實證醫學月會

皮膚科

R1 林曉郁

臨床情境

- 一位四十九歲女性，診斷為異位性皮膚炎已兩年，長期使用口服抗組織胺藥物，外用類固醇及普特皮藥膏治療，仍無法獲得良好控制，又擔心長期使用類固醇的副作用，最近聽朋友說有一種自費免疫抑制劑的藥物(Cyclosporine)可以使用，因此病患來到門診尋求醫師諮詢。

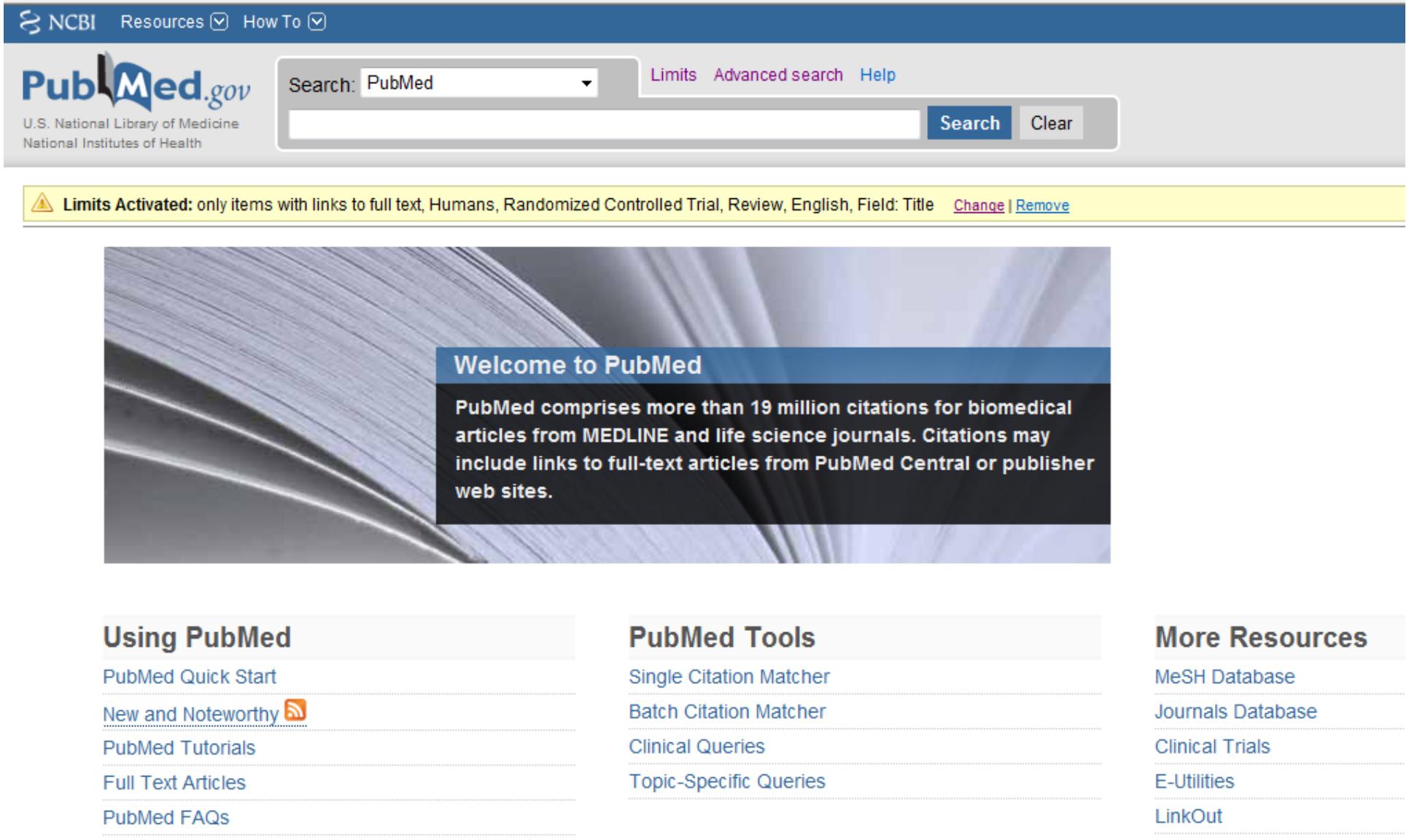
臨床問題

- 對於難治型的嚴重異位性皮膚炎, 免疫抑制劑(Cyclosporine)的使用是否有治療效果?

Asking Answerable Clinical Question (PICO)

- P (Patient/Problem)：atopic dermatitis
- I (Intervention)：cyclosporine
- C (Comparison)：placebo / conventional treatment
- O (Outcome)：decrease in severity of disease

