3) disallowed relationships and activities. *Manageable with minor constraints* usually refers to intellectual COIs only; members need to declare their COIs (e.g., affiliation with institutions, positions in an organization, authorship in a paper or CPG). *Manageable with major constraints* refers to some intellectual and financial conflicts of interest; panelists cannot vote, but they can share their expertise with the group during the discussion of recommendations. *Disallowed relationships and activities* refer to identified COI whose scope or nature precludes management and sometimes outweighs the content expertise of an individual who is supposed to serve as a full panelist, resulting in disqualification. If the panelist divests of a relationship before participating in the guideline formulation and for a minimum duration of 1 year post-publication, the panelist may not be disqualified.

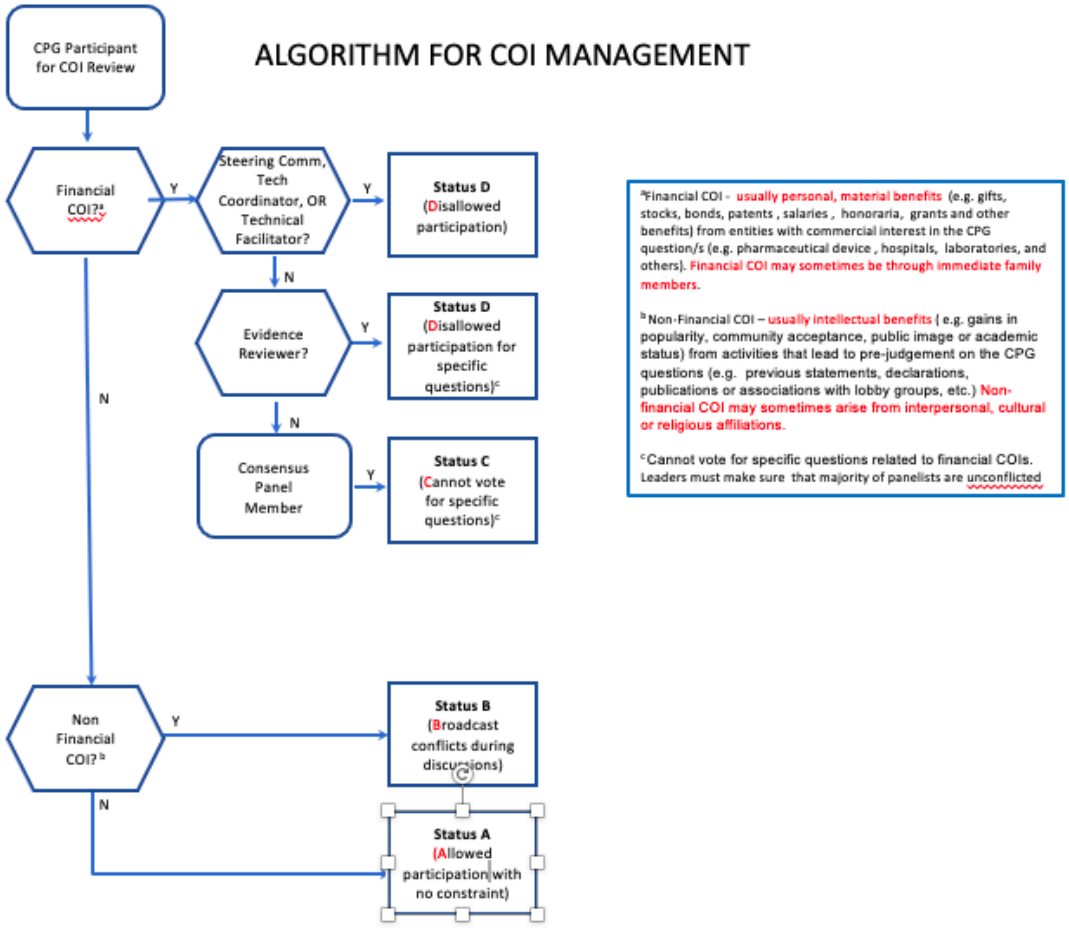

Figure 1. COI management algorithm

Refer to Appendix 8.2 for each member's declaration and management of declared COIs

3. Recommendations and Evidence Summaries

3.1. Should we use patch testing to diagnose allergic contact dermatitis?

Box 3.1. Recommendation: Patch Testing

We suggest the use of patch testing to diagnose allergic contact dermatitis.

(Very low certainty of evidence, Weak)

Key Findings

No studies compared the outcomes of performing a patch test versus no testing among patients with contact dermatitis. No diagnostic accuracy studies for patch testing for contact dermatitis were also found.

Eleven retrospective studies presented the positive rate of patch testing among adult patients with clinically diagnosed contact dermatitis. These rates ranged from 32.3% to 98%.

The certainty of the evidence was very low due to serious indirectness, imprecision, and risk of bias. The study included the pediatric population and those patients who are only suspected of having contact dermatitis, leading to indirectness.

Consensus Panel Issues

Despite the insufficient evidence on the use of patch testing, the panel suggested its utilization in diagnosing allergic contact dermatitis. This recommendation is based on several factors. First, patch testing is currently considered the gold standard for diagnosing this condition. Patch testing has moderate to large benefits since it has been extensively used in diagnosing allergic contact dermatitis and has been guiding clinicians in determining the most appropriate management, according to the panel. Additionally, medical societies have already acknowledged it as a useful tool for accurately diagnosing allergic contact dermatitis, so there has not been much interest in conducting studies on its clinical utility. Furthermore, it is worth noting that international dermatology societies have already endorsed the use of patch tests for the said dermatological condition in their guidelines. Lastly, it is also a mandatory requirement for regular employees seeking compensation for work-related contact dermatitis.

Because the panel also took into consideration the low affordability in private settings and limited accessibility of these tests, particularly in geographically isolated and disadvantaged areas, despite government hospitals providing subsidies for the test and the emergence of telemedicine, the statement garnered a weak recommendation.

Background

Patch testing is the standard procedure for diagnosing contact allergies resulting from type IV hypersensitivity.[12] The patch test is performed by applying allergens under occlusion to the skin under standardized conditions. The results will then be recorded and interpreted by expert dermatologists within a specified period. Diagnostic patch testing is an investigation undertaken on patients with a history of dermatitis to determine whether they have a contact allergy and then evaluate the relation of the contact allergen to their present dermatitis. This test also aids in determining cross–reactions between allergens of similar composition.[12]

Results

Diagnostic Accuracy

No studies compared the outcomes of performing a patch test versus no testing among patients with contact dermatitis. There were no diagnostic accuracy studies for patch testing for contact dermatitis, but 11 retrospective studies[13-23] reported positive rates from patch testing that ranged from 32.4% to 98% among adult patients with clinically diagnosed contact dermatitis.

Most of the studies involved patients in the adult population, with only three studies also including subjects from the pediatric population. All patients across all studies were previously diagnosed clinically with contact dermatitis by dermatologists based on the signs and symptoms they presented. Their records were gathered retrospectively, and these patients were subsequently recalled for having patch testing done. Chemotechnique Diagnostics produced the majority of patch test kits used across all studies (Table 5).

Table 5. Summary of findings: Proportion of patients with positive patch tests in each study on adult patients with clinically diagnosed contact dermatitis

AUTHOR, YEAR	NO. OF PARTICIPANTS	PATCH TEST-POSITIVE	PATCH TEST KIT USED	OTHER OUTCOMES
Akyol et al.,2005	1038	336 (32.4%)	European standard series excluding sesquiterpene lactone mix	
Zug et al., 2008	1497	734 (49%)	North American standard series Additional allergens deemed potentially relevant by the clinician	16% (n = 240) had at least one other relevant allergen not on the NACDG screening series
Li et al., 2004	48	45 (98%)	Modified European standard series	
Garg et al. 2017	58	36 (62.1%)	Indian standard series Indian cosmetic and fragrance series	

			Suspected personal cosmetics	
Lam et al., 2008	2,585	1,415 (54.7%)	European standard series	
Lee et al., 2012	584	240 (41.1%)	27 preservatives commonly found in cosmetics (Chemotechnique Diagnostics) Benzalkonium, thimerosal (Chemotechnique Diagnostics) Chlorphenesin (Serobilogique)	
Kolodziejczyk et al., 2016	79	29 (36.7%)	Specific series not mentioned	
Li et al., 2001	63	54 (85.7%)	Standard series of Beijing Medical University If the patient could supply suspected allergens, patch testing with patients' products	
Oosterhaven et al., 2016	33	14 (42.4%)	European baseline series Shoe series (Chemotechnique Diagnostics) Additional series with allergens specific for shoe factory work	
Wenk et al., 2012	100	88 (88%)	North American standard and fragrance series Patients' personal products	15% are standard series negative and fragrance series positive
Gilissen et al., 2017	15,980	8,942 (56%)	Modified European baseline series and/or other series The products used or their respective ingredients, including topical herbal remedy	In 125 patients (0.8%), a topical herbal remedy was the cause of dermatitis; this represents 1.4% of the contact-allergic patients

Safety Outcome

No adverse events were mentioned in any of the studies previously discussed. However, Cockayne and colleagues[24] reported 17 cases out of 1600 patch-tested patients of "angry back" or "excited skin syndrome," which arises in patch-testing when false-positive reactions occur close to true-positive ones. The reactions found were most commonly due to patch test

allergens regarded as marginal irritants, both in the patients with multiple reactions and those who had an exacerbation of pre-existing dermatitis. They can be due to hyperirritability resulting from pre-existing dermatitis or a fluctuation of humoral and cellular inflammation-modulating phenomena.[24]

Certainty of Evidence

The certainty of evidence was very low due to the serious risk of bias, indirectness, and imprecision. The serious risk of bias stemmed from the methodological design. The study also included the pediatric population and those patients who are only suspected of having contact dermatitis, leading to indirectness. A wide range of reported positive rates resulted in imprecision. Other values, such as sensitivity, specificity, PPV, and NPV, cannot be derived from the studies due to the lack of data.

Recommendations of Other Groups

Table 6. Recommendations of international societies in dermatology regarding the use of patch tests

GROUP	RECOMMENDATION	STRENGTH of RECOMMENDATION & CoE
European Society of Contact Dermatitis (2015)[25]	Patch testing should be considered in patients with the following conditions: • Suspected contact dermatitis, acute or chronic, including dermatitis related to occupational exposures. • Other types of (chronic) dermatitis (eczema) not improving with treatment. • Skin and mucous membrane eruptions (including delayed-type drug eruptions) in which delayed-type hypersensitivity is suspected.	Not stated
German Society of Dermatology (2019)[26]	Dermatitis, seen as the “final common pathway” of widely varying entities, is affected by multiple variables. Diagnosis requires a differentiated approach, usually involving patch testing.	Not stated
British Society of Dermatology (2017)[27]	Offer patients with suspected contact dermatitis a patch test with a baseline series of allergens.	Strong, CoE not stated

CoE: Certainty of evidence

Ongoing Studies

No ongoing study was found.

Evidence to Decision Considerations

Cost

No cost-effectiveness study was found. See Table 7 for the cost of patch tests.

Table 7. Cost of medical procedures and services: Patch test

	PATCH TEST (PUBLIC HOSPITAL)	PATCH TEST (PRIVATE HOSPITAL)
Cost of the Procedure	Php 1,500*	Php 7,000-8,000*
Dermatologist Consultation	-	Php 500-1000

***For a standard series of 30 allergens

Patients' Values and Preferences, Equity, Acceptability, and Feasibility

No formal studies with regard to patients' preferences, equity, acceptability, or feasibility were found.

3.2. Should we use a repeat open application test (ROAT) as an alternative test for patients suspected of allergic contact dermatitis?

Box 3.2. Recommendation: ROAT

Among patients with suspected allergic contact dermatitis, we recommend the use of ROAT as initial or presumptive test to identify potential contact allergens.

(Low certainty of evidence, Strong)

Key Findings

One case-control study compared ROAT and patch testing in diagnosing allergic contact dermatitis in patients with suspected hair dye allergies. Results showed that using the patch test as the reference standard, the sensitivity of ROAT was 83.33% (95% CI 67.19 to 93.63%), and the specificity was 100% (95% CI 76.84 to 100.00%). No adverse effects were reported.

The certainty of evidence was low due to serious indirectness and risk of bias. The risk of bias stems from the unclear selection of participants, unclear blinding of outcome assessors concerning the results of the reference test or the index test, and attrition rate.

No studies on ROAT as an alternative test for patients suspected of allergic contact dermatitis to identify potential allergens, reduce flares, and improve quality of life were found.

Consensus Panel Issues

The recommendation statement was revised from 'alternative test' to 'initial or presumptive test' after the clarification of the dermatologist in the consensus panel that it cannot replace

patch testing in establishing the exact contact allergen that causes the allergic contact dermatitis. Nevertheless, it can identify the potential causative factor of the said dermatological condition. The panel members' discourse also centered on the benefits of using ROAT, particularly for those patients who cannot easily afford patch testing or reside in regions where patch testing services are not readily available. Despite the low certainty of evidence on ROAT, the panel reached a unanimous decision to provide a strong recommendation. This decision was based on several factors: firstly, the test was perceived to be cost-effective and accessible; secondly, patients can carry out the test under the guidance of a dermatologist; thirdly, primary care physicians can be trained to administer the test; and finally, the test demonstrates a high level of sensitivity and specificity with patch testing as a reference standard.

Background

The gold standard in diagnosing allergic contact dermatitis was a combination of history and physical examination, clinical presentation, and a positive patch test.[12] However, the clinical relevance of patch test reactions is hard to evaluate. Thus, an alternative way of evaluating the clinical relevance of a positive patch test is needed.[13]

The repeat open application test[14] was recommended to be used when a patient had a suggestive history of contact allergy with questionable or negative patch test results or for patients with a positive patch test result for a new possible contact allergen.[14] The test was conducted by applying substances to the flexural (volar) aspect of the forearm near the antecubital fossa for up to 2 weeks.[19] Clinically, ROAT is used mostly for formulated products. It is a standardized exposure test mimicking the use of the product or situation.[19] This test can be used as an alternative method to patch testing in detecting allergic contact dermatitis as it is cheaper, imitates daily use situations, and is easier to be conducted.[28]

Results

No direct evidence on ROAT compared to no testing or another test used among patients with contact dermatitis in evaluating other treatment outcomes was found. No study also evaluated the use of ROAT as an alternative test for patients suspected of allergic contact dermatitis to identify potential allergens, reduce flares, and improve quality of life.

One case-control study[28] compared ROAT and patch test in diagnosing allergic contact dermatitis in patients (n = 50) with dermatitis and suspected of having a hair dye allergy. This study included patients aged >12 years who had dermatitis over the head and neck, trunk, or upper limbs and temporally correlated the condition with hair dye use. The patch test used the Indian standard series and followed the International Contact Dermatitis Research Group (ICDRG) guidelines. For ROAT, the patients applied a one-fourth fingertip unit of all brands of hair dye that they have used and Vaseline (negative control) on a marked area of 3 × 3 cm on the volar aspect of the forearm for 1 week.

The study included ten controls with no history of contact dermatitis or atopy. They were also asked to perform ROAT with two different commonly used brands of hair dye (Garnier and Godrej) and Vaseline as a control.

Among the sample of 50 patients who participated in the patch testing procedure, it was observed that a significant proportion (72%) exhibited positive reactions to paraphenylenediamine (PPD) in conjunction with various other allergens, including parthenium, nickel sulfate, nitrofurazone, thiuram mix, fragrance mix, colophony, and mercaptobenzothiazole.[28]

Diagnostic Accuracy

Sixty percent (60%) of the 50 patients who had positive reactions to ROAT also tested positive on the patch test.[28] Among the 30 ROAT-positive subjects, 49 positive reactions to different dyes were recorded on day 2 and 11 positive reactions on day 4. The correlation coefficient for ROAT and patch tests was 0.846 ($P < 0.0001$). Using the patch test as the standard test, the sensitivity of ROAT was 83.33% (95% CI 67.19 to 93.63%), and the specificity was 100% (95% CI 76.84 to 100.00%). All controls tested negative for ROAT. A significant difference was found between the controls and the cases ($P < 0.001$).[28] Table 8 shows the summary of findings on ROAT's diagnostic accuracy.

Table 8. Summary of findings: Sensitivity and specificity of ROAT as compared to a patch test (reference standard)

BASIS (NO. and TYPE of STUDY, NO. OF PARTICIPANTS)	SENSITIVITY (95% CI)	SPECIFICITY (95% CI)	ESTIMATE OF EFFECT PER 1000 TESTED		CERTAINTY OF EVIDENCE
1 case-control, n = 50	0.83 (0.67-0.94)	1.00 (0.77-1.00)	32 (26 to 37) true positives	0 (0 to 223) false positives	Low
			961 (738 to 961) true negative	7 (2 to 13) false negative	

Based on the study of Xue et al. (2022)[2], we used the prevalence of 3.9% to estimate the probability of correct diagnosis in 1000 people with a low probability of having suspected allergic contact dermatitis. Out of 1000 people, 32 will have a positive result and 968 will have a negative result. Among the 32 people who tested positive, 100% will have a true positive test result, and none will have a false positive result. Meanwhile, among those who tested negative, 99% (961/968) will have a true negative result and 1% (7/968) will have a false negative result or incorrect diagnosis.

Safety Outcomes

No adverse effects were reported in the study.[28]

Certainty of Evidence

The certainty of evidence was low due to indirectness and serious risk of bias. The risk of bias stems from the unclear selection of participants, unclear blinding of outcome assessors concerning the results of the reference test or the index test, and attrition rate.

Recommendations of Other Groups

Table 9. Recommendations of other professional membership bodies regarding the use of ROAT

GROUP	RECOMMENDATION	STRENGTH of RECOMMENDATION & CoE
The European Society of Contact Dermatitis (2015)[25]	Patch testing should be considered in patients with suspected contact dermatitis, acute or chronic, including dermatitis related to occupational exposures. The ROAT is used to clarify the relevance of selected positive and doubtful patch test reactions by testing (leave-on) cosmetics, topical drugs, and other suitable formulations.	Not stated
American Academy of Allergy, Asthma, & Immunology (AAAAI); the American College of Allergy, Asthma, and Immunology (ACAAI); and the Joint Council of Allergy (2015)[29]	Use the repeated open application test (ROAT) to further evaluate a patient suspected of ACD who exhibits doubtful or negative PT responses, to confirm that the patient is reacting to that particular product or to determine clinical tolerability to new cosmetic products	Moderate, C Evidence[†]
German Society of Dermatology (2019)[30]	A definitive diagnosis will require a confirmation test (ROAT) in particular.	Not stated

CoE: Certainty of evidence
[†]Moderate (strength of recommendation): The recommendation means the benefits exceed the harms (or that the harms exceed the benefits in the case of a negative recommendation), but the quality of evidence is not as strong.
C: Directly based on nonexperimental descriptive studies or extrapolated recommendation from meta-analysis of RCTs, from at least one RCT or quasi-experimental studies

Ongoing Studies

No ongoing study was found.

Evidence to Decision Considerations

Cost

No cost-effectiveness study was found. See Table 10 for the cost of ROAT.

Table 10. Cost of medical procedure and service: ROAT

	ROAT	PATCH TEST (PUBLIC HOSPITAL)	PATCH TEST (PRIVATE HOSPITAL)
Cost of the Procedure	Will depend on the products to be tested Usually, the patient's own product was used	Php 1,500*	Php 7,000-8,000*
Dermatologist Consultation	Php 300-1000	Php 300-1000	Php 300-1000

*For a standard series of 30 allergens

Patients' Values and Preferences, Equity, Acceptability, and Feasibility

No formal studies with regard to patients' preferences, equity, acceptability, or feasibility were found.

3.3. Should patients with suspected contact dermatitis use home remedies and/or over-the-counter topical products to alleviate their symptoms?

Box 3.3. Recommendation: Home remedies and/or OTC topical products

Among patients with suspected allergic contact dermatitis, we recommend against the use of home remedies and/or over-the-counter products.

(Very low certainty of evidence, Strong)

Key Findings

Four randomized controlled trials on the effect of herbal remedies (i.e., astaxanthin, henna, oral whey powder, and tea tree cream) on patients with allergic contact dermatitis were found. The use of astaxanthin, oral whey powder, and tea tree cream did not show any significant difference in alleviating symptoms of allergic contact dermatitis when compared with placebo. Henna cream, on the other hand, was associated with a significant improvement in symptoms of allergic contact dermatitis when compared with placebo. However, this was also associated with a significantly increased risk of skin redness. One RCT comparing tea tree cream with the current standard of treatment (topical corticosteroids) showed no difference in terms of symptom improvement.

The certainty of evidence is very low due to the serious risk of bias, imprecision, and indirectness.

Consensus Panel Issues

The prioritization of the clinical question by most panel members can be attributed to several factors, including the scarcity of topical corticosteroids, the significance of pharmacologic interventions, and the reliance on international organizations despite the lack of substantial evidence regarding the benefits and harms.

While the panel recognized the availability of these remedies, the majority of its members strongly recommended against their utilization or the use of over-the-counter products, citing various factors. First, they held the belief that the potential risks associated with utilizing these products surpassed the uncertain benefits. Second, they believed that the level of certainty of the available evidence was very low. Third, the potential costs incurred from the risks might outweigh any potential savings. Fourth, they pointed out the lack of sufficient data regarding patient preferences. Fifth, patient education aimed at preventing complications could be a more viable approach for managing occupational and chronic dermatitis than the use of these products. Lastly, these home remedies (e.g., Chinese medicine with fragrances) could potentially serve as a contributing factor to the development of allergic contact dermatitis.

Background

The mainstay of pharmacologic treatment of allergic contact dermatitis involves managing the inflammation with topical corticosteroids.[31] However, with prolonged and incorrect use, this treatment presents several side effects such as atrophy, striae, telangiectasia, tachyphylaxis, adrenal suppression, and the like.[31] It has been known that naturopathic and herbal treatment approaches predate modern medicine and the medications we know today. It is of utmost use and value to investigate and prove the efficacy of some of these homemade herbal remedies for allergic contact dermatitis.

Results

Four trials[32-35] examined the effect of herbal remedies (i.e., astaxanthin, henna, oral whey powder, and tea tree cream) among patients who were clinically diagnosed as well as patch test-confirmed to have allergic contact dermatitis. The participants were exposed to different types of home and over the counter remedies (topical henna cream, topical tea tree oil, topical zinc oxide, topical astaxanthin cream, oral whey protein). Three studies compared their intervention (topical henna cream[32], topical astaxanthin cream[33] and oral whey protein[35]) to placebo and one study[34] (topical tea tree oil, topical zinc oxide) compared their intervention to topical corticosteroids.

Outcome measures were DLQI questionnaire, the EASI scores and subjective total improvement assessed by visual analogue scale, and adverse events. Subjective improvement was the outcome in all four studies and adverse events were reported in the studies with henna or tea tree.

Efficacy Outcomes

The difference of using astaxanthin or oral whey powder versus placebo in alleviating symptoms of allergic contact dermatitis is still unclear (Table 11).[33,35] The study yielded inconclusive results for the elicited reactions to hair dye following the pretreated skin with

astaxanthin on day 2 and 7. Henna cream, on the other hand, was associated with significant improvement in symptoms of allergic contact dermatitis when compared with placebo.[32] However, this was also associated with a significantly increased risk for skin redness. One RCT comparing tea tree oil or zinc oxide with the current standard of treatment (clobetasone butyrate) showed inconclusive evidence in terms of symptom improvement.[34]

Table 11. Summary of findings: Use of herbal medicines or home remedies versus placebo or clobetasone for improvement of symptoms of allergic contact dermatitis

COMPARISONS	BASIS (NO. and TYPE of STUDY, NO. OF PARTICIPANTS)	EFFECT ESTIMATE	95% CI	INTERPRETATION	CERTAINTY OF EVIDENCE
Henna vs placebo	1 RCT n = 74	RR 5.50	1.31, 3.19	Benefit	Very Low
Astaxanthin vs placebo	1 RCT n = 24	RR 1.40	0.61, 3.19	Inconclusive	Very Low
Oral whey vs placebo	1 RCT n = 35	RR 1.48	0.75, 2.92	Inconclusive	Very Low
Zinc oxide vs clobetasone	1 RCT n = 21	RR 2.25	0.82, 6.18	Inconclusive	Very Low
Tea tree oil vs clobetasone	1 RCT n = 21	RR 1.29	0.59, 2.81	Inconclusive	Very Low

Safety Outcomes

Skin burning was less common in the henna group (9/28 participants) compared to the placebo group (3/34 participants), but this was not statistically significant (*P* = 0.052). On the other hand, in the placebo group of the henna study, some patients complained about worsening of dermatitis symptoms such as skin overmoistening and fragility.[32]

Moreover, skin redness significantly increased in the henna group (*P* value < 0.001). Tea tree oil at 50% concentration was applied to fifteen patients. As this concentration induced some redness in several patients, a concentration of 20% was administered to the remaining six patients.

The details of these findings on the safety of using henna versus placebo and tea tree oil versus clobetasone are shown in Table 12.

Table 12. Summary of findings: Safety of using herbal medicines or home remedies versus placebo or clobetasone

COMPARISONS	BASIS NO.AND TYPE OF STUDIES, NO. OF PARTICIPANTS)	EFFECT ESTIMATE	INTERPRETATION	CERTAINTY OF EVIDENCE
Henna vs. placebo	1 RCT, n = 74	Significantly more reports of erythema in the henna group	Harm	Very Low

Henna vs. placebo	1 RCT, n = 74	Skin burning was less common in the henna group (9/28 subjects) compared to the placebo group (3/34 subjects)	Inconclusive	Very Low
Tea tree oil vs.clobetasone	1 RCT, n = 21	Stat. insignificant reports of skin redness with 50% concentration on several patients	Inconclusive	Very Low

The various negative effects associated with topical application of pure henna were collated and listed in a separate evaluation by de Groot et al. that covered trials since the 1980s.[36] The adverse effects involved both the adult and pediatric age ranges who presented with signs and symptoms of contact dermatitis, from localized swelling, burning, pruritus, erythema, and edema to bullous eruptions and generalized contact dermatitis reactions to the topical agent applied. Various studies in the systematic review reported bullous eruption (n = 1 study), erythema and edema (n = 3 studies), clinically diagnosed ACD (n = 13 studies), and generalized ACD (n = 1 study) as adverse effects of topical pure henna.[36]

Certainty of Evidence

The overall certainty of evidence is very low due to the serious risk of bias, imprecision, and indirectness.

Recommendations of Other Groups

Table 13. Recommendations of other professional membership bodies regarding use of home remedies for suspected allergic contact dermatitis

GROUP	RECOMMENDATION	STRENGTH of RECOMMENDATION & CoE
British Guidelines[27]	No stated recommendation on the use of herbal medicine or home remedies	N/A
German Guidelines[26]	No stated recommendation on the use of herbal medicine or home remedies	N/A

Evidence to Decision Considerations

Cost

No cost-effectiveness study was found. See Table 14 for the cost of study-listed home remedies that are available in the Philippines.

Table 14. Cost of available home remedies in the studies

Item	Treatment Price per item

Topical Corticosteroids	Php 200-500 per 5cg tube
Topical Henna	Php 100-200 per 100 g tube
Topical Astaxanthin	Php 60-200 per 20-50g tube
Whey powder	Php 3500 per 2.5 kg tub
Topical Tea tree cream	Php 100-500 per 30-100ml container

Patients' Values and Preferences, Equity, Acceptability, Feasibility

No formal studies with regard to patients' preferences, equity, acceptability, or feasibility were found.

3.4. Among patients with contact dermatitis, should we recommend patient and/or family education versus none to improve outcomes?

Box 3.4. Recommendation: Patient/family education

Among patients with contact dermatitis, we recommend the provision of patient education.

(Moderate certainty of evidence, Strong)

Key Findings

No RCT was found that specifically addressed the clinical question. However, three RCTs investigated the effect of multidisciplinary interventions, including patient education, among patients with hand eczema.

Three RCTs were included in the quantitative analysis for the outcome of quality of life, which showed benefits for those in the patient education group. Pooled results from two RCTs showed improvement in symptoms among patients who received patient education versus patients who received the usual care.

All studies had a risk of bias as there were issues with allocation concealment, blinding, and attrition. The risk of bias contributed to the downgrading of the evidence to moderate certainty for outcomes, such as improvement in quality of life and symptoms.

Consensus Panel Issues

The statement was strongly recommended with a unanimous decision due to its feasibility and the moderate certainty of the evidence on benefits. The panel perceived the improvements in quality of life and symptoms as substantial, outweighing any potential negative effects. The panel also posited that the inclusion of patient education as a component of management strategies for patients has an impact on reducing the incidence of occupational contact dermatitis and increasing equity and cost savings.

Background

Patient and family education is part of the general management of any illness or disease. Health education and counseling by dermatologists are provided to patients with suspected occupational skin disorders through an insurance provider in Germany to help decrease the burden of illness and related societal and economic costs.[37] In the Philippines, although the physician educates patients, no formal study has been done to investigate the effect of individual and/or family education on contact dermatitis.

Results

No RCT was found that specifically addressed the clinical question. However, three RCTs investigated the effect of multidisciplinary interventions, including patient education, among patients with hand eczema in Denmark.[38-40]

All studies included individual counseling[38-40] regarding work-related skin-protective behavior[40], assessment-based skin care[38,39], or general skin care[38]. Other interventions in the experimental group included alternating lectures and workshops about skin-protective behavior, a pamphlet with information from the course (e.g., allergens, irritants, use of personal protective equipment and other protective behavior, rules and rights during an occupational injury, or a telephone hotline to repeat information from the course as needed)[40], patient self-management book or support from an intervention team of nurses or other trial participants[39], and work and domestic-related exposure assessments[38]. The comparator was medical examination done by a general practitioner and dermatologist[38,40] and treatment of dermatologic conditions[38-40], which may include an information video about hand eczema as a supplement to the oral and written information given by the dermatologist.[39]

Efficacy Outcomes

The outcomes measured included quality of life and severity of symptoms. Quality of life was based on the dermatology life quality index (DLQI), which is a validated 10-item questionnaire with a total score ranging from 0 to 30 points; the scores for each question are summed. The higher the score, the poorer the quality of life. It is a quality-of-life instrument designed for skin diseases in general, as no QoL instrument is specifically designed for people with hand eczema. Clinical severity was measured using the hand eczema severity index (HECSI) scores. This validated scoring system grades the intensity of erythema, induration, papules, vesicles, fissures, scaling, and edema for five areas of each hand (fingertips, fingers excluding the tips, palms, back of hands, wrists) on a scale from 0 to 3, with the scores added up for each of the areas. The extent of affected skin in each area is graded from 0 to 4. The intensity and extent of the eczema are multiplied, and the total score ranges from 0 to 360 (the higher the score, the more symptoms are present).

Three RCTs reported significant improvements in QoL for those in the patient education group compared to those in the usual care group (Table 15). Pooled results from two RCTs also showed improvement in symptoms among patients who received patient education versus patients who received usual care.

