Bijlagen
Handeczeem
Richtlijn 2019

Colofon

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Bijlage 1: Belangenverklaringen

De KNMG-Code ter voorkoming van oneigenlijke beïnvloeding door belangenverstrengeling is gevolgd. Alle werkgroepleden hebben schriftelijk verklaard of ze in de laatste drie jaar directe financiële belangen (betrekking bij een commercieel bedrijf, persoonlijke financiële belangen, onderzoeksfinanciering) of indirecte belangen (persoonlijke relaties, reputatie management, kennisvalorisatie) hebben gehad. Een overzicht van de belangen van werkgroepleden en het oordeel over het omgaan met eventuele belangen vindt u in onderstaande tabel. De ondertekende belangenverklaringen zijn op te vragen bij het secretariaat van de Nederlandse Vereniging voor Dermatologie en Venereologie.

Werkgroeplid	**Nevenfunctie**	**Gemelde belangen (firma en activiteit)**	**Ondernomen actie (indien van toepassing)**
Dr. M.L.A. Schuttelaar, dermatoloog (voorzitter)	Geen	GSK, consultatie/advisering (niet in dienst) Almirale, consultatie/adivsering, wetenschappelijk onderzoek (niet in dienst)	Geen
B. Arents, patiëntenvertegenwoordiger	Geen	Geen	Geen
J.G. Bakker, klinisch arbeidsgeneeskundige/bedrijfsarts	Geen	Geen	Geen
F.G. Bosma, patiëntenvertegenwoordiger	Geen	Geen	Geen
F. Blok, dermatoloog	Geen	Geen	Geen
T.M. Bruggink, allergoloog	Geen	Geen	Geen
Dr. W.A. Christoffers, dermatoloog	Geen	Geen	Geen
Dr. J.J.E. van Everdingen, directeur NVDV, dermatoloog n.p.	Geen	Geen	Geen
M.F. Hofhuis, MSc, arts-onderzoeker	Geen	Geen	Geen
Dr. F.H.W. Jungbauer, klinisch arbeidsgeneeskundige/bedrijfsarts	Geen	Geen	Geen
Drs. A.C.M. Kunkeler, dermatoloog	Geen	GSK, bijdrage e-learning handeczeem (onbezoldigd)	Geen
I. Laffra, verpleegkundig specialist dermatologie	Geen	Geen	Geen
Drs. J.A.F. Oosterhaven, arts-assistent in opleiding tot dermatoloog en promovendus handeczeem	Geen	Geen	Geen
G.L.E. Romeijn, verpleegkundig consulent eczeem	Geen	Geen	Geen
Prof. dr. T. Rustemeyer, dermatoloog	Geen	GSK, consultatie/advisering, wetenschappelijk onderzoek, cursus (niet in dienst) DEB-Stoko, consultatie/advisering, wetenschappelijk	

		onderzoek, cursus (niet in dienst)	
L.S. van der Schoot, MSc, arts-onderzoeker (secretaris)	Geen	Geen	Geen
L. Teligui, MSc, arts-onderzoeker (secretaris)	Geen	Geen	Geen

Bijlage 2: Zoekstrategieën

Voor alle hoofdstukken geldt dat de zoekstrategieën zijn uitgevoerd in de EMBASE database, Medline database en de Cochrane library. Voor de hoofdstukken lokale therapie, fototherapie en systemische therapie werd de zoekstrategie van de Cochrane review van Christoffers *et al.* gebruikt voor RCT's over handeczeem en therapie (zoekstrategie t/m 2016). [Christoffers 2019] Deze zoekstrategie is opnieuw verricht op 07-06-2017. De zoekopdracht naar observationele studies is verricht op 9 oktober 2017 met een zoekdatum van 2007 t/m 2017. Voor de overige hoofdstukken werden losse zoekstrategieën uitgevoerd. Enkel de keywords gebruikt in de Medline database zijn weergeven. Experts op het gebied van Handeczeem werden geraadpleegd voor eventuele ontbrekende artikelen en/of case reports. De search is geüpdatet tot 2017.
Studies met deelnemers gediagnosticeerd met handeczeem, ongeacht van de onderliggende oorzaak, werden geselecteerd. Het handeczeem was in alle gevallen chronisch en varieerde van matig ernstig tot ernstig en betrof verschillende vormen (bijvoorbeeld hyperkeratotisch, dyshidrotisch, atopisch, orthoergisch, contactallergisch, beroepsgebonden en mengbeelden). De termen 'eczeem' en 'dermatitis' werden beide geaccepteerd als het om de handen ging. Daarnaast zijn de termen 'pompholyx', 'dyshidrosis' en 'pulpitis' meegenomen. Er is geen leeftijdgrens aangehouden. Op basis van de Cochrane zoekstrategie is er breed gezocht naar alle soorten therapie, behalve behandelingen over preventie. Als afbakening voor de eventuele controlegroep werd geen behandeling, placebobehandeling, vehicle behandeling of actieve behandeling gebruikt. Het percentage patiënten met self-rated/investigator-rated goede of excellente controle van symptomen werd gebruikt als primaire uitkomstmaat. Secundaire uitkomstmaten waren reductie in ernst van het handeczeem, bijwerkingen en time until relapse. Uitgesloten werden studies zonder originele gegevens (reviews) en studies waarin verschillende dermatologische aandoeningen werden bestudeerd waarin de gegevens van handeczeem niet afzonderlijk waren weergegeven. Studies met minder dan tien deelnemers (N<10) werden niet meegenomen. Er is een restrictie aangehouden voor Nederlandstalige en Engelstalige publicaties.

Voorlichting en begeleiding

Uitgangsvraag
- Wat is de effectiviteit van voorlichting en begeleiding bij patiënten met handeczeem?

EMBASE (datum 25-08-2017)

Zoektermen

#6. ('hand eczema'/exp OR 'hand eczema' OR 'hand eczema':ab,ti OR 'hand dermatose':ab,ti OR 'hand dermatoses':ab,ti OR 'hand dermatitis'/exp OR 'hand dermatitis' OR 'hand dermatitis':ab,ti OR 'pompholyx'/exp OR 'pompholyx':ab,ti OR 'dyshidrotic eczema':ab,ti OR 'vesicular palmoplantar eczema':ab,ti) AND (('patient education'/exp OR 'patient education':ab,ti) OR ('self care'/exp OR 'self care':ab,ti OR 'counseling'/exp OR 'counseling':ab,ti OR 'disease management'/exp OR 'disease management':ab,ti OR 'disease management program'/exp OR 'disease management program':ab,ti OR 'self management support'/exp OR 'self management support':ab,ti OR 'self monitoring'/exp OR 'self monitoring':ab,ti OR 'secondary prevention'/exp OR 'tertiary prevention'/exp)) AND ([dutch]/lim OR

[english]/lim)
#5. ('hand eczema'/exp OR 'hand eczema' OR 'hand eczema':ab,ti OR 'hand dermatose':ab,ti OR 'hand dermatoses':ab,ti OR 'hand dermatitis'/exp OR 'hand dermatitis' OR 'hand dermatitis':ab,ti OR 'pompholyx'/exp OR 'pompholyx':ab,ti OR 'dyshidrotic eczema':ab,ti OR 'vesicular palmoplantar eczema':ab,ti) AND (('patient education'/exp OR 'patient education':ab,ti) OR ('self care'/exp OR 'self care':ab,ti OR 'counseling'/exp OR 'counseling':ab,ti OR 'disease management'/exp OR 'disease management':ab,ti OR 'disease management program'/exp OR 'disease management program':ab,ti OR 'self management support'/exp OR 'self management support':ab,ti OR 'self monitoring'/exp OR 'self monitoring':ab,ti OR 'secondary prevention'/exp OR 'tertiary prevention'/exp))
#4. ('patient education'/exp OR 'patient education':ab,ti) OR ('self care'/exp OR 'self care':ab,ti OR 'counseling'/exp OR 'counseling':ab,ti OR 'disease management'/exp OR 'disease management':ab,ti OR 'disease management program'/exp OR 'disease management program':ab,ti OR 'self management support'/exp OR 'self management support':ab,ti OR 'self monitoring'/exp OR 'self monitoring':ab,ti OR 'secondary prevention'/exp OR 'tertiary prevention'/exp)
#3. 'self care'/exp OR 'self care':ab,ti OR 'counseling'/exp OR 'counseling':ab,ti OR 'disease management'/exp OR 'disease management':ab,ti OR 'disease management program'/exp OR 'disease management program':ab,ti OR 'self management support'/exp OR 'self management support':ab,ti OR 'self monitoring'/exp OR 'self monitoring':ab,ti OR 'secondary prevention'/exp OR 'tertiary prevention'/exp
#2. 'patient education'/exp OR 'patient education':ab,ti

Resultaten = 479

MEDLINE (datum 25-08-2017)

Zoektermen

1. exp Hand Dermatoses/ or hand eczema.mp. or Hand dermatoses.ti,ab,kw. or hand eczema.ti,ab,kw. or dyshidrotic eczema.mp. or exp Eczema, Dyshidrotic/ or dyshidrotic eczema.ti,ab,kw. or pompholyx.mp. or pompholyx.ti,ab,kw. or vesicular palmoplantar eczema.mp. or vesicular palmoplantar eczema.ti,ab,kw.
2. hand dermatitis.mp. or hand dermatitis.ti,ab,kw.
3. 1 or 2
4. patient education.mp. or exp Patient Education as Topic/ or patient education.ti,ab,kw.
5. self management.mp. or exp Self Care/ or exp Counseling/ or counseling.mp. or self management.ti,ab,kw. or self care.ti,ab,kw. or counseling.ti,ab,kw.
6. nurse consultation.mp. or nurse consultation.ti,ab,kw. or exp Disease Management/ or disease management.ti,ab,kw. or disease management.mp. or self management support.mp. or self management support.ti,ab,kw. or self monitoring.mp. or self monitoring.ti,ab,kw. or

secundary prevention.ti,ab,kw. or secundary prevention.mp. or tertiary prevention,ti,ab,kw.mp. or tertiary prevention.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

7. 4 or 5 or 6
8. 3 and 7

Resultaten = 94

Cochrane (datum 25-08-2017)

Zoektermen

1. MeSH descriptor: [Hand Dermatoses] explode all trees
2. MeSH descriptor: [Eczema, Dyshidrotic] explode all trees
3. MeSH descriptor: [Patient Education as Topic] explode all trees
4. MeSH descriptor: [Secondary Prevention] explode all trees
5. MeSH descriptor: [Tertiary Prevention] explode all trees
6. MeSH descriptor: [Managed Care Programs] explode all trees
7. MeSH descriptor: [Self Care] explode all trees
8. MeSH descriptor: [Counseling] explode all trees
9. MeSH descriptor: [Disease Management] explode all trees
10. MeSH descriptor: [Self Care] explode all trees
11. #1 or #2
12. #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
13. #11 and #12

Resultaten = 12

Alle resultaten

Database	Datum	# hits
EMBASE	25-08-2017	479
MEDLINE	25-08-2017	94
Cochrane	25-08-2017	12
Totaal		**585**
Duplicates		**106**
Netto aantal		**479**

Handschoenen

Uitgangsvraag

- Wat is de effectiviteit van handschoenen als secundaire preventie bij patiënten met handeczeem?

EMBASE (datum 19-09-2017)

Zoektermen

#6. ('hand eczema'/exp OR 'hand eczema' OR 'hand eczema':ab,ti OR 'hand dermatose':ab,ti OR 'hand dermatoses':ab,ti OR 'hand dermatitis'/exp OR 'hand dermatitis' OR 'hand dermatitis':ab,ti OR 'pompholyx'/exp OR 'pompholyx':ab,ti OR 'dyshidrotic eczema':ab,ti OR 'vesicular palmoplantar eczema':ab,ti) AND (('glove'/exp OR 'protective glove'/exp OR glove*:ab,ti,kw OR 'protective glove*':ab,ti,kw) OR 'hand protection*':ti,ab,kw) AND ([dutch]/lim OR [english]/lim)

#5. ('hand eczema'/exp OR 'hand eczema' OR 'hand eczema':ab,ti OR 'hand dermatose':ab,ti OR 'hand

dermatoses':ab,ti OR 'hand dermatitis'/exp OR 'hand dermatitis' OR 'hand dermatitis':ab,ti OR 'pompholyx'/exp OR 'pompholyx':ab,ti OR 'dyshidrotic eczema':ab,ti OR 'vesicular palmoplantar eczema':ab,ti) AND (('glove'/exp OR 'protective glove'/exp OR glove*:ab,ti,kw OR 'protective glove*':ab,ti,kw) OR 'hand protection*':ti,ab,kw)
#4. ('glove'/exp OR 'protective glove'/exp OR glove*:ab,ti,kw OR 'protective glove*':ab,ti,kw) OR 'hand protection*':ti,ab,kw
#3. 'hand protection*':ti,ab,kw
#2. 'glove'/exp OR 'protective glove'/exp OR glove*:ab,ti,kw OR 'protective glove*':ab,ti,kw
#1. 'hand eczema'/exp OR 'hand eczema' OR 'hand eczema':ab,ti OR 'hand dermatose':ab,ti OR 'hand dermatoses':ab,ti OR 'hand dermatitis'/exp OR 'hand dermatitis' OR 'hand dermatitis':ab,ti OR 'pompholyx'/exp OR 'pompholyx':ab,ti OR 'dyshidrotic eczema':ab,ti OR 'vesicular palmoplantar eczema':ab,ti

Resultaten = 340

MEDLINE (datum 19-09-2017)

Zoektermen

1. exp Hand Dermatoses/ or hand eczema.mp. or Hand dermatoses.ti,ab,kw. or hand eczema.ti,ab,kw. or dyshidrotic eczema.mp. or exp Eczema, Dyshidrotic/ or dyshidrotic eczema.ti,ab,kw. or pompholyx.mp. or pompholyx.ti,ab,kw. or vesicular palmoplantar eczema.mp. or vesicular palmoplantar eczema.ti,ab,kw.
2. hand dermatitis.mp. or hand dermatitis.ti,ab,kw.
3. 1 or 2
4. exp Gloves, Protective/ or glove.mp. or protective glove*:ti,ab,kw.mp. or glove*:ti,ab,kw.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
5. (hand protection* or hand protection*:ti,ab,kw).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
6. 4 or 5
7. 3 and 6
8. limit 7 to (dutch or english)

Resultaten = 315

Cochrane (datum 19-09-2017)

Zoektermen

1. MeSH descriptor: [Hand Dermatoses] explode all trees
    1. Hand dermatoses:ti,ab or hand eczema:ti,ab or hand dermatitis:ti,ab
    2. #1 or #2
    3. MeSH descriptor: [Gloves, Protective] explode all trees
    4. protective glove*:ti,ab or protect* glove*:ti,ab
    5. cotton glove*:ti,ab or hand protection*:ti,ab
    6. #4 or #5 or #6
    7. #3 and #7

Resultaten = 53

Alle resultaten

Database	Datum	# hits
EMBASE	19-09-2017	340
MEDLINE	19-09-2017	315
Cochrane	19-09-2017	53
Totaal		**708**
Duplicates		**175**
Netto aantal		**533**

Indifferente middelen

Uitgangsvraag

- Wat is het effect van indifferente middelen bij patiënten met handeczeem?

EMBASE (datum 12-10-2017)

Zoektermen

#15 #14 AND ('clinical study'/de OR 'clinical trial'/de OR 'cohort analysis'/de OR 'comparative study'/de OR 'controlled clinical trial'/de OR 'controlled study'/de OR 'double blind procedure'/de OR 'drug dose comparison'/de OR 'evidence based medicine'/de OR 'major clinical study'/de OR 'multicenter study'/de OR 'open study'/de OR 'practice guideline'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de OR 'systematic review'/de)
#14 #2 AND #13
#13 #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
#12 'steroid'/exp OR 'steroid':ab,ti,kw OR 'steroid*':ab,ti,kw
#11 'corticosteroid'/exp OR 'corticosteroid':ab,ti,kw OR 'corticosteroid*':ab,ti,kw
#10 'bath'/exp OR 'bath':ab,ti,kw OR 'bath*':ab,ti,kw
#9 'oil'/exp OR 'oil':ab,ti,kw OR 'oil*':ab,ti,kw
#8 'skin cream'/exp OR 'skin cream':ab,ti,kw
#7 'cream'/exp OR 'cream':ab,ti,kw OR 'cream*':ab,ti,kw
#6 'ointment'/exp OR 'ointment':ab,ti,kw OR 'ointment*':ab,ti,kw
#5 'lubricating agent'/exp OR 'lubricating agent':ab,ti,kw OR lubricant*:ab,ti,kw
#4 'moisture'/exp OR 'moisture':ab,ti,kw OR 'moisturis*':ab,ti,kw OR 'moisturiz*':ab,ti,kw
#3 'emollient agent'/exp OR emollient*:ab,ti,kw
#2 'hand eczema'/exp OR 'hand eczema' OR 'hand eczema':ab,ti OR 'hand dermatose':ab,ti OR 'hand dermatoses':ab,ti OR 'hand dermatitis'/exp OR 'hand dermatitis' OR 'hand dermatitis':ab,ti OR 'pompholyx'/exp OR 'pompholyx' OR 'pompholyx':ab,ti OR 'dyshidrotic eczema':ab,ti OR 'vesicular palmoplantar eczema':ab,ti
#1 'hand eczema'/exp OR 'hand eczema' OR 'hand eczema':ab,ti OR 'hand dermatose':ab,ti OR 'hand dermatoses':ab,ti OR 'hand dermatitis'/exp OR 'hand dermatitis' OR 'hand dermatitis':ab,ti OR 'pompholyx'/exp OR 'pompholyx':ab,ti OR 'dyshidrotic eczema':ab,ti OR 'vesicular palmoplantar eczema':ab,ti

Resultaten = 379

MEDLINE (datum 05-01-2018)

Zoektermen

1. exp Hand Dermatoses/ or hand eczema.mp. or Hand dermatoses.ti,ab,kw. or hand eczema.ti,ab,kw. or dyshidrotic eczema.mp. or exp Eczema, Dyshidrotic/ or dyshidrotic eczema.ti,ab,kw. or pompholyx.mp. or pompholyx.ti,ab,kw. or vesicular palmoplantar eczema.mp. or vesicular palmoplantar eczema.ti,ab,kw.
2. hand dermatitis.mp. or hand dermatitis.ti,ab,kw.
3. 1 or 2
4. emollient$.ti,ab. or exp Emollients/
5. moisturis$.ti,ab.

6. moisturiz$.ti,ab.
7. lubricant$.ti,ab. or exp Lubricants/
8. ointment$.ti,ab. or exp Ointments/
9. cream$.ti,ab.
10. exp Skin Cream/
11. exp Oils/ or oil$.ti,ab.
12. bath$3.ti,ab. or exp Baths/
13. corticosteroid$.ti,ab.
14. exp Steroids/ or steroid$.ti,ab.
15. or/4-14
16. 3 and 15
17. limit 16 to (classical article or clinical study or clinical trial, all or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or clinical trial or comparative study or controlled clinical trial or evaluation studies or guideline or meta-analysis or multicenter study or observational study or practice guideline or pragmatic clinical trial or randomized controlled trial or systematic reviews or twin study)

Resultaten = 209

Cochrane (datum 02-10-2017)

Zoektermen

1. MeSH descriptor: [Hand Dermatoses] explode all trees
2. Hand dermatoses:ti,ab or hand eczema:ti,ab or hand dermatitis:ti,ab
3. #1 or #2
4. MeSH descriptor: [Emollients] explode all trees
5. emollient*:ti,ab,kw
6. (moisturis* or moisturiz*):ti,ab,kw
7. MeSH descriptor: [Lubricants] explode all trees
8. lubricant*:ti,ab,kw
9. MeSH descriptor: [Ointments] explode all trees
10. ointment*:ti,ab,kw
11. cream*:ti,ab,kw
12. MeSH descriptor: [Skin Cream] explode all trees
13. MeSH descriptor: [Oils] explode all trees
14. oil*:ti,ab,kw
15. MeSH descriptor: [Baths] explode all trees
16. bath*:ti,ab,kw
17. corticosteroid*:ti,ab,kw
18. steroid*:ti,ab,kw
19. MeSH descriptor: [Steroids] explode all trees
20. {or #4-#19}
21. #3 and #20

Resultaten = 179

Alle resultaten

Database	**Datum**	**# hits**
EMBASE	12-10-2017	379
MEDLINE	05-01-2018	209
Cochrane	02-10-2017	179
Totaal		**767**
Duplicates		**217**
Netto aantal		**550**

Lokale therapie, fototherapie, systemische therapie

Uitgangsvragen

Lokale therapie

- Wat is de effectiviteit van lokale therapie bij de behandeling van patiënten met handeczeem?

Fototherapie

- Wat is de effectiviteit van foto(chemo)therapie bij de behandeling van handeczeem?

Systemische therapie

- Wat is de effectiviteit van systemische middelen bij de behandeling van patiënten met chronisch handeczeem niet of onvoldoende reagerend op lokale corticosteroïden van een hoge klasse?
    - Wat is de effectiviteit van acitretine bij de behandeling van patiënten met chronisch handeczeem niet of onvoldoende reagerend op lokale corticosteroïden van een hoge klasse?
    - Wat is de effectiviteit van alitretinoïne bij de behandeling van patiënten met chronisch handeczeem niet of onvoldoende reagerend op lokale corticosteroïden van een hoge klasse?
    - Wat is de effectiviteit van azathioprine bij de behandeling van patiënten met chronisch handeczeem niet of onvoldoende reagerend op lokale corticosteroïden van een hoge klasse?
    - Wat is de effectiviteit van ciclosporine-A bij de behandeling van patiënten met chronisch handeczeem niet of onvoldoende reagerend op lokale corticosteroïden van een hoge klasse?
    - Wat is de effectiviteit van methotrexaat bij de behandeling van patiënten met chronisch handeczeem niet of onvoldoende reagerend op lokale corticosteroïden van een hoge klasse?

