

Cochrane Systematic Reviews the best evidence

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Disclosures

- Consultancies
 - BMS, CSL Behring, Grifols, LFB, Merck, Novartis
- Co-ordinating editor
 - Cochrane Neuromuscular Disease Group
1998 - 2008
- President
 - EFNS 2010 - 2014

Learning objectives

To be able to explain

- Differences between systematic and non-systematic reviews
- Risk of bias
- Forest plots
- Risk ratios, odds ratios, numbers needed to treat
- How to access the Cochrane library

Hierarchy of evidence 1

Class I: Adequately powered randomized, controlled trial or systematic review with masked outcome assessment in representative population with

- a. randomization concealment
- b. primary outcome(s) clearly defined
- c. exclusion/inclusion criteria are clearly defined
- d. dropouts and crossovers accounted for and few
- e. baseline characteristics equivalent or appropriately adjusted

Hierarchy of evidence 2

Class I: Adequately powered randomized, controlled trial or systematic review with masked outcome assessment in representative population fulfilling a-e

Class II: Prospective matched-group cohort study in representative population with masked outcome assessment meeting a–e or a randomized trial in a representative population lacking one of a–e

Class III: All other controlled trials where outcome assessment is independent of patient treatment

Class IV: Uncontrolled studies, case series, case reports, or expert opinion

Bell's palsy steroids case report

Rothendler HH 1951 J Nerv Ment Dis 114 340

A woman woke with a complete facial palsy, was given cortisone 100 mg four times daily, and recovered in 7 days.

It is indeed difficult, **though tempting**, to draw a conclusion from a single satisfactory case.

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell 2003 BMJ 327 1459-61

What this study adds

No randomised controlled trials of parachute use have been undertaken

The basis for parachute use is purely observational, and its apparent efficacy could potentially be explained by a “healthy cohort” effect

Individuals who insist that all interventions need to be validated by a randomised controlled trial need to come down to earth with a bump



See also Glasziou 2007 BMJ 334 349

Scurvy: controlled trial

Lind J 1753 A Treatise of the scurvy

- a quart of cider
- 75 drops of vitriol elixir
- 6 spoons of vinegar
- half a pint of seawater
- three nutmegs
- two oranges and a lemon



Bell's palsy steroids randomised controlled trial

Taverner D 1954 Lancet 2 1052

26 patients with complete facial palsy randomised within 9 days after onset to cortisone starting dose 200 mg orally daily for 3 days, 100 mg daily for 4 days and 50 mg daily for 2 days or placebo

Randomised double blind

Concealed allocation

Balanced clinical features at baseline

Complete follow-up

Intention to treat analysis

Risk ratio 0.85 (0.21 – 3.38)

Developed denervation

Steroid

4/14

Control

4/12

Mean (range) days to recovery

63 (27 –105)

69 (18-157)⁹

In 1972 one of the 'fathers' of Evidence-Based Medicine, Archie Cochrane, said

"It is surely a great criticism of our profession that we have not organised a critical summary, by speciality or sub-speciality, updated periodically, of all relevant randomised controlled trials."



A history of the Cochrane Collaboration

1972 - Publication of Archie Cochrane's ['Effectiveness and Efficiency: random reflections on health services'](#), which drew attention to our collective ignorance about the effects of health care



1985-90 - International collaboration to prepare systematic reviews of controlled trials in pregnancy and childbirth



1992 - 'The Cochrane Centre' opens in Oxford, UK



1993 - Formal launch of The Cochrane Collaboration at the 1st Cochrane Colloquium, in Oxford, UK



1998 - Neuromuscular Diseases Group registered



2002 - The Cochrane Library free at the point of use to anyone with Internet access in England and for developing countries



