



POST POLIO SYNDROME – a challenge of today

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Treatment for postpolio syndrome: results from a Cochrane Review

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Treatment for postpolio syndrome (Review)

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<http://www.thecochranelibrary.com>



Treatment for postpolio syndrome (Review)
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Title registration

Review Protocol

Cochrane Review

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> FACTS-2-PPS

> nieuwsbrieven en publicaties



Program

1 **Background**

2 **Methods**

3 **Results**

4 **Discussion**

5 **Questions**

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2 **Methods**

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5 **Questions**

1 Background

- European Federation of Neurological Societies (EFNS) task force: clinical guidelines 2006 (revision 2011)

European Journal of Neurology 2006, **13**: 795–801

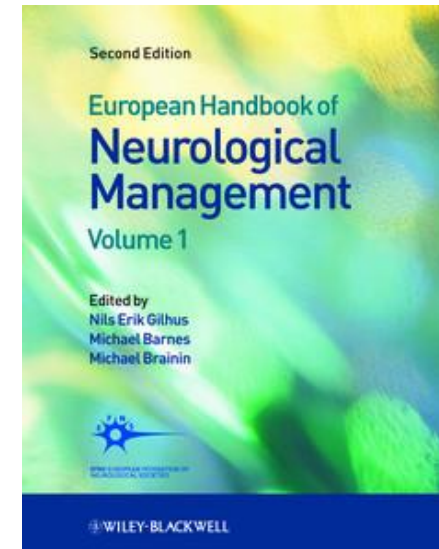
doi:10.1111/j.1468-1331.2006.01385.x

EFNS TASK FORCE/CME ARTICLE

EFNS guideline on diagnosis and management of post-polio syndrome.
Report of an EFNS task force

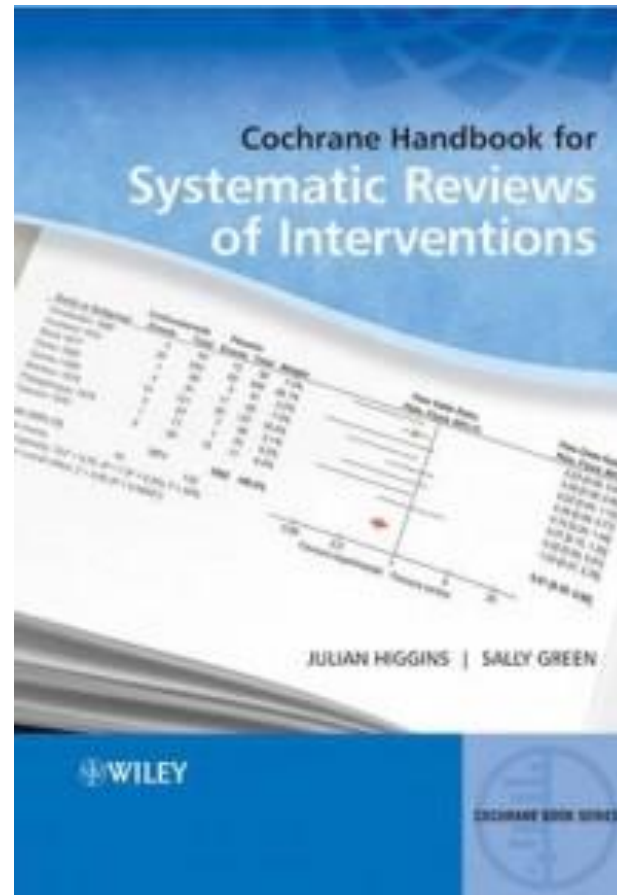
E. Farbu^{a,1}, N. E. Gilhus^a, M. P. Barnes^b, K. Borg^c, M. de Visser^d, A. Driessen^e, R. Howard^f,
F. Nollet^g, J. Opara^h and E. Stalberg^j

- No systematic review



1 Background

- Systematic methods
- Transparent
 - Inclusion, exclusion criteria
 - Search strategies
 - Methods of analyses
 - Interpretation of results (GRADE)
 - Presentation of results (SoF-tables)



1 Background

- Objective

To systematically review the evidence from **randomised** and **quasi-randomised** controlled trials for the effect of any **pharmacological** or **non-pharmacological** treatment for **PPS**, compared to **placebo**, **usual care** or **no treatment**.