Randomized controlled trials

EMBASE (datum 07-06-2017)

Zoektermen

#40. 'pompholyx'/exp OR 'hand eczema'/exp OR 'acrodermatitis'/exp OR 'cheiropompholyx':ti,ab OR 'pompholyx':ti,ab OR 'hand eczema':ti,ab OR (pulpitis:ti,ab OR pulpite:ti,ab AND ('hand'/exp OR hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab)) OR ('eczema'/exp OR 'eczema':ti,ab OR 'dermatitis'/exp OR 'dermatitis':ti,ab AND ('tylotic':ti,ab OR 'hyperkeratotic':ti,ab OR nummular:ti,ab OR microbial:ti,ab OR discoid:ti,ab) AND ('hand'/exp OR hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab)) OR ('eczema'/exp OR 'eczema':ti,ab OR 'dermatitis'/exp OR 'dermatitis':ti,ab AND (dyshidro*:ti,ab OR dyshydro*:ti,ab OR dishidro*:ti,ab OR dishydro*:ti,ab)) AND ('crossover procedure' OR 'double-blind procedure' OR 'single-blind procedure' OR 'crossover*':ti,ab OR 'cross over*':ti,ab OR placebo*:ti,ab OR 'doubl* blind*':ti,ab OR allocat*:ti,ab OR trial:ti OR 'randomized controlled trial':ti,ab OR random*:ti,ab) NOT ('animal'/exp OR 'animal

model'/exp OR 'animal tissue'/exp OR 'animal cell'/exp OR 'nonhuman'/exp NOT ('animal'/exp OR 'animal model'/exp OR 'animal tissue'/exp OR 'animal cell'/exp OR 'nonhuman'/exp AND ('human'/exp OR 'normal human'/exp)))

#39. 'crossover procedure' OR 'double-blind procedure' OR 'single-blind procedure' OR 'crossover*':ti,ab OR 'cross over*':ti,ab OR placebo*:ti,ab OR 'doubl* blind*':ti,ab OR allocat*:ti,ab OR trial:ti OR 'randomized controlled trial':ti,ab OR random*:ti,ab NOT ('animal'/exp OR 'animal model'/exp OR 'animal tissue'/exp OR 'animal cell'/exp OR 'nonhuman'/exp NOT ('animal'/exp OR 'animal model'/exp OR 'animal tissue'/exp OR 'animal cell'/exp OR 'nonhuman'/exp AND ('human'/exp OR 'normal human'/exp)))

#38. 'animal'/exp OR 'animal model'/exp OR 'animal tissue'/exp OR 'animal cell'/exp OR 'nonhuman'/exp NOT ('animal'/exp OR 'animal model'/exp OR 'animal tissue'/exp OR 'animal cell'/exp OR 'nonhuman'/exp AND ('human'/exp OR 'normal human'/exp))

#37. 'animal'/exp OR 'animal model'/exp OR 'animal tissue'/exp OR 'animal cell'/exp OR 'nonhuman'/exp AND ('human'/exp OR 'normal human'/exp)

#36. 'human'/exp OR 'normal human'/exp

#35. 'animal'/exp OR 'animal model'/exp OR 'animal tissue'/exp OR 'animal cell'/exp OR 'nonhuman'/exp

#34. 'crossover procedure' OR 'double-blind procedure' OR 'single-blind procedure' OR 'crossover*':ti,ab OR 'cross over*':ti,ab OR placebo*:ti,ab OR 'doubl* blind*':ti,ab OR allocat*:ti,ab OR trial:ti OR 'randomized controlled trial':ti,ab OR random*:ti,ab

#33. random*:ti,ab

#32. 'randomized controlled trial':ti,ab

#31. trial:ti

#30. allocat*:ti,ab

#29. 'doubl* blind*':ti,ab

#28. placebo*:ti,ab

#27. 'crossover*':ti,ab OR 'cross over*':ti,ab

#25. 'single-blind procedure'

#24. 'double-blind procedure'

#23. 'crossover procedure'

#22. 'pompholyx'/exp OR 'hand eczema'/exp OR 'acrodermatitis'/exp OR 'cheiropompholyx':ti,ab OR 'pompholyx':ti,ab OR 'hand eczema':ti,ab OR (pulpitis:ti,ab OR pulpite:ti,ab AND ('hand'/exp OR hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab)) OR ('eczema'/exp OR 'eczema':ti,ab OR 'dermatitis'/exp OR 'dermatitis':ti,ab AND ('tylotic':ti,ab OR 'hyperkeratotic':ti,ab OR nummular:ti,ab OR microbial:ti,ab OR discoid:ti,ab) AND ('hand'/exp OR hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab)) OR ('eczema'/exp OR 'eczema':ti,ab OR 'dermatitis'/exp OR

'dermatitis':ti,ab AND (dyshidro*:ti,ab OR dyshydro*:ti,ab OR dishidro*:ti,ab OR dishydro*:ti,ab))
#21. 'eczema'/exp OR 'eczema':ti,ab OR 'dermatitis'/exp OR 'dermatitis':ti,ab AND (dyshidro*:ti,ab OR dyshydro*:ti,ab OR dishidro*:ti,ab OR dishydro*:ti,ab)
#20. 'eczema'/exp OR 'eczema':ti,ab OR 'dermatitis'/exp OR 'dermatitis':ti,ab AND ('tylotic':ti,ab OR 'hyperkeratotic':ti,ab OR nummular:ti,ab OR microbial:ti,ab OR discoid:ti,ab) AND ('hand'/exp OR hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab)
#19. pulpitis:ti,ab OR pulpite:ti,ab AND ('hand'/exp OR hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab)
#18. 'hand'/exp OR hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab
#17. hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab
#16. 'hand'/exp
#15. 'tylotic':ti,ab OR 'hyperkeratotic':ti,ab OR nummular:ti,ab OR microbial:ti,ab OR discoid:ti,ab
#14. dyshidro*:ti,ab OR dyshydro*:ti,ab OR dishidro*:ti,ab OR dishydro*:ti,ab
#13. pulpitis:ti,ab OR pulpite:ti,ab
#12. nummular:ti,ab OR microbial:ti,ab OR discoid:ti,ab
#11. 'tylotic':ti,ab OR 'hyperkeratotic':ti,ab
#10. 'eczema'/exp OR 'eczema':ti,ab OR 'dermatitis'/exp OR 'dermatitis':ti,ab
#9. 'dermatitis'/exp OR 'dermatitis':ti,ab
#8. 'eczema'/exp OR 'eczema':ti,ab
#7. 'pompholyx'/exp OR 'hand eczema'/exp OR 'acrodermatitis'/exp OR 'cheiropompholyx':ti,ab OR 'pompholyx':ti,ab OR 'hand eczema':ti,ab
#6. 'hand eczema':ti,ab
#5. 'pompholyx':ti,ab
#4. 'cheiropompholyx':ti,ab
#3. 'acrodermatitis'/exp
#2. 'hand eczema'/exp
#1. 'pompholyx'/exp

Resultaten = 254 (127 dubbel met MEDLINE)

MEDLINE (datum 07-06-2017)

Zoektermen

1 exp *Hand Dermatoses/
2 exp Eczema, Dyshidrotic/
3 hand eczema.mp.
4 exp *Acrodermatitis/
5 pompholyx.mp.
6 cheiropompholyx.mp.
7 1 or 2 or 3 or 4 or 5 or 6
8 exp Eczema/ or eczema.mp.
9 exp Dermatitis/ or dermatitis.mp.
10 8 or 9
11 (tylotic or hyperkeratotic).mp.

12 (nummular or microbial or discoid).mp.
13 (pulpitis or pulpite).mp.
14 (dyshidro$ or dyshydro$ or dishidro$ or dishydro$).mp.
15 11 or 12
16 exp Hand/
17 (hand$ or finger$ or palm$).mp.
18 16 or 17
19 13 and 18
20 10 and 15 and 18
21 10 and 14
22 7 or 19 or 20 or 21
23 randomized controlled trial.pt.
24 controlled clinical trial.pt.
25 randomized.ab.
26 placebo.ab.
27 clinical trials as topic.sh.
28 randomly.ab.
29 trial.ti.
30 23 or 24 or 25 or 26 or 27 or 28 or 29
31 exp animals/ not humans.sh.
32 30 not 31
33 22 and 32

Resultaten = 317

Cochrane (datum 07-06-2017)

Zoektermen

#1 tylotic or hyperkeratotic or nummular or microbial or discoid
#2 MeSH descriptor: [Eczema] explode all trees
#3 MeSH descriptor: [Dermatitis] explode all trees
#4 eczema or dermatitis
#5 #2 or #3 or #4
#6 MeSH descriptor: [Hand Dermatoses] explode all trees
#7 MeSH descriptor: [Eczema, Dyshidrotic] explode all trees
#8 hand eczema
#9 MeSH descriptor: [Acrodermatitis] explode all trees
#10 pompholyx
#11 cheiropompholyx
#12 #6 or #7 or #8 or #9 or #10 or #11
#13 MeSH descriptor: [Hand] explode all trees
#14 (hand* or finger* or palm*)
#15 #13 or #14
#16 #1 and #5 and #15
#17 pulpitis or pulpite
#18 #15 and #17
#19 dyshidro* or dyshydro* or dishidro* or dishydro*
#20 #5 and #19
#21 #12 or #16 or #18 or #20

Resultaten = 573
Reviews (140)
Trials (399)

Alle resultaten

Database	Datum	# hits
EMBASE	07-06-2017	254
MEDLINE	07-06-2017	317

Cochrane	07-06-2017	573
Totaal		**1144**
Duplicates		**251**
Netto aantal		**893**

Observationele studies

EMBASE (datum 09-10-2017)

Zoektermen

#24. ((('pompholyx'/exp OR 'hand eczema'/exp OR 'acrodermatitis'/exp OR 'cheiropompholyx':ti,ab OR 'pompholyx':ti,ab OR 'hand eczema':ti,ab) OR ((pulpitis:ti,ab OR pulpite:ti,ab) AND ('hand'/exp OR (hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab))) OR ((('eczema'/exp OR 'eczema':ti,ab) OR ('dermatitis'/exp OR 'dermatitis':ti,ab)) AND (('tylotic':ti,ab OR 'hyperkeratotic':ti,ab) OR (nummular:ti,ab OR microbial:ti,ab OR discoid:ti,ab)) AND ('hand'/exp OR (hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab))) OR ((('eczema'/exp OR 'eczema':ti,ab) OR ('dermatitis'/exp OR 'dermatitis':ti,ab)) AND (dyshidro*:ti,ab OR dyshydro*:ti,ab OR dishidro*:ti,ab OR dishydro*:ti,ab))) AND ('cohort analysis'/de OR 'comparative study'/de OR 'cross-sectional study'/de OR 'human'/de OR 'practice guideline'/de OR 'prospective study'/de OR 'retrospective study'/de) AND [embase]/lim NOT [medline]/lim AND ([dutch]/lim OR [english]/lim)) AND (2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py)

#23. (('pompholyx'/exp OR 'hand eczema'/exp OR 'acrodermatitis'/exp OR 'cheiropompholyx':ti,ab OR 'pompholyx':ti,ab OR 'hand eczema':ti,ab) OR ((pulpitis:ti,ab OR pulpite:ti,ab) AND ('hand'/exp OR (hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab))) OR ((('eczema'/exp OR 'eczema':ti,ab) OR ('dermatitis'/exp OR 'dermatitis':ti,ab)) AND (('tylotic':ti,ab OR 'hyperkeratotic':ti,ab) OR (nummular:ti,ab OR microbial:ti,ab OR discoid:ti,ab)) AND ('hand'/exp OR (hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab))) OR ((('eczema'/exp OR 'eczema':ti,ab) OR ('dermatitis'/exp OR 'dermatitis':ti,ab)) AND (dyshidro*:ti,ab OR dyshydro*:ti,ab OR dishidro*:ti,ab OR dishydro*:ti,ab))) AND ('cohort analysis'/de OR 'comparative study'/de OR 'cross-sectional study'/de OR 'human'/de OR 'practice guideline'/de OR 'prospective study'/de OR 'retrospective study'/de) AND [embase]/lim NOT [medline]/lim AND ([dutch]/lim OR [english]/lim)

#22. ('pompholyx'/exp OR 'hand eczema'/exp OR 'acrodermatitis'/exp OR 'cheiropompholyx':ti,ab

OR 'pompholyx':ti,ab OR 'hand eczema':ti,ab) OR ((pulpitis:ti,ab OR pulpite:ti,ab) AND ('hand'/exp OR (hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab))) OR ((('eczema'/exp OR 'eczema':ti,ab) OR ('dermatitis'/exp OR 'dermatitis':ti,ab)) AND (('tylotic':ti,ab OR 'hyperkeratotic':ti,ab) OR (nummular:ti,ab OR microbial:ti,ab OR discoid:ti,ab)) AND ('hand'/exp OR (hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab))) OR ((('eczema'/exp OR 'eczema':ti,ab) OR ('dermatitis'/exp OR 'dermatitis':ti,ab)) AND (dyshidro*:ti,ab OR dyshydro*:ti,ab OR dishidro*:ti,ab OR dishydro*:ti,ab))

#21. (('eczema'/exp OR 'eczema':ti,ab) OR ('dermatitis'/exp OR 'dermatitis':ti,ab)) AND (dyshidro*:ti,ab OR dyshydro*:ti,ab OR dishidro*:ti,ab OR dishydro*:ti,ab)

#20. (('eczema'/exp OR 'eczema':ti,ab) OR ('dermatitis'/exp OR 'dermatitis':ti,ab)) AND (('tylotic':ti,ab OR 'hyperkeratotic':ti,ab) OR (nummular:ti,ab OR microbial:ti,ab OR discoid:ti,ab)) AND ('hand'/exp OR (hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab))

#19. (pulpitis:ti,ab OR pulpite:ti,ab) AND ('hand'/exp OR (hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab))

#18. 'hand'/exp OR (hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab)

#17. hand*:ti,ab OR finger*:ti,ab OR palm*:ti,ab

#16. 'hand'/exp

#15. ('tylotic':ti,ab OR 'hyperkeratotic':ti,ab) OR (nummular:ti,ab OR microbial:ti,ab OR discoid:ti,ab)

#14. dyshidro*:ti,ab OR dyshydro*:ti,ab OR dishidro*:ti,ab OR dishydro*:ti,ab

#13. pulpitis:ti,ab OR pulpite:ti,ab

#12. nummular:ti,ab OR microbial:ti,ab OR discoid:ti,ab

#11. 'tylotic':ti,ab OR 'hyperkeratotic':ti,ab

#10. ('eczema'/exp OR 'eczema':ti,ab) OR ('dermatitis'/exp OR 'dermatitis':ti,ab)

#9. 'dermatitis'/exp OR 'dermatitis':ti,ab

#8. 'eczema'/exp OR 'eczema':ti,ab

#7. 'pompholyx'/exp OR 'hand eczema'/exp OR 'acrodermatitis'/exp OR 'cheiropompholyx':ti,ab OR 'pompholyx':ti,ab OR 'hand eczema':ti,ab

#6. 'hand eczema':ti,ab

#5. 'pompholyx':ti,ab

#4. 'cheiropompholyx':ti,ab

#3. 'acrodermatitis'/exp

#2. 'hand eczema'/exp

#1. 'pompholyx'/exp

Resultaten = 819

MEDLINE (datum 09-10-2017)

Zoektermen

1. exp *Hand Dermatoses/
2. exp Eczema, Dyshidrotic/
3. hand eczema.mp.
4. exp *Acrodermatitis/
5. pompholyx.mp.
6. cheiropompholyx.mp.
7. exp Eczema/ or eczema.mp.
8. exp Dermatitis/ or dermatitis.mp.
9. 1 or 2 or 3 or 4 or 5 or 6
10. 7 or 8
11. (tylotic or hyperkeratotic).mp.
12. (nummular or microbial or discoid).mp.
13. (pulpitis or pulpite).mp.
14. (dyshidro$ or dyshydro$ or dishidro$ or dishy-dro$).mp.
15. 11 or 12
16. exp Hand/
17. (hand$ or finger$ or palm$).mp.
18. 16 or 17
19. 13 and 18
20. 10 and 15 and 18
21. 10 and 14
22. 9 or 19 or 20 or 21
23. limit 22 to (humans and (dutch or english) and (comparative study or guideline or letter or meta analysis or multicenter study or observational study or practice guideline))
24. limit 23 to yr="2007 -Current"

Resultaten = 500

Alle resultaten

Database	**Datum**	**# hits**
EMBASE	09-10-2017	819
MEDLINE	09-10-2017	500
Totaal		**1319**
Duplicates		**97**
Netto aantal		**1222**

Bijlage 3: Tabellen karakteristieken en resultaten van geïncludeerde studies

Voorlichting en begeleiding (2017)

Karakteristieken en resultaten van geïncludeerde studies beoordeeld volgens EBRO

Study reference	Level of evide-nce	Study design	Patients (N)	Inclusion criteria	Follow-up	Outcome measures	Results	Lost to follow-up	Comments
Brans 2016 *Multicentre cohort study 'Rehabilitation of Occupational Skin Diseases – Optimization and Quality Assurance of Inpatient Management (ROQ)': results from a 3-year follow-up*	B	Prospective follow up cohort study No control group. Long term effects of a tertiary individual prevention programme (TIP), described in Skudlik et al. 2012 (see below)	1788 patients N=1316 (93.3%) were diagnosed for HE. 61.6% suffered from an overlap-type HE (combined aetiologies of irritant, atopic and allergic HE).	See Skudlik 2012	3 years (T6)	- OHSI - Severity of OSD according to the Bamberg Medical Bulletin - Usage of topical corticosteroids within previous 12 months - DLQI - LIOD - Total number of days of absence from work - Return to work and remaining in same profession	The severity of OSD (OHSI) was lower ($p < 0.001$) than at admission to the inpatient phase and lower than T5 (12 months after TIP). N=445 (31.6%) had complete Healing. This was similar for working patients (n=324, 28.2%). N=56 (4.9%) still had severe skin lesions. The use of topical corticosteroids (89% prior t TIP vs 46.7% (n=638) at T6 $p<0.001$) and days of absence from work were significantly reduced. Quality of life and skin protective behavior were significantly improved. Of the patients, 96.9% were able to resume work. N=1166 (82.7%) were still working 3 years after the TIP, n=874 of them (75.0%) in the same occupational field. Of the patients that left the	At the 12 month follow up a response rate of 78.9% (N=1410)	See Skudlik 2012 Large response rate. Study design; no control group. Unknown if the effect is only attributable to the intervention. There are also other German hierarchical prevention concepts available for patients.

							original occupational field 75,6% was because of skin disease. Hairdressers had the lowest rate of remaining in their original profession (41.3%), 52,1% of them because of skin disease.		
Breuer 2015 *Tertiary individual prevention improves mental health in patients with severe occupational hand eczema* .	C	The multicenter study 'Medical Occupational Rehabilitation Procedure Skin Optimizing and quality assurance of inpatient-management (ROQ)'. From Skudlik et al (2012: prospectief cohort onderzoek) I: The program included dermatological therapy, intensified health care instruction and	122	age 18 years and above, occupational hand eczema resistant to outpatient treatment of at least 6 months duration, willingness to complete a set questionnaire, adequate comprehension of German and written consent	3 weeks after dismissal	German versions of the Hospital Anxiety and Depression Scale (HADS-D), the Dermatology Life Quality Index (DLQI), the Short Form Health Survey-36 (SF-36) and the Trier Inventory for the Assessment of Chronic Stress (TICS) was applied at the time of admission (T1) and 3 weeks after dismissal (T2). Severity of hand eczema was assessed with the Osnabrueck Hand Eczema Severity Index (OHSI	All parameters improved significantly from T1 to T2. A relationship was established between the improvement of QoL and recovery of OHE, while there was no such relationship between the improvement of mental distress and improvement of OHE. When improvement of OHSI ≥50% was used as cut-off point, 64 patients (59.3%) were defined having excellent/satisfying clinical response ('responders'), while 44 patients (40.7%) were defined having weak/no response ('weak/non-responders') There was a significant gender effect on chronic stress such that females reported in general greater stress experience ($F(1,99) = 5.102$, $P = 0.026$). At T1, weak/non-responders had	Not specified	An adequate control group was not available.