Table 15. Summary of findings: Effects of education in skin care vs. no education

CLINICAL OUTCOMES	BASIS (NO. AND TYPE OF STUDIES, TOTAL PARTICIPANTS)	EFFECT SIZE (MEAN DIFFERENCE)	95% CONFIDENCE INTERVAL	INTERPRETATION	CERTAINTY OF EVIDENCE
Quality of Life	3 RCTs n = 523	-1.05	-1.65, -0.45	Benefit	Moderate
Severity of symptoms	2 RCTs n = 245	-3.55	-4.93, -2.16	Benefit	Moderate

Certainty of Evidence

The overall certainty of evidence was downgraded to moderate for both outcomes (quality of life and severity of symptoms) due to a serious risk of bias. The serious risk of bias came from the lack of participant blinding and unclear outcome assessor blinding.

Recommendations of Other Groups

Table 16. Recommendations of other professional membership bodies regarding patient education among patients with contact dermatitis

GROUP	RECOMMENDATION	STRENGTH of RECOMMENDATION & CoE
British Association of Dermatologists [27]	Educational programs may help with secondary prevention and outcomes for chronic occupational contact dermatitis.	Not stated
Joint Task Force on Practice Parameters (Contact Dermatitis): American Academy of Allergy, Asthma & Immunology, American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma & Immunology [29]	The education of the workers with ACD or ICD should include prognosis and information that their disease may persist and need long-term management even after treatment and workplace modifications.	Moderate; C Evidence†
Ontario Agency for Health Protection and Promotion (Public Health Ontario) [41]	Recommendation for Skin Care Programs (Including Education) in Occupational Contact Dermatitis Employers should provide ongoing education, training, information, resources, and products that will reduce the incidence and prevalence of occupational contact dermatitis in healthcare workers. A multifaceted hand hygiene program is recommended to effect behavior change. The program should include: targeted and sustained education and training on hand hygiene best practices; a hand care program with education on skin self-screening and reporting; direction for appropriate selection and use of gloves, emollient hand creams and lotions; and provision of ready access to emollient hand creams and lotions, hand hygiene products and appropriate gloves.	IIA‡

CoE: Certainty of evidence

†**Moderate** (strength of recommendation): The recommendation means the benefits exceed the harms (or that the harms exceed the benefits in the case of a negative recommendation), but the quality of evidence is not as strong. **C**: Directly based on nonexperimental descriptive studies or extrapolated recommendation from meta-analysis of RCTs, from at least one RCT or quasi-experimental studies

‡**II**:Evidence from at least one-well designed clinical trial without randomization, **A**: Recommendations must be followed in all healthcare settings. The benefits outweigh the risks.

Evidence to Decision Considerations

Cost

No cost-effectiveness study was found.

Patients' Values and Preferences, Equity, Acceptability, Feasibility

No formal studies with regard to patients' preferences, equity, acceptability, or feasibility were found.

3.5. Among adult patients with contact dermatitis, should we use topical corticosteroids and emollients or barrier creams, as compared to topical corticosteroids alone to improve outcomes?

Box 3.5. Recommendation: Emollients

Among adult patients with contact dermatitis, we recommend the use of emollient or barrier cream as an adjunct to topical corticosteroids.

(Low certainty of evidence, Strong)

Key Findings

One randomized controlled trial (n = 63) on using fluocinolone 0.025% ointment and colloidal oatmeal 1% cream versus fluocinolone 0.025% ointment and base cream among patients with irritant contact dermatitis was identified. The results showed that symptom improvement using the hand eczema severity index (HECSI) and pruritus visual analog scale (VAS) showed statistically significant improvement in the intervention group versus a placebo group. The overall certainty of the evidence was low.

Consensus Panel Issues

The consensus panel was unanimous that it was important to compare using topical corticosteroids with and without emollients or barrier creams. All panel members except for one believed that the evidence presented moderate to large benefits (i.e., improvement in endpoints such as symptoms, pruritus, and QoL), and the majority perceived little concern for safety issues like burning sensation and itching. Other than the physiological benefits, the reasons for recommending the combined intervention were the feasibility of the recommendation and the translation of the improvement in skin condition into higher levels of self-esteem and work productivity among the patients with contact dermatitis.

Despite the apparent high to moderate costs, the panel heavily weighed the evidence of benefits. Cheaper alternative moisturizers and government's assistance were also thought to decrease the likely financial impact on patients and equity issues. Due to the aforementioned points, the panel strongly recommends using emollients or barrier creams as an adjunct to

topical corticosteroids, despite the overall low certainty of evidence.

Background

The management of a disrupted skin barrier is an area of consideration due to its association with allergy, atopic, and contact dermatitis. Repairing the skin barrier is a potential strategy for addressing this issue.[42]

Moisturizers help facilitate skin barrier repair and preserve skin integrity and function.[43] The term moisturizer has often been used synonymously with emollient. An emollient is a substance that helps soothe, soften, and increase moisture levels, particularly in the skin.[44] Others describe that moisturizer ingredients can be categorized into humectants, emollients, or occlusives. The term barrier repair cream can apply to any of the terms above. Humectants attract and bind water (e.g., urea, glycerin, hyaluronic acid, and polysaccharides). Emollients form an occlusive oil film on the stratum corneum, decreasing transepidermal water loss (e.g., lanolin, mineral oil, ceramide, dimethicone, polysaccharides, flavonoids, and lipids). While occlusives form a barrier to prevent water evaporation or reduce transepidermal water loss and are heavier than emollients (e.g., petroleum jelly, Aquaphor, lanolin, silicone, wax).[45]

According to the Institute for Quality and Efficiency in Health Care, it is important to continue using moisturizing products on the skin during treatment with steroids.[46] They recommended waiting about 15 minutes between applying a topical corticosteroid and applying the moisturizing product for the steroid to be absorbed properly.[46] On the other hand, there is no real consensus on the timing of applying emollients and topical steroids. There are no published controlled studies that have investigated this issue.[47]

Results

One randomized, double-blind, placebo-controlled trial (n = 63) examined the effects of using fluocinolone 0.025% ointment plus colloidal oatmeal 1% cream versus a control group with fluocinolone 0.025% ointment and base cream among adult patients clinically diagnosed with irritant contact dermatitis.[48] The base cream lacks the active ingredient of colloidal oatmeal, which has emollient properties. The participants were randomized into intervention (n = 32) and control (n = 31) groups. However, only 50 patients completed the study (24 in control, 26 in intervention). The outcome measures in the study were the HECSI, pruritus VAS, quality of life, and adverse effects. Only the 6-week outcome data on the HECSI and pruritus VAS are considered for this review.

The study had a drop-out rate of 21% (13/63) due to non-adherence to treatment (2 patients in intervention, 4 in control), non-tolerance of adverse events (1 in intervention and control), and loss to follow-up (3 patients in intervention, 2 in control). Based on the Risk of Bias (ROB) tool, there is a high risk of bias due to incomplete outcome data and selective outcome reporting.

Efficacy Outcomes

The results showed that symptom improvement using the HECSI and pruritus VAS showed statistically significant improvement in the intervention group versus the placebo group. The

mean difference between the intervention and control groups in HECSI at week 6 was -30.4 (-24.23 to -36.57). It indicates that the patients in the intervention group had a less severe skin condition (30 points lower in HECSI) when compared to those in the control group at week 6. The mean difference in pruritus VAS at week 6, on the other hand, was -3.16 (-2.74 to -3.58), indicating that the intervention group reported less itching (3 units lower in VAS) when compared to the control group (Table 17).

The mean difference in QoL measured by DLQI at week 6 was -5.34 (-0.01 to -10.69), showing that the patients who received fluocinolone 0.025% ointment plus colloidal oatmeal cream perceived that their lives were less severely affected (5 points lower in DLQI) by their skin disease when compared to those who received fluocinolone 0.025% ointment plus base cream.

Table 17. Summary of findings: Efficacy outcomes on the use of fluocinolone 0.025% ointment and colloidal oatmeal cream versus fluocinolone 0.025% ointment and base cream

OUTCOME	BASIS (NO. AND TYPE OF STUDY, NO. OF PARTICIPANTS)	EFFECT ESTIMATE	95% CONFIDENCE INTERVAL	INTERPRETATION	CERTAINTY OF EVIDENCE
Improvement of signs (HECSI) Week 6	1 RCT n = 50	MD -30.4	-24.23, -36.57	Benefit	Moderate
Improvement of symptoms (pruritus-VAS) Week 6	1 RCT n = 50	MD -3.16	-2.74, -3.58	Benefit	Moderate
QOL (DLQI)- Week 6	1 RCT n = 50	MD -5.34	-0.01, -10.69	Benefit	Moderate

Safety Outcomes

Results in the study revealed 3 out of 31 (9.7%) patients in the control group and 4 out of 32 (12.5%) patients in the intervention group reported adverse events. Table 18 shows the risk ratios for adverse events.

Table 18. Summary of findings: Safety outcomes on the use of fluocinolone 0.025% ointment and colloidal oatmeal cream versus fluocinolone 0.025% ointment and base cream

OUTCOME	BASIS (NO. AND TYPE OF STUDY, NO. OF PARTICIPANTS)	EFFECT ESTIMATE	95% CONFIDENCE INTERVAL	INTERPRETATION	CERTAINTY OF EVIDENCE
Adverse events	1 RCT n = 50	RR 1.29	0.31, 5.31	Inconclusive	Low
Adverse event that led to withdrawal	RCT n = 50	RR 0.97	0.06, 14.82	Inconclusive	Low

Certainty of Evidence

The overall certainty of the evidence was low due to the serious risk of bias and imprecision. There was a high risk of bias for outcome parameters due to the significant drop-out rate of more than 20%. Imprecision arose from safety outcomes with wide confidence intervals.

Recommendations of Other Groups

Table 19. Recommendations of other professional membership bodies regarding the use of emollients or barrier creams among patients with contact dermatitis

GROUP	RECOMMENDATION	STRENGTH of RECOMMENDATION & CoE
British Association of Dermatologists[27]	Consider skin care and skin protection creams when preventing occupational dermatitis.	Weak, Low CoE
German Contact Allergy Group (DKG) of the German Dermatology Society (DDG), the Information Network of Dermatological Clinics (IVDK), the German Society for Allergology and Clinical Immunology (DGAKI), the Working Group for Occupational and Environmental Dermatology (ABD) of the DDG, the Medical Association of German Allergologists (AeDA), the Professional Association of German Dermatologists (BVDD), and the DDG[26]	Basic moisturizing agents to promote skin barrier regeneration and protect against recurrence, combined with the use of skin protection creams, are beneficial when individually tailored to skin status and skin exposure.	Moderate, Low CoE

CoE: Certainty of evidence

Evidence to Decision Considerations

Cost

No cost-effectiveness study was found. See Table 20 for the cost of emollients.

Table 20. Cost of treatment in the country: emollients or barrier creams

Treatment	Cost
Fluticasone propionate ointment	Php 305.75/ 5 grams (tube)
Oatmeal cream	Php 1,200- 1,300/ 311 grams (jar)
Oatmeal lotion	Php 300-350/ 354 mL (bottle)

Patients' Values and Preferences, Equity, Acceptability, Feasibility

No formal studies with regard to patients' preferences, equity, acceptability, or feasibility were found.

3.6. Among individuals with contact dermatitis, should topical calcineurin inhibitors be used versus topical corticosteroids?

Box 3.6. Recommendation: TCIs

Among adult patients with contact dermatitis, we suggest against the use of topical calcineurin inhibitors over topical corticosteroids as pharmacologic therapy.

(Very low certainty of evidence, Weak)

Key Findings

Four randomized controlled trials were found on topical calcineurin inhibitors (TCI) compared with topical corticosteroids (TCS) in contact dermatitis. Studies showed that the two groups had no significant difference in visual and inflammatory outcomes. Harms or adverse events regarding using either TCI or TCS, if any, were not reported. Quality of life was not reported in any of the studies.

Most of the studies have serious risk of bias, imprecision, and indirectness. Due to these factors, the studies were assessed to have low to very low certainty of evidence.

Consensus Panel Issues

The panel prioritized this clinical question because there are some variations in practice. Certain dermatologists opt to use topical calcineurin inhibitors as steroid-sparer for those patients with prolonged use of topical corticosteroids who have a higher risk of skin atrophy or telangiectasia, particularly when the face or other thin areas are involved. Panel members who are experts in dermatitis explained that there are other treatments for contact dermatitis, but these two drugs in question are the more basic and available therapeutic options. Topical corticosteroids are used to relieve inflammation, and TCIs are administered when the flare-up has been controlled, especially for allergic contact dermatitis.

The CP suggested against the use of TCIs over TCS due to the insufficient evidence on benefit and the perceived small to moderate harm based on the evidence of an elevated risk of skin burning and pruritus when TCIs were compared to TCS. Other considerations that were taken into account were the repercussions of recommending TCIs, which are a more costly treatment. This may result in a greater financial burden and potential equity concerns for patients with contact dermatitis.

Background

Calcineurin inhibitors are immunosuppressants used in the management of certain autoimmune conditions. Topical forms, such as tacrolimus 0.1% and pimecrolimus 1%, have been US FDA-approved for use as second-line treatment of very severe atopic dermatitis involving a large body surface area among adults and mild to moderate atopic dermatitis, respectively.[49]

In contact dermatitis, it is known that topical corticosteroids are limited by their local and systemic side effects. Topical calcineurin inhibitors may be offered as steroid-sparing options for long-term topical treatment of allergic contact dermatitis.[49]

Results

Four randomized controlled trials (n = 124) were found on topical calcineurin inhibitors (TCI) compared with TCS in allergic contact dermatitis. All trials included adults with experimentally induced contact dermatitis in patches, 2 using nickel[50,51], 1 using various contact allergens[52], and 1 with diphenylcyclopropenone[53]. The areas applied were the upper extremities, including the hands and back. Each patient was his own control in all studies.

For the topical calcineurin inhibitors, two studies used only tacrolimus ointment in 0.1% concentration[50,52], while the others used both tacrolimus 0.1% and pimecrolimus 1%[51,53]. Topical corticosteroids were of high potency (clobetasol and betamethasone) and medium potency (hydrocortisone, triamcinolone, and mometasone).

The shortest and longest observation period from induction of contact dermatitis to the end of the study was from 2 days[50] to 90 days [52].

The clinical evaluation involved the use of various visual scoring systems and reported different units: three-point scoring per manifestation (erythema, papulation, vesiculation, and blistering), expressed in means and standard deviations[51]; a five-point Visual Assessment Scoring System per clinical manifestation (erythema, infiltration, vesiculation, desquamation, cracks, and itching)[52]; and a modified version of the International Contact Dermatitis Research Group clinical scoring system, reported in median scores[53]. One also used the proportion of patients who improved by the end of the study.[51]

Other parameters used were the erythema index by reflectance spectrophotometry[50] and skin thickness measured using skin ultrasound as a basis for improvement in inflammation.[53]

Efficacy Outcomes

All studies were inconclusive with regard to the advantage of treating contact dermatitis with either of the two TCIs (tacrolimus 0.1% or pimecrolimus 1%) over topical corticosteroids based on various visual scoring systems and skin thickness using skin ultrasound (Table 21). Quality of life, an outcome of interest, was not reported in any of the trials.

Table 21. Summary of findings: Comparison of the efficacy of topical calcineurin inhibitors vs. topical corticosteroids for contact dermatitis

EFFICACY OUTCOMES	BASIS (NO. AND TYPE OF STUDIES, NO. OF PARTICIPANTS)	EFFECT ESTIMATE	95% CONFIDENCE INTERVAL	INTERPRETATION	CERTAINTY OF EVIDENCE
Proportion of patients with improved visual scores[51]	1 RCT Pimecrolimus N = 42 Tacrolimus N = 42	Pimecrolimus RR 0.8 Tacrolimus RR 0.93	Pimecrolimus 0.43, 1.5 Tacrolimus 0.52, 1.68	Inconclusive	Very Low
Lesions with improved visual scores[52]	1 RCT Tacrolimus only N = 30	The mean scores from baseline to day 90 of each clinical parameter (erythema, infiltration, vesiculation, desquamation, cracks, and itching) for visual assessment between tacrolimus and mometasone did not differ at the end of the study. Neither of the two succeeded in the elimination of all parameters at the same time.		Inconclusive	Very Low
Percent reduction in inflammatory thickness based on skin ultrasound[53]	1 RCT Pimecrolimus Tacrolimus N = 45	At 72 h: pimecrolimus -13% (NS), tacrolimus by -26.5% ($P < 0.01$), hydrocortisone, butyrate, betamethasone, and clobetasol -15.3% ($P < 0.01$)		Inconclusive	Low
Lesions with improved visual score based on medians[53]	1 RCT Tacrolimus only N = 45	Median Scores (p-value) at 48 h for Diphenylcyclopropenone (DPCP)-induced reactions: Positive DPCP 3 Pimerolimus 3 ($P < 0.05$) Tacrolimus 0 ($P < 0.001$) Hydrocortisone butyrate 2 ($P < 0.001$) Betamethasone valerate 2 ($P < 0.001$) Clobetasol propionate 2 ($P < 0.001$)		Inconclusive	Very Low
Lesions with improved visual score based on visual scale and reflectance spectrophotometry[50]	1 RCT Tacrolimus only N = 44	SMD -0.39	-0.83, 0.03	Inconclusive	Low

Safety Outcomes

Harms or adverse events regarding using either TCI (tacrolimus 0.1% or pimecrolimus 1%) or TCS, if any, were not reported in these trials. However, two meta-analyses on atopic dermatitis showed that compared with topical corticosteroids (hydrocortisone butyrate 0.1% and hydrocortisone acetate 0.1%), tacrolimus 0.1% had a higher risk of skin burning and pruritus

(Table 22). Similarly, pimecrolimus 1% also resulted in a higher risk of skin burning when compared with topical corticosteroids (betamethasone valerate 0.1% or triamcinolone acetonide 0.1% for trunk and limbs and hydrocortisone acetate for face and neck). Trials on tacrolimus 0.1% or pimecrolimus 1% versus topical corticosteroids showed an inconclusive effect in terms of skin infection among patients with AD.

Table 22. Summary of findings: Comparison of safety of topical calcineurin inhibitors versus topical corticosteroids for contact dermatitis

SAFETY OUTCOMES	BASIS (NO. AND TYPE OF STUDIES, NO. OF PARTICIPANTS)	EFFECT ESTIMATE	95% CONFIDENCE INTERVAL	INTERPRETATION	CERTAINTY OF EVIDENCE
Tacrolimus 0.1% vs. Hydrocortisone butyrate 0.1% and Hydrocortisone acetate 0.1%					
Skin Burning	4 RCTs N = 1800	RR 3.2	2.72, 3.75	Tacrolimus more harmful	Low
Pruritus	3 RCTs N = 1720	RR 1.41	1.11, 1.80	Tacrolimus more harmful	Low
Skin Infection	3 RCTs N = 1710	RR 1.10	0.80, 1.52	Inconclusive	Low
Pimecrolimus 1% vs. Betamethasone valerate 0.1% or Triamcinolone acetonide 0.1% (trunk and limbs) and Hydrocortisone acetate (face and neck)					
Skin Burning	2 RCTs N = 746	RR 2.28	1.60, 3.24	Pimecrolimus more harmful	Low
Skin Infection	1 RCT N = 658	RR 0.87	0.65, 1.15	Inconclusive	Low

Certainty of Evidence

The overall certainty of evidence on efficacy is very low due to serious risks of bias, indirectness, and imprecision. All the studies involved subjects exposed to TCI and TCS at different sites. There was a risk of contamination. All studies were on experimentally induced dermatitis. The studies had small sample sizes, and the results showed wide confidence intervals, contributing to imprecision. The certainty of evidence on safety, on the other hand, was low due to the serious risk of indirectness and imprecision.

Recommendations of Other Groups

Table 23. Recommendations of other professional membership bodies and research group regarding the use of topical calcineurin inhibitors for contact dermatitis

GROUP	RECOMMENDATION	STRENGTH of RECOMMENDATION & CoE
European Society of Contact Dermatitis, 2021[54]	We suggest tacrolimus ointment for short-term treatment in the management of hand eczema. (Studies based on Tacrolimus vs. Vehicle)	Grade B, Moderate quality
Japanese Dermatological	Tacrolimus ointment is used after topical steroids to maintain remission and is also considered to be effective against inflammation	Grade C1, Level 2 quality

Association Guidelines 2020[55]	symptoms in atopic dermatitis, but in the case of contact dermatitis, careless use should not cloud the decision to eliminate the cause.	
Brod and colleagues (*UpToDate)*[56]	For acute, localized contact dermatitis involving the face or flexural areas, topical tacrolimus may be used until resolution and then taper. For chronic contact dermatitis, intermittent tacrolimus 0.1% ointment or low-potency corticosteroids may be used for the face or flexural areas.	Not stated

Ongoing Studies

No ongoing study was found.

Evidence to Decision Considerations

Cost

No cost-effectiveness study was found. See Table 24 for the cost of TCIs in the country.

Table 24. Cost of treatment: TCIs

Treatment	Estimated Price (Php)
Tacrolimus 0.1% Ointment 10 g tube	803.57 - 3,109.00
Pimecrolimus 1% Cream 10g tube	1,111.00
Clobetasol propionate 0.05% Cream 5g tube	50.21 - 350.00
Betamethasone dipropionate 0.1% 5g tube	41.74 to 357.75
Mometasone furoate 0.1% 5g tube	267.00 to 414.75

Tacrolimus 0.1% and pimecrolimus 1% are applied twice daily in the affected areas for up to 30 days. The dose is decreased to once daily thereafter up to 60 days (based on the longest study duration by Katsarou 2018). A patient whose treatment duration will be 90 days could consume 2 to 4 tubes of any TCI, costing a minimum of PHP 1,607.14 to a maximum of PHP 6,218.00.

Topical corticosteroids are applied twice daily for the first 7 days, then decreased to once daily for about 2 to 3 weeks (depending on the lesion's severity), tapered down to once daily, thrice a week for 2 weeks, and then once daily twice a week until resolution of lesions. A patient whose treatment duration will be 90 days could spend a minimum of PHP 168.00 to a maximum of PHP 2,488.50.

Patients' Values and Preferences, Equity, Acceptability, Feasibility

No formal studies with regard to patients' preferences, equity, acceptability, or feasibility were found.

3.7. Among adults with chronic, recurrent, or recalcitrant contact dermatitis, should we refer to a higher level of care to improve outcomes?

Box 3.7. Recommendation: Higher level of care

We recommend that patients with contact dermatitis who have frequent eruptions, co-existing atopic dermatitis, and those who have severe disease at baseline be referred to a higher level of care.

(Low certainty of evidence, Strong)

Key Findings

No evidence was found comparing the effectiveness of referral versus non-referral of adult patients with chronic, recurrent, or recalcitrant contact dermatitis to a higher level of care (dermatologist or allergologist) to improve outcomes (clinical improvement or resolution of symptoms, number of outpatient consults, quality of life, and adverse events).

Two cohort studies investigated factors associated with poor prognosis in patients with contact dermatitis. Frequent eruptions in the past 12 months and coexisting atopic dermatitis led to unchanged or aggravated severity at 6- and 12-month follow-up, respectively. Severe occupational hand eczema at baseline led to prolonged sick leave and loss of job at 12-month follow-up.

Consensus Panel Issues

Prior to the Delphi, the last round of voting on the strength of recommendation garnered 5 votes in favor of strongly recommending referral to a higher level of care for those with severe contact dermatitis conditions and 2 votes for a weak recommendation. Those who voted for a strong had the following reasons:

1. In a broader sense, the medical expert on severe contact dermatitis valued patients' perspectives based on clinical experience and multiple encounters with severe cases, despite no direct evidence. The panel considered the severity (frequent eruptions, co-existing atopic dermatitis, those who have severe disease at baseline) that has affected occupation and quality of life.
2. One believed that the weak evidence stems from the research gap that is not being tackled yet in the country.
3. Evidence-based medicine is not only based on RCTs but also on patients' values. The panel believes this research gap has not been tackled yet because other diseases are prioritized.
4. The panel considered their role as being adaptable and capable of weighing the evidence from foreign settings and taking into consideration Filipino patients' perspectives, particularly those with severe conditions at the onset.
5. The panel acknowledged that patients should see their primary health provider before going to a specialist. However, they believed that the population in the statement already have chronic conditions with frequent eruptions and might already suffer from

anxiety, poor quality of life, and decreased work productivity with an increased financial burden.

6. Members believed that the patients should not be misdiagnosed at that stage of their condition and subjected to several treatment protocols without determining the root cause of the problem. Specialists may have more clinical experience diagnosing compared to general practitioners.
7. Frequent visits to primary care physicians due to the difficulty of establishing the diagnosis can result in increased financial burden and productivity loss for the patient.
8. Supporting studies are mentioned in the Background of the evidence summary that those specific cases, such as recurrent contact dermatitis, are referred to specialists.
9. Regarding accessibility of services, there are now facilities that can take care of patients with chronic recalcitrant contact dermatitis, including those that provide telemedicine, and the Philippine Dermatological Society has taken the initiative to extend their services across the country, including areas of Benguet, Cebu, and Mindanao.
10. A strong recommendation has the potential to prompt the government to allocate funds for the creation of additional facilities aimed at addressing this condition and improving the healthcare system.

Those who voted for a weak recommendation, on the other hand, argued that:

1. The certainty of evidence supporting the recommendation statement is low. No studies have been done comparing the impact of referring to a higher level of care against not referring or managing by a general practitioner.
2. Based on the experience of a primary care physician, referring to a specialist or higher level of care is challenging for medical practitioners in remote areas.
3. Certain local government units (LGUs) may lack the necessary resources to provide these healthcare services in remote regions. However, telemedicine has the potential to serve as a viable solution.
4. Based on the panel discourse, there is a lack of compelling empirical data; the available information is solely based on the viewpoints of medical professionals. According to one panel member, some foreign countries adhere to evidence-based practices wherein patients are not initially evaluated by a specialist.
5. Recommending the statement would discourage primary care physicians from seeing patients with contact dermatitis and would opt to refer them immediately to a specialist.
6. Patients will incur increased charges if they are sent to a higher level of care based on a strong recommendation.
7. A weak recommendation may compel the government to investigate and rectify this inadequacy of services in the healthcare system.

The statement garnered a strong recommendation due to the aforementioned reasons. In addition, one panel shifted to voting for a strong recommendation after carefully weighing the balance between the benefit and harm of referring the patients to a higher level of care.

Background

Contact dermatitis can result in significant emotional, social, economic, and professional burdens for patients.[57] The pattern and morphology of dermatitis, particularly on the hands and face, are unreliable in predicting a cause and distinguishing atopic/ endogenous dermatitis clearly from irritant or allergic contact or exogenous dermatitis. Furthermore, it is not uncommon for atopic, irritant, and allergic etiologies to coexist, particularly in hand and foot dermatitis.[27] Referral to a higher level of care may be needed for a definitive etiologic diagnosis and a more targeted approach to treatment, which may help reduce the burden of the disease.

Results

No direct evidence compares the effectiveness of referral versus non-referral of adult patients with chronic, recurrent, or recalcitrant contact dermatitis to a higher level of care (dermatologist or allergologist) to improve outcomes (clinical improvement or resolution of symptoms, number of outpatient consults, quality of life, and adverse events).

Two cohort studies investigated factors associated with a poor prognosis in patients with contact dermatitis.[58,59] Both studies were conducted in Denmark and included adult patients with hand eczema. The data could not be pooled because of the differences in exposures and outcome measures. Hald and colleagues (n = 348) investigated the course of contact dermatitis in patients with frequent eruptions (≥ ½ of the time) in the past 12 months at 6 months. In another study (n = 540), the course of contact dermatitis in patients with atopic dermatitis and patients with severe occupational hand eczema at baseline and at 1 year follow-up was investigated.[59]

Factors Associated with Poor Prognosis

Frequent eruptions (≥ ½ of the time) in the past 12 months[58] and coexisting atopic dermatitis at 6- and 12-month follow-up led to unchanged or aggravated severity. Severe occupational hand eczema at baseline led to prolonged (> 5 weeks) sick leave and loss of job at 12-month follow-up. Table 25 shows the summary of findings from the two cohort studies.

Table 25. Summary of findings: Factors associated with poor prognosis in patients with contact dermatitis

OUTCOME	RISK FACTOR	BASIS (NO. AND TYPE OF STUDIES, NO. OF PARTICIPANTS)	EFFECT SIZE (95% CI)	INTERPRETATION	CERTAINTY OF EVIDENCE
Unchanged/ aggravated severity	Frequent eruptions	1 cohort (n = 348)	OR 1.96 (1.1, 3.7)	Positive association	Moderate[a]
	Atopic dermatitis	1 cohort (n = 540)	RR 1.53 (1.1, 2.2)	Positive association	Moderate[b]

Prolonged sick leave	Atopic dermatitis	1 cohort (n = 540)	RR 0.58 (0.2, 1.8)	Inconclusive	Low[b,c]
	Severe OHE at baseline	1 cohort (n = 540)	RR 5.29 (1.6, 17.7)	Positive association	Low[b,c]
Loss of job	Atopic dermatitis	1 cohort (n = 540)	RR 1.12 (0.2, 5.3)	Inconclusive	Low[b,c]
	Severe OHE at baseline	1 cohort (n = 540)	RR 14.0 (1.9, 102.9)	Positive association	Low[b,c]

OHE: occupational hand eczema. OR: odds ratio. RR: risk ratio
[a]Large drop-out for the outcome on severity assessment (n = 312), no adjustment for other prognostic factors
[b]No adjustment for important prognostic factors and concerns on outcome criteria used
[c]Wide confidence interval

Certainty of Evidence

The overall certainty of evidence is low. Both studies had a serious risk of bias due to the large attrition rate and the failure to perform statistical adjustments for other prognostic factors. One study also had serious imprecision issues with prolonged sick leave and loss of job outcomes due to a wide confidence interval.[59] These led to the downgrading of evidence to moderate for unchanged or aggravated severity outcomes and low for prolonged sick leave and loss of job outcomes.

Recommendations of Other Groups

Table 26. Recommendations of other groups regarding referring chronic contact dermatitis patients to specialists

GROUP	RECOMMENDATION	STRENGTH of RECOMMENDATION & CoE
Spanish Academy of Dermatology and Venereology (AEDV) 2020[60]	Patients with chronic hand eczema must always be referred to a dermatologist for additional tests and a definitive etiologic diagnosis.	Not stated
Danish Contact Dermatitis Group (DCDG) 2011[61]	It is suggested that if hand eczema has persisted for more than 1 month, the patient should be seen by a dermatologist.	Not stated

Ongoing Studies

No ongoing study was found.

Evidence to Decision Considerations

Cost

No cost-effectiveness study was found. See Table 27 for the cost of patch tests.

