UNRESOLVED ISSUES REGARDING INFECTIONS IN EMERGENCY SETTINGS.
Steroids in CNS infections

Prof Pasquale Pagliano

Infectious Diseases Unit

University of Salerno

AOU San Giovanni di Dio e Ruggi d'Aragona

Global, regional, and national burden of meningitis, its risk factors, and aetiologies, 1990–2023: a systematic analysis for the Global Burden of Disease Study 2023

*GBD 2023 Meningitis & Antimicrobial Resistance Collaborators**

Summary

Background Meningitis remains the leading infectious cause of neurological disabilities globally, disproportionately

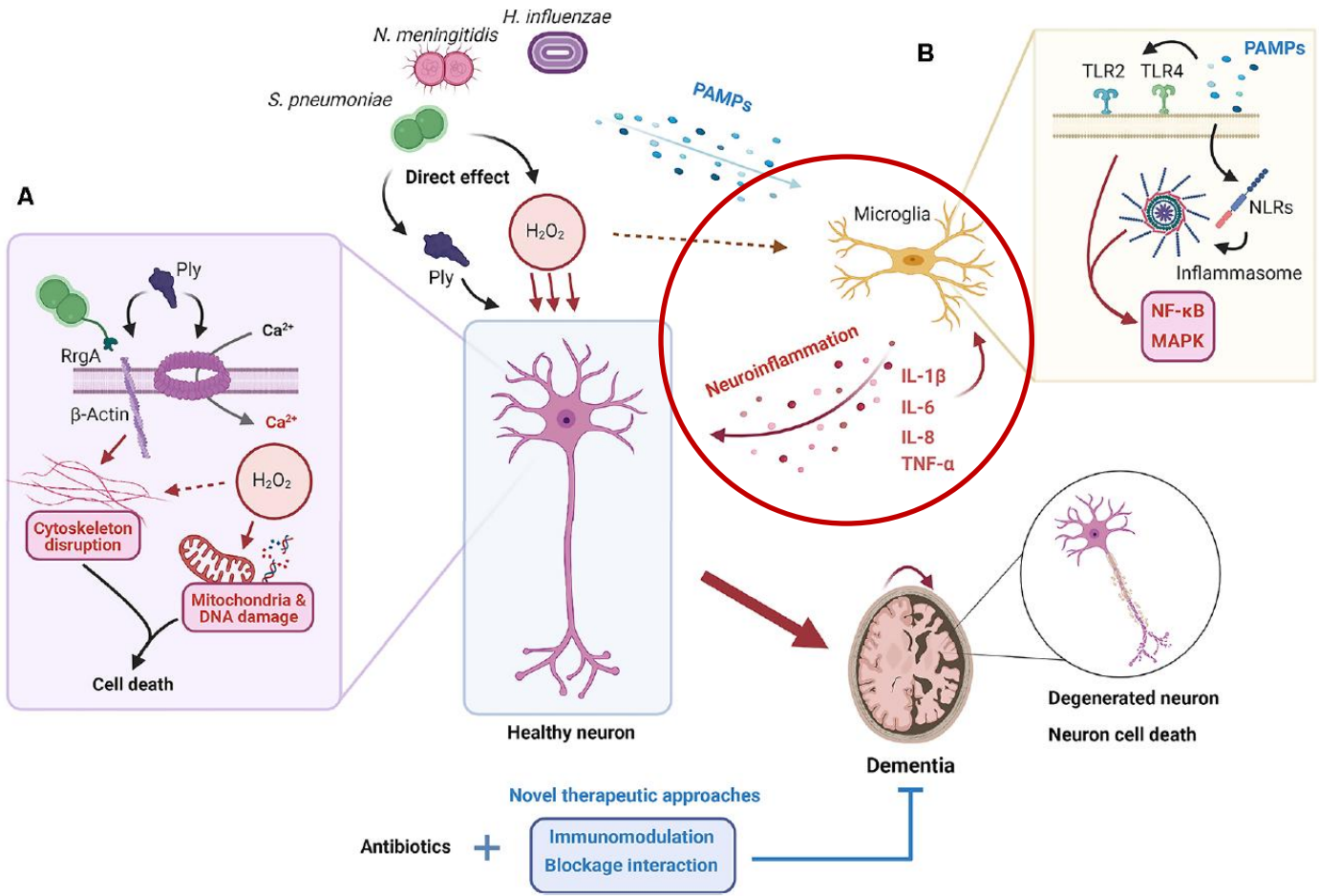
Lancet Neurol 2026; 25: 451–68

	1990		2015		2023		Percentage change in incidence rates between 1990 and 2023	Percentage change in incidence rates between 2015 and 2023
	Cases	Incidence rate per 100 000	Cases	Incidence rate per 100 000	Cases	Incidence rate per 100 000		
All ages	3 960 000 (3 290 000 to 4 710 000)	74·2 (61·7 to 88·3)	2 860 000 (2 470 000 to 3 340 000)	38·6 (33·3 to 45·0)	2 540 000 (2 200 000 to 2 930 000)	31·5 (27·2 to 36·4)	−57·5 (−60·5 to −54·5)	−18·5 (−20·0 to −17·1)
<5 years	2 230 000 (1 740 000 to 2 780 000)	363·2 (283·6 to 453·0)	1 170 000 (941 000 to 1 420 000)	172·1 (138·5 to 208·5)	953 000 (780 000 to 1 140 000)	148·1 (121·3 to 177·4)	−59·1 (−62·1 to −56·0)	−13·9 (−16·1 to −11·7)