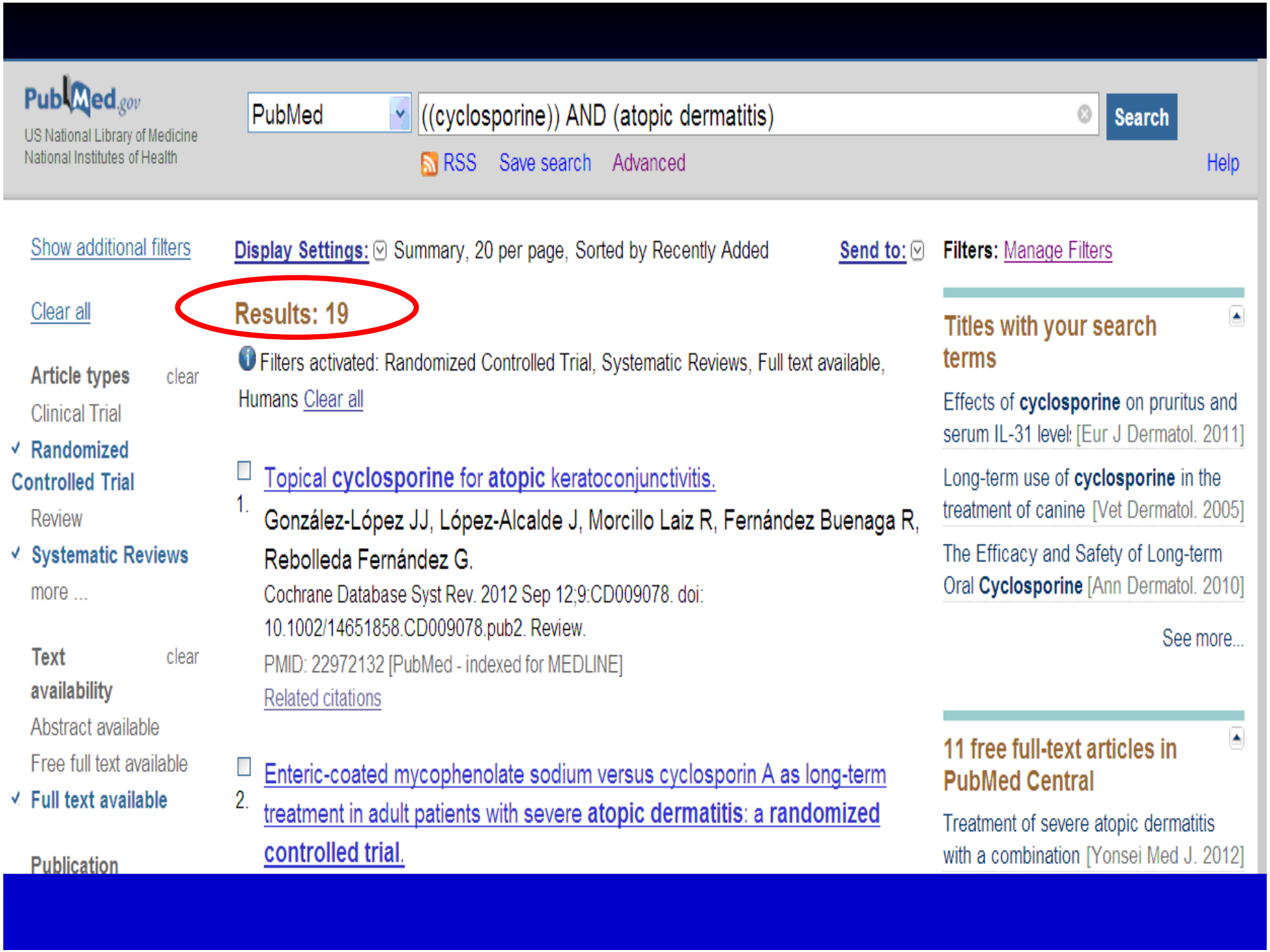
Search for Evidence



Search Strategy

- **Key words**
  - atopic dermatitis
  - Cyclosporine

- **Limitation**
  - Article type: RCT, systemic reviews
  - Species: human
  - English, full text available


PubMed.gov
US National Library of Medicine
National Institutes of Health
PubMed
((cyclosporine)) AND (atopic dermatitis)
Search
RSS
Save search
Advanced
Help
Show additional filters
Clear all
Article types clear
Clinical Trial
Randomized Controlled Trial
Review
Systematic Reviews
more ...
Text availability clear
Abstract available
Free full text available
Full text available
Publication
Display Settings: Summary, 20 per page, Sorted by Recently Added
Send to:
Filters: Manage Filters
Results: 19
Filters activated: Randomized Controlled Trial, Systematic Reviews, Full text available, Humans Clear all
1. Topical cyclosporine for atopic keratoconjunctivitis.
González-López JJ, López-Alcalde J, Morcillo Laiz R, Fernández Buenaga R, Rebolleda Fernández G.
Cochrane Database Syst Rev. 2012 Sep 12;9:CD009078. doi: 10.1002/14651858.CD009078.pub2. Review.
PMID: 22972132 [PubMed - indexed for MEDLINE]
Related citations
2. Enteric-coated mycophenolate sodium versus cyclosporin A as long-term treatment in adult patients with severe atopic dermatitis: a randomized controlled trial.
Titles with your search terms
Effects of cyclosporine on pruritus and serum IL-31 level [Eur J Dermatol. 2011]
Long-term use of cyclosporine in the treatment of canine [Vet Dermatol. 2005]
The Efficacy and Safety of Long-term Oral Cyclosporine [Ann Dermatol. 2010]
See more...
11 free full-text articles in PubMed Central
Treatment of severe atopic dermatitis with a combination [Yonsei Med J. 2012]

Related citations

5. Guidelines for management of **atopic dermatitis**.

Saeki H, Furue M, Furukawa F, Hide M, Ohtsuki M, Katayama I, Sasaki R, Suto H, Takehara K; COMMITTEE for GUIDELINES for the MANAGEMENT of **ATOPIC DERMATITIS** of JAPANESE DERMATOLOGICAL ASSOCIATION.

J Dermatol. 2009 Oct;36(10):563-77. doi: 10.1111/j.1346-8138.2009.00706.x.

PMID: 19785716 [PubMed - indexed for MEDLINE]

Related citations

6. Cyclosporin in the treatment of patients with **atopic** eczema - a **systematic** review and meta-analysis.

Schmitt J, Schmitt N, Meurer M.

J Eur Acad Dermatol Venereol. 2007 May;21(5):606-19. Review.

PMID: 17447974 [PubMed - indexed for MEDLINE]

Related citations

7. Systemic treatment of severe **atopic** eczema: a **systematic** review.

Schmitt J, Schäkel K, Schmitt N, Meurer M.

