



A Comprehensive Systematic Review of The Effect of Topical Corticosteroid and Vitamin D Analog Combination Therapy on Psoriasis Remission Duration

¹Dio Vaszdly Pramana Sukardi, ²Finda Rahmanisa

¹Faculty of Medicine, Islamic University of Indonesia, Special Region of Yogyakarta, Indonesia

²Ratu Aji Putri Botung Regional General Hospital, Penajam Paser Utara Regency, East Kalimantan, Indonesia

Corresponding Email : diosukardi@gmail.com

Article History :

Received date : 2025/09/15
Revised date : 2025/10/07
Accepted date : 2025/11/12
Published date : 2025/12/18



Copyright: © 2024 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (BY NC) license (<https://creativecommons.org/licenses/by-nc/4.0/>).

E-ISSN :

ISSN 3048-1368



P-ISSN

ISSN 3048-1376



ABSTRACT

Introduction: Topical therapy remains a cornerstone for mild-to-moderate psoriasis, but relapse after treatment cessation is a major challenge. The combination of topical corticosteroids (TCS) and vitamin D analogs (VDAs) has demonstrated superior efficacy over monotherapies for active treatment, yet comprehensive evidence on its long-term impact on remission duration is needed.

Methods: A systematic review was conducted based on a structured screening of literature from databases, adhering to predefined criteria. Studies involving adult patients with cutaneous psoriasis, evaluating concurrent topical TCS/VDA combination therapy, reporting remission duration or relapse data with ≥ 4 weeks follow-up, and employing controlled designs were included. Data on treatment regimens, remission definitions, relapse times, safety, and patient characteristics were extracted from 40 eligible sources.

Results: Proactive, long-term management with co-formulated calcipotriol/betamethasone dipropionate (Cal/BD) foam was the most effective strategy. The pivotal PSO-LONG trial demonstrated that twice-weekly proactive application nearly doubled the median time to first relapse (56 vs. 30 days) compared to reactive management, resulting in 41 additional days in remission per year (Lebwohl et al., 2020). Similar benefits were observed for other combinations, such as halobetasol/tazarotene lotion, which maintained treatment success in 38.2% of patients 4 weeks post-cessation versus 21.0% with halobetasol alone (Pariser et al., 2018). Systematic reviews confirmed the combination's superiority over VDA monotherapy (RR 2.28 for clearance) and a modest but significant benefit over potent corticosteroid monotherapy (RR 1.22) (Samarasekera et al., 2013; Queirós et al., 2017). The therapy was well-tolerated long-term, with no significant safety concerns over 52 weeks.

Discussion: The combination's efficacy stems from complementary anti-inflammatory, immunosuppressive, and keratinocyte-normalizing effects. The proactive regimen's success highlights the importance of treating subclinical inflammation to prevent relapse. Heterogeneity in outcomes is explained by differences in protocols (proactive vs. reactive), formulations (foam superiority), baseline disease severity, and combination types (co-formulated vs. sequential). The therapy offers a favorable risk-benefit profile, reducing overall corticosteroid exposure through sustained remission.

Conclusion: Proactive, long-term maintenance therapy with topical corticosteroid and vitamin D analog combinations, particularly Cal/BD foam, significantly prolongs psoriasis

remission, reduces relapse frequency, and is a safe and effective first-line strategy for long-term disease control.

Keywords: Psoriasis; Topical Therapy; Combination Therapy; Corticosteroids; Vitamin D Analogs; Remission Duration; Calcipotriol; Betamethasone Dipropionate; Proactive Management; Systematic Review.

INTRODUCTION

Background

Psoriasis is a chronic, immune-mediated inflammatory skin disease characterized by well-demarcated, erythematous, scaly plaques, affecting approximately 2-3% of the global population (Pariser et al., 2018). Its chronic and relapsing nature significantly impairs patients' quality of life, often requiring long-term management strategies. For mild-to-moderate plaque psoriasis, topical therapies remain the first-line treatment. Among these, topical corticosteroids (TCS) and vitamin D analogs (VDAs) are the most widely used classes. TCS provide potent anti-inflammatory and immunosuppressive effects, leading to rapid symptom control, but their long-term use is limited by potential local side effects (e.g., skin atrophy, telangiectasia) and a tendency for rapid relapse upon discontinuation ("rebound") (Gisondi et al., 2024). VDAs, such as calcipotriol, work by modulating keratinocyte differentiation and proliferation, and possess immunomodulatory properties, but their onset of action is slower and they can cause irritation (Yan et al., 2016).

The rationale for combining these two agents is rooted in their complementary and potentially synergistic mechanisms of action. The corticosteroid component provides swift anti-inflammatory relief, while the VDA component helps normalize the disrupted keratinocyte lifecycle characteristic of psoriasis and may mitigate some of the atrophic side effects associated with prolonged steroid use (Girolomoni et al., 2012). Fixed-dose combinations, such as calcipotriol plus betamethasone dipropionate (Cal/BD) in various vehicles (ointment, gel, foam), have been developed to enhance convenience, adherence, and efficacy.

Research Gap

While the short-term (4-8 week) efficacy of TCS/VDA combinations for reducing disease severity (e.g., achieving PASI-75) is well-established through numerous randomized controlled trials (RCTs) and systematic reviews, a critical evidence gap exists concerning their long-term impact on sustaining remission (Zhao et al., 2021). Most prior research has focused on the active

treatment phase, with comparatively less emphasis on the duration of clinical benefit after treatment is stopped or used intermittently. Key unanswered questions include: How does a proactive maintenance regimen compare to a traditional reactive ("as-needed") approach in delaying relapse? What is the median time to first and subsequent relapses with combination therapy versus monotherapy or vehicle? Do factors like formulation, application frequency, or baseline disease severity influence remission length? Addressing these questions is essential for developing optimized, long-term management protocols that maximize disease-free intervals and improve patient quality of life.

Novelty

This systematic review synthesizes evidence from a wide array of studies, with a specific and focused lens on remission duration as the primary outcome of interest. It moves beyond simply reporting efficacy scores at the end of an acute treatment phase. A significant novelty lies in its dedicated analysis of proactive management strategies (e.g., twice-weekly application to previously affected areas) versus standard reactive care, drawing heavily on landmark long-term trials like PSO-LONG (Stein Gold et al., 2020). Furthermore, it provides a detailed synthesis of factors that modify remission length, such as sex, disease severity, and formulation type, offering nuanced insights for personalized treatment. By integrating data from various combination types (Cal/BD, halobetasol/tazarotene, sequential therapies) and spanning over 20 years of research, this review presents a comprehensive, contemporary overview of how to best utilize these combinations for long-term disease control.

Hypothesis

This review operates on the central hypothesis that long-term, proactive maintenance therapy with topical combinations of corticosteroids and vitamin D analogs leads to a statistically significant and clinically meaningful prolongation of psoriasis remission and reduction in relapse rates compared to 1) reactive management strategies, 2) monotherapy with either agent alone, and 3) vehicle control.

Research Objectives

The primary objective of this systematic review is to evaluate the relationship between combination topical corticosteroid and vitamin D analog therapy and the duration of psoriasis remission. Secondary objectives include: 1) Comparing time to relapse between proactive and reactive management protocols; 2) Assessing the maintenance of therapeutic effect after treatment cessation; 3) Evaluating the comparative efficacy of combination therapy versus monotherapies on long-term outcomes; 4) Identifying patient- and treatment-related factors that influence remission duration; and 5) Summarizing the long-term safety and tolerability profile of such combinations.

Research Benefits

The findings of this review have direct clinical and practical implications. For clinicians, it provides an evidence-based framework for implementing long-term management plans for psoriasis, shifting the paradigm from purely reactive care to proactive maintenance. This can lead to better-controlled disease, fewer clinic visits, and reduced cumulative drug use. For patients, the adoption of effective proactive strategies can translate into longer periods of clear or almost-clear skin, fewer disease flares, and an improved quality of life. For healthcare systems, effective long-term control may reduce the overall economic burden associated with managing frequent relapses and complications. Finally, the review identifies areas for future research, particularly regarding optimal dosing frequency for maintenance and the long-term outcomes of newer combination formulations.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the effect of topical corticosteroid and vitamin d analog combination therapy on psoriasis remission duration.