5–14 years	659 000 (416 000 to 952 000)	58·9 (37·1 to 85·0)	504 000 (337 000 to 714 000)	39·4 (26·3 to 55·8)	447 000 (304 000 to 633 000)	32·3 (22·0 to 45·8)	−44·7 (−49·3 to −38·8)	−17·8 (−20·4 to −15·2)
15–49 years	662 000 (490 000 to 893 000)	24·4 (18·0 to 32·9)	713 000 (553 000 to 923 000)	18·7 (14·6 to 24·3)	684 000 (537 000 to 882 000)	17·1 (13·4 to 22·0)	−29·6 (−36·1 to −23·7)	−8·8 (−10·8 to −6·6)
50–69 years	244 000 (181 000 to 329 000)	35·8 (26·5 to 48·2)	253 000 (199 000 to 334 000)	20·4 (16·0 to 26·8)	241 000 (192 000 to 315 000)	16·1 (12·8 to 21·0)	−54·7 (−58·0 to −51·0)	−20·8 (−22·7 to −19·1)
≥70 years	164 000 (117 000 to 223 000)	80·5 (57·8 to 109·5)	222 000 (176 000 to 282 000)	54·0 (42·7 to 68·5)	212 000 (171 000 to 265 000)	39·4 (31·7 to 49·2)	−50·7 (−56·1 to −45·1)	−26·9 (−29·4 to −25·1)

Estimates are presented as rounded values and therefore might not sum to estimated aggregates. Data in parentheses are 95% uncertainty intervals.

Table 2: **Non-fatal estimates of meningitis globally by age in 1990, 2015, and 2023**

Are steroids useful for all these CNS infections?


N. meningitidis
H. influenzae
S. pneumoniae
PAMPs
Direct effect
A
Ply
RrgA
Ca2+
β-Actin
H2O2
Cytoskeleton disruption
Mitochondria & DNA damage
Cell death
Healthy neuron
B
Microglia
TLR2
TLR4
PAMPs
NLRs
Inflammasome
NF-κB
MAPK
Neuroinflammation
IL-1β
IL-6
IL-8
TNF-α
Dementia
Degenerated neuron
Neuron cell death
Novel therapeutic approaches
Antibiotics
Immunomodulation
Blockage interaction