Recent activity

Turn Off Clear

- Comparing tacrolimus ointment and oral cyclosporine in adult pat PubMed
- Cyclosporin greatly improves the quality of life of adults with se PubMed
- ((cyclosporine)) AND (atopic dermatitis) AND ((Randomize PubMed
- ((cyclosporine)) AND (atopic dermatitis) AND ((Randomize PubMed
- ((cyclosporine)) AND (atopic dermatitis) AND ((Review[pty PubMed

See more...

Search Results

1a ▪ ***Cyclosporin in the treatment of patients with atopic eczema - a systematic review and meta-analysis.***

- J Eur Acad Dermatol Venereol. 2007 May;21(5):606-19.

1b ▪ ***Cyclosporin greatly improves the quality of life of adults with severe atopic dermatitis.***

- Br. J. Dermatology 1993 Oct;129(4):422-30.
- A randomized, double-blind, placebo-controlled trial

2b ▪ ***Long-term efficacy and safety of cyclosporin in severe adult atopic dermatitis.***

- Br. J. Dermatology 1997 Jan;136(1):76-81.
- A one year Cohort study

2b ▪ ***Cyclosporin in atopic dermatitis: a multicentre placebo-controlled study.***

- Br. J. Dermatology 1994 May;130(5):634-40.
- A double-blind, placebo-controlled trial

The Evidence Pyramid

THE COCHRANE COLLABORATION

Meta-analysis
Forest plot

Meta - analysis

Hierarchy of evidence that arranges study designs by their susceptibility to bias.

Grade of Recommendation	Level of Evidence	Therapy
[A]	**1a**	**Systemic review of RCTs**
	1b	**Single RCT**
	1c	**‘All-or-none’**
[B]	**2a**	**Systemic review of cohort studies**
	2b	**Cohort study or poor RCT**
	2c	**‘Outcomes’ research**
	3a	**Systemic review of case-control studies**
	3b	**Case-control study**
[C]	**4**	**Case series**
[D]	**5**	**Expert opinion, physiology, bench research**

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REVIEW ARTICLE

Cyclosporin in the treatment of patients with atopic eczema – a systematic review and meta-analysis

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Keywords
atopic dermatitis, cyclosporin, immunosuppression, meta-analysis, systemic treatment

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accepted13 July 2006

Abstract

Objective To systematically assess the effectiveness of systemic cyclosporin in patients with severe atopic eczema.

Study design Systematic review and meta-analysis of controlled and uncontrolled trials. Electronic (MEDLINE, Cochrane databases) and hand search of published work. Independent standardized assessment of eligibility and data abstraction by two reviewers.

Methods For the qualitative review data on study design, study population, methodology, results, tolerability and methodological quality was independently extracted by two reviewers. Qualitatively homogeneous studies were pooled using a random-effects model. The mean relative change in objective disease severity was chosen as the main outcome measure for the quantitative

Journal of European Academy of Dermatology and Venereology
2007,21, 606– 619

Introduction

- Atopic eczema (AE) is a common inflammatory skin disorder that affects 20% of children and 10% of adults.
- Most common treatment included emollients, topical corticosteroids (TCS) and topical calcineurin inhibitors (TCI).
- **Cyclosporin**
  - inhibits the transcription of IL-2 and several other cytokines.
  - inhibition of the activation of T cells, the key role in the pathogenesis of atopic dermatitis.