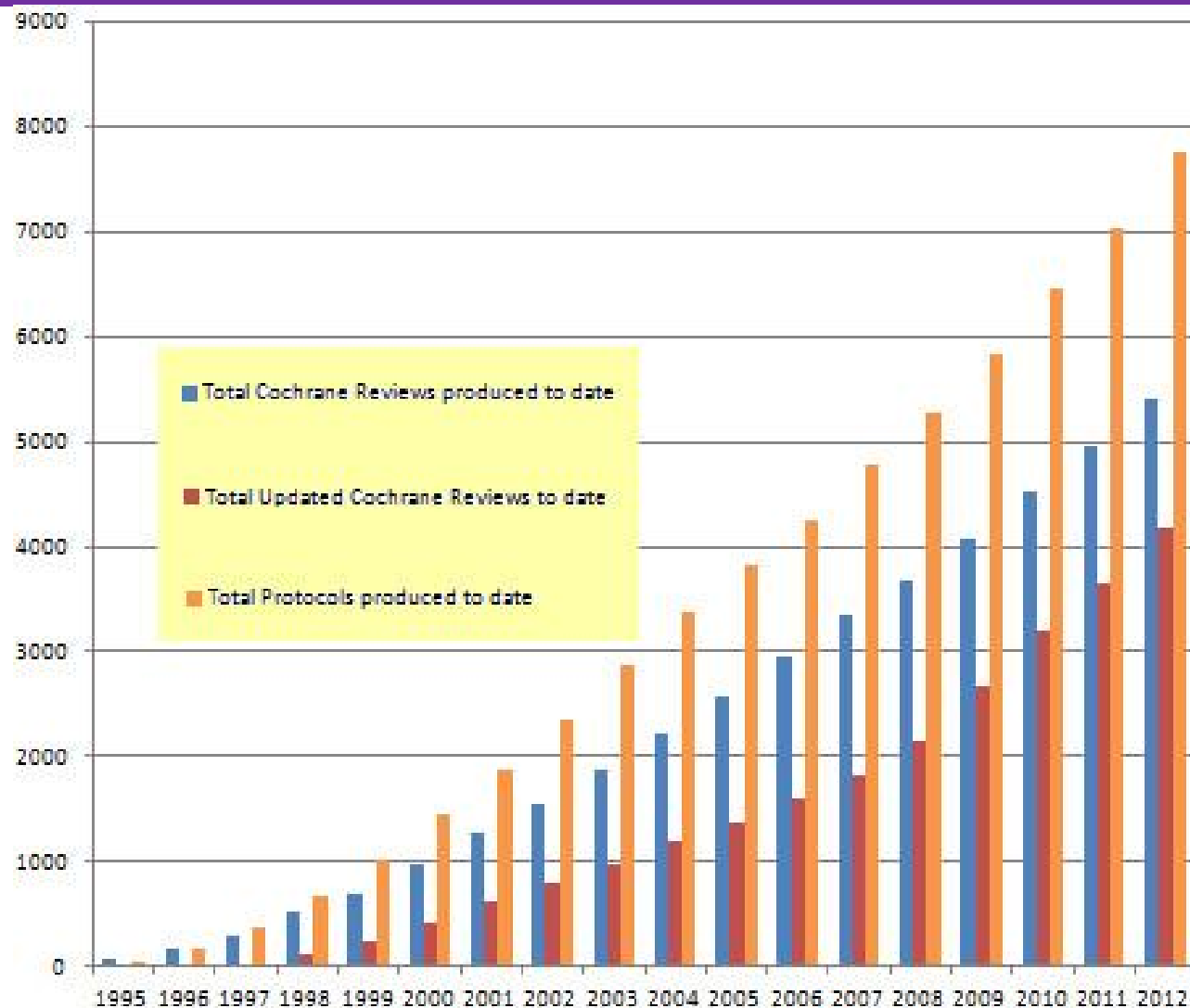
2012 - The number of Cochrane Reviews in the CDSR exceeds 5,000