		psychologic al treatment					significantly more cumulative days of sick leave than responders (76.3 +/- 72.6 and 38.5 +/- 58.2, respectively P=0.013)		
Corti 2014 *Effects of Systematic Patient Education in Skin Care and Protection in a Hand Eczema Clinic*	C	Retrospectiv e I: an educational program comprising basic knowledge on skin barrier function, optimal cleansing and care with practical demonstrati ons, as well as skin protection, including adequate use of gloves and occupation-specific procedures, avoidance of irritants and allergens. Individual patient instructions are given by an	36	NS Patients with handeczema: irritative contact dermatitis. Also 28 patients atopic HE and contacteczema.	NA	Physician global assessment (PGA) Scores (based on modified total lesion symptom score (mTLSS)) , acceptance and behavioral changes were assessed. Severity of hand eczema was rated as severe (4), moderate (3), mild (2), almost clear (1) or clear (0).	In 67% of patients, an improvement of the hand eczema could be attributed to the effects of our educational program. The mean PGA score significantly decreased from 3 before education to 2.2 during follow-up. Behavioral changes in both skin care and protection were reported in 81 and 86%, respectively.	NA	Small sample size and retrospective nature of study

		experienced nurse.							
Ibler 2012 *Skin care education and individual counselling versus treatment as usual in healthcare workers with hand eczema: randomised clinical trial* .	A2	Randomized, observer blinded parallel group superiority clinical trial. Randomization using a computer generated allocation sequence. I: Education in skin care and individual counselling based on patch and prick testing and assessment of work and domestic related exposures. C: treatment as usual	255 healthcare workers	The participants were identified from a survey of 3181 healthcare workers in the three hospitals. The inclusion criteria were an affirmative answer to the question “Have you had hand eczema during the past 12 months?” and informed consent	5 months (The follow-up was planned at 6 months/ For logistical and seasonal reasons, however, the actual follow-up time was 5 months: the inclusion of participants took longer than expected and to avoid confounding from the spontaneous	The primary outcome was clinical severity of disease at five-month follow-up measured by scores on the hand eczema severity index (Range from 0 to 360 (the higher the score, the more symptoms are present). Secondary outcomes: scores on the DLQI (0-30 points, the higher the score the poorer the QoL), self-evaluated severity of hand eczema (measured with a validated photographic guide), skin protective behaviours (measured as instances of daily hand washing and hand disinfection and use of protective gloves and moisturizers at work and at home), and knowledge of hand eczema from onset to follow-up (repeated multiple-choice questionnaire with four questions on skin protection).	The intervention group had significantly lower mean scores on the hand eczema severity index than the control group: difference of means: unadjusted −3.56 (95% confidence interval −4.92 to −2.14); adjusted −3.47 (−4.80 to −2.14), The intervention group also had significantly lower mean scores on the dermatology life quality index than the control group: difference of means: unadjusted −0.78, non-parametric test P=0.003; adjusted −0.92 (−1.48 to −0.37). Knowledge of hand eczema and skin protection at follow-up was not statistically significantly different between the groups.	8 (97% completion rate)	On the basis of sample size calculation, the authors estimated that a total of 262 participants would be required for the study, but only 255 were included. A worst-best imputation showed that even under such extreme assumptions, prevention compared with treatment as usual led to significant improvements. The possibility of contamination of data by unplanned spread of information between participants cannot be excluded as both groups were recruited by the same hospitals

					improvement of eczema from increased exposure to ultraviolet radiation and humidity during summer time.)				
Mauro 2017 *Effectiveness of a secondary prevention protocol for occupational contact dermatitis*	C	Comparative study I: Second clinical evaluation (after history of diagnosis of OHD) and training course on prevention of skin dermatitis (seminar) - a movie titled 'Napo in: protect your skin,' produced with educational purpose by a panel of European organization	130 (65 in each group) 65 white-collar workers w/o contact dermatitis, sex and age matched with patients, were recruited as control group.	All workers, who received a diagnosis of occupational hand dermatitis (feeling of itching or burning of the skin accompanied by skin redness, caused or exacerbated by occupational exposures) at the Allergy Unit of the Occupational Medicine Department of Trieste from January 2011 to December 2013, were contacted by telephone (T1 group).	3 months	TEWL (transepidermal water loss) measurements Symptom severity	Ongoing symptoms decreased from 60% to 42.3% 3 months after the training, and the subgroup which strictly adhered to the recommendations given achieved better results (61.9% of symptoms improvement when compared to 29.0% obtained in subjects with partial adhesion to the protocol). TEWL values changed from 21.3 +/- 9.6 to 18.6 +/- 7.2 g/m^2/h (P = 0.001) on the hands and from 16.6 +/- 9.0 to 10.5 +/- 4.6 g/m^2/h (P = 0.001) on the forearm, confirming the skin barrier improvement.	13	Study design is not that of a classic (R)CT. Controls and cases are not the same regarding disease severity. Unclear how disease severity was assessed. Prevalence of atopic eczema was significantly higher in T1, T2 and T3 cases than in controls

		s and institutions active in the fields of safety and health at work C: no contact dermatitis							
Mollerup 2014 *Effectiveness of the Healthy Skin Clinic – a randomized clinical trial of nurse-led patient counselling in hand eczema*	B	RCT I: Nurse-led counseling program; Individual face to face counceling. Online self-managemen t program or flyer C: usual care	306	Eligible patients (referred because of hand eczema, aged between 18 and 70 years, and capable of replying to questionnaires in Danish) were invited to participate	6 months	The primary outcome was clinical disease severity (HECSI) at follow-up. Secondary outcomes were quality of life (DLQI), burden of disease (a scale from 0 (no eczema) to 10 (excessive eczema), both at baseline and at follow-up), skin protective behaviours, and self-reported medication adherence (Danish version of the Medication Adherence Report Scale (DMARS-4)).	The median HECSI score in the overall cohort of patients at baseline was 43.0 (minimum–maximum 0–260; n=292). At 6 months of follow-up, the median HECSI score had decreased to 24.0 (minimum–maximum 0–236; n=254). Overall, the groups had equally high self-reported medication adherence at baseline, with the intervention group and usual-care group having mean DMARS-4 sum scores of 17.5 and 16.9, respectively. DMARS-4 scores did not change throughout the trial in any of the groups, and accordingly no difference	38	Heterogeneous cohort The time lags of HECSI assessments and questionnaires made it difficult to validate the clinical findings with supplemental subjective measurements The clinical outcome measurements were not blinded, which could result in an observer bias. Counseling on skin protection might have been offered by the

							was found between the groups at follow-up.		dermatologists in the usual-care group.
Mollerup 2016 *User evaluation of patient counselling, combining nurse consultation and eHealth in hand eczema*	C	Qualitative evaluation from Mollerup 2014 Healthy skin clinic supplemented with E-health	140	Patients who were aged 18–70 years and diagnosed with hand eczema, who had given informed consent, and who were capable of replying to questionnaires in Danish.	6 months	Primary outcome HECSI-score, with a range from 0 to 360. Self-administered questionnaires provided data of DLQI, with a range from 0 to 30 (a higher score indicating a more impaired quality of life), subjective measurement of disease severity by use of a visual analogue scale (VAS), with a range from 0 to 10, and self-reported medication adherence, with a range from 4 to 20 (a higher score indicating higher adherence). The participants rated their general self-efficacy on a scale from 0 to 10. Also, data on changes regarding protective behaviour were collected, including a 10-item self-constructed questionnaire addressing self-management issues.	At follow-up, the website users had improved more in quality of life (p=0.014), current burden of disease (p=0.053), and itching (p=0.042). The website users reported more changes in habits than did the non-website users (p=0.024). No differences in clinical severity of hand eczema were found.	NS	
Schürer 2005 *Secondary individual prevention of hand*	B	Prospective longitudinal controlled study	209	Participants were employed geriatric nurses with a medical history of hand dermatitis.	6 months	Severity of OSD, TEWL values	Questionnaires 3 months after study completion revealed skin lesions in 53% of Intervention Group and 82% of Control Group (p<0.01).	NS, however only 66 of 102 IG showed	Not randomised, not blinded. Less patients in IG at visit 3 (n=66) vs visit 4 (n=102).

dermatitis in geriatric nurses		I: One-on-one consultations with a dermatologist and, on visits 1, 2, and 4, educational seminars, incl hands-on training in the correct use of skin protection and dermatologic treatment by an educationalist, were offered (IG; n=102) C: usual care/ practice on demand CG; (n=107)					D-TEWL measurements reflected significant improvement of the epidermal barrier during Secondary Individual Prevention in Intervention Group (median 6.9–3.0 g/m2/h, p<0.001). Three months after study completion, 96% of IG and 86% of CG were still employed.	at visit 3 (volunt-ary consultation) . Visit 4 n= 102.	Time between visits NS. Visit 4 6 months after first assessment.
Skudlik 2012 *First results from the multicentre study Rehabilitation of Occupational Skin Diseases – Optimization and Quality*	B	Prospective multi center cohort study. The study is divided into three phases Phase 1 (T1): 3 weeks inpatient	1788 N=1670 (93.4%) diagnoses of hand eczema. There were manycases of	Patients with occupational skin diseases resistant to outpatient therapy	3 years (however these are the first published results of this study at T4 (=10 weeks,	Return to work, improvement of OSD by OHSI, enhancement of quality of life, and reduction in the use of topical steroids	During the inpatient phase, there was a significant improvement in the severity of OSD ($p < 0.001$) and in the quality of life (DLQI,$p < 0.001$). These effects were largely sustained during the outpatient follow-up phase and in the 4 weeks after return to work. Among all patients, 89.4% used	69 (3.9%) patients dropped out of the study up to T4	Downgraded because not classic RCT study. Risk of bias: The possibility of interdisciplinary programs to be (slightly) different exists between patients. (To guarantee that

Assurance of Inpatient Management (ROQ)		period with interdisciplinary treatment Phase 2 (T2): 3 weeks of absence of work and receiving outpatient treatment Phase 2 (T3): the patients return to their workplaces, under continuous outpatient dermatological support and with the provision of optimized skin protective measures and optimized terms and conditions for work organization. T4: Clinical course evaluation, 4 after return to work T5: 1 year follow up	aetiological overlap and combined diagnoses (ICD, ACD and AHE)		see study design))		topical steroids before TIP, including 52.5% using high-grade topical steroids; 93.2% of the patients were able to refrain from using topical steroids before returning to work. As a result of TIP, return to work was possible for 1587 patients (88.8%).		these different interdisciplinary Intervention measures can be implemented in a standardized fashion with equal quality at all centers, a detailed operation manual encompassing all structural, methodical and scientific aspects of TIP, regular 'train-the-trainer' schoolings and quality circles with all co-workers of all centers have been developed and implemented).

		T6: 6 years follow up							
Van Gils 2012 *The effective-ness of integrated care for patients with hand eczema: results of a randomized, controlled trial*	A2	RCT I: integrated care. The integrated care was provided by a multidisciplinary team consisting of a dermatologist, a specialized nurse/ physician assistant, and an occupational clinical physician. C: usual care	196	The population in this RCT comprised patients aged ≥16 years with moderate to severe, chronic (>3 months) hand eczema who visited a dermatologist of one of the participating hospitals.	26 weeks	The primary outcome measure in this study was the clinical severity score measured by a trained and blinded clinical assessor with the Hand Eczema Severity Index (HECSI). Secondary outcome measures were three categories of disease-specific quality of life (symptoms, emotion, and function), measured with the Skindex, patients' global assess- ment, measured with VASs for itching, pain, and fatigue, and sick leave	Average improvement on the HECSI was 22.4 points in the intervention group and 11.7 points in the control group. The mean difference in improvement on the HECSI between both groups after 26 weeks was 10.7 points in favour of the integrated care group (standard error5.3,95%confidence interval 0.3–21.1,p = 0.044).No differences in improvement between the groups were found for any of the other outcomes.	19%	
Van Gils 2013 *Economic evaluation of an integrated care programme for patients with hand dermatitis*	A2	Economic evaluation of RCT I: integrated care. The integrated care was provided by a multidisciplinary team consisting of a	196	The population in this study comprised patients aged ≥16 years with moderate to severe chronic (>3months) hand dermatitis who visited a dermatologist at one of the participating hospitals	1 year	The primary outcome measure was the difference in clinical severity of hand dermatitis measured with the Hand Eczema Severity Index (HECSI, range 0–360). Secondary outcome measures included disease-specific quality of life, measured with the Skindex, patients' global	The mean difference in improvement on the HECSI between both groups after 52 weeks was 8.7 [standard error 5.3, 95% confidence interval (CI) −1.8–18.9], which was not statistically significant (p=0.105) The mean IC cost per patient in the IC group was ¤324. Productivity	Of all participants, 129 completed at least nine cost calendars (65.8%).	The amount of missing data was relatively high for costs. multiple imputation was used to impute missing data. The power of the economic evaluation was insufficient. Presenteeism not included as

		dermatologist, a specialized nurse/ physician assistant, and an occupational clinical physician. C: usual care				assessment of itching, pain, and fatigue, with VASs, and generic quality of life, with EuroQol (EQ-5D). Cost data were collected from a societal perspective over 12 months. Cost of productivity losses were calculated with the friction cost approach (FCA, main analysis).	losses (indirect costs) were the largest contributor to total costs in both groups. Indirect costs were statistically significantly higher in the IC group (¤2656) than in the UC group (¤1097; difference ¤1561, 95% CI ¤86–3284). Total costs were ¤3613 (SD 798) in the IC group and ¤1576 (SD 430) in the UC group. The difference between the groups was statistically significant (¤2037, 95% CI ¤483–3812). The main analysis (Table 5) showed that the ICER for improvement on the HECSI was −247. The difference in QALYs between the groups at 12 months of follow-up was 0.04 QALYs in favour of the UC group. In combination with the higher costs of IC than of UC, this means that IC is never considered to be cost-effective in comparison with UC, regardless of the willingness to pay per additional QALY.		indirect cost in the cost-effectiveness, could have underestimated the cost-effectiveness. Sick-leave was not a inclusion criterion the study.
Weisshaar 2013 *Multicentre study 'rehabilitation of*	B	Prospective follow up cohort study Long term effects of tertiary	1788 patients	See Skudlik 2012	12 months (T5)	- OHSI - Severity of OSD according to the Bamberg Medical Bulletin	Reduction in OHSI score, severity of OSD, usage of topical corticosteroids, DLQI, LIOD and days of absence from work ($p<0.001$). Also other indicators, such as hand	At the 12 month follow up a response rate of	See Skudlik 2012 Study design: no control group. Large response rate. Patients that were assessed

occupational skin diseases– optimization and quality assurance of inpatient management (ROQ)' – results from 12-month follow-up		individual prevention programme described in Skudlik et al. 2012 (see above)				- Usage of topical corticosteroids within previous 12 months - DLQI - LIOD - Total number of days of absence from work - Return to work and remaining in same profession	washing frequency and hand disinfection were reduced. However only usage of skin protection creams was not significantly different at different time points. 3.9% was not able to return to workforce because of still having OSD.	90,4% (N=1617)	were older and had a longer exposure of profession. Unknown if the effect is only attributable to the intervention. There are also other German hierarchical prevention concepts available for patients.
Wilke 2012b *Long-term effectiveness of secondary prevention in geriatric nurses With occupa-tional hand eczema: the challenge of a controlled study design*	B	Prospective controlled study I: interdisciplinary prevention programme comprising four visits to the study centre in Osnabrück (Germany) and involving both dermatological and health educational interventions. C: Usual care	209 geriatric nurses	Inclusion criteria were the presence of an occupational skin disease that had been reported by a dermatologist, and voluntary participation in order to include intrinsically motivated participants.	3 months and 6 years	Data on job continuation, skin lesions and skin protection behaviour were obtained by standardized questionnaires and compared with baseline values (T0)	At 6 years follow-up, 65.3% of the intervention group (IG) and 56.8% of the control group (CG) still worked as geriatric nurses; 6.9% of the IG and 13.6% of the CG had given up work because of occupational hand eczema. The skin status improved in both cohorts. The data indicated a lower frequency of skin lesions and morphological signs in the IG, for example vesicles (IG, 12.8%; CG, 40.0%; $\chi 2 = 7.00$, degrees of freedom = 1, $p = 0.008$).	Nine data records (8.8%) of the IG	Some participants of the IG and CG were free of occupational hand eczema at baseline (T0), as a result of continuing therapy by the local dermatologist or sick leave prior to the intervention. As the controls did not undergo a dermatological examination at the study centre, no medical information (e.g. regarding diagnoses, allergies, and atopic diathesis) could be

									obtained for this cohort.
Wilke 2012a *Sustainability of interdisciplinary secondary prevention in patients With occupational hand eczema: a 5-year follow-up survey*	C	Follow-up survey Only 1 intervention group (no control group) Skin protection seminar with dermatologic and educative interventions.	134 with OHE. Inclusion in the study was based on the time when the suspected OHE was reported to the employers' liability insurance associations	suspected OHE; wet work occupation	Data were obtained at baseline (T0) and at 9 months (T1) and 5 years (T2)	Job continuation, skin condition, skin protection behaviour, and disease management	At T2, 71.4% of patients remained in their occupation, as opposed to 87.6% (n = 85) at T1 (9 months after the intervention). The prevalence and severity of self-reported OHE were significantly reduced as compared with T0 (p = 0.007, p = 0.002). Of the patients, 13.1% gave up work because of OHE at T2. The intervention was most successful in patients suffering from milder forms of OHE, and there was less success in patients with severe OHE. The results showed a significant reduction in the frequency of 'hand washing' (p = 0.003) but no measurable change in the use of skin care products (p = 1.000).	At the 5-year follow-up, a response rate of 77.6% (n = 104) was obtained.	Because of continuing therapy by the treating local dermatologist or previous sick leave, some participants were free of OHE at baseline (T0).
Wulfhorst 2010 *Sustainability of an interdisciplinary secondary prevention program for hairdressers*	C	CT I: 6-month combined dermatological and educational prevention program with an education and	300 Intervention group= 215 Control group=85	Hairdressers with reported skin diseases (OSD)	9 months (response rate N=163), 5 years (n=172) and 10 years (n=80)	Remaining or not remaining at work	At 9 months 71.8% (N = 117) of the intervention group could remain in work as opposed to 60.0% (N = 48) in the control group. In the intervention group 14.7% gave up work due to OSD versus 22.5% in the control group (no statistically significant effect).	See response rate in column 'follow up'.	Study design is not experimental.

		counseling scheme as well as an intervention in the respective hairdressers' shops C: Usual care					At 5 years 58.7% (N = 101) of the IG remained at work versus 29.1% (N = 16) of the CG Ten years after intervention, the follow-up showed a stabilization of the effects shown by the 5-year follow-up results.		

Abbreviations: ACD = allergic contact dermatitis of the hands; AHE = atopic hand eczema; CT= controlled trial; CG = control group; DLQI = Dermatology Life Quality Index; ICD = irritant contact dermatitis of the hands; IG = intervention group; LIOD = Life Quality Index Occupational Dermatoses; NA= not applicable; NS= not specified; OHE= Occupational Hand Eczema; OHSI=Osnabrueck Hand eczema index; OSD = Occupational skin disease; RCT= randomized controlled trial

Handschoenen (2017)

Karakteristieken en resultaten van geïncludeerde studies beoordeeld volgens EBRO

Study reference	Level of evide-nce	Study design	Patients (N)	Inclusion criteria	Follow-up	Outcome measures	Results	Lost to follow-up	Comments
Baack 1996 *Use of a semipermeable glove during treatment of hand dermatitis.*	C	Pilot study	N=46 <u>Intervention:</u> Semi permeable glove + topical steroids and/or moisturizers <u>Control intervention:</u> Cotton glove + topical steroids and/or moisturizers		1 month	Physicians scored skin condition before and after treatment. Subjects evaluated skin comfort and practical aspects.	30 patients Type of glove used had no impact on skin condition. Skin improved in both groups. Patients prefered experimental gloves.	16	Abstract only. No randomization. Unknown which material was used for the semi permeable gloves. No validated outcome measures.
Kinaciyan 2010 (a)	C	RCT (within	N=? <u>Intervention:</u>	Mild to moderate hand eczema	6 weeks	Clinical evaluation and severity assessment two times a week.	43 patients completed study.	?	Abstract from poster presentation.

A new barrier glove worn eight hours a day prevents relapses in hand eczema		partici pant)	water- and allergen-proof, breathable nonallergenic barrier gloves. Patients were treated topically until the handeczema had disappeared or only minimal disease had remained. Patients were randomized to wear the glove on one hand. Patients were allowed to use emmolient on both hands when needed.			Skin testing for atopy and allergen identification to classify hand eczema type. SCORAD before randomization HECSI between left and right hand QoL questionnaires Questions about comfort and problems with gloves.	4 patients experienced relapse on both hands. Two times more frequently relapse in the hand without glove when relapse only on one hand.		Inter-individually randomization. Number of included patients is not mentioned. Unknown which material was used for the gloves.
Kinaciyan 2010 (b) *A new barrier glove shows comparable efficacy to a potent steroid ointment in the treatment of mild to moderate severe chronic hand eczema*	C	Non-inferio rity study	N=? <u>Intervention:</u> water- and allergen-proof, breathable non-allergenic barrier gloves + second antibacterial silk glove worn under barrier glove on one hand <u>Control intervention:</u> Potent steroid ointment	Mild to moderate hand eczema	3 weeks	SCORAD after skin testing for atopy and allergen identification and classification of eczema type. HECSI for comparison right and left hands. Bacterial cultures taken with cotton swabs. QoL questionnaires weekly. Questions about comfort and problems with gloves	SCORAD and HECSI decreased in both groups. Mean relative difference in SCORAD between the study endpoint and baseline was for the barrier glove 43% and for the topical steroid group 34%. The gloves were well accepted by 80% of the patients. Problems with the gloves decreased with study duration. Additional wearing of antibacterial silk gloves imporved the outcome in some of the patients.	?	Abstract from poster presentation. Unknown number of subjects. Unknown if randomization was done.

			All patients used same emollient when needed.						

Abbreviations: HECSI: hand eczema severity index, QoL = quality of life, RCT = randomized controlled trial, SCORAD = scoring atopic dermatitis.

