Region Västra Götaland, HTA-centrum

Regional activity-based HTA
Health Technology Assessment
HTA-report 2014:74

Intravenous immunoglobulin for post-polio syndrome

Samuelsson O, Danielsson A, Nordin J, Sunnerhagen KS, Svanberg T.

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Intravenous immunoglobulin for post-polio syndrome [Intravenöst immunoglobulin vid post-polio syndrom]

Samuelsson O[1],Danielsson A[2], Nordin J[3], Sunnerhagen KS[4], Svanberg T[1].

[1] HTA-centrum of Region Västra Götaland, Sweden.
[2] Department of Physiotherapy, Sahlgrenska University Hospital, Göteborg Sweden
[3] Department of Rehabilitation, Södra Älvsborg Hospital, Borås, Sweden
[4] The Institution of Neuroscience and Physiology, Sahlgrenska Academy, University of Göteborg, Sweden

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Abbreviations

PPS	= post-polio syndrome
EMG	= electromyography
IVIG	= intravenous immunoglobulin
RCT	= randomised, controlled trial
MFI-20	= multidimensional fatigue index-20
FSS	= fatigue severity scale
VAS	= visual analogue scale
SF-36	= short form health survey
PCS	= physical component summary
6MWT	= 6 minute walk test

Summary of the Health Technology Assessment (1 & 2) from The Regional Health Technology Assessment Centre (HTA-centrum)

The Regional Health Technology Assessment Centre (HTA-centrum) of Region Västra Götaland, Sweden (VGR) has the task to make statements on HTA reports carried out in VGR. The English summary is a concise summary of similar outline as the summaries in the Cochrane systematic reviews. The Swedish summary summarises the question at issue, the results and quality of the evidence regarding efficacy and the risks, and gives economical and ethical aspects of the particular health technology. Finally, a concluding remark from HTA-centrum is given.

Christina Bergh, Professor, MD
Head of HTA-centrum of Region Västra Götaland, Sweden, 2014-09-24

Christina Bergh	Anders Larsson	Petteri Sjögren
MD, Professor	MD, PhD	DDS, PhD
Elisabeth Hansson-Olofsson	Christian Rylander	Maria Skogby
PhD, Senior lecturer	MD, PhD	RN, PhD
Magnus Hakeberg	Ola Samuelsson	Annika Strandell
OD, Professor	MD, Associate professor	MD, Associate professor
Lennart Jivegård	Ninni Sernert	Therese Svanberg
MD, Senior university lecturer	Associate professor	HTA-librarian
Jenny Kindblom	Henrik Sjövall	Kjell-Arne Ung
MD, Associate professor	MD, Professor	MD, Associate professor

1. Summary of the Health Technology Assessment

Background
Some patients with a previous polio infection with paralytic symptoms and a partial or complete recovery after the acute infection may develop new, late manifestations after many years of stable functioning. This is called the post-polio syndrome (PPS), and it is characterised by muscle weakness, fatigue, and musculoskeletal pain.

Objective
To describe and assess the evidence from controlled trials on the efficacy and tolerability of intravenous immunoglobulin (IVIG) treatment in patients with PPS.

Search methods and study selection criteria
Systematic searches were performed in PubMed, EMBASE, the Cochrane Library, CRD, and Cinahl. Reference lists of relevant articles were scrutinized for additional references. Studies were required to be a systematic review, a controlled trial of IVIG, or case series including more than 10 patients. The case series were used only for analysis of adverse effects. The certainty of evidence was graded using the GRADE system.

Main results
Four publications describing three randomised, controlled trials met the inclusion criteria (PICO). One of them was a multicentre trial that included 142 patients. One of the centres of this trial also reported their results after an extended follow-up. The other two trials were both single-centre trials, one of them being a small pilot-trial of only 20 patients. The other included 50 patients.
In comparison with placebo there were no differences in the effect of IVIG on fatigue (moderate certainty of evidence; GRADE ⊕⊕⊕O), pain (moderate certainty of evidence; GRADE ⊕⊕⊕O), physical capacity and walking ability (moderate certainty of evidence; GRADE ⊕⊕⊕O), muscle strength (low certainty of evidence; GRADE ⊕⊕ OO), and quality of life (moderate certainty of evidence; GRADE ⊕⊕⊕O) .

Concluding remark
Intravenous treatment with high doses of immunoglobulin is an expensive therapy. In controlled trials this treatment has not been shown to have any beneficial effects in patients with post-polio syndrome.

2. Swedish Summary of the Health Technology Assessment

Bakgrund

Poliovirusinfektion drabbar ryggmärgen med muskelsvaghet som följd. Muskelfunktionen kan återfås, men kvarstående neurologiska funktionsdefekter förekommer vilka stabiliseras efter den initiala sjukdomsfasen. Vissa patienter kan långt senare i livet drabbas av nytillkomna symtom. Detta benämns post-polio syndrom (PPS), och karakteriseras av muskelsvaghet, tilltagande uttröttbarhet och muskuloskeletala smärtor. Prevalensen av PPS i Sverige är inte studerad, men baserat på en tidigare undersökning från 1990-talet uppskattas förekomsten till 40 – 80 patienter per 100 000 innevånare.

Syfte

Att utvärdera den vetenskapliga dokumentationen av intravenöst immunoglobulin (IVIG) hos patienter med PPS avseende tolerabilitet och effekt på trötthet, smärta, fysisk kapacitet, gångförmåga, muskelstyrka och livskvalitet.

Resultat

Studier

Tre randomiserade, kontrollerade studier presenterade i fyra publikationer uppfyllde kriterierna att inkluderas i utvärdering av effekten av IVIG jämfört med placebo. Den största studien inkluderade 142 patienter vid fyra deltagande centra. Resultaten från en 12 månaders uppföljning av 41 patienter från ett av dessa centra har särredovisats i en separat senare publikation. De övriga två kontrollerade studierna var från en klinik i Norge och från en klinik i Spanien. Den norska studien var en pilotstudie med 20 patienter och 6 månaders uppföljning medan den spanska studien inkluderade 50 patienter som följdes i endast 4 månader.

Effekter

I jämförelse med placebo observerades inga skillnader i effekt på trötthet (Måttlig starkt vetenskapligt underlag; GRADE ⊕⊕⊕O), smärta (Måttligt starkt vetenskapligt underlag; GRADE ⊕⊕⊕O), fysisk kapacitet och gångförmåga (Måttligt starkt vetenskapligt underlag; GRADE ⊕⊕⊕O), muskelstyrka (Begränsat vetenskapligt underlag; GRADE ⊕⊕ OO) och livskvalitet (Måttligt starkt vetenskapligt underlag; GRADE ⊕⊕⊕O).

Komplikationer och biverkningar

Två av de tre kontrollerade studierna rapporterade biverkningar. Ingen allvarlig biverkan som kunde relateras direkt till IVIG-behandlingen rapporterades i studierna. Däremot hade drygt 50 % en hel del milda biverkningar i form av huvudvärk, illamående, feber och frossa eller lokala reaktioner vid administrationsstället.

Ekonomiska aspekter

Kostnaden för två IVIG behandlingar (den gängse behandlingsregimen är två injektioner med tre månaders intervall) med 90 g immunoglobulin vid varje behandlingstillfälle är idag cirka 100 000 kronor per patient. Antalet patienter med PPS i Västra Götaland är okänt men kan uppskattas till mellan 600 och 1 350 patienter. Behandling med IVIG av alla dessa patienter skulle innebära en total kostnad på 60 - 135 miljoner kronor.

Slutsats

Intravenöst immunoglobulin för post-polio syndrom är en dyr behandling. I kontrollerade studier har man inte observerat några behandlingseffekter av denna behandling vid jämförelse med placebo.