The Cochrane Collaboration

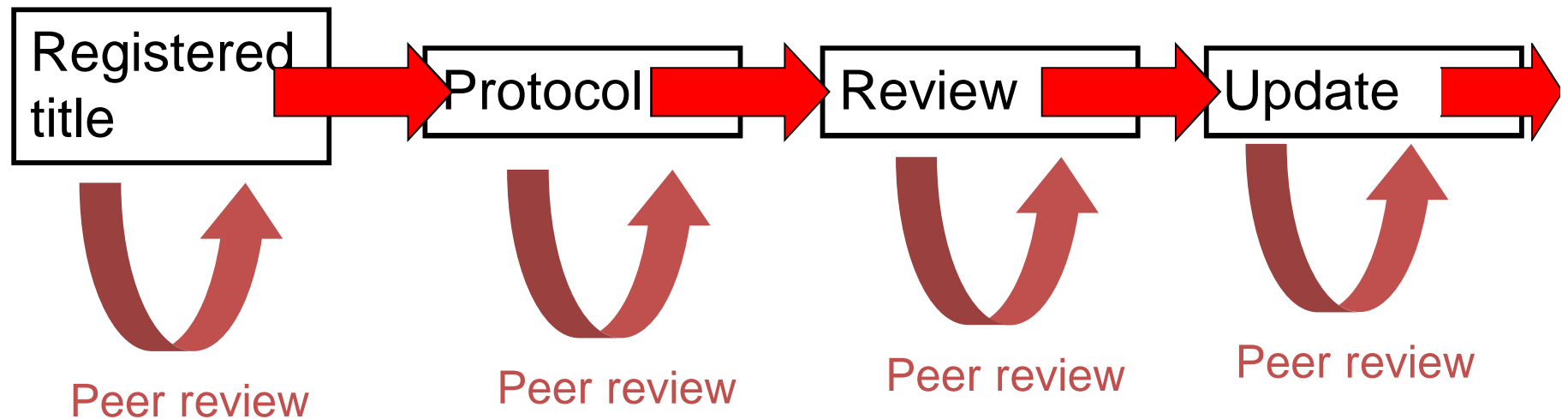
- International network of more than 28,000 people from over 100 countries.
- Over 5,000 Cochrane reviews so far, published online in the Cochrane Database of Systematic Reviews, part of *The Cochrane Library*.
- Each review takes hundreds of hours and a team of people to produce.
- Over 2,000 protocols for Cochrane Reviews available
- The latest estimate is that at least 10,000 Cochrane Reviews are needed to cover all healthcare interventions that have already been investigated in controlled trials
- These reviews will need to be updated at the rate of 5,000 per year.

[Source: <http://www.cochrane.org> (accessed 18 June 2013)]

Cochrane reviews progress



Preparing a Cochrane Review



Differences between a non-systematic review, systematic review and Cochrane review

