Original Research

Effectiveness of steroids and antiviral agents in the treatment of Bell's palsy

Christos Sialakis[1], Aikaterini Frantzana[2], Christos Iliadis[3], Peter Ouzounakis[4], Lambrini Kourkouta[5]

1) Otorhinolaryngology Private Practice, Thessaloniki, Greece

2) School of Sciences, Department of Health Sciences, School of Medicine, European University Cyprus, Nicosia, Cyprus; George Papanikolaou General Hospital of Thessaloniki, Greece

3) Private Diagnostic Health Center, Thessaloniki, Greece

4) General Hospital of Alexandroupoli, Greece

5) Nursing Department, International University of Greece, Thessaloniki, Greece

Abstract

Background. This study aims to investigate the effectiveness of steroids plus antivirals versus steroids alone in the treatment of Bell's palsy. Due to conflicting results in the existing literature, we conducted this meta-analysis to synthesize the available evidence and extract a more complete conclusion.

Methods. We searched electronic databases PubMed, CINAHL, ScienceDirect, MEDLINE, OVID, and Scopus. The last search was performed on March 2024. In this study, 7 randomized controlled trials were included. We used random and fixed effects for sensitivity analysis for each outcome, and we further proceeded to perform a Bayesian meta-analysis using priors and calculate the posterior distribution.

Results. Performing frequentist meta-analysis, both the random and fixed effects showed statistical significance, indicating the superiority of the combination treatment. The random log odds ratio was 0.5865 [95% CI: 0.0141 to 1.1589 and the Back-Transform Log Odds Ratio to Odds Ratio was 1.798 [95% CI: 1.014 to 3.186]. The fixed effect log odds ratio was 0.4377 [95%CI: 0.0819 to 0.7934] and the Back-Transform Log Odds Ratio to Odds Ratio was 1.549 [95% CI:1.085 to 2.211]. Neither the rank correlation nor the regression test in both models indicated any funnel plot asymmetry and publication bias.
Performing Bayesian meta-analysis, in the posterior distribution the model-averaged log odds ratio was 0.26 [0.00 to 0.90], showing no statistically significant results, as the log odds ratio contains the zero. The inclusion Bayes Factor (BF) for the effect was 1.225 showing anecdotal supporting evidence for the combination treatment. The inclusion BF for the heterogeneity was 0.979, showing no support for its existence in the analysis and the inclusion BF for the publication bias was 0.622, a lower of 1, indicating evidence of its absence in the analysis.

Conclusions. The combination of steroids plus an antiviral agent, is more efficacious than steroid monotherapy in treating Bell's palsy. This conclusion is supported by frequentist analysis, but not by the Bayesian approach as the Bayesian meta-analysis was inconclusive, suggesting some uncertainty in the effect size but this could be due to priors influence. Further research with advanced syntheses such as network and Bayesian meta-analysis is needed as well as more double-blinded randomized controlled trials.

Keywords: steroids, antiviral agents, Bell's palsy, idiopathic facial nerve paralysis, recovery, acyclovir, famciclovir, valacyclovir, prednisolone, randomized controlled trial

DOI: 10.15386/mpr-2786

Manuscript received: 11.08.2024
Received in revised form: 29.03.2025
Accepted: 28.05.2025

Address for correspondence:
Aikaterini Frantzana
mokaterinna1986@yahoo.gr

Introduction

Conflicting results exist in the literature about the effectiveness of antiviral agents added to the steroid treatment of Bell's palsy. This study aims to explore the efficacy of steroids plus antivirals versus steroids alone in the treatment of Bell's palsy.

In 1821 Sir Charles Bell described a condition characterized by partial or complete paralysis of facial muscles on the affected site. Bell's palsy is an acute peripheral lower motor neuron facial nerve palsy of idiopathic etiology [1]. The incidence of the disease is about 20 to 30 cases per 100,000 [1]. Bell's palsy is caused by a dysfunction of the peripheral part of the VII cranial nerve of unknown cause and manifests as an acute unilateral facial paralysis (complete loss of movement) or paresis (weakness) [2].

A multidisciplinary approach is needed, addressing the recommendations of both Otolaryngology-Head and Neck Surgery and Neurology Academies. The American Academy of Otolaryngology-Head and Neck Surgery [2] and the American Academy of Neurology [3] make recommendations about the treatment of Bell's palsy. Bell's palsy is a common case in otolaryngology and neurology.

According to the American Academy of Otolaryngology-Head and Neck Surgery [2], the current recommendations include that the clinicians should perform a physical examination and careful history assessment to exclude any other causes that can be identified, in patients who present acute onset unilateral facial paresis or paralysis. Secondly, oral steroids should be prescribed within 72 hours after symptoms manifest in patients 16 years and older. In addition, clinicians should not prescribe antivirals as monotherapy for patients with new-onset Bell's palsy. Fourth, eye protection in those patients with harmed eye closure is necessary. Other recommendations include that routine laboratory testing and diagnostic imaging should not obtained in patients presenting new-onset Bell's palsy symptoms. Furthermore, electrodiagnostic testing should not be obtained in patients with Bell's palsy, presenting incomplete facial paralysis. The American Academy of Otolaryngology-Head and Neck Surgery further recommends that clinicians should reassess patients with Bell's palsy, who present a new or a worsening neurologic symptom at any time during the disease course, if ocular symptoms emerge, and if facial recovery is incomplete after 3 months of symptoms onset. According to the same Clinical Practice Guideline, options in the treatment include oral antiviral therapy in addition to oral steroids within 72 hours of symptom onset and electrodiagnostic testing for Bell's palsy patients with complete facial paralysis. Finally, according to the American Academy of Otolaryngology-Head and Neck Surgery Foundation, this Clinical Practice Guideline does not recommend the surgical decompression, acupuncture, or physical therapy in patients with Bell's palsy [2].

According to the American Academy of Neurology [3] steroids have a high probability to be effective in treating Bell's palsy and should be suggested to increase the likelihood of recovery of facial nerve function. Furthermore, the combination of steroids and antiviral agents, in patients with new onset Bell's palsy does not increase the likelihood of facial nerve recovery by more than 7%. The American Academy of Neurology [3] suggests the addition of antiviral agents due to the modest increase of recovery that it may offer to the patients, but the patients have to be informed that the benefit of antiviral agents, if present, is modest.

Risk factors of the disease are hypertension, diabetes, upper respiratory disturbances, severe preeclampsia, pregnancy, and obesity [2]. Differential diagnosis can be difficult because other diseases may mimic the symptoms. Other etiologies of facial paralysis/paresis among others include Guillain-Barré syndrome, multiple sclerosis, Melkersson-Rosenthal syndrome, Mobius syndrome, sarcoidosis, encephalitis and meningitis, diabetes, human immunodeficiency virus (HIV), herpes simplex, otitis media, Lyme disease, mononucleosis, facial nerve tumor, skin cancer, parotid tumors, syphilis, Ramsay Hunt syndrome, heritable disorders, injury to facial nerve and stroke [2].

Common side effects of corticosteroid treatment are poorer control of glucose levels, high blood pressure, gastrointestinal disturbances, peptic ulcer reactivation, peripheral edema, and mood swings [2]. Pregnant patients and diabetic patients were routinely excluded from randomized trials and should be treated on an individualized basis [2]. Some common side effects of antiviral therapy include vomiting, nausea, diarrhea, and rare reactions including angioedema, hepatic and renal failure, hives, and bronchospasm.

Other options of treatment are described in the literature, such as physical therapy and surgical decompression. Inagaki et al [4] described transmastoid nerve decompression for Bell's palsy, preserving the ossicular chain. The authors of the study [4], conclude that this surgical technique, in the early phase, after symptoms arise, represents efficacious salvage in cases of severe Bell's palsy with more than 95% facial nerve degeneration. Furthermore, Kim et al [5] reported their findings of delayed facial nerve decompression in patients with Bell's palsy. According to the study, [5] decompression surgery did not provide a superior prognosis than treatment with medications but reduced the severe complications of facial palsy.

The study of Di Pietro et al [6], investigated the efficacy of selective electrical muscle stimulation for the treatment of patients with acute Bell's palsy. The authors concluded that the electrical stimulation, accelerated the recovery time, achieving excellent long-term results.

In another systematic review [7] the authors conclude

that synkinesis could be reduced in Bell's palsy patients if physiotherapy starts before synkinesis symptoms arise. The patient should be treated with oral steroids as soon as possible, receiving physical therapy at the same time.

