



Topical treatments for scalp psoriasis

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Introduction - Psoriasis



Clinical facts

- 2% of the population (western hemisphere)
- Auto-immune mediated
- Etiology: genes, environment
- Psoriasis vulgaris: 90%
- Higher risk for cardio-vascular and psychiatric co-morbidities, arthritis
→ systemic disease
- 79% present with scalp lesions

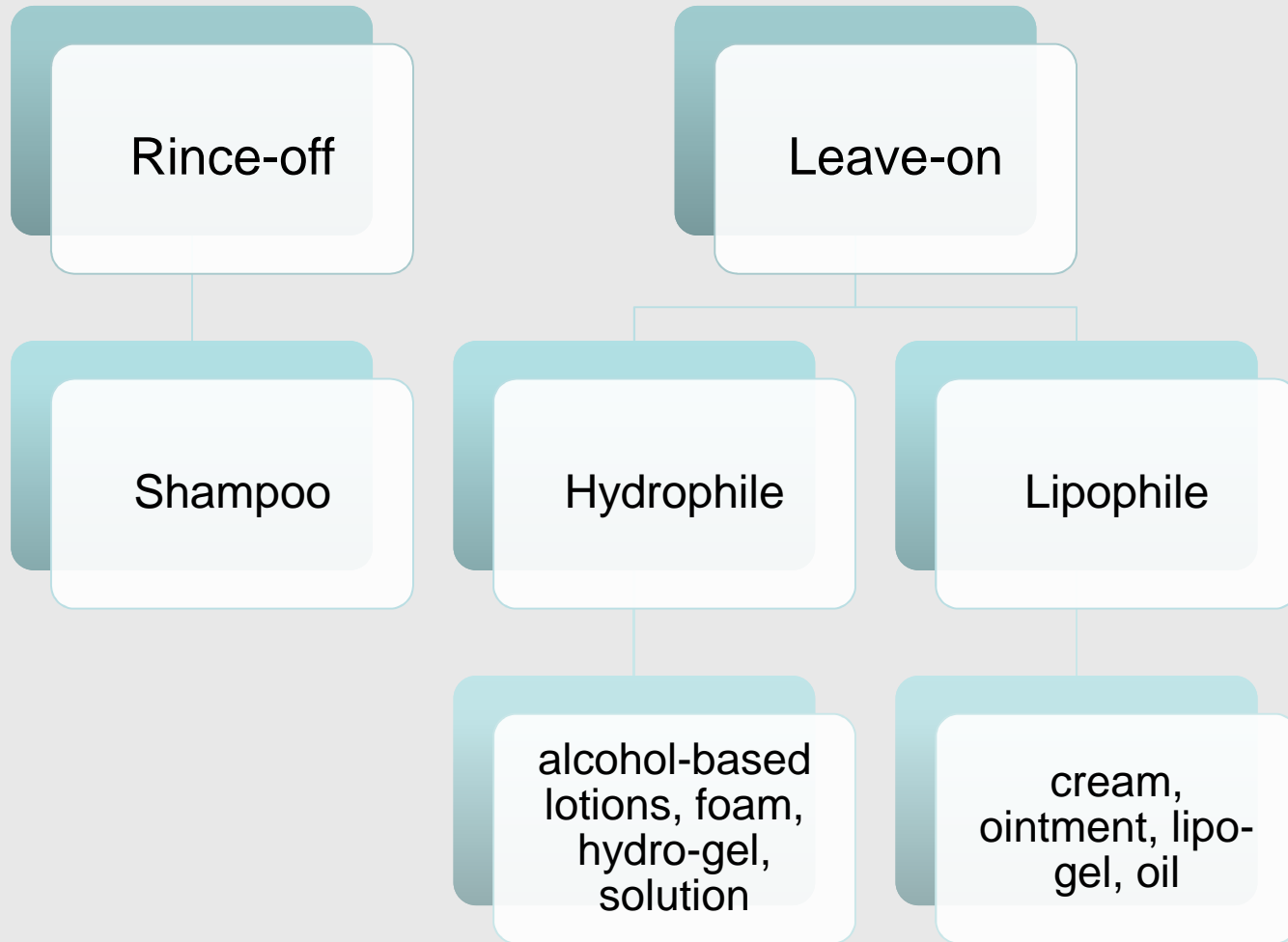
Introduction - Psoriasis of the scalp