3. Participants in the project

The question was posed by
Peter Lönnroth, Chairman, Program och Prioriteringsrådet, Region Västra Götaland, Sweden

Participants in the HTA group
First assessment (2009:12):
Katharina Stibrant Sunnerhagen, professor, The Institution of Neuroscience and Physiology, Sahlgrenska Academy, University of Göteborg, Sweden
Anna Danielsson, physiotherapist, Department of Physiotherapy, Sahlgrenska University Hospital, Göteborg Sweden
Jenny Nordin, MD, Department of Rehabilitation, Södra Älvsborg Hospital, Borås, Sweden

Participants from the HTA-centre
First assessment (2009:12):
Annika Strandell, MD, associate professor
Ola Samuelsson, MD, associate professor
Eva Alopaeus, librarian
Therese Svanberg, librarian

Updated assessment 2014:
Ola Samuelsson, MD, associate professor
Therese Svanberg, librarian

External reviewers
First assessment (2009:12
Ulla Molander, MD, associate professor. Department of geriatrics, Sahlgrenska University Hospital, Göteborg, Sweden.
Birgitta Archenholtz, occupational therapist, PhD, Strategic Department of Quality Development, Sahlgrenska University Hospital, Göteborg, Sweden.

Updated assessment (2014)
Maria Skogby, RN, PhD, Department of Radiology
Södra Älvsborgs Hospital, Borås, Sweden
Marie Studal, MD, associate professor, Department of Infectious Diseases, Sahlgrenska University Hospital, Göteborg, Sweden.

Conflicts of interest for the proposer or any of the participants in the work group
KSS was one of the investigators and authors of the randomised controlled trial of intravenous immunoglobulin for post-polio syndrome published in Lancet Neurology 2006.
None of the other participants in the HTA group had any conflicts of interest.

Project time
The first health technology assessment (2009:12) was accomplished during 2008– 2009.
The updated assessment was performed during the first half of 2014.

4. The post-polio syndrome

Post-polio syndrome

In 1-2% of all patients infected by the *Poliovirus* the anterior horn in the spinal cord is affected. This leads to an inflammation, and possible cell death, with loss of motor function. After the first acute phase with muscle weakness a second phase of recovery occurs. In many patients the recovery is complete. The term ***post-polio syndrome*** (PPS) was introduced in the 1980s as it became evident that some patients developed new, late manifestations of polio after many years of stable function following the initial recovery.

In 1995 the Halstead criteria for PPS were published (Halstead 1995):

- a prior episode of paralytic polio
- a period of partial or complete neurological recovery that have lasted several years
- an extended interval of neurological and functional stability over 15 years
- quick or progressive loss of endurance and/or muscular strength with or without muscular atrophy in previously unaffected and healthy muscles, associated to a general muscle and joint fatigue and cold intolerance
- the symptoms are specific by their unusual and lengthy characteristics progressing for more than one year

During an acute polio infection there is an initial denervation followed by a compensatory process that results in enlarged motor units. The neuromuscular symptoms of PPS can be explained by the loss of these enlarged motor units. There is a continuous reinnervation and denervation process. When PPS develops the equilibrium between reinnervation and denervation is disturbed resulting in peripheral denervation. However, the underlying pathophysiological mechanisms of PPS have not yet been clarified (Farbu 2010). One hypothesis is that genetic viral materials persist after the initial recovery, and that these materials stimulate and alter the regulation of the inflammatory and immune system response. Another hypothesis is that the loss of the enlarged motor neurons is due to an imbalance between degenerative and regenerative physiological processes that are related to a change of regulation mechanisms. A third hypothesis is that there are structural and functional abnormalities of the muscle fibers and/or abnormal sensory-motor integration (Boyer et al., 2010).

There are several observations that support that there is a non-infectious inflammation at the spinal level, and that these inflammatory changes play a significant role in the pathogenesis of PPS.

Post-polio syndrome is associated with definite risk of further impairment of disability and health-related quality of life.

Prevalence and incidence of post-polio syndrome

The exact prevalence of PPS is difficult to establish since various population studies have used different diagnostic criteria (Farbu, 2010). The reported prevalence of PPS in patients with a previous clinical polio infection varies in US and European polio populations between 15 - 80 %.

The last epidemic of polio in Sweden occurred in 1953. The vaccination programme in Sweden started in 1957, and only sporadic cases of polio have been reported after 1962. In a Swedish study published in 1993 the prevalence of post-polio sequelae was estimated to be between 92 to186 per 100,000 (depending on the source of data) in the general population (Ahlstrom et al. 1993). Eighty percent of these patients had late onset symptom, i.e. PPS. This corresponds to a prevalence of PPS of 74 to 159 per 100,000. The average age of the PPS patients in the survey in 1993 was 62 years. This means that currently, two decades later, the prevalence of PPS is most probably much lower since the incidence rate of acute polio infections has been dramatically lower after the introduction of the general polio vaccination programme, i.e. from the 1960s and henceforward.

Based on the assumption that the prevalence of PPS currently is half of that in 1993, i.e. between 37 to 80 per 100,000, the number of PPS patients in Region Västra Götaland is estimated to be somewhere between 600 to 1 350.

Present treatment of the post-polio syndrome in the outpatient setting

There is currently no available pharmacological treatment that can cure PPS. Most of these patients are treated with various forms of rehabilitation and physiotherapy.

At the out-patient clinic for patients with polio in Region Västra Götaland the patient will go through a thorough clinical work-up by a neurologist, a physiotherapist and an occupational therapist. The functional capacity and neurological deficits are evaluated by physical examinations and electromyography (EMG).

Based on the clinical evaluation each patient can be referred to individually adjusted physiotherapy, to try out assisted technologic devices, and pain-relieving therapy (pharmacological or non-pharmacological).

Number of patients per year who undergo treatment for post-polio syndrome

Presently, there are 865 patients registered patients at the out-patient clinic for post-polio patients at the Department of Neurorehabilitation, Sahlgrenska University Hospital, Göteborg, Sweden. Of these 93 %, i.e. 803 patients, are classified as PPS patients.

The normal pathway of a patient through the health care system

A patient with a previous history of an acute polio infection may either be referred by a general practitioner to the out-patient clinic for polio patients if late manifestations of polio are suspected, or may contact the out-patient clinic himself/herself directly. The latter is rather common since many physicians are not familiar with the symptoms of PPS.

Actual wait time in days for medical assessment and treatment

All new referrals will have a first clinical evaluation within three months. The wait time for an EMG examination is longer. Currently the wait time for specialized rehabilitation and physiotherapy may be long due to shortage of physiotherapists with experience of neuromuscular disorders.

5. Immunoglobulin in post-polio syndrome

The pathophysiology of PPS is still not clarified (see above). There are some indications that a chronic ongoing inflammatory process at the spinal level plays a role in the pathogenesis. It has been suggested that immunoglobulin may beneficially affect this immune-related disorder (Farbu 2007).

Intravenously administered high doses of immunoglobulin (IVIG) have been used in many neurological autoimmune disorders with beneficial effects. Theoretically, its immune-modulating effects may also have a positive effect on PPS (Farbu, 2007, Boyer et al., 2009). It has been shown that IVIG can reduce the levels of cytokines in the cereobrospinal fluid of PPS patients.

The doses that have been used in treatment in PPS have varied in different studies. Reported treatment regimens are 30 g daily during three consecutive days, repeated after three months, or a total dose of 2-4 g/kg body weight (given during 2-4 days) twice with a three month interval, or 0.4 g/kg body weight per day over five consecutive days twice. After two treatments no more IVIG will be administered.

