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Comparative efficacy and safety of antiviral therapy for herpes zoster ophthalmicus: a systematic review and Bayesian network meta-analysis

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Abstract

Background

Herpes zoster ophthalmicus (HZO) is reactivation of varicella zoster virus in the ophthalmic division of the trigeminal nerve. About half of untreated patients develop ocular complications. Acyclovir (oral, intravenous or topical), valacyclovir and famciclovir are all used, but no trial has compared more than two regimens. We compared these drugs and routes for acute HZO.

Methods

We searched PubMed, Embase and CENTRAL from inception to 15 March 2026 for randomised trials of antiviral treatment for acute HZO. Trials of herpes simplex eye disease and of long-term suppression were excluded. Systemic and topical acyclovir were analysed as separate treatments. Outcomes were treatment failure, resolution of ocular disease and adverse events. We fitted Bayesian random-effects network meta-analyses, which give odds ratios (ORs) with 95% credible intervals (CrIs). Risk of bias was assessed with RoB 2 and certainty with GRADE.

Results

Seven trials (933 participants, published 1983–2001) were included. Compared with placebo, systemic acyclovir reduced treatment failure (OR 0.19, 95% CrI 0.05–0.66; low certainty) and topical acyclovir did not (OR 1.00, 0.19–5.09; very low certainty). Topical acyclovir had higher odds of failure than systemic acyclovir (OR 5.15, 1.24–25.53; low certainty). Neither valacyclovir (OR 0.90, 0.19–4.99) nor famciclovir (OR 1.00, 0.24–4.87) differed from systemic acyclovir (low certainty). Systemic acyclovir also increased resolution of ocular disease (OR 8.50, 1.07–75.26; low certainty). Adverse events did not differ between treatments. No inconsistency was detected. Three trials were at high risk of bias and none at low risk.

Conclusions

Systemic antiviral therapy reduces ocular complications in acute HZO, and topical acyclovir ointment is not an adequate substitute. Valacyclovir and famciclovir perform similarly to oral acyclovir. The evidence is limited to seven small, older trials, so adequately powered head-to-head trials are needed.

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Introduction

Herpes zoster ophthalmicus (HZO) results from reactivation of latent varicella zoster virus (VZV) in the ophthalmic division of the trigeminal nerve. It accounts for approximately 10% to 20% of herpes zoster cases, and ocular involvement develops in about half of affected patients who receive no antiviral treatment [1]. The eye can be involved at any level, from conjunctivitis and epithelial keratitis to stromal keratitis, anterior uveitis, scleritis and, rarely, retinitis or optic neuritis, and late sequelae include neurotrophic keratopathy, corneal scarring, secondary glaucoma and postherpetic neuralgia [1, 2].

Placebo-controlled trials in the 1980s and early 1990s showed that systemic acyclovir started early in the course of HZO reduced the frequency of later ocular inflammation [3–5]. The prodrugs valacyclovir and famciclovir, which achieve higher drug exposure with three-times-daily dosing, were later compared with oral acyclovir in HZO [6, 7]. Topical acyclovir ointment, which reaches high concentrations in the aqueous humour, was also tested, both with topical corticosteroids in established ocular inflammation [8] and against oral acyclovir in acute disease [9].

These trials each compared two regimens. A Cochrane review of valacyclovir versus acyclovir for HZO found a single eligible trial and could not reach a conclusion on relative benefit [10]. A broader review of antivirals for herpes zoster pooled trials from all dermatomes with pain as its main outcome [11]. No review has compared all antiviral agents and routes on ocular outcomes. The Zoster Eye Disease Study has since addressed a different question, the use of long-term low-dose valacyclovir to suppress recurrent disease after an HZO episode [12].

Network meta-analysis combines direct comparisons within trials with indirect comparisons through common comparators, which allows treatments that were never compared head-to-head to be placed on one scale [13]. We conducted a systematic review and network meta-analysis of randomised trials of antiviral treatment for acute HZO, treating systemic and topical acyclovir as separate interventions, to compare their effects on treatment failure, resolution of ocular disease and adverse events.

Methods

Protocol and reporting

The review followed the Cochrane Handbook for Systematic Reviews of Interventions [16] and is reported according to PRISMA 2020 [15] and its extension for network meta-analyses [14]. The protocol was registered in PROSPERO (CRD420261423206). Three changes were made after registration: the review was restricted to VZV disease, trials of long-term suppression were excluded, and acyclovir was divided into systemic and topical nodes. The reasons are given in Supplementary Table S1.

Eligibility criteria

We included randomised controlled trials that enrolled patients with acute HZO, or trials of herpes zoster that reported ocular outcomes separately for patients with ophthalmic involvement. Eligible comparisons were an antiviral drug against placebo, against another antiviral, or against the same antiviral

given by a different route. Co-interventions were allowed if both arms received them. Where immune status was not reported, participants were assumed to be immunocompetent.