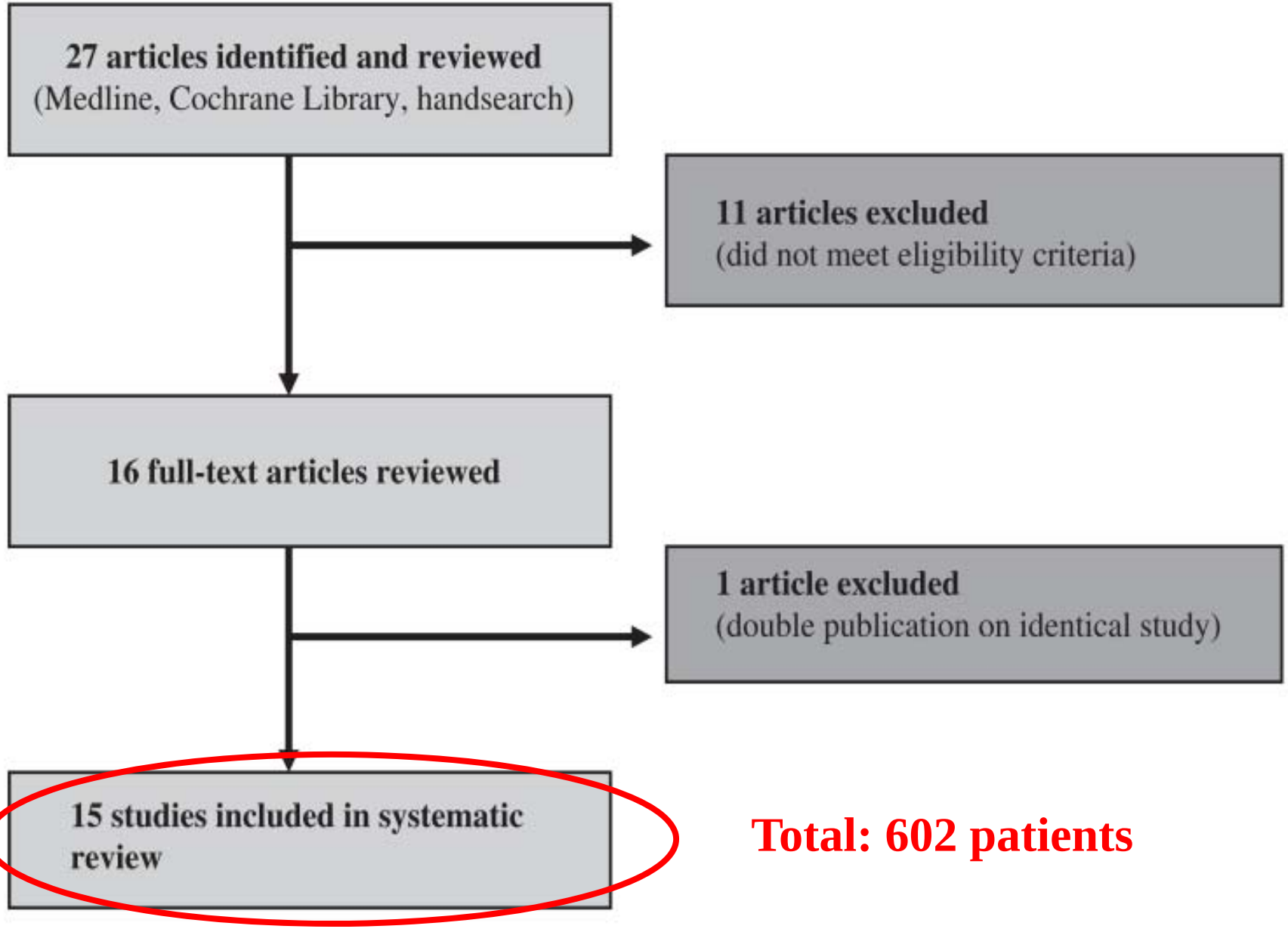
The Study

Objective

- To systematically assess the effectiveness of systemic cyclosporin in patients with severe atopic eczema.

Study Design

- Systematic review and meta-analysis of controlled and uncontrolled trials.
- Electronic (MEDLINE, Cochrane databases) and hand search of published work. (~Aug. 2005)
- Independent standardized assessment of eligibility and data abstraction by two reviewers.


27 articles identified and reviewed
(Medline, Cochrane Library, handsearch)
11 articles excluded
(did not meet eligibility criteria)
16 full-text articles reviewed
1 article excluded
(double publication on identical study)
15 studies included in systematic review
Total: 602 patients

Reference	Country	Study design	Comparators	Number of participants
Sowden *et al*. 1991[27]	U.K.	double-blind crossover RCT*	CyA vs. placebo	*n* = 33
Munro *et al*. 1994[30]	U.K.	double-blind crossover RCT	CyA vs. placebo	*n* = 24
van Joost *et al*. 1994[33]	Netherlands	double-blind parallel group RCT	CyA vs. placebo	*n* = 46
Zonneveld *et al*. 1996[28]	Netherlands	open label RCT	two dosages of CyA	*n* = 78
Zurbriggen *et al*. 1999[29]	Switzerland	double-blind crossover RCT	two formulations of CyA (Neoral® vs. Sandimmun®)	*n* = 14
Harper *et al*. 2000[23]	U.K.	open label RCT	continuous vs. intermittent long-term treatment	*n* = 43
Czech *et al*. 2000[26]	Germany	double-blind parallel group RCT	two dosages of CyA	*n* = 106
Pacor *et al*. 2004[34]	Italy	double-blind parallel group RCT	CyA vs. topical tacrolimus 0.1%	*n* = 30
Granlund *et al*. 1995[32]	Finland	open uncontrolled study	Not applicable	*n* = 43
Berth-Jones *et al*. 1996[25]	U.K.	open uncontrolled study	Not applicable	*n* = 27
Berth-Jones *et al*. 1997[24]	U.K.	open uncontrolled study	Not applicable	*n* = 100
Atakan and Erdem 1998[37]	Turkey	open uncontrolled study	Not applicable	*n* = 23
Caproni *et al*. 2000[36]	Italy	open uncontrolled study	Not applicable	*n* = 10
Bunikowski *et al*. 2001[31]	Germany	open uncontrolled study	Not applicable	*n* = 10
Pacor *et al*. 2001[35]	Italy	open uncontrolled study	Not applicable	*n* = 15

Method

Data extraction and Quality assessment

- methodology and results
- adequate case definition,
  definition of eligibility criteria,
  description of study population,
  randomization and blinding,
  use of validated outcomes,
  adequet follow-up date,
  conduct of intention-to-treat analysis
- Good: $\geq$ 6 Moderate: 4-5 Poor: $\leq$ 3

Table 3 Summary of quality criteria and rating of overall study quality

Reference	Clear case definiton[18,19]	Clearly defined eligibility criteria	Adequate description of study population	Double blind treatment	Validated outcome	Follow-up rate > 80%	Intention-to treat analysis	Overall study quality*
Sowden *et al*. 1991[27]	Yes	Yes	Yes	Yes	No	No	No	Moderate
Munro *et al*. 1994[30]	No	No	No	Yes	No	No	No	Poor
van Joost *et al*. 1994[33]	Yes	Yes	Yes	Yes	Yes	No	Yes	Good
Zonneveld *et al*. 1996[28]	Yes	Yes	No	No	No	No	No	Poor
Zurbriggen *et al*. 1999[29]	Yes	No	No	Yes	No	Yes	No	Poor
Harper *et al*. 2000[23]	No	Yes	No	No	Yes	No	No	Poor
Czech *et al*. 2000[26]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Good
Pacor *et al*. 2004[34]	Yes	No	Yes	Yes	Yes	Yes	No	Moderate
Granlund *et al*. 1995[32]	Yes	No	Yes	No	No	Yes	No	Poor
Berth-Jones *et al*. 1996[25]	No	Yes	Yes	No	Yes	Yes	No	Moderate
Berth-Jones *et al*. 1997[24]	No	Yes	No	No	Yes	No	No	Poor
Atakan & Erdem 1998,[37]	Yes	No	No	No	Yes	Yes	No	Poor
Caproni *et al*. 2000[36]	Yes	Yes	No	No	Yes	Yes	No	Moderate
Bunikowski *et al*. 2001[31]	Yes	Yes	No	No	Yes	Yes	No	Moderate
Pacor *et al*. 2001[35]	Yes	Yes	No	No	No	Yes	No	Poor

Method

Quantitative methods

- **Primary Outcome**

  relative change from mean clinical severity at baseline to mean clinical severity after 6–8 weeks of treatment.