The central question for the current HTA project

Can intravenous immunoglobulin therapy reduce fatigue and pain, and improve physical ability, muscle strength and quality of life in patients with post-polio syndrome?

PICO P= Patients, I= Intervention, C= Comparison, O=Outcome

P = Adult patients with late manifestations of polio following the initial complete recovery. The late-onset manifestations must occur after at least one year, and must be an objectively verified decrease in muscle strength or verified by typical EMG findings.

I = Intravenous immunoglobulin therapy (IVIG)

C = Placebo, no treatment or other pharmacologic therapy.

O = Fatigue
Pain
Physical capacity
Walking ability
Muscle strength
Activity of daily living
Quality of life

6. Review of Quality of Evidence

Search strategy, study selection and references (Appendix 1)

This is an updated revised version of the report published in 2009 (2009:12). An update of the previous literature search was made in February 2014. In the latter, systematic searches were performed in PubMed, Embase, the Cochrane Library, CINAHL, and a number of HTA-databases. Search strategies, eligibility criteria and a graphic presentation of the selection process are presented in Appendix 1. One librarian (TS) conducted the literature searches and together with one participant from HTA-centrum (OS) assessed the obtained abstracts independently of one another. Thereafter a final selection of full-text articles for inclusion or exclusion was made.

The updated literature search identified a total of 100 articles (after removal of duplicates). Eighty-seven articles were excluded after reading the abstracts, and 13 articles were read in full text. Four articles (two RCTs and two systematic reviews) were included in the report, together with two articles (RCT) from the previous report. The randomized, controlled trials have been critically appraised using modified checklists from SBU (Swedish Council on Health Technology Assessment). The systematic reviews have only been commented upon, but have not been critically appraised. The included articles are listed in appendix 2, and the excluded articles in appendix 3. The certainty of evidence was graded according to the GRADE system.

The present knowledge of immunoglobulin treatment in post-polio patients

The systematic literature searches (performed in 2009 and 2014) identified one Cochrane Review of any treatment for post-polio syndrome (PPS) (Koopman et al., 2011), one systematic review of IVIG in the treatment of neuromuscular disorders (Patwa, 2012), and three randomised controlled trials (RCT) that have studied the effects of intravenous immunoglobulin in comparison to placebo in patients with post-polio syndrome. There are two publications from one of the RCTs. The first one is the original publication of the trial with six months follow-up, and the second one is a prolonged follow-up of 12 months in a subset of the original study population. The design and the patient characteristics are presented in Appendix 2. Studies that were excluded from the assessment are presented in Appendix 3.

One of the RCT did not have any problems with regard to directness, study limitations or precision (see SoF-table Appendix 5), and another had only some minor problems with regard to study limitations. The third RCT was a pilot study with problems regarding both directness and precision.

The Cochrane review from 2011 concluded that there are insufficient evidence to make any definite conclusions on the effectiveness of different treatment options in people with PPS. With regard to immunoglobulin treatment the review concludes that “There is moderate quality evidence that intravenous immunoglobulin has no beneficial effect on activity limitations, and there is inconsistency for effectiveness on muscle strength and pain”. The review by Patwa et al.(2012) concluded that “Evidence is insufficient to support or refute use of IVIG in the treatment of postpolio syndrome”.

Fatigue *(*Appendix 4a)

There were no statistically differences between the IVIG-treated and the placebo-treated study groups in the fatigue index or fatigue severity scale that were used in any of the three RCTs.

Conclusion: Intravenous immunoglobulin results in little or no difference in fatigue in patients with post-polio syndrome compared to placebo.

Moderate certainty of evidence (GRADE ⊕⊕⊕O) (Appendix 5).

Pain *(*Appendix 4b)
There were no statistically significant differences between the IVIG-treated and the placebo-treated study groups in the VAS-scale or SF-36 bodily pain score in any of the three RCTs.
Conclusion: Intravenous immunoglobulin probably results in little or no difference in pain in patients with post-polio syndrome compared to placebo.
Moderate certainty of evidence (GRADE ⊕⊕⊕O) (Appendix 5).

Physical capacity and walking ability *(*Appendix 4c)
Two RCTs has reported on the SF-36 Physical component score or the 6 minute walk test. There were no statistically significant differences between the IVIG-treated and the placebo-treated study groups.
Conclusion: Intravenous immunoglobulin probably results in little or no difference in physical capacity or walking ability in patients with post-polio syndrome compared to placebo.
Moderate certainty of evidence (GRADE ⊕⊕⊕O) (Appendix 5).

Muscle strength *(*Appendix 4d)
The RCT with the largest sample size showed a statistically significant increase in muscle strength in selected muscles, whereas the other two RCT did not find any differences in various muscle groups.
Conclusion: Intravenous immunoglobulin probably results in little or no difference in muscle strength in patients with post-polio syndrome compared to placebo.
Low certainty of evidence (GRADE ⊕⊕OO) (Appendix 5).

Quality of life *(*Appendix 4e)
Two RCTs reported on various quality-of-life outcome variables. There were no statistically significant differences between the IVIG-treated and the placebo-treated study groups.
Conclusion: Intravenous immunoglobulin probably results in little or no difference in the quality of life in patients with post-polio syndrome compared to placebo.
Moderate certainty of evidence (GRADE ⊕⊕⊕O) (Appendix 5).

Complications
Mild reactions to the infusion of IVIG include headache, chills, muscle pain, and low-back pain. These adverse effects are not uncommon. They are reversible and can be minimized by slowing down the infusion rate. There are also severe adverse reactions to intravenous immunoglobulin therapy such as thromboembolic events and anaphylaxis in patients with severe IgA deficiency.

Ongoing research
A search in Clinicaltrials.gov (2014-02-18) using the search terms *(post-polio OR postpolio OR post polio OR post-poliomyelitis OR postpoliomyelitis OR (late AND (polio OR poliomyelitis))) AND (immuno-globulin OR immuno-globulins OR immunoglobulin OR immunoglobulins)* identified 26 trials. No one of them was relevant for the question at issue of the present assessment, i.e. there was no reported ongoing or planned study of IVIG in PPS.
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Medical societies or health authorities that recommend immunoglobulin in post-polio syndrome
None. IVIG treatment for PPS is presently not recommended in any guidelines from any international or national medical society or health authority.

7. Ethical consequences

Specialized out-patient neurological clinics have the responsibility for the care of patients with PPS. Treatment with high doses of intravenous immunoglobulin is costly (see below). Thus, there is a great risk that patients with other neuromuscular disorders who attend these out-patient clinics will receive less care if IVIG for PPS is introduced in the clinical routine.

8. Organisation

Intravenous immunoglobulin treatment can be put into practice

IVIG treatment could start immediately. An additional full-time registered nurse is needed at the out-patient clinic for polio patients.

Intravenous immunoglobulin treatment for post-polio syndrome in other hospitals in Region Västra Götaland of Sweden

No other hospital in the region use IVIG treatment för PPS. However, patients with PPS can get IVIG treatment in private clinics. The cost of the immunoglobulin will then be invoiced to Region Västra Götaland.

Consequences of intravenous immunoglobulin treatment for personnel

No, provided an extra nurse will be added to the staff of the Out-patient clinic for polio patients.

Consequences for other clinics or supporting functions at the hospital or in the whole Region Västra Götaland of Sweden

There will be no consequences for other clinics. However, patients who have a long distance to travel to the out-patient clinic for polio patients in Göteborg need to stay overnight during three days when the immunoglobulin is infused. The cost of travel and hotel stay needs to be accounted for.