The New England
Journal of Medicine

Copyright © 2002 by the Massachusetts Medical Society

VOLUME 347 NOVEMBER 14, 2002 NUMBER 20

DEXAMETHASONE IN ADULTS WITH BACTERIAL MENINGITIS

JAN DE GANS, PH.D., AND DIEDERIK VAN DE BEEK, M.D., FOR THE EUROPEAN DEXAMETHASONE IN ADULTHOOD BACTERIAL MENINGITIS STUDY INVESTIGATORS*

OUTCOME AND CULTURE RESULTS	DEXAMETHASONE GROUP	PLACEBO GROUP	RELATIVE RISK (95% CI)†	P VALUE
	no./total no. (%)			
Unfavorable outcome				
All patients	23/157 (15)	36/144 (25)	0.59 (0.37–0.94)	0.03
Streptococcus pneumoniae	15/58 (26)	26/50 (52)	0.50 (0.30–0.83)	0.006
Neisseria meningitidis	4/50 (8)	5/47 (11)	0.75 (0.21–2.63)	0.74
Other bacteria	2/12 (17)	1/17 (6)	2.83 (0.29–27.8)	0.55
Negative bacterial culture‡	2/37 (5)	4/30 (13)	0.41 (0.08–2.06)	0.40
Death				
All patients	11/157 (7)	21/144 (15)	0.48 (0.24–0.96)	0.04
S. pneumoniae	8/58 (14)	17/50 (34)	0.41 (0.19–0.86)	0.02
N. meningitidis	2/50 (4)	1/47 (2)	1.88 (0.76–20.1)	1.00
Other bacteria	1/12 (8)	1/17 (6)	1.42 (0.10–20.5)	1.00
Negative bacterial culture	0/37	2/30 (7)	—	0.20
Focal neurologic abnormalities				
All patients	18/143 (13)	24/119 (20)	0.62 (0.36–1.09)	0.13
S. pneumoniae	11/49 (22)	11/33 (33)	0.67 (0.33–1.37)	0.32
N. meningitidis	3/46 (7)	5/44 (11)	0.57 (0.15–2.26)	0.48
Other bacteria	3/11 (27)	3/16 (19)	1.45 (0.36–5.92)	0.66
Negative bacterial culture	1/37 (3)	5/26 (19)	0.14 (0.02–1.13)	0.07
Hearing loss				
All patients	13/143 (9)	14/119 (12)	0.77 (0.38–1.58)	0.54
S. pneumoniae	7/49 (14)	7/33 (21)	0.67 (0.25–1.69)	0.55
N. meningitidis	3/46 (7)	5/44 (11)	0.57 (0.15–2.26)	0.48
Other bacteria	2/11 (18)	1/16 (6)	2.91 (0.30–28.3)	0.55
Negative bacterial culture	1/37 (3)	1/26 (4)	0.70 (0.05–10.7)	1.00

2015

Cochrane Library

Cochrane Database of Systematic Reviews

Corticosteroids for acute bacterial meningitis (Review)

Brouwer MC, McIntyre P, Prasad K, van de Beek D

Summary of findings for the main comparison. Summary of findings table

Comparison of corticosteroids against placebo in patients with acute bacterial meningitis

Patient or population: acute bacterial meningitis
Setting: hospitals, low- and high-income countries
Intervention: corticosteroids
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with placebo	Risk with corticosteroids				
Mortality	Study population		RR 0.90 (0.80 to 1.01)	4121 (25 RCTs)	⊕⊕⊖⊖ MODERATE [1]	—
	199 per 1000	179 per 1000 (159 to 201)				
	Moderate					
	188 per 1000	169 per 1000 (150 to 189)				
Severe hearing loss	Study population		RR 0.67 (0.51 to 0.88)	2437 (17 RCTs)	⊕⊕⊕⊖ HIGH	—
	93 per 1000	62 per 1000 (47 to 82)				
	Moderate					
	40 per 1000	27 per 1000 (20 to 35)				
Any hearing loss	Study population		RR 0.74 (0.63 to 0.87)	2785 (20 RCTs)	⊕⊕⊕⊖ HIGH	—
	190 per 1000	141 per 1000 (120 to 166)				
	Moderate					
	233 per 1000	173 per 1000				