Non-systematic review

- Overview
- Search not defined
- Selection of studies not defined

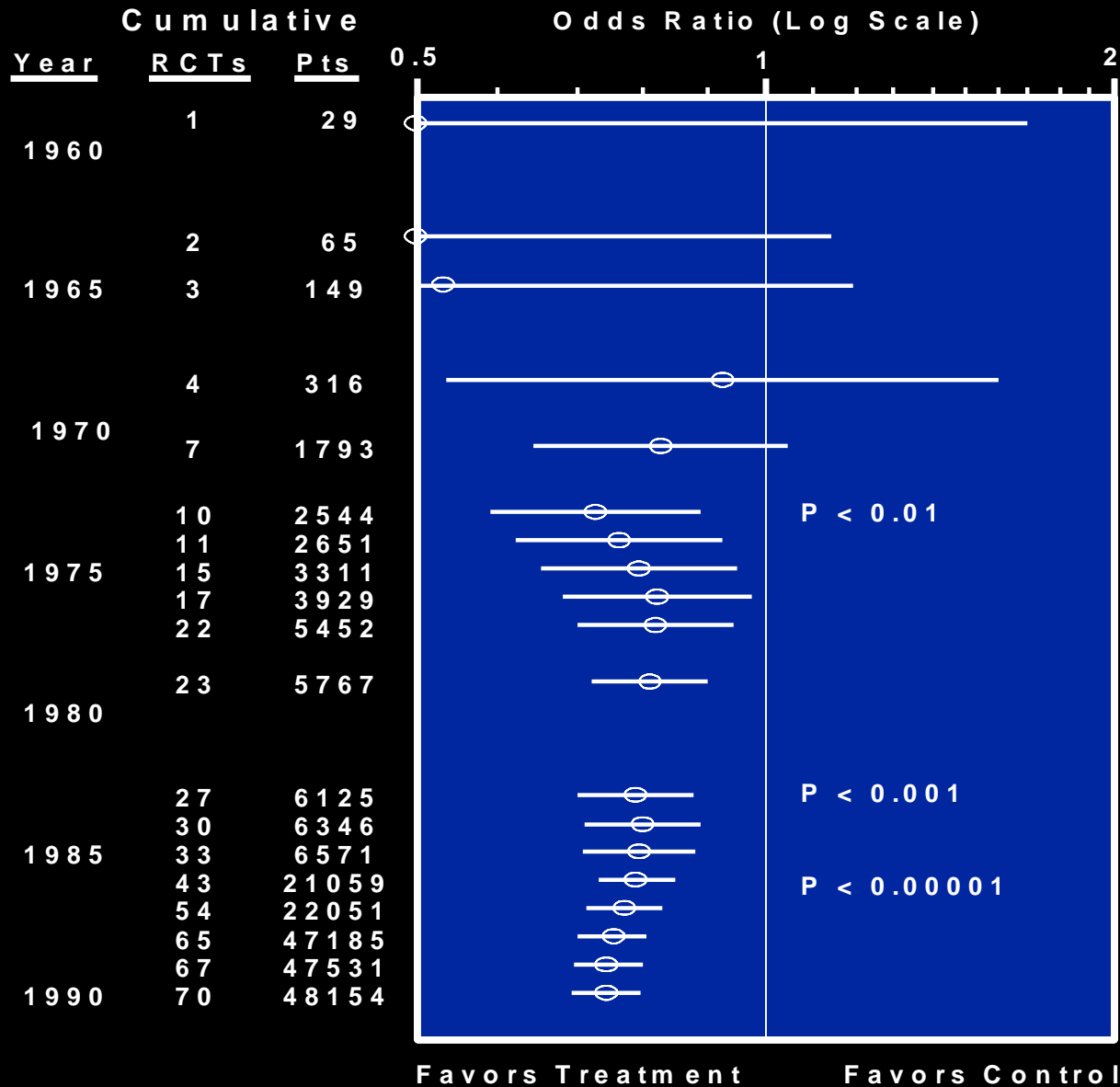
- Personal bias of the authors
- Paper publication

Cochrane systematic review

- Defined research question
- Search strategy
- Studies defined
 - type of study
 - participants
 - methodological quality
- Peer review
- Electronic publication
- Electronic criticisms
- Electronic updating

Cumulative meta-analysis

Thrombolytic Therapy for Acute MI



Textbook / Review Recommendations

Routine	Specific	Rare / New	Experimental	Not Mentioned
				21
				5
			1	10
			1	2
			2	8
				7
				8
	1			12
	1		8	4
	1		7	3
5	2		2	1
15	8			1
6	1			



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COCHRANE DATABASE OF SYSTEMATIC REVIEWS

Issue 6 of 12, June 2013

[\(Updated Daily\)](#) | [Contents](#)

BROWSE BY TOPICS

Note: numbers shown below are wrong and will be corrected soon.