9. Economy aspects

Present costs of out-patient care of patients with post-polio syndrome

The patients with PPS normally attend the out-patient clinic regularly, but the interval between visits vary. Some patients also need prescribed analgetics. Since the number of patients with polio in Sweden has decreased dramatically since the start of the vaccination programme in 1957 many of the patients with PPS have now reached retirement. However, some patients are still at a working-age but due to their disability may not be able to work. Due to all these circumstances it is difficult to estimate the current total cost of the care of patients with PPS.

Expected costs of intravenous immunoglobulin

Immunoglobulin for intravenous administration is available in Sweden as Octagam®, KIOVIG® and Gammagard®. The present cost for 1 g Octagam® is 550 SEK, and for 1g KIOVIG® 566 SEK. In 2006 the cost of 1 g Gammagard® was 416 SEK.

In the Swedish controlled trial the dose given was 90 g twice with an interval of three months. Thus, during a 6 month period each patient would receive 180 g immunoglobulin. This corresponds to about 100 000 SEK per patient.

If it is assumed that the number of patients with PPS in Region Västra Götaland is 600 and all of them are treated with IVIG this would yield a total cost for only the immunoglobulin of 60 million SEK. If it is assumed that the number of PPS patients is 1 350 the total cost is 135 million SEK.

Total change of cost

It is not expected that IVIG therapy to any major degree would reduce the need for regular visits to the out-patient clinic, or to any great extent change the ability to go back to work at full strength. Thus, it is not expected that the additional cost of the immunoglobulin will result in any substantial reduction in other costs.

Can intravenous immunoglobulin treatment in patients with post-polio syndrome be adopted and used within the present clinic budget?

No.

Available analyses of health economy with regard to immunoglobulin treatment in patients with post-polio syndrome

There are no such analysis.

10. Unanswered questions

Important gaps in scientific knowledge

1) Are there specific groups of patients with PPS that may benefit from immunoglobulin therapy, i.e. “responders”?
2) If there are “responders” to immunoglobulin therapy what is the optimal dose, and what is the optimal treatment cycle?
3) What are the long-term effects of immunoglobulin therapy?

Interest in Region Västra Götaland to start studies or trials within the research field at issue

There are currently no planned studies.

Appendix 1, Search strategy, study selection and references

PICO: (*P=Patient I=Intervention C=Comparison O=Outcome*)

Question at issue:
Can intravenous immunoglobulin therapy reduce fatigue and pain, and improve physical ability, muscle strength and quality of life in patients with post-polio syndrome?

P= Adult patients with late manifestations of polio following the initial complete recovery. The late-onset manifestations must occur after at least one year, and must be an objectively verified decrease in muscle strength or verified by typical EMG findings.

I= Intravenous immunoglobulin therapy

C= Placebo, no treatment or other pharmacologic therapy

O= Fatigue
Pain
Physical capacity
Walking ability
Muscle strength
Activity of daily living
Quality of life

Eligibility criteria

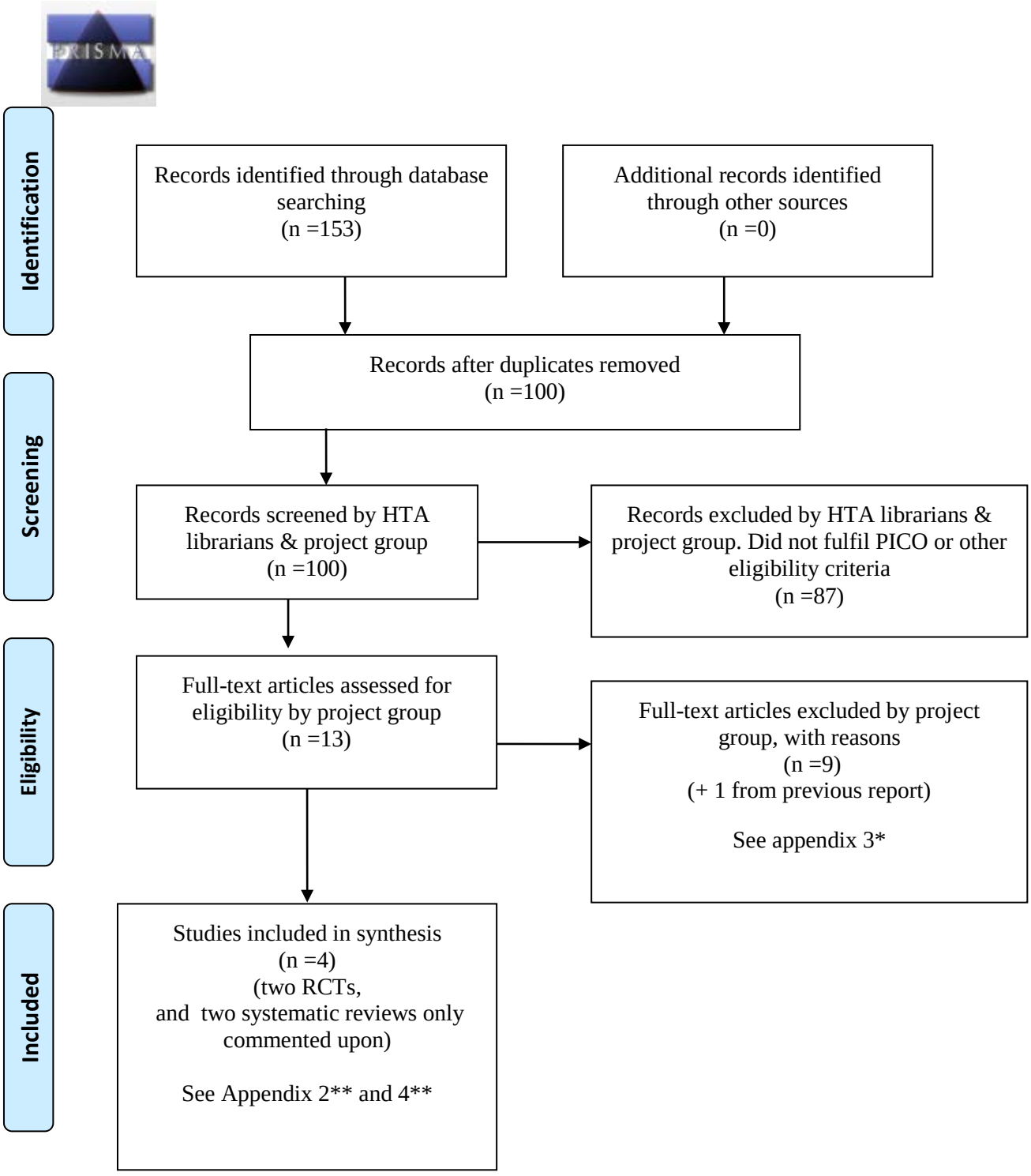
Study design:
Systematic reviews
Randomized controlled trials
Non-randomized controlled studies
Case series ≥ 10 patients

Language:
English, Swedish, Norwegian, Danish

Publication date:
This is an updated literature search of the HTA-report 2009:12 that covers the publication dates from 2008-01-01 until 2014-02-12. The initial literature search of the 2009:12 report had no limits concerning the publication dates.

Selection process – flow diagram

This flow diagram accounts for the updated searches made in February 2014. The total number of hits in the search of the 2009:12 report was 197. Three of them were then included in the first assessment. The current updated assessment includes four new articles and two from the previous report.



* Includes also one publication that was excluded in the 2009:12 report.

** Includes also two RCTs that were included in the 2009:12 report.

Search strategies

Database: EMBASE 1980 to Present*
Date: 2014-02-12
No of results: 83
* at the time of the previous report, the library had no subscription to Embase. A search with no limits to publication date was performed this time.