Search Strategy

The keywords used for this research based PICO :

Element	Keyword 1	Keyword 2	Keyword 3	Keyword 4
Population (P)	Psoriasis	Psoriasis Vulgaris	Plaque Psoriasis	Cutaneous Psoriasis
Intervention (I) / Exposure (E)	Combination Topical Therapy	Corticosteroid And Vitamin D Analog	Calcipotriol/Betamethasone	Topical Combination
Comparison (C)	Monotherapy	Topical Corticosteroid Alone	Vitamin D Analog Alone	Reactive Management
Outcome (O)	Remission Duration	Time To Relapse	Maintenance Of Remission	Relapse Rate

The Boolean MeSH keywords inputted on databases for this research are: (*"Psoriasis" OR "Psoriasis vulgaris" OR "Plaque psoriasis" OR "Cutaneous psoriasis"*) AND (*"Combination topical therapy" OR "Corticosteroid and vitamin D analog" OR "Calcipotriol/betamethasone dipropionate" OR "Topical corticosteroid vitamin D combination"*) AND (*"Monotherapy" OR "Topical corticosteroid alone" OR "Vitamin D analog alone" OR "Reactive management"*) AND (*"Remission duration" OR "Time to relapse" OR "Maintenance of remission" OR "Relapse rate"*)

Screening

We screened in sources based on their abstracts that met these criteria:

- **Population - Psoriasis Diagnosis:** Does the study involve patients with clinically diagnosed cutaneous psoriasis of any type (plaque, guttate, inverse, etc.) rather than focusing exclusively on psoriatic arthritis without skin involvement?
- **Intervention - Topical Combination Therapy:** Does the study evaluate true combination therapy (concurrent use) of topical corticosteroids and topical vitamin D analogs (not systemic formulations or sequential therapy)?
- **Outcome Measurement - Remission Duration:** Does the study report remission duration, time to relapse, or maintenance of clinical improvement with follow-up data beyond acute treatment response?
- **Study Design Quality:** Is the study design a randomized controlled trial, cohort study, case-control study, systematic review, or meta-analysis (not a case report, case series with fewer than 10 patients, editorial, letter, or conference abstract)?
- **Comparison Groups:** Does the study include appropriate control or comparison groups (such as placebo, monotherapy with corticosteroids alone, vitamin D analogs alone, or other standard treatments)?
- **Follow-up Duration:** Does the study have a follow-up duration of at least 4 weeks after treatment completion?
- **Population Age:** Does the study include adult populations (12 years and older) or provide separate adult data analysis (not exclusively pediatric populations under 12 years without separate adult data)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Data extraction

- **Treatment Regimens:**

Extract detailed information about all treatment groups including:

- Specific corticosteroid used (name, concentration, formulation)
- Specific vitamin D analog used (name, concentration, formulation)
- Whether combination was co-formulated or applied separately
- Application frequency and duration of initial treatment
- Maintenance/sequential therapy protocols if applicable
- Control/comparison groups (monotherapy, placebo, other treatments)

- **Remission Definition:**

Extract how remission was defined in the study including:

- Specific criteria used to define remission (e.g., PASI score threshold, lesion score, percentage improvement)
- Assessment scales used (PASI, PGA, lesion scores, etc.)
- Whether definition was based on clinician assessment, patient assessment, or both
- Time point when remission was assessed

- **Remission Duration:**

Extract all data related to maintenance of remission including:

- Mean/median duration of remission achieved
- Percentage of patients maintaining remission at different time points (e.g., 3 months, 6 months, 1 year)
- Time to relapse data if available
- Comparison of remission duration between treatment groups
- Statistical significance of differences in remission duration

- **Follow-up Protocol:**

Extract details about how remission duration was measured including:

- Total follow-up period length
- Frequency of follow-up assessments
- How relapse was defined and detected
- Methods used to track remission status over time
- Loss to follow-up rates during maintenance phase

- **Study Population:**

Extract patient characteristics including:

- Sample size for each treatment group
- Psoriasis type and severity at baseline
- Patient demographics (age range, gender distribution)
- Disease duration
- Prior treatment history if relevant
- Body areas treated (scalp, trunk/limbs, etc.)

- **Primary Outcomes:**

Extract the main efficacy findings including:

- Primary endpoint results for each treatment group
- Short-term efficacy results (typically 2-8 weeks)
- Long-term maintenance results
- Statistical comparisons between combination and monotherapy
- Effect sizes and confidence intervals where available

- **Study Design:**

Extract study methodology details including:

- Study design (RCT, open-label, etc.)

- Randomization and blinding methods
- Number of study centers
- Study duration (treatment + follow-up phases)
- Primary vs secondary analysis designation

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	("Psoriasis" OR "Psoriasis vulgaris" OR "Plaque psoriasis" OR "Cutaneous psoriasis") AND ("Combination topical therapy" OR "Corticosteroid and vitamin D analog" OR "Calcipotriol/betamethasone dipropionate" OR "Topical corticosteroid vitamin D combination" AND "Monotherapy" OR "Topical corticosteroid alone" OR "Vitamin D analog alone" OR "Reactive management") AND ("Remission duration" OR "Time to relapse" OR "Maintenance of remission" OR "Relapse rate")	2
Semantic Scholar	("Psoriasis" OR "Psoriasis vulgaris" OR "Plaque psoriasis" OR "Cutaneous psoriasis") AND ("Combination topical therapy" OR "Corticosteroid and vitamin D analog" OR "Calcipotriol/betamethasone dipropionate" OR "Topical corticosteroid vitamin D combination") AND ("Monotherapy" OR "Topical corticosteroid alone" OR "Vitamin D analog alone" OR "Reactive management") AND ("Remission duration" OR "Time to relapse" OR "Maintenance of remission" OR "Relapse rate")	250
Springer	("Psoriasis" OR "Psoriasis vulgaris" OR "Plaque psoriasis" OR "Cutaneous psoriasis") AND ("Combination topical therapy" OR "Corticosteroid and vitamin D analog" OR "Calcipotriol/betamethasone dipropionate" OR "Topical corticosteroid vitamin D combination") AND ("Monotherapy" OR "Topical corticosteroid alone" OR "Vitamin D analog alone" OR "Reactive management") AND ("Remission duration" OR "Time to relapse" OR "Maintenance of remission" OR "Relapse rate")	4
Google Scholar	("Psoriasis" OR "Psoriasis vulgaris" OR "Plaque psoriasis" OR "Cutaneous psoriasis") AND ("Combination topical therapy" OR "Corticosteroid and vitamin D analog" OR "Calcipotriol/betamethasone dipropionate" OR "Topical corticosteroid vitamin D combination") AND ("Monotherapy" OR "Topical corticosteroid alone" OR "Vitamin D analog alone" OR "Reactive management") AND ("Remission duration" OR "Time to relapse" OR "Maintenance of remission" OR "Relapse rate")	773
Wiley Online Library	("Psoriasis" OR "Psoriasis vulgaris" OR "Plaque psoriasis" OR "Cutaneous psoriasis") AND ("Combination topical therapy" OR "Corticosteroid and vitamin D analog" OR "Calcipotriol/betamethasone dipropionate" OR "Topical corticosteroid vitamin D combination") AND ("Monotherapy" OR "Topical corticosteroid alone" OR "Vitamin D analog alone" OR "Reactive management") AND ("Remission duration" OR "Time to relapse" OR "Maintenance of remission" OR "Relapse rate")	25