[Anaesthesia & pain control](#) (1051)

[Blood disorders](#) (678)

SPECIAL COLLECTIONS



World day for Safety and Health at Work 2013



Preventing falls and fall-related injuries in older people



Tuberculosis

EDITORIALS

[Folic acid supplementation for rheumatoid arthritis patients on methotrexate: the good gets better](#)

Jasvinder Singh

[Calling time on intravenous immunoglobulin for preterm infants?](#)

Roger Soll

All Results (135)

Cochrane Reviews (7)

All

Review

Protocol

Other Reviews (18)

Trials (106)

Methods Studies (1)

Technology Assessments (2)

Economic Evaluations (1)

Cochrane Groups (0)

All

Current Issue

Me Methodology

Dg Diagnostic

Ov Overview

Cc Conclusions changed

Ns New search

Mc Major change

Up Update

Wd Withdrawn

Cm Comment

Cochrane Database of Systematic Reviews : Issue 7 of 12, July 2013

Issue [updated daily](#) throughout month

There are 7 results from 8026 records for your search on 'Bells palsy in title abstract keywords in Cochrane Reviews'

Sort by Relevance

[Select all](#) | [Export all](#) | [Export selected](#)

- [Hyperbaric oxygen therapy for Bell 's palsy](#)
N Julian Holland , Jonathan M Bernstein and John W Hamilton
February 2012
Review

- [Acupuncture for Bell 's palsy](#)
Ning Chen , Muke Zhou , Li He , Dong Zhou and N Li
August 2010
Ns **Review**

- [Surgical interventions for the early management of Bell 's palsy](#)
Kerrie McAllister , David Walker , Peter T Donnan and Iain Swan
February 2011
Review

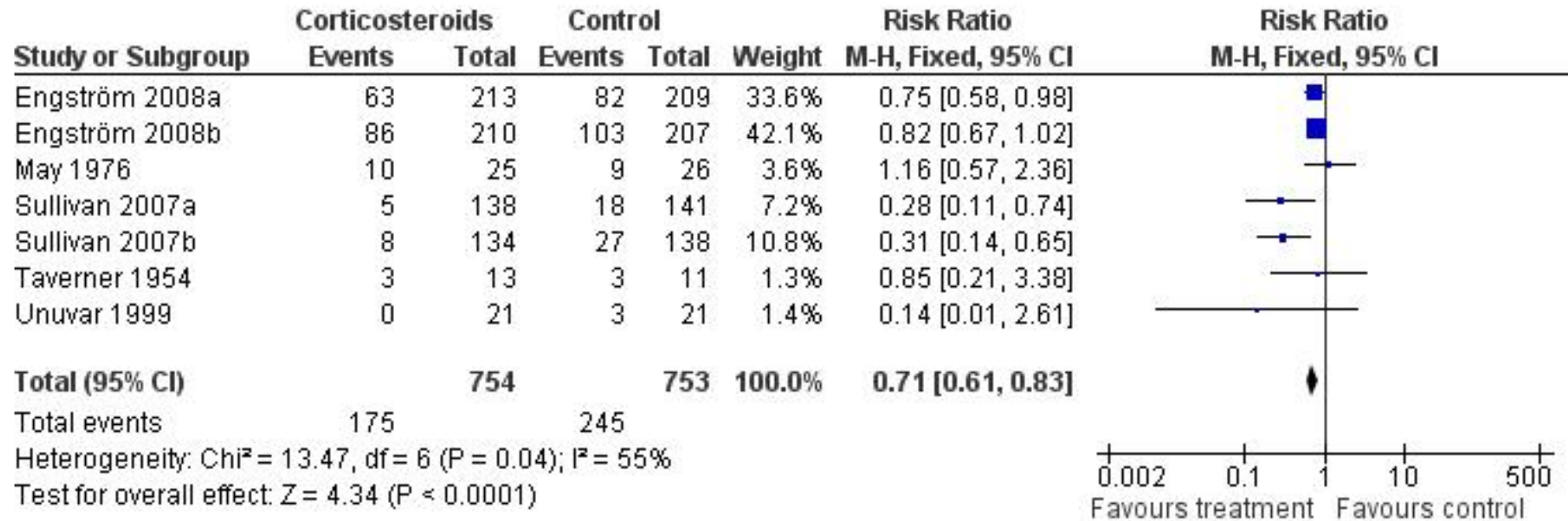
- [Antiviral treatment for Bell 's palsy \(idiopathic facial paralysis\)](#)
Pauline Lockhart , Fergus Daly , Marie Pitkethly , Natalia Comerford and Frank Sullivan
June 2010
Review