Table 27. Cost of treatment or medical services: Referral to a higher level of care

	Dermatologists	Allergologists
Number of a higher level of cares	1,325[a]	146[b]
Consultation fee (PHP)	500-1,500	500-1,500

[a]Camille B. Angeles, MD (Philippine Dermatological Society Secretary), e-mail communication, March 01, 2023
[b]Philippine Society of Allergy, Asthma & Immunology, Inc. Secretariat, e-mail communication, April 03, 2023

Patients' Values and Preferences, Equity, Acceptability, Feasibility

In one prospective cohort study that included 313 inpatient dermatology referrals, 20 (6.3%) of whom were diagnosed with contact dermatitis, referring services were surveyed on their perception of dermatology consultation regarding relevance and the negative impact on patient treatment if dermatology consultation was not available. Two hundred seventy-eight (89%) of the referring services thought that the dermatological consultation was either extremely relevant or important. Out of 313, 180 (58%) believed that it was important as it aided in the diagnosis or treatment of a dermatologic disease that was unrelated to the reason for admission, and 98 (31%) thought that it was extremely relevant as it helped to achieve a diagnosis and/or changed the treatment of the disease that led to admission. Two hundred forty-seven (79%) thought that the unavailability of dermatological consultations would negatively impact patient treatment. Of these, 150 (48%) thought that it would slightly impact patient treatment as the patient would have suffered longer with the dermatologic complaint until an outpatient consultation was available, and 97 (31%) thought that it would negatively impact patient treatment as the systemic disease would not have been diagnosed or a potentially severe dermatologic disease would not have been treated.

3.8. Should we use other modalities such as phototherapy as adjunct treatment among patients with chronic recalcitrant contact dermatitis?

Box 3.8. Recommendation: Phototherapy

Among patients with chronic recalcitrant contact dermatitis, we suggest the use of narrowband phototherapy as adjunct treatment.

(Low certainty of evidence, Weak)

Key Findings

Two randomized controlled trials investigated the effect of phototherapy as an adjunct treatment for patients with chronic recalcitrant contact dermatitis. Phototherapy, particularly narrowband UVB therapy (NB-UVB), showed a significant effect on improving dermatitis symptoms. The mean difference in the mean number of weeks in remission after treatment with NB-UVB therapy compared to placebo was 11.80. The risk of developing adverse events is inconclusive in both comparisons: (1) NB-UVB compared with placebo or no phototherapy; and (2) psoralen plus UVA (PUVA) compared with no phototherapy.

Both studies had serious risk of bias due to concerns about randomization, allocation concealment, and blinding. The risk of bias and indirectness contributed to the low certainty of evidence for the improvement of symptoms.

Consensus Panel Issues

No consensus issues were raised in suggesting the use of narrowband phototherapy as an adjunct treatment. The majority of the panel agreed that the benefits (remission and improvement of symptoms) of phototherapy as an adjunct in treating chronic conditions outweigh the potential risk of developing adverse events and the additional cost. The CP also perceived that improvement in patients' dermatological conditions correlates to increased work productivity and income.

Background

Phototherapy, or ultraviolet therapy, has been used to treat many forms of eczema in adults and children, especially for chronic skin diseases that do not respond to topical treatments.[62,63] It has been shown to have immunomodulatory properties. It has immunosuppressive effects on T-cell function and induces antigen-specific tolerance.[64] Phototherapy has been shown to cause clinical improvement due to its proapoptotic, antipruritic, pro-pigmentary, and anti-fibrotic effects.[65] The most common type of phototherapy used in clinical practice for chronic contact dermatitis and other eczemas is NB-UVB light, although other light options, such as PUVA, are also being used. Psoralens are phototoxic compounds given orally or topically as part of the PUVA treatment. The efficacy and safety of the different types of phototherapy as an adjunct therapy for those with chronic recalcitrant contact dermatitis have been studied.

Results

Two randomized controlled trials[66,67] (n = 75) investigated the effect of phototherapy as an adjunct treatment compared to standard treatment alone among patients with chronic recalcitrant contact dermatitis. Both studies were conducted in Sweden. The participants had chronic recalcitrant hand dermatitis for 2 to 10 years.

The main interventions were NB-UVB therapy (2 RCTs) and PUVA (1 RCT). In one trial[66], the participants were randomized to the NB-UVB or PUVA groups. In the NB-UVB group, the right hand was treated with NB-UVB therapy, and the left hand was not treated with phototherapy. Participants in the PUVA group received PUVA therapy on the left hand and no phototherapy on the right hand.[66] In another trial[67], NB-UVB was used on the hand and whole body. The mean number of treatments with PUVA was 16 (range 8-31), the mean duration of treatments was 44 days (range 16-96), and the mean total PUVA dose was 100J/cm^2 (range 21-329). The mean number of treatments with NB-UVB was 35 (range 26-44), the mean duration of treatments was 93 days (range 69-117), and the mean total NB-UVB dose was 11 J/cm^2 (range 2-27). The frequency of irradiation was three[66] to four times[67] a week.

The comparators for the studies were placebo (filtered light containing no UVB) or no phototherapy. Emollients were continued for all groups.

Outcomes measured in both studies were clearance or improvement of dermatitis, remission in weeks after the last treatment, and adverse events. The improvement of the following factors was assessed by an investigator every three weeks in the study of Rosen: desquamation, erythema, vesiculation, infiltration, and fissures.[66] In the other trial, a clinician assessed the improvement of dermatitis at 16 weeks and on or before 32 weeks of treatment.[67] No study reported on the quality of life.

Efficacy Outcomes

Phototherapy, particularly NB-UVB, showed a significant effect on improving the symptoms of dermatitis (Table 28). Subgroup analysis based on the UV type showed that the NB-UVB therapy resulted in a statistically significant improvement of symptoms. The improvement in symptoms among those who received PUVA therapy was inconclusive.

The mean difference in the mean number of weeks in remission after treatment with NB-UVB therapy compared to placebo was 11.80. This was based on only one RCT where the topical treatments were continued for all groups.[67]

Table 28. Summary of findings: Efficacy of phototherapy among patients with chronic contact dermatitis

OUTCOMES	BASIS (NO. AND TYPE OF STUDIES, NO. OF PARTICIPANTS)	EFFECT SIZE	95% CI	INTERPRETATION	CERTAINTY OF EVIDENCE
Improvement of symptoms	2 RCTs, N = 75	RR 1.39	1.10, 1.75	Benefit	Low
Subgroup: NB-UVB	2 RCTs n = 47	RR 1.47	1.05, 2.06	Benefit	Low
Subgroup PUVA	1 RCT n = 28	RR 1.26	0.94, 1.69	Inconclusive	Very Low
Remission (in weeks after the last treatment)	1 RCT N =15	MD 11.80 weeks	7.80, 15.80	Benefit	Low

Safety Outcomes

The risk of developing adverse events with phototherapy is higher than with placebo or no phototherapy (Table 29). However, in the subgroup analysis both comparisons were inconclusive: (1) NB-UVB compared with placebo or no phototherapy and (2) psoralen plus UVA (PUVA) compared with no phototherapy. The participants did not experience who received NB-UVB or PUVA therapy any serious adverse events.

Table 29. Summary of findings: Safety of using phototherapy among patients with chronic contact dermatitis

OUTCOMES	BASIS (NO. AND TYPE OF STUDIES, NO. OF PARTICIPANTS)	EFFECT SIZE	95% CI	INTERPRETATION	CERTAINTY OF EVIDENCE
Adverse Events	2 RCT N = 75	RR 19.0	1.16, 312.42	Harm	Very Low
Subgroup NB-UVB	2 RCT n = 47	RR 5.0	0.26, 96.59	Inconclusive	Very Low

Subgroup PUVA therapy	1 RCT n = 28	RR 15.0	0.94, 239.81	Inconclusive	Very Low

Certainty of evidence

The certainty of evidence for efficacy is low due to the serious risk of bias and indirectness. Both studies had a serious risk of bias due to concerns about randomization, allocation concealment, and blinding. Indirectness stemmed from including participants with other types of chronic recalcitrant hand dermatitis, although the majority had allergic contact dermatitis. The certainty of evidence for the subgroup analysis of the improvement of symptoms with PUVA therapy was further downgraded to very low due to the serious risk of bias, indirectness, and imprecision.

Recommendations of Other Groups

Table 30. Recommendations of other professional membership bodies regarding the use of phototherapy for chronic contact dermatitis

GROUP	RECOMMENDATION	STRENGTH of RECOMMENDATION & CoE
British Association of Dermatologists' guidelines for the management of contact dermatitis (2017)[27]	Consider PUVA therapy for treating patients with chronic hand eczema.	Weak, CoE not stated
Korean Society of Contact Dermatitis and Skin Allergy (Korean Consensus Guideline Working Group - Diagnosis and Treatment of Chronic Hand Eczema)[68]	The guideline working group recommends phototherapy as an auxiliary treatment in addition to other topical or systemic treatments.	Not stated
European Society of Contact Dermatitis (ESCD): Guidelines for diagnosis, prevention, and treatment of hand eczema (October 2021)[54]	Suggests phototherapy of the hands of adult patients with chronic hand eczema refractory to topical corticosteroids.	Weak, Moderate CoE
British Association of Dermatologists and British Photodermatology Group guidelines for narrowband ultraviolet B phototherapy (2022)[69]	Recommends offering NB-UVB as first-line phototherapy to people with eczema who have an inadequate response to topical therapy alone prior to offering systemic immunosuppression or immunomodulation therapies, including PUVA.	Strong, CoE not stated

Ongoing Studies

No ongoing study was found.

Evidence to Decision Considerations

Cost

No cost-effectiveness study was found. See Table 31 for the cost of phototherapy.

Table 31. Cost of treatment: phototherapy

	COST (PUBLIC HOSPITAL)	COST (PRIVATE HOSPITAL)
NB-UVB	Php 400/session	Php 980/session

Note: There are no economic evaluation studies on the use of phototherapy for recalcitrant allergic dermatitis in the Philippines. The estimated treatment cost for 36 sessions (3x a week for 3 months) is P14,400 to P35,280.

Patients' Values and Preferences, Equity, Acceptability, Feasibility

No formal studies with regard to patients' preferences and equity were found. Phototherapy is available in NCR, Region I, CAR, Region II, III, IV, V, VII, IX, XI clinics and hospitals.[70]

3.9. Among adults diagnosed with severe or recalcitrant chronic contact dermatitis, should we use systemic immunosuppressives (azathioprine, methotrexate, cyclosporine, mycophenolate mofetil, or janus kinase inhibitors) instead of oral corticosteroids and/or oral antihistamines in addition to topical corticosteroids and/or emollients

Box 3.9. Recommendation: Systemic immunosuppressives

Among adults diagnosed with severe or recalcitrant chronic contact dermatitis, we suggest against the use of systemic immunosuppressives (methotrexate, azathioprine, cyclosporin, mycophenolate mofetil, JAK inhibitors) compared to oral corticosteroids and/or oral antihistamines in addition to topical emollients and/or topical corticosteroids.

(Low certainty of evidence, Weak)

Key Findings

Two small RCTs investigated the use of azathioprine instead of oral corticosteroids in addition to topical corticosteroids and/or emollients for patients with chronic contact dermatitis.

The differences in clinical improvement and relapse between the azathioprine and oral corticosteroid groups were inconclusive. Although one study showed significantly fewer reports of acne, striae, and weight gain in patients who received azathioprine compared to those who received oral corticosteroids, the difference in adverse event rates that required discontinuation of therapy between the two groups was inconclusive. There were no studies available for other important outcomes.

The overall certainty of evidence is low.

No studies were found that looked into the use of methotrexate, cyclosporine, mycophenolate mofetil, and Janus kinase (JAK) inhibitors instead of oral corticosteroids and/or antihistamines in addition to topical corticosteroids and/or emollients for patients with chronic contact dermatitis.

Consensus Panel Issues

The panel unanimously voted against the use of systemic immunosuppressives such as methotrexate, azathioprine, cyclosporin, mycophenolate mofetil, and JAK inhibitors, citing insufficient evidence of benefits when compared to the use of oral corticosteroids. Although the current evidence regarding harm was inconclusive, the panel believed that larger trials may reveal adverse events associated with immunosuppressives. Moreover, the panel believed that the cost difference of immunosuppressives and standard of care is substantial.

Immunosuppressives are generally more costly than oral corticosteroids, particularly when used for chronic conditions.

Background

Several systemic therapies, such as systemic corticosteroids, methotrexate, azathioprine, mycophenolate mofetil, and cyclosporine, are used off-label to treat widespread and recalcitrant contact dermatitis. They act through nonspecific inhibition of the expression and actions of most cytokine cascades involved in the Th0, Th1, and Th2 pathways. Methotrexate, azathioprine, and mycophenolate mofetil are antimetabolites that suppress the proliferation of rapidly producing cells. Cyclosporine is a calcineurin inhibitor that inhibits Th1-mediated production of IL-2 and IFNγ needed for CD8+ activity and decreases histamine release from mast cells. It also inhibits CD8+ migration into the skin.

Although systemic corticosteroids are the most researched and widely used for recalcitrant dermatitis, long-term use is associated with adverse events such as hypothalamic-pituitary-adrenal axis inhibition, Cushing disease, diabetes, hypertension, peptic ulcer, osteonecrosis, osteoporosis, and the risk of opportunistic infections.[71] Thus, there is a need to review the evidence on the use of other immunosuppressive agents instead of oral corticosteroids for the treatment of chronic contact dermatitis.

Results

Two RCTs (n = 61) investigated the use of azathioprine instead of oral corticosteroids in addition to topical corticosteroids and/or emollients for patients with chronic contact dermatitis.

Both studies were conducted in India and included adult patients diagnosed with parthenium dermatitis (clinically and by patch test). The intervention group in both studies received azathioprine 100 mg/day divided into 2 doses for 6 months.[72,73] The control group received either prednisolone in tapering doses for 2 months followed by oral placebo for 4 months[72] or betamethasone 2 mg/day divided into 2 doses for 6 months[73]. In addition, the intervention and control groups in both studies received topical corticosteroids and antihistamines as needed. Outcome measures reported in the two trials were clinical improvement (≥ 50% improvement in severity score) measured at the end of treatment, relapse during treatment and up to 18 months after therapy, and adverse events.[72,73]

Efficacy Outcomes

The differences in clinical improvement and relapse between the azathioprine and oral corticosteroid groups were inconclusive (Table 32).

Table 32. Summary of findings: Efficacy of azathioprine vs. oral corticosteroids or oral placebo on chronic contact dermatitis

OUTCOMES	BASIS (NO. AND TYPE OF STUDIES, NO. OF PARTICIPANTS)	EFFECT SIZE	95% CI	INTERPRETATION	CERTAINTY OF EVIDENCE
Clinical improvement (≥50% improvement in severity score)	2 RCTs, N = 61	OR 1.50	0.28, 7.92	Inconclusive	Low
Relapse	2 RCTs N = 61	OR 0.58	0.20, 1.62	Inconclusive	Low

No studies investigating the use of methotrexate, cyclosporine, mycophenolate mofetil, and Janus kinase (JAK) inhibitors instead of oral corticosteroids and/or antihistamines in addition to topical corticosteroids and/or emollients for patients with chronic contact dermatitis was found.

Safety Outcomes

Based on two RCTs, the difference in adverse events that required discontinuation of therapy between the azathioprine and oral corticosteroid groups was inconclusive.[72,73] These adverse events leading to discontinuation included jaundice, anemia, and skin infections.

Although in one study[73] showed significantly less reports of acne, striae, weight gain in patients who received azathioprine compared to those who received oral corticosteroids, the difference in other adverse events (hirsutism, dyspepsia, nausea/vomiting, diabetes mellitus, cataract, glaucoma, infections, pigmentation, backache, fever, loss of appetite) that required discontinuation of therapy between the two groups was inconclusive.

The data on other adverse events could not be pooled because of incomplete reporting in one study.

Table 33. Summary of findings: Safety of azathioprine vs. oral corticosteroids or oral placebo on chronic contact dermatitis

OUTCOMES	BASIS (NO. AND TYPE OF STUDIES, NO. OF PARTICIPANTS)	EFFECT SIZE	95% CI	INTERPRETATION	CERTAINTY OF EVIDENCE
Adverse events that required discontinuation of therapy	2 RCTs, N = 61	OR 3.27	0.56, 19.09	Inconclusive	Low
Other adverse events	1 RCT, N = 41	-	-	-	Low
Acne		OR 0.09	0.01, 0.78	In favor of azathioprine	
Striae		OR 0.11	0.01, 0.97	In favor of azathioprine	

OUTCOMES	BASIS (NO. AND TYPE OF STUDIES, NO. OF PARTICIPANTS)	EFFECT SIZE	95% CI	INTERPRETATION	CERTAINTY OF EVIDENCE
Weight gain		OR 0.24	0.06, 0.93	In favor of azathioprine	
Cushingoid features		OR 0.13	0.01, 1.22	Inconclusive	
Hypertension		OR 0.13	0.01, 1.22	Inconclusive	

Certainty of Evidence

The certainty of evidence across all available outcomes is low due to the serious risk of bias and imprecision in both studies. The serious risk of bias was due to incomplete outcome data and issues with blinding in both studies. One trial also had issues in allocation concealment.[72] Wide confidence intervals in most of the outcomes resulted in serious imprecision.

Recommendation of Other Groups

Table 34. Recommendations of other professional membership bodies regarding the use of different immunosuppressants

Group	Recommendation	Strength of recommendation and certainty of evidence
Azathioprine		
German Dermatological Society (DDG), 2022[74]	The efficacy of immunosuppressants in contact dermatitis has not yet been sufficiently documented. For azathioprine, evidence of efficacy exists for airborne contact dermatitis. In addition, an RCT was performed for chronic hand eczema.	Not stated
European Society of Contact Dermatitis (ESCD), 2022 [54]	May be considered for *chronic hand eczema* patients refractory or contraindicated to first- and second-line therapy, although evidence for its efficacy is limited. Doctors and patients need to be aware that it is an off-label treatment.	Consensus-based recommendation (first round 100%, second round 100%)
Spanish Academy of Dermatology and Venereology (AEDV), 2020 [60]	Option for *hand eczema* when other treatments fail. Monitor for signs of hepatotoxicity due to the accumulation of azathioprine metabolites	Not stated
British Association of Dermatologists (BAD), 2017 [27]	The efficacy of systemic therapies – ciclosporin, azathioprine, and methotrexate – needs to be determined.	Not stated
Cyclosporine		
German Dermatological Society (DDG), 2022[74]	The efficacy of immunosuppressants in contact dermatitis has not yet been sufficiently documented. Cyclosporine may be helpful in chronic, recalcitrant hand eczema. The in-label use is restricted to atopic hand eczema. Off-label use with a maintenance dose of 3 mg/kg/day	Not stated

Group	Recommendation	Strength of recommendation and certainty of evidence
	may also be considered for non-atopic hand eczema in patients with long-term therapeutic need if first and second-line therapies have proved insufficient or are contraindicated.	
European Society of Contact Dermatitis (ESCD), 2022 [54]	We suggest cyclosporine for chronic hand eczema patients who are refractory or contraindicated to first- and second-line therapy. Doctors and patients need to be aware that it is an off-label treatment, except for patients with atopic hand eczema.	Consensus-based recommendation (first round 100%, second round 100%)
Korean Society of Contact Dermatitis and Skin Allergy, 2020 [68]	Recommends cyclosporine as a third-line treatment for patients with severe chronic hand eczema refractory to or relapsing after topical treatment, alitretinoin, and systemic steroids	Not stated
Spanish Academy of Dermatology and Venereology (AEDV), 2020 [60]	Option for hand eczema when other treatments fail. Effective in atopic dermatitis.	Not stated
British Association of Dermatologists, 2017[27]	The efficacy of systemic therapies–cyclosporine, azathioprine, and methotrexate–needs to be determined.	Not stated
Methotrexate		
German Dermatological Society (DDG), 2022 [74]	The efficacy of immunosuppressants in contact dermatitis is not yet sufficiently documented. Because of the limited data available on the use of mycophenolate mofetil, methotrexate, and other immunosuppressants in contact dermatitis, these cannot be considered standard therapy and should be reserved for special cases.	Not stated
European Society of Contact Dermatitis (ESCD) [54]	May be considered for chronic hand eczema patients who are refractory or contraindicated for first- and second-line therapy, although evidence for its efficacy is limited. Doctors and patients need to be aware that it is an off-label treatment.	Consensus-based recommendation (first round 100%, second round 100%)
Korean Society of Contact Dermatitis and Skin Allergy, 2020 [68]	Methotrexate could be recommended as a third-line treatment for hand eczema	Not stated
British Association of Dermatologists, 2017 [27]	The efficacy of systemic therapies–cyclosporine, azathioprine, and methotrexate–needs to be determined.	Not stated
Mycophenolate mofetil		
German Dermatological Society (DDG), 2022 [74]	The efficacy of immunosuppressants in contact dermatitis has not yet been sufficiently documented. Because of the limited data available on the use of mycophenolate mofetil, methotrexate, and other immunosuppressants in contact dermatitis, these cannot be	Not stated

Group	Recommendation	Strength of recommendation and certainty of evidence
	considered standard therapy and should be reserved for special cases.	

Ongoing Studies

No ongoing study was found.

Evidence to Decision Considerations

Cost

No cost-effectiveness study was found. See Table 35 for the cost of treatment.

Table 35. Cost of treatment: systemic immunosuppressives

	Prednisone	Azathioprine	Cyclosporine	Methotrexate	Mycophenolate mofetil	Tofacitinib
Cost per tablet[†]	8.50 (20 mg) + 5.50 (10 mg)	37.95 (50 mg)	164 (100 mg)	10.04 (2.5 mg)	119.87 (500 mg)	814.25 (5 mg)
Usual dose /dose in studies for dermatitis per day	30 mg	100 mg	2-3 mg/kg/day (~200 mg for a 70 kg patient)	15 mg	1-2 g	10 mg
Cost per day	14.00	75.90	328	60.24	479.48	1,628.50

[†] Prices available at Watsons [Internet]. https://www.watsons.com.ph

Patients' Values and Preferences, Equity, Acceptability, Feasibility

No formal studies with regard to patients' preferences, equity, acceptability, or feasibility were found.

4. Applicability Issues

4.1. Organizational Considerations to Implementation

The Evidence Review Experts searched for data on local feasibility, equity, availability, costs, cost-effectiveness of diagnostic tests and interventions for contact dermatitis. These data were considered and carefully discussed during the *en banc* meetings to finalize the recommendations.

Compliance and adherence to the strong recommendations for utilizing tests and interventions may become a challenge in certain regions across the country, primarily due to concerns regarding availability and costs. These issues, in turn, may exacerbate equity-related issues. The accessibility of patch tests and specialists, such as dermatologists and allergologists, for the purpose of establishing the diagnosis of contact dermatitis and providing management would likely vary in different areas and healthcare settings. While the cost of ROAT is lower than that of patch tests, the financial burden may escalate when both ROAT and patch tests are required to confirm the diagnosis of allergic contact dermatitis.

In addition to the requisite diagnostic protocols for patients suspected of having contact dermatitis, potential barriers to effective implementation of the strong recommendations for patients who have chronic contact dermatitis and their referral to a higher level of care may arise as a result of the limited availability of infrastructure and specialists in the field that may result in extended waiting period or delay in management. These challenges would be further compounded by issues of staff shortages in different institutions and resistance to adopting new policies, which may prioritize other medical conditions.

The public may also lack awareness on contact dermatitis and significance of the tests and interventions. Therefore, general practitioners and equipping them with knowledge and training are crucial in delivering the interventions, such as providing counseling for patient education on skin-protective behaviors and guiding the patients in using ROAT and/or patch tests in the primary care setting, as well as providing general information on contact dermatitis that could also reduce the probable stigma and misconceptions. Patients' knowledge of the condition can lead them to actively participate in the decision-making process and prioritize seeking help to improve their health and well-being. Language barriers, culture differences, and inadequate health literacy among patients should be taken into consideration when teaching communication strategies to healthcare providers.

Prescribing an emollient or barrier cream with the topical corticosteroids may also pose affordability issues for certain patients with contact dermatitis. Assistance from the government in the form of subsidies for these additional treatments and offering cheaper alternatives may result in improved compliance and better patient outcomes.

4.2. Resource Implications

It is imperative that our finite resources be allocated and utilized in an efficient manner as a country with a low-middle-income status. The panel meetings extensively deliberated on the

financial implications associated with the tests and interventions for contact dermatitis. This primarily encompassed the costs related to tests, referrals to higher levels of care, and the purchase of emollients and barrier creams. Health technology assessment (HTA) plays a crucial role as a gatekeeping mechanism to ensure the cost-effectiveness of all government payments facilitated by PhilHealth.

5. Monitoring and Evaluation

5.1. Dissemination

The SC planned to discuss with relevant stakeholders such as DOH and PhilHealth to prepare a dissemination plan that will actively promote the adoption of this guideline with strategies for copyrights.

To disseminate the guidelines, the following channels will be used: (a) webinars and scientific forums hosted by the collaborating specialty organizations; (b) websites of the collaborating specialty organizations; (c) publication in a reputable scientific journal; (d) inclusion of key recommendations in medical curricula; (e) lay forums organized by specialty societies; (f) training; and (g) social media platforms.

5.2. Implementation

An official department order may be issued to present this CPG for implementation to the various DOH hospitals. Once approved by the NGC's quality evaluation panel, the various groups that contributed to the creation of the CPG may also cascade and support the recommendations for implementation in their respective healthcare institutions.

The SC will be in charge of monitoring the compliance of relevant parties. A survey will be used as part of the monitoring and evaluation processes to determine the baseline knowledge and behaviors of the target users, as well as their perspectives on the recommendations in the guidelines and their relevance and practicality. These surveys will be conducted on a regular basis to see whether the target users' knowledge and behaviors have changed.

5.3. Updating of the guidelines

This CPG will be updated every three years. The SC will determine and carry out annual assessments of the evidence that might have an impact on the guideline's initial recommendations. The recommendations herein shall hold until such time that new evidence on interventions for contact dermatitis and/or patient and provider preferences require or contingencies dictate the revision and updating of practice guidelines.

In accordance with this, the SC may convene a meeting with the TWG to appraise and synthesize the evidence and the CP to determine if changes to the recommendations are required. The feedback of CPG's target users will also be reviewed on a yearly basis to assist implementers and policymakers with CPG-related concerns.

Table 36. Proposed process and timeline for updating the guideline

PROCESS	RESPONSIBLE UNIT/ORGANIZATION	FREQUENCY	TIMELINE
1. Review of current evidence relevant to contact dermatitis management	SC and TWG	Annual	2023-2025
2. Review of feedback on the contact dermatitis CPG by end users	SC	Annual	2023-2025
3. Amendment to the recommendations if new strong evidence becomes available	SC, TWG, and CP	N/A	2023-2025
4. Major update of the contact dermatitis CPG based on recent evidence and feedback obtained using the questionnaire	SC, TWG, and CP DOH	N/A	2025-2026

6. Research Implications or Gaps

The majority of the guideline topic questions, with the exception of one, exhibit a low to very low level of certainty in terms of evidence, thus necessitating additional research. Future studies may result in different effect estimates, thereby warranting consideration in the process of updating recommendations and guidelines. The following are the research gaps identified during the search for evidence and formulation of the recommendations:

1. Well-designed RCTs on methotrexate, cyclosporine, mycophenolate mofetil, and JAK inhibitors versus oral corticosteroids and/or oral antihistamines in addition to corticosteroids and/or emollients in patients with chronic contact dermatitis.
2. Studies on the effectiveness of referral versus non-referral of adult patients with chronic, recurrent, or recalcitrant contact dermatitis to a higher level of care
3. Studies on the effectiveness of patient or family education in improving clinical outcomes among patients with contact dermatitis
4. Well-designed RCTs on phototherapy as an adjunct treatment among patients with chronic recalcitrant contact dermatitis
5. High-quality RCTs on TCIs versus topical corticosteroids among patients with contact dermatitis with sufficient reporting of adverse events
6. Diagnostic accuracy studies on the use of ROAT for patients suspected of having allergic contact dermatitis to improve other patient outcomes such as reduction of flares and improvement of quality of life
7. Direct studies on the clinical utility of patch tests versus patch testing among patients with contact dermatitis, including diagnostic accuracy studies
8. Well-designed RCTs on emerging home remedies and/or over-the-counter topical products for alleviating symptoms in patients with suspected contact dermatitis.

Research on the cost-effectiveness of the test and interventions, along with formal studies conducted on Filipino patients and other relevant stakeholders' experiences and preferences, the feasibility and acceptability of the test and interventions (such as systemic immunosuppressives), and outcomes related to societal participation or work productivity in the management of contact dermatitis, will provide valuable insights for stakeholders involved in the update of this guideline.

7. References

1. Litchman G, Nair P, Atwater A, Bhutta B. Contact Dermatitis. In: StatPearls[Internet]: Treasure Island (FL); 2023. Accessed April 16, 2023.
2. Xue Y, Bao W, Zhou J, et al. Global burden, incidence and disability-adjusted life-years for dermatitis: A systematic analysis combined with socioeconomic development status, 1990–2019. *Frontiers in Cellular and Infection Microbiology.* 2022;12.
3. DOH. Manual for Clinical Practice Guideline Development. In: Department of Health Philippines; 2018.
4. Ejercito J, Recto R, Lima Ld, et al. Universal Health Care Act. *Republic Act No 11223.* 2019.
5. Higgins J, Altman D. Assessing risk of bias in included studies. In: Higgins J, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions*: Wiley; 2008.
6. Whiting P, Rutjes A, Westwood M, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med.* 2011;155(8):529-536.
7. Guyatt G, Oxman A, Sultan S, et al. GRADE guidelines: 9. Rating up the quality of evidence. *Journal of Clinical Epidemiology.* 2011;64:1311-1316.
8. Balshem H, Helfand M, Schünemann H, et al. GRADE guidelines: 3. Rating the quality of evidence. *Journal of Clinical Epidemiology.* 2011;64:401-406.
9. Alonso-Coello P, Schünemann H, Moberg J, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. *BMJ.* 2016;353:1-10.
10. Team A-RR. The Appraisal of Guidelines Research & Evaluation — Recommendation EXcellence (AGREE-REX) [Electronic version]. 2019.
11. ICE-NIH. Guidance on Review of COI. 2023.
12. Lazzarini R, Duarte I, Ferreira A. Patch tests. *Anais Brasileiros de Dermatologica.* 2013;88(6):879-888.
13. Akyol A, Boyvat A, Peksari Y, Gürgey E. Contact sensitivity to standard series allergens in 1038 patients with contact dermatitis in Turkey. *Contact Dermatitis.* 2005;52(6):333-337.
14. Zug K, Rietschel R, Warshaw E, et al. The value of patch testing patients with a scattered generalized distribution of dermatitis: retrospective cross-sectional analyses of North American Contact Dermatitis Group data, 2001 to 2004. *J Am Acad Dermatol.* 2008;59(3):426-431.
15. Li L, Wang J. Patch testing and aeroallergen intradermal testing in suspected allergic contact dermatitis, unclassified endogenous eczema and non-atopic chronic urticaria. *Contact Dermatitis.* 2001;45(2):84-88.
16. Oosterhaven J, Febriana S, Soebono H, Coenraads P, Schuttelaar M. Results of patch testing in Indonesian shoe factory workers. *Journal of the European Academy of Dermatology and Venereology.* 2016;31(1):e15–e17.
17. Wenk K, Ehrlich A. Fragrance series testing in eyelid dermatitis. *Dermatitis.* 2012;23(1):22-26.
18. Gilissen L, Huygens S, Goossens A. Allergic contact dermatitis caused by topical herbal remedies: importance of patch testing with the patients' own products. *Contact Dermatitis.* 2017;78(3):177-184.