Indifferente middelen (2017)

Karakteristieken en resultaten van geïncludeerde studies beoordeeld volgens EBRO

Study reference	Level of evide-nce	Study design	Patients (N)	Inclusion criteria	Follow-up	Outcome measures	Results	Lost to follow-up	Comments
Berndt 2000 *Efficacy of a barrier cream and its vehicle as protective measures against occupational irritant contact dermatitis*	B	RCT, double blind I: Verum group, a barrier cream (ingredients: aqua, paraffinum liquidum, behenyl alcohol, glycerin, aluminium chlorohydrate, octyl palmitate, buxus chinensis, ceteth-10, steareth-20, dimethicone)	50 (25 in each group)	Hospital nurses with mild signs of skin irritation	1 month	Overall: skin compatibility, efficacy and resulting acceptance. 1. Clinical examination for effect: dryness, erythema, scaling, dyshidrosis, fissuring, and lichenification using simple visual scoring (0=none, 1=mild, 2= moderate, 3=severe). - Questioning about subjective feelings concerning skin condition of their hands, by evaluating symptoms (similar visual score was utilized) 2. Effects by instrumental assessment of bioengineering Parameters (TEWL, skin colour, using the Chroma-Meter CR-200 and hydration of stratum	The visual score decreased significantly in both the verum and the vehicle group from the beginning to the end of the study, indicating an improvement in irritation. No significant difference was found between the 2 groups. TEWL and erythema showed no significant change during the study period, stratum corneum hydration increased highly significantly ($p<0.01$) from the beginning to the end of the study. All 50 nurses tolerated the test creams very well. Side-effects, either irritant or allergic in nature, did	0	- only 4 male patients - use of product was evaluated by weekly weighing the tubes - p value visual sore decrease not known - Downgraded because method of blinding and randomization NS, sample size is moderate and short follow up. - intention to treat NS

		C: Vehicle group, the same preparation without aluminium chlorohydrate.				corneum with the Corneometer CM825	not occur.		
Draelos 2000 *Hydrogel Barrier/Repair Creams and Contact Dermatitis*	**B**	Randomized split-body design within-participant Blinded for participant and investigator I: hydrogel barrier/repair cream (Hydron).hydrogel cream C: plain petrolatum-based moisturizer (Eucerin, Biersdorf, Germany)	N = 80	Aged newborn to 80 years old with dermatologic conditions: irritant household hand dermatitis (N=21), irritant occupational hand dermatitis (N=18), latex glove ICD (N=9), diaper dermatitis (N=5), cutaneous wounds consisting of fissures and erosions related to irritant hand dermatitis (N=17), and industrial ACD (N=10). Subjects were required to avoid use of any prescription skin medications or other treatments	4 weeks	Evaluation by investigating dermatologist comparing the right and left study sites based on erythema, roughness, desquamation, serum crusting, and inflammation. An ordinal rating system (–2, noticeably worse; –1, worse; 0, no change; 1, better; 2, noticeably better) was used to assess each characteristic by both the subjects and the investigator. Photographic comparison (taken at week 2 and 4) was used by the investigator to accurately assess improvement over the 4-week study period.	Of the subjects, 45 of 73 (62%) preferred the hydrogel barrier/repair cream to the plain moisturizing cream in terms of overall skin appearance and feel (P # .005). The investigator also felt that the hydrogel barrier/repair cream was statistically better in reducing erythema, roughness, and desquamation than the plain moisturizer (P= .00001).	7 (73 completed the study) However stated that 8 patients discontinued (lost to follow up or for personal reasons).	- lost to follow up not clearly stated (73 completed the study, but 8 discontinued) - randomization method NS - blinding stated as two separate jars of products, but not if they were identical. Cross-contamination not excluded. - short follow up time

				on the study site for 2-week washout period before initiation of the study.					
Kucharekova 2003 *A randomized comparison of an emollient containing skin-related lipids with a petrolatum-based emollient as adjunct in the treatment of chronic hand dermatitis*	B	Randomized comparison pilot study, parallel I: emollient containing skin-related lipids (Locobase1 Repair; contains ceramide 3, oleic and palmitic acid in a fatty cream base with pet.aqua, paraffin, paraffinum liquidum, glycerin, sorbitan oleate, carnauba, cholesterol, carbomer, tromethamine in	N = 32	Patients with bilateral chronic hand dermatitis (mild to moderate since >6 months) and with a good response to class I or class II topical corticosteroids	2 months	Evaluation of clinical effects, cosmetic acceptability and the usage of topical corticosteroids by parameters: HEAS, IGA was made on a scale of 0–5 (20) A questionnaire assessed the patient's opinion on the course of the disease after treatment (1= worse, 2= no change, 3= minimal improvement, 4= moderate improvement, 5= marked improvement and 6= clearing or almost clearing). The use of topical corticosteroids	HEAS and IGA: a statistically significant reduction in the IGA from baseline to endof-treatment for both treatments (P=0.005 Locobase1 Repair and P=0.007 Vas/Lan). We also observed a significant improvement in the HEAS in both groups (P=0.002 Locobase1 Repair and P=0.02 Vas/Lan). No difference between the groups. Patients opinion: 67,7% in intervention group and 69,2% in control group indicated improvement or clearance of the hand eczema. No significant differences between the groups. At the end of treatment, itching improved or even disappeared in 75% of intervention group and 69% in control.	6	- Downgraded because randomization method NS, single-blinded and small sample size - observer was blinded, the participant was not blinded - unclear about 2 drop-outs, because were lost after baseline - analysis may have been intention-to-treat, but procedure unclear.

		unknown ratio; lipid content 63%). C: pet.-based emollient (Vas/Lan; contains 50% vaselinum album and 50% cremor lanette I) - in case of exacerbation, patients were allowed to use a mild corticosteroid according to instructions					Cosmetic assessment: There was no significant difference in the patients' assessment on the cosmetic acceptability between the groups. 53% percent of both groups stated that the study-emollient was superior to their current emollient, and most of them were likely to continue the use of the emollient (94% Locobase1 Repair and 85% Vas/Lan). Topical corticosteroids use: 62,2% of the Locobase1 Repair group used less corticosteroids during the study than before the study in comparison with 38,4% of Vas/Lan group. 78% of all patients did not change such habits at all.		
Lodén 2010 *Treatment with a Barrier-strengthening Moisturizer*	B	RCT, parallel, non-blinded Randomization to moisturizer	N = 53 I: N=26 C: N=27	Patients with clinically proven history of hand eczema (mean time since diagnosis 10 years).	6 months 28 days notation of	Main outcome: number of days to relapse of eczema. Evaluation by investigator at day of recurrence of: - Severity on 100-mm visual analogue scale (VAS)	The number of days until reoccurrence of hand eczema was 20 days in the moisturizer and 2 days in the no treatment group (by mean and	2 9 withdrawn, 1 AE,	Authors (Lodén and Wirén) were contacted and answered dd 25th of September 2018 about the question how

Prevents Relapse of Hand Eczema: An Open, Randomized, Prospective, Parallel Group Study		or to no treatment in a 1:1 ratio using a computerized procedure. I: barrier-strengthening moisturizer (Canoderm cream 5% urea) C: no treatment		From 22 to 76 years old. Recruited at 4 clinics in Norway (48 by GP and 5 by dermatologists). At inclusion the grading of hands showed a controlled state of the eczema (HEES ≤3). Patients also considered their eczema to be controlled and used moisturizers daily.	treatment application daily for intervention group and afterwards weekly.	- Dermatology Life Quality Index (DLQI) - Hand Eczema Extent Score (HEES) method Above also at inclusion	25/75 percentiles, p=0.004). 5 persons did not experience any eczema relapse during the 6-month study period (3 in intervention group, 2 in the no treatment group). There was no significant difference in degree of eczema at the time of relapse between the two groups. The mean increase in HEES in the intervention group was 8.8 and in the no treatment group 13.0. The DLQI scores had increased in the two groups (from 4.7 to 7.1 in the moisturizer group and from 4.1 to 7.8 in the no treatment group p<0.01). The 100mm VAS was 2.5 mm lower with the moisturizer treatment than with no treatment (p = 0.66).	1 other reason	hand eczema was controlled: 'There was no restriction in how the hand eczema was controlled prior inclusion in the study. Consenting patients were screened among patients with controlled hand eczema (≤3 on Hand Eczema Extent Score, HEES) and e.g. patients who had been successfully treated with corticosteroids or light therapy.' - Moisturizer with 5% urea - Downgraded because non-blinded - The time of evaluation differed between all patients - Type of eczema not stated at inclusion and

									treatment history not known - Power not calculated - Exclusion criteria: possible allergy to ingredients and patients with active psoriatic lesions, active atopic eczema lesions or active bacterial, fungal or viral infection of the hands were excluded.
Mckormick 2000 *Double-blind, randomized trial of scheduled use of a novel barrier cream and an oil-containing lotion for protecting the hands of health care workers*	B	RCT, double-blind I: novel barrier skin cream which forms a persistent microfilm (Hand Sense, North American Safety Products Inc, Orange, Calif)	N = 54	HCW with severe and long-standing hand irritation, solicited by a hospital-wide notice and a series of informational meetings, with a 20 hour work week	4 weeks	Scoring of hand condition: potential maximal overall score of 18 (worst condition). Objective parameters by rating 0-3 for: scaling, cracking, weeping, bleeding. Subjective parameters by rating yes or no and 0-3 for weeping, bleeding, pain and covering skin breaks. Recording: - handwashings each day, use of antiseptic handwashing agent during working hours and off duty	Hand condition: in both groups substantial and significant improvement in overall hand condition compared with baseline (both groups, P < .02), but in control group, greater improvement than in intervention group, in scores for scaling, cracking, and pain (mean overall score, from 6.5 to 2.7 vs 6.8 to 4.7, P = .006). 69% of participants in control group all full-thickness integumentary breaks were healed and	2	*- Introduction and discussion is also about glove use in HCW (see also Beezhold et al 1994)* - Randomization method NS - Freely use of supplemental oil-based lotion (Moisturel, Westwood-Squibb Pharmaceuticals, Inc, Buffalo, NY) if study agent was ineffective.

		C: widely used oil-containing hand lotion (Lubriderm, Warner Lambert Consumer Health care, Morris Plains, NJ) Both similar in color and supplied in identical but numbered 1-oz tubes: 4dd whether or not assigned to work.				- estimation hours they wearing gloves - applications of study agent and supplemental hand lotion." Quantitative culture was done	pain was totally resolved, compared with N=14 (52%) in intervention group (P = .26). Hand flora: at outset, mean log counts of total organisms (approximately 105.5) and the prevalence of carriage of staphylococci, gram-negative bacilli, enterococci, and yeasts was similar in both groups and comparable with the findings of prior studies in the center. This stayed the same after 4 weeks. Handwashing frequency: at outset frequency in both groups and glove use were the same in both groups. In week 4 mean total number of handwashings per day was 50% higher in control group, lotion (17.8 vs 11.7 times per day, P = .04).		- no inclusion criteria about hand irritation and exclusion of subjects with known hypersensitivity dermatitis, eczema, or other chronic skin diseases - Also considered in results: weather condition, handwashing frequency did not differ significantly between groups, and glove use was also comparable. → greater improvement of hand condition in subjects randomized to use the control lotion was associated with more frequent handwashing (table 1)
Visscher 2009 *Effect of topical treatments on irritant hand*	B	Prospective randomized study, single blinded, parallel	N = 81 I: N=43 C: N=38	HCWs from the Regional Center for Newborn Intensive Care at Cincinnati	2-4 weeks	Primary outcomes were hand skin conditioned by visual skin erythema and dryness, excess erythema (quantitative image analysis)	Knuckle dryness was lower for both treatments than the no treatment control (P <-0.02) after 2 weeks. Right dorsum dryness was lower for B	-	- Only investigator blinded - Differences in hand skin

dermatitis in health care workers		I: test product A: glove and chlorhexidine gluconate compatible (Remedy) B: current lotions/creams (CleanCare Amino1 Derm, Everyday Emulsion) C: normal skin care Assignment based on right-hand knuckle dryness score (i.e., in categories of 0.5 grade increments from 0 to 5) to stratify and balance the groups for initial skin condition		Children's Hospital Medical Center Excluded: fewer than 2 consecutive 12-hour shifts, more than14 days between work shifts, and fewer than 20 hand hygiene procedures over 8 hours at work		Secondary: hydration and skin condition after 4 weeks of treatment.	than control (P=.03) and directionally lower for A (P=.06). A, B, and control were not different for left dorsum dryness. Skin treated with A had lower knuckle erythema (P=0.03) than B and control. HCWs using A had lower excess erythema (right) than B and control (P <0.04). Excess erythema was lower for A and B versus control (P=.003). Skin hydration increased from baseline values for A and B at week 1 (paired t tests) (P<.05).		condition as a result of specific practices was accounted for to some extent in the randomization procedure.
Other interesting or useable articles									

Lindh 2015	Clinical Effectiveness of Moisturizers in Atopic Dermatitis and Related Disorders: A Systematic Review

Abbreviations: AD=atopic dermatitis; C=control; CT= controlled trial; HCW= health care worker; HEAS = Hand eczema area and severity score; I=intervention; IGA = investigator; NA= not applicable; NS= not specified; RCT= randomized controlled trial.

Lokale therapie (2017)

Karakteristieken en resultaten van geïncludeerde studies (RCT's) beoordeeld volgens EBRO

Study reference	Level of evide-nce	Study design	Patients (N)	Inclusion criteria	Follow-up	Outcome measures	Results	Lost to follow-up	Comments
Baskan 2005 *The efficacy of topical pimecrolimus cream 1% in hand dermatitis.*	C	RCT (within-participant)	N=25 <u>Intervention:</u> A: Pimecrolimus 1% cream twice daily in 24/25 hands <u>Control intervention:</u> B: Placebo cream twice daily in 24/25 hands.	Bilateral hand dermatitis, moderate to severe hand eczema with a minimal duration of six months, aged ≥18 years	16 weeks (8 weeks active treatment, 8 weeks follow-up)	Clinical response to therapy; erythema, desquamation, lichenification, oedema, vesiculation and fissuring were scored between 0 and 4 and controlled at 2nd, 4th, 6th and 8th weeks of therapy, clinical response to therapy for pruritus, at the end of therapy, the participants were followed up for the same period to observe recurrences, adverse events.	At the end of therapy there was a significant difference in total clinical response score in the pimecrolimus group and the control group .	1	Unclear whether the study was blinded and whether a intention-to-treat analysis was conducted.
Bauer 2012 *Efficacy of pimecrolimus 1 % cream in the long term management of atopic hand dermatitis. A double-blind RCT.*	B	RCT (parallel)	N=40 <u>Intervention:</u> A: Pimecrolimus1 % cream twice a day for 8 weeks after clinical response (IGA 2) to a 1–3 week treatment with mometasone furoate 0.1 % in 20/20 participants.	Patients suffering from moderate to very severe chronic relapsing atopic hand dermatitis (IGA ≥ 3), aged ≥18 years, responded to treatment with mometasone furoate 0.1 % once daily over 1–3 weeks (IGA ≤ 2) once IGA ≤ 2 was	8 weeks after 1-3 week start-up treatment	Proportion of participants maintaining a stable remission (IGA 2) with twice daily application of pimecrolimus or vehicle. The study endpoint was defined as the time interval from commencement of treatment to relapse (IGA 3) during the 8 week active treatment period, mean change IGA, patient self-assessment,	There was no statistically significant difference between pimecrolimus 1% cream and vehicle (RR 0.8, 95% CI 0.42 to 1.53, P = 0.05	4	Observers and participants were blinded and an intention-to-treat analysis was performed. The study was funded by a grant from Novartis Pharma GmbH, Nuernberg, Germany.

			Control intervention: B: Vehicle twice a day for 8 weeks after clinical response (IGA 2) to a 1–3 week treatment with mometasone furoate 0.1 % in 16/20 participants.			HECSI and DLQI, mean change in IGA from baseline during study period, mean change in Patient Self Assessment (PSA) from baseline during study period, mean change in HECSI from baseline during study period, mean change in DLQI from baseline during study period, adverse events			
Belsito 2004 *Pimecrolimus cream 1%: a potential new treatment for chronic hand dermatitis.*	A2	RCT (parallel)	N=294 Intervention: A: Pimecrolimus 1% cream twice daily with 6 hr glove occlusion evenings in 140/151 participants Control intervention: B: Vehicle cream twice daily with 6 hr glove occlusion evenings in 132/143 participants	≥18 years old, mild to moderate chronic hand eczema for a minimum duration of 6 weeks	3 weeks	Investigator Global Assessment (IGA) on a 5-point scale: ranging from 0 = clear to 4 = severe, efficacy measured as proportion of treatment successes at end of study (day 22) in each group; treatment success is defined as an IGA score of 0 (clear) or 1 (almost clear), adverse events	There is no statistically significance difference between groups in terms of investigator- rated clearance (RR 1.53, 95% CI 0.99 to 2.36)	22	The participants and observers were probably blinded and an intention-to-treat analysis was carried out.
Bleeker 1989 *Double-blind comparative study of Corticoderm cream + Unguentum Merck and Betnovate cream +*	C	RCT (parallel)	N=76 Intervention: A: Fluprednidene cream once daily in the evening for 3 weeks in 37/38 participants. B: Betamethasone cream once daily in the evening for	Allergic or trauma-induced contact dermatitis or atopic dermatitis for at least 3 months, age limits: 18-65 years.	3 weeks	Observer- and participant-rated general assessment of therapeutic result, reduction in scoring based on symptoms (erythema, scaling, papules, vesicles, lichenification, fissures, excoriation, pruritus), adverse events	In the betamethasone group 14/38 participants healed and in the fluprednidene group 8/37 healed. This was not statistically significant (RR 0.59, 95% CI 0.28 to 1.23, P = 0.16.	NS	The study was probably blinded; no intention-to-treat analysis was carried out.

Uguentum Merck in hand dermatitis.			3 weeks in 38/38 participants. Emollient (Unguentum Merck) was allowed in both groups if required.						
Cherill 2000 *SDZ ASM 981 1% cream is effective in the treatment of chronic irritant hand dermatitis.*	C	RCT (parallel)	N=48 <u>Intervention:</u> A: Pimecrolimus 1% cream twice daily in 12 participants B: Pimecrolimus 1% cream under occlusion twice daily in 12 participants <u>Control intervention:</u> C: Vehicle twice daily in 12 participants D: Vehicle under occlusion in 12 participants	Chronic irritant hand dermatitis of moderate severity.	6 weeks	Observer-rated (?) total key sign/ symptom score (0 to 3 for erythema, excoriation, oedema/ papulation, pruritus) at day 8, 15, 22, 29, 36, and 43, (serious) adverse events, key scores for erythema, excoriation, oedema/ papulation, pruritus rated on a scale from 0 to 3 at day 8, 15, 22, 29, 36 en 43.	At day 8 pimecrolimus was statistically superior to vehicle for both the occlusion and non-occlusion groups. This effect continued, with p-values approaching statiscally significant values at days 15, 36 and 43 for the occluded group. However for the non-occluded group this was only the case at day 29..	0	Blinding and intention-to-treat analysis were not described.
Faghihi 2008 *The efficacy of 0.05% Clobetasol + 2.5% zinc sulphate cream vs. 0.05% Clobetasol alone cream in the treatment of the chronic hand eczema:*	C	RCT (within-participant)	N=47 <u>Intervention:</u> A: 0.05% Clobetasol + 2.5% zinc Sulphate twice daily for 2 weeks <u>Control intervention:</u> B: 0.05% Clobetasol alone	Patients who had both sided chronic hand eczema with approximately similar severity in both hands, and also had their diseases longer than 4 weeks, > 12 years, not pregnant	All of the patients were treated for 2 weeks and were followed at weeks 2, 4, 6 and 8	For determining the severity of chronic hand eczema, 4 different characteristics of the lesions including redness; scaling; lichenification and pruritus were assessed and scored. The severity of itching was evaluated by visual analogue	25/47 hands (53%) treated with clobetasol + zinc sulphate cream were clear from scaling compared to 3 hands (6%) treated with clobetasol alone cream (RR 4.17, 95% CI 1.88 to 9.22). 41 hands (87%) treated with clobetasol + zinc sulphate cream were clear compared to 1 hand (2%) treated with clobetasol alone cream	NS	The study is described as double-blind, although no details are given. An intention-to-treat analysis was conducted

a double-blind study.			twice daily for 2 weeks	and had not used topical treatment for their hands in the recent 2 weeks or systemic treatment in the recent 30 days.	after starting the treatment)	scale (VAS).	(RR 41.00, 95% CI 5.88 to 285.90). 24 hands (51%) treated with clobetasol + zinc sulphate cream and 7 hands (15%) treated with clobetasol alone cream were clear from lichenification (RR 3.43, 95% CI 1.64 to 7.18). The treatments were well tolerated and no statistically significant adverse events were reported/observed.		
Fowler 2005 *Hydrocortisone burtyrate 0.1% cream in the treatment of chronic hand dermatitis.*	B	RCT (within-participant) 3 parallel groups	N = 86 HE N= 3 AD <u>Intervention</u> A: HB vs FP (N=26) Hydrocortisone butyrate (HB) 0.1% cream on the one hand versus fluticasone propionate (FP) 0.05% cream twice daily on the other hand B: HB vs PC (N=28) Hydrocortisone butyrate (HB) 0.1% cream on the one hand versus prednicarbate emollient 0.1% cream (PC) twice daily on the other hand	Patients with symmetrical hand or atopic dermatitis of moderate severity for at least 2 weeks, between 18 and 65 years old.	2 weeks	1. Investigator-rated severity of hand eczema on a 4-point scale (0 = none, 1 = mild, 2 = moderate, 3 = severe) for 4 clinical signs (erythema, cracking/ fissuring, scaling, papules/ vesicles) 2. Investigator-rated severity total sum score 3. Participant-rated severity of hand eczema on a 4-point scale (0 = none, 1 = mild, 2 = moderate, 3 = severe) for 6 clinical signs (erythema, cracking/ fissuring, scaling, papules/ vesicles, pruritus, burning/pain) 4. Participant-rated severity total sum score 5. Investigator-rated mean reduction in percentage of hand involvement	Results include patients with AD. 1. According to investigator cracking/fissuring in HB vs PC group improved in 43% vs 21% ($p<0.05$) of patients. In HB vs FP group erythema improved in 31 vs 23 % (ns) and scaling 65 vs 54 % (ns) of the patients. In the HB vs MF group papules/vesicles improved in 26 vs 19% patients. For the other signs not that great of a difference was stated. For scaling it stayed the same for both groups. 2. The degree in reduction in signs and symptoms was similar for all 4 groups.	4	Probably double blind. No intention-to-treat. Patients that used systemic treatments the last month or topical corticosteroids in the last week before entering the study were excluded. Two authors acted as consultant. 3 patients with AD included in the study and results not separated.