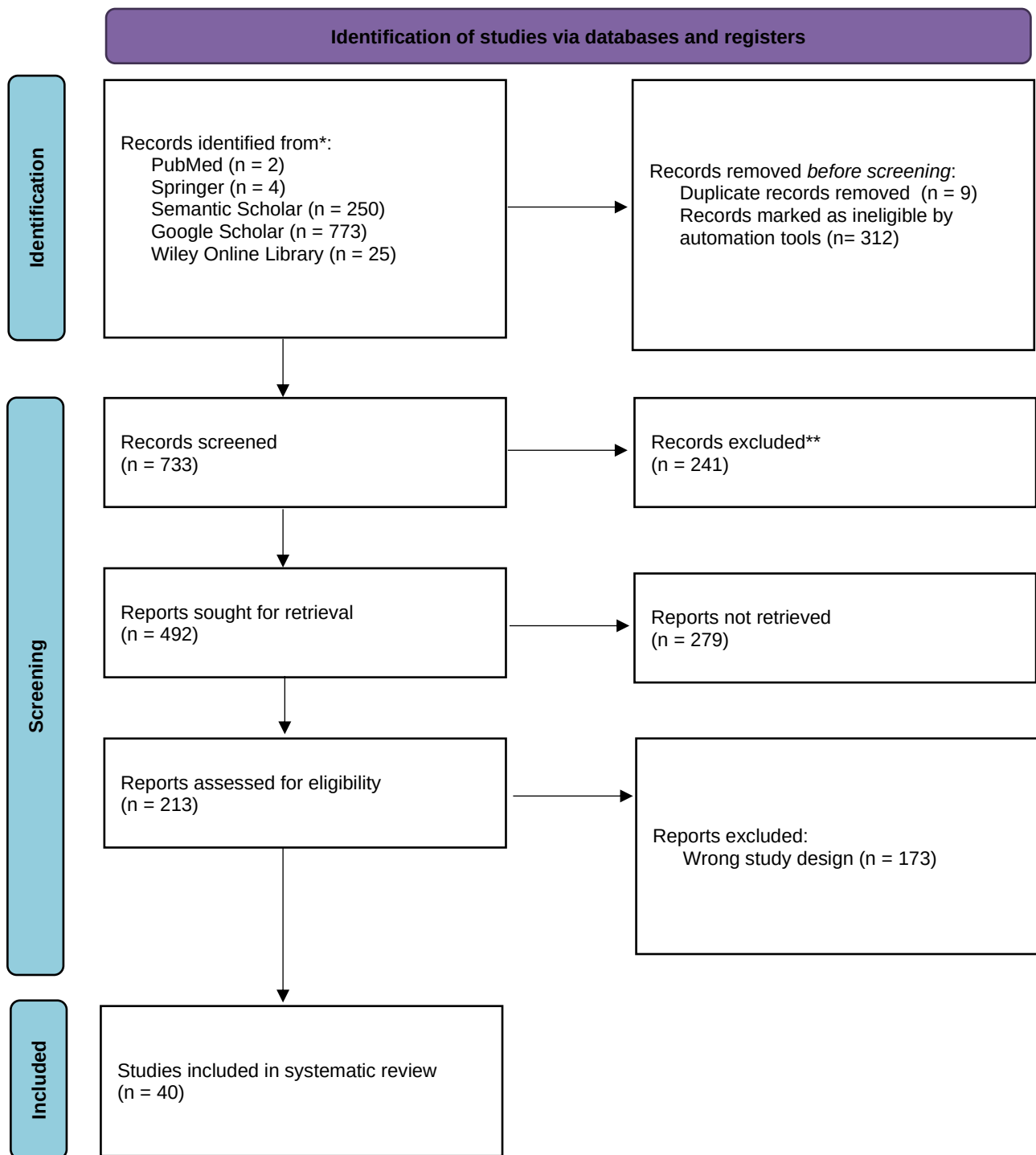


Figure 1. Article search flowchart

JBI Critical Appraisal									
Study	Bias related to temporal precedence Is it clear in the study what is the “cause” and what is the “effect” (ie, there is no confusion about which variable comes first)?	Bias related to selection and allocation Was there a control group?	Bias related to confounding factors Were participants included in any comparisons similar?	Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Were the outcomes of participants included in any comparisons measured in the same way?	Were outcomes measured in a reliable way?	Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Statistical conclusion validity Was appropriate statistical analysis used?
M. Lebwohl et al., 2020									
M. Lebwohl et al., 2020a									

Yi Zhao et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
L. S. Stein Gold et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Lebwohl et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
K. Papp et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Lebwohl et al., 2020b	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Lebwohl et al., 2020c	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Lebwohl et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
L. S. Stein Gold et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
G. Girolomon i et al., 2012	✓	✓	✓	✗	✓	✗	✓	✓	✓
K. Kragballe et al., 2006	✓	✓	✓	✗	✓	✗	✓	✓	✓

A. Bakulev et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
Hao Chen et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
T. Luger et al., 2008	✓	✓	✓	✗	✓	✗	✓	✓	✓
L. Kircik et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
D. Pariser et al., 2018	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Takhar et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
朱品华 et al., 2015	✓	✓	✓	✗	✓	✗	✓	✓	✓
E. Samarasekera et al., 2013	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Koo et al., 2006	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. G. Schlager et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓
P. Gisondi et al., 2024	✓	✓	✓	✗	✓	✗	✓	✓	✓

R. Saraceno et al., 2007	✓	✓	✓	✗	✓	✗	✓	✓	✓
G. Vena et al., 2005	✓	✓	✓	✗	✓	✗	✓	✓	✓
L. Gold et al., 2020	✓	✓	✓	✗	✓	✗	✓	✓	✓
Jacqueline Liu et al., 2023	✓	✓	✓	✗	✓	✗	✓	✓	✓
L. Gold et al., 2020a	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Lahfa et al., 2003	✓	✓	✓	✗	✓	✗	✓	✓	✓
Marjorie Heim et al., 2022	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Mason et al., 2002	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. G. Schlager et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
N. Katoh et al., 2003	✓	✓	✓	✗	✓	✗	✓	✓	✓
J. Ortonne et al., 2004	✓	✓	✓	✗	✓	✗	✓	✓	✓

Ru Yan et al., 2016	✓	✓	✓	✗	✓	✗	✓	✓	✓
M. Sindhuja et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
R. Warren et al., 2021	✓	✓	✓	✗	✓	✗	✓	✓	✓
A. Dattola et al., 2019	✓	✓	✓	✗	✓	✗	✓	✓	✓
P. Peeters et al., 2005	✓	✓	✓	✗	✓	✗	✓	✓	✓
C. Queirós et al., 2017	✓	✓	✓	✗	✓	✗	✓	✓	✓

RESULTS

Characteristics of Included Studies

This systematic review encompasses 40 sources examining the relationship between combination topical corticosteroid and vitamin D analog therapy and psoriasis remission duration. The studies varied considerably in design, population characteristics, and outcome measures.

Study	Combination Used	Treatment Duration	Body Area
M. Lebwohl et al., 2020	Cal/BD foam (co-formulated)	52 weeks maintenance	Trunk/limbs

Study	Combination Used	Treatment Duration	Body Area
M. Lebwohl et al., 2020a	Cal/BD foam (co-formulated)	52 weeks maintenance	Not specified
Yi Zhao et al., 2021	Cal/BD various formulations	Up to 52 weeks	Body/scalp
L. S. Stein Gold et al., 2020	Cal/BD foam (co-formulated)	52 weeks maintenance	Trunk/limbs
M. Lebwohl et al., 2021	Cal/BD foam (co-formulated)	52 weeks maintenance	Trunk/limbs
K. Papp et al., 2021	Cal/BD foam (co-formulated)	Not specified	Not specified
M. Lebwohl et al., 2020b	Cal/BD foam (co-formulated)	52 weeks	Trunk/limbs
M. Lebwohl et al., 2020c	Cal/BD foam (co-formulated)	52 weeks	Trunk/limbs
M. Lebwohl et al., 2022	Cal/BD foam (co-formulated)	52 weeks	Not specified
L. S. Stein Gold et al., 2018	HP/TAZ lotion (co-formulated)	8 weeks + 4 weeks follow-up	Not specified
G. Girolomoni et al., 2012	Cal/BD ointment/gel (co-formulated)	Up to 52 weeks	Body/scalp
K. Kragballe et al., 2006	Cal/BD two-compound product	52 weeks	Not specified