We excluded trials of herpes simplex virus (HSV) eye disease, trials of suppressive treatment in patients without active acute disease at entry, trials comparing the same drug and route at different durations or doses (both arms would form a single node), non-randomised studies, and trials that reported none of the review outcomes in a form that could be converted to event counts.

Information sources and search

PubMed, Embase and the Cochrane Central Register of Controlled Trials were searched from inception to 15 March 2026 using controlled vocabulary and free-text terms for ocular herpes zoster and herpetic eye disease, combined with terms for antiviral drugs (Supplementary Table S2). Reference lists of included trials and relevant reviews were checked by hand.

Study selection and data extraction

Two reviewers independently screened titles and abstracts and then full texts in Rayyan, and disagreements were resolved by discussion or by a third reviewer. From each trial we extracted design, setting, eligibility criteria, sample size, age, sex, ethnicity, immune status, time from rash onset to treatment, drug, dose, route and duration, co-interventions, follow-up, and arm-level counts for each outcome together with the trial's own outcome definition. Where a trial reported percentages only, counts were derived from the percentage and the arm denominator. Each derived value is marked in Supplementary Table S5.

Treatment nodes

The network had five nodes: placebo, systemic acyclovir (oral or intravenous), topical acyclovir (ophthalmic ointment), valacyclovir and famciclovir. Oral doses of acyclovir ranged from 600 mg to 800 mg five times daily for 7 to 10 days and were pooled within the systemic node, because each dose was tested in a different trial and a dose effect could not be separated from a trial effect. In the three-arm trial by Marsh and Cooper [8], the comparison of acyclovir ointment plus dexamethasone drops with placebo ointment plus dexamethasone drops was used, since the steroid was common to both arms. The trial by McGill and colleagues [5] enrolled herpes zoster at any site, and only the patients with ocular involvement contributed to the ocular outcome.

Outcomes

Treatment failure was defined as the development or progression of ocular complications during follow-up, or the need for additional treatment of ocular disease such as topical corticosteroids or intravenous antiviral therapy. Resolution of ocular disease was defined as the absence of active ocular disease at the trial's final ocular assessment. Adverse events were defined as the proportion of patients with at least one adverse event. Two trials reported adverse events only as counts by symptom, and one reported percentages for individual events; these data were used in the main adverse-event analysis and removed in a sensitivity analysis. The definition used in each trial is listed in Supplementary Table S5.

Risk of bias

Risk of bias was assessed with the Cochrane RoB 2 tool [17] across its five domains: the randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each domain and the overall judgement were rated low risk, some concerns or high risk.

Statistical analysis

For each outcome we fitted an arm-based Bayesian network meta-analysis with a binomial likelihood and logit link [18], assuming consistency and a common between-trial standard deviation (τ). The primary model used random effects with a half-normal(0, 1) prior on τ [19], normal(0, 5^2) priors on the basic treatment effects and normal(0, 10^2) priors on trial-specific baselines. Models were run in JAGS 4.3.2 through rjags 4–15 in R 4.3.3 [20], with three chains, 20,000 burn-in iterations and 60,000 sampling iterations thinned by 5. Convergence was checked with the Gelman–Rubin statistic (R-hat below 1.01 for all parameters) [21] and trace plots. Model fit was assessed from the posterior mean residual deviance against the number of data points and from the deviance information criterion (DIC). Trials with no events in either arm, or with events in every patient in both arms, carry no information on the odds ratio and were left out of the network for that outcome.

Results are posterior medians of odds ratios (ORs) with 95% credible intervals (CrIs). Treatments were ranked using the surface under the cumulative ranking curve (SUCRA) [13]. Inconsistency was assessed by node-splitting for every comparison lying in a closed loop [22]. Sensitivity analyses were a fixed-effect model, a random-effects model with a uniform(0, 5) prior on τ, a frequentist random-effects network meta-analysis fitted by restricted maximum likelihood in metafor [23] with a 0.5 continuity correction for trials with a zero cell, exclusion of the McGill trial for treatment failure, and restriction of the adverse-event network to trials that counted patients rather than events. Small-study effects could not be assessed because no comparison had more than three trials.

Transitivity was examined by comparing time from rash onset to treatment, age, immune status, co-interventions and outcome definitions across the direct comparisons. Certainty of evidence for each network estimate was rated with the GRADE approach for network meta-analysis [24, 25], considering risk of bias, inconsistency, indirectness (including intransitivity), imprecision, publication bias and incoherence between direct and indirect estimates.