Bell's palsy caused by a virus is characterized by inflammation and demyelination of the facial nerve [5]. Although Bell's palsy is considered of idiopathic etiology, there is evidence of viral infection or reactivation of facial nerve ganglion. Considering the possible evidence of viral infection as an etiologic factor of Bell's palsy, several trials investigated the effectiveness of antiviral agents, in treating the disease [2].The facial nerve innervates facial muscles, stapedius muscle, lacrimal glands, salivary glands, and it also contains sensory fibers from the tympanic membrane and posterior ear canal, and taste fibers from the anterior tongue. As a result, patients with Bell's palsy may have symptoms such as facial muscle paresis or paralysis, taste loss, hyperacusis, dryness of the eye and mouth, and dropping of the eyelid and corner of the mouth [2].

The prognosis of Bell's palsy can be more accurately predicted according to the degree of facial nerve degeneration [4]. Electroneurography, measuring ≥90% facial nerve degeneration, suggests a poor prognosis for recovery [4]. Although Bell's palsy is typically self-limited, possible long-term poor outcomes could cause discomfort to the patient [2]. Up to 30% of patients with Bell's palsy do not succeed in recovering completely the facial function [3]. As a result, many patients experience permanent facial weakness each year [3]. Complete recovery occurs in 70% of patients with no treatment, and in about 90% of patients treated with steroids and antivirals [6]. Caution should be exercised when evaluating patient outcomes, especially when using questionnaires or other measurement tools to assess quality of life, as these tools can potentially lead to misleading conclusions or patient discrimination [8]. Therefore, clinicians can focus on a compassionate and supportive environment that prioritizes the patients's well-being, influencing positively their treatment, and increasing their life expectancy [8].

Methods

This study adheres to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 checklist [9]. The study aims to investigate the effectiveness of the treatment of steroids plus antivirals versus steroids alone in the treatment of Bell's palsy.

Inclusion and exclusion criteria

The inclusion criteria were studies of patients with Bell's palsy. We used the PICOS framework to describe the inclusion criteria.

1. Population: Adults or mixed populations of patients with Bell's palsy, with the majority of participants being adults. Studies focused solely on pediatric patients were excluded.

2. Intervention: Combination therapy consisting of standard steroid treatment (e.g., prednisolone or prednisone) plus antiviral agents (e.g. acyclovir, valacyclovir).

3. Comparison: Standard steroid treatment alone (e.g. prednisolone or prednisone), without the addition of antiviral agents.

4. Outcome: Recovery of facial nerve function, assessed using recognized standardized scales such as the House-Brackmann, Sunnybrook, and Yanagihara scales.

5. Study Design: Randomized Controlled Trials (RCTs), including double-blinded, single-blinded, or non-blinded studies.

The exclusion criteria were set as follows:

1. studies that are not randomized controlled trials.

2. studies assessing facial palsy treatments other than steroids and antivirals, such as acupuncture, physical therapy, and surgical decompression.

3. animal studies.

4. observational studies.

5. cohort studies.

6. case reports.

7. editorial letters.

Information Resources and Search Strategy

Electronic research was performed on PubMed, OVID, ScienceDirect, Cumulative Index to Nursing & AlliedHealth (CINAHL), and MEDLINE in October 2022, to identify relevant studies according to the inclusion criteria. The new research was performed during March 2024 on Scopus. We used keywords 'steroids', 'antivirals', 'Bell's palsy', 'facial paralysis', 'recovery', 'acyclovir', 'famciclovir', 'valaciclovir', 'prednisolone'. We proceed to de-duplication and exclusion of irrelevant studies, screening abstracts and full-text articles and exclude them with specific reasons, if the inclusion criteria were not met. Furthermore, three relevant studies not identified in the database search and nor in the reference lists were identified in Google Scholar search. This additional search strategy, enabled us to increase the range of literature searched, thus increasing the comprehensiveness and rigor of our search strategy. Finally, 7 RCTs were included for qualitative and quantitative analysis. The last search was performed in March 2024.

Selection process and data collection process

Two authors independently worked. The screening process included the abstract and full text of relevant studies. The data collection process included the year of publication, size of the study arms, age range or mean age of patients, assessment scale of Bell's palsy, dosage of steroids, and antivirals. During the selection and data collection process, any disagreement was resolved by discussion.

Effect measures

In this meta-analysis, we measured the efficiency of steroids plus antivirals versus steroids monotherapy in the treatment of Bell's palsy. For the effect measures, the

log odds ratio was preferred, and 95% confidence intervals (95%CIs), with random and fixed effects. Furthermore, a regression test was performed for publication bias.

In Robust Bayesian Meta-Analysis, log odds ratios with 95% credible intervals (95% CrI) were calculated for the effect size and heterogeneity in the posterior distribution. Furthermore, the Bayes factor was calculated for effect size, heterogeneity, and publication bias.

Recovery of facial palsy is assessed by specific scales. These are:

1. House-Brackmann scale score [10] involving six grades I-VI according to the severity of the palsy

2. Yanagihara 40-point scoring system. A score of 40 points is considered normal, lower than 10 as severe, and zero is considered as no movement [11]

3. Sunnybrook scale score, using a score of 100 points as a normal facial function, and zero as complete facial paralysis [12].

Evaluation of the quality of the included studies

The quality assessment for the included studies was performed separately by two authors. The Cochrane Collaboration Tool for Assessing Risk of Bias [13] was used in the Revman program [14]. According to this tool [13] there are five elements of evaluation. These are:

1. random sequence generation (selection bias)

2. allocation concealment (selection bias)

3. blinding of participants and personnel (performance bias)

4. incomplete outcome data (attrition bias)

5. selective reporting (reporting bias)

6. other bias. The assessment of the risk of bias can be evaluated as low, high, or unclear risk of bias for each element.

Statistical methods

To evaluate the effectiveness of combination therapy (steroids plus antivirals) versus steroids alone for treating Bell's palsy, we performed both frequentist and Bayesian meta-analysis approaches.

Frequentist meta-analysis

We conducted the frequentist meta-analysis using the Jamovi software [15], which uses the metafor package in R [16][17]. Frequentist meta-analysis compares the number of patients who recovered, on antiviral plus steroid therapy, against those treated with steroids alone. We calculated the log odds ratios (log OR) to measure the effect of recovery with combination therapy compared to steroids alone. Confidence intervals (CIs) provide the range of values in which the true effect likely lies. Furthermore, we investigated how the treatment effects vary across different studies, and we assessed heterogeneity using the Q test, I^2, and τ^2. Low heterogeneity indicates that the treatment effect is similar across studies, enhancing the reliability of our findings. In addition, we identified any unusual or highly influential studies by calculating studentized residuals to find outliers and Cook's distances to detect studies that disproportionately affect the results.

To ensure that our results aren't skewed by only positive findings being published, we performed funnel plot asymmetry tests using rank correlation and regression tests. Symmetrical funnel plots suggest low publication bias, while asymmetry may indicate potential bias [15-17].

Bayesian meta-analysis

We advanced our research approach and, we performed a Robust Bayesian Meta-Analysis using JASP software [18,19]. Bayesian meta-analysis combines prior knowledge with current study data to estimate the probability of different treatment effects. To perform the Bayesian meta-analysis, we used the RoBMA-original model [18], which includes 12 combinations of prior assumptions for effect size, heterogeneity, and publication bias. We used a model-averaged approach [18-20], to account for multiple potential models, providing a more balanced and reliable estimate of treatment effects.

Bayes Factors (BF10) were calculated to evaluate the strength of evidence [21,22]. A Bayes Factor (BF10) of 1 indicates that the evidence is inconclusive for or against the treatment effect, on the other hand, a Bayes Factor of more than 1 suggests that the evidence supports the treatment effect, with values ranging from 1 to 3 suggest weak evidence, from 3 to 10 suggest moderate, and more than 10 suggest strong evidence. Finally, a Bayes Factor less than 1 suggests evidence against the treatment effect. The results are reported as log odds ratios to align with the frequentist analysis, ensuring consistency and ease of comparison [21,22].

To assess the reliability of our Bayesian results, we conducted several diagnostic tests such as the Markov Chain Monte Carlo (MCMC) algorithm Diagnostics to simulate the posterior distributions accurately [23]. These diagnostic tests include the Effective Sample Size (ESS), in which a minimum ESS of 500 suggests that our estimates are based on sufficient independent data points [23-25]. In addition, the Gelman–Rubin Diagnostic (R-hat), having values close to 1 (ideally between 1.00 and 1.05) indicates that the MCMC chains have mixed well, suggesting stable and reliable estimates [23-25]. Finally, we performed MCMC Error Checks, in which low maximum MCMC error and MCMC error/SD values (close to zero) confirm that the simulations are precise and converged [24,25]. Performing both frequentist and Bayesian methods, our meta-analysis provides a robust estimate of the treatment's effectiveness. The frequentist approach offers a traditional comparison of recovery rates, while the Bayesian method delivers a probability-based assessment that incorporates prior knowledge and accounts for uncertainty.