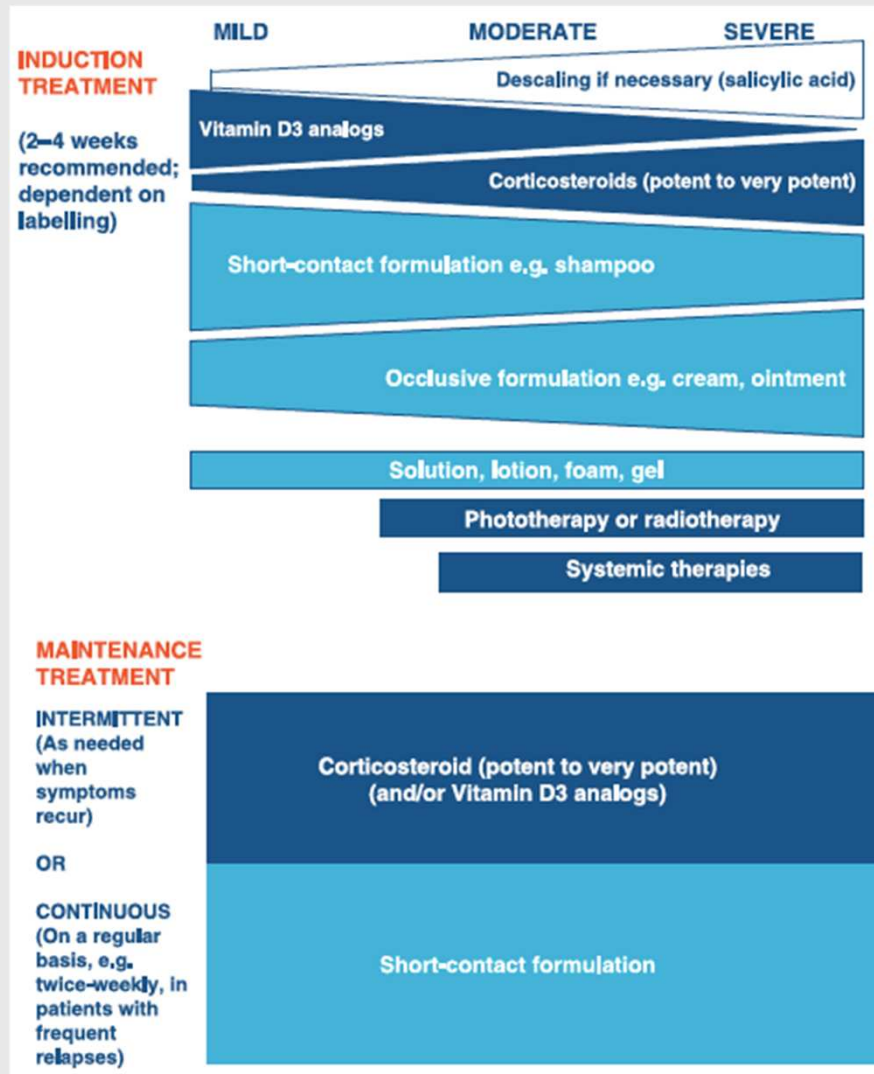
Introduction - Psoriasis of the scalp



Introduction - Topical vehicles

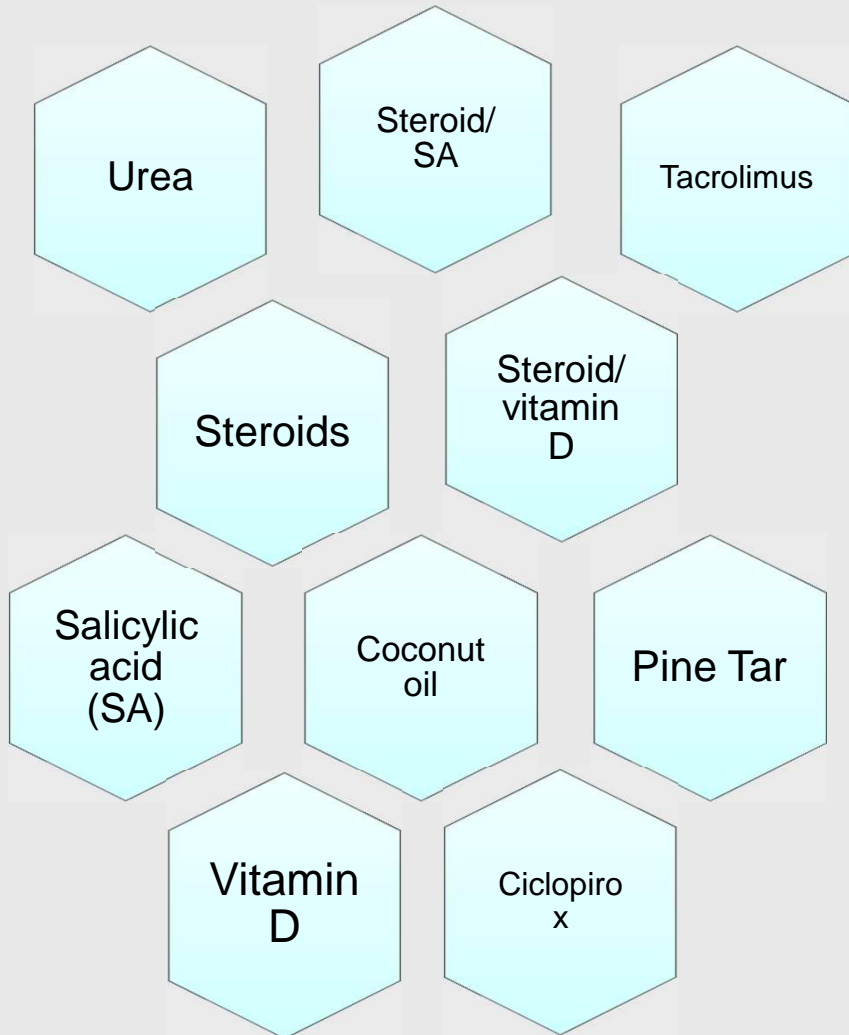


Introduction – Consensus treatment algorithm



Ortonne, JP. et al.
Scalp psoriasis: European consensus on grading and treatment algorithm. J Eur Acad Dermatol Venereol. 2009 Dec;23(12):1435-44. doi: 10.1111/j.1468-3083.2009.03372.x.

Introduction - Topical treatment options



Why is this review necessary?