Results

Study selection

The search identified 1,104 records. After removal of 444 duplicates, 660 records were screened by title and abstract and 592 were excluded. All 68 remaining reports were retrieved and assessed in full, and 61 were excluded (Fig. 1; Supplementary Table S3). The commonest reasons were the absence of an antiviral intervention (25 reports), herpes zoster without ocular involvement (11) and HSV eye disease (18). The Zoster Eye Disease Study was excluded as a suppression trial [12], the trial by Hoang-Xuan and colleagues because both arms received the same oral acyclovir regimen for different durations [26], and the valacyclovir trial by Beutner and colleagues because it did not report outcomes for its HZO subgroup [27]. Seven trials were included [3–9].

Characteristics of included trials

The seven trials randomised 933 participants and were published between 1983 and 2001 (Table 1). Four were conducted in the United Kingdom [4, 5, 8, 9], one in four centres in the United States [3], one in five centres in France [6] and one in 87 centres internationally [7]. Trial size ranged from 40 to 499 randomised participants, and mean age, where reported, ranged from 58 to 71 years. Three trials compared systemic acyclovir with placebo: oral acyclovir 600 mg five times daily for 10 days [3], oral acyclovir 800 mg five times daily for 10 days [4] and intravenous acyclovir 5 mg/kg every 8 hours for 5 days [5]. One trial compared acyclovir ointment with placebo ointment, both given with dexamethasone drops [8], one compared acyclovir ointment with oral acyclovir 800 mg five times daily [9], and two compared a prodrug with oral acyclovir 800 mg five times daily for 7 days: valacyclovir 1 g three times daily [6] and famciclovir 500 mg three times daily [7].

Table 1
Baseline characteristics of included trials

Study	Design and setting	Intervention / Control	Sample size, I / C randomised (analysed)	Age, mean ± SD (y)		Male %		White %		Black %		Time from rash onset to treatment	Ocular status / disease at entry
				I	C	I	C	I	C	I	C		
Randomised controlled trials included in the network meta-analysis (n = 7)													
Cobo 1986 [3]	RCT, double-masked, placebo-controlled; 4 centres, USA	Oral acyclovir 600 mg 5×/day for 10 days / oral placebo	36 / 35	NR	NR	36.1	60.0	88.9	88.6	11.1	11.4	< 72 h: 20 / 23 72 h–7 days: 16 / 12	Acute HZO
Colin 2000 [6]	RCT, double-masked; 5 centres, France	Valacyclovir 1000 mg 3×/day for 7 days / oral acyclovir 800 mg 5×/day for 7 days	56 / 54	58 ± 18	62 ± 17	53.6	42.6	100	100	0	0	≤ 48 h: 49 / 46 > 48 h: 7 / 8	Acute HZO
Harding 1991 [4]	RCT, double-masked, placebo-controlled; Liverpool, UK	Oral acyclovir 800 mg 5×/day for 10 days / oral placebo	24 (23) / 22 (19)	62.1[a]	70.6[a]	26.1[a]	47.4[a]	NR	NR	NR	NR	< 72 h	Acute HZO, no intraocular complication at entry
Marsh 1991 [8][b]	RCT, three-arm, double-masked; Moorfields, London, UK	Acyclovir ointment + dexamethasone drops / placebo ointment + dexamethasone drops	97 in 3 arms (27 / 26)	NR	NR	NR	NR	NR	NR	NR	NR	< 3 weeks	HZO with established ocular inflammation
McGill 1983 [5][c]	RCT, double-blind, placebo-controlled; UK	Intravenous acyclovir 5 mg/kg every 8 h for 5 days / intravenous placebo	40 entered (17 / 20); ocular subgroup 8 / 10	70.4	68.8	17.6	35.0	NR	NR	NR	NR	Mean 1.69 / 1.80 days (≤ 96 h)	Herpes zoster, any dermatome; trigeminal 11 / 14
Neoh 1994 [9][d]	RCT, open-label; 3 centres, UK	Acyclovir 3% ointment 5×/day for 7 days / oral acyclovir 800 mg 5×/day for 7 days	70 in total (26 / 31)	64.6 (all)	–	31.6 (all)	–	NR	NR	NR	NR	< 72 h	Acute HZO, no ocular complication at entry
Tyring 2001 [7]	RCT, double-masked, double-dummy; 87 centres, international	Famciclovir 500 mg 3×/day for 7 days / oral acyclovir 800 mg 5×/day for 7 days	251 / 246 (203)[e]	59	58	47.8	45.8	94	96	4	3	0–48 h: 135 / 117 49–72 h: 116 / 86	Acute HZO (V1)

Values are given as intervention / control (I / C) in the order listed in the third column. Sample size is the number randomised, with the number analysed in p herpes zoster ophthalmicus; NR, not reported; RCT, randomised controlled trial; V1, ophthalmic division of the trigeminal nerve.