Program

1 Background

2 **Methods**

3 Results

4 Discussion

5 Questions

2 Methods

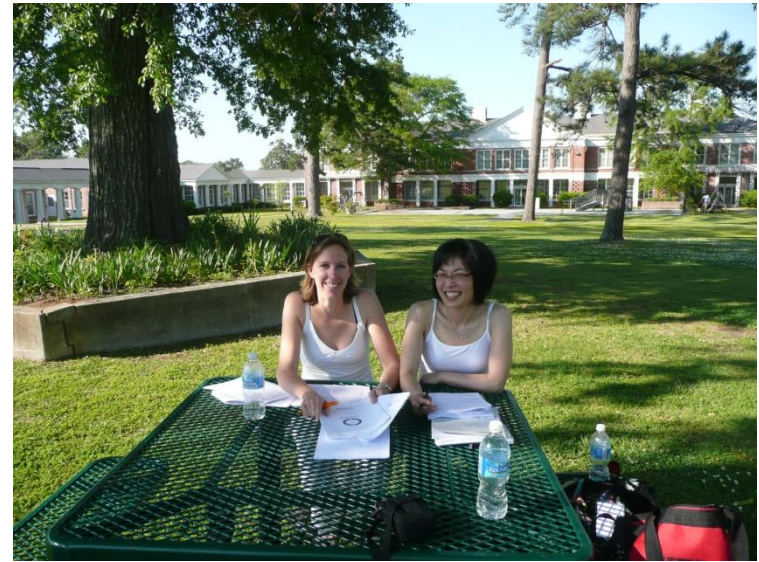
- Criteria for considering studies for the review:
 - **Study design:** RCT or quasi RCT
 - **Patients:** diagnosis of PPS (broad criteria)
 - **Intervention:** any form of pharmacological or non-pharmacological treatment
 - **Comparison:** placebo, usual care or no treatment
 - **Outcomes:** activity limitations, muscle strength, muscle endurance, fatigue, pain, adverse events

2 Methods

- Search methods for identification of studies
 - Databases: Cochrane Neuromuscular Disease Group Specialized Register, Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, PsycINFO, CINAHL (September 2010) > update of the review expected in 2012
 - Reference lists of all relevant articles
 - Databases of ongoing trials
 - Investigators known in this research area

2 Methods

- Data collection and analysis
 - Selection of studies, risk of bias assessment and data extraction: 2 independent reviewers
 - Risk of bias:
 - Randomisation sequence generation
 - Allocation concealment
 - Blinding
 - Incomplete outcome data
 - Selective outcome reporting
 - Other sources of bias



April 2009, Roosevelt Warm Springs, Georgia.

2 Methods

- Data collection and analysis
 - Data synthesis (meta-analysis) > trials with a comparable treatment, patient characteristics and outcomes



2 Methods



- Grading the quality of the evidence

Study design	Initial quality of a body of evidence	Lower if	Higher if	Quality of a body of evidence
Randomised trials	High	Risk of Bias	Large effect	High (⊕⊕⊕⊕)
		Inconsistency	Dose response	Moderate (⊕⊕⊕○)
		Indirectness	All plausible residual confounding & bias	Low (⊕⊕○○)
Observational studies	Low	Imprecision	-Would reduce a demonstrated effect -Would suggest a spurious effect if no effect was observed	Very low (⊕○○○)
		Publication bias		