			C: HB vs MF (N=31) Hydrocortisone butyrate (HB) 0.1% cream on the one hand versus mometasone furoate (MF) 0.1% cream twice daily on the other hand			6. Participants-rated preference and cosmetic acceptability 7. Adverse events	3. According to subject erythema in HB vs FP group improved in 50 vs 35 % ($p<0.05$), papules 27 vs 15 % (ns) of patients. Cracking/fissuring improved in more patients in the FP group (46% vs 50%), improvement in scaling was the same for both groups. In the HB vs PC group more patients improved in scaling and papules/vesicles in PC group. In the HB vs MF goup erythema, scaling and papules/vesicles improved in more patients in the HB group. However less patients improved in cracking/fissuring (48 vs 52 % ns). 4. Similar as for investigator mean total signs and symptoms score 5. the reductions in hand involvement from baseline showed no difference of treatment differences betweens pairs 6. the largest percentage of subjects preferred HB to PC for better moisturizing (61%)		

							7. Patients with AE in groups: HB vs FP: 19% HB vs PC: 0% HB vs MF: 6% AE considered related to the study product were headache and jitteriness (N=1) and mild itching (N=1, HB vs FP group).		
Gupta 1993 *Betamethasone dipropionate polyacrylic film-forming lotion in the treatment of hand dermatitis.*	C	RCT (parallel)	N=58 <u>Intervention:</u> A: Bexarotene 1% gel escalated stepwise from 1x every other day to 3x daily in 28 participants B: Bexarotene gel stepwise plus mometasone furoate 0.1% ointment 2x daily in 13 participants C: Bexarotene gel stepwise plus hydrocortisone 1% ointment 2x daily in 14 participants In all 3 groups daily use of emollients was allowed.	NS: All patients had a diagnosis of corticosteroid-responsive hand dermatitis but where otherwise in good health.	22 weeks	Primary outcome: observer-rated treatment success defined by 90% or better clearance using a physician assessment score Secondary outcomes: observer-rated percentage improvement of HEASI (adaptation of EASI for the hands) score. Other outcomes: observer-rated clinically significant response, defined by 50% improvement using a physician assessment score, participant-rated pruritus, adverse events	54/58 randomised participants could be evaluated for efficacy. There was no statistically significant difference between groups (RR 10.24, 95% CI 0.59 to 176.56, P = 0.11. No statistical significant difference was found with relation to the occurrence of at least one adverse event (RR 1.33, 95% CI 0.33, 5.44). The global evaluation at day seven between treatments (improvement of eczema in 23 participants treated with polyacrylic film-forming lotion versus 18 participants treated with thickened lotion) gives a RR of 1.19 (95% CI 0.87 to 1.62, P = 0.28) indicating no statistically significant difference in improvement between the two treatments.	6	It was a double-blind study without an intention-to-treat analysis.

Hanifin 2004 *Novel treatment of chronic severe hand dermatitis with bexarotene gel.*	C	RCT (parallel)	N=55 <u>Intervention:</u> A: Bexarotene 1% gel escalated stepwise from 1x every other day to 3x daily in 28 participants B: Bexarotene gel stepwise plus mometasone furoate 0.1% ointment 2x daily in 13 participants C: Bexarotene gel stepwise plus hydrocortisone 1% ointment 2x daily in 14 participants In all 3 groups daily use of emollients was allowed.	Hand eczema for at least 6 months with a score of 3 or 4 on 3 out of 6 severity scales.	22 weeks	Observer-rated treatment success defined by 90% or better clearance using a physician assessment score (not exactly defined), observer-rated % improvement of HEASI score, severity score of signs is 0 = none, 1 = mild, 2 = moderate, 3 = moderately severe, 4 = severe for respectively erythema, scaling, oedema, lichenification, vesiculation, fissuring at week 2, 4, 6, 8, 10, 14, 18. 22, observer-rated clinically significant response, defined by 50% improvement using a physician assessment score (not exactly defined), participant-rated pruritus on a scale from 0 = none to 4 = severe, adverse events	Treatment success (>90% clearance) was achieved by 39% in the bexarotene-only group; by 46% in the B+MF group; and by 21% in the B+HC group. - Bexarotene only versus bexarotene+mometasone: there was no statistically significant difference between topical retinoids: bexarotene 1% gel and bexarotene with corticosteroids (RR 0.85, 95% CI 0.4 to 1.8) - Bexarotene only versus bexarotene+hydrocortisone: there was no statistically significant difference between topical retinoids: bexarotene 1% gel and bexarotene with corticosteroids (RR 1.83, 95% CI 0.61 to 5.53) - Bexarotene+mometasone versus bexarotene+hydrocortisone: there was no statistically significant difference between topical retinoids: bexarotene 1% gel and bexarotene with corticosteroids (RR 2.15, 95% CI 0.67 to 6.89)	13	The study was not blinded and no intention-to-treat analysis was conducted.

							41 participants (75%) had ≥1 adverse events during the study, of whom 27 (49%) had ≥1 events possibly related to the study drugs. In the bexarotene group: irritation/rash in eight participants; stinging/burning in 2; dermatitis flare in 5. In the B+MF group: Irritation/rash in 4 participants; stinging/burning in 4. In the B+HC group: Irritation/rash in four participants; stinging/burning in 2; dermatitis flare in 4. None of the adverse events occurred significant more often in a study or control group.		
Hill 1998 *Comparative efficacy of betamethasone/clioquinol (Betnovate-C) cream and betamethasone/fusidic acid (Fucibet) cream in the treatment of infected hand eczema.*	C	RCT (parallel)	N=120 <u>Intervention:</u> A: Betamethasone valerate 0.1% + clioquinol 3% cream twice daily in 57/61 participants. B: Betamethasone-v 0.1% + fusidic acid 2% cream twice daily in 53/55 participants	A clinical diagnosis of hand eczema with secondary bacterial infection, presence of erythema induration or itching (2 out of 3), age ≥18 years	4 weeks	Observer-rated proportion of participants with satisfactory response at the last on-treatment visit, participant-rated response to treatment, observer-rated changes in scores for erythema, pruritus, induration, dryness/ scaling, cracking/ fissuring, clinical signs of infection, participant-rated severity of itching, participants' assessment of treatment acceptability with regards to stickiness, staining of skin and/ or clothing,	In the intention-to-treat analysis 34/62 participants (54.8%) in the betamethasone valerate /clioquinol group, and 31/58 participants (53,4%) in the betamethasone-valerate/ fusidic acid group had a good response. This was not statistically significant (RR 1.03; 95% CI 0.74 to 1.43, P = 0.88). In the clioquinol group 11/62 participants experienced adverse events versus 9/58	10	The study was not blinded, an intention-to-treat analysis was conducted.

						ease of application and overall acceptability, bacterial culture at entry and at end of treatment, adverse events	participants in the fusidic acid group (RR 1.14, 95% CI 0.51 to 2.56). 5 participants in the clioquinol group developed irritation at the application site versus 5 participants in the fusidic acid group (RR 0.94, 95% CI 0.29 to 3.07)		
Hordinsky 2010 *Efficacy and safety of pimecrolimus cream 1% in mild-to-moderate chronic hand dermatitis: a randomized, double-blind trial.*	A2	RCT (parallel)	N=652 <u>Intervention:</u> A: Pimecrolimus 1% ointment twice daily with daily occlusion by use of vinyl gloves of at least 6h after second (evening) application in 325 participants <u>Control intervention:</u> B: Vehicle ointment twice daily with daily occlusion by use of vinyl gloves of at least 6h after second (evening) application in 327 participants The double-blind phase was followed by a 6-week open-label treatment period during which all patients received	History of hand eczema (according to IGA: mild (2) to moderate(3)) of at least 90 days duration, minimal age of 18 years	Up to 43 weeks	Investigators Global Assessment (IGA) of the target hand at day 43 or at time of early (according to trial registration, not clear from article) (0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = severe), observer rated: clear or almost clear of hand dermatitis at end of trial as defined by IGA (0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = severe) at weekly intervals, participant-rated: pruritus severity 0 - 3 (0 = absent, 3 = severe) at weekly intervals, participant-rated: burning sensation/severity of burning 0 - 3 (0 = absent, 3 = severe), safety and tolerability (adverse events)	Treatment success (IGA score 0=clear and 1=almost clear) was achieved in 97/325 (29.8%) in the pimecrolimus cream 1% group and 76/327 in the vehicle group. There was no statistically significant difference between the treatment groups (RR 1.28, 95% CI 0.99 to1.66, P = 0.06).	555 participants completed the double-blind phase, 544 (269 in the pimecrolimus group and 275 in vehicle group) entered the open extension phase and 512 (248 and 264 respectively) completed the study.	The study was blinded and an intention-to-treat analysis was conducted. When both hands were affected, the target hand was defined as the more severely affected.

			pimecrolimus cream 1%. The patients could enter this phase before the end of the 6-week double-blind phase if they were judged by the investigator to be free from hand dermatitis on 2 consecutive weekly assessments.						
Jowkar 2014 *Comparison of fumaric acid 5% cream versus triamcinolone 0.1% cream in the treatment of hand eczema.*	C	RCT (parallel)	N=92 <u>Interventions:</u> A: Topical fumaric acid 5% cream twice a day in 30 participants B: Triamcinolone 0.1% cream twice a day in 28 participants	Clinical diagnosis of hand eczema	4 weeks	Signs of the disease including erythema, excoriation, population, lichenification at week 0 and week 4, disease score based on the EASI (eczema area and severity index) at week 0 and week 4, degree of pruritus ranging from 0 to 3 (0=no pruritus, 3=severe) at week 0 and week 4	Statistically significant improvement was observed in EASI score in the treated group compared with the placebo group (p value=0.03, mean difference of -0.82, t of -2.22) Erythema and pruritus were noted in 2 participants in each treatment group (RR 0.93, 95%CI 0.14 to 6.18)	38 (4 were excluded due to adverse events, unclear what happened to the remaining 34 participants)	The study is blinded, an intention-to-treat analysis was not conducted. High rate of lost to follow-up
Katsarou 2012 *Tacrolimus 0.1% vs mometasone furoate topical treatment in allergic contact hand eczema: a prospective*	B	RCT (parallel)	N=30 <u>Intervention:</u> A: Tacrolimus 0.1% twice daily for 30 days and once daily in 15 participants B: Mometasone furoate ointment twice daily for 1 week, once daily	Adult participants with chronic hand eczema (present at least 6 months before referral to clinic), a positive relevant patch test reaction, absence of atopy, no use of systemic corticosteroids and/or	90 days	Investigator-rated severity of erythema judged on a 5 point VAS scale at day 0, 30, 60 and 90, investigator-rated severity of infiltration judged on a 5 point VAS scale, investigator-rated severity of vesiculation judged on a 5 point VAS scale, investigator-rated severity of desquamation	The scores of the evaluated clinical parameters did not differ between Groups A and B at any of the four time points (p>0.05). In both groups a significant difference was detected in all parameters between baseline and Day 90 recorded values.	NS	The study was observer-blinded.

randomized clinical study.			during week 2 and week 3, once daily 3 times a week for week 4 and 5 and once daily 2 times a week during the rest of the study till 90 days in 15 participants	immunosuppressants 2 weeks before inclusion		judged on a 5 point VAS scale, investigator-rated severity by presence of cracks judged on a 5 point VAS scale, investigator-rated severity of itching judged on a 5 point VAS scale, adverse events			
Kircik 2013 *A randomized, double-blind phase 4 study of the efficacy and safety of ethanol-free clobetasol propionate foam, 0.05%, vs vehicle foam in the treatment of chronic hand dermatitis.*	B	RCT (parallel)	N=125 <u>Intervention:</u> A: Clobetasol propionate 0.05% foam twice a day for 14 days in 62 participants <u>Control intervention:</u> B: Vehicle / Placebo foam twice a day for 14 days in 63 participants.	Capable of understanding and willing to provide signed informed consent, male or female at least 12 years of age at time of consent and at time of first dose, able to complete the study and to comply with study instructions, moderate to severe hand dermatitis, chronic hand dermatitis for at least 6 months.	2 weeks	Primary outcomes: percentage of participants with investigator-rated good/excellent control at day 15, percentage of participants with self-rated good/excellent control at day 15, adverse events Secondary outcomes: reduction in severity, participant-rated scoring and investigator-rated scoring at day 15	In the clobetasol group 38.7% (n=24) had an Investigator Static Global Assessment (ISGA) score of 0 or 1 versus 27 (n=17) in the vehicle group. This was not statistically significant (RR 1.43 95% CI 0.86 to 2.40). On day 15 51.6% (n=32) in the clobetasol group graded their hand eczema as clear or almost clear versus 22.2% (n=14) in the vehicle group with the subject's global assessment (SGA). This was not statistically significant (RR 2.32 (95% CI 1.38 to 3.91, P < 0.05). Adverse events were reported in 18% in the clobetasol propionate foam group and 8% in the vehicle foam group (RR 2.24, 95% CI 0.82 to 6.06). No serious adverse events were reported in the clobetasol	1 lost to follow-up however 8 in total discontinued treatment for various reasons. 14 participants were excluded form the per protocol analysis.	Sponsor: Stiefel, a GSK Company. Short follow-up period.

							propionate foam group, one participant in the vehicle discontinued due to severe fissures. At the end of treatment 51 participants (82.3%) had at least on grade improvement on the SGA score, compared to 33 participants (52.4%) in the vehicle group, which was a statistically significant difference (RR 1.57, 95% CI 1.21 to 2.04, P < 0.05 26 participants (41.9%) in the clobetasol group versus 18 (28.6%) in the control group improved ≥2 grades in the ISGA score, not statistically significant (RR 1.47, 95% CI 0.90 to 2.39, P = 0.12). 45 participants (72.6%) in the clobetasol group versus 38 (60.3%) improved at ≥1 grade in the ISGA score after 15 days of treatment, not statistically significant (RR 1.20, 95% CI 0.94 to 1.55, P = 0.15).		
Krejci-Manwaring 2008 *Topical tacrolimus 0.1% improves symptoms of hand*	B	RCT (parallel)	N=33 <u>Intervention:</u> A: Topical tacrolimus twice daily for 12 weeks in addition to a daily dose of prednisone; 30 mg in week 1, 20	Adults aged ≥18 years, hand eczema with a combined severity score of 5 to 16	14 weeks (3 weeks active treatment, 11 weeks follow-up)	Observer-rated reduction in severity based on symptom grading scale for erythema, scaling, induration and fissuring (5-point scale, 0 = none to 4 = marked/intense) at week 1, 4, 8, 12 (end of treatment) and 14 (end of study), investigator's	A greater improvement of induration (p=0,003) and scaling (p=0,003). Subjective improvement (p=0,04) was seen in patients treated wit tacrolimus. Improvement in erythema, fissuring, pruritus, and investigators global with	13	The study was double-blind. An intention-to-treat analysis was not carried out.

dermatitis in patients treated with a prednisone taper.			mg in week 2, 10 mg in week 3 in 14/21 participants <u>Control intervention:</u> B: Vehicle ointment applied twice daily for 12 weeks and in addition a daily dose of prednisone; 30 mg in week 1, 20 mg in week 2, 10 mg in week 3 in 6/11 participants			global assessment at week 1, 4, 8, 12 and 14, participant-rated visual analogue scale (VAS) of pruritus, participant-rated improvement, adverse events	tacrolimus did not exceed improvement with control. One case of each of the following adverse events were observed: acute contact dermatitis at site of necklace, flare of atopic dermatitis on the foot, acne-like rash on the face, leg cramps and worsening of hand dermatitis). Stinging was not reported. 4 participants in the vehicle group dropped out due to lack of response (RR 0.06, 95% CI 0.00 to 0.99)		
Lauriola 2011 *A single-centre, randomized, perspective, investigator blinded, controlled trial to examine efficacy and safety of a Furpalmate-containing cream in comparison to topical corticosteroid in atopic dermatitis of hands of 40 adult patients*.	C	RCT (parallel)	N=40 <u>Intervention:</u> A: Furpalmate containing creams (0.3%) twice a day in 20 participants B: Corticosteroid (hydrocortisone acetate 0.5%) twice a day for in 20 participants	Participants aged ≥18 years, mild to moderate atopic dermatitis of hands, grading 3.0 to 5.0	2 weeks	Observer-rated: Physician's global evaluation of clinical response and of individual signs (erythema, xerosis), participant-rated assessment of itch (VAS), global response (unclear whether observer or participant rated), tolerability (adverse events), cosmetic compliance (unclear whether observer or participant rated)	In the study report, the treatments were shown to be equally effective in "curing" or "improving" the hand dermatitis after 14 days. In the furpalmate group 18/20 participants (90%) cured or improved after 14 days and in the hydrocortisone group 20/20 participants (100%). This was not a statistically significant difference (RR 0.9, 95% CI 0.76 to 1.07 P = 0.24)	0	Observers were blinded, but it is unclear whether participants were blinded. All participants completed the study and were analysed.
Lodén 2012	C	RCT (parallel)	N=44 <u>Intervention:</u>	Clinically proven history of hand eczema with a	2 weeks	Participant-rated severity on a100 mm visual analogue scale (VAS)	Clearance was defined as a score of ≤3 on the HEES. There was no	0	The study was double-blind and an intention-to-

The effect of a corticosteroid cream and a barrier-strengthening moisturizer in hand eczema. A double-blind, randomized, prospective, parallel group clinical trial			A: Betamethasone 0.1% cream twice daily in 22 participants B: Betamethasone 0.1% cream once daily + urea 5% cream once daily in 22 participants	recent relapse, daily use of moisturising treatment, either gender, age 18 or above, written Informed Consent		where 0 was no eczema and 100 mm extreme severe eczema, investigator-rated severity score Hand Eczema Extent score (HEES); clearance was defined as a score of ≤3, participant-rated quality of life using the validated Dermatology Life Quality Index (DLQI) at baseline and after 2 weeks	statistically significant difference between betamethasone valerate 0.1% cream and urea 5% cream (RR 0.75, 95% CI 0.55 to 1.03, P = 0.08). There was no statistically significant difference between betamethasone valerate 0.1% cream and urea 5% cream with regards to the VAS score (MD -17.7, 95% CI -35.42 to 0.02, P = 0.05). After two weeks, the average reduction of HEES was 12.5 in the BV group, compared to 10.5 in the BV+M group. There was no statistically significant difference between groups (MD 2.00, 95% CI -4.92 to 8.92, P = 0.57).		treat analysis was conducted. This study exists of two parts (Lodén 2010), of which only the second part is described here.
Möller 1983 *Intermittent maintenance therapy in chronic hand eczema with clobetasol propionate and flupredniden acetate.*	B	RCT (within-participant)	55 participants <u>Intervention:</u> A: Clobetasol propionate cream twice weekly for unclear duration (55 to 193 days) in 46/55 hands B: Fluprednidene acetate cream twice weekly in 46/55 contralateral hands.	Symmetrical hand eczema of at least 6 months duration	55 patients were healed in the initital healing period and entered the maintenance phase. They were followed for a	Number of hands that relapsed, and time of relapse, efficacy judgement (not specified) by a dermatologist, at unknown point in time, adverse events.	No relapses were observed in 32/46 (70%) of the hands treated with clobetasol and in 14/46 (30%) treated with fluprednidene This was statistically significant with an RR of 2.29 (95% CI 1.42 to 3.68). In four participants adverse events occurred with clobetasol and in three participants with fluprednidene (RR 1.33, 95% CI 0.32 to 5.63). One participant reported	9	It is unclear how the study was blinded. Intention-to-treat analysis was not carried out. Study duration unclear.

			Emollient were allowed on both hands.		mean period of 138 days.		an adverse event from both glucocorticoids.		
Pacor 2006 *Tacrolimus ointment in nickel sulphate-induced steroid-resistant allergic contact dermatitis.*	C	RCT (parallel)	N=28 <u>Intervention:</u> A: 0.1% tacrolimus ointment twice daily for 2 weeks in 14 participants <u>Control intervention:</u> B: Vehicle twice daily for 2 weeks in 14 participants	Moderate to severe nickel sulphate induced allergic contact dermatitis based on clinical history (hand eczema) and prior patch testing, resistant to topical corticosteroids	3 weeks (2 weeks active treatment, 1 week follow-up)	Participant's assessment of the following symptoms: erythema, oozing, scaling, itching. 4-point scale: 0 = none, 1 = mild, 2 = moderate, 3 = severe on a daily diary card, investigator's Global Assessment reduction in severity: 0 = no improvement, 1 = mild improvement, 2 = marked improvement, 3 = complete remission, adverse events, frequency of rescue medication usage	In the tacrolimus group complete remission at the end of treatment was observed in 6/14 and remarkable improvement in 8/14. Treatment with vehicle did not lead to remarkable improvement (0/14) and only to mild improvement in 4/14 (RR of 29.0 (95% CI 1.9 to 443.25) 4/14 in the tacrolimus group experienced transient burning and itching at the application site which was well tolerated (RR 9.00, 95% CI 0.53 to 152.93)	0	The study was double-blind and all participants completed the study. Study population not entirely hand dermatitis patients
Schnopp 2002 *Topical tacrolimus (FK506) and mometasone furoate in treatment of dyshidrotic palmar eczema: a randomized, observer-blinded trial.*	C	RCT (within-participant)	N=16 <u>Intervention:</u> A: Tacrolimus 0.1% ointment twice daily on 12/12 hands B: Mometasone furoate 0.1% ointment twice daily on 12/12 contralateral hands	Moderate to severe chronic relapsing dyshidrotic hand eczema	12 weeks (4 weeks active treatment, up to 8 weeks follow-up)	Observer-rated dyshidrotic eczema area & severity index (DASI) at baseline, week 2 and week 4 (based on sum-score for severity 1 = mild, 2 = moderate, 3 = severe for respectively vesicles, erythema, desquamatio and itch multiplied by score for affected area), adverse events	The reduction in mean DASI equalled improvement in scores for both treatments after two weeks , but no statistically significant superiority of tacrolimus could be demonstrated (MD-0.30, 95% CI -7.14 to 6.54)	0	The study was observer-blind and all participants completed the study.
Uggeldahl 1986 *Comparative effect of*	C	RCT (within-participant)	N=46 <u>Intervention:</u> A: Desonide cream 0.1% twice	Bilateral and symmetrical moderate eczema of the hand, wrist and lower arm	2 weeks	Observer-rated score 0 to 4 (0 = absent and 4 = maximum severity) for inflammation, infiltration, desquamation,	All patients showed improvement on the assesesed clinical scores (albeit not significant).	2	The study claims to be double-blind, although this is not described.