[a] Reported for the 23 and 19 analysed patients. [b] Not reported; assumed immunocompetent in the analysis. [c] Third arm (acyclovir ointment + placebo drops no matching comparator; 14 of 97 patients were not analysed. [d] Herpes zoster at any site; 25 patients had trigeminal zoster and the 18 with ocular involvem contributed treatment-failure data. [e] 13 of 70 patients were excluded from analysis (9 lost to follow-up, 4 ointment patients given oral acyclovir or steroids b gives 26 / 31 analysed while Table I of the report gives 25 / 32, and the outcome analysis uses Table I. Age and sex were reported for all 57 analysed patient 499 randomised in total; 43 acyclovir patients who received a non-bioequivalent batch were excluded from the efficacy analysis.

Four trials enrolled patients within 72 hours of rash onset [4, 6, 7, 9], one within 96 hours [5] and one within 7 days [3]. The trial by Marsh and Cooper differed from the others: it enrolled patients who already had ocular inflammation, up to 3 weeks after the rash, and all patients received a topical corticosteroid [8]. Five trials enrolled immunocompetent adults and two did not report immune status [4, 8]. Follow-up ranged from 24 weeks to 12 months.

Risk of bias

No trial was at low risk of bias overall. Four trials raised some concerns [3, 4, 6, 7] and three were at high risk (Supplementary Figure S1; Supplementary Table S4). The trial by Marsh and Cooper was rated high risk for the randomisation process because the authors reported significant differences between groups in initial disease severity, with milder disease in the acyclovir-plus-steroid arm, and in sex distribution [8]. The McGill trial was rated high risk for missing outcome data because ocular outcomes were available only for the post-randomisation subgroup with eye involvement, and the report gives inconsistent

numbers for that subgroup [5]. The trial by Neoh and colleagues was open-label, and four patients in the ointment group who were given oral acyclovir or steroids by their general practitioner were removed from the analysis, which led to a high-risk rating for deviations from intended interventions [9]. All seven trials raised some concerns for selection of the reported result, as none had a published protocol or analysis plan.

Network geometry

The treatment-failure network included all seven trials, five nodes and 792 analysed patients (Supplementary Figure S2). It contained one closed loop, formed by placebo, systemic acyclovir and topical acyclovir. Valacyclovir and famciclovir were each connected to the network by a single trial against systemic acyclovir. The resolution network included four trials [4, 6, 8, 9], four nodes and 242 patients, with the same closed loop. The adverse-event network included four trials [3–6], three nodes and 264 patients, and had no closed loop. The Marsh trial reported no drug-related adverse events in either arm and therefore did not contribute to that network.

Treatment failure

Systemic acyclovir reduced the odds of treatment failure compared with placebo (OR 0.19, 95% CrI 0.05–0.66), whereas topical acyclovir did not (OR 1.00, 0.19–5.09) (Fig. 2). Topical acyclovir had higher odds of failure than systemic acyclovir (OR 5.15, 1.24–25.53). Point estimates for valacyclovir (OR 0.17, 0.02–1.31) and famciclovir (OR 0.20, 0.03–1.26) against placebo were similar to that of systemic acyclovir, but their intervals crossed 1 because they were linked to placebo only through acyclovir. Compared with systemic acyclovir, the OR was 0.90 (0.19–4.99) for valacyclovir and 1.00 (0.24–4.87) for famciclovir, and valacyclovir compared with famciclovir gave an OR of 0.89 (0.10–8.55) (Supplementary Table S6). SUCRA values were 76.3% for valacyclovir, 72.8% for systemic acyclovir, 71.2% for famciclovir, 15.2% for topical acyclovir and 14.5% for placebo (Supplementary Table S7; Supplementary Figure S3). Between-trial heterogeneity was moderate (τ 0.43, 95% CrI 0.02–1.64).

Resolution of ocular disease

Systemic acyclovir increased the odds of resolution compared with placebo (OR 8.50, 95% CrI 1.07–75.26) (Fig. 3). The estimates for topical acyclovir (OR 3.64, 0.45–31.91) and valacyclovir (OR 3.52, 0.07–115.29) were imprecise. Topical acyclovir compared with systemic acyclovir gave an OR of 0.43 (0.05–4.06), and valacyclovir compared with systemic acyclovir an OR of 0.41 (0.01–7.85). Systemic acyclovir ranked highest (SUCRA 83.3%), followed by topical acyclovir (54.1%), valacyclovir (50.5%) and placebo (12.2%). The direct evidence for systemic acyclovir against placebo came from one trial of 39 patients [4]. Heterogeneity was τ 0.59 (0.03–2.01).