Program

1 Background

2 Methods

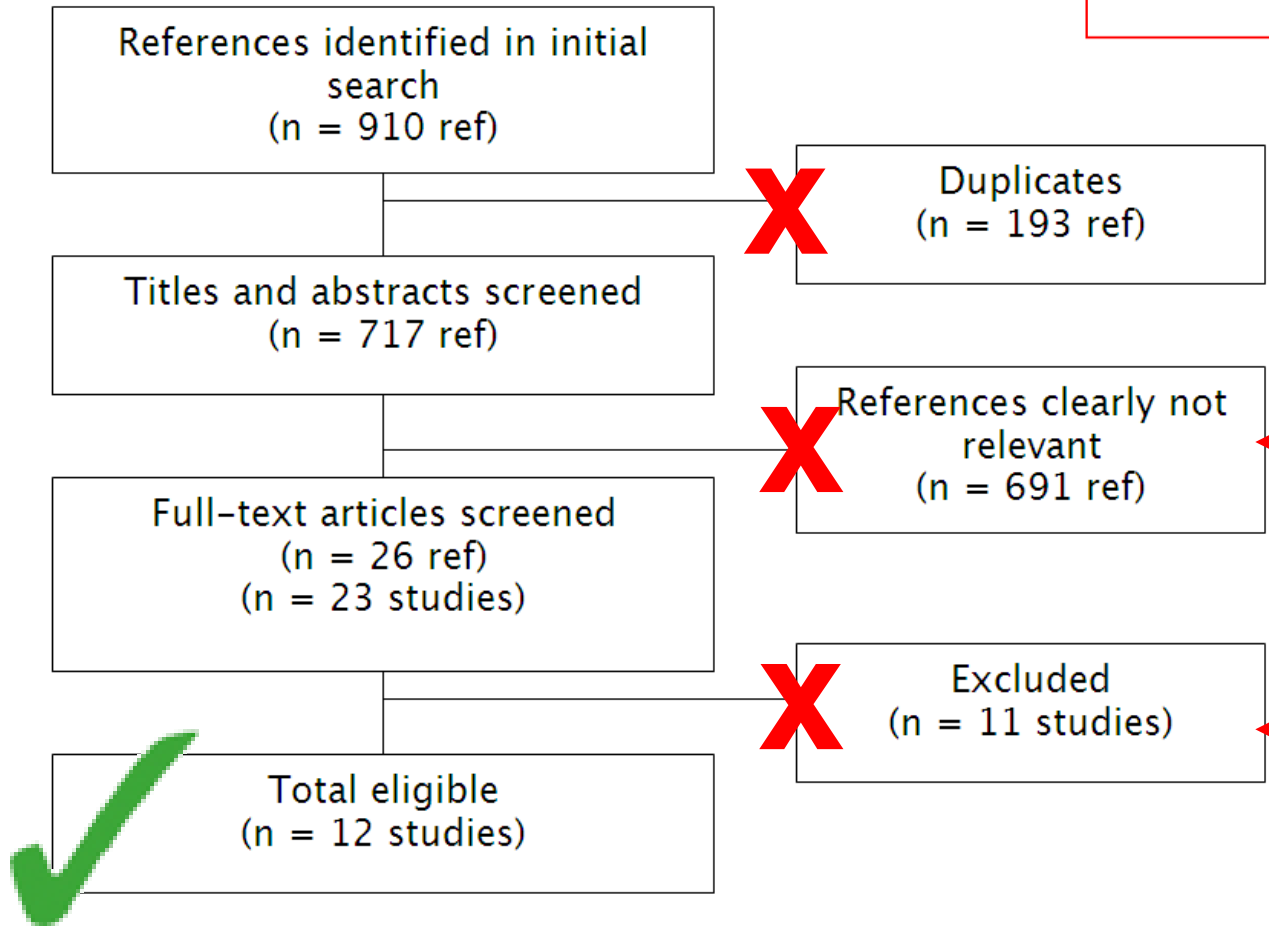
3 Results

4 Discussion

5 Questions

3 Results

- Criteria for considering studies for the review:
- Study design: RCT or quasi RCT
 - Patients: diagnosis of PPS (broad criteria)
 - Intervention: any form of pharmacological or non-pharmacological treatment
 - Comparison: placebo, usual care or no treatment
 - Outcomes: activity limitations, muscle strength, muscle endurance, fatigue, pain, adverse events



3 Results

- Included studies (12 studies):
 - Pharmacological studies (9 studies)
 - Modafinil (Chan 2006, Vasconcelos 2007)
 - IVIG (Gonzalez 2006, Farbu 2007)
 - Pyridostigmine (Trojan 1999, Horemans 2003)
 - Lamotrigine (On 2005)
 - Amantadine (Stein 1995)
 - High dose prednisone (Dinsmore 1995)
 - Non-pharmacological studies (3 studies)
 - Muscle strengthening (Chan 2003)
 - Rehabilitation in warm and cold climate (Strumse 2003)
 - Static magnetic fields (Vallbona 1997)

3 Results

Chen 2003	+	?	-	-	?	?	?	?	+
Chen 2006	?	+	+	+	+	?	?	?	+
Dinsmore 1995	?	+	+	+	-	?	?	?	+
Farbu 2007	+	+	-	-	+	+	+	+	+
Gonzalez 2006	+	+	-	-	-	+	+	+	-
Horemans 2003	?	?	+	+	-	+	?	?	+
On 2005	?	?	-	-	?	?	?	?	-
Stein 1995	?	?	-	-	?	?	?	?	+
Stumse 2003	?	?	-	-	?	?	?	?	-
Trojan 1999	+	+	-	-	+	+	?	?	-
Vallbona 1997	+	+	+	+	+	+	-	-	+
Vasconcelos 2007	+	+	+	+	-	+	+	+	+
	Adequate sequence generation?	Allocation concealment?	Blinding? (All outcomes - patients?)	Blinding? (All outcomes - administrators of the intervention?)	Blinding? (All outcomes - outcome assessors?)	Incomplete outcome data addressed? (Missing outcome data?)	Incomplete outcome data addressed? (ITT-analyses performed?)	Free of selective reporting?	Free of other bias?