#	Searches	Results
1	exp immunoglobulin/	348414
2	(immuno-globulin or immuno-globulins or immunoglobulin or immunoglobulins).af.	491602
3	1 or 2	505888
4	exp postpoliomyelitis syndrome/	871
5	(post-polio or postpolio or post polio or post-poliomyelitis or postpoliomyelitis).af.	1337
6	(late adj4 (polio or poliomyelitis)).af.	212
7	4 or 5 or 6	1433
8	**3 and 7**	**83**

Database: PubMed
Date: 2014-02-12
No of results: 37

Search	Query	Items found
#12	**Search #5 AND #10 Filters: Publication date from 2008/09/01**	**37**
#10	Search #7 OR #8 OR #9	1653
#9	Search late and (polio or poliomyelitis)	432
#8	Search post-polio or postpolio or post polio or post-poliomyelitis or postpoliomyelitis	1370
#7	Search "Postpoliomyelitis Syndrome"[Mesh]	683
#5	Search #3 OR #4	765353
#4	Search immuno-globulin or immuno-globulins or immunoglobulin or immunoglobulins	765353
#3	Search "Immunoglobulins"[Mesh]	726886

Database: The Cochrane Library
Date: 2014-02-12
No of results: 20
Cochrane reviews 12
Trials 6
Technology assessment 1
Cochrane groups 1

ID	Search	Hits
#1	MeSH descriptor: [Immunoglobulins] explode all trees	13976
#2	immuno-globulin or immuno-globulins or immunoglobulin or immunoglobulins	7908
#3	#1 or #2	16487
#4	MeSH descriptor: [Postpoliomyelitis Syndrome] explode all trees	25
#5	post-polio or postpolio or post polio or post-poliomyelitis or postpoliomyelitis	124

#6	late and (polio or poliomyelitis)	70
#7	#4 or #5 or #6	160
#8	#3 and #7	40
#9	**#8 from 2008**	**20**

Database: CRD
Date: 2014-02-12
No of results: 2

Line	Search	Hits
1	(post-polio or postpolio or post polio or post-poliomyelitis or postpoliomyelitis) OR (late and (polio or poliomyelitis))	8
2	(post-polio or postpolio or post polio or post-poliomyelitis or postpoliomyelitis) OR (late and (polio or poliomyelitis)) FROM 2008 TO 2014	2

Database: Cinahl
Date: 2014-02-12
No of results: 11

#	Query	Results
S8	**S3 AND S7**	**11**
S7	S4 OR S5 OR S6	678
S6	TI (late and (polio or poliomyelitis)) OR AB (late and (polio or poliomyelitis))	113
S5	TI (post-polio or postpolio or post polio or post-poliomyelitis or postpoliomyelitis) OR AB (post-polio or postpolio or post polio or post-poliomyelitis or postpoliomyelitis)	485
S4	(MH "Postpoliomyelitis Syndrome")	514
S3	S1 OR S2	12,440
S2	TI (immuno-globulin or immuno-globulins or immunoglobulin or immunoglobulins) OR AB (immuno-globulin or immuno-globulins or immunoglobulin or immunoglobulins)	4,426
S1	(MH "Immunoglobulins+")	10,432

The web-sites of **SBU, Kunnskapssenteret** and **Sundhedsstyrelsen** were visited

Nothing relevant to the question at issue was found

Reference lists
A comprehensive review of reference lists brought no new records

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Reference lists

Included studies:

Bertolasi L, Frasson E, Turri M, Gajofatto A, Bordignon M, Zanolin E, et al. A randomized controlled trial of IV immunoglobulin in patients with postpolio syndrome. Journal of the neurological sciences. 2013;330(1-2):94-9.

Gonzalez H, Khademi M, Borg K, Olsson T. Intravenous immunoglobulin treatment of the post-polio syndrome: sustained effects on quality of life variables and cytokine expression after one year follow up. Journal of neuroinflammation. 2012;9:167.

From previous report:
Farbu E, Rekand T, Vik-Mo E, Lygren H, Gilhus NE, Aarli JA. Post-polio syndrome patients treated with intravenous immunoglobulin: a double-blinded randomized controlled pilot study. Eur J Neurol. 2007 Jan;14(1):60-5.

Gonzalez H, Sunnerhagen KS, Sjöberg I, Kaponides G, Olsson T, Borg K. Intravenous immunoglobulin for post-polio syndrome: a randomised controlled trial. Lancet Neurol. 2006 Jun;5(6):493-500.

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Werhagen L, Borg K. Effect of intravenous immunoglobulin on pain in patients with post-polio syndrome. Journal of rehabilitation medicine : official journal of the UEMS European Board of Physical and Rehabilitation Medicine. 2011;43(11):1038-40.

From previous report:
Kaponides G, Gonzalez H, Olsson T, Borg K. Effect of intravenous immunoglobulin in patients with post-polio syndrome -- an uncontrolled pilot study. J Rehabil Med. 2006 Mar;38(2):138-40.

Other references:

Ahlstrom G, Gunnarsson LG, Leissner P, Sjödén PO. Epidemiology of neuromuscular diseases, including postpolio sequelae, in a Swedish county. Neuroepidemiology 1993;12:262-69.

Boyer FC, Tiffreau V, Rapin A, Laffont I, Percebois-Macadre L, Supper C, et al. Post-polio syndrome: Pathophysiological hypotheses, diagnosis criteria, drug therapy. Annals of physical and rehabilitation medicine. 2010;53(1):34-41.

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Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009 Jul 21;6(7):e1000097.

Stibrant Sunnerhagen K, Danielsson A, Nordin J, Strandell A, Samuelsson O, Alopaeus E, Svanberg T. Post-polio: effekt av intravenöst immunglobulin (IvIG) hos patienter med post-polio problematik [Internet]. Göteborg: Västra Götalandsregionen, Sahlgrenska Universitetssjukhuset, HTA-centrum; 2009. HTA-rapport 2009:12. [citerat 26 September 2014]. Tillgänglig från: http://www.sahlgrenska.se/upload/SU/HTA-centrum/HTA-rapporter/Postpolio%20HTA-rapport%20Protokoll,%20inkl%20bilagor%202011-12-08%20till%20publicering.pdf

Appendix 2 – Included studies of post-polio syndrome – design and patient characteristics.

Author, Year, Country	Study Design	Follow-up (months)	Study Groups; Intervention vs control	Patients (n)	Age (years) Mean and sd/range	Women/ Men (%)	Outcome variables
Gonzalez 2006 Sweden	RCT	6	IVIG Placebo	73 69	61.5 (9.2) 59.0 (10.0)	71/29 58/42	Primary: Muscle strength SF-36 Physical Component Summary (PCS) Secondary: SF-36 Vitality 6 Minute Walk Test (6MWT) Pain (VAS-scale) Fatigue (Multidimensional fatigue index; MFI-20)
Gonzalez 2012 Sweden	RCT Extended follow-up of subgroup	12	IVIG Placebo	20 21	61.7 (52-75) 61.9 (46-75)	70/30 57/43	Physical activity of the elderly (PASE) SF-36 (8 domains) SF-36 Physical Component Summary (PCS) SF-36 Mental Component Summary (MCS) 6 Minute Walk Test (6MWT) Pain (VAS-scale)
Farbu 2007 Norway	RCT	6	IVIG Placebo	10 10	59.9 (6.2) 58.7 (6.8)	60/40 70/30	Primary: Pain (VAS-scale) Fatigue (Fatigue Score System ;FSS) Muscle strength (on Carolus)
Bertolasi 2013 Italy	RCT	4	IVIG Placebo	26 24	54.9 (5.7) 58.3 (5.6)	50/50 50/50	Primary: SF-36 Physical Component Summary (PCS) Secondary: SF-36 Mental Component Summary (MCS) Muscle strength (MRC scale) 6 Minute Walk Test (6MWT) Pain (VAS-scale) Fatigue (Fatigue Score System ;FSS)

Appendix 3. Excluded articles – IVIG in post-polio syndrome.