Following Cochrane review:

- only marginal effects could be observed in terms of mortality
- an advantage was reported in terms of hearing loss

ORIGINAL ARTICLE

ESCMID guideline: diagnosis and treatment of acute bacterial meningitis

D. van de Beek[1], C. Cabellos[2], O. Dzupova[3], S. Esposito[4], M. Klein[5], A. T. Kloek[1], S. L. Leib[6], B. Mourvillier[7], C. Ostergaard[8], P. Pagliano[9], H. W. Pfister[5], R. C. Read[10], O. Resat Sipahi[11] and M. C. Brouwer[1], for the ESCMID Study Group for Infections of the Brain (ESGIB)

Key Question 6. Does dexamethasone have a beneficial effect on death, functional outcome and hearing loss in adults and children with bacterial meningitis?

Recommendation

Grade A	Empiric treatment with dexamethasone is strongly recommended for all adults (10 mg qid for 4 days) and children (0.15 mg/kg qid for 4 days) with acute bacterial meningitis in the setting of high-income countries.
Grade A	Treatment with dexamethasone is strongly recommended to be initiated with the first dose of antibiotic treatment.
Grade C	If intravenous antibiotic treatment has already been started, dexamethasone can still be administered up to 4 hours after start of the first dose of intravenous antibiotics.
Grade B	It is recommended to stop dexamethasone if the patient is discovered not to have bacterial meningitis or if the bacterium causing the meningitis is a species other than *H. influenzae* or *S. pneumoniae*, although some experts advise that adjunctive treatment should be continued irrespective of the causative bacterium.

SUGGESTED CORTICOSTEROID REGIMEN

Recommended corticosteroid regimen for community-acquired bacterial meningitis in international guidelines

	IDSA [16]	ESCMID [15]	NICE [17]	WHO [14]
Year of publication	2004	2016	2024 (updated from 2010)	2025
Corticosteroid	Dexamethasone	Dexamethasone	Dexamethasone	Dexamethasone
Dose, duration	10 mg four times a day for 4 days	10 mg four times a day for 4 days	10 mg four times a day for 4 days	10 mg four times a day for 4 days
Start	Suspected or proven pneumococcal meningitis	All bacterial meningitis patients	All bacterial meningitis patients	All bacterial meningitis patients, except during meningococcal meningitis epidemic
Timing	Before or with first dose of i.v. antibiotics	With first dose of i.v. antibiotics, if forgotten up to 4 hours after start i.v. treatment	Before or with first dose of i.v. antibiotics, if forgotten up to 12 hours after start i.v. treatment	With first dose of i.v. antibiotics
Stop	If cause is NOT *Streptococcus pneumoniae* or *H. influenzae*	If *Listeria monocytogenes* is identified	If cause if NOT *S. pneumoniae* or *H. influenzae*	If cause is NOT *S. pneumoniae* or *H. influenzae* DXM can be discontinued

Brouwer, CMI 2026

Which evidence guides steroids administration for viral CNS infection?

Journal of Neurology (2023) 270:3603–3615
https://doi.org/10.1007/s00415-023-11715-0

ORIGINAL COMMUNICATION

Steroids for the treatment of viral encephalitis: a systematic literature review and meta-analysis

Emira Hodzic[1] · Rodrigo Hasbun[2] · Alejandro Granillo[2] · Anna R. Tröscher[3] · Helga Wagner[1] · Tim J. von Oertzen[3,4] · Judith N. Wagner[3,4]