This meta-analysis includes 7 RCTs that are compatible with the inclusion criteria.

Figure 1 [26] shows the screening process and study selection.

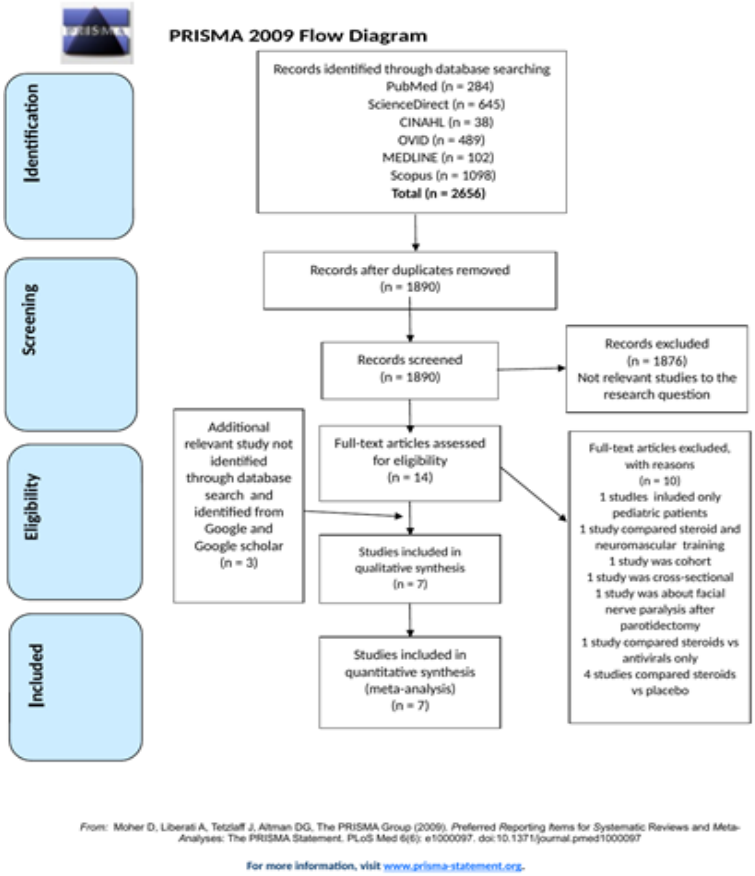

Figure 1. Screening process and study selection.

Results

Table I. Basic characteristics of included studies.

Study	Characteristics
Engström et al 2008 [27]	Study type: Double-blind RCT, participants were allocated into 1 of 4 treatment groups, valaciclovir with prednisolone, valaciclovir with placebo, placebo with prednisolone, or double placebo. Age: 18–75 years Duration between palsy and treatment: 0-72h Grading system and Recovery criteria: Sunnybrook scale score [26] of 100 points or House-Brackmann scale score [27] of I * in our review we used recovery events from the House-Brackmann scale Treatment Antiviral-steroid: 1000 mg valaciclovir three times per day for 7 days, prednisolone 60 mg/d for 5 days then reduced by 10 mg per day for a total treatment time of 10 days. Steroid: Prednisolone 60 mg/d for 5 days then reduced by 10 mg per day for a total treatment time of 10 days Follow-up (maximum duration): 12 months Study arms (complete recovery events as described in the study/total number) **data used for the meta-analysis Prednisolone plus valaciclovir: 164 / 206 Prednisolone plus placebo: 160 / 210 **Exclusion criteria: psychiatric disease, or any other condition that was at risk of being influenced by the study medication or that might have affected completion of the study, systemic antiherpetic medication within the past 2 weeks, ongoing systemic steroid medication, allergy to aciclovir, valaciclovir, famciclovir, or ganciclovir, pregnancy, other neurological diseases, diabetes, badly controlled hypertension, current or a history of serious heart disease, history of renal or hepatic disease, gastric or duodenal ulcer, history of glaucoma, acute otitis or history of ipsilateral chronic otitis, recent head injury, history of tuberculosis, history of immunodeficiency syndromes, breastfeeding, being a woman of childbearing age who was unwilling to use contraceptives during the medication period.**

Table I. Basic characteristics of included studies (continuation).

Study	Characteristics
Hato et al 2007 [28]	Study type: Single-blind RCT Age: *15-80* ***years*** *(Valacyclovir + prednisolone) , 15-84* ***years*** *(placebo + prednisolone)* Duration between palsy and treatment: 2.4 days (Valacyclovir + prednisolone) , 1.9 days (placebo + prednisolone) Grading system and Recovery criteria: score higher than 36 using Yanagihara 40-point scoring system [28] without facial contracture or synkinesis Treatment Antiviral-steroid: valacyclovir 1,000 mg/d for 5 days or a placebo with identical appearance and weight for 5 days. Each was administered orally twice daily. Prednisolone 60 mg/d for 5 days,30 mg/d for 3 days, and 10 mg/d day for 2 days. Steroid: Prednisolone 60 mg/d for 5 days,30 mg/d for 3 days, and 10 mg/d day for 2 days. Follow-up (maximum duration): 6 months Study arms (complete recovery events as described in the study/total number) **data used for the meta-analysis Valacyclovir plus prednisolone: 110 / 114 Prednisolone plus placebo: 96 / 107 **Exclusion criteria: not contraindicated for corticosteroid or antiviral agent, systemic disease, such as severe diabetes, peptic ulcer, renal disease, hepatic dysfunction, and psychosis. Neoplasms, trauma, Ramsay Hunt syndrome, or zoster sine herpete (ZSH), which is a form of Ramsay Hunt syndrome without manifestation of herpetic vesicles at the auricle or ear canal, otitis media, facial palsy attributable to central nervous system disorders.**
Inanli et al 2001 [29]	Study type: a prospective, controlled, and randomized study Age: ***19 to 74 years***, mean: 38 (Acyclovir + prednisolone), 42 (Prednisolone) Duration between palsy and treatment: evaluated within the first 96 hours Grading system and Recovery criteria: House – Brackmann [27] ≤ 2 Treatment Antiviral-steroid: Acyclovir dosage was 2400 mg for 10 days, prednisolone given as a daily dose of 1 mg/kg over the next 12 days Steroid: Prednisolone given as a daily dose of 1 mg/kg over the next 12 days Follow-up : 3 months Study arms (complete recovery events as described in the study/total number) **data used for the meta-analysis Acyclovir plus prednisolone: 17 / 20 Prednisolone: 20 / 22 **Exclusion criteria: severe hypertension exceeding 140/90 mmHg despite antihypertensive drug treatment or diet, pregnancy, cardiac disease, hepatic-renal dysfunction, severe diabetes mellitus, immunodeficiency, and psychosis were considered contraindications for the use of prednisolone and acyclovir in the study participants, tuberculosis, glaucoma.**
Kawaguchi et al 2007 [30]	Study type: Not blind RCT Age: 15 to 85 (mean, 50.3) years Duration between palsy and treatment: Mean ± SD, 2.5 ±1.8 days (prednisolone-valacyclovir), 2.1 ± 1.6 days (prednisolone) Grading system and Recovery criteria: Yanagihara scale [28] Points equal to or greater than 36 without sequelae, such as synkinesis and contracture, were defined as recovery from facial paralysis. Treatment Antiviral-steroid: Valacyclovir was administered as 500 mg two times daily (1,000 mg/d) from days 1 to 5. Prednisolone was administered at 20 mg three times daily (60 mg/d) from days 1 to 5, 10 mg three times daily (30 mg/d) from days 6 to 8, and 10 mg once daily on days 9 and 10. Steroid: prednisolone was administered at 20 mg three times daily (60 mg/d) from days 1 to 5, 10 mg three times daily (30 mg/d) from days 6 to 8, and 10 mg once daily on days 9 and 10 Follow-up (maximum duration): 6 months Study arms (complete recovery events as described in the study/total number) **data used for the meta-analysis, *** recovery events presented as percentage rates in a graph Prednisolone-Valacyclovir: 76 / 84 Prednisolone: 57 / 66 **Exclusion criteria: Patients were excluded if they had been diagnosed with Ramsay Hunt syndrome (RHS), or if they had contraindications for treatment with prednisolone or valacyclovir because of complications such as severe psychologic disease, peptic ulcer, connective tissue disease, or renal dysfunction, diabetes mellitus, pregnancy.**

Table I. Basic characteristics of included studies (continuation).