- Variety of treatment options
- No evidence-based consensus



Clinical guidance

Methods

Types of studies

Randomised controlled trials (RCTs) - parallel-group, cross-over, within-patient design.

Types of patients

- All ages
- Diagnosed with scalp psoriasis

Major exclusion criteria

- Systemic treatments
- Grenz-Ray
- Psoralen-UVA (PUVA)

Methods - Literature search

Literature Search	
Electronic search (4 February 2015)	<ul style="list-style-type: none">• Cochrane Skin Group Specialised Register• Cochrane Central Register of Controlled Trials (CENTRAL) 2015, Issue 1, in <i>The Cochrane Library</i>• LILACS (Latin American and Caribbean Health Science Information database, from 1982)• The Salford Database of Psoriasis trials (from inception)
Trials registers (2 April 2014)	<ul style="list-style-type: none">• The metaRegister of Controlled Trials• The US National Institutes of Health Ongoing Trials Register• The Australian New Zealand Clinical Trials• The World Health Organization International Clinical Trials Registry platform• The EU Clinical Trials Register
Reference lists	Included studies
Handsearching	<ul style="list-style-type: none">• American Academy of Dermatology (AAD)• European Academy of Dermatology and Venerology (EADV)• Deutsche Dermatologische Gesellschaft (DDG)• Psoriasis - From Gene to Clinic• Psoriasis International Network – Paris• International Federation of Psoriasis Associations (IFPA)

Methods - Assessment of risk of bias

Adequate randomisation?

Adequate allocation concealment?

Knowledge of the allocated interventions after assignment prevented?

Incomplete outcome data adequately addressed?

Are reports of the study free of suggestion of selective reporting?

Was the study apparently free of other bias?



High risk



Unclear



Low risk

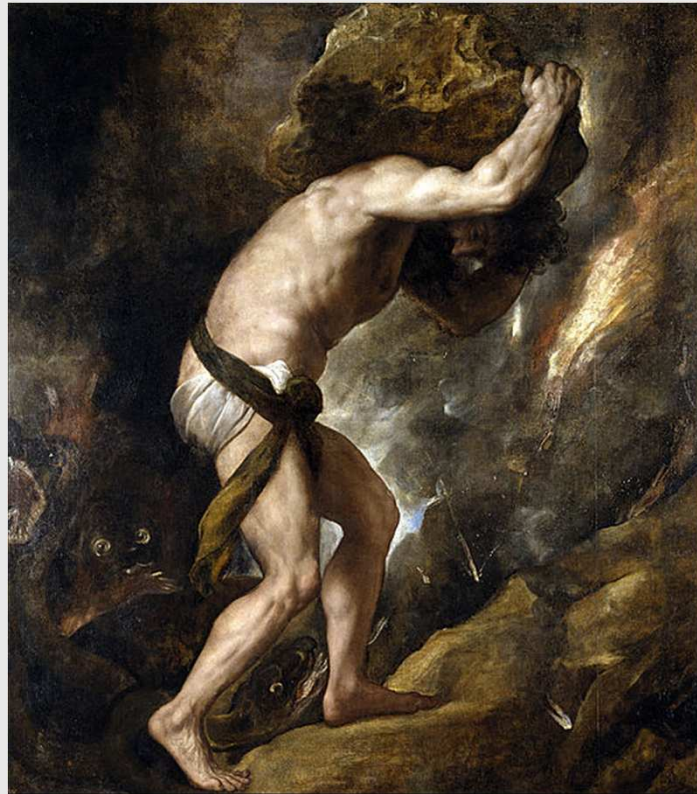
Higgins JPT, Altman DG, Sterne JAC (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Methods - Outcomes

Outcomes		Tools
Primary	<ul style="list-style-type: none">• Reduction in clinician assessed severity• Improvement in quality of life• Number of patients withdrawing due to AEs	IGA / TSS
Secondary	<ul style="list-style-type: none">• Subjective reduction in severity of psoriasis• Number of patients with at least one AEs• Time free of disease until relapse to baseline severity	PGA