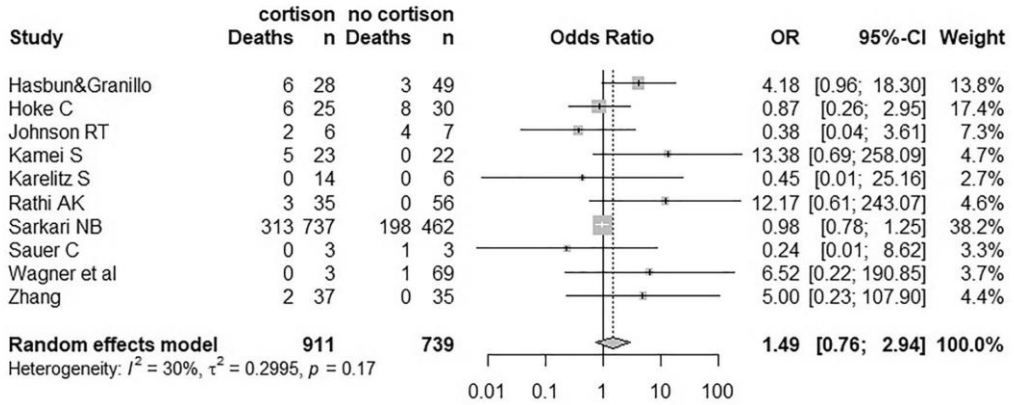


Fig. 3 Forest Plot of the odds ratio (OR) for the risk of dying in patients who received steroids (C.P.) vs. those who did not (no C.P.)

	Houston cohort (Hasbun and Granillo)	Linz cohort (Wagner et al.)
Total number of patients; *n*	83	72
Immunosuppressed; *n*	19	7
Pathogen; *n*		
Cytomegalovirus	4	1
Enterovirus	2	0
Epstein–Barr virus	4	4
Herpes simplex virus	19	12
Influenza A virus	0	1
Parvovirus B19	0	0
St. Louis Encephalitis virus	4	0
Tick-borne Encephalitis virus	0	27
Unspecified	0	22
Varicella zoster virus	17	6
West Nile virus	33	0
Intensive care treatment; *n*	33	26
Median CSF cell count (range); cells/µl	75 (0–1100)	80.5 (2–840)
Median admission GCS (range); score	14 (3–15)	n.a
Steroid therapy; patients; *n*	28	3
Antiviral therapy; patients; *n*	69	65
Median modified Ranking scale score at last contact (range); score	3 (0–6)	1 (0–6)
Patients dead at last contact; *n*	9	1

Which is the effect on HSV encephalitis?

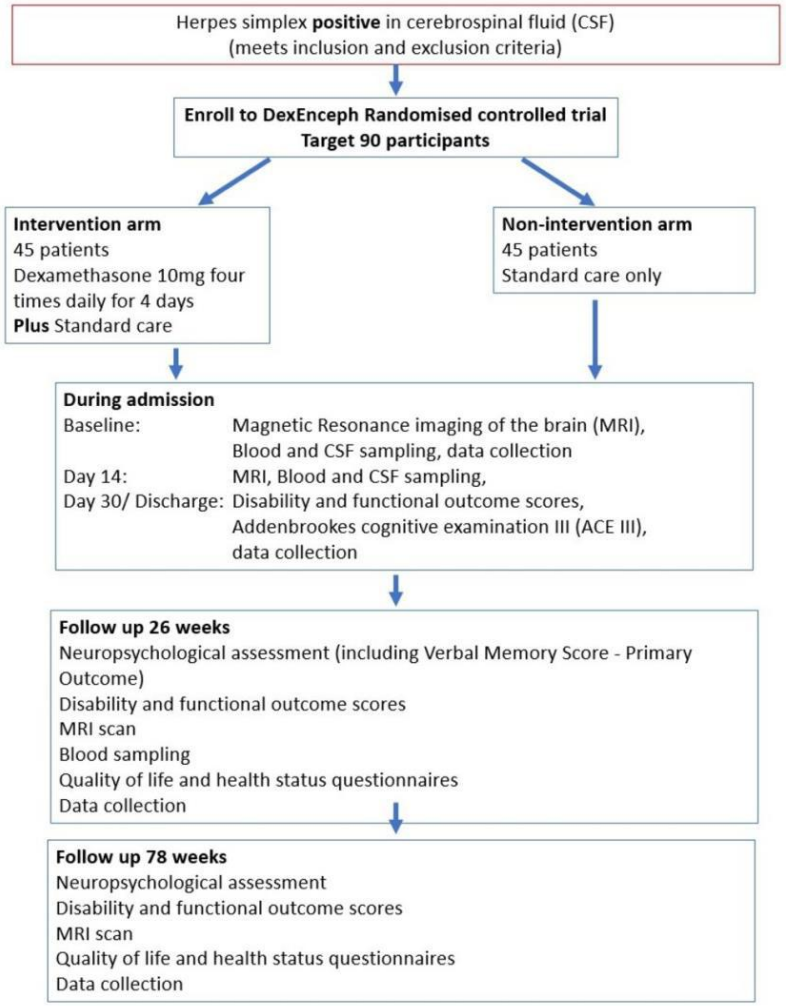
Safety and efficacy of adjunct dexamethasone in adults with herpes simplex virus encephalitis in the UK (DexEnceph): a multicentre, observer-blind, randomised, phase 3, controlled trial