- **The dose–response relationship**
  - meta-analysis for mean relative effectiveness after 2 weeks of cyclosporin treatment.
  - initial cyclosporin dose < 3 mg/kg (BW) vs. >3 mg/kg.

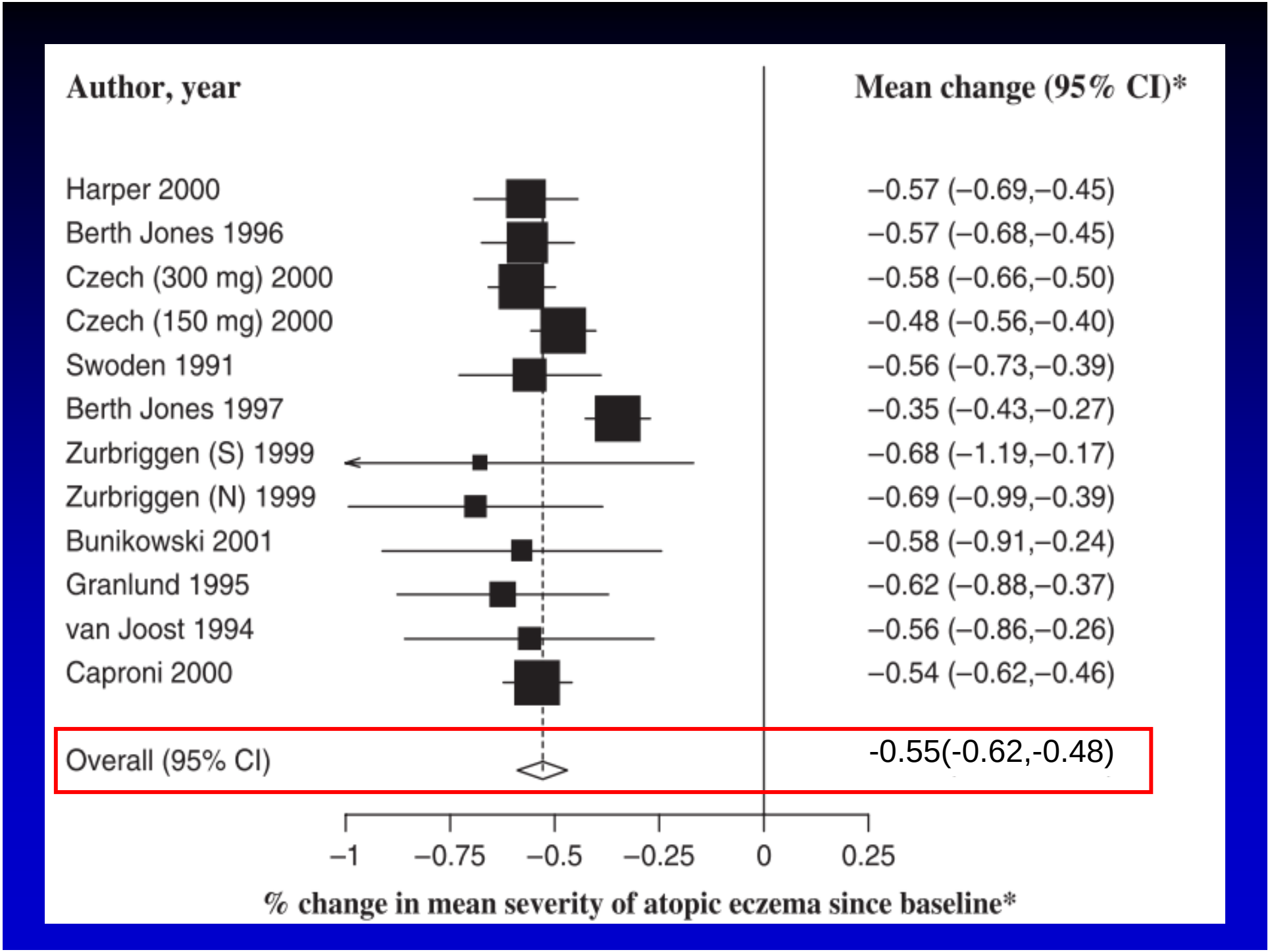
	Treatment characteristics				Results	
Reference	Duration of cyclosporin treatment	Initial dose	Allowed dose adjustment	Concurrent treatment	Relative improvement compared to baseline	Comparative efficacy
Sowden *et al.* 1991[27]	8 weeks	5 mg/kg BW‡	None	Topical steroids	56% reduction in mean severity score	Mean severity score with CyA vs. placebo: 16.5 vs. 40.5; $P < 0.01$
Munro *et al.* 1994[30]	8 weeks	5 mg/kg BW	None	Topical steroids	About 90% reduction in mean extent	Mean extent after CyA vs. placebo: 2% BSA vs. 14% BSA; $P < 0.01$
van Joost *et al.* 1994[33]	6 weeks	5 mg/kg BW	None	Antihistamines	55% reduction in mean severity score	4% increase in mean severity score in placebo group; significant superiority of CyA; $P < 0.05$
Zonneveld *et al.* 1996[28]	1 years	3 mg/kg BW vs. 5 mg/kg BW	After 2 weeks adjustment of 1 mg/kg every other week	Topical steroids, antibiotics, antihistamines	After 2 weeks: 46% vs. 29% reduction in mean severity score in high- vs. low-dose group; $P = 0.05$	After 1 year: 70% vs. 60% of patients in high- vs. low-dose group rated overall efficacy as good or very good; $P > 0.05$
Zurbriggen *et al.* 1999[29]	8 weeks	4–4.5 mg/kg BW	None	Topical steroids	After 8 weeks: 70% reduction in mean severity score in both groups; $P > 0.05$	After 2 weeks: Significant improvement in Neoral-treated group, but not in Sandimmun-treated group
Harper *et al.* 2000[23]	12 weeks short course vs. 1 years continuous	5 mg/kg BW	After 4 weeks 25% dose reduction per month	Topical steroids	After 12 : weeks 50% reduction in mean SASSAD	After 1 year: 42% vs. 56% mean SASSAD reduction after shourt couse vs. contiunous therapy; $P > 0.05$
Czech *et al.* 2000[26]	8 weeks	150 mg vs. 300 mg	50% dose reduction after 2 weeks	Topical steroids, antibiotics, antihistamines	After 2 weeks: 45% vs. 33% reduction in mean severity in high- vs. low-dose group; $P < 0.05$	After 8 weeks: 58% vs. 48% reduction in mean severity in high- vs. low-dose group; $P > 0.05$
Pacor *et al.* 2004[34]	6 weeks	3 mg/kg BW	None	Antihistamines	88% reduction in mean SCORAD	89% reduction in mean SCORAD in tacrolimus group; no difference