Adverse events

Adverse events did not differ between systemic acyclovir and placebo (OR 1.06, 95% CrI 0.37–3.48) or between valacyclovir and placebo (OR 0.78, 0.08–7.75), and valacyclovir compared with systemic acyclovir gave an OR of 0.74 (0.10–5.39) (Fig. 4). SUCRA values were 61.6% for valacyclovir, 47.5% for placebo and 41.0% for systemic acyclovir. Only the Harding trial counted patients with at least one adverse event (12 of 24 on acyclovir, 11 of 22 on placebo; OR 1.00, 95% CI 0.31–3.18) [4]. Famciclovir and topical acyclovir could not be included in this network.

Inconsistency, model fit and sensitivity analyses

Node-splitting found no disagreement between direct and indirect evidence in the treatment-failure loop ($p = 0.42$ for systemic acyclovir against placebo, 0.61 for topical acyclovir against placebo and 0.59 for topical against systemic acyclovir) or in the resolution loop ($p = 0.40$, 0.59 and 0.50) (Supplementary Table S8). With a single loop in each network, these tests had little power. Posterior mean residual deviance was close to the number of data points in every model (13.1 for 14 arms in the treatment-failure network), and all R-hat values were 1.006 or lower (Supplementary Table S10).

The benefit of systemic acyclovir on treatment failure was consistent across the fixed-effect model (OR 0.20, 0.06–0.58), the uniform-prior random-effects model (OR 0.19, 0.03–0.96), the frequentist model (OR 0.23, 95% CI 0.08–0.67) and the analysis without the McGill trial (OR 0.24, 0.06–0.94) (Supplementary Table S9). Removing McGill also left the comparison of topical with systemic acyclovir unchanged (OR 4.90, 1.12–23.32). In the fixed-effect and frequentist models the intervals for valacyclovir and famciclovir against placebo excluded 1 (for example, valacyclovir OR 0.18, 0.04–0.67 under fixed effect). For resolution, the effect of systemic acyclovir held in the fixed-effect (OR 8.70, 1.99–52.06) and frequentist (OR 7.70, 1.38–42.93) models, but under the uniform(0, 5) prior on τ its interval widened to include 1 (OR 7.67, 0.20–170.97).

Certainty of evidence

Certainty was low for the effect of systemic acyclovir against placebo on treatment failure and on resolution, low for the comparison of topical with systemic acyclovir on treatment failure, and low for the comparisons of valacyclovir and famciclovir with systemic acyclovir (Supplementary Table S11). The comparisons of topical acyclovir, valacyclovir and famciclovir with placebo were rated very low, as were all adverse-event comparisons. The main reasons for downgrading were imprecision, risk of bias in the Marsh, McGill and Neoh trials, and the different disease stage and steroid co-treatment in the Marsh trial.

Discussion

In seven randomised trials of acute HZO, systemic acyclovir reduced the odds of treatment failure by about four-fifths compared with placebo, and this result held across fixed-effect, random-effects and frequentist models and after removing the trial with the weakest ocular data. Topical acyclovir ointment did no better than placebo and was inferior to systemic acyclovir. Valacyclovir and famciclovir were indistinguishable from oral acyclovir. Adverse events did not differ between any of the treatments that could be compared.

The placebo-controlled evidence for systemic acyclovir is old and small, with about 30 failure events across three trials, but the direction of effect was the same in each trial. In the two oral trials, treatment failure occurred in 2 of 36 and 1 of 23 patients on acyclovir against 6 of 35 and 5 of 19 on placebo [3, 4]. The resolution outcome rests on a single direct trial of 39 patients [4], and its interval included 1 when a vaguer heterogeneity prior was used, so it supports the treatment-failure finding rather than standing as independent evidence.

The result for topical acyclovir is the clearest difference this network adds to the individual trials. Acyclovir ointment produces substantial aqueous humour concentrations [28], higher than those reached after oral dosing [29], and this was the rationale for testing it in HZO [9]. In the trial by Neoh and colleagues, however, patients given ointment alone had more ocular complications and more anterior uveitis than those given oral acyclovir [9]. In the network, the indirect evidence through placebo pointed the same way as this direct comparison, and the topical node sat at the same rank as placebo. Systemic treatment reaches viral replication in the skin and along the nerve as well as in the eye, which may explain why higher local drug levels did not translate into fewer complications. Topical acyclovir should not be used in place of systemic antiviral therapy for acute HZO.

Valacyclovir and famciclovir each entered the network through one trial against oral acyclovir [6, 7], and neither trial found a difference in ocular outcomes. The network adds an indirect comparison with placebo, which is imprecise because there is no placebo-controlled trial of either prodrug and because between-trial heterogeneity widens indirect intervals. Under fixed-effect and frequentist models, which assume no heterogeneity, both prodrugs were superior to placebo. Our findings agree with the Cochrane review of valacyclovir against acyclovir, which rated the same comparison as low to very low certainty [10]. Across herpes zoster of all sites, valacyclovir and famciclovir reduced zoster-associated pain compared with acyclovir [11]. With similar ocular efficacy and three-times-daily rather than five-times-daily dosing, either prodrug is a reasonable first choice.