Methods

Challenge: variety of efficacy outcomes



Methods – Investigator's/Patient's Global Assessment

IGA
↓
objective

&

PGA
↓
subjective

Absent

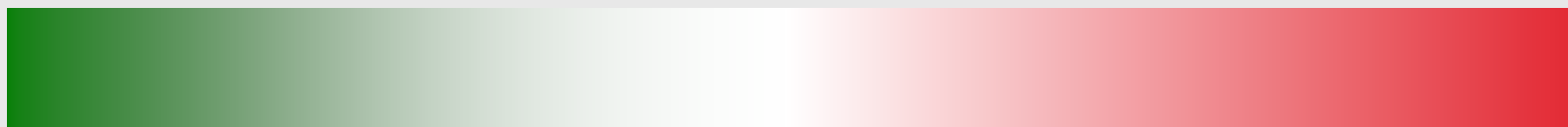
very mild

mild

moderate

severe

very severe



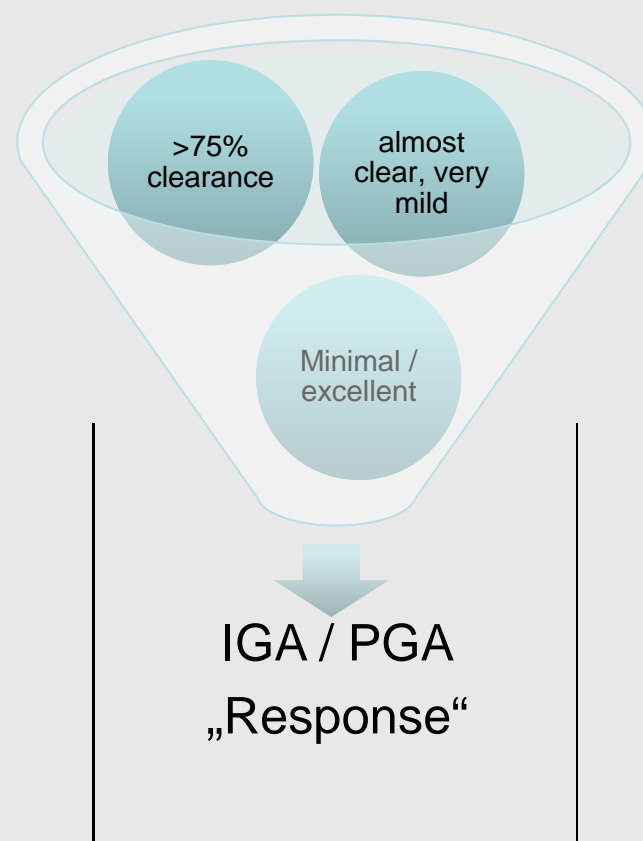
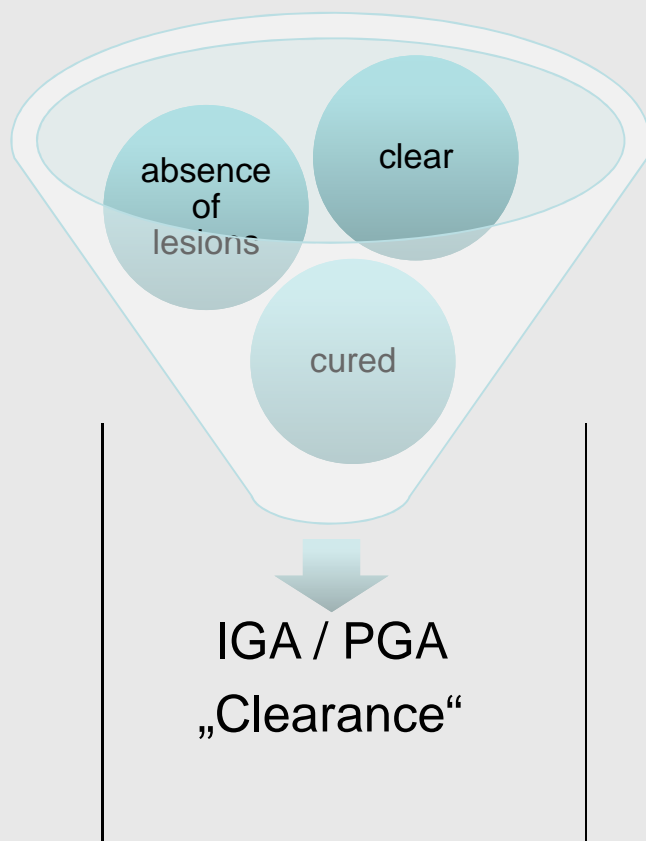
Methods - dichotomous efficacy outcomes

Author	Score	
Luger et al. 2008	„IGA“ or „PGA“	Absent, very mild, mild, moderate, severe, very severe
Sofen et al. 2011	„GSS“ (Global severity score)	Clear, minimal, mild, moderate, severe, very severe
Ellis et al. 1988	„Overall therapeutic efficacy assessed by investigator“	Clear (100%), excellent (>75%), good (>50%), fair (>25%), poor (<25%), no effect, exacerbation
Curley et al. 1990	„Overall evaluation“	Cured - worse

- Different definition of IGA:

Curley 1990	Franz 2000	Sofen 2011
5-point scale	7-point scale	6-point scale
- Some studies only reported number of patients with cleared lesions

Methods - dichotomous efficacy outcomes



Methods - continuous efficacy outcomes

- IGA / PGA – mean

- Total Sign Score (TSS):

Erythema + Scaling + Thickness = TSS

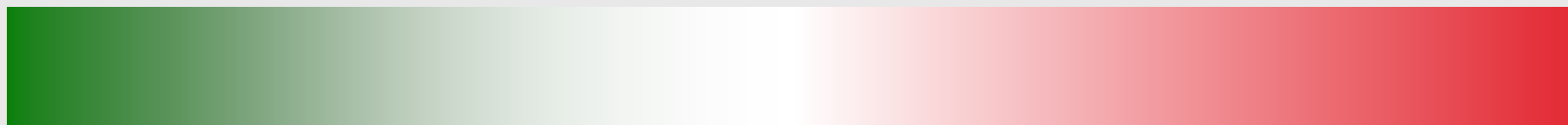
0-4

0-4

0-4

0-12

0 1 2 3 4 5 6 7 8 9 10 11 12



Methods - continuous efficacy outcomes

Authors	Score	Clinical signs			
Sofen et al. 2011 Tyring et al. 2010	TSS	Erythema	Scaling	Thickness	
	0-12	0-4	0-4	0-4	
Katz et al. 1995 Swinehart et al. 1989	TSS	Erythema	Scaling	Thickness	Pruritus
	0-12	0-3	0-3	0-3	0-3
Andres et al. 2006	DSS	Erythema	Desquamation	Thickness	
	0-9	0-3	0-3	0-3	
He et al. 2008	Severity score of sign and symptoms	Erythema	Dander	Thickness	Pruritus
	0-16	0-4	0-4	0-4	0-4