3 Results

- **Modafinil (Chan 2006, Vasconcelos 2007)**
 - No reduction in activity limitations, fatigue and pain as compared to placebo
 - Causes adverse events in substantial proportion of medication group

Conclusion:

- There is high quality evidence that there is no beneficial effect of modafinil.

3 Results

- IVIG (Gonzalez 2006, Farbu 2007)
 - No effects on activity limitations and fatigue
 - Inconsistent effects on muscle strength
 - Effect on pain only in subgroup of patients who report much pain
 - Causes adverse events in substantial proportion of medication group

Conclusion:

- There is moderate quality evidence that IVIG has no beneficial effect on activity limitations and there is inconsistency in the evidence on muscle strength and pain.

Recommendations:

- More studies needed to validate results!

3 Results

- **Pyridostigmine (Trojan 1999, Horemans 2003)**
 - No beneficial effects on activity limitations, muscle function, fatigue and pain
 - Causes adverse events in substantial proportion of medication group

Conclusion:

- There is moderate quality evidence of no beneficial effect of pyridostigmine.

Recommendations:

- Effects of individually adjusted doses?

3 Results

- **Lamotrigine (On 2005)**

- Beneficial effect on activity limitations and pain.
- Effects on fatigue are inconsistent
- No adverse events

Conclusion:

- There is very low quality evidence that lamotrigine has a positive effect on activity limitations and pain.

Recommendations:

- Placebo-controlled studies with larger sample size, a longer follow-up period and adequate blinding needed!

3 Results

- **Amantadine (Stein 1995)**

- No effects on fatigue

Conclusion:

- There is very low quality evidence of no beneficial effect of amantadine for fatigue in PPS.

- **High dose prednisone (Dinsmore 1995)**

- No effects on fatigue

Conclusion:

- There is very low quality evidence of no beneficial effect of high-dose prednisone for fatigue in PPS.

3 Results

- **Muscle strengthening of thumb muscles (Chan 2003)**
 - Beneficial effect on muscle strength
 - No negative effect on motor unit survival

Conclusion:

- There is very low quality evidence that progressive resistance training of thumb muscles has a beneficial effect on muscle strength.

Recommendations:

- Effects on larger muscle groups? Effects on activity limitations? Effects on long term?

3 Results

- **Rehabilitation in warm ($\pm 25^{\circ}$ C, dry, sunny) and cold climates ($\pm 0^{\circ}$ C, rainy or snowy) (Strumse 2003)**
- No beneficial effect on activity limitations, muscle strength, fatigue and pain

Conclusion:

- There is low quality evidence of no beneficial effect of rehabilitation in warm and cold climates three months after treatment.

Recommendations:

- Effects of comprehensive rehabilitation with varying program components?

3 Results

- **Static magnetic fields (Vallbona 1997)**
 - Beneficial effect on pain directly after treatment.
 - No adverse events

Conclusion:

- There is moderate quality evidence of a beneficial effect of application of static magnetic fields over a pain trigger point in reducing pain immediately post treatment.

Recommendations:

- Effects on activity limitations and long term effects need to be investigated.

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Discussion

- Absence of evidence \neq absence of effectiveness
 - Amount of evidence is limited
 - Quality of evidence is rather low > blinding!
 - Other reasons for many non-significant results:
 - PPS is highly heterogeneous group
 - Slow progression > need for long term follow up
 - Specific outcome measures are lacking
- Evidence based medicine: use the **current best available evidence** in making decisions about the care of individual patients

TAKE HOME

- This Cochrane review on treatment for PPS indicates that **IVIg**, **lamotrigine**, **muscle strengthening**, and **static magnetic fields** may be **beneficial** in treating symptoms of PPS.
- Due to insufficient good quality data and lack of randomized studies, it is **impossible to draw definite conclusions** on the effectiveness of interventions for PPS.
- **Future research** should focus on novel trials of interventions in PPS to establish evidence on the effect of treatment, which will improve patient care.



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