Study	Combination Used	Treatment Duration	Body Area
A. Bakulev et al., 2019	Cal/BD gel (co-formulated)	Up to 52 weeks	Body
Hao Chen et al., 2020	TAZ/BM cream (co-formulated)	6 weeks + 8 weeks follow-up	Not specified
T. Luger et al., 2008	Cal/BD scalp formulation (co-formulated)	52 weeks	Scalp
L. Kircik et al., 2020	Cal/BD foam + apremilast	16 weeks	Not specified
D. Pariser et al., 2018	HP/TAZ lotion (co-formulated)	8 weeks + 4 weeks follow-up	Not specified
A. Takhar et al., 2020	Cal/BD foam (co-formulated)	52 weeks	Not specified
朱品华 et al., 2015	Tacalcitol + Sicorten (separate)	8 weeks	Not specified
E. Samarasekera et al., 2013	Various combinations	Up to 52 weeks intermittent	Trunk/limbs/scalp
J. Koo et al., 2006	Calcipotriene + clobetasol (separate)	6 months	Trunk
J. G. Schlager et al., 2017	Cal/BD combination	Short-term (<6 months)	Scalp
P. Gisondi et al., 2024	Cal/BDP (co-formulated)	Not specified	Not specified

Study	Combination Used	Treatment Duration	Body Area
R. Saraceno et al., 2007	Cal/BD ointment (co-formulated)	12 weeks	Not specified
G. Vena et al., 2005	Cal/BD ointment (co-formulated)	12 weeks	Not specified
L. Gold et al., 2020	HP/TAZ lotion (co-formulated)	1 year	Not specified
Jacqueline Liu et al., 2023	Cal/BD foam (co-formulated)	8 weeks	Not specified
L. Gold et al., 2020a	HP/TAZ lotion (co-formulated)	1 year	Not specified
M. Lahfa et al., 2003	Calcitriol/calcipotriol + clobetasol (separate)	12 weeks	Not specified
Marjorie Heim et al., 2022	Cal/BD foam (co-formulated)	4 weeks	Not specified
J. Mason et al., 2002	Potent steroid + calcipotriol	Short duration	Not specified
J. G. Schlager et al., 2016	Not specified	Up to 12 months	Scalp
N. Katoh et al., 2003	Calcipotriol + clobetasol (premixed)	Not specified	Trunk
J. Ortonne et al., 2004	Cal/BD ointment (co-formulated)	8 weeks	Not specified
Ru Yan et al., 2016	Cal/BD ointment/gel (co-formulated)	4-8 weeks	Not specified

Study	Combination Used	Treatment Duration	Body Area
M. Sindhuja et al., 2021	Calcipotriol + betamethasone	6 weeks	Not specified
R. Warren et al., 2021	Cal/BD foam (co-formulated)	4 weeks	Not specified
A. Dattola et al., 2019	Cal/BD foam (co-formulated)	8 weeks	Not specified
P. Peeters et al., 2005	Cal/BD ointment (co-formulated)	8 weeks	Not specified
C. Queirós et al., 2017	Cal/BD combination	Up to 6 months	Scalp

The majority of studies (28/40) employed randomized controlled trial designs or systematic reviews of RCTs. The predominant combination studied was calcipotriene/calcipotriol with betamethasone dipropionate in co-formulated preparations, with foam formulations being most common in recent trials. Study durations ranged from 4 weeks to 52 weeks, with the PSO-LONG trial providing the most comprehensive long-term data on remission maintenance.

Effects on Remission Duration

Definition and Assessment of Remission

Remission definitions varied across studies but most commonly utilized the Physician Global Assessment (PGA) scale. The most frequently used criterion was PGA score of "clear" or "almost clear" with at least a 2-grade improvement from baseline. Some studies employed PASI-based criteria, with PASI-75 (75% improvement from baseline) serving as a

common threshold . The Investigator Global Assessment (IGA) was utilized in studies examining halobetasol/tazarotene combinations .

Time to First Relapse

Study	Treatment Group	Comparator	Median Time to Relapse	Hazard Ratio (95% CI)	P-value
M. Lebwohl et al., 2020	Cal/BD foam twice weekly	Vehicle	56 days vs 30 days	0.57 (0.47-0.69)	<0.0001
M. Lebwohl et al., 2020a	Proactive Cal/BD	Reactive management	56 days vs 30 days	Not reported	<0.001
K. Papp et al., 2021 (HPA subgroup)	Proactive Cal/BD	Reactive management	111 days vs 31 days	0.49	0.029
M. Lebwohl et al., 2021	Proactive Cal/BD	Reactive management	56 days vs 30 days	0.56	<0.001
M. Lebwohl et al., 2022 (second relapse)	Proactive Cal/BD	Reactive management	169 days vs 90 days	0.53 (0.43-0.66)	<0.001

The PSO-LONG trial and its associated analyses provide the most robust data on time to relapse. Proactive twice-weekly application of Cal/BD foam nearly doubled the median time to first relapse compared to reactive management (56 days versus 30 days) . The risk reduction was substantial, with a 43% lower risk of first relapse in the proactive

management group . Notably, in patients with moderate-to-severe psoriasis undergoing HPA-axis testing, the median time to first relapse was even longer at 111 days with proactive management versus 31 days with reactive management .

Analysis of time to second relapse confirmed the sustained benefit of proactive management, with median time extended by 79 days (169 days versus 90 days) . This demonstrates that the benefit of combination therapy in maintaining remission persists over multiple treatment cycles.

Days in Remission and Relapse Rates

Study	Metric	Proactive/Combination	Reactive/Control	Difference	P-value
M. Lebwohl et al., 2020	Days in remission (1 year)	Higher	Lower	41 additional days	<0.0001
M. Lebwohl et al., 2020a	Days in remission (1 year)	Higher	Lower	41 additional days	<0.001
M. Lebwohl et al., 2020	Predicted relapses/year	4.0	7.5	46% reduction	<0.001
M. Lebwohl et al., 2020a	Relapses/year exposure	3.1	4.8	35% reduction	Not reported
K. Papp et al., 2021	Proportion of days in remission	17% more	Reference	17% increase	0.001
K. Papp et	Relapse rate	Lower	Reference	60%	<0.001

Study	Metric	Proactive/Combination	Reactive/Control	Difference	P-value
al., 2021				reduction	

Patients receiving proactive management with Cal/BD foam experienced 11% more days in remission than those receiving reactive management, translating to 41 extra days over one year . The rate of relapse over one year was 46% lower with Cal/BD foam compared to vehicle . In the HPA subgroup analysis, the relapse rate reduction was even more pronounced at 60% .

Maintenance of Effect After Treatment Cessation

Study	Treatment	Assessment Point	Remission Maintenance Rate
D. Pariser et al., 2018	HP/TAZ lotion	4 weeks post-treatment	38.2% treatment success
D. Pariser et al., 2018	HP alone	4 weeks post-treatment	21.0% treatment success
D. Pariser et al., 2018	TAZ alone	4 weeks post-treatment	12.8% treatment success
L. Gold et al., 2020	HP/TAZ lotion	Variable	28.6% no retreatment needed
L. Gold et al., 2020	HP/TAZ lotion	≥85 days	53.6% no retreatment
L. Gold et al., 2020	HP/TAZ lotion	≥57 days	62.5% no retreatment
L. Gold et al.,	HP/TAZ lotion	≥29 days	83.9% no

Study	Treatment	Assessment Point	Remission Maintenance Rate
2020			retreatment
Hao Chen et al., 2020	TAZ/BM cream	8-week follow-up	10.62% relapse rate
Hao Chen et al., 2020	BM cream alone	8-week follow-up	29.63% relapse rate
A. Dattola et al., 2019	Cal/BD foam	4 weeks post-suspension	91.7% maintained improvement
J. Koo et al., 2006	Calcipotriene + weekend clobetasol	6 months	92% improvement maintained
J. Koo et al., 2006	Calcipotriene + weekend vehicle	6 months	62% improvement maintained

The halobetasol/tazarotene combination demonstrated significant maintenance of effect post-treatment, with 38.2% of patients remaining treatment successes at 4 weeks after cessation compared to 21.0% with halobetasol alone and 12.8% with tazarotene alone . Among patients achieving clear skin with HP/TAZ lotion, 28.6% did not require any retreatment, and over half maintained remission for at least 85 days .