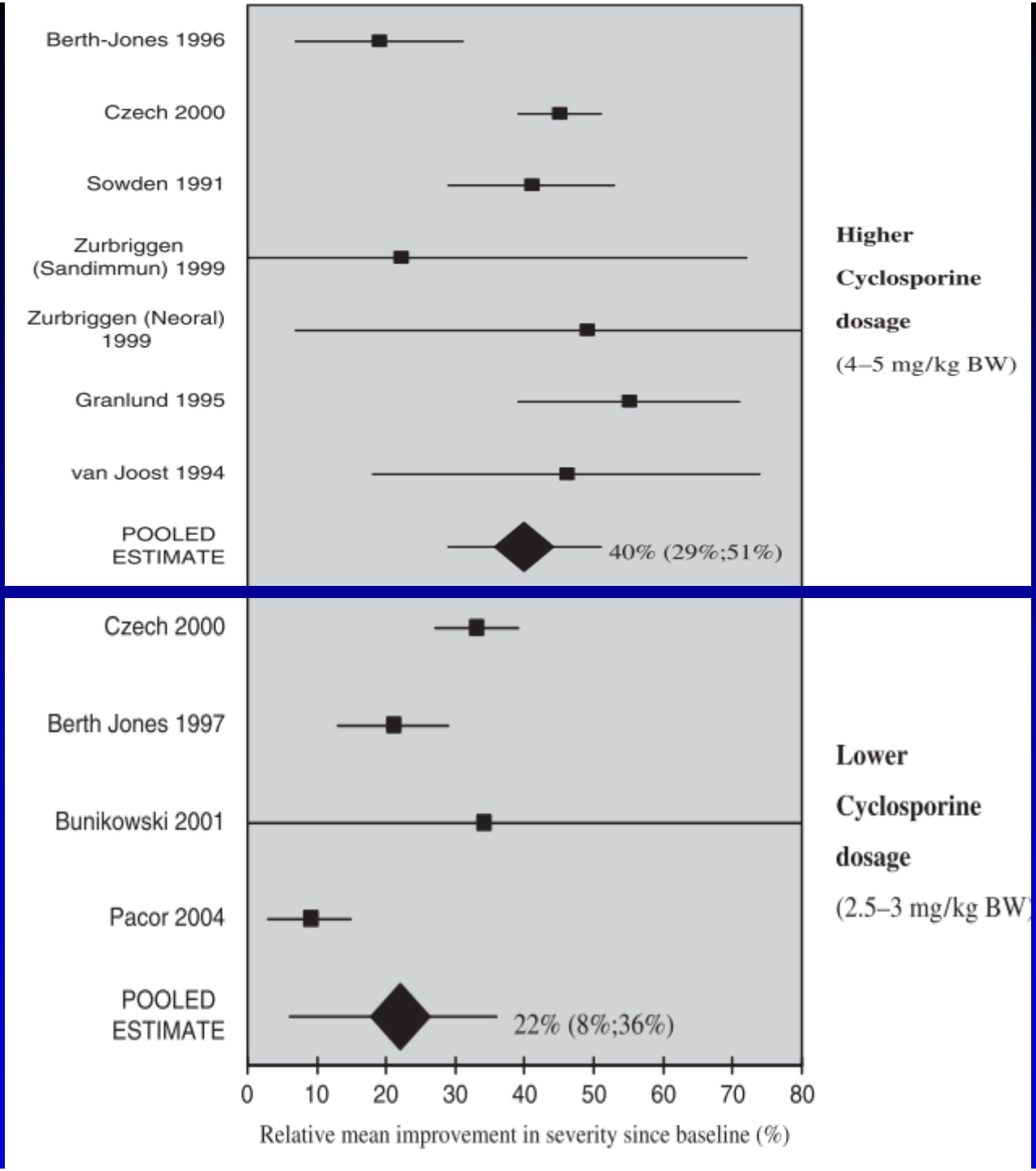
	Treatment characteristics				Results
Reference	Duration of cyclosporin treatment	Initial dose	Allowed dose adjustment	Concurrent treatment	Relative improvement compared to baseline
Granlund *et al.* 1995[32]	6 weeks	5 mg/kg BW	None	1%hydrocortisone ointment	53% reduction in mean severity score
Berth-Jones *et al.* 1996[25]	6 weeks	5 mg/kg BW	None	Topical steroids, antihistamines	57% reduction in mean SASSAD
Berth-Jones *et al.* 1997[24]	48 weeks	2.5 mg/kg BW	After 8 weeks adjustments to minimum effective levels	Topical steroids, antihistamines	39% reduction in mean SASSAD
Atakan and Erdem 1998[37]	10 weeks	3 mg/kg BW	Stepwise dose increase up to 5 mg/kg	Topical steroids	90% reduction in mean SCORAD
Caproni *et al.* 2000[36]	6 weeks	5 mg/kg BW	None	Not reported	54% reduction in mean Costa's Index
Bunikowski *et al.* 2001[31]	8 weeks	2.5 mg/kg BW	After 2 weeks, 1 mg/kg change every other week	Topical steroids	58% reduction in mean SCORAD
Pacor *et al.* 2001[35]	8 weeks	5 mg/kg BW	Not reported	Not reported	About 90% reduction in mean extent score