- [Corticosteroids for Bell 's palsy \(idiopathic facial paralysis\)](#)
Rodrigo A Salinas . Gonzalo Alvarez . Fergus Daly and Joaquim Ferreira

Bell's palsy steroids Cochrane review

Salinas et al 2010 *Cochrane Database of Systematic Reviews* Issue 2

Incomplete recovery after 6 months or more



Risk of bias

	Adequate sequence generation?	Allocation concealment?	Blinding?	Incomplete outcome data addressed?	Free of selective reporting?	Free of other bias?
Engström 2008a	+	+	+	-	+	-
Engström 2008b	+	+	+	-	+	-
Lagalla 2002	+	?	+	+	+	-
May 1976	+	+	+	-	+	+
Sullivan 2007a	+	+	+	+	+	+
Sullivan 2007b	+	+	+	+	+	+
Taverner 1954	+	+	+	+	+	-
Unuvar 1999	?	+	-	+	+	+

odds versus risk ratios

	+	-	Total
Placebo	a	b	a + b
Treatment	c	d	c + d

Odds ratio (OR) = $(a/b)/(c/d)$

Risk ratio (RR) = $[a/(a+b)]/[c/(c+d)]$

Relative risk reduction = $1 - RR$

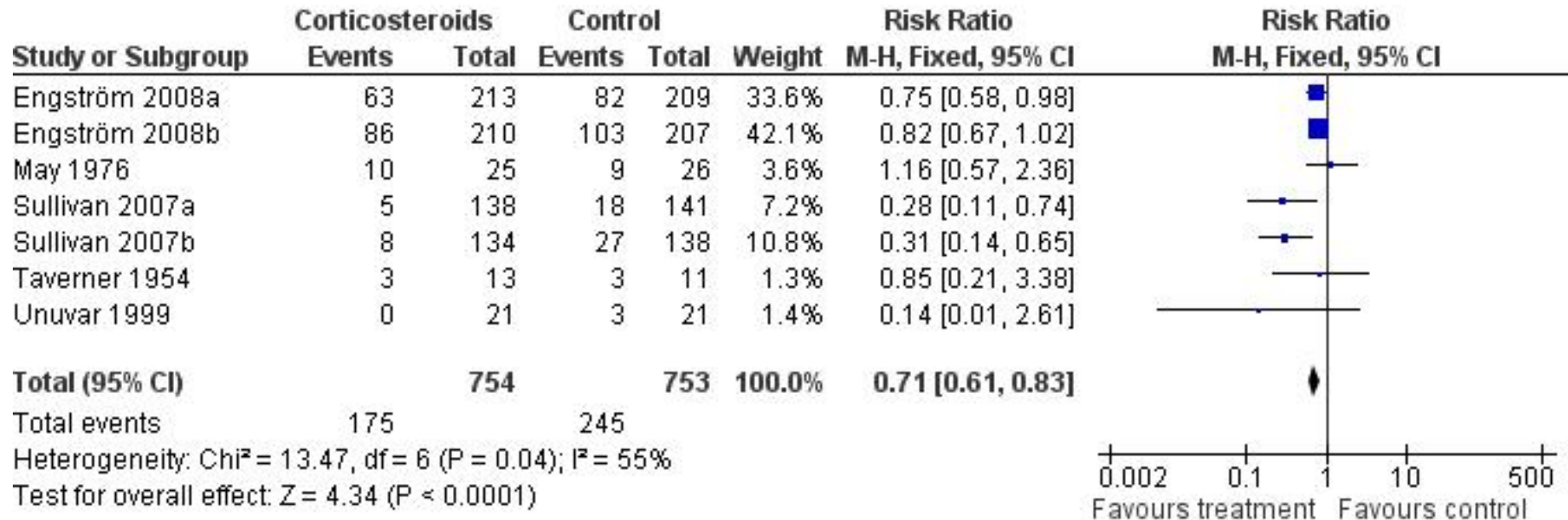
Absolute risk reduction (ARR) = $a/(a+b) - c/(c+d)$