Study	Characteristics
Li et al 1997 [31]	Study type: Double-blind RCT Age: mean 39.2 years (Acyclovir+prednisone), 40.3 years (Prednisone) Duration between palsy and treatment: within 4 days of presentation Grading system and Recovery criteria: House-Brackmann scale [27] Grade I and Grade II Treatment Antiviral-steroid: Acyclovir or a matched placebo was administered orally 800 mg five times daily for 7d, Prednisone was administered orally at 60mg/d for the first 5 days, 50mg, 40mg, 30mg, 20mg, 10mg, daily for other 5 days. Steroid: Prednisone was administered orally at 60mg/d for the first 5 days, 50mg, 40mg, 30mg, 20mg, and 10mg, daily for other 5 days. Follow-up (maximum duration): 6 months Study arms (complete recovery events as described in the study/total number) **data used for the meta-analysis Acyclovir plus prednisone: 21 / 25 Prednisone: 8 / 21 **Exclusion criteria: Contraindication to corticosteroid therapy, peptic ulcer disease, active tuberculosis, pregnancy, diabetes mellitus, hypertension.**
Vázquez et al 2008 [32]	Study type: Double-blind RCT Age: 14-82 years Duration between palsy and treatment: less than 72h of presentation Grading system and Recovery criteria: facial grading system, Sunnybrook scale [26] > 90 Treatment Antiviral-steroid: valacyclovir, 2 g per day for seven days, Prednisone 1 mg/kg for 7 days, followed by tapering doses for 14 days Steroid: Prednisone 1 mg/kg for 7 days, followed by that tapering the doses for 14 days Follow-up (maximum duration): 12 months Study arms (complete recovery events as described in the study/total number) **data used for the meta-analysis Valacyclovir plus prednisone: 19 / 22 Prednisone plus placebo: 17 / 19 **Exclusion criteria: Chronic kidney disease, HIV infection, Tuberculosis, Pregnant or breastfeeding women, Hypertonus > 160/100 mmHg, Decompensated heart failure, Ramsay-Hunt Syndrome, Peptic ulcer, Glaucoma.**
Yeo et al 2008 [33]	Study type: Double-blind RCT Age: mean 42.7 ± 15.7 years (Acyclovir+prednisone) , 40.2 ± 18.4 years (Prednisone) Duration between palsy and treatment: Early treatment start: ≤3 Day after onset. Late treatment start: 3 days after onset. Grading system and Recovery criteria: House-Brackmann scale [27] Grade ≤ 2 Treatment Antiviral-steroid: Acyclovir (2400 mg/d) for 5 days, oral prednisone 1mg/kg per day (max. 80 mg/d) for 4 days, reduced to 60 mg/d on days 5 and 6, 40 mg on days 7 and 8, and 20 mg on days 9 and 10. Steroid: oral prednisone 1 mg/kg per day (max. 80mg/d) for 4 days, reduced to 60 mg/d on days 5 and 6, 40 mg on days 7 and 8, and 20 mg on days 9 and 10. Follow-up (maximum duration): 6 months Study arms (complete recovery events as described in the study/total number) **data used for the meta-analysis Acyclovir and prednisone: 41 / 44 Prednisone: 40/ 47 **Exclusion criteria: Those who could not be treated with corticosteroids or acyclovir because of uncontrollable diabetes or duodenal ulcer, patients with central nervous system abnormalities, neoplasms, acute or chronic middle ear disease, patients with facial palsy caused by temporal bone fracture, patients with facial nerve paralysis caused by surgery, patients with Ramsay Hunt syndrome.**

Quality Assessment of included studies

Quality assessment of included studies according to Cochrane Collaboration's tool for assessing the risk of bias (Figure 2) in randomized trials [13] in Revman statistical software [14].

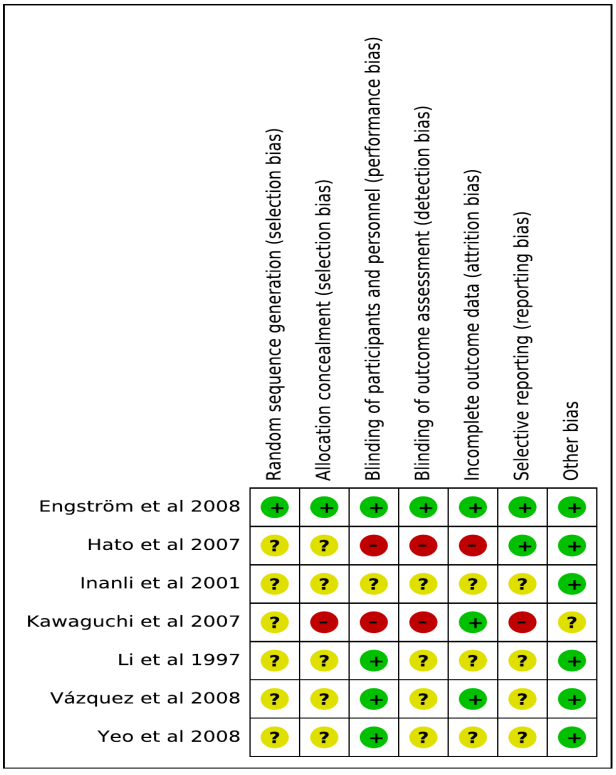

Figure 2. Risk of bias summary.

Frequentist meta-analysis

Figure 3 shows the funnel plot of comparison of steroids plus antivirals vs. steroid plus placebo, Jamovi [15-17].

Funnel plot assessing potential publication bias. Each dot represents a study included in the meta-analysis. Symmetry in the plot suggests low publication bias, while asymmetry would indicate potential publication bias. Studies falling outside the funnel shape may suggest small-study effects or other biases.

Figure 4 shows the Forest plot of comparison of steroids plus antivirals vs steroid plus placebo, Jamovi statistical software [15-17]

Forest plot summarizing effect sizes of each study included in the meta-analysis. Each horizontal line represents the confidence interval for the effect size of an individual study, with squares indicating the estimated effect size for each study. Studies with lines that cross the center line (no-effect line) do not show a statistically significant effect. Studies positioned to the right of the center line favor combination therapy, suggesting a potential benefit of this approach for Bell's palsy treatment.

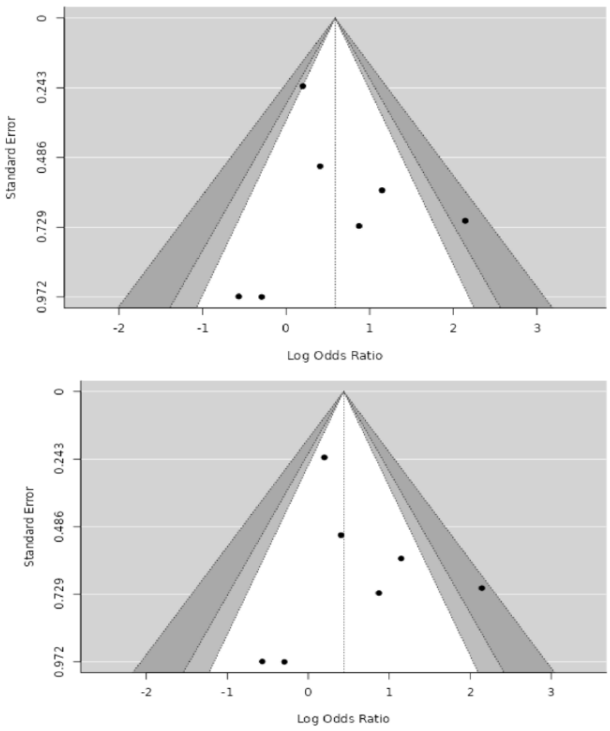

Figure 3. Funnel plot of comparison of steroids plus antivirals vs. steroid plus placebo. **Figure 3a.** Funnel plot random effect. **Figure 3b.** Funnel plot fixed effect.

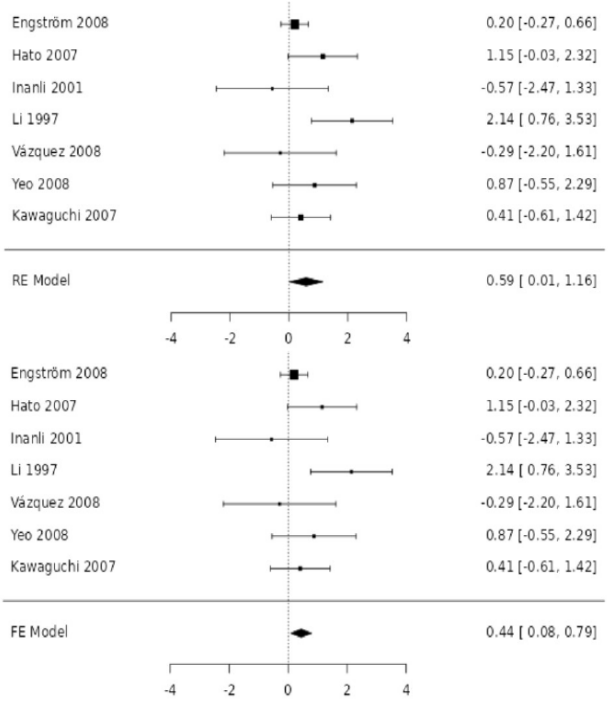

Figure 4. Forest plot of comparison of steroids plus antivirals vs steroid plus placebo. **Figure 4a.** Forrest plot log odds ratio random effect. **Figure 4b.** Forest plot log odds ratio fixed effect.