- **Missing Standard Deviation (SD)**
- Some studies provided only **single sign scores**

Methods - continuous efficacy outcomes

Our solution:

1. TSS → ✗ SD → ✗ Meta-analysis → ✓ %-change

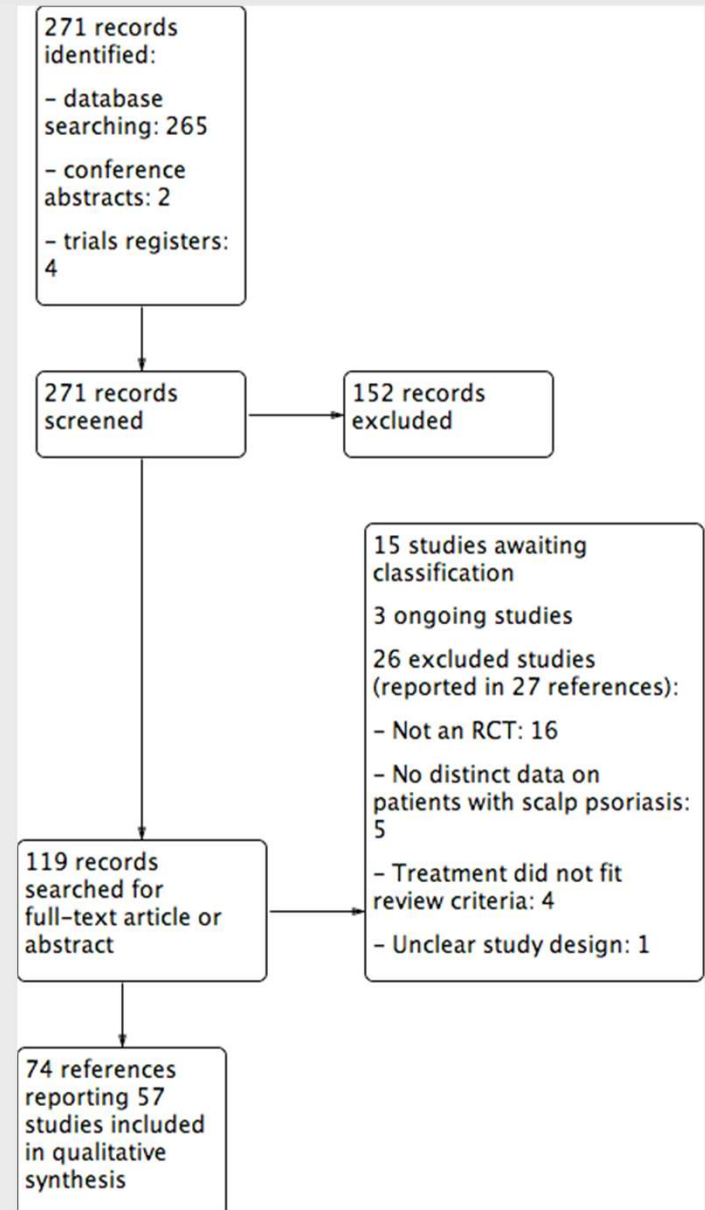
1. IGA or PGA-mean → ✓ SD → Forest Plot

3. If only **single scores** provided:

Computation of the TSS → %-change from baseline

Results - Literature search

- 271 records identified
- 119 records searched for full-text
- **57** studies included
→ 11,491 participants



Results - Quality and Outcomes

Quality

- varied considerably

Outcomes

- Only three studies assessed QoL
- None assessed time until relapse to baseline severity occurred
- Most findings based on short-term therapies

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)
Andres 2006	?	?	?	?	?	?	?
Bergstrom 2003	?	?	?	?	?	?	?
Breneman 1992	?	?	?	?	?	?	?
Buckley 2008	?	?	?	?	?	?	?
Curley 1990	?	?	?	?	?	?	?
De Cuyper 1995	?	?	?	?	?	?	?
Duweb 2000	?	?	?	?	?	?	?
Ellis 1988	?	?	?	?	?	?	?
Ellis 1989	?	?	?	?	?	?	?
Feldman 2001	?	?	?	?	?	?	?
Feldman 2013	?	?	?	?	?	?	?
Franz 1999	?	?	?	?	?	?	?
Franz 2000	?	?	?	?	?	?	?
Fredriksson 1976	?	?	?	?	?	?	?
Gip 1981	?	?	?	?	?	?	?
Green 1994	?	?	?	?	?	?	?
Griffiths 2006	?	?	?	?	?	?	?
Harris 1972	?	?	?	?	?	?	?
He 2008	?	?	?	?	?	?	?
Hillstrom 1978	?	?	?	?	?	?	?
Hillstrom 1982	?	?	?	?	?	?	?
Hillstrom 1984	?	?	?	?	?	?	?
Housman 2002	?	?	?	?	?	?	?
Jarratt 1991	?	?	?	?	?	?	?
Jarratt 2004	?	?	?	?	?	?	?
Jemec 2008	?	?	?	?	?	?	?
Josse 2005	?	?	?	?	?	?	?
Katz 1995	?	?	?	?	?	?	?
Kiss 1996	?	?	?	?	?	?	?
Kiss 1996a	?	?	?	?	?	?	?
Klaber 1994	?	?	?	?	?	?	?
Klaber 2000	?	?	?	?	?	?	?
Kose 1997	?	?	?	?	?	?	?
Kragballe 2009a	?	?	?	?	?	?	?
Lassus 1976	?	?	?	?	?	?	?
Lepaw 1978	?	?	?	?	?	?	?
Luger 2008	?	?	?	?	?	?	?
Medansky 1974	?	?	?	?	?	?	?
Monk 1995	?	?	?	?	?	?	?
NCT01195831	?	?	?	?	?	?	?
Olsen 1991	?	?	?	?	?	?	?
Pauporte 2004	?	?	?	?	?	?	?
Regaia 2009	?	?	?	?	?	?	?
Reygagne 2002b	?	?	?	?	?	?	?
Reygagne 2005	?	?	?	?	?	?	?
Ruzicka 2004	?	?	?	?	?	?	?
Shuttleworth 1998	?	?	?	?	?	?	?
Sofen 2011	?	?	?	?	?	?	?
Swinehart 1989	?	?	?	?	?	?	?
Tyring 2010	?	?	?	?	?	?	?
van de Kerkhof 2002	?	?	?	?	?	?	?
van de Kerkhof 2009	?	?	?	?	?	?	?
Van der Ploeg 1989	?	?	?	?	?	?	?
Wall 1999	?	?	?	?	?	?	?
Willis 1986	?	?	?	?	?	?	?
Wright 1985	?	?	?	?	?	?	?
Yilmaz 2005	?	?	?	?	?	?	?