The tazarotene/betamethasone combination showed a relapse rate of only 10.62% at 8-week follow-up, significantly lower than the 29.63% relapse rate with betamethasone alone (P=0.0269) . Sequential treatment with clobetasol foam plus weekday calcipotriene demonstrated 92% maintenance of improvement at 6 months compared to 62% with vehicle weekend treatment .

Long-Term Efficacy Data

Study	Duration	Key Finding
T. Luger et al., 2008	52 weeks	92.3% of visits with satisfactorily controlled disease
A. Bakulev et al., 2019	52 weeks	PsGA improved from 3.0 to 1.1
K. Kragballe et al., 2006	52 weeks	Trend toward better efficacy with two-compound product (p=0.025)
Yi Zhao et al., 2021	Up to 52 weeks	Combination efficacious up to 1 year on as-needed basis

Long-term studies demonstrated sustained efficacy of combination therapy. In a 52-week scalp psoriasis trial, disease was satisfactorily controlled in 92.3% of visits in the two-compound group versus 80.0% in the calcipotriol group (p<0.001). The BODYGUARD observational study showed sustained improvement with PsGA scores improving from 3.0 at baseline to 1.3 at 8 weeks and 1.1 at 52 weeks.

Comparative Efficacy: Combination vs Monotherapy

Combination	Monotherapy	Outcome Measure	Result
Cal/BD	Vitamin D	Clearance (IGA)	RR 2.28 (1.87-2.78)
Cal/BD	Steroid	Clearance (IGA)	RR 1.22 (1.08-1.36)
Cal/BD	Vitamin D	Treatment response (IGA)	RR 2.31 (1.75-3.04)

Combination	Monotherapy	Outcome Measure	Result
Steroid + calcipotriol	Calcipotriol	TSS improvement	SWMD 0.42 (0.12-0.72)
Cal/BD then calcipotriol	Tacalcitol	PASI reduction	65.0% vs 33.3% at week 4

Cochrane systematic review data demonstrated that the two-compound combination was superior to vitamin D monotherapy for achieving clearance (RR 2.28; 95% CI 1.87-2.78; NNTB=6) . The combination showed statistically significant but clinically modest superiority over corticosteroid monotherapy (RR 1.22; 95% CI 1.08-1.36; NNTB=17) . Polytherapy using potent steroid and calcipotriol was more effective than calcipotriol alone with a standardized weighted mean difference of 0.42 (95% CI 0.12-0.72) .

Factors Influencing Remission Duration

Baseline Disease Severity

Analysis of the PSO-LONG trial revealed that baseline disease severity significantly influenced time to first relapse. Patients with moderate baseline PGA had a hazard ratio of 1.42 for relapse compared to those with mild disease, while those with severe baseline disease had a hazard ratio of 2.32 . Similarly, baseline mPASI severity was associated with time to first relapse (moderate vs mild HR 1.19; severe vs mild HR 1.77; overall p=0.009) .

However, the treatment effect of proactive management remained consistent regardless of baseline characteristics. The benefit of proactive versus reactive management (HR 0.56; p<0.001) did not vary across any baseline parameters including body surface area, mPASI, PGA, BMI, age, sex, DLQI, or duration of psoriasis .

Sex Differences

Female sex was associated with shorter time to first relapse compared to male sex (HR 1.26; $p=0.030$), though the treatment effect remained beneficial for both sexes.

Application Frequency

Systematic review evidence suggests no significant differences in efficacy between once-daily and twice-daily application of Cal/BD combination for a 4-week treatment period . Once-daily application appears sufficient during the active treatment phase, while twice-weekly application provides effective maintenance .

Safety and Tolerability

Cal/BD foam was well tolerated during long-term proactive management. The rate of adverse events per 100 patient-years was comparable between Cal/BD (165.1) and vehicle (156.1) groups . Serious adverse events were low and similar between groups (8.2 per 100 patient-years for Cal/BD; 7.8 for vehicle). Only two adverse events were adjudicated as related to long-term corticosteroid use (chorioretinopathy and pain of skin).

Rebound was four times more likely with vehicle ($n=17$) compared with Cal/BD ($n=4$) following relapse . No clinically relevant effects on calcium metabolism or HPA axis function were observed in subgroup analysis . Adverse drug reactions were less frequent with the two-compound formulation (17.2%) compared to calcipotriol alone (29.5%; $p<0.001$) .

Synthesis

The evidence consistently demonstrates that combination topical therapy with corticosteroids and vitamin D analogs prolongs psoriasis remission duration compared to either reactive treatment approaches or vitamin D monotherapy. The most robust evidence

comes from the PSO-LONG trial, which showed that proactive twice-weekly application of Cal/BD foam nearly doubled median time to first relapse (56 vs 30 days) and resulted in 41 additional days in remission over one year .

Reconciling Apparent Heterogeneity

The magnitude of benefit varied across studies, which can be explained by several factors:

Treatment Protocol Differences : Studies employing proactive maintenance protocols showed more pronounced remission prolongation than those using reactive approaches. The PSO-LONG trial's twice-weekly proactive regimen demonstrated superior outcomes compared to as-needed treatment strategies . This suggests that scheduled preventive application to previously affected areas is more effective than waiting for visible relapse.

Formulation Effects : Foam formulations showed consistently strong efficacy in maintaining remission , which may be attributed to superior drug delivery characteristics. The aerosol foam vehicle enhances skin penetration and patient adherence compared to traditional ointments and gels .

Population Severity : The HPA subgroup analysis demonstrated even longer time to first relapse (111 days vs 31 days) in patients with more severe disease (10-30% BSA affected) , suggesting that combination therapy may provide proportionally greater benefit in more severe presentations, though baseline severity also predicts faster relapse overall .

Combination Type : Co-formulated products consistently outperformed separately applied combinations in convenience and adherence , though both approaches demonstrated efficacy superior to monotherapy. The halobetasol/tazarotene combination showed particularly sustained post-treatment effects , potentially due to tazarotene's mechanism of normalizing keratinocyte differentiation .

Clinical Implications

For patients with mild-to-moderate plaque psoriasis, combination Cal/BD therapy provides meaningful extension of remission duration when used proactively. The treatment effect is robust across patient subgroups and baseline characteristics . The combination's superior efficacy over vitamin D monotherapy (RR 2.28 for clearance) combined with a safety profile similar to or better than monotherapy supports its use as first-line topical therapy .

The marginal additional benefit of combination over potent corticosteroid monotherapy (NNTB=17) must be weighed against the advantages of reduced relapse rates and potentially lower long-term corticosteroid exposure through the proactive maintenance approach. Sequential therapy protocols initiating with combination followed by vitamin D maintenance also show promise for sustaining remission.

DISCUSSION

This systematic review of 40 studies provides robust and consistent evidence that combination topical therapy with corticosteroids and vitamin D analogs significantly prolongs the remission duration of plaque psoriasis compared to monotherapies or reactive treatment approaches. The discussion will interpret these findings, explore the underlying mechanisms, reconcile heterogeneity, and consider clinical implications.