Random-Effects Model

The log odds ratio based on the random-effects model was 0.5865 (95% CI: 0.0141 to 1.1589), and the back-transformed odds ratio was 1.798 (95% CI: 1.014 to 3.186). This suggests that combination therapy increases the recovery of patients with Bell's palsy compared to steroids alone, with a significant positive effect ($z = 2.0082$, $p = 0.0446$).

Clinical interpretation: This finding indicates a likely benefit of combination therapy for Bell's palsy, although the effect size may vary across different study populations.

Heterogeneity and prediction intervals

The Q-test showed no significant heterogeneity ($Q = 10.2428$, $p = 0.1148$, $\tau^2 = 0.2249$, $I^2 = 41.42\%$), meaning that treatment effects were fairly consistent across studies. The 95% prediction interval (-0.5051 to 1.6781) suggests that while combination therapy generally has a positive effect, individual study results might vary, with some studies potentially showing no effect or even a slight negative effect.

Clinical interpretation: This consistency in effect supports the reliability of combination therapy's benefits, though clinicians should note that results may vary slightly by patient group.

Outlier and Influence Analysis

The studentized residuals showed no outliers, and Cook's distances identified no overly influential studies, suggesting that the individual studies did not influence the overall effect size. However, the study of Engström et al [27] was identified to have a relatively large weight due to its larger sample size, which provided more precise effect estimates in the analysis.

Clinical interpretation: In this test, no outliers nor overly influential studies were identified. This shows more strength to the average treatment effect, so no single study overly influenced the findings. The larger weight of Engström et al [27] reflects its precision, giving it slightly more influence in the analysis.

Publication bias

Neither the rank correlation test ($p = 1.0000$), nor the regression test ($p = 0.9773$) indicated funnel plot asymmetry, suggesting minimal publication bias. This means there is no evidence that the results are skewed by selective publication of studies with positive findings.

Clinical interpretation: The low publication bias enhances the reliability of the results of the meta-analysis, suggesting that the positive effect of combination therapy is not due to selective reporting of favorable studies.

Fixed-Effects Model

The estimated average log odds ratio based on the fixed-effects model was 0.4377 (95% CI: 0.0819 to 0.7934), and the back-transformed odds ratio was 1.549 (95% CI: 1.085 to 2.211). This indicates a statistically significant positive effect of combination therapy on the recovery of patients with Bell's palsy, compared to steroid treatment alone ($z = 2.4113$, $p = 0.0159$).

Clinical interpretation: In this test, the combination therapy shows improvement in the odds of recovery events, compared to steroids alone. The statistically significant effect suggests that combination therapy could be beneficial, although the effect size is slightly smaller than in the random-effects model, reflecting more uniform effects across studies.

Heterogeneity and Study Influence

The Q-test result ($Q(6) = 10.2428$, $p = 0.1148$) and the $I^2 = 41.42\%$ suggest a moderate variability among studies. While the effect is fairly consistent, one study, Engström et al [27], had a relatively large influence due to its larger sample size. Studentized residuals showed no outliers, but Cook's distance indicated that Engström et al [27] may be somewhat overly influential.

Clinical interpretation: The moderate heterogeneity suggests that the treatment effect may vary slightly among included studies, but not significantly. The larger weight of Engström's study makes sense given its large sample, which provides a precise effect estimate, but it means that its findings contribute more heavily to the overall result.

Publication Bias

Neither the rank correlation test ($p = 1.0000$) nor the regression test ($p = 0.3061$) indicated any funnel plot asymmetry, suggesting no evidence of publication bias.

Clinical interpretation: The fact that no publication bias was identified suggests that the estimated effect of combination therapy reflects a true benefit and not the result of selective reporting of positive outcomes.

Robust Bayesian meta-analysis

Table II. Summary of results.

Model Summary				
	Models	P(M)	P(M|data)	Inclusion BF
Effect	6/12	0.500	0.551	1.225
Heterogeneity	6/12	0.500	0.495	0.979
Publication bias	8/12	0.500	0.383	0.622
Model averaged estimates				
The estimates are summarized on the log(OR) scale (priors were specified on the Cohen's d scale).				
	Mean	Median	95% CI Lower	95% CI Upper
Effect size (log(OR))	0.255	0.169	0.000	0.901
Heterogeneity (τ)	0.199	0.000	0.000	0.983
Model averaged weights (ω)				
Estimated publication weights omega correspond to two-sided p-values.				
Lower p-values interval	Upper p-values interval	Mean	Median	95% CI Lower	95% CI Upper
0.000	0.050	1.000	1.000	1.000	1.000
0.050	0.100	0.878	1.000	0.291	1.000
0.100	1.000	0.825	1.000	0.181	1.000

Table III. Models overview.

	Prior Distribution						
#	Effect Size	Heterogeneity	Publication Bias	P(M)	P(M|data)	log(MargLik)	Inclusion BF
1	Spike(0)	Spike(0)		0.125	0.102	−1.945	0.793
2	Spike(0)	Spike(0)	omega[two-sided:.05] ~ CumDirichlet(1, 1)	0.063	0.051	−1.941	0.808
3	Spike(0)	Spike(0)	omega[two-sided: .1,.05] ~ CumDirichlet(1,1, 1)	0.063	0.062	−1.755	0.983
4	Spike(0)	InvGamma(1,0.15)		0.125	0.145	−1.590	1.189
5	Spike(0)	InvGamma(1,0.15)	omega[two-sided: .05] ~ CumDirichlet(1, 1)	0.063	0.047	−2.025	0.739
6	Spike(0)	InvGamma(1,0.15)	omega[two-sided: .1, .05] ~ CumDirichlet(1,1, 1)	0.063	0.043	−2.116	0.672
7	Normal(0,1)	Spike(0)		0.125	0.185	−1.345	1.594
8	Normal(0,1)	Spike(0)	omega[two-sided: .05] ~ CumDirichlet(1, 1)	0.063	0.057	−1.838	0.900
9	Normal(0,1)	Spike(0)	omega[two-sided: .1,.05] ~ CumDirichlet(1,1, 1)	0.063	0.049	−1.986	0.770
10	Normal(0,1)	InvGamma(1,0.15)		0.125	0.184	−1.352	1.580
11	Normal(0,1)	InvGamma(1,0.15)	omega[two-sided: .05] ~ CumDirichlet(1, 1)	0.063	0.044	−2.099	0.684
12	Normal(0,1)	InvGamma(1,0.15)	omega[two-sided: .1,.05] ~ CumDirichlet(1,1, 1)	0.063	0.032	−2.411	0.495

Table IV. Model diagnostics.

	Prior Distribution						
Model	Effect Size	Heterogeneity	Publication Bias	max(MCMC error)	max(MCMC error/SD)	min(ESS)	max(R-hat)
1	Spike(0)	Spike(0)					
2	Spike(0)	Spike(0)	omega[two-sided: .05] ~ CumDirichlet(1, 1)	0.003	0.014	5479	1.000
3	Spike(0)	Spike(0)	omega[two-sided: .1,.05] ~ CumDirichlet(1,1, 1)	0.003	0.015	4226	1.001
4	Spike(0)	InvGamma(1,0.15)		0.003	0.014	4902	1.002
5	Spike(0)	InvGamma(1,0.15)	omega[two-sided: .05] ~ CumDirichlet(1, 1)	0.003	0.015	4632	1.001
6	Spike(0)	InvGamma(1,0.15)	omega[two-sided: .1,.05] ~ CumDirichlet(1,1, 1)	0.003	0.017	3423	1.001
7	Normal(0,1)	Spike(0)		0.001	0.010	9778	1.000
8	Normal(0,1)	Spike(0)	omega[two-sided: .05] ~ CumDirichlet(1, 1)	0.003	0.015	4386	1.000
9	Normal(0,1)	Spike(0)	omega[two-sided: .1,.05] ~ CumDirichlet(1,1, 1)	0.003	0.016	3814	1.000
10	Normal(0,1)	InvGamma(1,0.15)		0.002	0.013	5778	1.002
11	Normal(0,1)	InvGamma(1,0.15)	omega[two-sided: .05] ~ CumDirichlet(1, 1)	0.003	0.015	4739	1.001
12	Normal(0,1)	InvGamma(1,0.15)	omega[two-sided: .1,.05] ~ CumDirichlet(1,1, 1)	0.003	0.017	3551	1.001

Figure 5 shows the posterior distribution plot based on the Bayesian meta-analysis. This plot represents the updated belief about the treatment effect size after combining prior information with the current data. Higher peaks indicate a greater likelihood of specific effect sizes. Regions to the right of zero suggest a positive treatment effect of combination therapy compared to steroids alone.