19. Garg T, Agarwal S, Chander R, Singh A, Yadav P. Patch testing in patients with suspected cosmetic dermatitis: A retrospective study. *J Cosmet Dermatol.* 2018;17(1):95-100.
20. Lam W, Chan L, Ho S, Chong L, So W, Wong T. A retrospective study of 2585 patients patch tested with the European standard series in Hong Kong (1995-99). *International Journal of Dermatology.* 2008;47(2):128-133.
21. Lee S, Hong D, Lee N, et al. Multicenter study of preservative sensitivity in patients with suspected cosmetic contact dermatitis in Korea. *The Journal of Dermatology.* 2012;39(8):677-681.
22. Li L, Guo J, Wang J. Environmental contact factors in eczema and the results of patch testing Chinese patients with a modified European standard series of allergens. *Contact Dermatitis.* 2004;51(1):22-25.
23. Kolodziejczyk J, Wojciechowska M. Retrospective analysis of the incidence of allergy in patients with contact eczema. *World Allergy Organization Journal.* 2016;9:A266.
24. Cockayne S, Gawkrodger D. Angry back syndrome is often due to marginal irritants. *Contact Dermatitis.* 2000;43(5):280-282.
25. Johansen J, Aalto-Korte K, Agner T, et al. European Society of Contact Dermatitis guideline for diagnostic patch testing - recommendations on best practice. *Contact Dermatitis.* 2015;73(4):195-221.
26. Brasch J, Becker D, Aberer W, et al. Guideline contact dermatitis: S1-Guidelines of the German Contact Allergy Group (DKG) of the German Dermatology Society (DDG), the Information Network of Dermatological Clinics (IVDK), the German Society for Allergology and Clinical Immunology (DGAKI), the Working Group for Occupational and Environmental Dermatology (ABD) of the DDG, the Medical Association of German Allergologists (AeDA), the Professional Association of German Dermatologists (BVDD) and the DDG. *Allergo J Int.* 2014;23(4):126-138.
27. Johnston G, Exton L, Mustapa M, et al. British Association of Dermatologists' guidelines for the management of contact dermatitis 2017. *Br J Dermatol.* 2017;176(2):317-329.
28. Khambra A, Ramesh V, Kathuria S. Correlation of patch test with repeated open application test in patients with suspected hair-dye dermatitis. *Indian J Dermatol Venereol Leprol.* 2020;86(733-736).
29. Fonacier L, Bernstein D, Pacheco K, Holness D, Blessing-Moore J, Khan D. Contact dermatitis: A practice parameter–update 2015. *The Journal of Allergy and Clinical Immunology.* 2015;3(3).
30. Mahler V, Nast A, Bauer A, Becker D, Brasch J, Breuer K. S3 guidelines: Epicutaneous patch testing with contact allergens and drugs – short version, part 1. *JDDG: Journal der Deutschen Dermatologischen Gesellschaft.* 2019;17(10):1076-1093.
31. Gabros S, Nessel T, Zito P. Topical Corticosteroids. In: StatPearls [Internet]: StatPearls Publishing LLC, Treasure Island (FL); 2023.
32. Niazi M, Mehrabani M, Namazi M, et al. Efficacy of a topical formulation of henna (Lawsonia inermis L.) in contact dermatitis in patients using prosthesis: A double-blind randomized placebo-controlled clinical trial. *Complement Ther Med.* 2020;49:102316.
33. Trakanwittayarak S, Meephansan J. The effect of astaxanthin on allergic contact dermatitis in response to hair dye containing p-phenylenediamine. *Eur J Dermatol.* 2019;29(6):647-648.

34. Wallengren J. Tea tree oil attenuates experimental contact dermatitis. *Archives of Dermatological Research.* 2010;303(5):333-338.
35. Alyasin S, Nabavizadeh S, Esmaeilzadeh H, et al. Efficacy of oral supplementation of whey protein in patients with contact dermatitis: A pilot randomized double-blind placebo-controlled clinical trial. *Dermatologic Therapy.* 2020;33(6):e14260.
36. Groot A. Side-effects of henna and semi-permanent "black henna" tattoos: a full review. *Contact Dermatitis.* 2013;69(1):1-25.
37. Ahlstrom M, Dietz J, Wilke A, Johansen J, John S, Brans R. Evaluation of the secondary and tertiary prevention strategies against occupational contact dermatitis in Germany: A systematic review. *Contact Dermatitis.* 2022;87:142-153.
38. Ibler K, Jemec G, Diepgen T, et al. Skin care education and individual counselling versus treatment as usual in healthcare workers with hand eczema: andomized clinical trial. *BMJ.* 2012;345(7887):1-14.
39. Mollerup A, Veien N, Johansen J. Effectiveness of the healthy skin clinic – a randomized clinical trial of nurse-led patient counselling in hand eczema. *Contact Dermatitis.* 2014;71(4):202-214.
40. Fisker M, Ebbøhøj N, Vejlstrup S, Lindschou J, Gluud C, Winkel P. Prevention of hand eczema: effect of an educational program versus treatment as usual - results of the randomized clinical prevex trial. *Scand J Work Environ Health.* 2018;44(2):212-218.
41. Recommendations for the prevention, detection and management of occupational dermatitis in health care settings. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Published 2019. Accessed2023.
42. Eberting C. Repairing a compromised skin barrier in dermatitis: Leveraging the skin's ability to heal itself. *Journal of Allergy & Therapy.* 2014;5(5).
43. Purnamawati S, Indrastuti N, Danarti R, Saefudin T. The role of moisturizers in addressing various kinds of dermatitis: a review. *Clin Med Res.* 2017;15(3-4):75-87.
44. Emollients. Cleveland Clinic. Treatments & Procedures Web site. https://my.clevelandclinic.org/health/treatments/23305-emollients. Accessed.
45. Difference Between Humectant, Emollient, Occlusive. The Derm Review. https://thedermreview.com/difference-between-humectant-emollient-occlusive/. Accessed.
46. IQWiG. Eczema: Steroids and other topical medications. In: InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care; 2017.
47. Yuen N, Ibrahim K, Begum S. Does order of application of emollient and topical corticosteroids make a difference to severity in children with atopic eczema? . *European Journal of Pediatric Dermatology.* 2012;22(1):14-15.
48. Sobhan M, Hojati M, Vafaie S, Ahmadimoghaddam S, Mohammadi Y, Mehrpooya M. The efficacy of colloidal oatmeal cream 1% as add-on therapy in the management of chronic irritant hand eczema: a double-blind study. *Clin Cosmet Investig Dermatol.* 2020;13:241-251.
49. Safarini O, Keshavamurthy C, Patel P. Calcineurin Inhibitors. In: Treasure Island (FL): StatPearls Publishing; 2022.
50. Alomar A, Puig L, Gallardo C, Valenzuela N. Topical tacrolimus 0.1% ointment (protopic) reverses nickel contact dermatitis elicited by allergen challenge to a similar degree to mometasone furoate 0.1% with greater suppression of late erythema. *Contact Dermatitis.* 2003;49(4):185-188.

51. Bhardwaj S, James J, Liu A, Washaw E. A double-blind randomized placebo-controlled pilot study comparing topical immunomodulating agents and corticosteroids for treatment of experimentally induced nickel contact dermatitis. *Dermatitis.* 2007;18(1):26-31.
52. Katsarou A, Makris M, Papagiannaki K, Lagogianni E, Tagka A, Kalogeromitros D. Tacrolimus 0.1% vs mometasone furoate topical treatment in allergic contact hand eczema: a prospective randomized clinical study. *Eur J Dermatol.* 2012;22(2):192-196.
53. Mose K, Flemming A, Ropke M, Skove L, Friedman P, Andersen K. Anti-inflammatory potency testing of topical corticosteroids and calcineurin inhibitors in human volunteers sensitized to diphenylcyclopropenone. *Br J Clin Pharmacol.* 2018;84:1719-1728.
54. Thyssen J, Schuttelaar M, Alfonso J, et al. Guidelines for diagnosis, prevention, and treatment of hand eczema. *Contact Dermatitis.* 2022;86(5):357-378.
55. Takayama K. for the Japanese Dermatological Association Guidelines. Japanese Dermatological Contact Dermatitis Treatment Guidelines Revision: Contact dermatitis clinical practice guideline 2020. *Journal of Nissinkai.*130(4):523-567.
56. Brod B. Management of allergic contact dermatitis. https://www.uptodate.com/contents/management-of-allergic-contact-dermatitis. Published 2023. Accessed 7 February 2023.
57. Milam E, Cohen D. Contact dermatitis: Emerging Trends. *Dermatol Clin.* 2019;37(1):21-28.
58. Hald M, Agner T, Blands J, Veien N, Laurberg G, Avnstorp C. Clinical severity and prognosis of hand eczema. *Br J Dermatol.* 2009;160(6):1229-1236.
59. Cvetkovski R, Zachariae R, Jensen H, Olsen J, Johansen J, Agner T. Prognosis of occupational hand eczema: A follow-up study. *Arch Dermatol.* 2006;142.
60. Salvador J, Mendaza F, Garcés M, Palacios-Martínez D, Camacho R, Sanz R. Guidelines for the diagnosis, treatment, and prevention of hand eczema. *Actas Dermo-Sifiliográficas.* 2020;111(1):26-40.
61. Menné T, Johansen J, Sommerlund M, Veien N. Hand eczema guidelines based on the Danish guidelines for the diagnosis and treatment of hand eczema. *Contact Dermatitis.* 2011;65(1):3-12.
62. Christoffers W, Coenraads P, Svensson A, et al. Interventions for hand eczema. *Cochrane Database of Systematic Reviews.* 2019(4).
63. Musters A, Mashayekhi S, Harvey J, et al. Phototherapy for atopic eczema. *Cochrane Database of Systematic Reviews.* 2021;10(10):CD013870.
64. Bernard J, Gallo R, Krutmann J. Photoimmunology: how ultraviolet radiation affects the immune system. *Nat Rev Immunol.* 2019;19(11):688-701.
65. Vieyra-Garcia P, Wolf P. A deep dive into UV-based phototherapy: Mechanisms of action and emerging molecular targets in inflammation and cancer. *Pharmacol Ther.* 2021;222:107784.
66. Rosén K, Mobacken H, Swanbeck G. Chronic eczematous dermatitis of the hands: a comparison of PUVA and UVB treatment. *Acta Derm Venereol.* 1987;67(1):48-54.
67. Sjövall P, Christensen O. Local and systemic effect of UVB irradiation in patients with chronic hand eczema. *Acta Derm Venereol.* 1987;67(6):538-541.
68. Kim H, Bang C, Kim H, et al. K2020 Korean Consensus Guidelines for Diagnosis and Treatment of Chronic Hand Eczema. *Ann Dermatol.* 2021;33(4):351-360.

69. Goulden V, Ling T, Babakinejad P, et al. British Association of Dermatologists and British Photodermatology Group guidelines for narrowband ultraviolet B phototherapy 2022. *Br J Dermato.* 2022;187(3):298-308.
70. PDS. PDS Photodermatology Directory. Philippine Dermatological Society. https://www.pds.org.ph/wp-content/uploads/2023/01/PDS-Photodermatology-Directory-as-of-Jun-2020-FINAL.pdf. . Accessed 02 March 2023.
71. Sung C, McGowan M, Machler B, Jacob S. Systemic treatments for allergic contact dermatitis. *Dermatitis.* 2019;30(1):46-53.
72. Davis S, Shenoi S, Prabhu S, Pai S, Balachandran B. Single blind randomized controlled trial of 'azathioprine versus corticosteroids in parthenium hysterophorus induced contact dermatitis. *Clin Dermatology Ther.* 2014;1:1-4.
73. Verma K, Mahesh R, Srivastava P, Ramam M, Mukhopadhyaya A. Azathioprine versus betamethasone for the treatment of parthenium dermatitis: A randomized controlled study. *Indian J Dermatol Venereol Leprol.* 2008;74(5):453-457.
74. Dickel H, Bauer A, Brehler R, Mahler V, Merk H, Neustädter I. German S1 guideline: Contact dermatitis. *JDDG - J Ger Soc Dermatology.* 2022;20(5):712-734.

8. Appendices

8.1. Members of the CPG Task Force

UP Manila Institute of Clinical Epidemiology

Program Leader: Marissa M. Alejandria, MD, MSc, FPCP, FPSMID
Project Leader: Maria Carmela M. Lapitan, MD, MSc, FPCS, FPUA
Technical Consultants: Aldrich Ivan D. Lois Burog, MD; Ian Theodore M. Cabaluna, RPh, MD, GDip (Epi)

Jose R. Reyes Memorial Medical Center

Project Manager: Elaine Marie C. Gutierrez-Villaroman, MD, FPDS
Administrative Officer: Joseph John S. Tayag, MD, Mary Darice R. Wong-Ong, MD

COI Review Committee

1. Camille Berenguer-Angeles, MD, FPDS (*Philippine Dermatological Society)*
2. Mary Jo Kristine S. Bunagan, MD, MPH, FPDS, FISHRS (*Philippine Dermatological Society)*
3. Mara Therese P. Evangelista-Huber, MD, FPDS, FDSP, MClinRes (*Philippine Dermatological Society)*

Steering Committee

Chair: Lillian L. Villafuerte, MD, MOH, FPDS
(*Philippine College of Occupational Medicine, Philippine Dermatological Society)*
Vice-Chair: Katherine Joy B. Sayo-Aguiling, MD, DPDS (*Philippine Dermatological Society*)
Members:

1. Peter Julian A. Francisco, MD, FPAFP, DIH, MHM (*Philippine Academy of Family Physicians*)
2. Matilde Krisha P. Montenegro, MD, DPDS (*Philippine Dermatological Society*)
3. Michelle Yau Otayco, MD, FPCP, FPSN, MMHoA (*Philippine College of Physicians*)
4. Evelyn O. Salido, MD MSc, FPCP FPRA (Methodologist)
5. Pauline Florence R. Santos Estrella, MD, FPPS, DPSAAI (*Philippine Society of Allergy, Asthma and Immunology)*

Evidence Review Experts

Technical Coordinator: Zharlah Gulmatico-Flores, MD, MMPHA, FPDS
Evidence Reviewers:

1. Imelda Caole-Ang, MD, FPCP, FPCC

2. Czarina P. Chavez, MD, FPDS
3. Regina Dionisio-Capulong, MD, FPPS, FPSAAI
4. Melanie Joy C. Doria-Ruiz, MD, FPDS
5. Mia C. Fojas, MD, FPCP, FPCEDM
6. Anna Maria Vida P. Garcia, RPh, D Clin Epi
7. Mary Darice R. Wong-Ong, MD

Consensus Panel

1. Lonabel P. Ancheta-Encarnacion, MD, FPDS (*Philippine Dermatological Society*)
2. Caroline C. Aquino, MD, FPPS, DPSAAI (*Philippine Society of Allergy, Asthma and Immunology*)
3. Nelia Medina, RSW (*Philippine Alliance of Patient Organization*)
4. Enrique T. Pagulayan, MD, FPCOM (*Philippine College of Occupational Medicine*)
5. Ma. Doris Rosales-Obias EdD, RN, CSCM (*Philippine Nurses Association*)
6. Ofelia M. Samar-Sy, MD, FPCP, PhD (*Philippine College of Physicians*)
7. Emerie Gold P. Vallestero, MD, DFM (*Philippine Academy of Family Physicians*)
8. Julie Mart C. Rubite, MD, FPAFP, MMHeA (*Non-Voting Member, Medical Specialist IV*, *Disease Prevention and Control Bureau, Department of Health)*

Consensus Panel Facilitator: Ma. Angela M. Lavadia, MD, FPDS, IFAAD
Technical Writer: Myzelle Anne Infantado-Alejandro, PTRP

8.2. Summary of COI Declarations

Name	Affiliation*	Specialization/ Content Expertise	Summary of Declared Conflicts of Interest	Management
Steering Committee				
Lillian L. Villafuerte, MD, MOH, FPDS	*Philippine College of Occupational Medicine, Philippine Dermatological Society*	*Dermatology; Dermatologic Surgery ; Environmental and Occupational Dermatology*	Nil	Approved without constraints†
Elaine Marie C. Gutierrez-Villaroman, MD, FPDS	*Philippine Dermatological Society*	*Dermatology; Contact Dermatitis and Environmental Dermatology; Patch Testing*	Nil	Approved without constraints†
Katherine Joy B. Sayo-Aguiling, MD, DPDS	*Philippine Dermatological Society*	*Dermatology*	Nil	Approved without constraints†
Matilde Krisha P. Montenegro, MD, DPDS	*Philippine Dermatological Society, Pediatric Dermatology Society of the Philippines*	*Adult and Pediatric Dermatology*	Nil	Approved without constraints†
Peter Julian A. Francisco, MD, FPAFP, DIH, MHM	*Philippine Academy of Family Physicians*	*Family and Community Medicine*	Nil	Approved without constraints†
Michelle Yau Otayco, MD, FPCP, FPSN, MMHoA	*Philippine College of Physicians, Philippine Society of Nephrology, Asia Pacific Society of Dialysis*	*Adult Interventional Nephrology*	Nil	Approved without constraints†

Pauline Florence R. Santos Estrella, MD, FPPS, DPSAAI	*Philippine Society of Allergy, Asthma and Immunology*	*Adult and Pediatric Allergy, Asthma & Immunology*	Financial COI	Broadcast conflict‡
Evelyn O. Salido, MD MSc, FPCP FPRA	*UP-Philippine General Hospital*	*Rheumatology, Internal Medicine, Clinical Epidemiology*	Financial COI	Broadcast conflict‡
Evidence Review Experts				
Zharlah Gulmatico-Flores, MD, MMPHA, FPDS	*Philippine Dermatological Society*	*Dermatologic Surgery, Procedural Dermatology, Research*	Financial COI	Cannot vote for certain questions‡
Imelda Caole-Ang, MD, FPCP, FPCC	*Philippine College of Physicians, Philippine Heart Association*	*Internal Medicine, Cardiology*	Nil	Approved without constraints†
Regina Dionisio-Capulong, MD, FPPS, FPSAAI	*Philippine Pediatrics Society, Philippine Society of Allergy, Asthma and Immunology*	*Allergy and Immunology*	Nil	Approved without constraints†
Melanie Joy C. Doria-Ruiz, MD, FPDS	*Philippine Dermatological Society*	*Immunodermatology, Research*	Nil	Approved without constraints†
Czarina P. Chavez, MD, FPDS	*Philippine Dermatological Society*	*Dermatology, Clinical Research*	Financial COI	Cannot vote for certain questions‡
Mia C. Fojas, MD, FPCP, FPCEDM	*UP College of Medicine*	*Internal Medicine, Endocrinology*	Nil	Approved without constraints†
Anna Maria Vida P. Garcia, RPh, D Clin Epi	*ClinChoice Inc.-Manila*	*Pharmacology, Epidemiology*	Nil	Approved without constraints†
Mary Darice R. Wong-Ong, MD	*JRRMMC*	*Dermatology*	Nil	Approved without constraints†
Voting Members of Consensus Panel				
Lonabel P. Ancheta-Encarnacion, MD, FPDS	*Philippine Dermatological Society*	*Environmental Dermatology; Contact Dermatitis & Patch*	Nil	Approved without constraints†

		Testing; Occupational Dermatology		
Caroline C. Aquino, MD, FPPS, DPSAAI	*Philippine Society of Allergy, Asthma and Immunology*	*Allergy and Immunology*	Nil	Approved without constraints†
Nelia Medina, RSW	*Philippine Alliance of Patient Organization*	*Social Work, Patient Advocate*	Nil	Approved without constraints†
Enrique T. Pagulayan, MD, FPCOM	*Philippine College of Occupational Medicine*	*Occupational Medicine*	Nil	Approved without constraints†
Ma. Doris Rosales-Obias EdD, RN, CSCM	*Philippine Nurses Association*	*Nursing, Infectious/Communicable Disease Management & Infection Control, Health Management, Research*	Nil	Approved without constraints†
Ofelia M. Samar-Sy, MD, FPCP, PhD	*Philippine College of Physicians*	*Cardiology, Medical Education*	Nil	Approved without constraints†
Emerie Gold P. Vallestero, MD, DFM	*Philippine Academy of Family Physicians*	*Family and Community Medicine*	Nil	Approved without constraints†
Administrative Officers				
Joseph John S. Tayag, MD	*JRRMMC*	*Dermatology*	Nil	Approved without constraints†
Mary Darice R. Wong-Ong, MD	*JRRMMC*	*Dermatology*	Nil	Approved without constraints†
Technical Facilitator				
Ma. Angela M. Lavadia, MD, FPDS, IFAAD	*Philippine Dermatological Society*	*Dermatology; Contact Dermatitis and Environmental Dermatology*	*Nil*	Approved without constraints†
Technical Writer				
Myzelle Anne Infantado-Alejandro, PTRP	*UPCM Department of Clinical Epidemiology*	*Physical Therapy*	Nil	Approved without constraints†

† May be involved in the CPG development activities

‡ May be involved in the CPG development activities but must declare COI

*Complete affiliation details can be found below

Affiliation Details

Project Manager: Elaine Marie C. Gutierrez-Villaroman, MD, FPDS
Specialization/Content Expertise: Dermatology; Contact Dermatitis and Environmental Dermatology; Patch Testing
Affiliations:
- Dr. Jose R. Reyes Memorial Medical Center, Department of Dermatology (National Specialty Center for Dermatology)
- Diplomate and Fellow, Philippine Dermatological Society
- Philippine Medical Association – Malabon-Navotas Chapter

COI Review Committee

1. Camille Berenguer-Angeles, MD, FPDS
   Specialization: Dermatology, Cosmetic Dermatology, Research
   Affliations:
   - UERMMMCI
   - Philippine Dermatological Society

2. Mary Jo Kristine S. Bunagan, MD, MPH, FPDS, FISHRS
   Specialization/Content Expertise: Dermatology
   Affiliations:
   - Southern Philippines Medical Center
   - Philippine Dermatological Society

3. Mara Therese P. Evangelista-Huber, MD, FPDS, FDSP, MClinRes
   Specialization/Content Expertise: Dermatopathology, Research
   Affiliations:
   - Levana Dermatology Clinic
   - Philippine Dermatological Society
   - Dermatopathology Society of the Philippines
   - Philippine Medical Association
   - Quezon City Medical Society

Steering Committee

Chair: Lillian L. Villafuerte, MD, MOH, FPDS
Specialization : Dermatology; Dermatologic Surgery ; Environmental and Occupational Dermatology
Affiliations :
- Dr . Jose R. Reyes Memorial Medical Center, Department of Dermatology (National Specialty Center for Dermatology)
- The Medical City
- Manila Doctors Hospital
- Diplomate and Fellow, Philippine Dermatological Society
- Member, Philippine College of Occupational Medicine

Vice-Chair: Katherine Joy B. Sayo-Aguiling, MD, DPDS (Philippine Dermatological Society)
Specialization/Content Expertise: Dermatology
Affiliations:
- Dr. Jose R. Reyes Memorial Medical Center, Department of Dermatology (National Specialty Center for Dermatology)
- Diplomate, Philippine Dermatological Society

Members:

1. Peter Julian A. Francisco, MD, FPAFP, MHM, DIH
   Specialization/Content Expertise: Family and Community Medicine
   Affiliations:
   - University of the Philippines Manila - College of Medicine, Department of Family and Community Medicine
   - Jose R. Reyes Memorial Medical Center, Department of Family and Community Medicine
   - Manila Doctors Hospital, Department of Family and Community Medicine
   - Fellow, Philippine Academy of Family Physicians

2. Matilde Krisha P. Montenegro, MD, DPDS
   Specialization/Content Expertise: Adult & Pediatric Dermatology
   Affiliations:
   - Jose R. Reyes Memorial Medical Center, Department of Dermatology (National Specialty Center for Dermatology)
   - Diplomate, Philippine Dermatological Society
   - Member, Pediatric Dermatology Society of the Philippines

3. Michelle Yau Otayco, MD, FPCP, FPSN, MMHoA
   Specialization/Content Expertise: Adult Interventional Nephrologist
   Affiliations:
   - Philippine College of Physician
   - Philippine Society of Nephrology
   - Asia Pacific Society of Dialysis Access

4. Evelyn O. Salido, MD MSc, FPCP FPRA
   Specialization/Content Expertise: Rheumatology, Internal Medicine, Clinical Epidemiology
   Affiliations:
   - University of the Philippines Manila
   - De la Salle Health Sciences Institute
   - Asian Hospital and Medical Center
   - Perpetual Help Dalta Medical Center
   - Philippine College of Physicians
   - Philippine Rheumatology Association

5. Pauline Florence R. Santos Estrella, MD, FPPS, DPSAAI
   Specialization/Content Expertise: Adult and Pediatric Allergy, Asthma & Immunology
   Affiliations:
   - St. Luke's Medical Center Global City and Quezon City
   - Providence Hospital Inc.
   - Philippine Children's Medical Center
   - Pasig City Children's Hospital
   - Dermatologic Council of Philippine Society of Allergy, Asthma and Immunology
   - Philippine Pediatric Society

Evidence Review Experts

Technical Coordinator: Zharlah Gulmatico-Flores, MD, MMPHA, FPDS, FPADSFI
Specialization: Dermatology
Specialty/Content Expertise: Dermatologic Surgery, Procedural Dermatology, Research
Affiliations:
- Dr. Jose R. Reyes Memorial Medical Center, Department of Dermatology (National Specialty Center for Dermatology)
- Fatima Medical Center
- Diplomate and Fellow; Board of Director 2023-2024, Philippine Dermatological Society

Evidence Reviewers:

1. Imelda Caole-Ang, MD, FPCP, FPCC
   Specialization/Content: Internal Medicine Cardiology
   Affiliations:
   - Pamantasan ng Lungsod ng Maynila
   - Ospital ng Maynila

2. Czarina P. Chavez, MD, FPDS
   Specialization/Content Expertise: Dermatology & Clinical Research
   Affiliations:
   - The Medical City Clinics
   - Rizal Medical Center

3. Regina Dionisio-Capulong, MD, FPPS, FPSAAI
   Specialization/Content Expertise: Allergy and Immunology
   Affiliations:
   - ManilaMed
   - Manila Doctors Hospital
   - Philippine Society of Allergy, Asthma and Immunology
   - Philippine Pediatric Society

4. Melanie Joy C. Doria-Ruiz, MD, FPDS, MMHOA
   Specialization/Content Expertise: Immunodermatology, Research
   Affiliations:
   - Dr. Jose R. Reyes Memorial Medical Center, Department of Dermatology (National Specialty Center for Dermatology)
   - ACE Baypointe Hospital and Medical Center
   - Floridablanca Doctors Hospital

5. Mia Chavez Fojas, MD, FPCP, FPCEDM
   Specialization/Content Expertise: Internal Medicine - Endocrinology
   Affiliation:
   - UP College of Medicine

6. Anna Maria Vida P. Garcia, RPh, D Clin Epi
   Specialization/Content Expertise: Pharmacology, Epidemiology

7. Mary Darice R. Wong-Ong, MD
   Specialization/Content Expertise: Dermatology
   Affiliations:
   - Philippine Dermatological Society

Consensus Panel

1. Lonabel P. Ancheta-Encarnacion, MD, FPDS
   Specialization/Content Expertise: Environmental Dermatology; Contact Dermatitis & Patch Testing; Occupational Dermatology
   Affiliations:
   - St. Luke's Medical Center
   - Philippine Dermatological Society
   - Philippine College of Occupational Medicine SMarT chapter
   - Philippine Medical Association – Quezon City Chapter

2. Caroline C. Aquino, MD, FPPS, DPSAAI
   Specialization/Content Expertise: ALLERGY AND IMMUNOLOGY
   Affiliations:
   - Makati Medical Center
   - Unihealth Parañaque Hospital and Medical Center
   - Calamba Doctors Hospital
   - Philippine Society of Allergy, Asthma and Immunology

3. Nelia Medina, RSW
   Specialization/Content Expertise: Social Work/Patient Advocate
   Affiliations:
   - Philippine Alliance of Patient Organization
   - The Max Foundation

4. Enrique T. Pagulayan, MD, FPCOM
   Specialization: Occupational Medicine
   Affiliations:
   - Philippine College of Occupational Medicine,Pasig Chapter
   - Philippine Medical Association, Valenzuela Chapter

5. Ma. Doris Rosales-Obias EdD, RN, CSCM
   Specialization/Content Expertise: Nursing Education - Medical-Surgical Nursing (Pathophysiology),Infectious/Communicable Disease Management & Infection Control ; Health Management.; Research. Nursing Admin.(ret)
   Affiliations:
   - Philippine Nurses Association
   - St.Paul University Iloilo, Tuguegarao, San Miguel.
   - Central Colleges of the Philippines,
   - Adamson University
   - Naga College Foundation
   - Bukidnon Colleges

6. Ofelia M. Samar-Sy, MD, FPCP, PhD
   Specialization/Content Expertise: Internal Medicine - Cardiology, Medical Education
   Affiliations:
   - Bicol University
   - Philippine College of Physicians
   - Philippine Heart Association
   - Philippine Medical Association
   - American College of Physicians

7. Emerie Gold P. Vallestero, MD, DFM
   Specialization/Content Expertise: Family and Community Medicine
   Affiliations:
   - Rizal Provincial Hospital System Jalajala, Rizal
   - Philippine Academy of Family Physicians

Non-Voting Member/ DOH Representative:
Julie Mart C. Rubite, MD, FPAFP, MMHeA
Medical Specialist IV
Disease Prevention and Control Bureau
Department of Health

Consensus Panel Facilitator: Ma. Angela M. Lavadia, MD, FPDS, IFAAD
Specialization/Content Expertise: Dermatology; Contact Dermatitis and Environmental Dermatology
Affiliations:
- Philippine Dermatological Society
- Philippine Medical Association
- American Academy of Dermatology
- East Avenue Medical Center
- St Lukes Medical Center, QC
- National Kidney &Transplant Institute
- UP Health Service

Technical Writer: Myzelle Anne Infantado-Alejandro, PTRP
Specialization/Content Expertise: Physical therapy
Affiliation: University of the Philippines Manila

External Reviewers:
1. Hester Gail Lim, MD, FPDS
   Specialization/Content Expertise: Dermatology; Translational Research
   Affiliations:
   - Vicente Sotto Memorial Medical Center
   - Chong Hua Hospital Mandaue
   - Cebu Institute of Medicine
   - Editor in Chief, Journal of the Philippine Dermatological Society
   - Fellow, Philippine Dermatological Society

2. Bryan Edgar K. Guevara, MD, FPDS, FDSP-PDS
   Specialization/Content Expertise: Dermatopathology, Immunodermatology
   Affiliations:
   - Southern Philippines Medical Center, Davao
   - Research Committee Chair, Philippine Dermatological Society,
   - Associate-Editor, Australasian Journal of Dermatology