Study (author, publication year)	Reason for exclusion
Aguila-Maturana, 2010	Systematic review in Spanish with only an English abstract.
Borg, 2010	Abstract.
Boyer, 2010	Non-systematic review.
Dalakas, 2010	Non-systematic review of IVIG in patients with neuroinflammatory and neurodegenerative disorders..
Farbu, 2010	Non-systematic review.
Goebel, 2010	Non-systematic review of IVIG in patients with chronic pain.
Kaponides, 2006	Case series without any data on side effects or other types of complications.
Tamburin, 2014	Non-systematic review of IVIG in patients with chronic pain.
Werhagen, 2011	Case series without any data on side effects or other types of complications.
Östlund, 2012	Case series without any data on side effects or other types of complications.

Appendix 4a – Post-polio syndrome
Outcome variable: Fatigue. MFI-20 = Multidimensional Fatigue Index (5 scales with 4 items each). FSS = Fatigue Severity Scale

* + No problem
? Some problems
- Major problems

Author, year	Country	Study design	Number of patients Follow-up	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Intravenous immunoglobulin	Placebo				
Gonzalez, 2006	Sweden	RCT	I=73 C=69 FU: 6 m	I = 6 C = 1	<u>MFI-20 General fatigue</u> Baseline 13.2 (sd 4.4) Δ = -1.0 (95 CI: -4.0;1.0) NS between study groups <u>MFI-20 Physical fatigue</u> Baseline 13.4 (sd 4.3) Δ = ±0 (95 CI: -2.5;2.0) NS between study groups	<u>MFI-20 General fatigue</u> Baseline 14.6 (sd 4.5) Δ = -1.0 (95 CI: -2.0;1.0) <u>MFI-20 Physical fatigue</u> Baseline 14.0 (sd 4.8) Δ =±0 (95 CI: -2.0;2.0)		+	+	+
Farbu, 2007	Norway	RCT	I=5 C=5 FU:6		<u>FSS</u> Baseline = 5.3 (sd 1.4) 3 months = 4.5 (95 CI: 3.5;5.5) 6 months= 5.0 (95 CI: 4.2;5.8) NS between study groups	<u>FSS</u> Baseline = 5.6 (sd 1.5) 3 months = 5.1 (95 CI: 4.1;6.2) 6 months= 5.5 (95 CI: 4.4;6.7)		?	+	-
Bertolasi, 2013	Italy	RCT	I = 26 C= 24	I = 1 C= 0	<u>FSS</u> Baseline = 5.5 (sd 1.4) 2 months = 5.0 (sd 1.2) 4 months= 4.8 (sd 1.4) NS between study groups	<u>FSS</u> Baseline = 5.6 (sd 1.2) 2 month s= 4.5 (sd 2.3) 4 months = 5.3 (sd 1.4)		+	?	+

Appendix 4b– Post-polio syndrome
Outcome variable: Pain. SF36-Bodily pain – scale 0-100; the higher score the more pain

* + No problem
? Some problems
- Major problems

Author, year	Country	Study design	Number of patients Follow-up	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Intravenous immunoglobulin	Placebo				
Gonzalez, 2006	Sweden	RCT	I=73 C=69 FU: 6 m	I = 6 C = 1	<u>VAS</u> Baseline = 26.3 (sd 23.5) Δ = -1.5 (95 CI: -14;6.0) NS between study groups	<u>VAS</u> Baseline = 29.8 (sd 24.4) Δ = ±0 (95 CI: -6.5;14.0))		+	+	+
Farbu, 2007	Norway	RCT	I=5 C=5 FU:6		<u>VAS</u> Baseline = 45 (sd 16) 3 months = 29 (95 CI: 17;42) p=0.001 between study groups 6 months= 50 (95 CI: 37;62) NS between study groups	<u>VAS</u> Baseline = 46 (sd 29) 3 months = 61 (95 CI: 44;78) 6 months= 56 (95 CI: 37;76	VAS-pain scale (0-100 mm)	?	+	-
Bertolasi, 2013	Italy	RCT	I = 26 C= 24	I = 1 C= 0	<u>SF-36 Bodily pain</u> Baseline = 47.4 (sd 24.6) 2 months = 60.4 (sd 25.9) 4 months = 54.6 (sd 24.7) NS between study groups	<u>SF-36 Bodily pain</u> Baseline = 49.4 (sd 26.7) 2 months = 51.1 (sd 26.4) 4 months = 54.8 (sd 26.5)		+	?	+

Appendix 4c -Post-polio syndrome

Outcome variable: Physical capacity and walking ability measured by SF36-PCS = Physical component score (0 -100; the higher score the better) and by 6MWT =6 minute walk test. Results in meters.

* + No problem
? Some problems
- Major problems

Author, year	Country	Study design	Number of patients Follow-up	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Intravenous immunoglobulin	Placebo				
Gonzalez, 2006	Sweden	RCT	I=73 C=69 FU: 6 m	I = 6 C = 1	<u>PCS</u> Baseline 33.7 (sd 9.7) Δ = +1.5 (95 CI: -3.6;6.0) NS between study groups <u>6MWT</u> Baseline 335 (sd 115) Δ = +6.6 % (95 CI: -2.2;17.4) NS between study groups	<u>PCS</u> Baseline 34.0 (sd 10.0) Δ = -0.8 (95 CI: -4.1;6.0) <u>6MWT</u> Baseline 313 (sd 102) Δ =+3.9 % (95 CI: -2.4;11.4)		+	+	+
Gonzalez 2012	Sweden	RCT	I = 20 C = 21 FU: 12 m		<u>PCS</u> Baseline = 28.9 (sd 6.1) 12 months = 32.8 (sd 8.2) P=0.02 between study groups <u>6MWT</u> Baseline = 351 (sd 110) 12 months = 400 (sd 112) NS between study groups	<u>PCS</u> Baseline = 34.0 (sd 10.0) 12 months = 33.1 (sd 11.3) <u>6MWT</u> Baseline = 306 (sd 111) 12 months = 325 (sd 125)	Extension of Gonzalez 2006. Subgroup analysis in patients from 1 out 4 participating centers. Significant improvement pre- to post-treatment within IVIG-group for both PCS and 6MWT	?	?	?

Appendix 4c -Post-polio syndrome
Outcome variable: Physical capacity and walking ability measured by SF36-PCS = Physical component score (0 -100; the higher score the better) and by 6MWT =6 minute walk test. Results in meters.