Efficacy in Prolonging Remission: The Core Finding

The most compelling evidence comes from the PSO-LONG trial and its analyses, which represent a paradigm shift in topical psoriasis management. The trial demonstrated that a proactive, twice-weekly application of Cal/BD foam to previously affected areas nearly doubled the median time to first relapse compared to a reactive strategy (56 days vs. 30 days) (Lebwohl et al., 2020). This translated into a substantial 41 extra days in remission over one year, a difference that is not

only statistically significant but also clinically meaningful for patients (Lebwohl et al., 2021). The hazard ratio of 0.57 indicates a 43% reduction in the risk of relapse with proactive management. Importantly, this benefit persisted over multiple relapse cycles, as the median time to a *second* relapse was also significantly longer in the proactive group (169 vs. 90 days) (Lebwohl et al., 2022). This confirms that the strategy is effective for sustained, long-term disease control, not just a single extension of remission.

The benefit extends beyond the Cal/BD combination. The fixed combination of halobetasol propionate and tazarotene (HP/TAZ) lotion showed impressive durability of effect after cessation. Four weeks post-treatment, 38.2% of patients were still treatment successes, compared to only 21.0% and 12.8% with halobetasol or tazarotene monotherapy, respectively (Pariser et al., 2018). Among clear patients, over half (53.6%) did not require retreatment for at least 85 days (Gold et al., 2020). Similarly, a tazarotene/betamethasone cream showed a significantly lower relapse rate at 8-week follow-up compared to betamethasone alone (10.62% vs. 29.63%) (Chen et al., 2020). These findings across different combination molecules underscore a class effect: combining an anti-inflammatory agent with one that normalizes epidermal function leads to more sustained outcomes.

Superiority Over Monotherapy: Quantifying the Advantage

Systematic review data quantitatively confirms the advantage of combination therapy. When compared to vitamin D analog monotherapy, the combination is markedly superior for achieving clearance, with a relative risk (RR) of 2.28 (Samarasekera et al., 2013). This means patients are more than twice as likely to achieve clear or almost-clear skin with the combination. The Number Needed to Treat for Benefit (NNTB) of 6 is highly favorable (Queirós et al., 2017). Compared to potent corticosteroid monotherapy, the combination still shows a statistically significant, though clinically more modest, benefit (RR 1.22, NNTB=17) (Samarasekera et al., 2013). This modest edge in acute efficacy is crucially augmented by the combination's superior ability to *maintain* remission, as seen in the relapse data, and its potential to allow for a lower cumulative steroid dose over time through the proactive regimen.

The International Journal of Medical Science and Health Research

Mechanistic Rationale for Prolonged Remission

The prolonged remission observed can be attributed to the complementary and potentially synergistic mechanisms of the two drug classes. Corticosteroids provide rapid suppression of the key inflammatory cytokines (e.g., IL-17, IL-23, TNF- α) and immune cell infiltration that drive psoriasis plaques (Heim et al., 2022). Vitamin D analogs, like calcipotriol, not only inhibit keratinocyte proliferation but also promote their normal differentiation and have direct immunomodulatory effects on T-cells and dendritic cells (Gisoni et al., 2024). By simultaneously targeting inflammation and the underlying epidermal dysregulation, the combination therapy may more effectively "reset" the pathological skin microenvironment. The proactive strategy of treating subclinical disease in previously affected areas is likely suppressing nascent inflammatory processes before they become clinically apparent plaques, thereby preventing relapse rather than merely treating it (Stein Gold et al., 2020). Tazarotene, a retinoid, adds another dimension by directly modulating gene expression involved in keratinocyte differentiation, which may explain the particularly sustained post-treatment effects of the HP/TAZ combination (Stein Gold et al., 2018).

Reconciling Heterogeneity: Factors Influencing Outcomes

The magnitude of benefit varied across studies, which can be explained by several key factors:

1. **Treatment Protocol (Proactive vs. Reactive):** This is the most significant modifier. Studies employing scheduled, proactive maintenance (like PSO-LONG) showed dramatically better remission outcomes than those using traditional "as-needed" reactive approaches (Lebwohl et al., 2021; Kragballe et al., 2006). The protocol itself is a major determinant of success.
2. **Formulation:** Foam formulations of Cal/BD consistently demonstrated strong efficacy. Foams are cosmetically elegant, spread easily, and are preferred by patients, which likely improves adherence (Dattola et al., 2019). Furthermore, the aerosol foam vehicle may

enhance drug delivery and penetration compared to ointments or gels, contributing to better outcomes (Warren et al., 2021).

3. **Baseline Disease Severity:** While patients with more severe baseline disease (higher PGA or mPASI) relapsed faster overall, the *relative benefit* of proactive combination therapy was consistent across all severity subgroups (Lebwohl et al., 2021). Interestingly, in the HPA-axis subgroup of the PSO-LONG trial (patients with moderate-to-severe disease), the median time to relapse with proactive management was even more impressive (111 days), suggesting this group may derive proportionally greater benefit (Papp et al., 2021).
4. **Type of Combination:** Co-formulated products offer superior convenience and adherence compared to separately applied agents, which is a practical advantage for long-term use (Girolomoni et al., 2012). However, sequential regimens (e.g., weekday calcipotriol + weekend clobetasol) also proved highly effective in maintaining improvement for up to 6 months (Koo et al., 2006), offering a viable alternative.
5. **Follow-up Duration:** Studies with shorter follow-up (<12 weeks) naturally captured less data on relapse, underscoring the importance of long-term trials like PSO-LONG (52 weeks) to fully appreciate the remission-prolonging effects (Zhao et al., 2021).

Safety and Tolerability in Long-Term Use

A major concern with any long-term topical therapy, especially involving corticosteroids, is safety. Reassuringly, the long-term data, particularly from the 52-week PSO-LONG trial, indicates that proactive management with Cal/BD foam is well-tolerated. Adverse event rates were similar to vehicle control, serious adverse events were low and comparable between groups, and there was no evidence of clinically relevant HPA-axis suppression or effects on calcium metabolism in monitored subgroups (Lebwohl et al., 2020). Importantly, rebound was significantly *less* likely with Cal/BD foam than with vehicle (4 vs. 17 events) (Lebwohl et al., 2020a). Furthermore, the combination's superior efficacy may allow for a reduction in the total cumulative dose of potent

corticosteroid compared to repeated courses of monotherapy for frequent relapses. The fixed combination of HP/TAZ also demonstrated a favorable safety profile with minimal evidence of atrophy or irritation associated with long-term use (Stein Gold et al., 2018).

Clinical Implications and Practical Guidance

The evidence strongly supports a shift towards proactive, long-term management for appropriate patients with chronic plaque psoriasis. For patients who achieve initial clearance with a 4-week daily course of combination therapy (e.g., Cal/BD foam), transitioning to a twice-weekly proactive maintenance regimen to previously affected areas should be considered standard of care to extend remission (Lebwohl et al., 2020; Zhao et al., 2021). This approach is effective for both trunk/limb and scalp psoriasis (Luger et al., 2008; Schlager et al., 2017).

The choice of agent can be individualized. Cal/BD foam is a first-line option with the most extensive long-term data. HP/TAZ lotion is a potent alternative, particularly useful for thicker plaques and offering very durable post-treatment effects (Pariser et al., 2018). For cost-conscious settings or where specific formulations are unavailable, sequential therapy with a potent steroid and a VDA remains an effective strategy (Koo et al., 2006; Lahfa et al., 2003). The treatment effect is robust across different patient demographics, including skin of color (Liu et al., 2023), and is not influenced by factors like age, sex, or BMI, making it widely applicable (Lebwohl et al., 2021).

Economic Considerations

While not the primary focus of this review, the improved clinical outcomes have economic implications. A cost-effectiveness analysis from the UK suggested that proactive management with Cal/BD foam is likely cost-effective compared to reactive management, due to reduced relapse rates and associated healthcare resource utilization (Takhar et al., 2020). Fewer flares mean fewer physician visits, prescriptions, and treatments for complications, offsetting the cost of the maintenance therapy.