Figure 5a shows the Model-Averaged Effect Size Estimate. This plot estimates the effect size of combination therapy compared to steroids alone for Bell's palsy treatment. Positive values on the x-axis (log odds ratio) suggest a beneficial effect of combination therapy, which may increase recovery chances. The y-axis shows probability density, indicating which effect sizes are most credible based on the data. The peak of the black curve to the right of zero suggests that combination therapy likely improves recovery outcomes, though the tail crossing zero reflects some uncertainty, underscoring the need for careful patient evaluation.

Figure 5b shows the Model-Averaged Heterogeneity Estimate. This plot estimates the variability in treatment effectiveness across studies. Low heterogeneity (τ near zero) suggests that the effect of combination therapy on recovery in Bell's palsy is relatively consistent across different patient populations and study settings. This consistency strengthens the generalizability of findings, suggesting that the treatment may provide similar benefits for a broad range of patients.

Figure 5c shows the Model-Averaged Weight Function Estimate.This plot assesses potential publication bias, which could affect how treatment effects are interpreted. The x-axis represents p-value intervals, and the y-axis shows weights (ω), indicating the influence of each p-value range on the analysis. High weights near 1 for low p-values (0.000–0.050) suggest that studies reporting strong effects are credible, with less likelihood of publication bias. This reliability supports the conclusion that combination therapy may be beneficial in clinical practice.

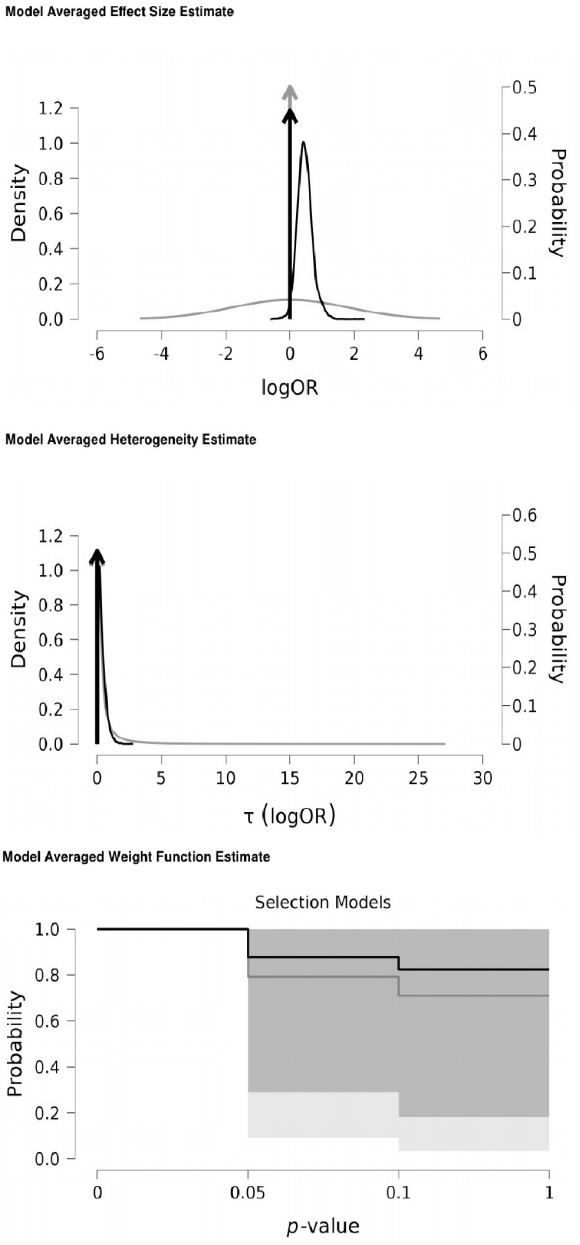

Figure 5. Posterior distribution plot based on the Bayesian meta-analysis

Figure 5a. Model averaged effect size estimate, **5b**. Model averaged heterogeneity estimate, **5c**. Model averaged weight function estimate.

Figure 6 presents the Model Averaged Forest Plot. This plot displays the range of plausible treatment effect sizes based on Bayesian analysis, with the shaded region representing the credible interval, where the true effect size likely falls with high probability. Although the credible interval includes zero, indicating statistical uncertainty, the interval is shifted to the right, suggesting a potential benefit of combination therapy for Bell's palsy recovery. This rightward trend hints at a possible positive effect favoring combination therapy, though further research is needed to confirm this conclusively.

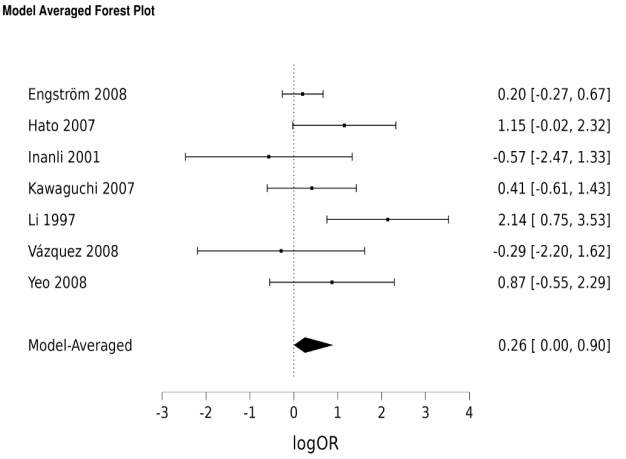

Figure 6. Model Averaged Forest Plot.

A Bayesian meta-analysis was performed using JASP [18] software. We preferred the Robust Bayesian Meta-Analysis (RoBMA) method, which offers three sets of prior models. We selected the RoBMA-original set which includes 12 models, to balance existing knowledge with new data, to avoid overly strong assumptions.

The effect sizes, heterogeneity, and publication bias were assessed. The log odds ratios and confidence intervals from the frequentist meta-analysis were used, to perform the Bayesian meta-analysis.

Effect size

The posterior probability of the effect size was 0.551, indicating a slight increase in the belief that combination therapy may have a positive effect on recovery of facial function, compared to steroids alone. The inclusion Bayes Factor (BF) for effect size was 1.225, suggesting weak evidence in favor of combination therapy's effectiveness.

Clinical interpretation: This result provides weak but positive support for the idea that combination therapy could improve recovery rates in Bell's palsy compared to steroids alone, though further evidence is needed.

Heterogeneity

The posterior probability of heterogeneity was 0.495. These results show moderate variation across studies. The inclusion Bayes Factor of heterogeneity was 0.979. That means that there is no strong evidence of variation in the treatment effect in the included studies.

Clinical interpretation: These findings suggest that the treatment effect of the combination therapy was relatively stable across the studies, providing confidence for the application of the combined treatment across patient groups.

Publication Bias

The posterior probability of publication bias was 0.383, and the inclusion Bayes Factor was 0.622. This suggests only minimal evidence of publication bias presence, in the Bayesian meta-analysis.

Clinical interpretation: Minimal publication bias enhances confidence that the overall effect size is a reliable indicator of combination therapy's potential benefits.

Model-Averaged Estimates

The model-averaged estimates provided a mean effect size of 0.255 (median 0.169) with 95% credible intervals (CrI) of [0.000, 0.901]. Although the average effect suggests a moderate positive impact of combination therapy, the credible intervals include zero, indicating that, there is uncertainty about the significance of this effect.

Clinical interpretation: The credible intervals CrI, showed some uncertainty in the true effect size. That means that, although a positive effect is likely, it is not definitively established.

Model Diagnostics

The diagnostic tests of the Bayesian meta-analysis showed good convergence of the (MCMC) Markov Chain Monte Carlo algorithm. The R-hat values were close to 1, ranging between 1.000 and 1.002, indicating stability in model estimates [24,25]. Furthermore, the Effective Sample Size (ESS) ranged from 3423 to 9778, suggesting sufficient independent sampling [24,25]. In addition, the low MCMC error values, ranging from 0.001 to 0.017, indicated accurate estimates with low uncertainty [24, 25].

Clinical interpretation: According to the diagnostic tests, the Bayesian analysis is reliable, and the results show that the estimates are well-converged and accurate.