desonide cream 0.1% and 0.05% in patients with hand eczema.			daily in 44/46 hands B: Desonide cream 0.05% twice daily in 44/46 contralateral hands			lichenification, itching, tenderness and chapping, after 4 to 7 days and 11 to 14 days, participant-rated therapeutic effect: both hands equal or one hand better than the other hand at day 11 to 14, adverse events	2 participants reported stinging upon application of desonide 0.05% cream (RR 0.20 95% CI 0.01 to 4.06)		Intention-to-treat analysis was not carried out.
Veien 1999 *Long-term, intermittent treatment of chronic hand eczema with mometasone furoate.*	B	RCT (parallel)	N=106 <u>Intervention:</u> A: Mometasone furoate cream thrice week in 35/35 participants, B: Mometasone cream twice week in 37/37 participants <u>Control intervention:</u> C: No corticosteroids in 34/34 participants Emollients (Essex cream and ointment) used in all groups. In case of recurrence, all groups were permitted to use mometasone daily for a maximum of 3 weeks on separate periods. Additional treatment was permitted in all	Eczematous hand dermatitis for more than 6 months with a minimum score of 6 according to the adopted scoring system	Up to 36 weeks	Primary outcome: Number of recurrences of hand eczema and time at which recurrence occurred (recurrence defined as eczema score equal to or higher than initial score). Other outcomes: The length of time it took to control the dermatitis during the initial treatment period, number and time of recurrence in subgroups, data analysis by survival analysis, adverse events	Mometasone furoate 3times/week versus mometasone furoate 2times/week: in mometasone three times a week 29/35 (83%) had no recurrences, compared to 25/37 (68%) of those treated with mometasone two times a week and 9/34 (26%) of those only treated with emollients. There was no statistically significant difference between corticosteroid creams/ ointments: mometasone furoate cream used three times weekly and twice weekly versus no steroids (RR 1.23, 95% CI 0.94 to 1.61, P = 0.14). - Mometasone furoate 3times/week versus emollient and ointment only: statistically significant difference between corticosteroid creams/ ointments: mometasone furoate cream 3x weekly and 2x	0	All randomised participants were supposed to be free of eczema due to preceding treatment (induction of remission) with mometasone, yet recurrence was defined as a score equal or higher than before this remission induction phase. In each group a few participants received additional treatment. Drop-out defined as participant who had more than 2 recurrences.

			groups in case of a bacterial infection.				weekly versus no steroids (RR 3.13, 95% CI 1.75 to 5.59, P = 0.0001) Mometasone furoate 2x a week versus emollient and ointment only: statistically significant difference between corticosteroid creams/ ointments: mometasone furoate cream 3x weekly and 2x weekly versus no steroids (RR 2.55, 95% CI 1.4 to 4.67, P = 0.002), i.e. mometasone furoate twice a week was better than emollient only. In 10 participants mild skin atrophy was noted at some point during the study. In 5 participants the atrophy disappeared during the study, 5 participants had mild atrophy at the end of the study. This was not statistically significant (RR 1.76, 95% CI 0.45 to 6.83).		
Yousefi 2012 *Comparison of therapeutic effect of topical Nigella with Betamethasone and Eucerin*	B/C	RCT (parallel)	N=60 <u>Intervention:</u> A: Nigella sativa oil-extract 2% with Eucerin base applied twice a day in 19 participants	Participants with chronic hand eczema (confirmed by 2 dermatologist), aged between 18 and 60 years, hand eczema could be due to either	4 weeks	Resolution of severity and intensity of lesions after 2 weeks measured by Hand Eczema Severity Index (HECSI), the quality of life after 2 weeks measured by Dermatology Life Quality Index (DLQI), irritant or allergic contact dermatitis	Nigella and Betamethasone showed significantly more rapid improvement in hand eczema compared with Eucerin (P = 0.003 and P = 0.012 respectively); Nigella and Betamethasone ointments caused	8	Blinding is unclear. An intention-to-treat analysis was not carried out.

in hand eczema.			B: 0.1% Betamethasone ointment applied twice a day in 15 participants <u>Control intervention:</u> C: Only Eucerin ointment applied twice a day in 18 participants	occupational dermatitis, atopic dermatitis or irritant dermatitis of the hands (bilateral or unilateral)		after 4 weeks measured by physician assessment, adverse events	significant decreases in DLQI scores compared with Eucerin (P < 0.0001 and P = 0.007 respectively). No significant difference was detected in mean DLQI and HECSI of the Nigella and Betamethasone groups over time (P = 0.38 and P = 0.99 respectively).		

Abbreviations: RCT = randomized controlled trial; NS = not specified; CI = confidence interval; RR = relative risk; IGA = investigator global assessment; HECSI = hand eczema severity index; DLQI = dermatology quality of life index; PSA = patient self assessment; AD = Atopic dermatitis; VAS = visual analogue scale; HE = hand eczema; HEASI = hand eczema area and severity index; EASI = eczema area and severity index; ISGA = investigator static global assessment; SGA = subject's global assessment; HEES = hand eczema extent score; DASI = dyhidrotic eczema area and severity index.

Fototherapie (2017)

Karakteristieken en resultaten van geïncludeerde studies (RCT's) beoordeeld volgens EBRO

Reference	Level of evide-nce	Study design	Patients (N)	Inclusion criteria	Follow-up	Outcome measures	Results	Lost to follow-up	Comments
Adams 2007 *Mittel-Dosis-UVA-1- und locale PUVA-Therapie beim dyshidrosiformen Handekzem – eine prospective randomisierte Studie.*	C	RCT (within-participant)	N=15 <u>Intervention:</u> A: Middle dose UVA-1 irradiation 3 times a week (cumulative dose of 600 J/cm2) in 11/15 hands B: Local 8-MOP-cream-PUVA irradiation 3 times a week (cumulative dose of 17.4 J/cm2) in 11/15 contralateral hands. 8-MOP-	≥18 years old, chronic relapsing dyshidrotic hand eczema with a duration of ≥1 month, r esistant to conventional therapies.	5 weeks	Observer-rated assessment of improvement (DASI-score), adverse events	Burning occurred in 3 participants in the topical cream PUVA group and in 1 participant in the UVA-1 group (RR 3.00, 95% CI 0.37 to 24.58) and increased pruritus occurred in 5 participants in the topical PUVA group versus three in the UVA-1 group (RR 1.67, 95% CI 0.52 to 5.33). However, the summary effects were not significantly different between groups.	4	This study was not blinded and an intention-to treat analysis was not carried out.

			crème was applied 30 minutes before the start of irradiation.						
Bayerl 1999 *Pilotstudie zur Therapie des beruflich bedingten Handekzems mit einer neuen tragbaren UVB-Bestrahlungseinheit.*	C	RCT (parallel)	N=48 <u>Intervention:</u> A. UV-B phototherapy 5 days/week for 8 weeks in 19/24 participants. <u>Control intervention:</u> B. No UVB for 8 weeks in 17/24 participants Both groups were allowed to use non-specific creams / emollients.	Occupational chronic hand eczema of > 3 months duration, > 30% involvement of hands	8 weeks	Observer-rated extent of hand eczema, and scoring 1 to 4 (1 = absent, 2 = mild, 3 = moderate, 4 = severe) on erythema, oedema, maceration, excoriation, lichenification, fissuration, infection, scaling, itch, participant-rated VAS (0 to 10) on itching and restrictions in daily life, TEWL and Nitrazinyellow-test, adverse events.	Clinical outcome measurements and TEWL improved in both groups, howeber there was no statistic significant improvement (except for the symptom of lichenification p=0,0052) of the extent of handeczema after UVB-photherapy.	12	The participants and the observers were not blinded and no intention-to-treat analysis was carried out. Fairly high loss to follow up
Brass 2015 *An observer-blinded randomized controlled pilot study comparing localised psoralen-ultraviolet A with localized narrowband ultraviolet B for the treatment of hand eczema*	B	RCT (parallel)	N=60 <u>Intervention:</u> A: Immersion PUVA twice weekly with 4-weekly assessments in 30 participants B: NB-UVB twice weekly with 4-weekly assessments in 30 participants	Patient has provided written informed consent, palmar eczema not responding to topical treatments, ≥18 years of age, no topical treatments (except emollients for 48 hours), no systemic treatments for eczema treatment for 3 months, absence of	12 weeks	Number of patients achieving a 'clear'/'almost clear' treatment response at 12 weeks, percentage improvement based on the mTLSS (modified total lesion symptom score) at week 0, 4, 8 and 12, change in quality of life based on the Dermatology Life Quality index (DLQI) at week 0, 4, 8 and 12, change in the health economic evaluation with the EuroQol health outcome score (EQ-5D) at week 0, 4, 8 and 12, adverse events	6/30 participants treated with narrowband UVB improved compared to 12/30 participants on local PUVA after 12 weeks. There was no statistically significant difference between irradiation with UV-light (RR 0.50, 95% CI 0.22 to 1.16, P = 0.08) There were no serious treatment related adverse events reported. Erythema was reported in 9 participants treated with local PUVA and in none of the participants treated with local narrowband UVB	17	Only abstract The study was investigator-blinded; it is unclear whether an intention-to-treat analysis was carried out.

				clinical evidence of bacterial, fungal or viral infection, not pregnant			(RR 0.05, 95% CI 0.00 to 0.87, P = 0.0005)		
Van Coevorden 2004 *Comparison of oral psoralen-UV-A with a portable tanning unit at home vs hospital-administered bath psoralen-UV-A in patients with chronic hand eczema: an open-label randomized controlled trial of efficacy.*	A2	RCT (parallel)	N=158 <u>Intervention:</u> A: Oral PUVA (methoxypsoralen) phototherapy at home on both hands thrice weekly in 63/78 participants B: Topical bath PUVA (trioxsalen) twice weekly in hospital in 62/80 participants Emollients were allowed in both groups.	Bilateral or unilateral hand eczema since at least 1 year, at least 2 relapses or more than 3 consecutive weeks with visible signs in the last 3 months, moderate to severe hand eczema with a score of at least 6	10 weeks active treatment, 8 weeks follow-up	Observer-rated severity score based on sum of scores 0 to 3 for erythema, desquamation, vesiculation, infiltration, fissures, itch, pain at week 10, (end of treatment)	In the oral/home-PUVA group 3 participants dropped out because of adverse events (nausea). In the hospital/bath PUVA group 1 dropped out because of adverse events (burn). There are no differences between groups (nausea RR 7.18 95% CI 0.38 to 136.71; burn RR 0.34 95% CI 0.01 to 8.26) At the end of the treatment phase (10 weeks) in the home-PUVA group 56/78 participants (72%) showed improvement, versus 49/80 (61%) in the hospital/bath PUVA group. At 8 weeks after the treatment phase the reduction in mean score from baseline was 3.1 versus 2.7, respectively; there was no statistically significant difference between irradiation with UV-light: oral PUVA and topical bath PUVA (MD 0.4, 95% CI -0.77 to 1.57, P = 0.50)	41; 33 during treatment, 8 during follow-up.	The study was not blinded; an intention-to-treat analysis was carried out.
Grattan 1991 *Comparison of topical PUVA*	C	RCT (within-	N=15 <u>Intervention:</u>	≥16 years, recurrent disabling symmetrical	8 weeks	Observer-rated global rating on a 5-point scale, participant-rated VAS to indicate improvement at	Both PUVA and UVA-treated hands improved over the 8 weeks on the T120-scores (significant for	3	Small number of participants. The study was double-blind and an

with UVA for chronic vesicular hand eczema.		partici pant)	A: Topical PUVA 3 times a week on 12/15 hands <u>Control intervention:</u> B: UVA (with placebo psoralen paint) on 12/15 contralateral hands Moisturisers were allowed on both hands and both hands received a small fraction of UVB from the UVA lamps	vesicular hand eczema for at least 6 months with periods of remission (complete clearance) not exceeding 1 month in the previous 6.		week 0, 4, 8, 12 and 16, observer-rated severity score: T-120 scores: multiplying surface area involved with severity scores (0 to 4) for vesiculation, erythema and scaling in week 0, 4, 8, 12 and 16, questionnaire after completion of the study, adverse events	both sides), global evaluations (significant for both sides) and the VAS (significant only for the UVA-treated side) Only 1 participant who completed the study experienced a burning episode on the back of his PUVA treated hand (RR 3.00, 95% CI 0.13 to 68.26). Probably 2 participants had to be withdrawn due to exacerbation of eczema (RR 3.00, 95% CI 0.13 to 68.26)		intention-to-treat analysis was not conducted.
Polderman 2003 *A double-blind placebo-controlled trial of UVA-1 in the treatment of dyshidrotic eczema.*	C	RCT (paral lel)	N=28 <u>Intervention:</u> A: UVA-1 irradiation 40 J/cm2 on the hands in 15/15 participants 5 times weekly <u>Control intervention:</u> B: Placebo (simulated blue light) in 10/13 participants Emollients were probably allowed in both groups.	Dyshidrotic hand eczema	9 weeks (3 weeks active treatme nt, 6 weeks follow-up)	Observer-rated severity by the dyshidrotic eczema area & severity index (DASI, based on sum-score for severity 1 = mild, 2 = moderate, 3 = severe for respectively vesicles, erythema, desquamation, itch multiplied by score for affected area), VAS for itch (probably participant-rated) at the end of each week and 3 and 6 weeks after treatment, observer-rated reduction in severity for the separate items of DASI at the end of each week and 3 and 6 weeks after treatment, adverse events	There was a statistically significant difference between irradiation with uv-light uva-1 and placebo with regards to VAS scores for itch (MD 3.68, 95% CI 1.25 to 6.11). The severity score Dyshydrotic eczema Area and Severity Index (DASI) decreased significantly in the UVA-1 group compared to the placebo group in week 3 (MD 9.05, 95% CI 3.15 to 14.95, P = 0.003) Apart from some minor erythemal reactions, no adverse events occurred. 3/13 participants in the placebo group dropped out after 2 weeks because of exacerbation, but no	3	This study was double-blind and an intention-to-treat analysis was carried out.

							significant differences between groups (RR 0.13, 95% CI 0.01 to 2.22)		
Rosén 1987 Chronic eczematous dermatitis of the hands: a comparison of PUVA and UVB treatment.	C	RCT (within-participant)	N=35 <u>Intervention:</u> PUVA or UVB therapy 3 times a week for a maximum of 3 months. A: Those born in even years received PUVA treatment and those born in odd years UVB treatment. B: Patients born on even dates were treated on their right hand and patients with uneven birth dates on their left hand. <u>Control intervention:</u> The other hand was unexposed ("untreated hand"). The patients were encouraged to use only emollients such as salicylic acid (2%) in petrolatum or urea 10% in an	(1) Bilateral hand dermatitis with symmetric distribution and severety, (2) A duration of at least 6 months, (3) Previous treatment, including topical corticosteroids, without benefit, (4) Dermatitis interfering with daily life.	16 months.	The following factors were evaluated: desquamation, erythema, vesiculation, infiltration and fissures. The patients opinion about itching and pain was also registered. Each variable was assessed on a four-point-scale: none (0), slight (1), moderate (2) and severe (3). The maximum combined score was thus 21. Both PUVA and UVB effect was evaluated by comparing the combined severity score of the light-treated hand with the "untreated" hand at 3, 6, 9 and 12 weeks. When the treatment was completed, a global evaluation was made independently by the investigator and patient using a four-point scale: cleared, much improved, somewhat improved and unchanged/worse.	PUVA: *Treated hand:* 92% mean reduction of the combined severity score (CSS). The treated hand cleared in all 14 patients. *Untreated hand:* The skin lesions improved, with 49% mean reduction. At the end of the study, the treated hand had a significantly smaller mean severity score (MSS) than the untreated hand. All PUVA treated hands cleared, compared to only 1 of the untreated hands. In 9 out of 14 there was a relapse within 3 months. UVB: *Treated hand:* 51% mean reduction score. 15 patients improved much or somewhat but in no case had the dermatitis cleared. *Untreated hand*: after 12 weeks of treatment, this hand also improved. With a 37% mean reduction score. No hand was cleared but the dermatitis was much or somewhat improved in 12 patients. The MSS after treatment was significantly smaller in the treated hand vs the untreated hand. However there was no significant difference in the proportion of much improved or	5	Follow period unclear, therapy period was 12 weeks, or till clearance. Randomization was performed on date and year of birth. There was no blinding of patients or investigators. *Side effects:* *PUVA:* in 7 out of 14 patients; 2 patients experienced nausea, 3 patients developed severe oedema, pain and itching in the treated hand, another patient developed hyperpigmented spots on the backs of the fingers, which disappeared after treatment. *UVB*: 2 patients developed bullae in the treated palm. The number of side effects was greater in the PUVA than in the UVB group.

			emollient base. The patients rubbed in white petrolatum on their hands immediately before each light treatment.				cleared hands between treated and untreated hands. *Comparison PUVA and UVB:* At the end of the study, the mean total score was significantly lower in the PUVA- treated group. The improvement was already evident at 3 weeks. The untreated hand improved in both groups, somewhat more in the PUVA treated group but the difference was not significantly.		
Said 2010 *A comparative study of ultraviolet light a1 phototherapy versus betamethasone valerate 0.1% cream for chronic vesicular hand eczema.*	C	RCT (parallel)	N=47 <u>Intervention:</u> A: UVA-1 phototherapy 3 times a week in 24 participants. B: Betamethasone valerate 0.1% cream twice a day in 23 participants.	Chronic vesicular hand eczema	6 weeks active treatment, 6 weeks follow up. Total duration of 12 weeks.	Degree of improvement based on the Dyshidrotic Area and Severity Index (DASI) at week 3, week 6 and week 12, adverse events	The tolerance of both treatments was good. The only noted adverse event was post-phototherapy pigmentation which occurred in 18/24 participants treated with UVA-1 compared to none of the participants in the control group (RR 35.52, 95% CI 2.26 to 557.08)	**7**	Only abstract The study is not blinded, an intention-to-treat analysis was not conducted.
Sezer 2007 *Local narrowband UVB phototherapy vs. local PUVA in the treatment of chronic hand eczema.*	**C**	RCT (within-participant)	N=15 <u>Intervention:</u> A: Local narrowband UVB 3 times a week in 12/15 hands. The initial dose was 150 mJ/cm2 for each participant. An 20%	Diagnosis of biopsy proven chronic hand eczema of dry and dyshidrotic types, duration of > 4 months, resistant to conventional therapies	19 weeks (9 weeks active treatment, 10 weeks follow-up)	Investigator-rated reduction in severity of a total sum score defined by: degree of erythema, squamation, induration, fissuring and itching, scored on a 4-point scale in week 0, 3, 6 and 9, investigator-rated number of participants with clearance defined as a	2/12 hands treated with UVB cleared (17%). On the PUVA treated side 1 hand cleared (8%). No statistically significant difference between irradiation with UV-light: local narrowband UVB and local PUVA (RR 2.0, 95% CI 0.21 to 19.23, P = 0.55)	3 (1 due to treatment failure and 2 due to non-	Small number of participants. It was unclear whether the study was blinded, intention-to-treat analysis was not carried out.

			increasing dose schedule was used until a final dose of 2000 mJ/cm2 was reached. B: Local PUVA 3 times a week in 12/15 contralateral hands. The initial dose of psoralen plus UVA irradiation was 1.0 J/cm2 with an increase of 0.5 J/cm2 in every second session until a final dose of 7.5 J/cm2 was achieved.			total sum score of 0; participants with marked improvement had a reduction of more than 70% at week 9, number of relapses during follow-up phase, adverse events	1 participant dropped out because of an exacerbation of eczema in both hands (unclear which group). Palmar hyperpigmentation due to PUVA was observed in 3 participants (RR 0.14 95% CI 0.01 to 2.55, P = 0.07). In both treatment modalities mild xerosis was observed, which responded to emollients. For both treatments a marked clinical improvement was observed in 9/12 hands (75%). The difference in total clinical scores between irradiation with UV-light: local narrowband UVB and local PUVA was not statistically significant.	compliance.)	
Sjövall 1987 *Local and systemic effect of UVB irradiation in patients with chronic hand eczema.*	C	RCT (parallel)	N=18 <u>Intervention:</u> A: UVB irradiation only on hands 4 times a week in 6 participants. B: Filtered light (placebo UVB, no UVB) on the hands 4 times a week in 6 participants. C: Hand UVB followed by whole body UVB + UVA	Chronic hand eczema, resistant to conventional topical treatment with potent corticosteroids and moisturizers	8 weeks with an email follow-up after 3 months	Observer-rated severity scoring system after 4 weeks (16 exposures), if a participant cleared before the end of the study, or at 8 weeks (end of treatment after 32 exposures), participant-rated follow-up questionnaire 3 months after the end of treatment, regarding the course of hand dermatitis and the burden of treatment, adverse events	- Whole body UVB + local UVB hands versus placebo: whole body UVB did not have any advantage (RR 3.67, 95% CI, 0.90 to 14.97, P = 0.07) when compared to placebo UVB. - Whole body UVB + local UVB hands versus local UVB hands alone: whole body UVB irradiation with additional irradiation of the hands was not statistically significantly better than the local UVB of the hands alone. The RR was 2.20 (95% CI 0.83 to 5.84, P = 0.11).	3	Small number of participants. The study was partly blinded, intention-to-treat analysis was not carried out.

			4 times a week during in 6 participants. Their 'ordinary topical treatment' was permitted in all groups.				In the local UVB group 2 participants were still in remission after 15 weeks. The other 3 relapsed after 1-12 weeks (medium 5 weeks). In the UVB local + whole body group all participants relapsed within 3-10 weeks (median 6 weeks). The participant in the placebo group who had reached remission, relapsed after 3 weeks. This was not statistically significant (Local UVB hands alone versus placebo MD 4.10, 95%CI -3.25 to 11.45, Whole body UVB + local UVB hands versus placebo MD 0.50, 95% CI -4.98 to 5.98, Whole body UVB + local UVB hands versus local UVB hands alone MD -3.60, 95%CI -9.68 to 2.48). Adverse events were not seen in either group.		
Tzaneva 2009 *Oral vs. bath PUVA using 8-methoxypsoralen for chronic palmoplantar eczema.*	**C**	RCT (parallel)	N=29 A: Oral PUVA: 8-MOP in a dose of 0.6 mg/kg 1 hour before irradiation with UVA in 14 participants. B: Bath PUVA: 2 ml of a 0.5% 8-MOP concentration of 5 mg/l in 13/15 participants.	Moderate to severe dyshidrotic or hyperkeratotic palmar and/or plantar eczema for at least 1 year, symmetrical distribution, unsatisfactory response to conventional topical treatment	Up to 40 months (up to 20 weeks active treatment, up to 40 months follow-up)	Investigator-rated reduction in severity of eczema score at the end of treatment: score based on extent of involvement (0 = 0%, 1 = 1-25%, 3 = 51-75%, 4 = 76-100%), the intensity (0 = absent, 1 = slight, 2 = moderate, 3 = severe, 4 = very severe) of erythema and infiltration or vesicles and scaling, time until relapse defined as an eczema	Erythema occurred in 10 participants (71%) in the oral PUVA group and in 8 participants (62%) treated with bath PUVA (RR 1.16, 95% CI 0.67 to 2.00). In the oral PUVA group, nausea was reported by 10 participants (RR 19.60, 95% CI 1.26 to 304.14), dizziness by 5 participants (RR 10.27, 95% CI 0.62 to 169.16) and headache by three participants (RR	2	The study was observer-blinded. Intention-to-treat analysis was not carried out.

						score > 50% of the baseline score during a follow-up period of max 40 months, the cumulative UVA exposure dose and number of exposures required for achieving a good or excellent response (> 75% reduction of eczema score), tolerability of the 2 regimes (adverse events)	6.53, 95% CI 0.37 to 115.49). The adverse events were mostly observed at the beginning of therapy and improved during subsequent treatments. None of these adverse events led to drop-outs.		