Limitations and Future Research

This review has limitations. The included studies varied in their definitions of remission and relapse, though PGA "clear/almost clear" was common. Most long-term data comes from industry-sponsored RCTs; more real-world evidence on proactive management is needed. Future research should focus on: determining the optimal minimum effective frequency and duration of proactive therapy; directly comparing different combination formulations (foam vs. lotion vs. ointment) for maintenance; investigating biomarkers that predict long-term response; and evaluating the role of combination topical therapy within treatment sequences that include systemic or biologic agents (Kircik et al., 2020).

CONCLUSION AND RECOMMENDATIONS

Conclusion

This comprehensive systematic review conclusively demonstrates that long-term, proactive management with topical combinations of corticosteroids and vitamin D analogs, particularly the fixed-dose combination of calcipotriol and betamethasone dipropionate (Cal/BD) in a foam vehicle, is a highly effective and well-tolerated strategy for significantly prolonging remission in patients with mild-to-moderate chronic plaque psoriasis. Compared to reactive ("as-needed") approaches, proactive twice-weekly application nearly doubles the time to relapse, provides over 40 additional remission days per year, and reduces relapse rates by approximately half. The combination therapy is substantially more effective than vitamin D analog monotherapy and provides a meaningful, sustained advantage over potent corticosteroid monotherapy, all while maintaining a favorable safety profile over 52 weeks of use. The benefits are consistent across various patient subgroups and are also evident with other combinations like halobetasol/tazarotene.

Recommendations

1. **For Clinical Practice:** Adopt a paradigm of proactive, long-term maintenance for suitable patients with chronic plaque psoriasis. After achieving initial disease control (e.g., with a 4-week daily course), implement a twice-weekly application of a combination product like Cal/BD foam to previously affected areas as a standard strategy to prolong remission.
2. **For Treatment Selection:** Consider fixed-dose combination products (foam, ointment, lotion) as first-line topical therapy due to their proven superior efficacy in maintaining remission and enhanced patient adherence. The choice can be tailored based on disease location, plaque morphology, and patient preference.
3. **For Patient Management:** Educate patients on the concept and benefits of proactive maintenance to set realistic expectations and improve adherence. Emphasize that this strategy aims to prevent flares rather than just treat them.
4. **For Research:** Future studies should focus on real-world effectiveness data for proactive regimens, refine the optimal dosing protocols for maintenance, and explore the integration of these topical strategies with systemic therapies for more severe disease. Long-term studies beyond one year are also warranted to confirm sustained safety and efficacy.

REFERENCES

- A. Bakulev, A. Л. Бакулев, D. Petrunin, and Д Д Петрунин. "Results of the Long-Term Observational Noninterventional Prospective Study BODYGUARD in Psoriasis Patients." *Vestnik Dermatologii i Venerologii*, 2019.
- A. Dattola, M. Silvestri, L. Bennardo, Maria Passante, F. Rizzuto, S. Dastoli, C. Patruno, L. Bianchi, and S. Nisticò. "A Novel Vehicle for the Treatment of Psoriasis." *Dermatologic Therapy*, 2019.
- A. Takhar, H. Thoning, B. Petersen, F. Salih, V. Kontogiannis, and N. Nyholm. "PSS10 Cost-Effectiveness of Proactive Management Versus Reactive Management with

Calcipotriol/Betamethasone Dipropionate Foam for Treatment of Psoriasis Vulgaris in the UK,” 2020.

C. Queirós, G. Duarte, João Costa, and A. Vaz-Carneiro. “[Analysis of the Cochrane Review: Topical Treatments for Scalp Psoriasis. Cochrane Database Syst Rev. 2016;2:CD009687].” *Acta Médica Portuguesa*, 2017.

D. Pariser, L. Green, L. S. Stein Gold, J. Sugarman, Tina Lin, and R. Pillai. “Halobetasol 0.01%/Tazarotene 0.045% Lotion in the Treatment of Moderate-to-Severe Plaque Psoriasis: Maintenance of Therapeutic Effect After Cessation of Therapy.” *Journal of Drugs in Dermatology*, 2018.

E. Samarasekera, L. Sawyer, D. Wonderling, R. Tucker, and Catherine Smith. “Topical Therapies for the Treatment of Plaque Psoriasis: Systematic Review and Network Meta-analyses.” *British Journal of Dermatology*, 2013.

G. Girolomoni, G. Vena, F. Ayala, S. Cannavò, O. De Pità, S. Chimenti, and A. Peserico. “Consensus on the Use of the Fixed Combination Calcipotriol/Betamethasone Dipropionate in the Treatment of Plaque Psoriasis.” *Giornale Italiano Di Dermatologia e Venereologia : Organo Ufficiale, Societa Italiana Di Dermatologia e Sifilografia*, 2012.

G. Vena, N. Cassano, C. Agnusdei, M. Bellini, S. Calabretta, S. Centofanti, G. Cervadoro, et al. “Treatment of Psoriasis Vulgaris with Calcipotriol Betamethasone Dipropionate Combination Followed by Calcipotriol and Assessment of the Adjuvant Basic Use of Urea-Based Emollients,” 2005.

Hao Chen, Jianfang Sun, Haizhen Yang, Qiuning Sun, Jianzhong Zhang, J. Gu, Hai Wen, et al. “Fixed Combination of Tazarotene and Betamethasone Dipropionate for Treatment of Psoriasis Vulgaris: The Result of a Phase 3, Multicenter, Randomized Controlled Trial.” *Journal of Dermatology (Print)*, 2020.

J. G. Schlager, S. Rosumeck, R. Werner, A. Jacobs, J. Schmitt, C. Schlager, and A. Nast. “Topical Treatments for Scalp Psoriasis.” *Cochrane Database of Systematic Reviews*, 2016.

J. G. Schlager, S. Rosumeck, R. Werner, A. Jacobs, Jochen Schmitt, C. Schlager, and A. Nast. “Topical Treatments for Scalp Psoriasis: Summary of a Cochrane Systematic Review.” *British Journal of Dermatology*, 2017.

J. Koo, Robin R. Blum, and M. Lebwohl. “A Randomized, Multicenter Study of Calcipotriene Ointment and Clobetasol Propionate Foam in the Sequential Treatment of Localized Plaque-Type Psoriasis: Short- and Long-Term Outcomes.” *Journal of American Academy of Dermatology*, 2006.

J. Mason, A. Mason, and Michael J. Cork. “Topical Preparations for the Treatment of Psoriasis in Primary Care: A Systematic Review,” 2002.

J. Ortonne, R. Kaufmann, M. Lecha, and M. Goodfield. “Efficacy of Treatment with Calcipotriol/Betamethasone Dipropionate Followed by Calcipotriol Alone Compared with Tacalcitol for the Treatment of Psoriasis Vulgaris: A Randomised, Double-Blind Trial.” *Dermatology*, 2004.

Jacqueline Liu, Ahuva Cices, B. Kaufman, Ingrid Sanabria-Gonzalez, and A. Alexis. “Efficacy and Safety of Calcipotriene/Betamethasone Dipropionate Foam in the Treatment of Psoriasis in Skin of Color.” *Journal of Drugs in Dermatology*, 2023.

K. Kragballe, J. Austad, L. Barnes, A. Bibby, M. Brassinne, F. Cambazard, C. Fleming, et al. “Efficacy Results of a 52-Week, Randomised, Double-Blind, Safety Study of a Calcipotriol/Betamethasone Dipropionate Two-Compound Product (Daivobet®/Dovobet®/Taclonex®) in the Treatment of Psoriasis Vulgaris.” *Dermatology*, 2006.

K. Papp, Z. Adamski, L. Guenther, M. Liljedahl, Agnieszka Miasik-Pogodzinska, Anna Szponar-Bojda, C. Lynde, et al. “Efficacy and Safety of Proactive Treatment with Twice-Weekly Topical

Cal/BD Foam in Patients with Plaque Psoriasis Undergoing HPA-Axis Testing: A PSO-LONG Subgroup Analysis.” *Journal of Dermatological Treatment (Print)*, 2021.