Tom Solomon, Cory Hooper, Ava Easton, Anna Rosala-Hallas, Bethany Facer, Perry Moore, Simon S Keller, Thomas Whitfield, Cristina Fernandez, Rachel Kneen, Michael J Griffiths, Kumar Das, Shona C Moore, Kelly Davies, Dianne Wheatley, Jean Paul Stahl, Ben Hardwick, Sylviane Defres, Benedict D Michael, DexEnceph Study Group*, Girvan Burnside†, Mark A Ellul†

Lancet Neurol 2026; 25: 136–46

Summary

Background Herpes simplex virus (HSV) encephalitis is characterised by inflammation and swelling of the brain,



We included patients who had positive PCR for HSV type 1 or type 2 DNA in CSF, reported no longer than 7 days before randomisation and receiving intravenous aciclovir 10 mg/kg three times daily, or reduced dose if clinically indicated

Safety and efficacy of adjunct dexamethasone in adults with herpes simplex virus encephalitis in the UK (DexEnceph): a multicentre, observer-blind, randomised, phase 3, controlled trial

Tom Solomon, Cory Hooper, Ava Easton, Anna Rosala-Hallas, Bethany Facer, Perry Moore, Simon S Keller, Thomas Whitfield, Cristina Fernandez, Rachel Kneen, Michael J Griffiths, Kumar Das, Shona C Moore, Kelly Davies, Dianne Wheatley, Jean Paul Stahl, Ben Hardwick, Sylviane Defres, Benedict D Michael, DexEnceph Study Group*, Girvan Burnside†, Mark A Ellul†

Lancet Neurol 2026; 25: 136–46

Summary

Background Herpes simplex virus (HSV) encephalitis is characterised by inflammation and swelling of the brain,

Implications of all the available evidence

Although earlier retrospective studies hinted at a beneficial effect of corticosteroids in HSV encephalitis, our randomised trial did not show an improvement in outcome. Nevertheless, corticosteroid use did not appear to be associated with harm. Currently, in patients with suspected encephalitis for whom the aetiology might be HSV or autoimmune, corticosteroids are not usually given until HSV has been excluded. Our data suggest that corticosteroids could be given safely to all such patients as soon as encephalitis is suspected. Future studies should explore more targeted immune therapies as adjuncts to aciclovir in HSV encephalitis.

When TBM is suspected, which is the optimal treatment?

Does an adjunctive steroid reduce mortality from tuberculous meningitis?