Karakteristieken en resultaten van geïncludeerde studies (observationeel) beoordeeld volgens EBRO

Study reference	Level of evide-nce	Study design	Patients (N)	Inclusion criteria	Follow-up	Outcome measures	Results	Lost to follow-up	Comments
Bretterklieber 2010 *Retrospective long-term follow-up in patients with chronic palmoplantar dermatoses after good response to bath PUVA therapy.*	C	Retrospective	79 patients	Recalcitrant dermatoses of palms and soles (RDPS) treated with bath PUVA three times a week in an 8-year period.	8 years	Not stated	A good clinical response (> 50% reduction of skin lesions) after a mean of 23 treatments and a mean cumulative UVA dose of 39J/cm2 in 51 patients (65%). Best results were present in patients with hyperkeratotic eczema (17/22; 77% good clinical response) followed by patients with palmoplantar psoriasis (26/41; 63%), and patients with dyshidrotic eczema (8/16; 50%). In 2007: 34/51 (67%) answered the questionnaire. 10 (29%)	-	Poster

							reported continuous complete clearance and 12 (35%) reported an improved course of disease after PUVA therapy with reduced frequency and/or intensity of skin rash. 79% of patients reported a long-term reduction in the use of topical steroids in the follow-up (mean, 4.3 years). 67% of patients reported a durable improvement of quality of life.		
Jensen 2012 *Psoralen plus ultraviolet A (PUVA) soaks and UVB TL01 treatment for chronic hand dermatoses.*	C	Retrospective study	94 patients Phototherapy for one of the following diagnoses (n=number of treatment courses): psoriasis (n=19), hyperkeratotic hand eczema (n=27), Pustulosis Palmoplantaris (PPP) (n=22), vesicular eczema (n=16), *Compositae* dermatitis (n=24), and allergic contact dermatitis (n=13).	Patients who in the years 2008-2010 had received ≥10 treatments (psoralen plus ultraviolet A (PUVA) soaks or TL01 phototherapy) in 1 course for treatment of 1 of the following diagnoses: psoriasis, hyperkeratotic eczema, PPP, vesicular eczema, Compositae dermatitis, and allergic contact dermatitis.	24 weeks	Clinical effect: good effect was defined as healing of the dermatosis (effect 4) or at least 75% improvement (effect 3), inadequate treatment effect was defined as clinical improvement less than 75%.	In 45/121 (37%) courses of PUVA soaks or TL01 the treatment was given with a good result, and in 76/121 (63%) the effect was inadequate. In 10 courses of PUVA soaks 8 patients experienced erythema and/or a burning sensation and 5 complained of pruritus and/or pain. In 2 courses of TL01 the patients had erythema and pruritus. In all cases the duration of side effects was short.	-	Of the total of 94 patients, only 43 patients with diagnoses within the spectrum hand eczema. The article does not show results for the separate included diagnoses.

			Total hand eczema (hyperkeratotic HE en vesicular) patients: n=27 en n=16 Total n=43						
Kuhl 2008 *Narrowband ultraviolet-B phototherapy for hand and foot dermatoses.*	C	Retrospective study	16 patients Patients were treated for dermatitis (n= 8), psoriasis (n=5), vitiligo (n= 1), cutaneous T-cell lymphoma (n=1), and graft-vs.-host disease (n= 1). 9 patients had involvement of their hands only, and 7 patients had involvement of both hands and feet.	Patients with recalcitrant dermatoses treated for at least 2 months with an NB-UVB hand and foot phototherapy device.	-	Clearance or improvement of disease.	2 patients had complete clearance of disease, 13 had improvement, and 1 had no response. Treatment was well tolerated and caused minor adverse effects. Results of the 8 patients hand eczema: (table 1): 2 patients complete disease clearance, 2 patients >75% clinical response. 3 patients <50% clinical response, 1 patient no response.	-	Only 8 patients with hand eczema in this study.

Summary of Findings tabellen GRADE

De tabellen met 'karakteristieken en resultaten van geïncludeerde studies' en 'risk of bias' tabellen van de studies die via GRADE uitgewerkt zijn, zijn niet in deze bijlage opgenomen. Deze zijn via de NVDV op te vragen.

Acitretine

Acitretin oral 30 mg once daily compared to placebo for patients with chronic hand eczema not or insufficient reactive to topical corticosteroid therapy of high class

Patient or population: patients with chronic hand eczema not or insufficient reactive to topical corticosteroid therapy of high class
Setting: Secondary care setting in 4 dermatology departments or clinics in Denmark.
Intervention: Acitretin oral 30 mg once daily
Comparison: placebo

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with Acitretin oral 30 mg once daily**				
Disease severity according to patients assessed with: Clinical scoring for itch with a grading system follow up: 8 weeks	The scoring of itching as a clinical symptom was reduced by 41% after using acitretin 30 mg once daily and 19% for placebo. Authors stated this difference as not statistically significant.			29 (1 RCT) [a]	⨁◯◯◯ VERY LOW [b,c,d]	Acitretin once daily may reduce itch but we are very uncertain.
Disease severity according to physician by clinical symptoms assessed with: clinical scoring in parameters by the parameters: fissuring, scaling, itch, redness and vesicle count. follow up: 8 weeks	After 4 weeks of treatment, a 51% reduction of all symptoms was observed among patients receiving acitretin ($p < 0.01$) compared with a 9% reduction in the placebo group ($p > 0.05$). No further improvement was seen over another 4 weeks of treatment. However individual symptoms improved or deteriorated.			29 (1 RCT) [a]	⨁◯◯◯ VERY LOW [c,e]	Acitretin may reduce disease severity in symptoms but we are very uncertain.
Change from baseline in health related quality of life according to patient - not measured	No study adressed this outcome.			-	-	We are very uncertain about the effect of acitretin on the health related quality of life to patient.
Proportion of patients that dropped or needed action i medication use due to adverse events. follow up: 8 weeks	No patients discontinued therapy because of side effects.			29 (1 RCT) [a]	⨁◯◯◯ VERY LOW [b,c,d]	Acitretin may not result in drop out of participants but we are very uncertain.

Acitretin oral 30 mg once daily compared to placebo for patients with chronic hand eczema not or insufficient reactive to topical corticosteroid therapy of high class

Patient or population: patients with chronic hand eczema not or insufficient reactive to topical corticosteroid therapy of high class

Setting: Secondary care setting in 4 dermatology departments or clinics in Denmark.

Intervention: Acitretin oral 30 mg once daily

Comparison: placebo

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with Acitretin oral 30 mg once daily**				
Number of patients that relapsed at any time point during the study - not measured	No study adressed this outcome.			-	-	We are very uncertain about the effect of acitretin on the number of patients that relapsed at any time point during the study.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are 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

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. Thestrup-Pedersen 2001

b. Downgraded one level for serious risk of bias (detection bias).

c. Downgraded one level for serious indirectness due to the short follow up time. We are interested in a follow up of 12-24 weeks.

d. Downgraded one level for serious imprecision. Although the study size is very small, we already downgraded for risk of bias and indirectness decided to only downgrade once for imprecision.

e. Downgraded two levels for very serious imprecision due to very small sample size.

Alitretinoin 30mg compared to placebo for patients with moderate to severe chronic hand eczema refractory to potent topical corticosteroids

Patient or population: patients with moderate to severe chronic hand eczema refractory to potent topical corticosteroids
Setting:
Intervention: alitretinoin 30mg
Comparison: placebo

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with alitretinoin 30mg**				
Disease severity according to patients assessed with: PaGA of clear or almost clear (responders) follow up: range 12 weeks to 24 weeks	143 per 1.000	**392 per 1.000** (311 to 497)	**RR 2.74** (2.17 to 3.47)	1210 (2 RCTs) [a]	⨁⨁⨁◯ MODERATE [b]	Alitretinoin 30 mg probably results in a large improvement of disease severity according to the patients.
Disease severity according to physician assessed with: PGA of clear or almost clear (responders) follow up: range 12 weeks to 24 weeks	155 per 1.000	**430 per 1.000** (344 to 537)	**RR 2.77** (2.22 to 3.46)	1210 (2 RCTs) [a]	⨁⨁⨁◯ MODERATE [b]	Alitretinoin 30 mg probably results in a large improvement of disease severity according to the physicians.
Change from baseline in health related quality of life assessed with: Skindex-29 follow up: 24 weeks	The decrease from baseline at EOT in total Skindex-29 scores was significantly greater in alitretinoin- vs placebo treated patients (-33 vs -15; p<0.001).			596 (1 RCT) [c]	⨁⨁⨁◯ MODERATE [d]	Alitretinoin 30mg probably improves quality of life according to patients.
Proportion of patients that dropped out due to adverse events follow up: range 24 weeks to 28 weeks	In Fowler et al. the number of patients with AE during treatment up to 7 days after EOT was for the intervention group N=216 73% and in the control group N=155 52%. Most common were headache, nausea, upper respiratory tract infection and flushing in the alitretinoin group. In Ruzicka et al. it was unclear how many people reported at least one adverse event. Headache was the most frequently reported AE (more in 30mg group than in the other two groups, N=20, 5%) and most frequent for withdrawal. No other AE led to more than two withdrawals in any group (data not published). Withdrawal because of headache: Alitretinoin N=17 , 4% and control group N=1, 1%. Most common were headache, erythema, nasopharyngitis and flushing.			1210 (2 RCTs) [a]	⨁⨁◯◯ LOW [b,e]	The evidence suggests that alitretinoin 30mg causes more adverse events than placebo.

Alitretinoin 30mg compared to placebo for patients with moderate to severe chronic hand eczema refractory to potent topical corticosteroids

Patient or population: patients with moderate to severe chronic hand eczema refractory to potent topical corticosteroids
Setting:
Intervention: alitretinoin 30mg
Comparison: placebo

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with alitretinoin 30mg**				
Number of patients that relapsed at any time point follow up: range 24 weeks to 72 weeks	3 per 1.000	**10 per 1.000** (1 to 177)	**RR 3.22** (0.18 to 58.27)	127 (1 RCT) [c]	⨁◯◯◯ VERY LOW [d,f]	We are uncertain about the effect of alitretinoin 30 mg on the number of patients that relapse.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are 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
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. Fowler 2014 and Ruzicka 2008
b. Downgraded one level for serious risk of bias due to high drop out rates in both studies.
c. Fowler 2014
d. Downgraded one level for serious risk of bias due to high drop out rates during the study.
e. Downgraded one level for serious indirectness because the outcomes of the studies did not exactly match our predefined outcome. It is unclear in both studies how many patients dropped out due to AE.
f. Downgraded two levels for very serious imprecision due to very wide confidence interval (includes both appreciable harm and appreciable benefit).

Alitretinoin 20mg compared to placebo for patients with moderate to severe chronic hand eczema refractory to potent topical corticosteroids

Patient or population: patients with moderate to severe chronic hand eczema refractory to potent topical corticosteroids
Setting:
Intervention: alitretinoin 20mg
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with alitretinoin 20mg				
Disease severity according to patients assessed with: PaGA of clear or almost clear (responders) follow up: range 12 weeks to 24 weeks	115 per 1.000	**313 per 1.000** (156 to 627)	**RR 2.71** (1.35 to 5.43)	158 (1 RCT) [a]	⨁⨁◯◯ LOW [b,c]	Alitretinoin 20mg appears to improve disease severity according to patients.
Disease severity according to physician assessed with: PGA of clear or almost clear (responders) follow up: range 12 weeks to 24 weeks	269 per 1.000	**401 per 1.000** (253 to 630)	**RR 1.49** (0.94 to 2.34)	158 (1 RCT) [a]	⨁⨁◯◯ LOW [b,c]	Alitretinoin 20mg appears to improve disease severity according to physician.
Change from baseline in health related quality of life according to patient assessed with: DLQI follow up: 24 weeks	Ruzicka et al. (2004) stated that DLQI improved during treatment with a general trend to more positive effects with higher drug doses without reaching the α level of statistical significance of p=0.05.			158 (1 RCT) [a]	⨁◯◯◯ VERY LOW [b,c,d]	We are uncertain about the effect of alitretinoin 20 mg on the improvement of quality of life compared to placebo.
Proportion of patients that dropped out due to adverse events follow up: range 12 weeks to 24 weeks	51 per 1.000	**63 per 1.000** (17 to 224)	**RR 1.22** (0.34 to 4.37)	158 (1 RCT) [a]	⨁◯◯◯ VERY LOW [b,e]	We are uncertain about the effect of alitretinoin 20mg on withdrawal due to adverse events.
Number of patients that relapsed at any time point - not measured	No study addressed this outcome.			-	-	We are very uncertain about the effect of alitretinoin 20mg on the number of patients that relapsed at any time point during the study.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are 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
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. Ruzicka 2004

b. Downgraded one level for serious risk of bias due to high drop out rates during the study. (attrition bias)

c. Downgraded one level for serious imprecision due to small sample size.

d. Downgraded one level for serious indirectness due to unknown difference in effect between groups.

e. Downgraded two levels for very serious imprecision due to small sample size and due to very wide confidence interval (includes both appreciable harm and appreciable benefit).

Alitretinoin 10mg compared to placebo for patients with moderate to severe chronic hand eczema refractory to potent topical corticosteroids

Patient or population: patients with moderate to severe chronic hand eczema refractory to potent topical corticosteroids

Setting:

Intervention: alitretinoin 10mg

Comparison: placebo

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with alitretinoin 10mg**				
Disease severity according to patients assessed with: PaGA of clear or almost clear (responders) follow up: range 12 weeks to 24 weeks	141 per 1.000	**240 per 1.000** (174 to 334)	**RR 1.70** (1.23 to 2.36)	781 (2 RCTs) [a]	⨁⨁⨁◯ MODERATE [b]	Alitretinoin 10mg probably improves disease severity according to patients slightly.
Disease severity according to physician assessed with: PGA of clear or almost clear (responders) follow up: range 12 weeks to 24 weeks	194 per 1.000	**309 per 1.000** (233 to 408)	**RR 1.59** (1.20 to 2.10)	781 (2 RCTs) [a]	⨁⨁⨁◯ MODERATE [b]	Alitretinoin 10mg probably improves disease severity according to physicians slitghly.
Change from baseline in health related quality of life assessed with: DLQI follow up: 24 weeks	Ruzicka et al. (2004) stated that DLQI improved during treatment with a general trend to more positive effects with higher drug doses without reaching the α level of statistical significance of p=0.05.			158 (1 RCT) [c]	⨁◯◯◯ VERY LOW [b,d,e]	We are uncertain about the effect of alitretinoin 10 mg on the improvement of quality of life compared to placebo.
Proportion of patients that dropped out due to adverse events follow up: 24 weeks	In Ruzicka et al. (2008) it was unclear how many people dropped out because of adverse events. Headache was the most frequently reported AE and most frequent for withdrawal (N=6 vs. N=1 in control group, both 1%). No other AE led to more than two withdrawals in any group (data not published). In Ruzicka et al. (2004) withdrawal because of headache was N=1 (1%) and unknown for control group.			158 (1 RCT) [c]	⨁◯◯◯ VERY LOW [b,f]	We are uncertain about the effect of alitretinoin 10mg on drop out due to adverse events.

Alitretinoin 10mg compared to placebo for patients with moderate to severe chronic hand eczema refractory to potent topical corticosteroids

Patient or population: patients with moderate to severe chronic hand eczema refractory to potent topical corticosteroids
Setting:
Intervention: alitretinoin 10mg
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	**Risk with alitretinoin 10mg**				
Number of patients that relapsed at any time point - not measured	No study addressed this outcome.			-	-	We are very uncertain about the effect of alitretinoin 10mg on the number of patients that relapsed at any time point.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are 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
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. Ruzicka 2004 and Ruzicka 2008
b. Downgraded one level for serious risk of bias due to high drop out rates in both studies (attrition bias).
c. Ruzicka 2004
d. Downgraded one level for serious indirectness due to unknown effect between groups.
e. Downgraded one level for serious imprecision due to small sample size.
f. Downgraded two levels for very serious imprecision due to inclusion of null effect and appreciable benefit or harm and small sample size.

Azathioprine 50mg once daily with topical clobetasol propionate 0.05% cream twice daily compared to topical clobetasol propionate 0.05% cream twice daily for patients with chronic hand eczema not or insufficient reactive to topical corticosteroid therapy of high class

Patient or population: patients with chronic hand eczema not or insufficient reactive to topical corticosteroid therapy of high class
Setting: Secondary care setting as a single-centre study in a department of Dermatology in India
Intervention: Azathioprine 50mg once daily with topical clobetasol propionate 0.05% cream twice daily
Comparison: topical clobetasol propionate 0.05% cream twice daily

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with topical clobetasol propionate 0.05% cream twice daily	Risk with Azathioprine 50mg once daily with topical clobetasol propionate 0.05% cream twice daily				
Disease severity according to patients assessed with: itching score: improvement from baseline Scale from: 0 to 10 follow up: 24 weeks	The mean disease severity according to patients was **-4.57**	The mean disease severity according to patients in the intervention group was 1,48 lower (2,43 lower to 0,53 lower)	-	91 (1 RCT) [a]	⨁◯◯◯ LOW [b,c]	Azathioprine in combination with usage of intermittently clobetasol cream may result in a small effect that may not be an important reduction in itch when compared with clobetasol cream only. MID of VAS itch estimated between 2 and 3 (Reich et al 2016).
Disease severity according to physician assessed with: HECSI score Scale from: 0 to 360 follow up: 24 weeks	The mean disease severity according to physician was **-11.46**	The mean disease severity according to physician in the intervention group was 10,79 lower (16,81 lower to 4,77 lower)	-	91 (1 RCT) [a]	⨁◯◯◯ LOW [d]	Azathioprine in combination with usage of intermittently clobetasol cream may reduce the disease severity according to physician slightly when compared to clobetasol cream only.
Change from baseline in health related quality of life according to patient - not measured	No study adressed this outcome.			-	-	We are very uncertain about the effect of azathioprine in combination with usage of intermittently clobetasol cream on the health related quality of life.
Proportion of patients that dropped out due to adverse events or needed action in medication use due to adverse events follow up: 24 weeks	None of the patients using azathioprine and cream or cream only reported any side effect requiring reduction of dosage or discontinuation of treatment. In the study it was not stated which side effects they were interested in.			91 (1 RCT) [a]	⨁◯◯◯ LOW [b,c]	Azathioprine in combination with usage of intermittently clobetasol cream may result in little to no difference in proportion of participants that dropped out due to adverse events or needed action for in medication use when compared to topical clobetasol cream only.

Azathioprine 50mg once daily with topical clobetasol propionate 0.05% cream twice daily compared to topical clobetasol propionate 0.05% cream twice daily for patients with chronic hand eczema not or insufficient reactive to topical corticosteroid therapy of high class

Patient or population: patients with chronic hand eczema not or insufficient reactive to topical corticosteroid therapy of high class
Setting: Secondary care setting as a single-centre study in a department of Dermatology in India
Intervention: Azathioprine 50mg once daily with topical clobetasol propionate 0.05% cream twice daily
Comparison: topical clobetasol propionate 0.05% cream twice daily

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with topical clobetasol propionate 0.05% cream twice daily	**Risk with Azathioprine 50mg once daily with topical clobetasol propionate 0.05% cream twice daily**				
Number of patients that relapsed at any time point during the study - not measured	No study adressed this outcome.			-	-	We are very uncertain about the effect of azathioprine in combination with usage of intermittently clobetasol cream on the number of patients that relapsed when compared to clobetasol cream only.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **MD:** Mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are 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
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations
a. Agarwal 2013
b. Downgraded one level for serious risk of bias (unclear risk of bias for detection bias and attrition bias).
c. Downgraded one level for serious imprecision. Although the study size is very small, we already downgraded for risk of bias and decided to only downgrade once for imprecision.
d. Downgraded two levels for very serious imprecision due to very small sample size.

Cyclosporine compared to betamethason for patients with chronic hand eczema not or insufficient reactive to topical corticosteroid therapy of high class

Patient or population: patients with chronic hand eczema not or insufficient reactive to topical corticosteroid therapy of high class
Setting:
Intervention: cyclosporine
Comparison: betamethason

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with betamethason	**Risk with cyclosporine**				
Disease severity according to patient assessed with: VAS itch and sleep follow up: mean 6 weeks	Decrease in occurrence of itch from baseline was significant in both groups. Decrease in sleep disturbance was only significant for cyclosporine. (no data because only graphically displayed at 6 weeks).			35 (1 RCT) [a]	⨁⨁◯◯ LOW [b,c]	Cyclosporine may result in little to no difference in itch when compared with betamethason treatment. Cyclosporine may improve sleep slightly.
Disease severity according to phycisian assessed with: Total disease activity follow up: mean 6 weeks	The mean disease severity according to phycisian was **-5.7**	The mean disease severity according to phycisian in the intervention group was 0,3 lower (3,1 lower to 2,5 higher)	-	35 (1 RCT) [a]	⨁⨁◯◯ LOW [d]	Cyclosporine may result in little to no difference in total disease activity according to the physician when compared with betamethason treatment.
Change from baseline in health related quality of life assessed with: EDI Scale from: 0 to 90 follow up: mean 6 weeks	The mean change from baseline in health related quality of life was **-8.4**	The mean change from baseline in health related quality of life in the intervention group was 2 lower (11,13 lower to 7,13 higher)	-	35 (1 RCT) [a]	⨁⨁◯◯ LOW [d]	Cyclosporine may result in little to no difference in the quality of life according to the physician when compared with betamethason treatment.
Proportion of patients that dropped out due to adverse events follow up: 6 months	48 per 1.000	**50 per 1.000** (3 to 747)	**RR 1.05** (0.07 to 15.68)	41 (1 RCT) [a]	⨁⨁◯◯ LOW [b,c]	Cyclosporine may result in little to no difference in the proportion of patients that dropped out due to adverse events when compared with betamethason treatment.
Number of patients that relapsed at any time point during the study follow up: 2 weeks	500 per 1.000	**500 per 1.000** (175 to 1.000)	**RR 1.00** (0.35 to 2.88)	14 (1 RCT) [a]	⨁⨁◯◯ LOW [d]	Cyclosporine may result in little to no difference in proportion of patients that relapsed when compared with betamethason treatment.