Results - Steroid vs vitamin D

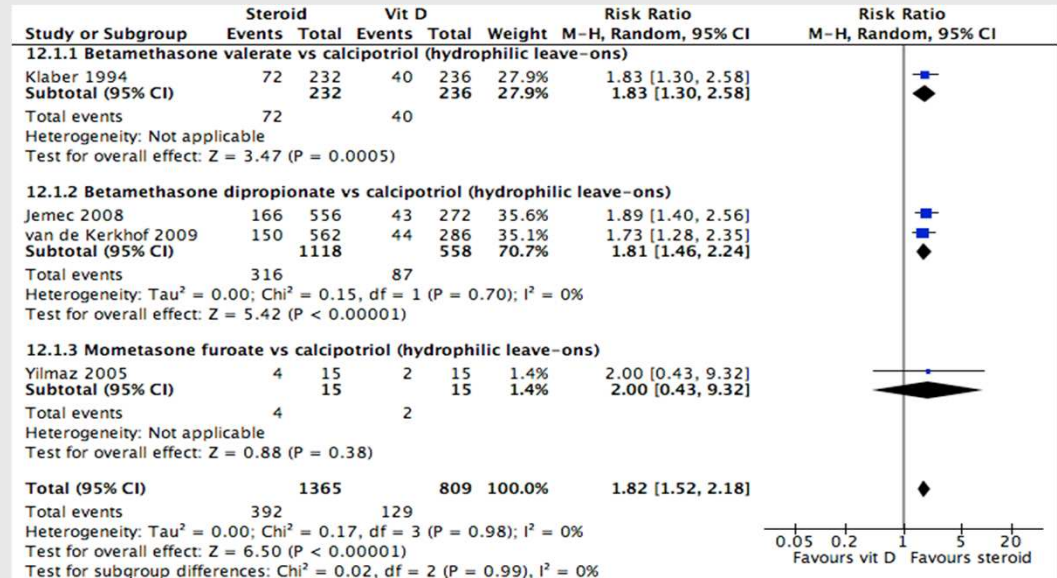


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Results - Steroid vs vitamin D

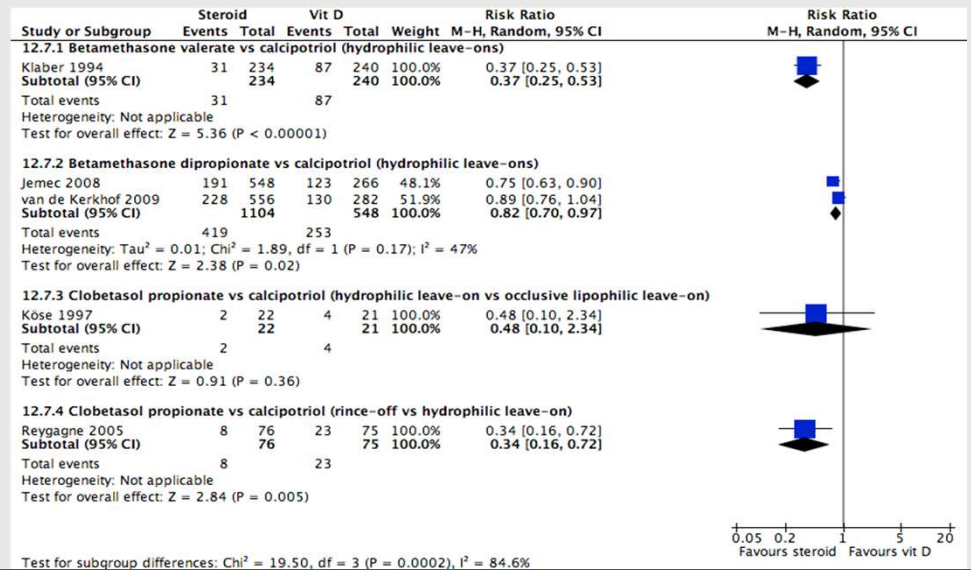
Efficacy analysis

IGA: clearance



Safety analysis

N° of patients with at least one AE



Results – combination vs monotherapy

Together or alone - what is better?