8.3. Search Strategy

Table 8.3.1. Search strategy for the evidence review on diagnostic accuracy of patch testing for contact dermatitis (last search date: April 6, 2023)

DATABASE	QUERY	RESULTS
MEDLINE	((contact dermatitis) AND (patch testing)) AND (sensitivity)	1639
	((contact dermatitis) AND (patch testing)) AND (diagnosis)	10508
	(((contact dermatitis) AND (patch testing)) AND (diagnosis)) AND (sensitivity)	829
	(((((contact dermatitis) AND (patch testing)) AND (diagnosis)) AND (sensitivity)) NOT (children)) NOT (atopic)	663
	(((((suspected contact dermatitis) AND (patch testing)) AND (diagnosis)) AND (sensitivity)) NOT (children)) NOT (atopic)	80
Cochrane Library	contact dermatitis and patch testing and diagnosis	90
	contact dermatitis and patch testing and diagnosis and sensitivity	43
	patch testing and diagnosis	536

Table 8.3.2. Search strategy for the evidence review on safety of patch testing for contact dermatitis in MEDLINE (last search date: April 6, 2023)

DATABASE	QUERY	RESULTS
MEDLINE	contact dermatitis AND patch testing AND side effects	5071
	contact dermatitis AND patch testing AND adverse effects	5061
	contact dermatitis AND patch testing AND excited skin syndrome	6
	contact dermatitis AND patch testing AND angry back syndrome	5
Cochrane Libary	contact dermatitis AND patch testing AND side effects	34
	contact dermatitis AND patch testing AND adverse effects	103
	contact dermatitis AND patch testing AND excited skin syndrome	0
	contact dermatitis AND patch testing AND angry back syndrome	0

Table 8.3.3.Search strategy for the evidence review on repeat open application test for contact dermatitis

DATABASE	#	SEARCH STRATEGY / SEARCH TERMS	LAST DATE OF SEARCH	RESULTS
MEDLINE	1	ROAT	February 20, 2023	337
	2	"repeat open application test"		10
	3	"repeated open application test"		99
	4	#1 OR #2 OR #3		386
	5	contact dermatitis[MeSH Terms]		36,099
	6	"Contact Dermatitis"		34,842
	7	"Contact Dermatitides"		9
	8	"Contact Sensitivities"		24
	9	"Contact Sensitivity"		1,527
	10	"Contact Eczema"		613
	11	"Contact Hypersensitivities"		8
	12	"Contact Hypersensitivity"		2,452

DATABASE	#	SEARCH STRATEGY / SEARCH TERMS	LAST DATE OF SEARCH	RESULTS
	13	"allergic contact dermatitis"		15,421
	14	allergic contact dermatitis[MeSH Terms]		13,579
	15	"contact allergy"		3,387
	16	#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15		42,281
	17	#4 AND #16		130
	18	#4 AND #16 Filter: Humans, English		112
Cochrane Library	1	"repeat open application test"	February 24, 2023	1
	2	ROAT		39
	3	"repeated open application test"		21
	4	#1 OR #2 OR #3		44
	5	"allergic contact dermatitis"		263
	6	"contact allergy"		152
	7	"Contact Dermatitis"		1203
	8	"Contact Dermatitides"		2
	9	"Contact Sensitivities"		1
	10	"Contact Sensitivity"		16
	11	"Contact Eczema"		30
	12	"Contact Hypersensitivities"		0
	13	"Contact Hypersensitivity"		62
	14	#5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13		1336
	15	#4 AND #14		25
HERDIN PLUS	1	(("Contact Dermatitis") OR ("Contact Dermatitides") OR ("Contact Sensitivities") OR ("Contact Sensitivity") OR ("Contact Eczema") OR ("Contact Hypersensitivities") OR ("Contact Hypersensitivity") OR ("allergic contact dermatitis") OR OR ("contact allergy")) AND (("repeated open application test") OR ("repeat open application test") OR (ROAT))	February 24, 2023	0
ClinicalTrials.gov	1	Contact dermatitis | ("repeated open application test") OR ("repeat open application test") OR (ROAT) | Adult, Older Adult	February 24, 2023	1

Table 8.3.4. Search strategy for the evidence review on home remedies or over-the-counter topical products for contact dermatitis (last search date: February 23, 2023)

DATABASE	QUERY	RESULTS
MEDLINE	Allergic contact dermatitis and home remedy	4
	Contact dermatitis and home remedy	8
	Allergic contact dermatitis and herbal	10
	Allergic contact dermatitis and menthol	3
	Allergic contact dermatitis and zinc oxide	16
Cochrane Library	(contact dermatitis) AND (treatment)	608
	(contact dermatitis) AND (home remedy)	8
	(contact dermatitis) AND (herbal)	8
	(((contact dermatitis) AND (treatment)) NOT (atopic)) NOT (psoriasis)	108
	((((contact dermatitis[MeSH Terms]) AND (herbal[MeSH Terms])) NOT (irritant[MeSH Terms])) NOT (atopic[MeSH Terms])) NOT (psoriasis[MeSH Terms])	0
	(contact dermatitis) AND (traditional medicine)	8
	(contact dermatitis) AND (menthol)	1
	(allergic contact dermatitis) AND (zinc oxide)	1

Table 8.3.5. Search strategy for the evidence review on patient education for contact dermatitis (last search date: March 1, 2023)

DATABASE	QUERY	RESULTS
MEDLINE	(contact dermatitis) AND (patient education)	162
	((clinical severity) OR (exacerbation)) OR ("clinical severity")	889,888
	((contact dermatitis) AND (patient education)) AND (((clinical severity) OR (exacerbation)) OR ("clinical severity"))	20
	(contact dermatitis) AND (family education)	96
	(patient education) OR (family education)	363, 418
	(contact dermatitis) AND ((patient education) OR (family education))	245
	(contact dermatitis) AND (secondary prevention)	166
Cochrane Library	Contact dermatitis and patient education	15
	Contact dermatitis and patient education and secondary prevention	3
Google Scholar	Contact dermatitis 'patient education' secondary prevention	218
HERDIN PLUS	Contact dermatitis	21
	Contact dermatitis and education	0
ClinicalTrials.gov	Contact dermatitis and patient education	1

Table 8.3 6. Search strategy for the evidence review on topical corticosteroids and emollient or barrier cream for contact dermatitis (last search date: March 7, 2023)

DATABASE	QUERY	RESULTS
MEDLINE	Contact Dermatitis AND Steroid AND Cream	8
	Contact Dermatitis AND Steroid AND Moisturizer	6
	Contact Dermatitis AND Steroid (Clinical Trial)	8
Cochrane Library	Contact dermatitis and steroid and cream	39
	Contact dermatitis and steroid and moisturizer	1
	Contact dermatitis and steroid and emollient	2
Google Scholar	Contact Dermatitis OR steroid OR moisturizer	757
	Contact dermatitis AND cream	38
	Contact dermatitis AND steroid OR moisturizer	4
	Contact dermatitis AND steroid AND moisturizer	0
	Contact dermatitis AND steroid AND cream	0
	Contact Dermatitis AND emollient	69
ClinicalTrials.gov	Contact dermatitis AND steroid, cream	0
	Contact dermatitis AND steroid AND moisturizer	0
	Contact dermatitis AND steroid AND emollient	0
	Contact dermatitis AND steroid	1
	Contact dermatitis	15
	Contact dermatitis AND steroid, cream	0

Table 8.3.7. Search strategy for the evidence review on topical calcineurin inhibitors vs. topical corticosteroids for contact dermatitis

DATABASE	SEARCH STRATEGY / SEARCH TERMS	LAST DATE AND TIME OF SEARCH	RESULTS	
			Yield	Eligible

Medline	(("dermatitis, contact"[MeSH Terms] OR ("dermatitis"[All Fields] AND "contact"[All Fields]) OR "contact dermatitis"[All Fields] OR ("contact"[All Fields] AND "dermatitis"[All Fields])) AND (("topical"[All Fields] OR "topically"[All Fields] OR "topicals"[All Fields]) AND ("adrenal cortex hormones"[MeSH Terms] OR ("adrenal"[All Fields] AND "cortex"[All Fields] AND "hormones"[All Fields]) OR "adrenal cortex hormones"[All Fields] OR "corticosteroid"[All Fields] OR "corticosteroids"[All Fields] OR "corticosteroidal"[All Fields] OR "corticosteroide"[All Fields] OR "corticosteroides"[All Fields])) AND (("topical"[All Fields] OR "topically"[All Fields] OR "topicals"[All Fields]) AND ("calcineurin inhibitors"[Pharmacological Action] OR "calcineurin inhibitors"[MeSH Terms] OR ("calcineurin"[All Fields] AND "inhibitors"[All Fields]) OR "calcineurin inhibitors"[All Fields]))) AND (clinicaltrial[Filter] OR meta-analysis[Filter] OR randomizedcontrolledtrial[Filter] OR review[Filter] OR systematicreview[Filter]	15 January 2023 07:40	53	4
Google Scholar	Colchicine AND COVID AND randomized trial	28 February 2023 16:45	0	0
ClinicalTrials.gov	Topical calcineurin inhibitors and contact dermatitis	28 February 2023 16:53	2	0

Table 8.3.8. Search strategy for the evidence review on higher level of care for severe or recalcitrant contact dermatitis (last search date: February 21, 2023)

DATABASE	QUERY	RESULTS
MEDLINE	(((chronic contact dermatitis) OR (recurrent contact dermatitis)) OR (recalcitrant contact dermatitis)) AND (a higher level of care referral)	3
	(((chronic contact dermatitis) OR (recurrent contact dermatitis)) OR (recalcitrant contact dermatitis)) AND ((dermatology referral) OR (allergology referral))	21
	((dermatology referral) OR (allergology referral)) AND (contact dermatitis)	158
Cochrane Library	Population: contact dermatitis Intervention: specialized physician	0
	Population: contact dermatitis Intervention: dermatologist	0
Google Scholar	a higher level of care referral "contact dermatitis"	5,600
	"contact dermatitis, a higher level of care referral"	0
	"contact dermatitis, dermatology referral"	0
	contact dermatitis "dermatology referral"	1,030
	contact dermatitis "allergology referral"	3
	All in title: contact dermatitis a higher level of care referral	0
	All in title: contact dermatitis referral	5
HERDIN PLUS	a higher level of care referral AND contact dermatitis	0
	contact dermatitis	39
medRxiv	contact dermatitis, a higher level of care referral	6
	contact dermatitis, referral	18
	Condition: contact dermatitis Other terms: a higher level of care referral	0

DATABASE	QUERY	RESULTS
	Condition: contact dermatitis	86

Table 8.3.9. Search strategy for the evidence review on narrowband phototherapy for chronic contact dermatitis

DATABASE	SEARCH STRATEGY / SEARCH TERMS	LAST DATE AND TIME OF SEARCH	RESULTS	
			Yield	Eligible
MEDLINE	((((("dermatitis, contact"[MeSH Terms] OR ("dermatitis"[All Fields] AND "contact"[All Fields]) OR "contact dermatitis"[All Fields] OR ("contact"[All Fields] AND "dermatitis"[All Fields])) AND ("meta analysis"[Publication Type] OR "randomized controlled trial"[Publication Type] OR "systematic review"[Filter])) OR "dermatitis, contact"[MeSH Terms] OR "dermatitis, allergic contact"[MeSH Terms] OR "allergic contact dermatitis"[All Fields] OR "irritant contact dermatitis"[All Fields]) AND (("Phototherapy"[All Fields] AND "ultraviolet radiation A"[All Fields]) OR "UVA"[All Fields] OR (("ultraviolet rays"[MeSH Terms] OR ("ultraviolet"[All Fields] AND "rays"[All Fields]) OR "ultraviolet rays"[All Fields] OR ("ultraviolet"[All Fields] AND "radiation"[All Fields]) OR "ultraviolet radiation"[All Fields]) AND ("ficusin"[MeSH Terms] OR "ficusin"[All Fields] OR "psoralen"[All Fields] OR "psoralene"[All Fields] OR "furocoumarins"[MeSH Terms] OR "furocoumarins"[All Fields] OR "psoralens"[All Fields] OR "psoralenes"[All Fields])) OR "PUVA"[All Fields] OR "ultraviolet radiation B"[All Fields] OR "UVB"[All Fields] OR "narrowband UVB therapy"[All Fields] OR "NB-UVB"[All Fields] OR "Phototherapy"[MeSH Terms] OR "PUVA Therapy"[MeSH Terms])) AND (meta-analysis[Filter] OR randomizedcontrolledtrial[Filter] OR systematicreview[Filter])	February 18, 2023 14:37:17	41	2
Cochrane Library	Contact dermatitis MeSH descriptor: [Phototherapy] explode all trees or phototherapy or (MeSH descriptor: [PUVA Therapy] explode all trees and PUVA) or psoralen plus UVA or UVA1 or narrowband UVB or NBUVB and (MeSH descriptor: [Dermatitis, Allergic Contact] explode all trees or allergic contact dermatitis or MeSH descriptor: [Dermatitis, Contact] explode all trees or contact dermatitis)	January 15, 2023 17:06:31	77	2
Google Scholar	Phototherapy AND chronic recalcitrant contact dermatitis AND randomized controlled trial	February 20,2023 15:20:10	3280	
HERDIN	Phototherapy and allergic contact dermatitis		0	0
ClinicalTrials.gov	Phototherapy and allergic contact dermatitis		1	0

Table 8.3.10. Search strategy for the evidence review on systemic immunosuppressives for contact dermatitis in MEDLINE (last search date: March 10, 2023)

DATABASE	QUERY	RESULTS
MEDLINE	((severe contact dermatitis) OR (recalcitrant contact dermatitis)) AND (((((methotrexate) OR (azathioprine)) OR (cyclosporine)) OR (mycophenolate mofetil)) OR (JAK inhibitors))	34
	(contact dermatitis) AND (((((methotrexate) OR (azathioprine)) OR (cyclosporine)) OR (mycophenolate mofetil)) OR (JAK inhibitors))	103
	(immunosuppressive) AND (contact dermatitis)	0
Cochrane Library	methotrexate, OR azathioprine, OR cyclosporine, OR mycophenolate OR mofetil, OR janus OR kinase OR inhibitors "contact dermatitis"	1,010
	“contact dermatitis” AND “cyclosporine”	4
	“contact dermatitis” AND “azathioprine”	9

DATABASE	QUERY	RESULTS
	“contact dermatitis” AND “mycophenolate mofetil”	0
	“contact dermatitis” AND “janus kinase inhibitors”	0
Google Scholar	a higher level of care referral "contact dermatitis"	5,600
	contact dermatitis azathioprine	14,400
	allintitle: contact dermatitis azathioprine	7
	allintitle: contact dermatitis methotrexate	5
	allintitle: contact dermatitis cyclosporine	8
	allintitle: contact dermatitis mycophenolate mofetil	1
	allintitle: contact dermatitis janus kinase inhibitors	1
HERDIN PLUS	Contact dermatitis AND methotrexate	0
	Contact dermatitis AND azathioprine	0
	Contact dermatitis AND mycophenolate mofetil	0
	Contact dermatitis AND cyclosporine	0
	Contact dermatitis AND janus kinase inhibitors	0
ClinicalTrials.gov	Condition: contact dermatitis Other terms: methotrexate	0
	Condition: contact dermatitis Other terms: cyclosporine	0
	Condition: contact dermatitis Other terms: azathioprine	0
	Condition: contact dermatitis Other terms: mycophenolate mofetil	0
	Condition: contact dermatitis Other terms: janus kinase inhibitors	0
	Condition: contact dermatitis Other terms: baricitinib	1
	Condition: contact dermatitis Other terms: upacitinib	0

8.4. PRISMA Flow Diagram

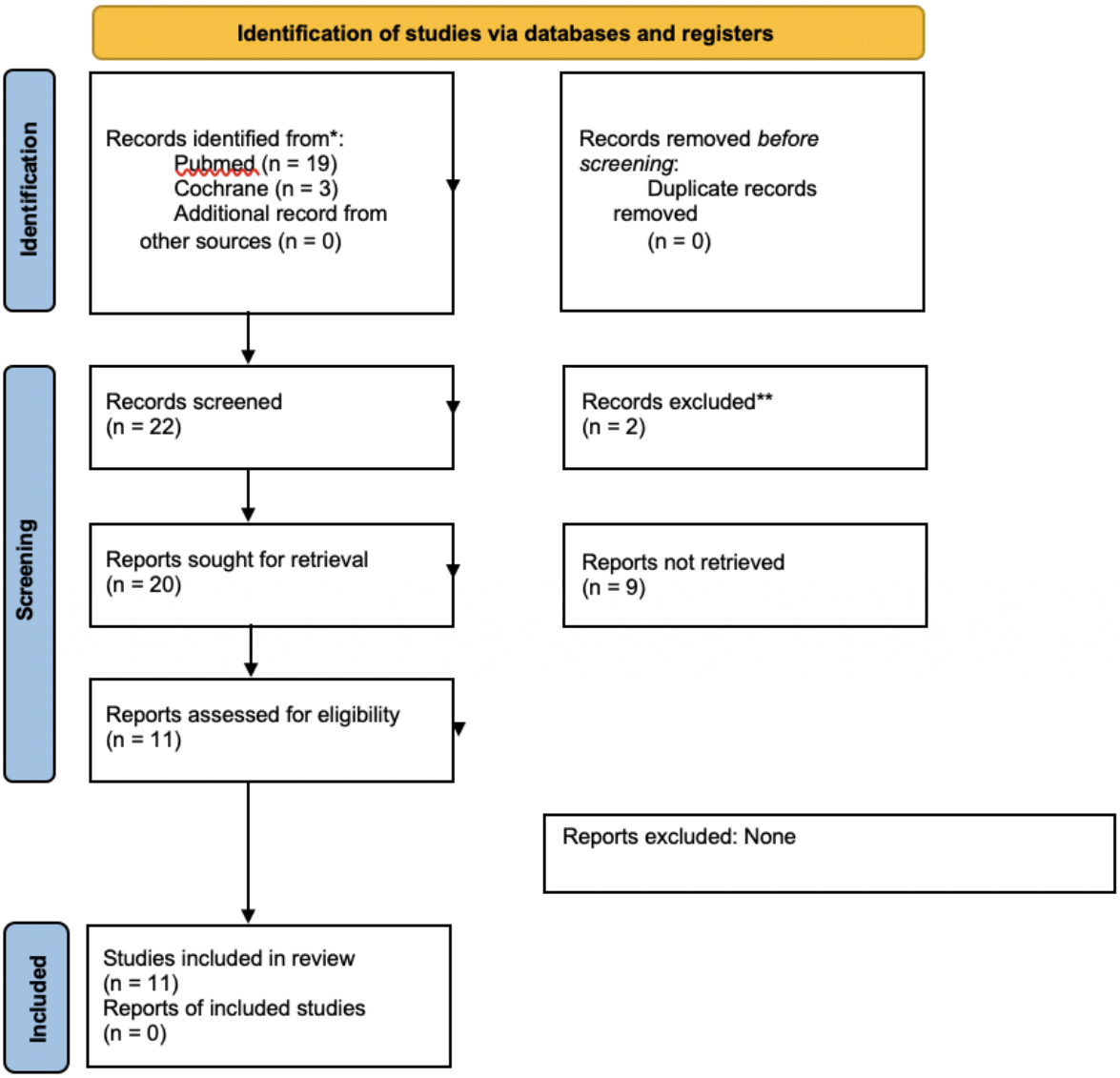

Figure 8.4.1. PRISMA flow diagram for identification and inclusion of studies on the use of patch testing: efficacy outcomes

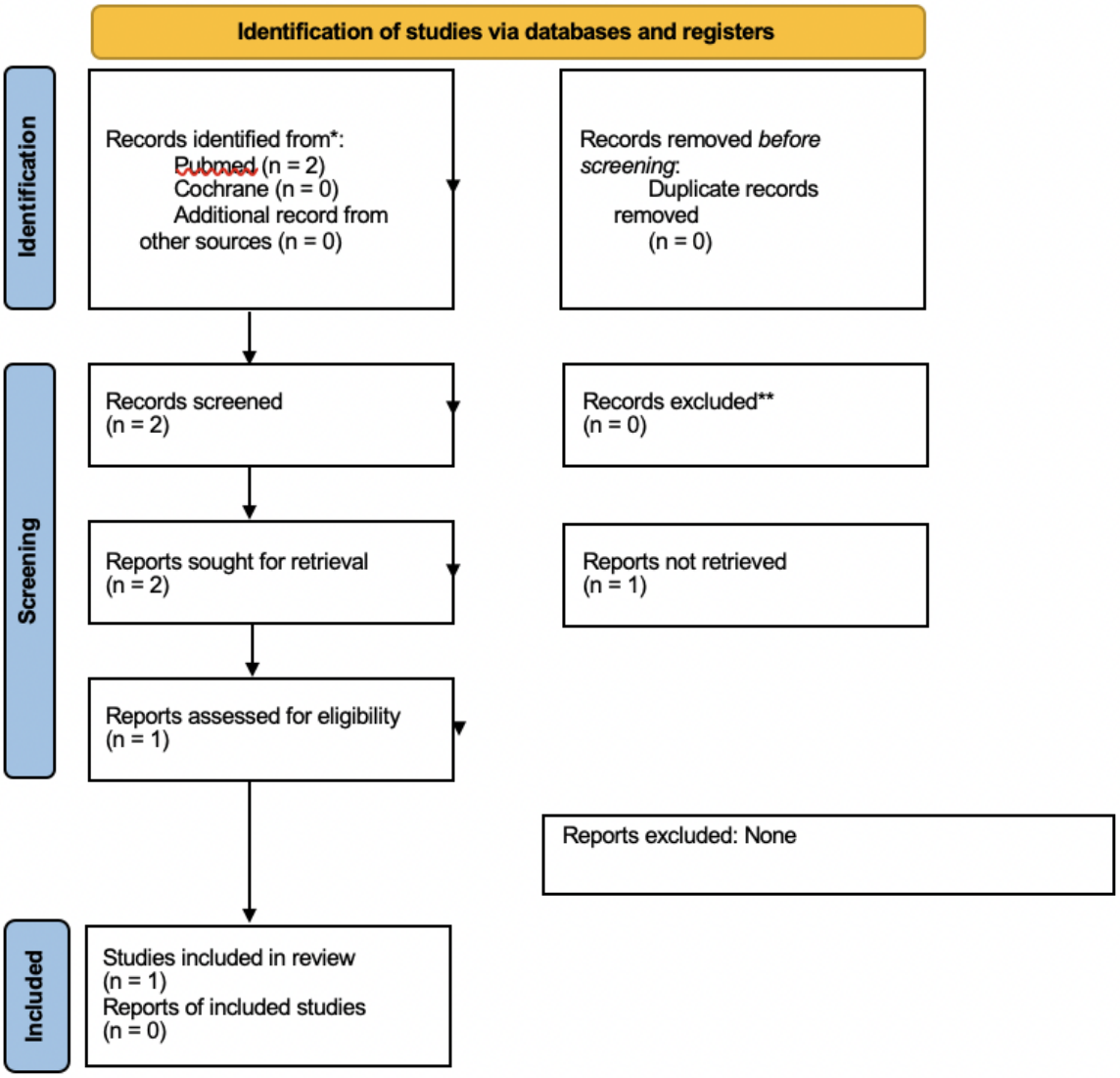

Figure 8.4.2. PRISMA flow diagram for identification and inclusion of studies on the use of patch testing: safety outcomes

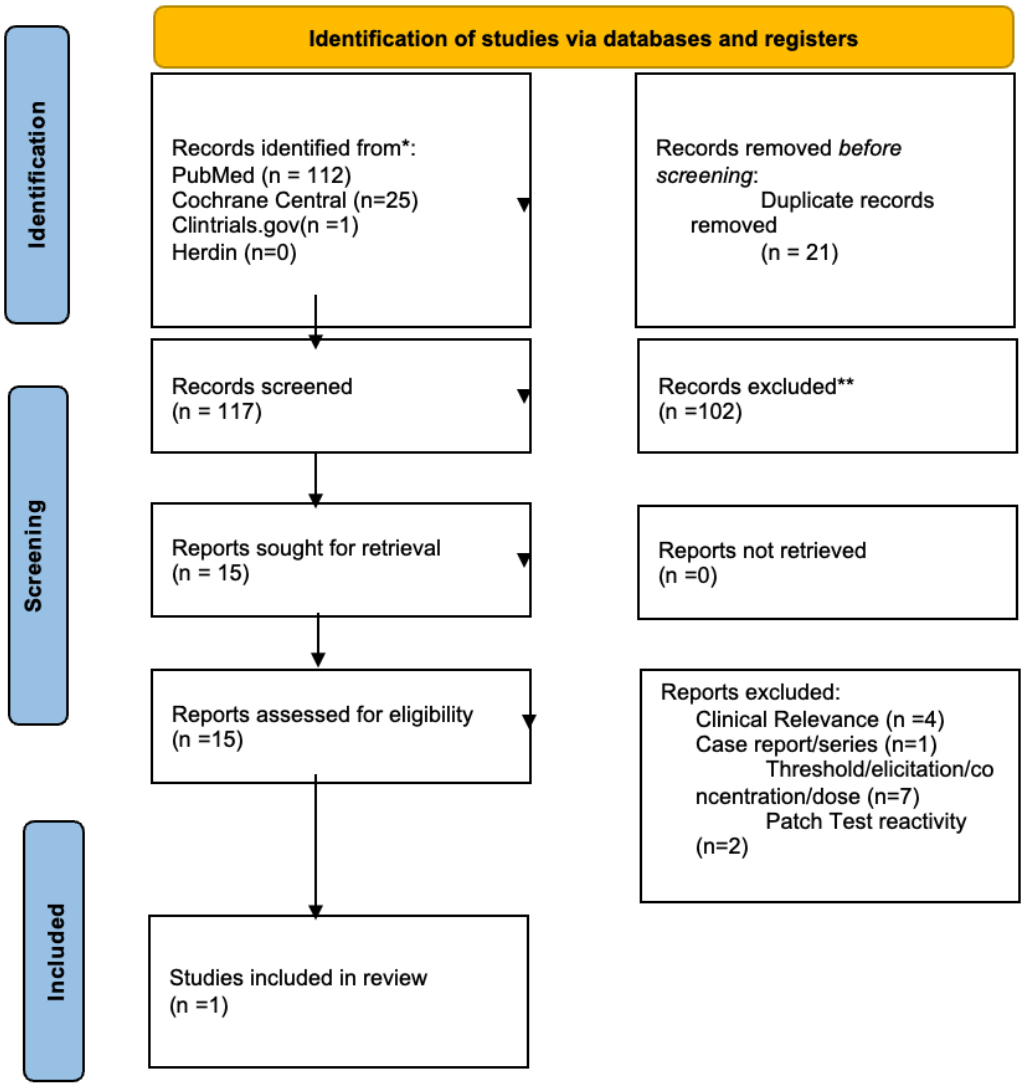

Figure 8.4.3. PRISMA flow diagram for identification and inclusion of studies on the use of ROAT

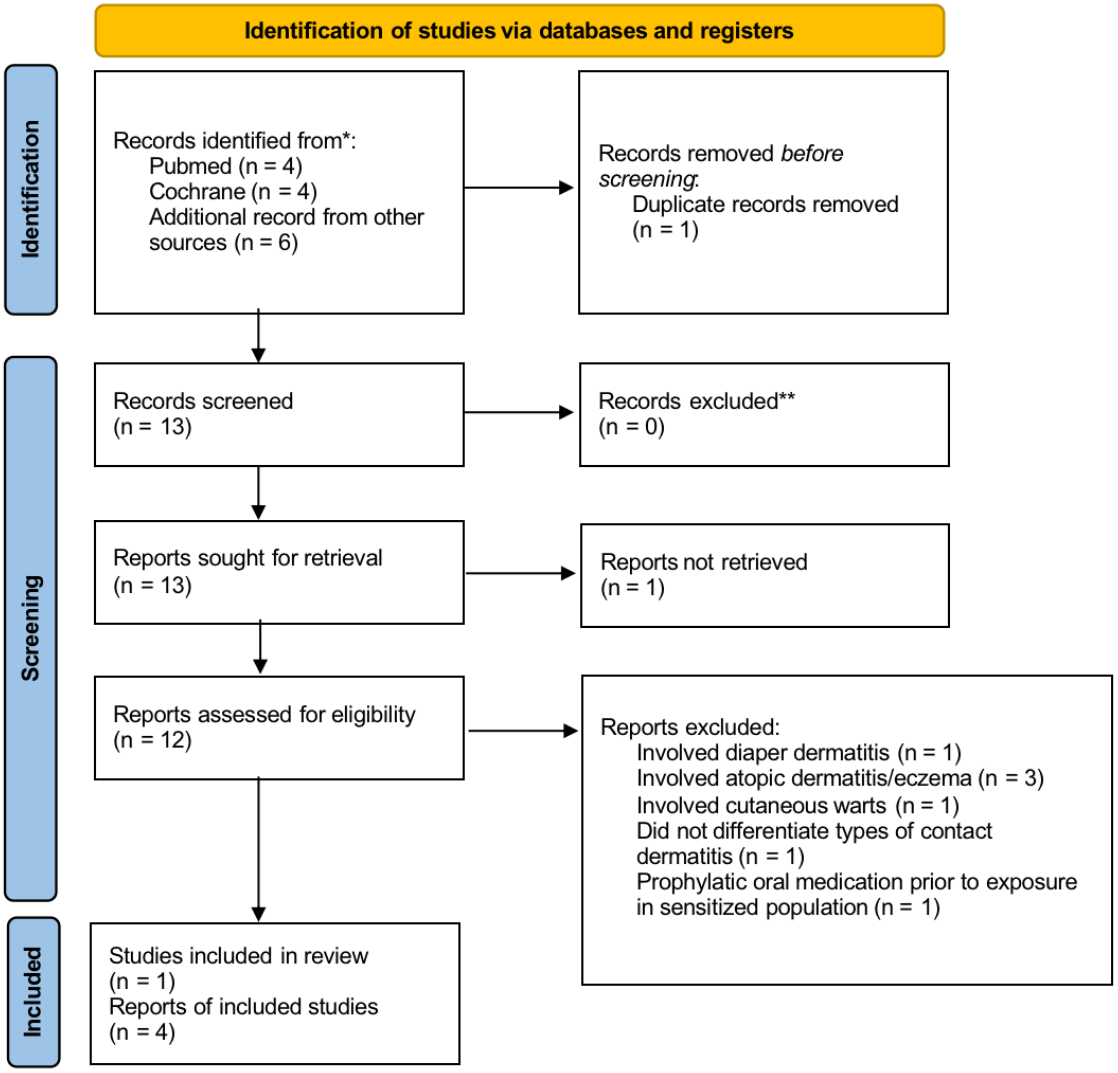

Figure 8.4.4. PRISMA flow diagram for identification and inclusion of studies on the use of home remedies for ACD