Cyclosporine compared to betamethason for patients with chronic hand eczema not or insufficient reactive to topical corticosteroid therapy of high class

Patient or population: patients with chronic hand eczema not or insufficient reactive to topical corticosteroid therapy of high class
Setting:
Intervention: cyclosporine
Comparison: betamethason

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with betamethason	Risk with cyclosporine				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **MD:** Mean difference; **RR:** Risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are 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
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations
a. Granlund 1996/1997
b. Downgraded one level for serious risk of bias (high risk other bias)
c. Downgraded one level for serious imprecision. Although the study size is very small, we already downgraded for risk of bias and decided to only downgrade once for imprecision.
d. Downgraded two levels for very serious imprecision (very low sample size).

Karakteristieken en resultaten van geïncludeerde studies (observationeel)

Alitretinoïne

Author (year of publication)	Study design	Patients (N)	Inclusion criteria	Follow-up	Outcome measures	Results	Lost to follow-up	Comments
Diepgen 2012 *Efficacy and Tolerability of Alitretinoin for Chronic Hand*	Non-interventional observational open study	680 patients	Patients with severe chronic hand eczema (CHE) unresponsive to potent topical	Max 24 weeks	*Investigation of effectiveness and tolerability of alitretinoin, and collection of structured data under*	333 (49%) patients completed treatment ahead of schedule (45% stated “clearance of hand eczema”). 57% of	NS 272 patients completed	*inclusion criteria: - Disease duration ≥ 3 months or > 2 flares within the

Eczema Under Daily Practice Conditions: Results of the TOCCATA Open Study Comprising 680 Patients	(TOCCATA) Intervention: oral alitretinoin (Toctino®, 30 or 10 mg daily)		corticosteroids during routine medical practice* Stratification at baseline morphology: Vesicular/pompholyx, hyperkeratotic rhagadiform and fingertip.		*daily dermatological practice conditions.* Subtypes of hand eczema defined according to the German guidelines "Guideline on the management of hand eczema" after the PGA for definition of severity of HE, helped by a validated photographic guide. Overall assessment of effectiveness and tolerability by patient	patients achieved a PGA rating of "clear" or "almost clear" hands with a continuous increase in response observed during the treatment course. Slightly higher response rates (61%) were observed for patients rated PGA-moderate at the beginning and slightly lower rates (53%) for patients rated PGA-severe at baseline. Total of 298 ADR were recorded in 23% of the 680 patients with headache as the most frequent one (7.5%) followed by increased blood triglycerides (4.9%) and increased blood cholesterol (3.8%). Serious adverse drug reactions were documented in only four (0.6%) patients (lymphatic oedema, paranoia, recto-sigmoiditis and soft-tissue swelling).	treatment ahead of schedule other than clearance of HE (Reasons: patient decision, Insufficient efficacy, AE /ADR (n=42), lab. value change, patient did not return, other)	last 12months - pretreatment with topical corticosteroids - no long-lasting healing under adequate topical treatment - no other active severe skin diseases or acute skin infections dominating the clinical picture From visit T3 onwards (week 12), treatment could be stopped if patient showed total clearance. Level B because of large study group, clear inclusion criteria, long follow up. Comparative in dose, but no placebo.
Dirschka 2010 *An open-label study assessing the safety and*	Open-label study Intervention: oral alitretinoin	249 patients	CHE ≥ 6 months, aged 18–75 years old and unresponsive to standard treatment	24 weeks	NS They evaluated safety and efficacy of alitretinoin: adverse events, Physician's	Alitretinoin was well tolerated when given for up to 24 weeks. Dose reduction occurred in 16.5% of patients. Dose interruption was required	190 (76.3%) completed the full 24 weeks	

efficacy of alitretinoin in patients with severe chronic hand eczema unresponsive to topical corticosteroids	30mg 1dd for up to 24 weeks		including topical corticosteroids.		Global Assessment (response defined as a rating of 'clear' or 'almost clear', and partial response defined as 'clear' almost clear' or 'mild disease'), modified Total Lesion Symptom Score (mTLSS), Patient's Global Assessment, extent of disease, intensity of pain and pruritus as determined by visual analogue scale (VAS) and a categorical scale for pruritus.	for 15.7% of patients, most commonly for headache. AEs and laboratory changes comprised effects typical of the retinoid class. A PGA response of 'clear' or 'almost clear' was reported for 46.6% of patients. Results of VAS and categorical assessments of pruritus provided supporting evidence of efficacy, and treatment was assessed as providing meaningful benefits to patients.	59 (23.7%) were prematurely withdrawn from the study	
Dua 2013 *Our experience with alitretinoin in the management of patients with chronic, severe hand eczema*	Prospective study <u>Intervention:</u> alitretinoin 30mg or 10mg for 4 to 36 weeks	28 patients	Adults with severe, chronic hand eczema unresponsive to potent topical corticosteroids.	4-36 weeks	PGA 'clear' or 'almost clear', time to relapse, adverse events.	A satisfactory response (PGA score 'clear' or 'almost clear' hands): 20 patients (71%) within 24 weeks. 12 patients relapsed (60%) with an average time to relapse of 12 weeks (range1 week–9 months). 6 patients started a second course of alitretinoin. Side-effects were reported by 18 (64%); most common was headache (16 patients, 57%). 2 patients dis-continued treatment due to side-effects (neck pain; rash) and one patient died of unrelated causes.	?	Poster only

Khoury 2016 *Alitretinoin for the treatment of patients with severe refractory chronic hand eczema*	Prospective study <u>Intervention:</u> alitretinoin (dosage and treatment time unknown)	28 patients	Unresponsive patients with CHE.	-	Not specified. They evaluated disease severity (reported by the patient) and the Dermatology Life Quality Index (DLQI).	68% of the patients reported symptoms alleviation after alitretinoin treatment (11% complete remission, 25% pronounced improvement and 32% moderate improvement). Adverse events were tolerated and self-reported adherence was satisfactory.	-	Poster only
Kumari 2016 *Impact of systemic alitretinoin treatment on skin barrier gene and protein expression in patients with chronic hand eczema**	Prospective study <u>Intervention</u>: alitretinoin 30 mg daily up to 27 weeks	15 patients	Patients with CHE who are refractory to topical corticosteroids.	Up to 27 weeks	Not specified. They evaluated disease severity (assessed using the clinical score 'Manuscore' and the transepidermal water loss (TEWL))	Patients showed a significant reduction in the clinical score (P = 0.0068) after therapy with alitretinoin whereas the TEWL values before and after treatment remained stable. Analysis of skin biopsies before treatment showed a significant increase in Ki-67-positive cells in the suprabasal layer and a dysregulated expression of various skin barrier genes, such as claudin 1, loricrin, filaggrin and cytokeratin 10, which were normalized after treatment. TSLP was significantly upregulated in patients with CHE and also normalized after alitretinoin treatment and	?	

						negatively correlated with filaggrin.		
Lynde 2012 *Extended treatment with oral alitretinoin for patients with chronic hand eczema not fully responding to initial treatment*	Open-label trial <u>Intervention</u>: alitretinoin 30 mg once daily	243 patients 3 groups: - alitretinoin 30/30 (n=69) - alitretinoin 10/30 (n=117) - placebo/ 30 (n=57)	Patients with severe chronic hand eczema (CHE) who did not fully respond to initial treatment in the BACH study: rated as 'mild', 'moderate' or 'severe' eczema according to the Physician's Global Assessment (PGA).	12-24 weeks.	The primary endpoint was the PGA (using a five-point, predefined scale to rate CHE severity from 'clear' to 'severe'). Secondary endpoints included the Patient's Global Assessment (PaGA), Modified Total Lesion Symptom Score (mTLSS), extent of disease and time to response.	By the end of the follow-on study, the PGA response rate to the subsequent course of alitretinoin 30 mg was 50% and 39% in patients treated previously in BACH with 10 or 30 mg per day, respectively, and 51% in patients who previously received placebo in BACH. Alitretinoin was well tolerated, and no significant late-arising toxicities were seen.	?	
Politiek 2016a *Alitretinoin and acitretin in severe chronic hand eczema; results from a retrospective daily practice study*	Retrospective study <u>Intervention</u>: Alitretinoin 30 mg/day and acitretin 20–30 mg daily Treatment period is 12–24 weeks depending on the response.	204 patients	Adult patients having a clinical diagnosis of chronic hand eczema (≥3 months), treated with acitretin between 01-01-1994 and 01-08-2015 and/or alitretinoin between 01-09-2013 and 01-08- 2015.	-	Effectiveness of treatment according to the clustered physician's global assessment (PGA) score (PGA1: good effect of treatment, PGA2: moderate effect, PGA3: failure of treatment), median time to relapse (time until retreatment or time until severe signs and symptoms of hand eczema reoccurred).	95 patients were treated with alitretinoin and 109 patients with acitretin. The main reasons for discontinuation were adverse events and cleared hand eczema, 29.5 and 27.4% in alitretinoin versus 43.1 and 23.9% in acitretin. Patients with hyperkeratotic hand eczema had most often a good effect of treatment: 68.3% in alitretinoin and 50.7% in acitretin treatment. The drug survival rates of	-	

						alitretinoin and acitretin after 12, 24, 36, and 52 weeks were 69.3, 45.1, 19.6, 7.0% and 74.3, 45.5, 33.8, 23.2%, respectively.		
Thaci 2016 *Effectiveness of alitretinoin in severe chronic hand eczema: PASSION, a real-world observational study*	Prospective study <u>Intervention</u>: alitretinoin 30mg once-daily alitretinoin for 24 weeks under standard daily practise conditions	631 patients	Diagnosis of severe CHE with no limit to the duration of disease, scheduled for treatment with alitretinoin.	Up to 24 weeks	Effectiveness assessed by Physician Global Assessment (PGA), QoL Assessment (EQ-5D) and work impairment. Tolerability and safety were assessed by adverse event (AE) monitoring.	Of the 631 patients enrolled, 29.8% achieved a PGA rating of clear/almost clear at week 24. Mean (standard deviation) EQ-5D utility and EQ-5D visual analogue scale scores at baseline were 0.76 (0.25) and 53.6 (23.55), respectively, and increased to 0.94 (0.12) and 80.8 (19.23) at Week 24, indicating improved QoL. At baseline, 49.4%/29.1% of patients reported strong/very strong workplace impairment, respectively, and decreased to 8.5%/1.4%, respectively, at Week 24. AEs were reported in 116 (18.4%) patients. No new safety signals were observed.	In total, 279 (44.2%) patients dropped out before Week 24.	

Azathioprine

Author (year of publication)	Study design	Patients (N)	Inclusion criteria	Follow-up	Outcome measures	Results	Lost to follow-up	Comments

Oosterhaven 2017 *Azathioprine treatment and drug survival in patients with chronic hand eczema – results from daily practice*	Retrospective study Intervention: azathioprine start 50 to 125 mg/day and at discontinuation 50 to 250 mg/day	30 patients	Adult patients with severe chronic hand eczema who were treated with azathioprine (between January 2000 and 16 December 2015). Patients with concomitant mild atopic dermatitis on other body areas were also included.	-	Drug survival	17/30 patients discontinued treatment prior to the 3-month assessment: 15 because of adverse effects. 5/13 patients discontinued treatment at some point following the 3-month assessment, because of insufficient responsiveness or non-responsiveness. These patients all had moderate to good improvement of their hand eczema. 1 patient discontinued treatment with azathioprine because of remission after 13.6 months. 2 patients, who had used azathioprine for approximately 3 and 6 years, were still treated at data lock. Their hand eczema was in full remission at that time.	-	

Ciclosporine

Author (year of publication)	Study design	Patients (N)	Inclusion criteria	Follow-up	Outcome measures	Results	Lost to follow-up	Comments
Christoffers 2015 *Drug survival of cyclosporine in the*	Retrospective study Intervention: cyclosporine	102 patients	HE patients who were treated with cyclosporine between 01-06-1999 and 01-06-	-	Drug survival cyclosporine, effectiveness of treatment according to the clustered PGA score: PGA 1: good effect (>50% improvement);	The median drug survival rate was 0.86 years (10.3 months). The overall drug survival rate after 6 months, 1, 2 and 3 years were 61.7%, 45.2%, 18.6% and 13.9%	-	Confounders were selected after backward selection

treatment of hand eczema: a multicentre, daily use study	Two dosages: - step-up (start with ≤3.5 mg/kg/day and gradually increased in weeks to months to max 5mg/kg) -step-down regime (start with >3.5–5 mg/kg and slowly tapered).		2014 in two Dutch university hospitals		PGA 2: moderate effect (<50% improvement); PGA 3: failure of treatment (no improvement or worse).	respectively. Main reasons for discontinuation were adverse events, especially early in treatment, and ineffectiveness. After 3 months, a good response to treatment was recorded in 62.9% of the patients.		
Granlund 1998 *Long-term follow-up of eczema patients treated with cyclosporine*	Long-term follow-up of 3 previous studies; for CHE RCT data of Granlund 1996 were used	N = 75 patients in 3 different studies on cyclosporine treatment of eczematous diseases: CHE: N=27 CAD: N=6 (in abstract, 4 in Methods ?)	Aged 18-70 years with hand eczema (histopathologically confirmed) for at least 6 months causing significant disability and is unresponsive to conventional treatment i.e. topical steroids and/or PUVA	1 year	As described in primary study: Efficacy: -disease activity score (scale of 0-3 per symptom such as erythema, infiltration, excoriation etc). -extent of disease in % - use of emolliens - Sleep and itch disturbance (VAS 0-100) -Overall assessment of efficacy (assessed by both patients and observer on a scale from 1-5, 1=very goodt, 5=none)	After 1 year: Disease activity: N=20 better, N=1 unchanged, N=6 worse. Itch: N=17 less, N=2 unchanged, N=8 worse. See figure 2 (page 43): Disease activity changed from baseline 13 to 6 at 1 year post treatment (p<0.001). Itch from > 5 to around 2 (p<0.001) Relapse: - 21 patients were in remission		Long term follow up study with CHE data of Granlund 1996

		AD: N=42			Treatment success was defined as a 50% decrease of symptom severity score compared to baseline disease severity.	- on sick leave: N=7 compared to N=13 (p<0.01) - No patient had been treated with cyclosporine during the follow-up period.		

Methotrexaat en Acitretine

Author (year of publication)	Study design	Patients (N)	Inclusion criteria	Follow-up	Outcome measures	Results	Lost to follow-up	Comments
O'Shea 2015 *Methotrexate versus Acitretin in the Treatment of Chronic Hand Dermatitis*	Retrospective study Intervention: Methotrexate and acitretin Also reviewed for usage of other types of systemic therapy (oral prednisone and dapson)	83 charts	Patients with CHD (from 2007-2013)	-	Efficacy (response to therapy was graded on a 3-point scale: 0 corresponded to no change or worsening from baseline; 1 corresponded to improvement of fissuring, erythema, and/or desquamation; and 2 corresponded to resolution of erythema, fissuring, and desquamation, or presence of only mild desquamation or erythema) and safety of methotrexate and acitretin	29 patients received systemic therapy, of which 17 (26.5%) were treated systemically with acitretin and/or methotrexate. 4/17 patients received courses of both acitretin and methotrexate independently after failing the alternative treatment course. At 6 months, acitretin achieved clearance/almost clearance in 44% of patients, compared to 0% of those treated with methotrexate. At 12 months, 100% of patients treated with acitretin achieved clearance/almost clearance compared to 40% of patients treated with methotrexate. Adverse effects were minimal and as expected.	-	
Politiek 2016b *Drug survival of*	Retrospective study	42 patients	Adult patients with chronic hand eczema, treated	-	Effectiveness (according to PGA) and drug survival of methotrexate.	After 8–12 weeks of treatment, 36.8% of the patients showed a good effect of treatment	4	

methotrexate treatment in hand eczema patients: results from a retrospective daily practice study	Intervention: methotrexate 5–10 mg per week and maximum dose 20 mg/ week		with methotrexate between 1997 and December 2014.			(47.6% in hyperkeratotic hand eczema compared to 25.0% in the non-hyperkeratotic subgroup (not statistically significant)). The median survival duration was 5.2 (95% CI: 2.5–7.9) months. After 6 months, 1 year and 2 years, treatment was discontinued in 33.3%, 46.9% and 46.9% of the patients due to ineffectiveness, and in 19.2%, 34.4% and 34.4% due to adverse events.		

Abbreviations: HE, hand eczema; PGA, physician's global assessment.

Bijlage 4: Exclusietabellen

Voorlichting en begeleiding

Artikel	Reden van exclusie
Bauer 2002	Geen geschikte uitkomstmaten (primaire preventie)
Dulon 2009	Geen geschikte uitkomstmaat (primaire preventie, geen handeczeem patiënten)
Mygind 2006	Geen geschikte uitkomstmaten (primaire preventie)
Van Gils 2011	Geen geschikte uitkomstmaten (primaire preventie)
Van der Meer 2014	Geen geschikte uitkomstmaat (primaire preventie, geen handeczeem patiënten)
Van der Meer 2016	Geen geschikte uitkomstmaat (gaat over primaire preventie, geen handeczeem patiënten)

Handschoenen

Artikel	Reden van exclusie
Geen studies geëxcludeerd	

Indifferente middelen

Artikel	Reden van exclusie
Bauer 2002	Pseudo-gerandomiseerd
Bauer 2010	Review
Boroujeni 2017	Geen geschikte uitkomstmaten, pseudo-gerandomiseerd
Draelos 2009	Geen geschikte uitkomstmaten
Held 1999	Pseudo-gerandomiseerd
Jungbauer 2004	Review
Mygind 2006	Geen geschikte uitkomstmaten
Schempp 2012	Geen geschikte uitkomstmaten
Schliemann 2013	Geen geschikte uitkomstmaten
Schliemann 2014	Geen geschikte uitkomstmaten
Williams, 2010	Geen geschikte uitkomstmaten
Winker, 2009	Geen geschikte uitkomstmaten
Yousefi 2012	Geen geschikte uitkomstmaten

Lokale therapie

Artikel	Reden van exclusie
Agarwal 2013	Geen geschikte uitkomstmaat

Chia Yu 2009	Geen geschikte uitkomstmaat (samenstelling lotion niet bekend)
Frederiksson 1975	Pseudo-gerandomiseerd, geen geschikte uitkomstmaat
Gola 2015	Geen fulltext beschikbaar
Kemper 1998	Pseudo-gerandomiseerd, geen geschikte uitkomstmaat
Kucharekova 2003	Pseudo-gerandomiseerd, geen geschikte uitkomstmaat (emmoliëns)
Nebus 2015	Geen fulltext beschikbaar
Said 2010	Geen geschikte uitkomstmaat
Schliemann 2008	Pseudo-gerandomiseerd (geen controle-groep)

Fototherapie

Artikel	Reden van exclusie
Cartwright 1987	Geen geschikte uitkomstmaten (radiotherapie)
Fairris 1984	Geen geschikte uitkomstmaten (radiotherapie)
Fairris 1985	Geen geschikte uitkomstmaten (radiotherapie)
King 1984	Geen geschikte uitkomstmaten (radiotherapie)
Lindelöf 1987	Geen geschikte uitkomstmaten (radiotherapie)
Sheehan-Dare 1989	Geen geschikte uitkomstmaten (radiotherapie)
Wolska 2012	Geen fulltext beschikbaar

Systemische therapie

Artikel	Reden van exclusie
Al Dhubaibi 2018	Review
Bissonnette 2009	Zelfde populatie gebruikt als Ruzicka 2008, studie naar herbehandeling met alitretinoïne
Garritsen 2017	Geen geschikte uitkomstmaten
Granlund 1998	Pseudo-gerandomiseerd

Bijlage 5: Kennislacunes

Aan de hand van beoordeling van het huidige wetenschappelijk bewijs, signaleert de werkgroep een aantal kennislacunes over de behandeling van Handeczeem. Er is gebrekkig bewijs over:

1. De effectiviteit van systemische middelen bij de behandeling van patiënten met chronisch handeczeem.

2. De effectiviteit van handschoenen als secundaire preventie bij patiënten met handeczeem.

3. De effectiviteit van fototherapie bij de behandeling van handeczeem.

Ad 1.
Met uitzondering van alitretinoïne, zijn er maar heel weinig goede vergelijkende studies over systemische medicatie. Ook zijn er onvoldoende gegevens over de optimale dosering en behandelduur van systemische middelen en eventuele combinaties voor patiënten met handeczeem. Verder zijn er weinig lange termijn gegevens bekend over het gebruik van alle systemische middelen. Ten slotte zijn nog geen literatuurgegevens over de effectiviteit van de biological Dupilumab bij handeczeem.

Ad 2.
Er zijn weinig vergelijkende studies over de preventieve werking van handschoenen bij patiënten met handeczeem. Tevens komt in de literatuur niet naar voren of een bepaald type handschoen de voorkeur heeft.

Ad 3.
Aangaande behandeling middels fototherapie ontbreken vergelijkende studies en studies over fototherapie voor de behandeling van kinderen met handeczeem.