vs



Steroid/vitamin D combination

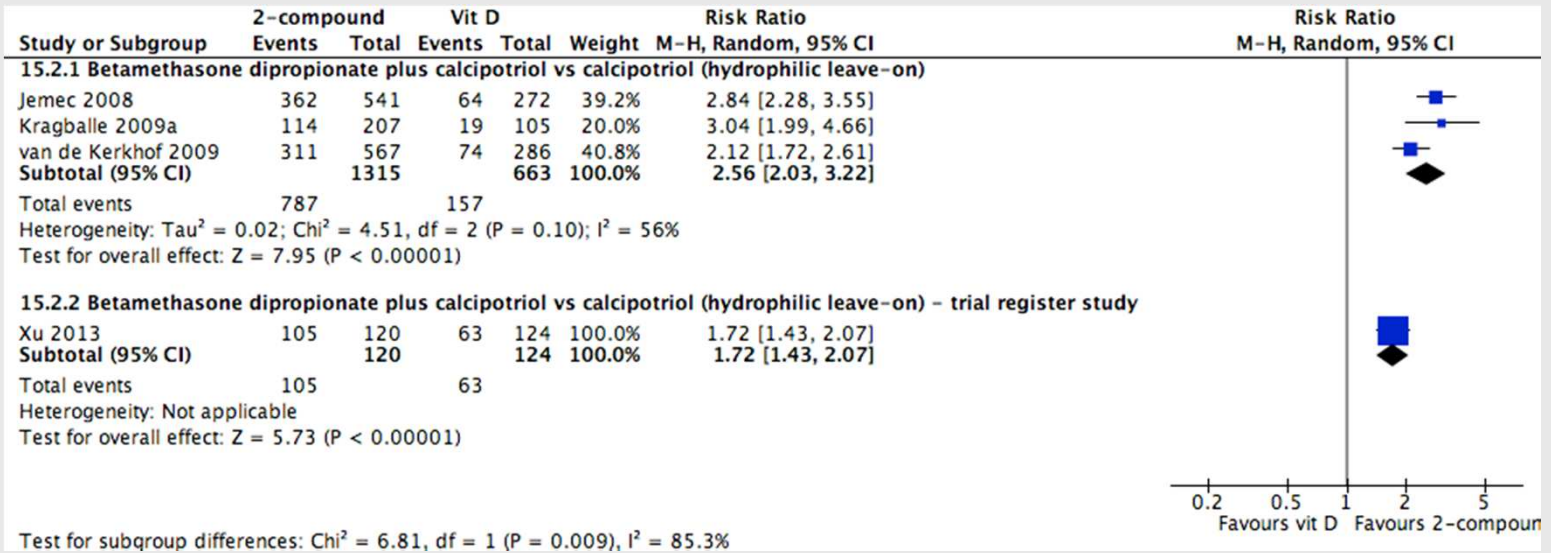
Monotherapy

(steroids or vitamin D)