* + No problem
? Some problems
- Major problems

Author, year	Country	Study design	Number of patients Follow-up	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Intravenous immunoglobulin	Placebo				
Bertolasi, 2013	Italy	RCT	I = 26 C= 24	I = 1 C= 0	<u>PCS</u> Δ Baseline -2 months = 5.2 NS between study groups <u>6MWT</u> Baseline = 317.3 (sd 105.6) 2 months = 330.0 (sd 103.5) 4 months = 323.5 (sd 100.8) NS between study groups	<u>PCS</u> Δ Baseline -2 months = 2.9 <u>6MWT</u> Baseline = 297.8 (sd 108.5) 2 months = 311.5 (sd 109.3) 4 months = 318.8 (sd 113.9)		+	?	+

Appendix 4d - Post-polio syndrome
Outcome variable: Muscle strength

* + No problem
? Some problems
- Major problems

Author, year	Country	Study design	Number of patients n= Follow up	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Intravenous immunoglobulin	Placebo				
Gonzalez, 2006	Sweden	RCT	I=73 C=69 FU: 6 m	I = 6 C = 1	Change in muscle strength: + 2.3 % p = 0.029	Change in muscle strength: + -6.3 %	Study muscle was selected as a polio-affected muscle with 25-75% expected strength (for age and sex). Muscle strength in the upper legs was studied in 88 subjects, and in in 45 subjects it was studied in the lower legs . A clinical significant effect was defined as a difference between groups of more than 15 %.	+	+	+
Farbu, 2007	Norway	RCT	I=10 C=10 FU:6 m	I = 0 C = 0	<u>Right elbow flexion (Nm)</u> Baseline: 17.1 6 months: 24.2 <u>Left elbow flexion (Nm)</u> Baseline: 19.1 6 months: 22.5 <u>Right knee extension (Nm)</u> Baseline: 62.2 6 months: 66.6 <u>Right knee extension (Nm)</u> Baseline: 59.5 6 months: 67.6 NS between study groups for all 4 outcomes	<u>Right elbow flexion (Nm)</u> Baseline: 24.4 6 months: 25.4 <u>Left elbow flexion (Nm)</u> Baseline: 25.1 6 months: 27.0 <u>Right knee extension (Nm)</u> Baseline: 56.9 6 months: 53.6 <u>Right knee extension (Nm)</u> Baseline: 64.7 6 months: 63.3	Isometric muscle strength measured with a dynamometer (Carolus).	?	+	-

Appendix 4d - Post-polio syndrome
Outcome variable: Muscle strength

* + No problem
? Some problems
- Major problems

Author, year	Country	Study design	Number of patients n= Follow up	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Intravenous immunoglobulin	Placebo				
Bertolasi, 2013	Italy	RCT	I = 26 C= 24 FU : 4 m.	I = 1 C= 0	<u>Right elbow flexion (Nm)</u> Baseline: 13.0 4 months: 13.3 <u>Left elbow flexion (Nm)</u> Baseline: 12.1 4 months: 12.5 <u>Right knee extension (Nm)</u> Baseline: 3.6 4 months: 4.4 <u>Right knee extension (Nm)</u> Baseline: 5.1 4 months: 7.5 NS between study groups for all 4 outcomes	<u>Right elbow flexion (Nm)</u> Baseline: 13.1 4 months: 14.3 <u>Left elbow flexion (Nm)</u> Baseline: 10.2 4 months: 10.8 <u>Right knee extension (Nm)</u> Baseline: 7.8 4 months: 7.7 <u>Right knee extension (Nm)</u> Baseline: 5.3 4 months: 4.0	Peak isometric strength measured by a dynamometer (Force Gauge PCE-FM 100). Muscle strength assessed with the MRC scale did not show any differences between study groups.	+	?	+

Appendix 4e - Post-polio syndrome
Outcome variable: Quality of life assessed by SF36 scales. 0-100; the higher score the better.

* + No problem
? Some problems
- Major problems

Author, year	Country	Study design	Number of patients n= Follow up	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Intravenous immunoglobulin	Placebo				
Gonzalez, 2006	Sweden	RCT	I=73 C=69 FU: 6 m	I = 6 C = 1	<u>SF-36 PCS</u> Baseline = 33.7 (sd 9.7) Δ Baseline-6 months: 1.5 NS between study groups	<u>SF-36 Vitality</u> Baseline = 34.0 (sd 10.0) Δ Baseline-6 months: -0.8	For all other SF-subscales (Physical functioning, General health, Social functioning, Roel emotional, Mental health) only baseline data were reported, but no follow-up data.	+	+	+
Gonzalez 2012	Sweden	RCT	I = 20 C = 21 FU: 12 m		<u>SF-36 General health</u> Baseline = 53.1 (sd 22.4) 12 months = 61.3 (sd 24.2) <u>SF-36 Vitality</u> Baseline = 43.0 (sd 22.6) 12 months = 49.3 (sd 27.3) <u>SF-36 Social functioning</u> Baseline = 66.9 (sd 24.1) 12 months = 73.8 (sd 26.6) <u>SF-36 Role emotional</u> Baseline = 61.7 (sd 43.6) 12 months = 66.7 (sd 40.5) <u>SF-36 Mental health</u> Baseline = 74.4 (sd 17.9) 12 months = 76.0(sd 19.3) NS between study groups for all outcomes	<u>SF-36 General health</u> Baseline = 58.1 (sd 22.5) 12 months = 61.8 (sd 24.2) <u>SF-36 Vitality</u> Baseline = 46.4 (sd 23.8) 12 months = 47.3 (sd 22.2) <u>SF-36 Social functioning</u> Baseline = 70.8 (sd 26.3) 2 months = 71.4 (sd 23.8) <u>SF-36 Role emotional</u> Baseline = 63.5 (sd 43.3) 12 months = 73.0 (sd 38.9) <u>SF-36 Mental health</u> Baseline = 72.6 (sd 17.2) 12 months = 72.5 (sd 17.6)	Extension of Gonzalez 2006. Subgroup analysis in patients from of the 4 original participating centers.	?	?	?

Appendix 4e - Post-polio syndrome
Outcome variable: Quality of life assessed by SF36 scales. 0-100; the higher score the better.

* + No problem
? Some problems
- Major problems

Author, year	Country	Study design	Number of patients n= Follow up	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Intravenous immunoglobulin	Placebo				
Bertolasi, 2013	Italy	RCT	I = 26 C= 24 FU : 4 m.	I = 1 C= 0	<u>SF-36 General health</u> Baseline = 50.3 (sd 23.0) 2 months = 59.7 (sd 22.2) 4 months = 55.1 (sd 19.6) <u>SF-36 Vitality</u> Baseline = 45.2 (sd 20.7) 2 months = 57.1 (sd 18.5) 4 months = 51.9 (sd 19.8) <u>SF-36 Social functioning</u> Baseline = 57.1 (sd 26.6) 2 months = 69.1 (sd 22.4) 4 months = 65.0 (sd 26.09 <u>SF-36 Role emotional</u>* Baseline = 59.5 (sd 39.3) 2 months = 76.2 (sd 30.4) 4 months = 54.0 (sd 41.6) <u>SF-36 Mental health</u> Baseline = 60.5 (sd 16.4) 2 months = 74.8 (sd 14.8) 4 months = 68.8 (sd 14.9) NS between study groups for all outcomes with one exception*	<u>SF-36 General health</u> Baseline = 47.8 (sd 22.9) 2 months = 48.8 (sd 22.6) 4 months = 52.2 (sd 24.3) <u>SF-36 Vitality</u> Baseline = 43.8 (sd 17.7) 2 months = 49.0 (sd 18.0) 4 months = 48.6 (sd 18.8) <u>SF-36 Social functioning</u> Baseline = 55.3 (sd 21.1) 2 months = 57.3 (sd 24.7) 4 months = 61.8 (sd 25.7) <u>SF-36 Role emotional</u> Baseline = 59.8 (sd 42.0) 2 months = 47.9 (sd 44.2)* 4 months = 51.4 (sd 45.7) <u>SF-36 Mental health</u> Baseline = 60.3 (sd 14.7) 2 months = 67.5 (sd 15.4) 4 months = 60.9 (sd 17.5)	SF-Role emotional significantly different at 2 months.	+	?	+