Publication Weights

The model-averaged weights for publication bias (ω) were close to 1 for low p-values (0.000–0.050), with slightly lower weights for p-values between 0.050 and 1.000. This weighting reflects the confidence level in each study's contribution, where studies with lower p-values provide more reliable estimates.

Clinical interpretation: The even distribution of weights supports the consistency of the evidence, suggesting that individual studies are not overly influencing the overall result [19].

Discussion

This meta-analysis shows that combining steroids and antivirals improves recovery odds for Bell's palsy compared to steroids alone. Both frequentist and Bayesian analyses support this, though the Bayesian results highlight some uncertainty about the exact effect size.

The findings suggest that combination therapy is a reliable option, but further research is needed to confirm the best dosage, timing, and response in different patient groups. With more studies, we can better tailor treatment plans and clarify how this therapy can benefit Bell's palsy patients.

Heterogenicity was observed in antiviral treatment in studies. Valacyclovir was used by Engström et al [27], Hato et al [28], Kawaguchi et al [30], and Vázquez et al [32]. Acyclovir was used by Inanli et al [29], Li et al [31] and Yeo et al [33]. Concerning steroids, prednisone was used by Yeo et al [33], Vázquez et al [32], and Li et al [31]. Prednisolone was used by Inanli et al [29], Engström et al [27], Hato et al [28], and Kawaguchi et al [30].

The quality assessment indicated some studies with possible risk of bias. We observed a possible risk of bias in the studies of Kawaguchi et al [30], and Hato et al [28]. A very low risk of bias was observed in the studies of Engtorm et al [27]. The reason that a risk of bias exists is that the studies of Kawaguchi et al [30] were not blinded and the study of Hato et al [28] was single-blinded RCT.

Also, the study of Inanli et al [29] is stated as a prospective, controlled, and randomized study, but no other data are given about randomization and blinding.

In the existing literature, some studies focus on the use of medications, such as steroids and antivirals, for the treatment of Bell's palsy, while others explore alternative treatment options.

In a network meta-analysis of Jalali et al [34], the authors included 21 trials comprising 2,839 participants. Measuring the good recovery, they report that corticosteroids plus antivirals were more effective than compared to placebo RR 1.25 (95% CrI: 1.10, 1.43) in short term and 1.26 (95% CrI: 1.11, 1.45) for intermediate and long term recovery. Finally, the authors conclude that combined therapy remains the best choice for recovery in patients with Bell's palsy.

In a network meta-analysis of Cao et al [35], the authors concluded that famciclovir could be better than a placebo and the effectiveness of other antiviral treatments are similar. According to the study, famciclovir showed the best results, followed by valacyclovir, acyclovir, and finally placebo.

In a retrospective cohort study by Kim et al [36], assessing 1710 patients treated for Bell's palsy from January 2005 to December 2019, the authors concluded that combination therapy with steroids plus antiviral agents resulted in higher favorable rates compared to steroids alone in severe Bell's palsy patients.

In another retrospective study, Rim et al [37], evaluated 1504 patients with Bell's palsy from January 1986 to May 2023. The authors of the study concluded that the management of Bell's palsy should be applied according to the patient's characteristics, such as the severity of the condition. Steroid monotherapy, within 72 hours, showed favorable results, although an antiviral and steroid treatment combination could offer an advantage in patients with severe Bell's palsy.

In a meta-analysis of Abdu et al [38], comparing oral versus intravenous steroids for the treatment of Bell's palsy, the authors, suggest that a full recovery can be achieved in one month, when intravenous methylprednisolone is given to the patients, compared to oral prednisolone. Furthermore, no difference was observed after 3 months, between the two treatment options.

De Jongh et al [39], investigated the Botulinum toxin A treatment, for synkinesis in peripheral facial nerve injury. However, they concluded that this treatment is patient-specific and personalized to the patient, so studies should focus on this direction, rather than trying to standardize this treatment.

In another meta-analysis, by Fujiwara et al [40], the authors concluded that intratympanic administration of corticosteroids showed a reduced non-recovery rate of facial function in patients with Bell's palsy and Ramsay Hunt syndrome, although the quality of evidence was very low.

Nakano et al [41], performed a meta-analysis on the effect of physical therapy on peripheral facial palsy. They suggested that physical therapy, improves the Sunnybrook facial grading score, although its efficiency in reducing palsy sequelae is uncertain. According to the study, the certainty of the evidence was low to very low.

In a retrospective case review of Kim et al [42], the authors concluded that Facial nerve decompression surgery, in patients with severe Bell's palsy did not improve prognosis compared to the conservative treatment alone.

Limitations of the evidence included and the review process

Several limitations exist in our study. First heterogenicity was observed among studies using antiviral treatment. We extracted the data from the included studies without further analysis of antiviral treatment. Among the antiviral agents used are acyclovir, and valacyclovir. Differences in efficiency may exist. In this review, an overall statistical analysis was performed without analyzing further outcomes according to the antiviral agent used. Second, in the included studies different risk of bias was observed. We did not analyze outcomes according to the risk of bias of included studies. Another limitation was the degree of facial palsy. The degree of facial paralysis may affect the patient's recovery. The fourth limitation was the degree of recovery. In this review, we tried to analyze the complete

recovery events accordingly as the data was given in the included studies. Different criteria were set as what is good recovery among studies. Furthermore, another limitation was observed by the heterogenicity in the scoring system, as some studies used the House-Brackmann scale [10], but some studies used another scale such as the Sunnybrook scale score [12] and Yanagihara scoring system [11]. Sixth, although we used the original RoBMA set with 12 models of prior combinations for the effects, the priors could be strong enough, affecting the posterior distribution, leading to non-significant results for the effect size.

Seventh, we did not perform an analysis for the treatment of adverse events. Finally, although we performed a comprehensive search in electronic databases, we may have missed some relevant studies.

Implications of the results for practice, policy, and future research

Implications for research and practice

Clinical practice

Our meta-analysis suggests that combined treatment with steroids and antivirals could improve the recovery rates in patients with Bell's palsy compared to steroids alone. Given the moderate consistency in treatment effects across studies, combination therapy appears to have broad applicability, though individual responses may vary.

The pooled effect size estimate of frequentist and Bayesian meta-analysis, help healthcare providers to make informed decisions regarding the effectiveness of combination therapy for Bell's palsy. The fact that no significant publication bias was observed and moderate heterogenicity across studies, provides combination therapy as a reliable option for clinicians.

In addition, beyond the clinical effectiveness of the treatment itself, a compassionate approach that communicates positive recovery expectations to patients is essential. A patient-centered perspective, which prioritizes the patients' health improvement and well-being is necessary, avoiding quality-of-life measurement tools that may undervalue patients' needs. Furthermore, a supporting and empathetic approach should be a priority.

Future research

The results of our study show the need for further research on the role of combination therapy and, to update treatment protocols. Future research could focus on optimal timing, dosage, and, duration of combined treatment for Bell's palsy, to help standardize protocols for clinical practice.

Our study contributes methodological insights that future research can build on. We performed frequentist meta-analyses using diagnostics like Cook's distances for influential studies, studentized residuals for outliers, and tests for publication bias. In addition, performing Bayesian meta-analysis using priors may inspire future studies to apply similar methods. These approaches ensure a robust evaluation of evidence quality.

It is important to address the uncertainty observed in the Bayesian credible intervals, which included zero. Randomized controlled trials with larger samples, would help to verify the positive effect size observed in this meta-analysis and establish the generalizability of findings. Future research, investigating these knowledge gaps, can offer healthcare providers more definitive guidance on combination therapy effectiveness, supporting a more evidence-based approach to managing Bell's palsy.

Implications for policy and health services

Policymakers can develop evidence-based guidelines for implementing combination therapy. In addition, evaluating healthcare services' effectiveness and responsiveness to patients' needs will provide health services with opportunities for continuous improvement in patient care and recovery support. It is important to create a compassionate healthcare environment providing comprehensive information to the patients about the treatment options. Supporting the patients with positive messages is of paramount importance, as this could influence positively the patients' phychological well-being and overall recovery.

Conclusions

In this study, we confirm the superior efficacy of steroid plus antiviral therapy for Bell's palsy, compared to steroid monotherapy. Although this conclusion is supported by the traditional frequentist meta-analysis, it is not supported by the Bayesian meta-analytical approach, as the Bayesian meta-analysis was inconclusive, suggesting some uncertainty in the effect size, but this could be due to priors influence. Well-designed double-blinded randomized controlled trials of lower risk of bias are needed. More advanced synthesis of the evidence with direct and indirect comparisons as well as with Bayesian approaches may provide insights and further elucidate the efficiency of various treatment modalities for Bell's palsy.