We restricted the review to VZV disease. HSV keratitis is a different disease with different outcome measures, chiefly healing of an epithelial ulcer, and a large trial literature of its own [30]. VZV is also two to eight times less susceptible to acyclovir than HSV in vitro, which is why zoster doses are higher [31]. In an exploratory network that combined zoster and simplex trials, the between-trial standard deviation for treatment failure rose from 0.43 to about 1.0. Long-term suppression is also a separate question. In the Zoster Eye Disease Study, 12 months of valacyclovir 1 g daily did not significantly delay new or worsening keratitis or iritis at 12 months (hazard ratio 0.77, 95% CI 0.56–1.05), although it reduced these events at 18 months (hazard ratio 0.73, 0.55–0.97) [12]. Those results apply to patients with established eye disease after HZO, not to acute treatment.

This review has several limitations. The evidence base is seven trials, all published before 2002, and most comparisons rest on one trial. The single closed loop in each efficacy network gave the node-splitting tests little power. Outcome definitions varied between trials, from ocular complications needing steroids to any ocular manifestation, and follow-up ranged from 24 weeks to 12 months. The McGill trial contributed only a small post-randomisation subgroup, although excluding it did not change the results. The Marsh trial enrolled a later stage of disease with steroid co-treatment, and the Neoh trial was open-label. Adverse events were poorly reported, and only one trial counted patients with any event. We could not examine dose, duration or time to treatment, could not assess small-study effects, and could not analyse immunocompromised patients, who were absent or unreported in every trial. The strengths of the review are its restriction to a single virus and a clinically homogeneous question, separate nodes for each route of administration, re-extraction of arm-level data from the full trial reports, and the use of several models and GRADE to judge how much the findings depend on modelling choices.

New trials would ideally compare valacyclovir, famciclovir and acyclovir directly in patients treated within 72 hours, use a common definition of ocular complications with masked assessment, and report adverse events as the number of patients affected. Trials enrolling immunocompromised patients and older adults, in whom HZO is most frequent, are also needed.

Conclusion

Systemic antiviral therapy reduces ocular complications of acute herpes zoster ophthalmicus, and topical acyclovir ointment alone is not an adequate substitute. Valacyclovir and famciclovir perform similarly to oral acyclovir, with more convenient dosing. The certainty of these conclusions is low because the evidence comes from seven small trials published between 1983 and 2001.

Declarations

Ethics Approval and Consent to Participate: Not applicable.

Consent for Publication: Not applicable.

Availability of Data and Material: Provided in the Supplementary Material.