Results – Steroid/vitamin D-combination vs vitamin D

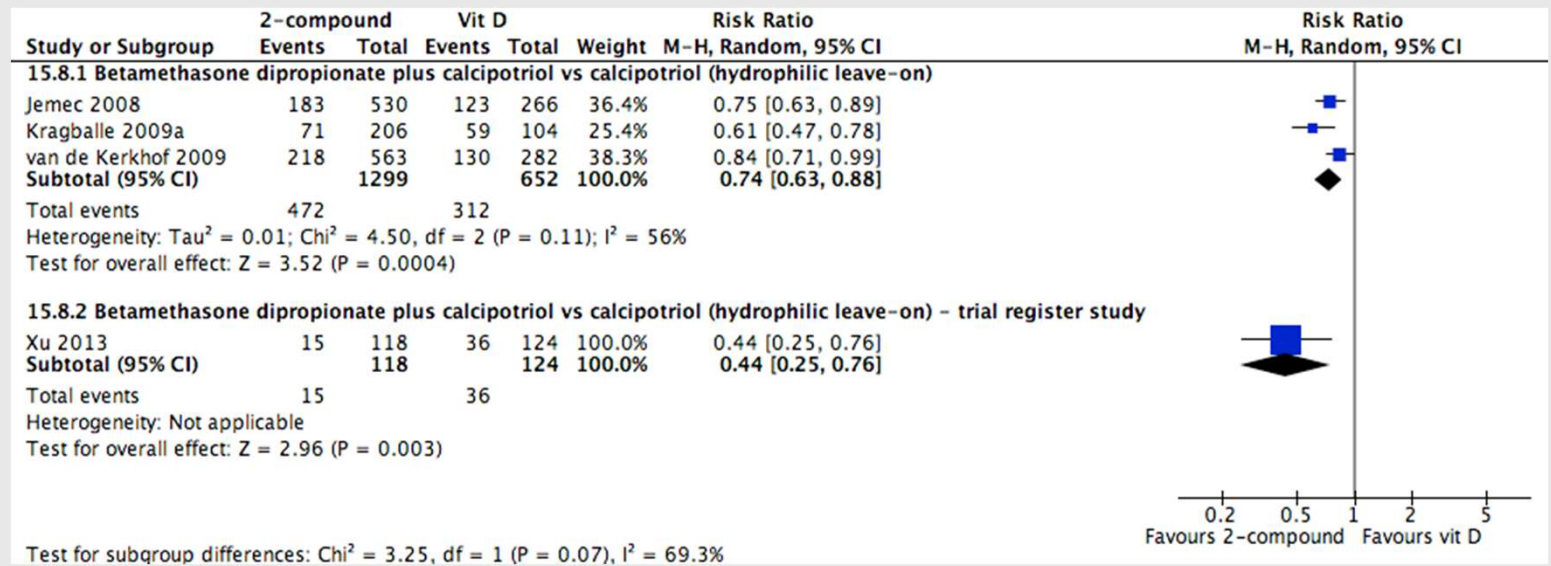
Efficacy analysis

IGA: response



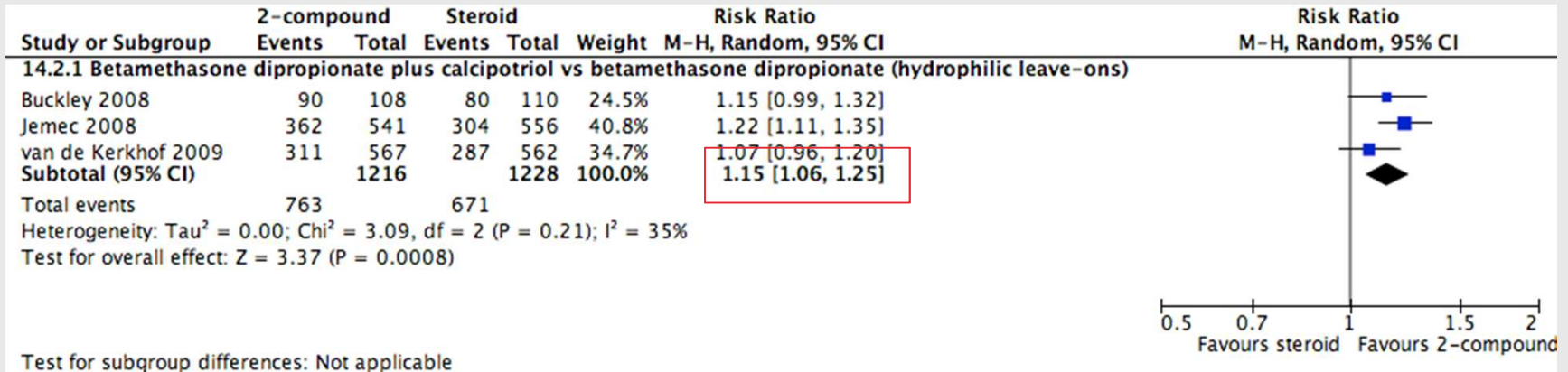
Safety analysis

N^o of patients with at least one AE

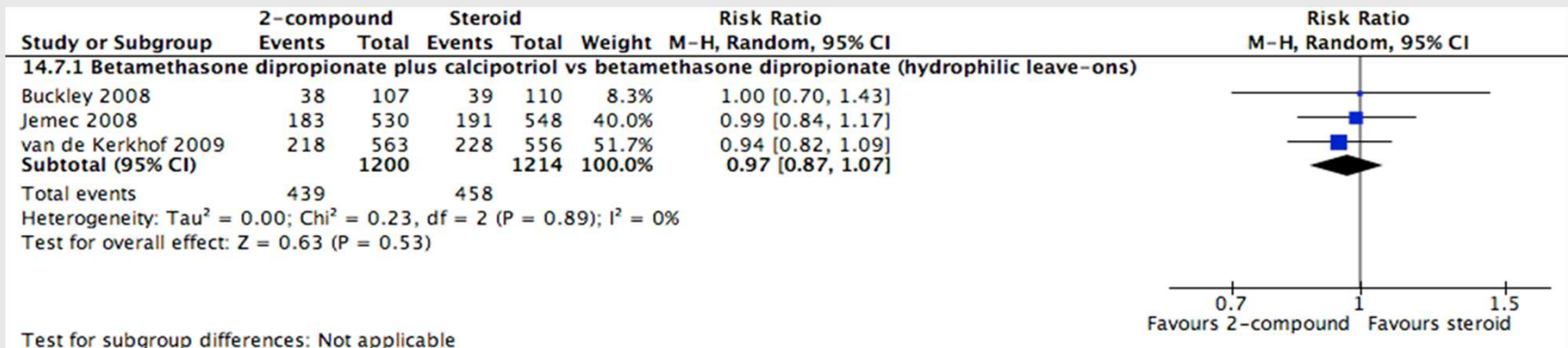


Results - Steroid/vitamin D-combination vs steroid

Efficacy analysis (IGA: response)



Safety analysis (N^o of patients with at least one AE)



Results - other comparisons



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Results - other comparisons

Steroids / vitamin D / 2-compound vs placebo

- significantly more effective
- similar rate of adverse event

Corticosteroids of different potency

- similar efficacy and safety profile

Treatments with insufficient evidence

- Salicylic acid, tar, dithranol, steroid vehicles, cocois, urea, tacrolimus, anti-fungals, coconut oil

Quality of Life

- Clobetasol > Placebo

Discussion

Major limitations

- No evidence for most topical treatments
- Evidence based on short-term therapy
- Lack of quality of life data

Discussion



Interesting finding

Steroid/vitamin D-combination > corticosteroid monotherapy

→ Higher treatment costs justified?

→ Mono-therapy of generic topical corticosteroids fully acceptable?

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