Authors contributions

C.S., and L.K. the concept and design of the study; A.F and C.I. data acquisition; C.S. statistical analysis; C.S., A.F., C.I. interpreted the results; C.S., A.F. and P.O. analyzed the data and drafted the manuscript. All authors critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

References

1. Yuan J, Johari S, Seneviratna A, Chong YK. Bell's palsy workup: Does audiometry add value? J Otol. 2021;16:61-64.
2. Baugh RF, Basura GJ, Ishii LE, Schwartz SR, Drumheller CM, Burkholder R, et al. Clinical practice guideline: Bell's palsy. Otolaryngol Head Neck Surg. 2013;149:S1-27.
3. Gronseth GS, Paduga R; American Academy of Neurology. Evidence-based guideline update: steroids and antivirals for Bell palsy: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2012;79:2209-2213.
4. Inagaki A, Takahashi M, Murakami S. Facial and hearing outcomes in transmastoid nerve decompression for Bell's palsy, with preservation of the ossicular chain. Clin Otolaryngol. 2021;46:325-331.
5. Kim SH, Jung J, Lee JH, Byun JY, Park MS, Yeo SG. Delayed facial nerve decompression for Bell's palsy. Eur Arch Otorhinolaryngol. 2016;273:1755-1760.
6. Di Pietro A, Cameron M, Campana V, Leyes L, Zalazar Cinat JAI, et al. Efficacy of adding selective electrical muscle stimulation to usual physical therapy for Bell's palsy: immediate and six-month outcomes. Eur J Transl Myol. 2023;33:11630.
7. Kim DR, Kim JH, Jung SH, Won YJ, Seo SM, Park JS, et al. Neuromuscular retraining therapy for early stage severe Bell's palsy patients minimizes facial synkinesis. Clin Rehabil. 2023;37:1510-1520.
8. Wyatt JS. What's Wrong with Quality of Life as a Clinical Tool?. Virtual Mentor. 2005;7:183-186.
9. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
10. House JW, Brackmann DE. Facial nerve grading system. Otolaryngol Head Neck Surg. 1985;93:146-147.
11. Hato N, Fujiwara T, Gyo K, Yanagihara N. Yanagihara facial nerve grading system as a prognostic tool in Bell's palsy. Otol Neurotol. 2014;35:1669-1672.
12. Ross BR, Fradet G, Nedzelski JM. Development of a sensitive clinical facial grading system. Eur Arch Otorhinolaryngol. 1994:S180-S181.
13. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343:d5928.
14. Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager 5 (RevMan 5). Version 5.4.1 Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration.
15. The jamovi project (2024). jamovi. (Version 2.5) [Computer Software]. Available from https://www.jamovi.org.
16. R Core Team (2023). R: A Language and environment for statistical computing. (Version 4.3) [Computer software]. Available from: https://cran.r-project.org . (R packages retrieved from CRAN snapshot 2024-01-09).
17. Viechtbauer, W. Conducting Meta-Analyses in R with the metafor Package. Journal of Statistical Software, 2010;36, 1–48.
18. JASP Team (2024). JASP (Version 0.18.3)[Computer software]. Available from: https://jasp-stats.org/
19. Bartoš F, Maier M, Wagenmakers EJ, Doucouliagos H, Stanley TD. Robust Bayesian meta-analysis: Model-averaging across complementary publication bias adjustment methods. Res Synth Methods. 2023;14:99-116.
20. Berkhout SW, Haaf JM, Gronau QF, Heck DW, Wagenmakers EJ. A tutorial on Bayesian model-averaged meta-analysis in JASP. Behav Res Methods. 2024;56:1260-1282.
21. Kelter R. Bayesian alternatives to null hypothesis significance testing in biomedical research: a non-technical introduction to Bayesian inference with JASP. BMC Med Res Methodol. 2020;20:142.
22. Johnson VE, Pramanik S, Shudde R. Bayes factor functions for reporting outcomes of hypothesis tests. Proc Natl Acad Sci U S A. 2023;120:e2217331120.
23. Vivekananda RA. Convergence Diagnostics for Markov Chain Monte Carlo Annual Review of Statistics and Its Application Rev Stat Appl. 2020;7:387–412.
24. Quintana DS. How to perform a Bayesian meta-analysis. The benefits of Bayesian meta-analysis and how to perform one in R, 2021. Available from: https://www.dsquintana.blog/how-to-perform-a-bayesian-meta-analysis-in-r/
25. František Bartoš. Package 'RoBMA'. Robust Bayesian Meta-Analyses, Version 3.1.0. 2023. Available from: https://cran.r-project.org/web/packages/RoBMA/RoBMA.pdf
26. 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;6:e1000097.
27. Engström M, Berg T, Stjernquist-Desatnik A, Axelsson S, Pitkäranta A, Hultcrantz M, et al. Prednisolone and valaciclovir in Bell's palsy: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet Neurol. 2008;7:993-1000.
28. Hato N, Yamada H, Kohno H, Matsumoto S, Honda N, Gyo K, et al. Valacyclovir and prednisolone treatment for Bell's palsy: a multicenter, randomized, placebo-controlled study. Otol Neurotol. 2007;28:408-413.
29. İnanlı S, Tutkun A, Öztürk Ö, Batman Ç, Üneri C, Şehitoğlu MA. Idiopathic Facial Nerve Paralysis Treatment with Acyclovir and Prednisolone Compared with Prednisolone Alone. Turk Arch Otorhinolaryngol. 2001;39:19-24.
30. Kawaguchi K, Inamura H, Abe Y, Koshu H, Takashita E, Muraki Y, et al. Reactivation of herpes simplex virus type 1 and varicella-zoster virus and therapeutic effects of combination therapy with prednisolone and valacyclovir in patients with Bell's palsy. Laryngoscope. 2007;117:147-156.
31. Li Y, Gao P, Mao X, Cao P. Randomized clinical trial of acyclovir plus prednisone versus prednisone alone in Bell's palsy. Ceylon Journal of Medical Science 1997;40:37-41.
32. Vázquez MC, Sánchez N, Calvo J, Perna A. Efficacy of antiviral agents in Bell's paralysis. Revista Médica del Uruguay. 2008;24:67-174.
33. Yeo SG, Lee YC, Park DC, Cha CI. Acyclovir plus steroid

vs steroid alone in the treatment of Bell's palsy. Am J Otolaryngol. 2008;29:163-166.

34. Jalali MM, Soleimani R, Soltanipour S, Jalali SM. Pharmacological Treatments of Bell's Palsy in Adults: A Systematic Review and Network Meta-Analysis. Laryngoscope. 2021;131:1615-1625.
35. Cao J, Zhang X, Wang Z. Effectiveness comparisons of antiviral treatments for Bell palsy: a systematic review and network meta-analysis. J Neurol. 2022;269:1353-1367.
36. Kim Y, Doo JG, Chon J, Lee JH, Jung J, Lee JM, et al. Steroids plus antiviral agents are more effective than steroids alone in the treatment of severe Bell's palsy patients over 40 years of age. Int J Immunopathol Pharmacol. 2021;35:20587384211042124.
37. Rim HS, Byun JY, Kim SH, Yeo SG. Optimal Bell's Palsy Treatment: Steroids, Antivirals, and a Timely and Personalized Approach. J Clin Med. 2023;13:51.
38. Abdu SH, Alsubhi AH, Alzahrani A, Alshehri A, Al Taylouni N, Rammal A. Comparison of oral versus intravenous steroid in the management of Bell's palsy: a systematic review and meta-analysis of randomized clinical trials. Eur Arch Otorhinolaryngol. 2024;281:1095-1104.
39. de Jongh FW, Schaeffers AWMA, Kooreman ZE, Ingels KJAO, van Heerbeek N, Beurskens C, et al. Botulinum toxin A treatment in facial palsy synkinesis: a systematic review and meta-analysis. Eur Arch Otorhinolaryngol. 2023;280:1581-1592.
40. Fujiwara T, Iwata S, Hosokawa Y, Mitani S. Intratympanic corticosteroid for Bell's palsy and Ramsay Hunt syndrome: Systematic review and meta-analysis. Auris Nasus Larynx. 2022;49:599-605.
41. Nakano H, Fujiwara T, Tsujimoto Y, Morishima N, Kasahara T, Ameya M, et al. Physical therapy for peripheral facial palsy: A systematic review and meta-analysis. Auris Nasus Larynx. 2024;51:154-160.
42. Kim Y, Yeo SG, Rim HS, Lee J, Kim D, Kim SS, et al. Comparison of Medical and Surgical Treatment in Severe Bell's Palsy. J Clin Med. 2022;11:888.