Number needed to treat = $1/ARR$

Bell's palsy steroids Cochrane review

Salinas et al 2010 *Cochrane Database of Systematic Reviews* Issue 2

Incomplete recovery after 6 months or more



	steroid	control
Risk	23%	33%
Absolute risk reduction		10%
Number needed to treat		10

IVIg for CIDP

First trial IVIg for CIDP

Vermeulen et al 1993

4/15 IVIg

3/13 placebo r

Not signif

Last trial IVIg for CIDP

Hughes et al 2008

42/59 IVIg

20/58 placebo responded

p=0.0002 – statistically significant

Which trial do we believe?

Summary of findings

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Placebo	IVIg			
Significant improvement in disability scale used in original study Follow-up: 2 to 6 weeks	18 per 100	44 per 100 (32 to 62)	RR 2.4 (1.72 to 3.36)	269 ¹ (5 studies)	⊕⊕⊕⊕ high

CIDP Treatment

Overall 70% patients respond to Rx in short term

Corticosteroids for chronic inflammatory demyelinating
Polyradiculoneuropathy 2002 Updated 2007 and 2012

Man Mohan Mehndiratta¹, Richard AC Hughes²

Authors' conclusions

A single randomised controlled trial with 35 participants provided weak evidence to support the conclusion from non-randomised studies that oral corticosteroids reduce impairment in CIDP. Corticosteroids are known to have serious long-term side effects. The long-term risk and benefits have not been adequately studied.

[NB worsening may occur in motor CIDP]



Plasma exchange for chronic inflammatory demyelinating
Polyradiculoneuropathy 2004 updated 2010

Man Mohan Mehndiratta¹, Richard AC Hughes², Puneet Agarwal³

Authors' conclusions

Moderate to high quality evidence from two small trials [47 patients] showed that PEx provides significant short-term improvement in disability, clinical impairment and motor nerve conduction velocity in CIDP but rapid deterioration may occur afterwards. Adverse eventsare not uncommon.



Intravenous immunoglobulin for chronic inflammatory
demyelinating polyradiculoneuropathy 2004 Updated 2010

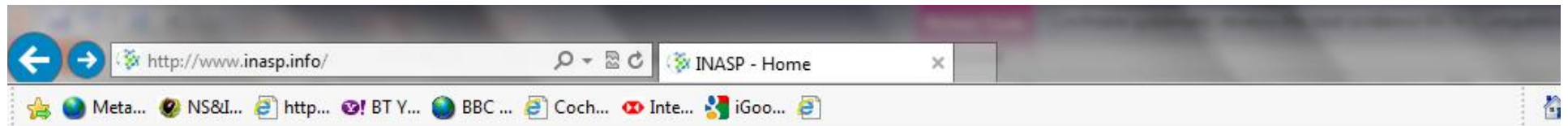
F Eftimov¹, JB Winer², M Vermeulen³, R de Haan⁴, I vanSchaik¹

Authors' conclusions

The evidence shows that IVIG improves disability for at least two to six weeks compared with placebo, with a number needed to treat of 3.00..... it has similar efficacy to plasma exchange and oral prednisolone. In one large trial, benefit of IVIg persisted for 24 and possibly 48 weeks.



Access to the Cochrane library



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publication

Investigating capacity to use evidence

Time for a more objective approach? This reflective paper discusses why so many capacity building programmes fail to thoroughly assess skills gaps and determine what capacity is required before starting their activities.

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