L. Gold, J. Weiss, L. Green, L. Kircik, Tina Lin PharmD, and S. Harris. “15324 Long-Term Management of Moderate to Severe Plaque Psoriasis: Maintenance of Treatment Success Following Cessation of Fixed Combination Halobetasol Propionate 0.01% and Tazarotene 0.045% Lotion in Patients with Baseline Body Surface Area of 6%-12%,” 2020.

L. Gold, M. Lebwohl, N. Bhatia, Tina Lin, and R. Pillai. “605 Long-Term Management of Moderate-to-Severe Plaque Psoriasis: Maintenance of Treatment Success Following Cessation of Halobetasol Propionate 0.01%/Tazarotene 0.045% Lotion,” 2020.

L. Kircik, T. Schlesinger, and E. Tanghetti. “Efficacy and Safety of Calcipotriene 0.005%/Betamethasone Dipropionate 0.064% Foam With Apremilast for Moderate Plaque Psoriasis.” *Journal of Drugs in Dermatology*, 2020.

L. S. Stein Gold, J. Alonso-Llamazares, J. Lacour, R. Warren, S. Tying, L. Kircik, P. Yamauchi, and M. Lebwohl. “PSO-LONG: Design of a Novel, 12-Month Clinical Trial of Topical, Proactive Maintenance with Twice-Weekly Cal/BD Foam in Psoriasis.” *Advances in Therapy*, 2020.

L. S. Stein Gold, J. Bagel, M. Lebwohl, Tina Lin, Gina Martin, and R. Pillai. “Halobetasol and Tazarotene: Further Defining the Role of a Unique Fixed Combination Topical Lotion in Moderate-to-Severe Plaque Psoriasis.” *Journal of Drugs in Dermatology*, 2018.

M. Lahfa, U. Mrowietz, Miriam Koenig, and J. Simon. “Calcitriol Ointment and Clobetasol Propionate Cream: A New Regimen for the Treatment of Plaque Psoriasis.” *EJD. European Journal of Dermatology*, 2003.

M. Lebwohl, J. Lacour, M. Liljedahl, C. Lynde, M. Mørch, Anja Snel-Prentø, D. Thaçi, and R. Warren. “12797 Safety of Long-Term Proactive Management with Fixed-Dose Combination Calcipotriene 0.005% and Betamethasone Dipropionate 0.064% Foam in Patients with Psoriasis

Vulgaris: Results of a Phase III, Multicenter, Randomized, 52-Week, Vehicle-Controlled Trial,” 2020.

———. “18223 Long-Term Proactive Management of Psoriasis Vulgaris with Fixed-Dose Combination of 0.005% Calcipotriene and 0.064% Betamethasone Dipropionate Foam: Results of a Phase III Randomized Controlled Trial,” 2020.

M. Lebwohl, Jean Philippe LACOUR, M. Liljedahl, C. Lynde, M. Mørch, Anja Snel-Prentø, L.E.O. Pharma, D. Thaçi, and R. Warren. “16830 Results from the Open-Label Treatment Period of a Long-Term Proactive Management Phase III Trial Using Fixed-Dose Combination Calcipotriene 0.005% and Betamethasone Dipropionate 0.064% Foam,” 2020.

M. Lebwohl, K. Papp, M. Mørch, and J. Andersen. “32805 Analysis of Time to Second Relapse Confirms the Superiority of Long-Term Proactive Management with Cal/BD Foam Vs Reactive Management of Psoriasis.” *Journal of American Academy of Dermatology*, 2022.

M. Lebwohl, K. Papp, M. Mørch, Marie Y. Jablonski Bernasconi, and R. Warren. “Long-Term Proactive Treatment of Plaque Psoriasis with Calcipotriene/Betamethasone Dipropionate Foam Prolongs Remission and Reduces Relapses Irrespective of Patient Baseline Characteristics.” *Dermatologic Therapy*, 2021.

M. Lebwohl, L. Kircik, J. Lacour, M. Liljedahl, C. Lynde, M. Mørch, K. Papp, et al. “Twice-Weekly Topical Calcipotriene / Betamethasone Dipropionate Foam as Proactive Management of Plaque Psoriasis Increases Time in Remission and Is Well Tolerated over 52 Weeks (PSO-LONG Trial).” *Journal of American Academy of Dermatology*, 2020.

M. Sindhuja, and N. Muthiah. “Efficacy and Safety of Topical Calcipotriol Plus Betamethasone Dipropionate Versus Topical Betamethasone Dipropionate Alone in Mild to Moderate Psoriasis.” *Journal of Pharmaceutical Research International*, 2021.

- Marjorie Heim, M. Irondelle, L. Duteil, N. Cardot-Leccia, S. Rocchi, T. Passeron, and M. Tulic. "Impact of Topical Emollient, Steroids Alone or Combined with Calcipotriol, on the Immune Infiltrate and Clinical Outcome in Psoriasis." *Experimental Dermatology*, 2022.
- N. Katoh, and S. Kishimoto. "Combination of Calcipotriol and Clobetasol Propionate as a Premixed Ointment for the Treatment of Psoriasis." *EJD. European Journal of Dermatology*, 2003.
- P. Gisondi, T. Gracia-Cazaña, Hjalmar Kurzen, and Jordi Galván. "Calcipotriol/Betamethasone Dipropionate for the Treatment of Psoriasis: Mechanism of Action and Evidence of Efficacy and Safety Versus Topical Corticosteroids." *Journal of Clinical Medicine*, 2024.
- P. Peeters, J. Ortonne, René Sitbon, and E. Guignard. "Cost-Effectiveness of Once-Daily Treatment with Calcipotriol/Betamethasone Dipropionate Followed by Calcipotriol Alone Compared with Tacalcitol in the Treatment of Psoriasis Vulgaris." *Dermatology*, 2005.
- R. Saraceno, L. Andreassi, F. Ayala, M. Bongiorno, A. Giannetti, P. Lisi, P. Martini, K. Peris, A. Peserico, and S. Chimenti. "Efficacy, Safety and Quality of Life of Calcipotriol/Betamethasone Dipropionate (Dovobet®) Versus Calcipotriol (Daivonex®) in the Treatment of Psoriasis Vulgaris: A Randomized, Multicentre, Clinical Trial." *Journal of Dermatological Treatment (Print)*, 2007.
- R. Warren, M. Gold, M. Gooderham, L. Kircik, J. Lacour, P. Laws, M. Liljedahl, et al. "Four-Week Daily Calcipotriene/Betamethasone Dipropionate Foam Is Highly Efficacious in Patients With Psoriasis (PSO-LONG Lead-in Phase)." *Journal of Drugs in Dermatology*, 2021.
- Ru Yan, Shi-Bin Jiang, Yan Wu, Xing-Hua Gao, and Hong-Duo Chen. "Topical Calcipotriol/Betamethasone Dipropionate for Psoriasis Vulgaris: A Systematic Review." *Indian Journal of Dermatology, Venereology and Leprology*, 2016.
- T. Luger, F. Cambazard, F. G. Larsen, M. Bourcier, G. Gupta, F. Clonier, P. Kidson, and N. Shear. "A Study of the Safety and Efficacy of Calcipotriol and Betamethasone Dipropionate Scalp Formulation in the Long-Term Management of Scalp Psoriasis." *Dermatology*, 2008.

Yi Zhao, A. Asahina, P. Asawanonda, M. Frez, S. Imafuku, Dong Hyun Kim, C. Theng, Liang-Chou Wang, Jiang-an Zhang, and S. Zimmo. “Systematic Review and Practical Guidance on the Use of Topical Calcipotriol and Topical Calcipotriol with Betamethasone Dipropionate as Long-term Therapy for Mild-to-moderate Plaque Psoriasis.” *Journal of Dermatology (Print)*, 2021.

朱品华. “卡他西醇和卤米松联合nb-Uvb治疗寻常型银屑病 Tacalcitol and Sicorten Combined NB-UVB Treatment of Psoriasis Vulgaris,” 2015.