Cochrane Library

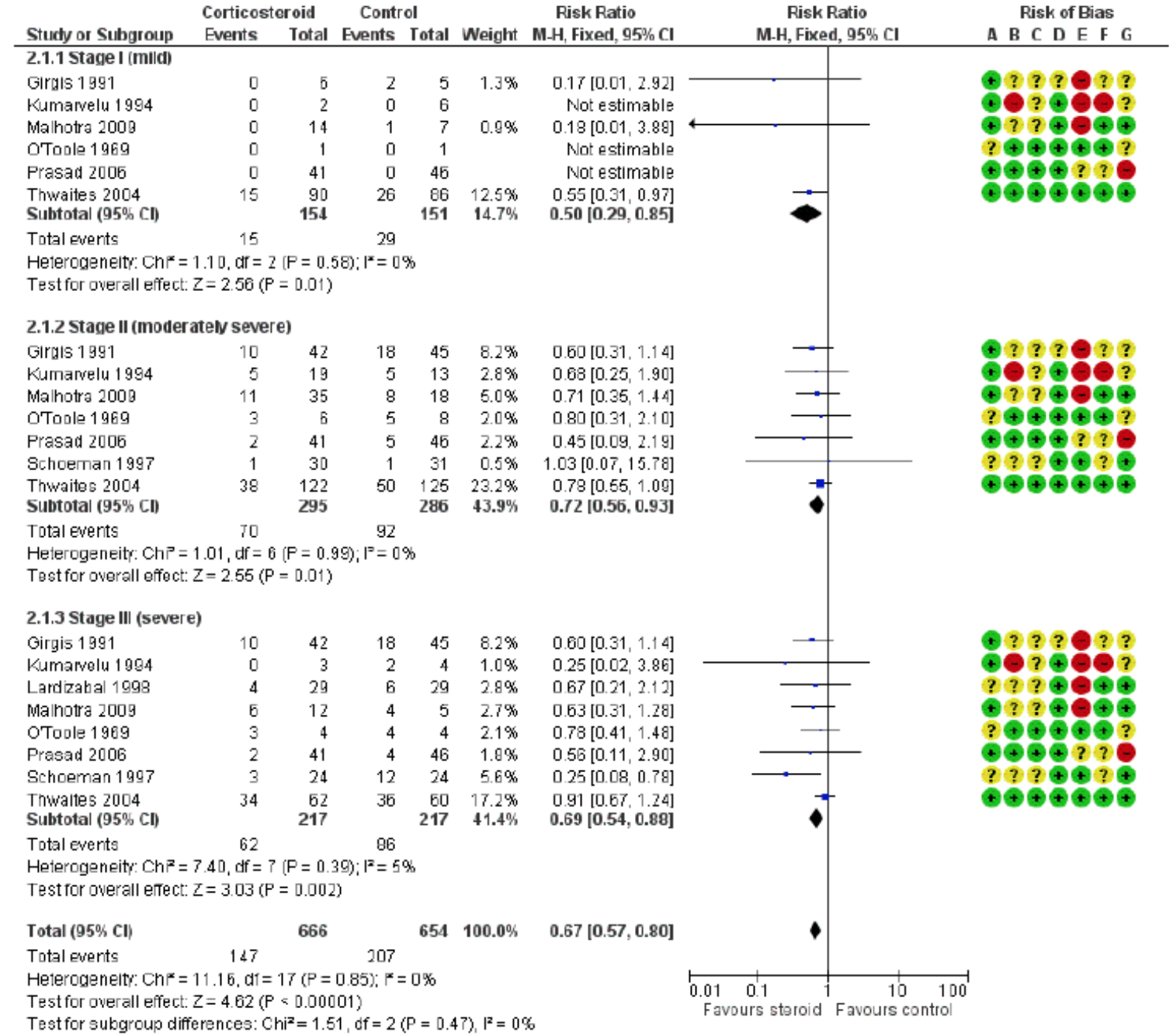
Cochrane Database of Systematic Reviews

Corticosteroids for managing tuberculous meningitis (Review)

Prasad K, Singh MB, Ryan H

2016

Figure 7. Forest plot of comparison: 2 Any corticosteroid versus control: stratified by severity of illness, outcome: 2.1 Death.



Conclusions

Dexamethasone reduces mortality and hearing loss in pneumococcal meningitis, but further data on Listeria meningitis should be produced;
Corticosteroids reduce mortality by ~25% in HIV-negative tuberculous meningitis, but show only a non-significant benefit in HIV-associated disease;
Viral CNS infections have comparatively weak evidence, so steroid use there is reserved for specific indications (edema/herniation risk) rather than routine practice