Results

Results

- The relative effectiveness appeared homogeneous across studies.
  - all studies found a decrease in mean severity of AE after cyclosporin treatment.
- In terms of comparative efficacy, cyclosporin was superior to placebo in all placebo-controlled RCTs.
- In comparing different dosing regimens of cyclosporin, higher initial dose consistently led to more rapid response after 2 weeks of treatment.
  - after 2 weeks, the mean benefit was about 40% at this dose.


Author, year
Mean change (95% CI)*
Harper 2000
Berth Jones 1996
Czech (300 mg) 2000
Czech (150 mg) 2000
Swoden 1991
Berth Jones 1997
Zurbriggen (S) 1999
Zurbriggen (N) 1999
Bunikowski 2001
Granlund 1995
van Joost 1994
Caproni 2000
−0.57 (−0.69,−0.45)
−0.57 (−0.68,−0.45)
−0.58 (−0.66,−0.50)
−0.48 (−0.56,−0.40)
−0.56 (−0.73,−0.39)
−0.35 (−0.43,−0.27)
−0.68 (−1.19,−0.17)
−0.69 (−0.99,−0.39)
−0.58 (−0.91,−0.24)
−0.62 (−0.88,−0.37)
−0.56 (−0.86,−0.26)
−0.54 (−0.62,−0.46)
Overall (95% CI)
-0.55(-0.62,-0.48)
−1
−0.75
−0.5
−0.25
0
0.25
% change in mean severity of atopic eczema since baseline*


Berth-Jones 1996
Czech 2000
Sowden 1991
Zurbriggen (Sandimmun) 1999
Zurbriggen (Neoral) 1999
Granlund 1995
van Joost 1994
POOLED ESTIMATE
40% (29%;51%)
Higher Cyclosporine dosage
(4–5 mg/kg BW)
Czech 2000
Berth Jones 1997
Bunikowski 2001
Pacor 2004
POOLED ESTIMATE
22% (8%;36%)
Lower Cyclosporine dosage
(2.5–3 mg/kg BW)
0
10
20
30
40
50
60
70
80
Relative mean improvement in severity since baseline (%)

Results

- Long-term effectiveness was evaluated in three studies, each with a follow-up time of approximately 1 year. The mean relative improvement was about 50% in each study.

- Health-related quality of life (HRQL) was assessed in three studies, and consistently found significant improvements in HRQL.

Results

- The likelihood of adverse drug reaction (ADR) increased by cyclosporine dosage.
- Withdrawals from treatment due to adverse events were also more likely in patients with higher initial cyclosporin dosages.

Table 4 Adverse events and withdrawals due to adverse events in patients treated with cyclosporin for atopic eczema

Reference	Age range of study population	Initial dose (mg/kg BW††)	Creatinine increase¶ (n/percent per month of treatment)	Hypertention‡‡ (n/percent per month of treatment)	Infections (n/percent per month of treatment)	Gastrointestinal symptom§ (n/percent per month of treatment)	Paraesthesia (n/percent per month of treatment)	Headache (n/percent per month of treatment
Sowden *et al*. 1991[27]	17–56 years	5	0	0	3/4.5%	15/22.7%	8/12.1%	3/4.5%
Munro *et al*. 1994[30]	19–48 years	5	2/4.2%	0	5/10.4%	1/2.1%	7/14.6%	0
van Joost *et al*. 1994[33]	17–68 years	5	not reported	2/5.8%	not reported	not reported	not reported	not reported
Zonneveld *et al*. 1996[28]	18–70 years	3 resp. 5	low-dose: 6/0.9% high-dose: 2/0.4%	low-dose: 4/0.9% high-dose: 7/1.5%	not reported	not reported	not reported	not reported
Zurbriggen *et al*. 1999[29]	20–64 years	4–4.5	not reported	not reported	not reported	not reported	not reported	not reported
Harper *et al*. 2000[23]	2–16 years	5	not reported	not reported	1/0.4%	7/2.8%	3/1.2%	2/0.8%
Czech *et al*. 2000[26]	18 years or older	fixed dosages: 150 mg vs. 300 mg†	low-dose: 2/1.9% high-dose: 4/3.8%	low-dose: 2/1.9%* high-dose: 1/0.9%*	not reported	low-dose: 6/5.6% high-dose: 8/7.4%	not reported	not reported
Pacor *et al*. 2004[34]	13–45 years	3	0	0	0	1/4.4%	0	3/13.3%
Granlund *et al*. 1995[32]	16–80 years	5	7/10.9%	1/1.6%	8/12.4%	26/40.3%	16/24.8%	8/12.4%
Berth-Jones *et al*. 1996[25]	2–16 years	5	0	0	3/7.4%	13/32.2%	2/4.9%	7/17.3%
Berth-Jones *et al*. 1997[24]	12 years or older	2.5	45/4.1%	5/0.5%	48/4.4%	66/6.0%	16/1.5%	26/2.4%
Atakam & Erdem 1998[37]	13–70 years	3.0	0	0	2/1.1%	4/2.3%	1/0.6%	1/0.6%
Caproni *et al*. 2000[36]	17–45 years	5	not reported	not reported	not reported	not reported	not reported	not reported
Bunikowski *et al*. 2001[31]	1–15 years	2.5	1/5.0%	0	not reported	not reported	not reported	not reported
Pacor *et al*. 2001[35]	35.5 years (median)	5	0	0	0	0	0	0
TOTAL (percent per month treatment)			high-dose§§: 2.8 low-dose§§: 2.0 children***: 2.5 adults†††: 3.2	high-dose: 1.2 low-dose: 0.6 children: 0.0 adults: 1.6	high-dose: 5.9 low-dose: 1.8 children: 3.9 children: 9.1	high-dose: 15.4 low-dose: 4.6 children: 17.5 adults: 18.1	high-dose: 9.6 low-dose: 0.7 children: 3.1 adults: 12.9	high-dose: 7.(low-dose: 5.4 adults: 9.1 adults: 5.8