Appendix 4f - Post-polio syndrome
Complications and adverse events

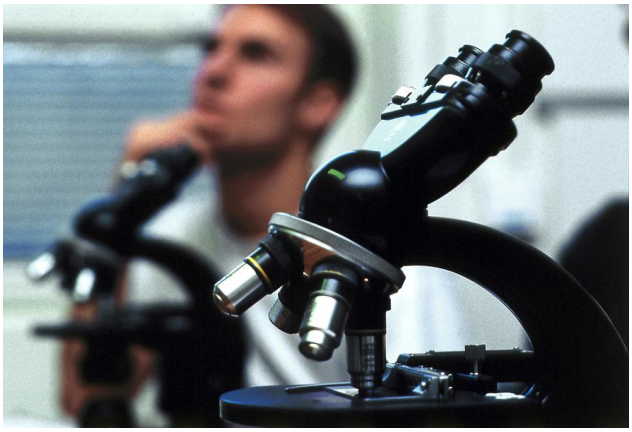
Author, year	Country	Study design	Number of patients	Complications and adverse events		
					IVIG n (%)	Placebo n (%)
Gonzalez, 2006	Sweden	RCT	IVIG = 73 Placebo = 69	<u>Serious Adverse Events</u> Not related to treatment <u>Adverse Events</u> Gastrointestinal disorders General disorders and administration site conditions Nervous system disorders Skin and subcutaneous skin disorders	 1 16 (22 %) 14 (19%) 43 (59%) 27 (37%)	 2 2 (3%) 6 (9%) 13 (19%) 5 (7%)
Gonzalez 2012	Sweden	RCT	IVIG = 20 Placebo = 21	Not reported		
Farbu 2007	Norway	RCT	IVIG = 10 Placebo = 10	<u>Adverse Events</u> Chills and fever Flu-like illness Chest myalgia (after 5 months)	 7 1 1	 1 0 0
Bertolasi, 2013	Italy	RCT	IVIG = 26 Placebo = 24	Not reported		

Appendix 5 – Summary of Findings
Immunoglobulin in post-polio syndrome

Outcome variable Number of studies	Design	Study limitations	Consistency	Directness	Precision	Publication bias	Magnitude of effect	Relative effect (95%CI)	Absolute effect	Quality of evidence GRADE
Fatigue 3	RCT	No serious limitations (0)	No important inconsistency (0)	Some uncertainty (?)	No imprecision (0)	Unlikely	Not relevant	No difference between study groups		⊕⊕⊕◯ Moderate
Pain 3	RCT	No serious limitations (0)	Some inconsistency (?)	Some uncertainty (?)	No imprecision (0)	Unlikely	Not relevant	No difference between study groups		⊕⊕⊕◯ Moderate
Physical capacity and walking ability 2	RCT	No serious limitations (0)	Some inconsistency (?)	Some uncertainty (?)	No imprecision (0)	Unlikely	Not relevant	No difference between study groups		⊕⊕⊕◯ Moderate
Muscle strength 3	RCT	Serious limitations (-1)	Some inconsistency (?)	Some uncertainty (?)	No imprecision (0)	Unlikely	Not relevant	No difference between study groups		⊕⊕◯◯ Low
Quality of life 2	RCT	No serious limitations (0)	No important inconsistency (0)	Serious indirectness (-1)	No imprecision (0)	Unlikely	Not relevant	No difference between study groups		⊕⊕⊕◯ Moderate

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA



HTA

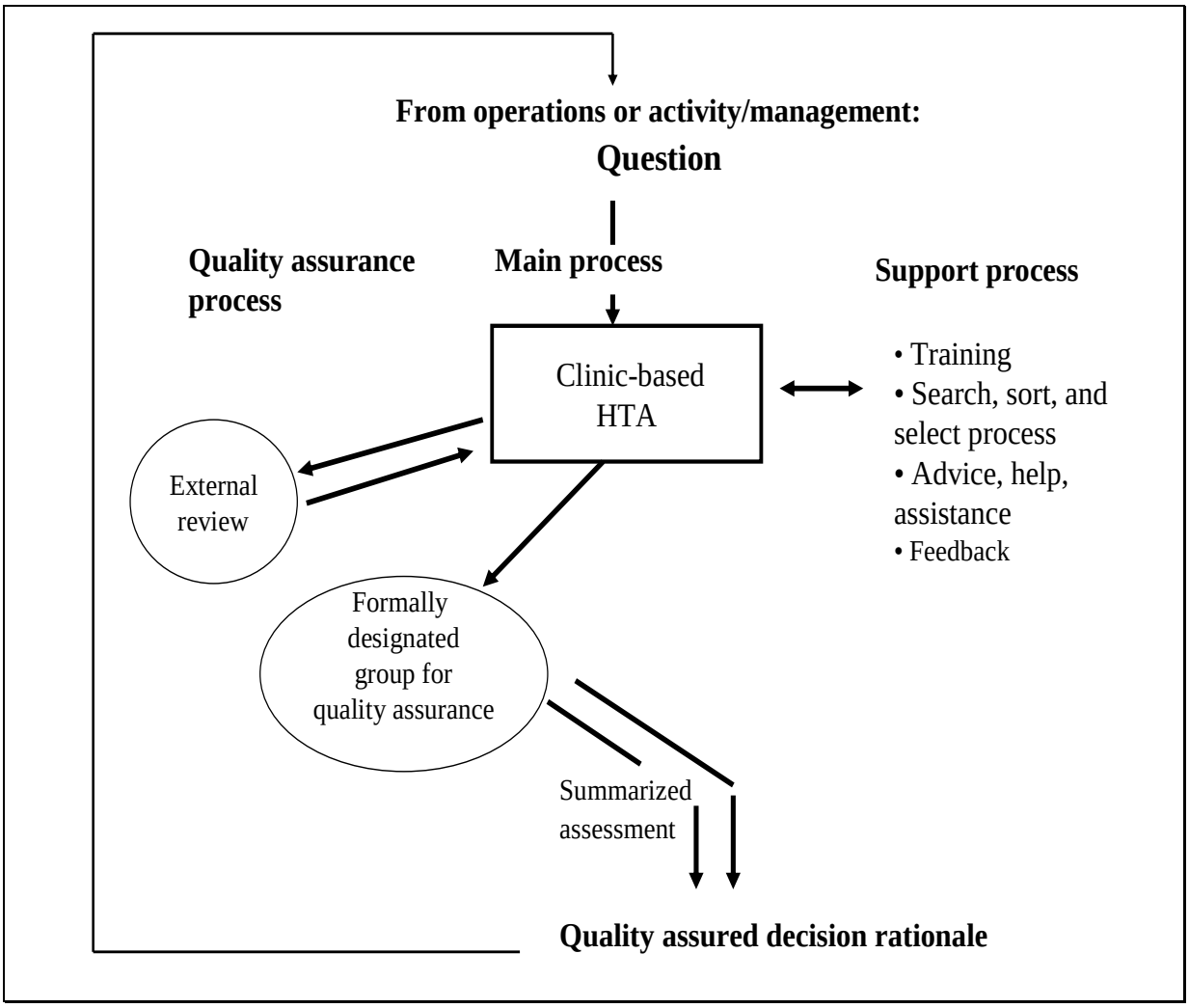
Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the quality of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High quality of evidence	= (GRADE⊕⊕⊕⊕)
Moderate quality of evidence	= (GRADE ⊕⊕⊕O)
Low quality of evidence	= (GRADE ⊕⊕OO)
Very low quality of evidence	= (GRADE ⊕OOO)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh, Professor, MD.
Head of HTA-centrum


From operations or activity/management:
Question
Quality assurance process
Main process
Support process
Clinic-based HTA
• Training
• Search, sort, and select process
• Advice, help, assistance
• Feedback
External review
Formally designated group for quality assurance
Summarized assessment
Quality assured decision rationale

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Sahlgrenska Universitetssjukhuset, HTA-centrum
Röda Stråket 8, 413 45 Göteborg
www.sahlgrenska.se/hta-centrum