Competing Interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Figures

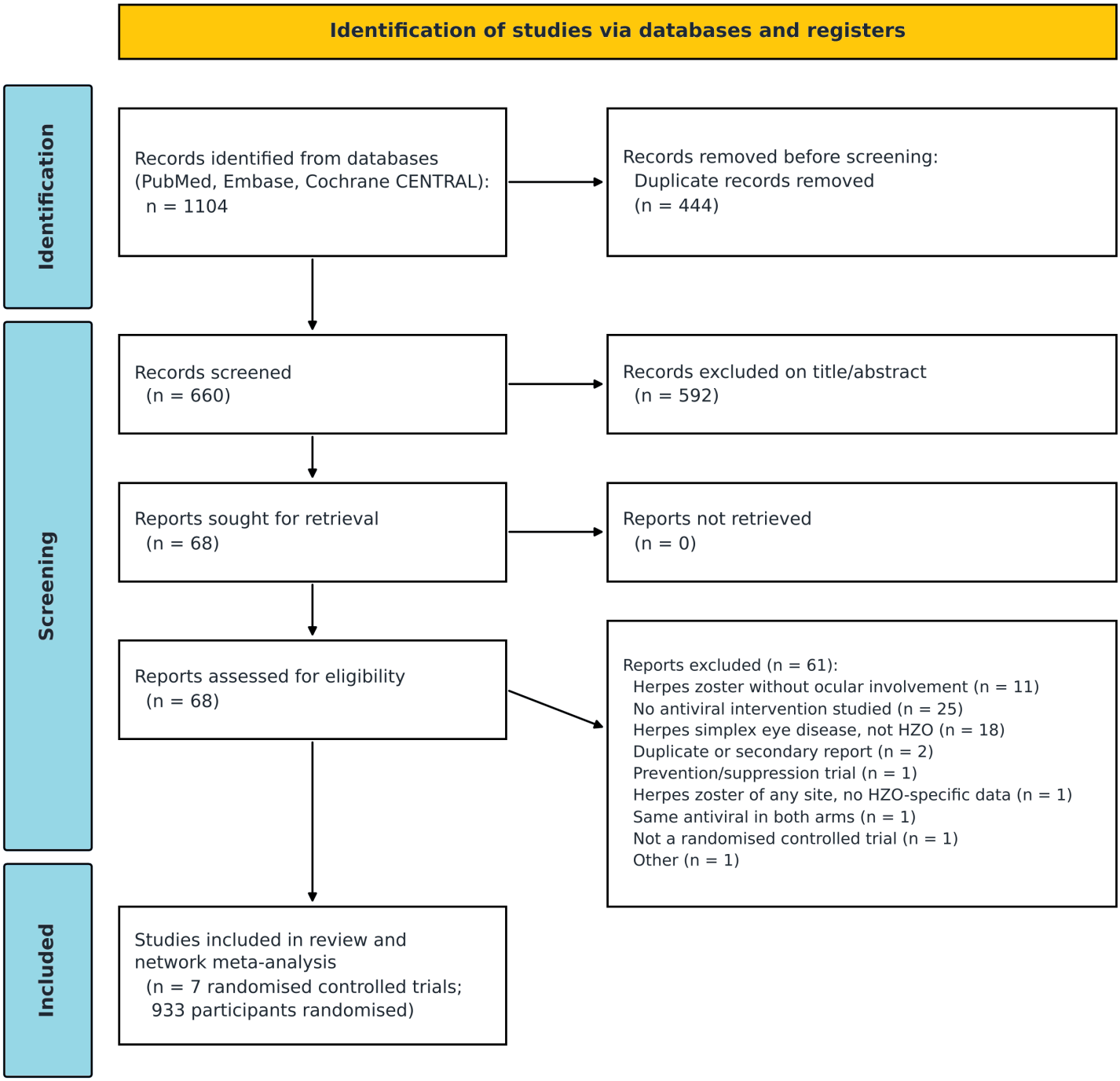


Figure 1

PRISMA 2020 flow diagram of study selection.

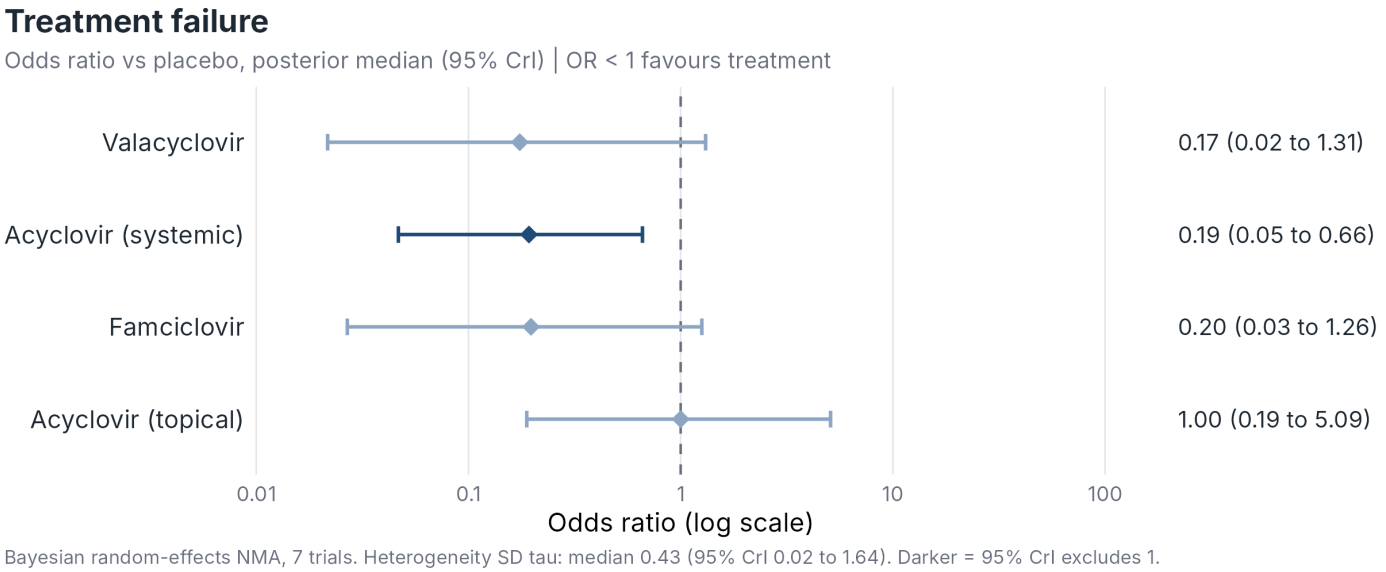


Figure 2

Treatment failure: odds ratios for each treatment compared with placebo from the Bayesian random-effects network meta-analysis (posterior median and 95% credible interval). An odds ratio below 1 favours the treatment.