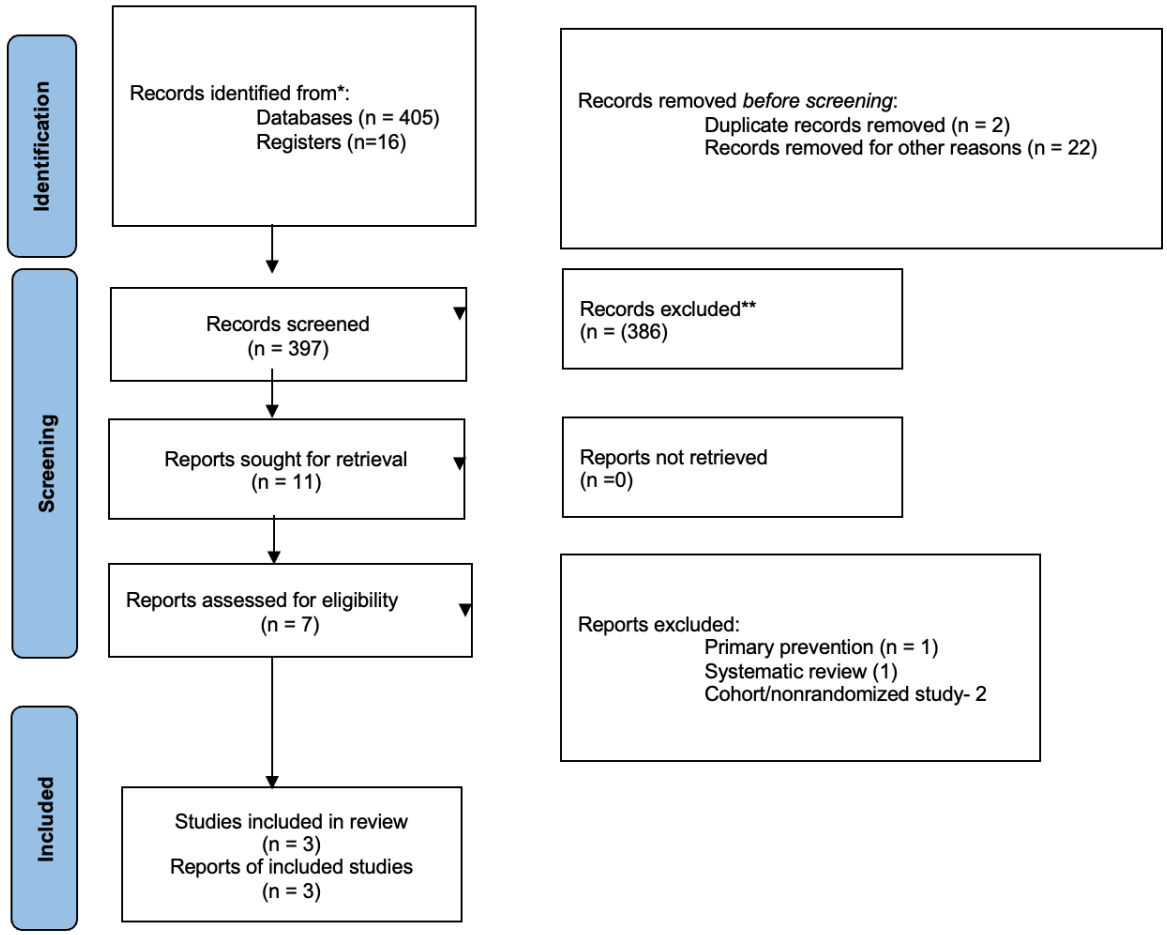

Figure 8.4.5. PRISMA flow diagram for identification and inclusion of studies on the provision of patient education for contact dermatitis

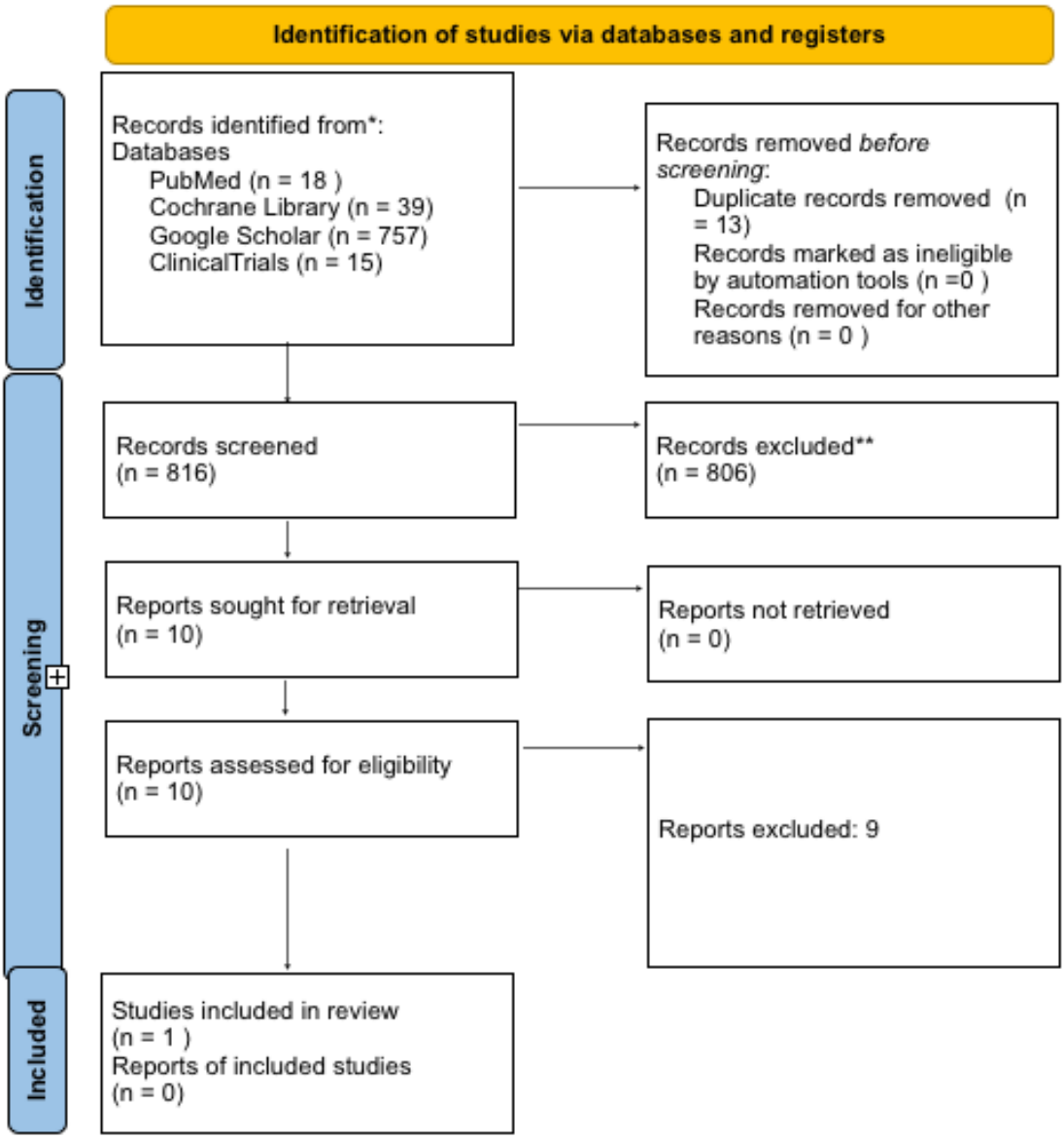

Figure 8.4.6. PRISMA flow diagram for identification and inclusion of studies on the use of emollients or barrier cream for contact dermatitis

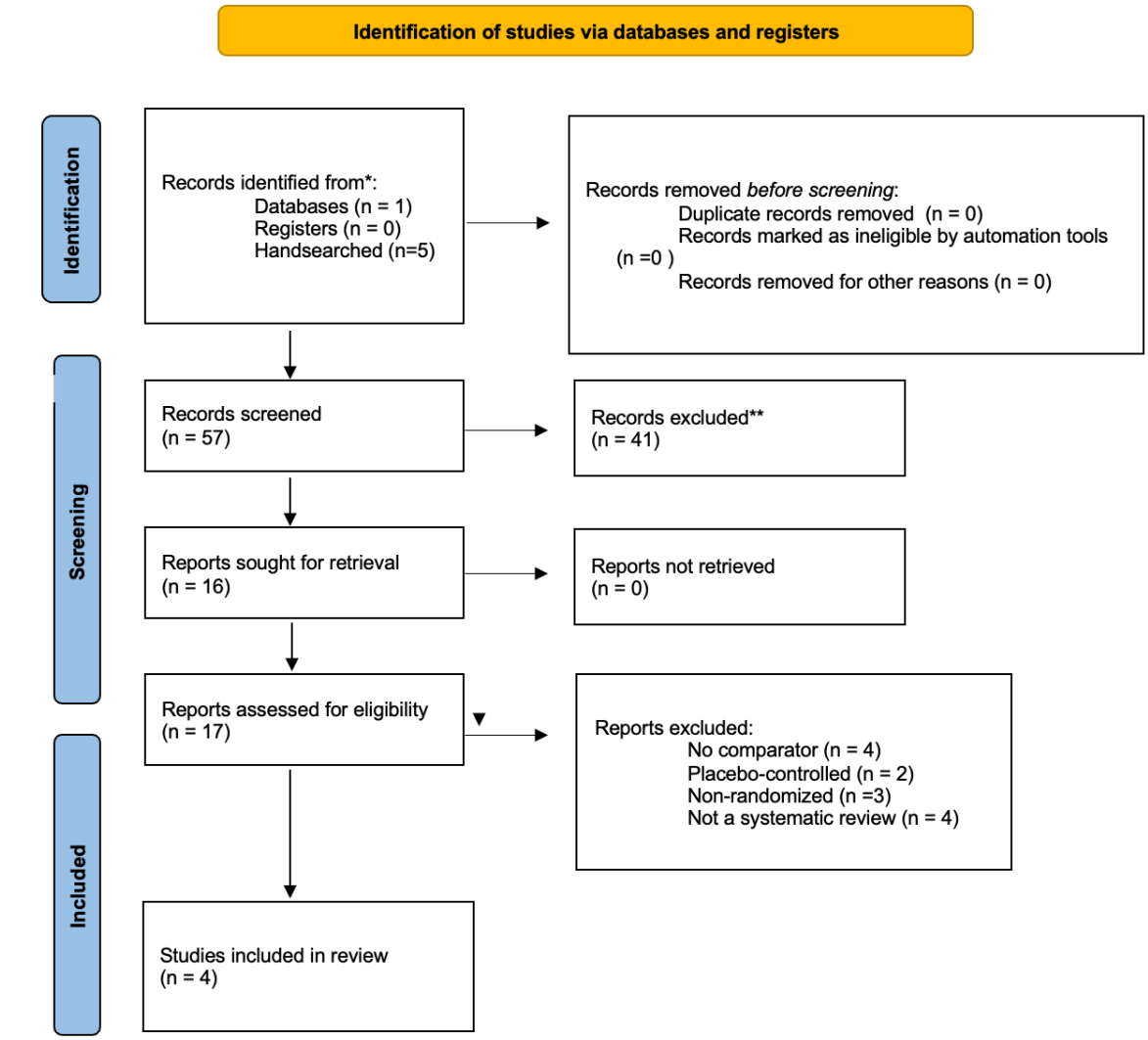

Figure 8.4.7. PRISMA flow diagram for identification and inclusion of studies on the use topical calcineurin inhibitors for contact dermatitis

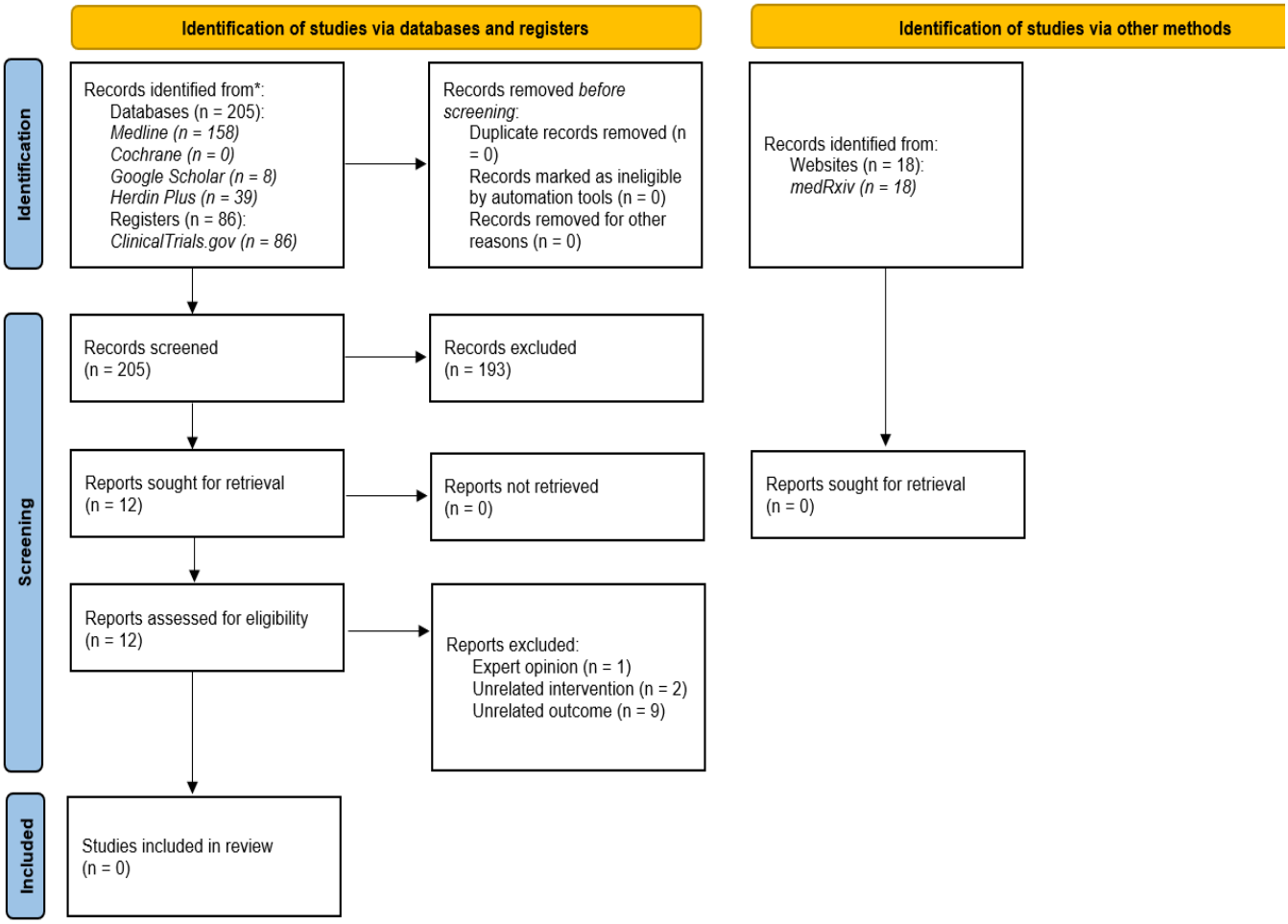

Figure 8.4.8. PRISMA flow diagram for identification and inclusion of studies on referring patients with chronic, recurrent, or recalcitrant dermatitis to a higher level of care

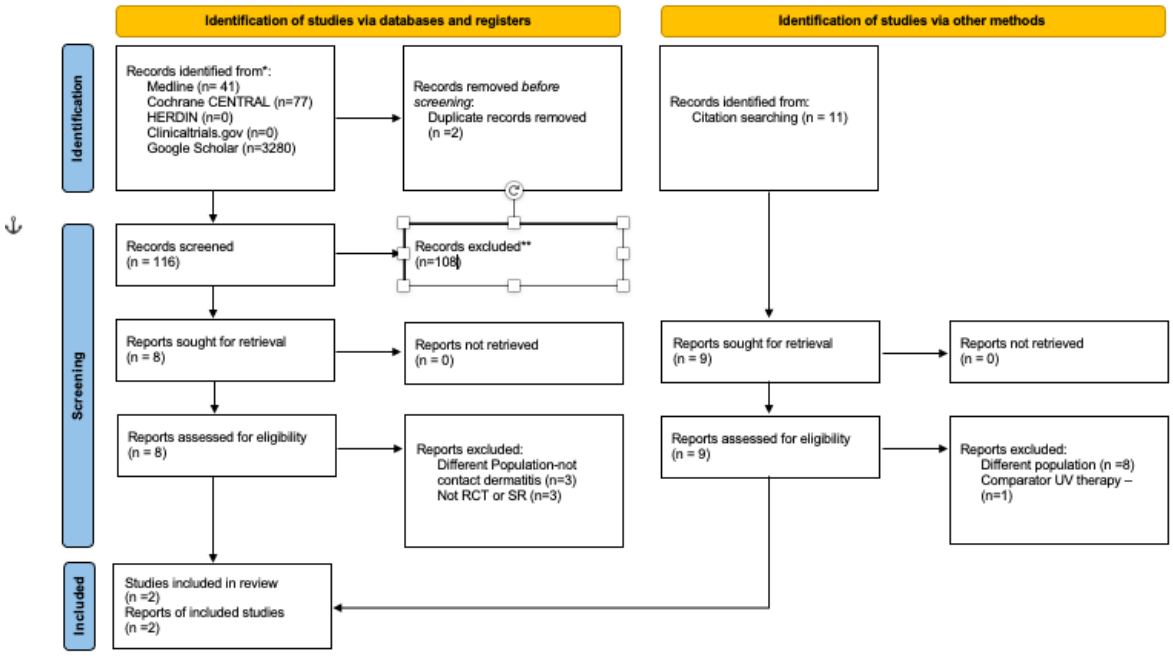

Figure 8.4.9. PRISMA flow diagram for identification and inclusion of studies on the use of phototherapy as an adjunct treatment for patients with chronic recalcitrant contact dermatitis

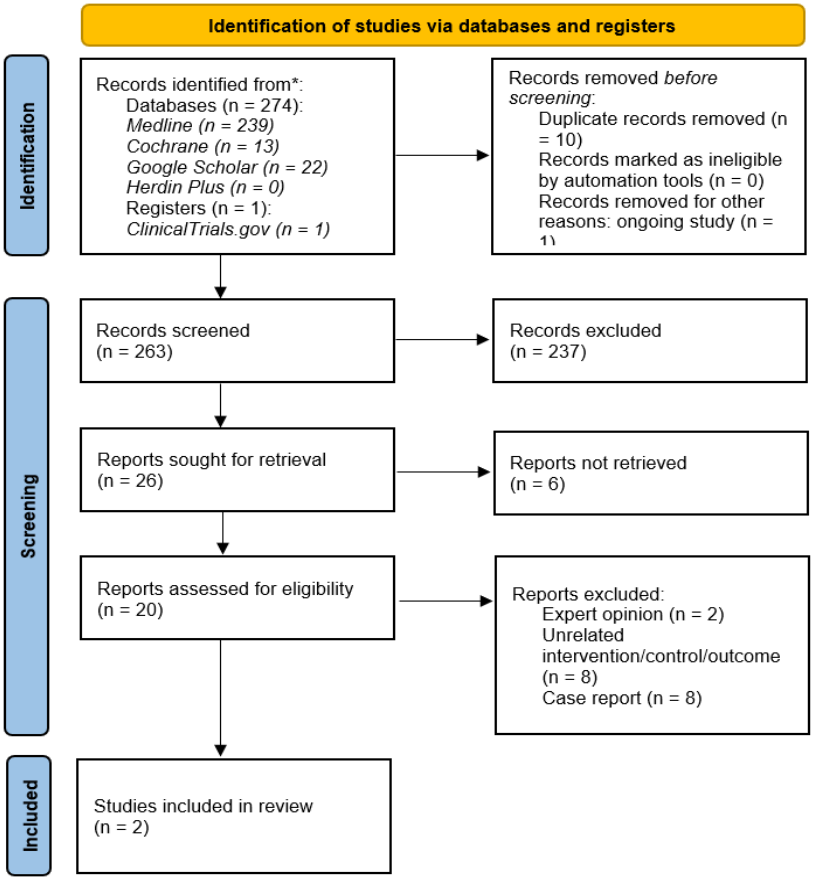

Figure 8.4.10. PRISMA flow diagram for identification and inclusion of studies on the use of systemic immunosuppressives (methotrexate, azathioprine, cyclosporin, mycophenolate mofetil, JAK inhibitors) in severe recalcitrant contact dermatitis

8.5. Characteristics of Included Studies

Table 8.5.1. **Characteristics of included studies: Patch testing**

AUTHOR/YEAR	SETTING	INDEX TEST AND REFERENCE STANDARD	POPULATION	SAMPLE SIZE	OUTCOMES
Akyol et al., 2005	Department of Dermatology, Ankara University School of Medicine	Index Test: Patch Test Reference Standard: Clinical Diagnosis	705 patients were female and 333 patients were male The patients were from 6 years of age to 77 years of age (mean age 33.40 ± 13.70 years)	1038	336 patients (32.3%) had one or more positive patch test reactions
Zug et al., 2008	Lebanon, New Hampshire; Tucson, Arizona; Minneapolis, Minnesota; Kansas City, Missouri; Cleveland and Cincinnati, Ohio; San Francisco, California; Louisville, Kentucky; Hershey, Pennsylvania; New York, New York; Ottawa, Ontario, and Montreal, Quebec, Canada; and Portland, Oregon	Index Test: Patch Test Reference Standard: Clinical Diagnosis		1497	734 (49%) had at least one positive patch test deemed of definite, probable, or possible current relevance
Li et al., 2004	Department of Dermatology, Peking University Third Hospital, Beijing, China	Index Test: Patch Test Reference Standard: Clinical Diagnosis		48	45 patients (98%) in the ACD group went on to have relevant patch test result

AUTHOR/YEAR	SETTING	INDEX TEST AND REFERENCE STANDARD	POPULATION	SAMPLE SIZE	OUTCOMES
Garg et al., 2017	Department of Dermatology and STD, Lady Hardinge Medical College, New Delhi, India	Index Test: Patch Test Reference Standard: Clinical Diagnosis	The age group of our patients ranged from 9 to 60 years, with the mean age of 36.28 11.76 years. There were 50 females and eight male	58	Thirty-six study patients (62.1%) out of 58 clinically diagnosed with contact dermatitis reacted positively to patch test with either one or more allergens of ICFS/ISS, or suspected personal cosmetics or both
Lam et al., 2008	Social Hygiene Service, Department of Health, and Department of Community and Family Medicine, Chinese University of Hong Kong, Hong Kong, China	Index Test: Patch Test Reference Standard: Clinical Diagnosis	All 2585 patients patch tested during the study period were included in the analysis. Of the 1535 female patients, 1000 (65.1%) were aged 40 years or below. For the male patients, 477 (45.4%) were aged 40 years or below.	2585	A total of 1415 patients (54.7%) had one or more positive responses to the allergens in the European standard series
Lee et al., 2012	Department of Dermatology Chungnam National University Hospital, 640 Daesa-dong Chung-gu, Daejon	Index Test: Patch Test Reference Standard: Clinical Diagnosis	The study involved 480 female (82.1%) and 104 (17.9%) Patient age ranged from 16 to 83 years	584	A positive reaction to one or more preservatives occurred in 240 (41.1%) patients.

AUTHOR/YEAR	SETTING	INDEX TEST AND REFERENCE STANDARD	POPULATION	SAMPLE SIZE	OUTCOMES
Kolodziejczyk et al., 2016	Nicolaus Copernicus University in Toruñ, Ludwik Rydygier Medical College in Bydgoszcz, Poland	Index Test: Patch Test Reference Standard: Clinical Diagnosis	The study analyzed the histories of 79 patients with contact eczema: 61 women in age 18-83 years (mean age 46.5 years) and 18 men in age 22-80 years (mean age 54.3 years).	79	Positive patch tests results were obtained in 29 (36.7%) patients
Li et al., 2001	Department of Dermatology, Peking University, The Third Hospital, Beijing, China	Index Test: Patch Test Reference Standard: Clinical Diagnosis	63 cases of suspected ACD, 18 males and 45 females, with an average age of 36.7+/-14.9 years	63	The highest positive rate (85.7%) was found in the suspected ACD group
Oosterhaven et al., 2016	1Department of Dermatology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands,	Index Test: Patch Test Reference Standard: Clinical Diagnosis	Thirty-nine workers (8%) had Occupational Contact Dermatitis Mean age was 32 years (range: 19–47)	39	Fourteen workers (35.8%) of were diagnosed with OACD (patch test positive)
Wenk et al., 2012	Department of Dermatology, The George Washington University Medical Center, Washington, DC.	Index Test: Patch Test Reference Standard: Clinical Diagnosis	The patch test population consisted of 96 females and 4 males, with a mean age of 47 years.	100	Eighty-eight patients (88%) tested positive to at least 1 relevant allergen on the standard and/or fragrance trays

AUTHOR/YEAR	SETTING	INDEX TEST AND REFERENCE STANDARD	POPULATION	SAMPLE SIZE	OUTCOMES
Gilissen et al., 2017	Department of Dermatology, University Hospitals KU Leuven, 3000, Leuven, Belgium	Index Test: Patch Test Reference Standard: Clinical Diagnosis	5,387 (34%) were men and 10,593 (66%) were women; the mean age was 41 years in both subgroups.	15,980	8,942 (56%) showed a positive reaction to at least one of the allergens tested

Table 8.5.2. **Characteristics of included studies: ROAT**

AUTHOR/YEAR	SETTING	INDEX TEST AND REFERENCE STANDARD	POPULATION	SAMPLE SIZE	OUTCOMES
Khambra A, 2020	Department of Dermatology and STD, Safdarjung Hospital and Vardhaman Mahavir Medical College, New Delhi, India	Index Test: Repeat Open Application Study Reference Standard: Patch Test	Patients (>12 years) having dermatitis over head and neck, trunk or upper limbs and temporal correlation with hair dye	50	Sensitivity Repeat Open Application Test (ROAT):0.83 (95% CI: 0.67 to 0.94)| Specificity: ROAT:1.00 (95% CI: 0.77 to 1.00)

Table 8.5.3 **Characteristics of included studies: Home remedies for suspected ACD**

AUTHOR/YEAR	STUDY DESIGN	COUNTRY	NUMBER OF PATIENTS	POPULATION	INTERVENTION GROUP(S)	CONTROL	OUTCOMES
M. Niazi, et al, 2020	Randomized, double-blind, placebo-controlled	Iran	95	Adult patients with contact dermatitis	Topical henna	Topical placebo	Improvement in CD symptoms in the intervention group compared to the placebo group Adverse effects such as skin redness
Trakanwittayarak et al., 2019	Experimental, superiority study	Thailand	13	Adult patients with allergic contact dermatitis	Pre-treated with an emulsion containing astaxanthin	Pre-treated with an emulsion without astaxanthin	Effects on the elicited reaction to p-phenylenediamine in sensitized subjects
Wallengren et al., 2010	Randomized, placebo-controlled	Sweden	21	Adult patients with allergic and irritant contact dermatitis	Tea tree oil on CD caused by nickel and benzalkonium chloride patch test	physiological saline, zinc oxide, petrolatum jelly, clobetasone butyrate, ichthammol, menthol	Reduction of signs and symptoms of allergic contact dermatitis reactions.
Alyasin et al., 2020	randomized, double arm, double blind, placebo-controlled	Iran	35	Adult patients with allergic contact dermatitis	Whey protein 30 g in 200 mL warm water at fasting time for 4 weeks	Oral placebo	Improvement in EASI, DLQI, and reports of subjective total improvement

Table 8.5.4. **Characteristics of included studies:** Patient education for contact dermatitis

AUTHOR/ YEAR	STUDY DESIGN	COUNTRY	NUMBER OF PATIENTS	POPULATION	INTERVENTION GROUP(S)	CONTROL	OUTCOMES
Fisker 2018 PREVEX	RCT	Denmark	756	Newly notified occupational hand eczema	Low-cost group counseling (one-time, 2-hour, group-based education in skin-protective behavior)	treatment as usual	total sickness absence, health-related quality of life (HR-QoL), and self-reported severity of hand eczema.
Ibler 2012 (HET)	RCT	Denmark	255	Hand eczema	Education in skin care and individual counselling based on patch and prick testing and assessment of domestic-related related exposures.	Treatment as usual	1. clinical severity of disease at five-month follow-up measured by scores on the hand eczema severity index 2. scores on the dermatology life quality index, self-evaluated severity of hand eczema, skin protective behaviours, and knowledge of hand eczema from onset to follow-up
Mollerup 2014	RCT	Denmark	306	Outpatient hospital and dermatology clinic patients with hand eczema	nurse-led counselling consultation Skin profile generated by responses from the baseline questionnaire described each patient's susceptibility, knowledge, co-morbidities, social support, known allergies, and suspected aggravating factors. The purpose of this profile was to focus on the relevant areas for individual counseling. Second, a patient self-management book was offered on a secure website with information, educational videos, and tools for self-monitoring. Patients who did not use the internet were given a folder containing almost the same features. Third, self-management support was offered through ad hoc communication and networking. The patients could contact either the intervention team of nurses or other trial participants by using the website.	Usual care	clinical disease severity at follow-up. Quality of life, burden of disease, skin protective behaviours, and self-reported medication adherence.