Results

- The likelihood of adverse drug reaction (ADR) increased by cyclosporine dosage.
- Withdrawals from treatment due to adverse events were also more likely in patients with higher initial cyclosporin dosages.

Results

- By means of meta-regression, we did not detect any significant influence of
  - Study type (RCTs vs. Uncontrolled studies) (P = 0.63)
  - Inclusion of children (P = 0.91)
  - Overall study quality (P = 0.76)
  - Concomitant topical treatment with corticosteroids (P = 0.82).

Conclusions

- Short-term use of cyclosporin effectively decreases the severity of AE in patients inadequately controlled with conventional topical therapies.
  - Effectiveness is similar in adults and children
  - Tolerability might be better in children
- The mean clinical improvement in disease severity after 6–8 weeks of cyclosporin treatment is about 55%.
- Higher initial dosages (4–5 mg/kg) led to a more rapid response.
  - adjustments to the individual minimum effective levels are recommended according to the evidence available.

Conclusions

- However, due to uncertainty concerning rare ADRs with long latencies, close long-term monitoring is important in all patients treated with cyclosporin, particularly in children.

Apprasel（文獻評讀）

Answer	文獻試圖回答什麼問題？**Treatment effect**	是否回答我的問題？**yes**
Author	作者是誰，是否為這方面的專家? **yes**	有無利益衝突? **Not sure**
Method	**Systemic review** **RCT,cohort, case-control,** **case series**	**case report, expert opinion**
Patient	是否隨機取樣 **(randomization)** **not all of it**	取樣是否具代表性 **(representative) yes**
Intervention	是否有清楚的描述(Ascertain), 是否為臨床實際可行? yes	
Comparasion		
Outcome	是否有客觀雙盲的測量(MBO) not all of it	是否有統計學或臨床上的意義？**yes**
Time	是否清楚描述研究取樣、操作、結果測量的時間點，追蹤時間是否夠長? 有些study追蹤時間不夠久	

Apply (臨床應用)

- Q: 對於難治型的嚴重異位性皮膚炎, 免疫抑制劑(Cyclosporine)的使用是否有治療效果?

- A: 對於傳統外用類固醇或Tarcorlimus難以控制的嚴重異位性皮膚炎患者, 短期使用(6~8週)Cyclosporine 對於臨床症狀之改善確實有其助益, 但需定期追蹤藥物之副作用.

醫療現況	病人意願
對於部分難治型異位性皮膚炎患者,傳統外用類固醇或tarcrolimus確實難以提供良好療效,口服類固醇因有其副作用亦不適合長期使用	異位性皮膚炎為慢性皮膚疾病,亦容易反覆惡化,病人多半不堪其擾而希望並願意接受更方便有效的治療方法
生活品質	**社會經濟脈絡**
異位性皮膚炎為慢性皮膚疾病,長期並嚴重影響病人生活品質,cyclosporine之療效有其助益	Cyclosporine目前須自費使用,對病人來說經濟上可能會是一負擔

Audit（自我評估）

在「提出臨床問題」方面的自我評估

- 提出的問題是否具有臨床重要性？有
- 我是否明確的陳述了我的問題？
  - 我的foreground question 是否可以清楚的寫成PICO？可以
  - 我的background question是否包括what, when, how, who等字根？有
- 我是否清楚的知道自己問題的定位？（亦即可以定位自己的問題是屬於診斷上的、治療上的、預後上的或流行病學上的），並據以提出問題？知道
- 對於無法立刻回答的問題，我是否有任何方式將問題紀錄起來以備將來有空時再找答案？還沒有

在「搜尋最佳證據」方面的自我評估

- 我是否已盡全力搜尋？我盡力了…
- 我是否知道我的問題的最佳證據來源？知道
- 我是否從大量的資料庫來搜尋答案？ 是
- 我工作環境的軟硬體設備是否能支援我在遇到問題時進行立即的搜尋？ 能, 但PubMed有些無法閱讀全文
- 我是否在搜尋上愈來愈熟練了？是
- 我會使用「斷字」、布林邏輯、同義詞、MeSH term，限制 (limiters)等方法來搜尋？部份會
- 我的搜尋比起圖書館人員或其他對於提供病人最新最好醫療有熱情的同事如何？仍有許多地方要學習

Thank you