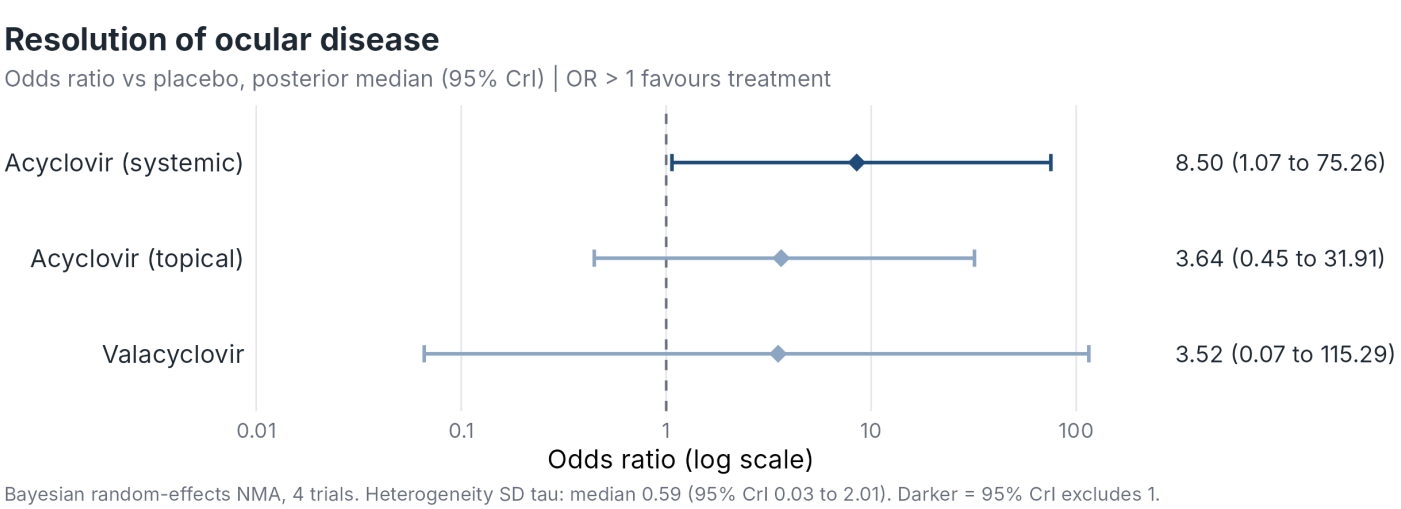


Figure 3

Resolution of ocular disease: odds ratios for each treatment compared with placebo. An odds ratio above 1 favours the treatment.

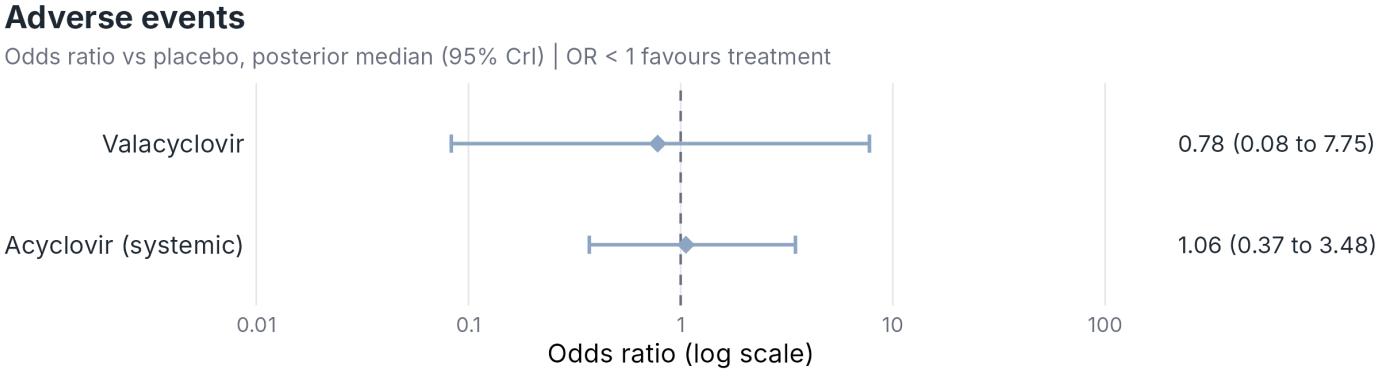


Figure 4

Adverse events: odds ratios for each treatment compared with placebo. An odds ratio below 1 indicates fewer adverse events with the treatment.

Supplementary Files

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- SupplementaryFile.docx