Table 8.5.5. **Characteristics of included studies:** Emollients or barrier cream for contact dermatitis

AUTHOR/ YEAR	STUDY DESIGN	COUNTRY	NUMBER OF PATIENTS	POPULATION	INTERVENTION GROUP(S)	CONTROL	OUTCOMES
Sobhan et al., 2020	RCT Double-blind	Iran	50 out of 63 completed study	18-65 year-old Chronic irritant hand eczema/dermatitis	Colloidal oatmeal + Fluoci- nolone 0.025% ointment versus	Placebo + Fluocin-olone 0.025% oint- ment	Hand eczema severity index (HECS) Pruritus Visual Analaog Scale (VAS)

Table 8.5.6. **Characteristics of included studies:** Topical calcineurin inhibitors for patients with contact dermatitis

AUTHOR/ YEAR	STUDY DESIGN	COUNTRY	NUMBER OF PATIENTS	POPULATION	INTERVENTION GROUP(S)	CONTROL	OUTCOMES
Alomar et al. 2003	Double blind, randomized, petrolatum and mometasone furoate 0.1% ointment controlled trial	Spain	28	Adults with a history of ACD to nickel	Tacrolimus 0.1% ointment	Mometasone furoate 0.1% ointment	Visual assessment scores Erythema index via reflectance spectrophotometry - from baseline to 7 days
Bhardwaj et al., 2007 .	Double blind, randomized, placebo-controlled	United States	21	Age 18 years and older with history of ACD to nickel (arm)	Tacrolimus Pimecrolimus	Triamcinolone Clobetasol	Proportion of patients with improvement in Visual scores from baseline to 14 days Visual scoring (NACDG) Total Reaction scores (Erythema+ Induration + Papules/ Vesicles)
Katsarou, et al., 2012	Single-centre, randomized comparative protocol	Greece	30 (2 groups of 15)	age ≥ 18 years, chronic hand eczema present at least 6 months before referral	Tacrolimus 0.1%	Mometasone furoate 0.1%	Improvement in Visual scoring (erythema, infiltration, vesiculation, desquamation, presence of cracks

AUTHOR/ YEAR	STUDY DESIGN	COUNTRY	NUMBER OF PATIENTS	POPULATION	INTERVENTION GROUP(S)	CONTROL	OUTCOMES
							and itching) on Days 30, 60 and 90
Mose, et al., 2018	Two randomized, double-blind, vehicle-controlled studies Study 2 compared TCS vs Calcineurin inhibitors	Denmark	45	Healthy adults aged 26-44 years old	Pimecrolimus Tacrolimus	Hydrocortisone Hydrocortisone butyrate Betamethasone valerate Clobetasol	Improvement in Median Visual Scores from baseline to 72 h Improvement in skin thickness based on skin ultrasound from baseline to 72 h

Table 8.5.7.**Characteristics of included studies:** Referral to a higher level of care

AUTHOR/ YEAR	STUDY DESIGN	COUNTRY	NUMBER OF PATIENTS	POPULATION	EXPOSURE	OUTCOME	FINDINGS
Hald M et al. 2009	Multicenter cohort	Denmark	348	Patients ≥18 years of age diagnosed with hand eczema	Frequent eruptions (≥ ½ of the time) in the past 12 months	Unchanged/aggravated severity at 6 months follow-up	OR 1.96 (95% CI 1.05-3.66)
Cvetkovski et al. 2006	Registry-based cohort	Denmark	540	Patients ≥18 years of age diagnosed with occupational hand eczema	Atopic dermatitis	Persistently severe/aggravated occupational hand eczema	RR 1.53 (95% CI 1.1-2.2)
						Prolonged sick leave (>5 weeks)	RR 0.58 (95% CI 0.2-1.8)

		Loss of job at 1 year follow-up	RR 1.12 (95% CI 0.2-5.3)
	Severe OHE at baseline	Prolonged sick leave (>5 weeks)	RR 5.29 (95% CI 1.6-17.7)
		Loss of job at 1 year follow-up	(RR 14.0, 95% CI 1.9-102.9)

Table 8.5.8.**Characteristics of included studies:** Phototherapy

AUTHOR/ YEAR	STUDY DESIGN	COUNTRY	NUMBER OF PATIENTS	POPULATION	INTERVENTION GROUP(S)	CONTROL	OUTCOMES
Rosen 1987	RCT	Sweden	N=35 Allergic contact dermatitis (n=22) Irritant contact dermatitis (n=6) Hyperkeratotic dermatitis (n=6)	Adults (mean age 47 for PUVA, 52 for UVB) with the following hand dermatitis: ● Bilateral hand dermatitis with symmetric distribution and severity ● Duration of at least 6 months Previous treatment, including topical corticosteroids, without improvement Dermatitis interfering with daily life	Allergic contact dermatitis , both the PUVA and UVB groups were treated 3x a day for 3 months 1. PUVA group (n=13) -Waldmann PUVA 180+200 unit with initial dose at 2 Joules/cm^2 and increased per visit (max dose of 15 Joules/cm^2 and 8-methoxypsoralen (Puvamet, Draco, Lund, Sweden) 2. UVB group (n=9) lamp with 6 Philips TL12	No phototherapy	*PUVA group vs no phototherapy (n=14)* mean difference in severity score 4.6 ± 0.7 (SEM) Dermatitis cleared for all (n=14) hands treated with PUVA, only 1 for untreated Recurrence of dermatitis (n=9) after 1-8 months (mean 3 months) Side effects (7/14) Severe nausea sec to 8-methoxypsoralen tablets (n=4) severe edema, pain, and itching (n=3) soreness and stiffness (n=2) spread of dermatitis to face and arm (2 with ACD) *UVB group vs no phototherapy (n=16)*

					tubes of 60 cm length with light dose increased per visit		Mean difference in severity score 1.4 ± 0.6 (SEM) Improved but no clearance of dermatitis Side effects- bullae (n=2), S. aureus infection (n=1) *Discontinued treatment:* PUVA group = 4 (2 did not tolerate the Puvamet tablets and experienced nausea,lassitude, and headache; 2 dropped out due to personal reasons not related to the treatment UVB group =1 (dermatitis worsened at 6 weeks after S. aureus infection)
Sjovall 1987	RCT	Sweden	N=18 Drop-outs=3	Age: Mean 45 (26-67 years) Gender: 15 females, 3 males Chronic hand eczema, resistant to conventional topical treatment Allergic contact dermatitis – 11 Atopic dermatitis -4 Constitutional endogenous eczema =3 All with one or more patch test proven allergic reactions	Group 1 :UVB-exposure of hand (n=5) 4x a week for 8 weeks Group 3: Whole body UVB (n=5) exposure with additional radiation of hands 4x a week for 8 weeks *all groups allowed to use “their ordinary topical treatment”	Group 2: Placebo (n=5) (irradiation of hands with filtered light containing no detectable ultraviolet radiation 4x a week for 8 weeks	Cleared: UVB hand 2/5 UVB body and hand 5/5 Placebo 1/5 Improved UVB hand 3/5 Placebo 1/5 Unchanged Placebo 3/5 Follow-up after 3 months of treatment: UVB hand 2/5 still improved, 3/5 with exacerbations after 1-12 weeks UVB body + hand 5/5 clear 3-10 weeks after treatment Placebo Exacerbation after 2-3 weeks

Table 8.5.9. **Characteristics of included studies:** Systemic immunosuppressives

AUTHOR/YEAR	STUDY DESIGN	COUNTRY	NUMBER OF PATIENTS	POPULATION	INTERVENTION GROUP(S)	CONTROL	OUTCOMES
Azathioprine							
Davis et al., 2014	RCT	India	N=20	20-80 years of age, diagnosed with parthenium induced airborne-contact dermatitis (clinically and by positive patch test)	N=7 Azathioprine 50 mg BID x 6 months + topical betamethasone valerate OD + pheniramine maleate 25 mg BID prn	N=13 Prednisolone in tapering doses (30 mg x 2 weeks → 20 mg x 2 weeks → 10 mg x 4 weeks → oral placebo x 4 months) + topical betamethasone valerate OD + pheniramine maleate 25 mg BID prn + antacids	1) Dermatitis Assessment Severity Index (DASI) 2) Side effects – clinically and laboratory 3) Relapse
Verma et al., 2008	RCT (single center)	India	N=41	≥18 years of age, diagnosed with parthenium dermatitis (clinically and by positive patch test)	N=20 Azathioprine 50 mg BID x 6 months + cetirizine 10 mg OD and topical clobetasol propionate prn	N=21 Betamethasone 1 mg BID x 6 months + cetirizine 10 mg OD and topical clobetasol propionate prn	1) Clinical severity score (CSS) – itching, morphology, areas of involvement 2) Side effects 3) Relapse

8.6. GRADE Evidence Profiles

Table 8.6.1. GRADE: Evidence on patch testing

Sensitivity	-- (95% CI: -- to --)	Effect per	1,000
Specificity	-- (95% CI: -- to --)	Prevalences	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	pre-test probability of 0%	
True positives (patients with allergic contact dermatitis)	11 studies 11933 patients	cross-sectional (cohort type accuracy study)	serious	serious	serious	serious		0 (0 to 0)	-
False negatives (patients incorrectly classified as not having allergic contact dermatitis)								0 (0 to 0)	
True negatives (patients without allergic contact dermatitis)	11 studies 10132 patients	cross-sectional (cohort type accuracy study)	serious	serious	serious	serious		0 (0 to 0)	-
False positives (patients incorrectly classified as having allergic contact dermatitis)								1000 (1000 to 1000)	

Table 8.6.2. GRADE: Evidence on ROAT

Patient or population: suspected allergic contact dermatitis
New test: Patch Test |Cut-off value:
Single study sensitivity Repeat Open Application Test (ROAT):0.83 (95% CI: 0.67 to 0.94)|Single study specificity Repeat Open Application Test (ROAT):1.00 (95% CI: 0.77 to 1.00)

Test result	Number of results per 1,000 patients tested (95% CI)		Number of participants (studies)	Certainty of the Evidence (GRADE)
	Prevalence3.9% Typically seen in			
	Repeat Open Application Test (ROAT)	Patch Test		
True positives	**32** (26 to 37)	**28** (22 to 33)		

Test result	Number of results per 1,000 patients tested (95% CI)		Number of participants (studies)	Certainty of the Evidence (GRADE)
	Prevalence3.9% Typically seen in			
	Repeat Open Application Test (ROAT)	Patch Test		
	4 more TP in Repeat Open Application Test (ROAT)		50 (1)	⨁⨁◯◯ **Low**[a,b]
False negatives	**7** (2 to 13)	**11** (6 to 17)		
	4 fewer FN in Repeat Open Application Test (ROAT)			
True negatives	**961** (738 to 961)	**0** (0 to 0)	50 (1)	⨁⨁◯◯ **Low**[a,b]
	961 more TN in Repeat Open Application Test (ROAT)			
False positives	**0** (0 to 223)	**961** (961 to 961)		
	961 fewer FP in Repeat Open Application Test (ROAT)			

CI: confidence interval

Explanations

a. Unclear if a random sample of patients was enrolled; Unclear if the index test results were interpreted without knowledge of the results of the reference standard • Unclear if the reference standard results were interpreted without knowledge of the results of the index test; Not all patients enrolled in the study were included in the analysis

b. Specific for hair dye

Table 8.6.3.GRADE: Evidence on home remedies vs. placebo/usual care for suspected ACD

Certainty assessment							Summary of findings						
							№ of patients		Effect		Certainty	Importance	
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Improvement	Placebo	Relative (95% CI)	Absolute (95% CI)			
Astaxanthin (assessed with: placebo)													
1	randomised trials	not serious	not serious	serious [a]	not serious	none	7/12 (58.3%)	5/12 (41.7%)	**RR 1.40** (0.61 to 3.19)	**167 more per 1,000** (from 163 fewer to 913 more)	⨁⨁⨁◯ Moderate		
Henna (assessed with: plalcebo)													
1	randomised trials	not serious	not serious	serious	not serious	none	11/37 (29.7%)	2/37 (5.4%)	**RR 5.50** (1.31 to 23.12)	**243 more per 1,000** (from 17 more to 1,000 more)	⨁⨁⨁◯ Moderate		
Oral Whey (assessed with: placebo)													
1	randomised trials	not serious	not serious	serious	not serious	none	11/18 (61.1%)	7/17 (41.2%)	**RR 1.48** (0.75 to 2.92)	**198 more per 1,000** (from 103 fewer to 791 more)	⨁⨁⨁◯ Moderate		
tea tree (assessed with: zinc)													
1	randomised trials	not serious	not serious	serious	not serious	none	9/21 (42.9%)	4/21 (19.0%)	**RR 2.25** (0.82 to 6.18)	**238 more per 1,000** (from 34 fewer to 987 more)	⨁⨁⨁◯ Moderate		
tea tree (assessed with: clobetasone)													
1	randomised trials	not serious	not serious	serious	not serious	none	9/21 (42.9%)	5/21 (23.8%)	**RR 1.29** (0.59 to 2.81)	**69 more per 1,000** (from 98 fewer to 431 more)	⨁⨁⨁◯ Moderate		

Table 8.6.4.GRADE: Evidence on patient/family education for CD

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Patient education	usual treatment/ none	Relative (95% CI)	Absolute (95% CI)		
Quality of Life												
3	randomised trials	serious[a]	not serious	not serious	not serious	none	523	531	-	MD 1.05 lower (1.65 lower to 0.45 lower)	⊕⊕⊕◯ Moderate	
Symptom Improvement												
2	randomised trials	serious[a]	not serious	not serious	not serious	none	245	264	-	MD 3.55 lower (4.93 lower to 2.16 lower)	⊕⊕⊕◯ Moderate	

Explanations

a. blinding not possible for participants and unclear for outcome assessors

Table 8.6.5.GRADE: Evidence on emollient or barrier cream as an adjunct treatment for CD

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Colloidal Oatmeal + Fluocinone 0.025% ointment	Placebo + Fluocinone 0.025% ointment	Relative (95% CI)	Absolute (95% CI)		
Hand Eczema Severity index (6 weeks)												
1	RCT	serious[a]	not serious	not serious	not serious	none	26	24	-	mean difference -30.4 (-24.23 to -36.57)	⊕⊕⊕ Moderate	
Visual Analog Scale (6 weeks)												
1	RCT	serious[a]	not serious	not serious	not serious	none	26	24	-	mean difference -3.16 (-2.74 to 3.58)	⊕⊕⊕ Moderate	
QOL (6 weeks)												
	RCT	serious[a]	not serious	not serious	not serious	none	26	24	-	mean difference -5.34 (-0.01 to -10.69)	⊕⊕⊕ Moderate	
Adverse Effect												
1	RCT	serious[a]	not serious	serious	serious	none	32	31	-	1.29 (0.31 to 5.31)	⊕⊕ Low	
Adverse Effect that led to withdrawal												
1	RCT	serious	not serious	serious	serious	none	32	31	-	0.97 (0.06 to 14.82)	⊕⊕⊕ Low	

Table 8.6.6.GRADE: Evidence on TCIs for CD -- Efficacy of Tacrolimus 0.1% or Pimecrolimus 1% vs. topical corticosteroids

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical Calcineurin Inhibitors	Topical Corticosteroids	Relative (95% CI)	Absolute (95% CI)		
Visual improvement based on the number of patients (Bhardwaj, 2007) (assessed with: North American Contact Dermatitis Group (NACDG) scoring system)												
1	randomised trials	serious[a]	not serious	serious	serious[b]	none	26/84 (31.0%)	30/84 (35.7%)	RR 0.87 (0.57 to 1.33)	5 fewer per 100 (from 15 fewer to 12 more)	⊕◯◯◯ Very low	
Visual improvement based on the size and intensity of lesions (Katsarou, 2012) (assessed with: Visual Assessment Score)												
1	randomised trials	serious	not serious	serious[c]	serious[d]	none	Visual assessment scores based on erythema, infiltration, vesiculation, desquamation, cracks and itching from baseline to day 90 were compared. Mean scores were taken for each clinical manifestation. The differences of the visual assessment scores for all the clinical parameters from baseline to day 90 between tacrolimus and mometasone did not differ at the end of the study. Neither of the two succeeded in the elimination of all parameters at the same time.				⊕◯◯◯ Very low	
Visual scoring based on the intensity of reactions (Mose, 2018) (assessed with: Modified International Contact Dermatitis Research Group Clinical Scoring System)												
1	randomised trials	serious[a]	not serious	serious[c]	serious[b]	none	Median Scores (p value) at 48h for Diphenylcyclopropenone (DPCP)-induced reactions: Positive DPCP 3 Pimerolimus 3 (<0.05) Tacrolimus 0 (<0.001) Hydrocortisone butyrate 2 (<0.001) Betamethasone valerate 2 (<0.001) Clobetasol propionate 2 (<0.001)				⊕◯◯◯ Very low	
Percent Reduction in Inflammatory Thickness (Mose 2018) (assessed with: Skin ultrasound)												
1	randomised trials	serious[a]	not serious	serious[c]	serious[b]	all plausible residual confounding would reduce the demonstrated effect	Skin thickness at 72h: pimecrolimus -13% (NS) tacrolimus -26.5% (p<0.01) hydrocortisone, butyrate, betamethasone, and clobetasol -15.3% (p<0.01)				⊕⊕◯◯ Low	

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical Calcineurin Inhibitors	Topical Corticosteroids	Relative (95% CI)	Absolute (95% CI)		
Visual assessment score using a scale (Alomar, 2003) (assessed with: Visual Scale; Scale from: 0 to 3)												
1	randomised trials	serious	not serious	serious[c]	serious[b]	all plausible residual confounding would reduce the demonstrated effect	28	28	-	SMD 0.32 SD lower (0.85 lower to 0.2 higher)	⊕⊕◯◯ Low	
Erythema via Colourimetry (Alomar, 2003) (assessed with: Erythema index values; Scale from: 0 to 30)												
1	randomised trials	serious	not serious	serious[e]	serious[b]	all plausible residual confounding would reduce the demonstrated effect	16	16	-	SMD 0.52 SD lower (1.22 lower to 0.19 higher)	⊕⊕◯◯ Low	

CI: confidence interval; MD: mean difference; RR: risk ratio; SMD: standardised mean difference

Explanations
a. Contamination may have been done by neighboring medication sites as the study used differnt topical medications in several sites in the same person.
b. Wide confidence interval or Confidence interval crossed 1.
c. Evaluation done after a short duration of treatment, and not until resolution of symptoms.
d. Different allergens were used and allergen contact sensitization was not equal in both groups.
e. Use of reflectance spectrophotometry may have errors with regard amount of skin pigmentation.

Table 8.6.7.GRADE: Evidence on TCIs for CD -- Safety of tacrolimus 0.1% or pimecrolimus 1% vs. topical corticosteroids

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical Calcineurin Inhibitors	Topical Corticosteroids	Relative (95% CI)	Absolute (95% CI)		
Skin burning associated with Tacrolimus 0.1% vs TCS (follow-up: range 3 weeks to 12 months; assessed with: No. of Events)												
4	randomised trials	not serious	not serious	serious[b]	not serious	none	446/904 (49.3%)	138/896 (15.4%)	RR 3.20 (2.72 to 3.75)	339 more per 1,000 (from 265 more to 424 more)	⊕⊕⊕◯ Moderate	
Pruritus associated with Tacrolimus 0.1% vs TCS (follow-up: range 3 weeks to 6 months; assessed with: No. of Events)												
3	randomised trials	not serious	not serious	serious[b]	not serious	none	138/864 (16.0%)	97/856 (11.3%)	RR 1.41 (1.11 to 1.80)	46 more per 1,000 (from 12 more to 91 more)	⊕⊕⊕◯ Moderate	
Skin infection associated with Tacrolimus 0.1% vs. TCS (follow-up: range 3 weeks to 6 months; assessed with: No. of Events)												
3	randomised trials	not serious	not serious	serious[b]	serious[a]	none	87/854 (10.2%)	80/856 (9.3%)	RR 1.10 (0.80 to 1.52)	9 more per 1,000 (from 19 fewer to 49 more)	⊕⊕◯◯ Low	
Skin burning associated with Pimecrolimus 1% vs TCS (follow-up: range 8 days to 12 months; assessed with: No. of Events)												
2	randomised trials	not serious	not serious	serious[b]	not serious	none	86/371 (23.2%)	38/375 (10.1%)	RR 2.28 (1.60 to 3.24)	130 more per 1,000 (from 61 more to 227 more)	⊕⊕⊕◯ Moderate	
Skin infection associated with Pimecrolimus 1% vs TCS (follow-up: range 8 days to 12 months; assessed with: No. of Events)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical Calcineurin Inhibitors	Topical Corticosteroids	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	not serious	not serious	serious[b]	serious[a]	none	69/328 (21.0%)	80/330 (24.2%)	RR 0.87 (0.65 to 1.15)	32 fewer per 1,000 (from 85 fewer to 36 more)	⊕⊕◯◯ Low	

Table 8.6.8.GRADE: Evidence on referral of patients with chronic CD to a higher level of care

Course of contact dermatitis in patients with frequent eruptions over 6 months

Bibliography: Hald M, Agner T, Blands J, et al. Clinical severity and prognosis of hand eczema. Br J Dermatol. 2009;160(6):1229-1236. doi:10.1111/j.1365-2133.2009.09139.x
Authors: Chavez, C

Certainty assessment							Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Unchanged/aggravated severity									
1	observational studies	serious[a]	not serious	not serious	not serious	none	OR 1.96 (95% CI 1.05-3.66)	⊕⊕⊕◯ Moderate	CRITICAL

[a]Large drop-out for the outcome on severity assessment (n=312), no adjustment for other prognostic factors

Course of contact dermatitis in patients with atopic dermatitis over 1 year

Cvetkovski RS, Zachariae R, Jensen H, Olsen J, Johansen JD, Agner T. Prognosis of Occupational Hand Eczema: A Follow-Up Study. Arch Dermatol. 2006;142.
Authors: Chavez, C; Cabaluna, I

Certainty assessment							Effect	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Persistently severe/aggravated eczema									
1	observational studies	serious[a]	not serious	not serious	not serious	none	RR 1.53 (95% CI 1.1-2.2)	⊕⊕⊕◯ Moderate	CRITICAL
Prolonged sick leave									

1	observational studies	serious[a]	not serious	not serious	serious[b]	none	RR 0.58 (95% CI 0.2-1.8)	⊕⊕◯◯ Low	CRITICAL
Loss of job									
1	observational studies	serious[a]	not serious	not serious	serious[b]	none	RR 1.12 (95% CI 0.2-5.3)	⊕⊕◯◯ Low	CRITICAL

[a]No adjustment for important prognostic factors and concerns on outcome criteria used
[b]Wide confidence interval

Table 8.6.9.GRADE: Evidence on phototherapy as an adjunct treatment for chronic recalcitrant CD

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Phototherapy	placebo/standard of care	Relative (95% CI)	Absolute (95% CI)		
Improvement of symptoms												
2	randomised trials	serious[1,2,a,b]	not serious	serious[c]	not serious	none	39/40 (97.5%)	25/35 (71.4%)	RR 1.39 (1.10 to 1.75)	279 more per 1,000 (from 71 more to 536 more)	⊕⊕◯◯ Low	CRITICAL
Subgroup analysis -Improvement of sympotms UVB therapy												
2	randomised trials	serious[1,a]	not serious	serious[c]	not serious	none	25/26 (96.2%)	14/21 (66.7%)	RR 1.47 (1.05 to 2.06)	313 more per 1,000 (from 33 more to 707 more)	⊕⊕◯◯ Low	CRITICAL
Subgroup analysis - Improvement of symptoms with PUVA therapy												

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Phototherapy	placebo/standard of care	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious[a]	not serious	serious[c]	serious[d]	none	14/14 (100.0%)	11/14 (78.6%)	RR 1.26 (0.94 to 1.69)	204 more per 1,000 (from 47 fewer to 542 more)	⨁◯◯◯ Very low	-

-
Remission

1	randomised trials	serious[b,e]	not serious	not serious	serious[f]	none	10	5	-	MD 11.8 weeks higher (7.8 higher to 15.8 higher)	⨁⨁◯◯ Low	

Adverse Events

2	randomised trials	serious[a]	not serious	serious[c]	serious[g]	none	9/40 (22.5%)	0/35 (0.0%)	RR 19.00 (1.16 to 312.42)	0 fewer per 1,000 (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	-

UVB adverse events

2	randomised trials	serious[a,b]	not serious	serious[c]	serious[d]	none	2/31 (6.5%)	0/21 (0.0%)	RR 5.00 (0.26 to 96.59)	0 fewer per 1,000 (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	-

PUVA Adverse events

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Phototherapy	placebo/standard of care	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious[a]	not serious	serious[h]	serious[i]	none	7/14 (50.0%)	0/14 (0.0%)	RR 15.00 (0.94 to 239.81)	0 fewer per 1,000 (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	-

CI: confidence interval; MD: mean difference; RR: risk ratio

Explanations

a. High risk of bias for randomization and allocation concealment; unclear risk of bias for blinding of outcome assessors (Rosen)
b. Unclear risk of bias for randomization and allocation concealment
c. Participants for both studies included other types of chronic hand dermatitis although most of them had contact dermatitis. All participants had positive patch test (Sjovall)
d. 95% CI 0.94, 1.69
e. No baseline characteristics presented to compare the groups
f. small events (n=15)
g. Small events
h. Included participants had other types of chronic hand dermatitis although most had contact dermatitis
i. 95% CI 0.94 to 239.81; small events

Table 8.6.10.GRADE: Evidence on systemic immunosuppressives for severe recalcitrant CD

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	azathioprine	oral corticosteroid and/or antihistamine	Relative (95% CI)	Absolute (95% CI)		
Clinical improvement >50% (assessed with: Dermatitis assessment severity index (DASI), clinical severity score (CSS))												
2	randomised trials	serious[a]	not serious	not serious	serious[b]	none	25/27 (92.6%)	29/34 (85.3%)	OR 1.50 (0.28 to 7.92)	44 more per 1,000 (from 234 fewer to 126 more)	⊕⊕◯◯ Low	
Relapse (follow-up: 6 months)												
2	randomised trials	serious[a]	not serious	not serious	serious[b]	none	12/27 (44.4%)	19/34 (55.9%)	OR 0.58 (0.20 to 1.62)	135 fewer per 1,000 (from 357 fewer to 114 more)	⊕⊕◯◯ Low	
Adverse events requiring discontinuation of therapy												
2	randomised trials	serious[a]	not serious	not serious	serious[b]	none	2/27 (7.4%)	0/34 (0.0%)	OR 3.27 (0.56 to 19.09)	0 fewer per 1,000 (from 0 fewer to 0 fewer)	⊕⊕◯◯ Low	
Other adverse events												
1	randomised trials	serious[c]	not serious	not serious	serious[d]	none			not estimable		⊕⊕◯◯ Low	

CI: confidence interval; OR: odds ratio

Explanations

a. Verma 2008 - high risk of bias due to incomplete outcome data and concerns on blinding and outcome reporting; Davis 2014 - high risk of bias due to incomplete outcome data and concerns on allocation concealment, blinding and outcome reporting

8.7. Study Quality Assessment

Table 8.7.1. Appraisal of included studies on ROAT using QUADAS-2

ITEM	AUTHORS' JUDGMENT	RISK OF BIAS	APPLICABILITY CONCERNS
DOMAIN 1: Patient Selection			
Was a consecutive or random sample of patients enrolled?	Unclear	Unclear	None
Was a case-control design avoided?	No	Low-risk	None
Did the study avoid inappropriate exclusions?	Low-Risk	Low-Risk	None
Could the selection of patients have introduced bias?	Unclear	Unclear	None
Are there concerns that the included patients and setting do not match the review question?	Yes	N/A	Specific to hair dye allergens
DOMAIN 2: Index Test			
Were the index test results interpreted without knowledge of the results of the reference standard?	No	High-Risk	None
If a threshold was used, was it pre-specified?	Yes	Low-Risk	None
Could the conduct or interpretation of the index test have introduced bias?	Yes	High-Risk	None
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	None	N/A	None
DOMAIN 3: Reference Standard			

Is the reference standards likely to correctly classify the target condition?	Yes	Low-Risk	None
Were the reference standard results interpreted without knowledge of the results of the index tests?	No	High-Risk	None
Could the reference standard, its conduct, or its interpretation have introduced bias?	Yes	High-Risk	None
Are there concerns that the target condition as defined by the reference standard does not match the question?	None	N/A	None
DOMAIN 4: Flow and Timing			
Was there an appropriate interval between index test and reference standard?	Unclear	Unclear	None
Did all patients receive the same reference standard?	Yes	Low-Risk	None
Were all patients included in the analysis?	No	High-Risk	None
Could the patient flow have introduced bias?	Yes	High-Risk	None

Table 8.7.2. Appraisal of included studies on home remedies

Study ID	R1	R2	R3	R4	R5	Overall	Comments
Niazi 2017	L	L	L	L	L	**L**	Computer generated randomization was done.All the participants and researchers were blind to their allocation. Placebo topical preparation was similar to topical henna preparation in the same color, viscosity and weight, the physician, patients, drug deliverer, and data analyst were blinded to the type of intervention.
Trakanwittaryak2020	H	L	L	H	H	**H**	No mention of method of randomization. It was not specified if the researchers and investigators were blinded.
Wallengren 2010	L	H	L	H	H	**H**	No method of randomization mentioned. The study did not specify how each intervention was labelled and concealed to the investigators
Alyasin 2020	L	L	L	L	L	**L**	A nonstratified block randomization list was created by an epidemiologist using Number Cruncher Statistical System. Then, the eligible patients were assigned into two arms by the researchers using the mentioned randomization list. Physicians, patients, drug deliverer, and data analyst were blinded to the allocation of the intervention. It should be noted that the drugs' containers were the same. Additionally, placebo powder was similar to whey powder regarding the color, odor, and taste.

Table 8.7.3.Appraisal of included study on emollient or barrier cream as an adjunct treatment vs. usual care for CD

Study ID	R1	R2	R3	R4	R5	Overall	Comments
Sobhan, et al, 2022	L	L	L	H	H	H	High risk of bias

R1- sequence generation; R2-allocation concealment; R3 – blinding; R4 – incomplete outcome data
R5 – selective outcome reporting; L – low risk of bias; H – high risk of bias; U – uncertain / no information

Table 8.7. 4.Appraisal of included studies on referral of patients with chronic CD to a higher level of care

Study ID	R1	R2	R3	R4	R5	Overall	Comments
Hald 2009	L	H[1]	L	L	H[2]	H	High risk of bias due to inadequate follow-up and lack of adjustment for important prognostic factors
Cvetkovski 2006	L	L	U[3]	L	H[2]	L	High risk of bias due to lack of adjustment for important prognostic factors and concerns on outcome criteria used

[1]Large drop-out for outcome on severity assessment (n = 312)
[2]No adjustment for other prognostic factors
[3]Incomplete information on the severity score (outcome criteria) used.

Table 8.7.5.Appraisal of included studies on narrowband phototherapy as adjunct treatment for chronic recalcitrant CD

Rosen 1986

Bias	Judgment	Support for Judgment
Random sequence generation (selection bias)	High risk	"Those born in even years received PUVA treatment and those born in odd years UVB treatment. Patients born on even dates were treated on their right hand and patients with uneven birth rates on their left hand."
Allocation concealment (selection bias)	High risk	Use of birthdates
Blinding of participants and personnel (performance bias)	Unclear	-
Blinding of outcome assessment	Unclear	Although assessment were made by the same investigator, it was not stated whether he was blinded to treatment assignments.
Incomplete outcome data (attrition bias)	Low risk	Last observed score was substituted for the missing value
Selective reporting (reporting bias)	Low risk	All outcomes pre-specified were reported
Other bias	Low risk	Baseline characteristics were similar

Sjovall 1987

Bias	Judgment	Support for Judgment
Random sequence generation (selection bias)	Unclear	Not mentioned how patients were "randomly divided into 3 groups"
Allocation concealment (selection bias)	Unclear	-
Blinding of participants and personnel (performance bias)	Low risk	Use of placebo for UVB (local) but not for whole body
Blinding of outcome assessor	Unclear	Double-blind but not mentioned if outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Per protocol analysis but 15/18 were able to complete study; 3 did not complete the study due to personal reasons
Selective reporting (reporting bias)	Low risk	No difference between methods, prespecified outcomes and results reported
Other bias	Unclear	Baseline characteristics were not reported

Table 8.7.6. Appraisal of included studies on systemic immunosuppressives vs. oral corticosteroids for severe or recalcitrant CD

Study ID	R1	R2	R3	R4	R5	Overall	Comments
Verma KK 2008	L	L	U[1]	H[2]	U[3]	H	See below
Davis SJ 2014	L	U[4]	U[5]	H[6]	U[3]	H	See below

[1]Did not specify if assessors were blinded
[2]For 10 participants lost to follow-up, reasons were not known; 14 participants who did not complete the study were excluded from analysis
[3]Protocol not available
[4]Did not describe allocation
[5]Stated that the study is single blind but did not specify who were blinded and how they were blinded
[6]Disproportionally high drop out rate in intervention group (58.8% vs. 23.5%); reasons were not known

8.8. Costs of Diagnostic Tests/Interventions

Table 8.8.1. Cost of medical procedure and service: Patch test

	PATCH TEST (PUBLIC HOSPITAL)	PATCH TEST (PRIVATE HOSPITAL)
Cost of the Procedure	Php 1,500*	Php 7,000-8,000*
Dermatologist Consultation	-	Php 500-1000

***For standard series of 30 allergens**

Table 8.8.2. Cost of medical procedure and service: ROAT

	ROAT	PATCH TEST (PUBLIC HOSPITAL)	PATCH TEST (PRIVATE HOSPITAL)
Cost of the Procedure	Will depend on the products to be tested Usually, the patient's own product was used	Php 1,500*	Php 7,000-8,000*
Dermatologist Consultation	Php 300-1000	Php 300-1000	Php 300-1000

* For standard series of 30 allergens

Table 8.8.3 Cost of available home remedies in the studies

Item	Treatment Price per item
Topical Corticosteroids	Php 200-500 per 5cg tube
Topical Henna	Php 100-200 per 100 g tube
Topical Astaxanthin	Php 60-200 per 20-50g tube
Whey powder	Php 3500 per 2.5 kg tub
Topical Tea tree cream	Php 100-500 per 30-100ml container

Table 8.8.4 Cost of treatment in the country: emollients or barrier creams

Treatment	Cost
Fluticasone propionate ointment	PHP 305.75/ 5 grams (tube)
Oatmeal cream	PHP 1,200- 1,300/ 311 grams (jar)
Oatmeal lotion	PHP 300-350/ 354 mL (bottle)

Table 8.8.5. Cost of treatment: TCIs

Treatment	Estimated Price (PHP)
Tacrolimus 0.1% Ointment 10 g tube	803.57 - 3,109.00
Pimecrolimus 1% Cream 10g tube	1,111.00
Clobetasol propionate 0.05% Cream 5g tube	50.21 - 350.00
Betamethasone dipropionate 0.1% 5g tube	41.74 to 357.75
Mometasone furoate 0.1% 5g tube	267.00 to 414.75

Note: Tacrolimus 0.1% and Pimecrolimus 1% are applied twice daily in the affected areas for up to 30 days. The dose is decreased to once daily thereafter up to 60 days (based on the longest study duration by Katsarou 2018). A patient whose treatment duration will be 90 days could consume 2 to 4 tubes of any TCI, costing a minimum of PHP 1,607.14 to a maximum of PHP 6,218.00.

Topical corticosteroids are applied twice daily for the first 7 days, then decreased to once daily for about 2 to 3 weeks (depending on the lesion's severity), tapered down to once daily, thrice a week for 2 weeks, and then once daily twice a week until resolution of lesions. A patient whose treatment duration will be 90 days could spend a minimum of PHP 168.00 to a maximum of PHP 2,488.50.

Table 8.8.6. Cost of treatment or medical services: Referral to a higher level of care

	Dermatologists	Allergologists
Number of a higher level of cares	1,325[a]	146[b]
Consultation fee (PHP)	500-1,500	500-1,500

[a]Camille B. Angeles, MD (Philippine Dermatological Society Secretary), e-mail communication, March 01, 2023
[b]Philippine Society of Allergy, Asthma & Immunology, Inc. Secretariat, e-mail communication, April 03, 2023

Table 8.8.7. Cost of treatment: phototherapy

	COST (PUBLIC HOSPITAL)	COST (PRIVATE HOSPITAL)
NB-UVB	Php 400/session	Php 980/session

Note: There are no economic evaluation studies on the use of phototherapy for recalcitrant allergic dermatitis in the Philippines. The estimated treatment cost for 36 sessions (3x a week for 3 months) is P14,400 to P35,280.

Table 8.8.8. Cost of treatment: systemic immunosuppressives

	Prednisone	Azathioprine	Cyclosporine	Methotrexate	Mycophenolate mofetil	Tofacitinib
Cost per tablet[†]	8.50 (20 mg) + 5.50 (10 mg)	37.95 (50 mg)	164 (100 mg)	10.04 (2.5 mg)	119.87 (500 mg)	814.25 (5 mg)
Usual dose /dose in studies for dermatitis per day	30 mg	100 mg	2-3 mg/kg/day (~200 mg for a 70 kg patient)	15 mg	1-2 g	10 mg
Cost per day	14.00	75.90	328	60.24	479.48	1,628.50

[†] Prices available at Watsons [Internet]. https://www.watsons.com.ph

8.9. Research on Cost-Effectiveness of Intervention, Patients' Values and Preference, Equity, Acceptability, and Feasibility

TOPIC	STUDY	FINDINGS
Patch test	No available studies	N/A
ROAT	No available studies	N/A
Home remedies	No available studies	N/A
Patient education	No available studies	N/A
Emollients or barrier creams	No available studies	N/A
TCIs	No available studies	N/A
Referral to a higher level of care	Mancusi et al, 2010	In one prospective cohort study that included 313 inpatient dermatology referrals, 20 (6.3%) of whom were diagnosed with contact dermatitis, referring services were surveyed on their perception of dermatology consultation regarding relevance and negative impact on patient treatment if dermatology consultation was not available. Two hundred seventy-eight (89%) of referring service thought that the dermatological consultation was either extremely relevant or important. Out of 313, 180 (58%) believed that it was important as it aided in a diagnosis or treatment of a dermatologic disease that was unrelated to the reason for admission and 98 (31%) thought that it was extremely relevant as it helped to achieve a diagnosis and/or changed the treatment of the disease that led to admission. Two hundred forty-seven (79%) thought that unavailability of dermatological consultation would negatively impact patient treatment [150 (48%) thought that it would slightly impact patient treatment as the patient would have suffered longer with the dermatologic complaint until an outpatient consultation was available, and 97 (31%) thought that it would negatively impact patient treatment as the systemic disease would not have been diagnosed or a potentially severe dermatologic disease would not have been treated].
Phototherapy	Philippine Dermatological Society	Phototherapy is available in NCR, Region I, CAR, Region II, III, IV, V, VII, IX, XI clinics and hospitals.
Systemic immunosuppressives	No available studies	N/A

Sources:

1. Mancusi S, Neto CF. Inpatient dermatological consultations in a university hospital. Clinics [Internet]. 2010;65(9):851–5. Available from: http://dx.doi.org/10.1590/S1807-59322010000900007
2. Philippine Dermatological Society. PDS Photodermatology Directory. https://www.pds.org.ph/wp-content/uploads/2023/01/PDS-Photodermatology-Directory-as-of-Jun-2020-FINAL.pdf. Accessed 02 March 2023.

8.10. Forest Plots

Patient Education

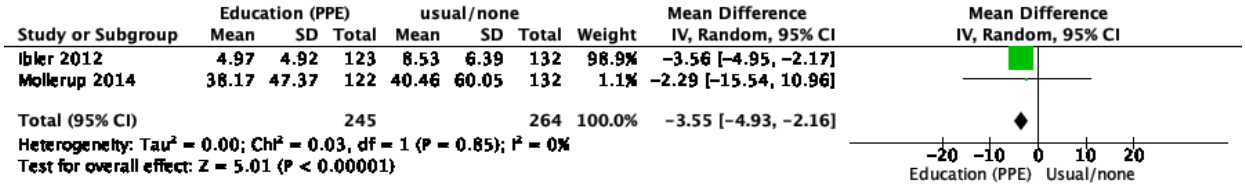

Figure 8.12.1. Forest plot of comparison: Education (use of PPE) vs usual care, outcome: Severity of symptoms

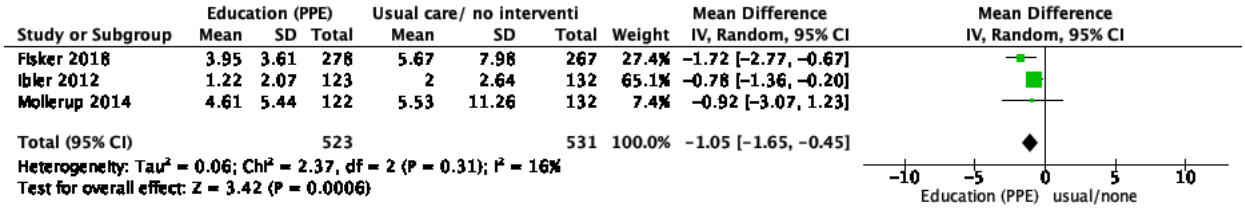

Figure 8.12.2.Forest plot of comparison: Education (use of PPE) vs usual care, outcome: Quality of life

TCI

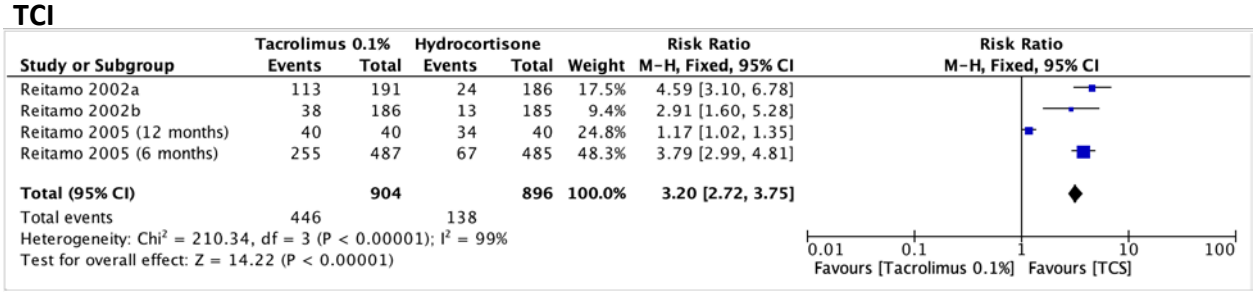

Figure 8.12. 3. Forest plot of comparison: Proportion of Patients with Improvement TCI vs TCS, outcome: Proportion of patients with improved visual scores.

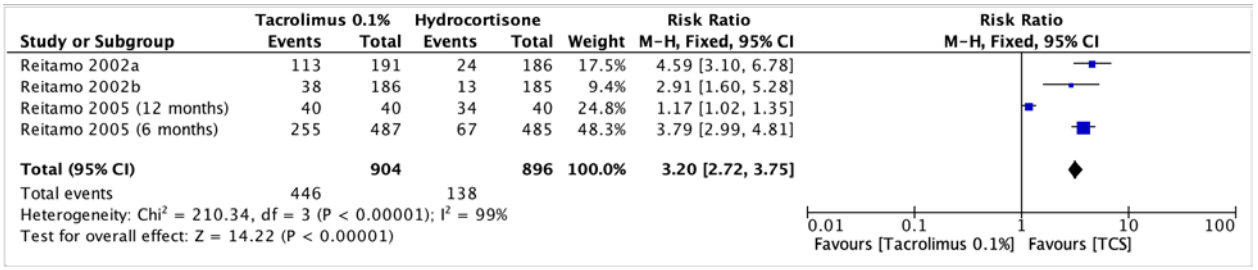

Figure 8.12. 4. Forest plot of comparison: Tacrolimus 0.1% vs TCS, outcome: Skin Burning.

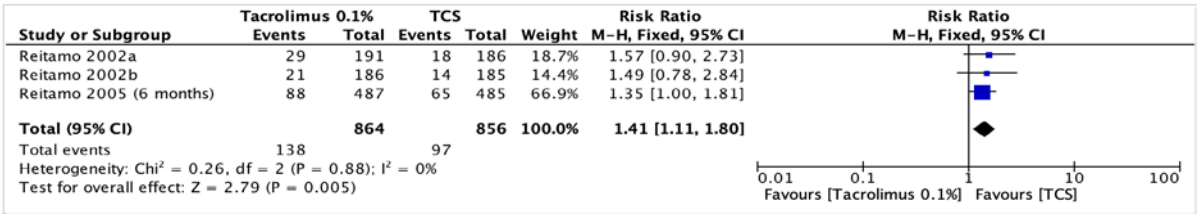

Figure 8.12.5. Forest plot of comparison: Tacrolimus 0.1% vs TCS, outcome: Pruritus.

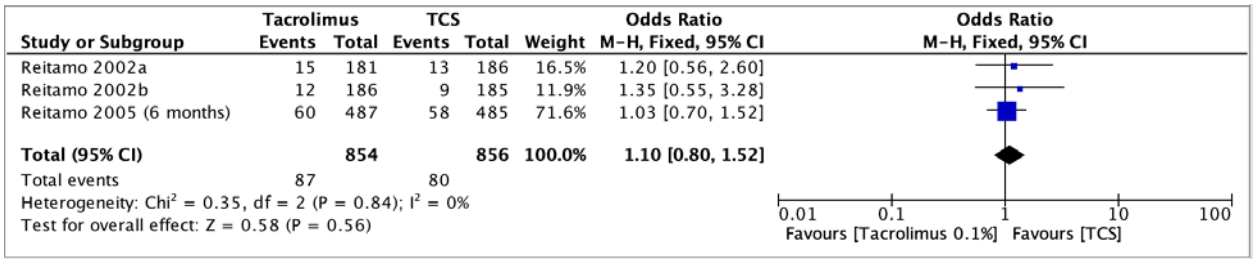

Figure 8.12.6.Forest plot of comparison: Tacrolimus 0.1% vs TCS, outcome: Skin Infection.

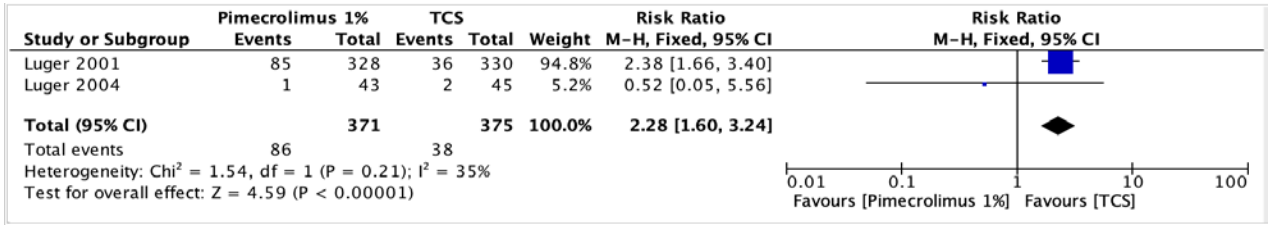

Figure 8.12.7. Pimecrolimus 1% vs TCS, outcome: Skin Burning

Phototherapy

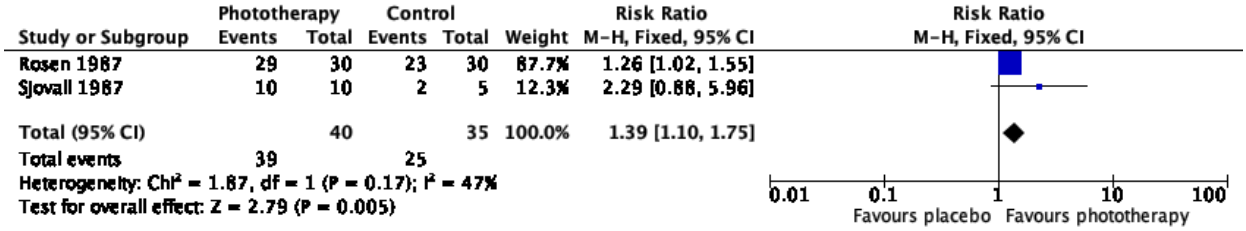

Figure 8.12.8. Improvement of symptoms with phototherapy versus placebo or no phototherapy

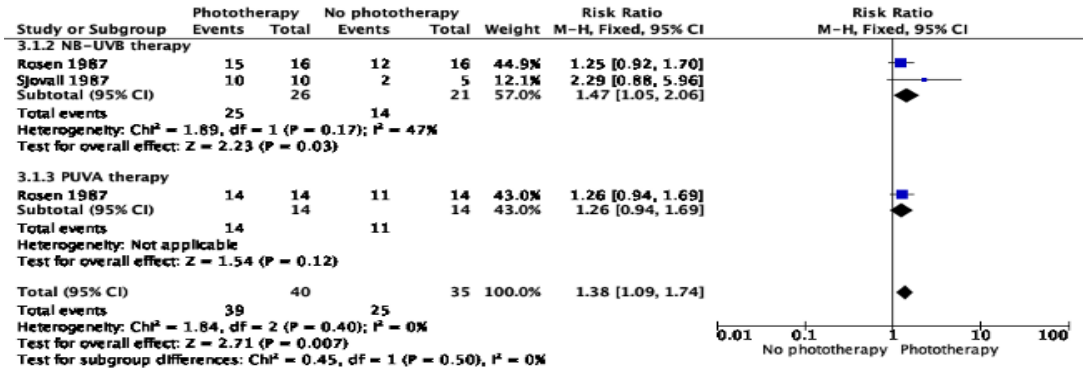

Figure 8.12.9. Subgroup analysis: Improvement of symptoms with (3.1.2) NB-UVB phototherapy versus placebo/no phototherapy, (3.1.3) PUVA therapy versus no placebo

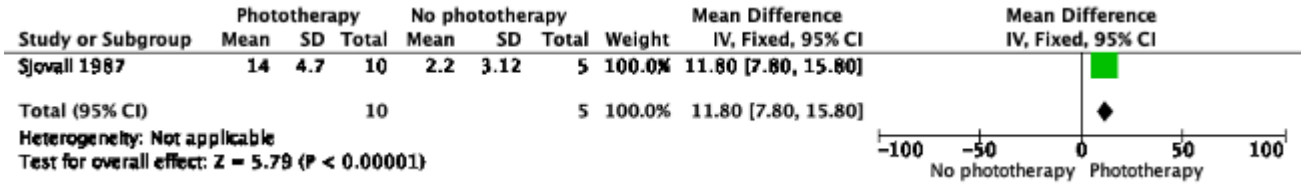

Figure 8.12. 10.Remission of dermatitis (in weeks) with NB-UVB vs placebo or no phototherapy

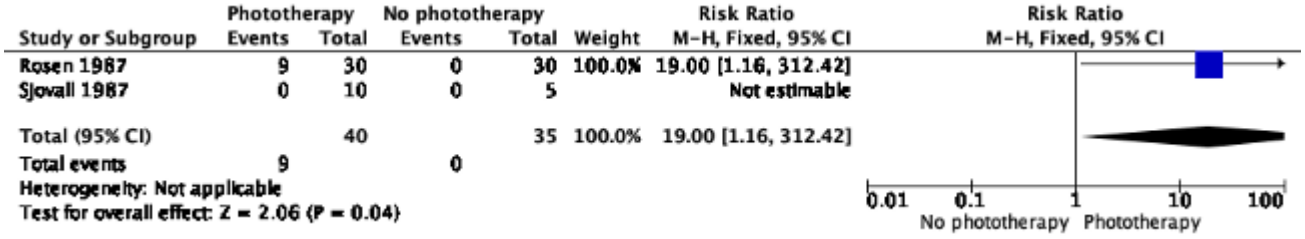

Figure 8.12. 11. Adverse events with phototherapy

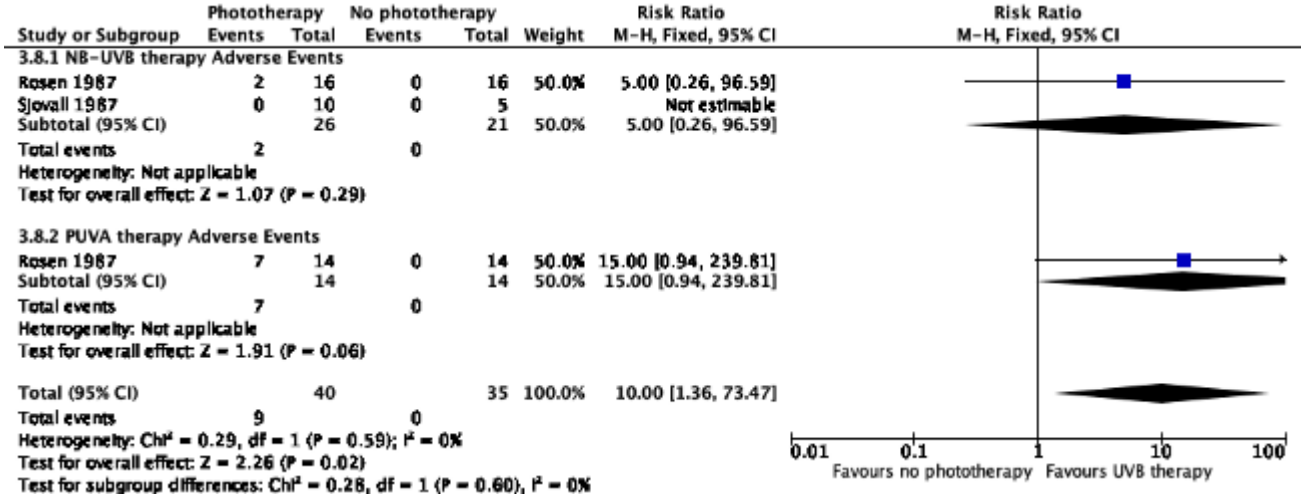

Figure 8.12.12. Subgroup analysis: Adverse events with (3.8.1) NB-UVB therapy versus placebo or no phototherapy, (3.8.2) PUVA therapy versus placebo

8.11. AGREE Reporting Checklist (Self Evaluation)

Fillable forms may be downloaded here: http://www.agreetrust.org/resource-centre/agree-reporting-checklist/

This checklist is intended to guide the reporting of clinical practice guidelines.

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
DOMAIN 1: SCOPE AND PURPOSE		
1. OBJECTIVES *Report the overall objective(s) of the guideline. The expected health benefits from the guideline are to be specific to the clinical problem or health topic.*	☒ Health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.) ☒ Expected benefit(s) or outcome(s) ☒ Target(s) (e.g., patient population, society)	**pp. 13, 15,** Executive Summary, Sections 1.1. – 1.5
2. QUESTIONS *Report the health question(s) covered by the guideline, particularly for the key recommendations.*	☒ Target population ☒ Intervention(s) or exposure(s) ☒ Comparisons (if appropriate) ☒ Outcome(s) ☒ Health care setting or context	**p. 16,** Section 1.6; **pp. 25-67**, Section 3
3. POPULATION *Describe the population (i.e., patients, public, etc.) to whom the guideline is meant to apply.*	☒ Target population, sex and age ☒ Clinical condition (if relevant) ☒ Severity/stage of disease (if relevant) ☒ Comorbidities (if relevant) ☐ Excluded populations (if relevant)	**p.15,** Section 1.4 **pp. 25-67**, Section 3;
DOMAIN 2: STAKEHOLDER INVOLVEMENT		
4. GROUP MEMBERSHIP *Report all individuals who were involved in the development process. This may include members of the steering group, the research team involved in selecting and reviewing/rating the evidence and individuals involved in formulating the final recommendations.*	☒ Name of participant ☒ Discipline/content expertise (e.g., neurosurgeon, methodologist) ☒ Institution (e.g., St. Peter's hospital) ☐ Geographical location (e.g., Seattle, WA) ☒ A description of the member's role in the guideline development group	**p. 17,** Section 2.1; **pp. 77-79,** Appendices 8.1-8.2
5. TARGET POPULATION PREFERENCES AND VIEWS *Report how the views and preferences of the target population were sought/considered and what the resulting outcomes were.*	☒ Statement of type of strategy used to capture patients'/publics' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences) ☒ Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups) ☒ Outcomes/information gathered on patient/public information ☒ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	**p. 19** Section 2.3. Formulating Recommendations: Patients' Views and Preferences and Evidence to Decision Framework

6. TARGET USERS *Report the target (or intended) users of the guideline.*	☒ The intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators) ☒ How the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)	**pp. 13, 15,** Executive Summary & Sections 1.1, 1.5
DOMAIN 3: RIGOUR OF DEVELOPMENT		
7. SEARCH METHODS *Report details of the strategy used to search for evidence.*	☒ Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL) ☒ Time periods searched (e.g., January 1, 2004 to March 31, 2008) ☒ Search terms used (e.g., text words, indexing terms, subheadings) ☒ Full search strategy included (e.g., possibly located in appendix)	**pp. 17-19** Section 2.2 Evidence Synthesis- Search Methods and Strategies, **p. 76-81**, Appendix 8.3
8. EVIDENCE SELECTION CRITERIA *Report the criteria used to select (i.e., include and exclude) the evidence. Provide rationale, where appropriate.*	☒ Target population (patient, public, etc.) characteristics ☒ Study design ☒ Comparisons (if relevant) ☒ Outcomes ☒ Language (if relevant) ☒ Context (if relevant)	**pp. 17-19** Search Methods and Strategies, Inclusion criteria and Exclusion criteria, **p. 82-90** PRISMA flow diagram
9. STRENGTHS & LIMITATIONS OF THE EVIDENCE *Describe the strengths and limitations of the evidence. Consider from the perspective of the individual studies and the body of evidence aggregated across all the studies. Tools exist that can facilitate the reporting of this concept.*	☒ Study design(s) included in body of evidence ☒ Study methodology limitations (sampling, blinding, allocation concealment, analytical methods) ☒ Appropriateness/relevance of primary and secondary outcomes considered ☒ Consistency of results across studies ☒ Direction of results across studies ☒ Magnitude of benefit versus magnitude of harm ☒ Applicability to practice context	**pp. 25-67;** Section 3 Evidence and Recommendations **pp. 95-123,** Appendices 8.5, 8.6, 8.7
10. FORMULATION OF RECOMMENDATIONS *Describe the methods used to formulate the recommendations and how final decisions were reached. Specify any areas of disagreement and the methods used to resolve them.*	☒ Recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered) ☒ Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures) ☒ How the process influenced the recommendations (e.g., results of Delphi technique influence final	**pp. 18-19** Section 2.3 Formulation of Recommendations, **pp. 25-67;** Section 3 Evidence and Recommendations

	recommendation, alignment with recommendations and the final vote)	
11. CONSIDERATION OF BENEFITS AND HARMS *Report the health benefits, side effects, and risks that were considered when formulating the recommendations.*	☒ Supporting data and report of benefits ☒ Supporting data and report of harms/side effects/risks ☒ Reporting of the balance/trade-off between benefits and harms/side effects/risks ☒ Recommendations reflect considerations of both benefits and harms/side effects/risks	**pp. 25-67;** Section 3 Evidence and Recommendations
12. LINK BETWEEN RECOMMENDATIONS AND EVIDENCE *Describe the explicit link between the recommendations and the evidence on which they are based.*	☒ How the guideline development group linked and used the evidence to inform recommendations ☒ Link between each recommendation and key evidence (text description and/or reference list) ☒ Link between recommendations and evidence summaries and/or evidence tables in the results section of the guideline	**pp. 25-67;** Section 3 Evidence and Recommendations
13. EXTERNAL REVIEW *Report the methodology used to conduct the external review.*	☒ Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence) ☒ Methods taken to undertake the external review (e.g., rating scale, open-ended questions) ☒ Description of the external reviewers (e.g., number, type of reviewers, affiliations) ☒ Outcomes/information gathered from the external review (e.g., summary of key findings) ☒ How the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)	**p. 21** Section 2.4 External Review
14. UPDATING PROCEDURE *Describe the procedure for updating the guideline.*	☒ A statement that the guideline will be updated ☒ Explicit time interval or explicit criteria to guide decisions about when an update will occur ☒ Methodology for the updating procedure	**p. 69**, Section 5. Monitoring and Evaluation – Dissemination and Implementation
DOMAIN 4: CLARITY OF PRESENTATION		
15. SPECIFIC AND UNAMBIGUOUS RECOMMENDATIONS	☒ A statement of the recommended action	**pp. 25-67;**

Describe which options are appropriate in which situations and in which population groups, as informed by the body of evidence.	☒ Intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects) ☒ Relevant population (e.g., patients, public) ☒ Caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply) ☒ If there is uncertainty about the best care option(s), the uncertainty should be stated in the guideline	Section 3 Evidence and Recommendations
16. MANAGEMENT OPTIONS *Describe the different options for managing the condition or health issue.*	☒ Description of management options ☒ Population or clinical situation most appropriate to each option	**pp. 25-67;** Section 3 Evidence and Recommendations
17. IDENTIFIABLE KEY RECOMMENDATIONS *Present the key recommendations so that they are easy to identify.*	☒ Recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms ☒ Specific recommendations grouped together in one section	**pp. 25-67;** Section 3—Evidence to Decision Considerations **p. 13,** Section 1.1. Executive Summary - Summary of Recommendations
DOMAIN 5: APPLICABILITY		
18. FACILITATORS AND BARRIERS TO APPLICATION *Describe the facilitators and barriers to the guideline's application.*	☒ Types of facilitators and barriers that were considered ☒ Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation) ☒ Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the population receive mammography) ☒ How the information influenced the guideline development process and/or formation of the recommendations	**pp. 25-67;** Section 3—Evidence to Decision Considerations p**. 68**, Section 4-Applicability Issues

19. IMPLEMENTATION ADVICE/TOOLS *Provide advice and/or tools on how the recommendations can be applied in practice.*	☒ Additional materials to support the implementation of the guideline in practice. For example: o Guideline summary documents o Links to check lists, algorithms o Links to how-to manuals o Solutions linked to barrier analysis (see Item 18) o Tools to capitalize on guideline facilitators (see Item 18) o Outcome of pilot test and lessons learned	**p. 69**, Section 5. Monitoring and Evaluation – Dissemination and Implementation
20. RESOURCE IMPLICATIONS *Describe any potential resource implications of applying the recommendations.*	☒ Types of cost information that were considered (e.g., economic evaluations, drug acquisition costs) ☒ Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.) ☒ Information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course) ☒ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	**pp. 19-20** Section 2.3 Formulating Recommendations: Evidence to Decision Framework; **pp. 25-67;** Section 3— Evidence to Decision Considerations **p. 68**, Section 4- Applicability Issues **pp. 125-127**; Appendices 8.8 and 8.9
21. MONITORING/ AUDITING CRITERIA *Provide monitoring and/or auditing criteria to measure the application of guideline recommendations.*	☒ Criteria to assess guideline implementation or adherence to recommendations ☒ Criteria for assessing impact of implementing the recommendations ☒ Advice on the frequency and interval of measurement ☒ Operational definitions of how the criteria should be measured	**p. 69**, Section 5. Monitoring and Evaluation – Dissemination and Implementation
DOMAIN 6: EDITORIAL INDEPENDENCE		
22. FUNDING BODY *Report the funding body's influence on the content of the guideline.*	☒ The name of the funding body or source of funding (or explicit statement of no funding) ☒ A statement that the funding body did not influence the content of the guideline	**p.21**; Section 2.5 Editorial Independence- Funding Source
23. COMPETING INTERESTS *Provide an explicit statement*	☒ Types of competing interests considered	**p.21**; Section 2.5 Editorial

that all group members have declared whether they have any competing interests.	☒ Methods by which potential competing interests were sought ☒ A description of the competing interests ☒ How the competing interests influenced the guideline process and development of recommendations	Independence-Management of Conflicts of Interest; **pp. 79-80** – Appendix 8.2. Summary of COI Declarations