PICO

- A way of characterizing a trial
- A way of designing a systematic review
- A way of identifying/searching for a systematic review
- A way of structuring a question for a recommendation

Do steroids work in patients with TB meningitis? Design a research study

Steroids for TBM?

Steroids for TBM?

• Design: RCT

• Participants: patients with TB meningitis

• Intervention: steroids

Outcome: death or disability

RCT of adults

• 274 to steroids

• 271 to placebo

• 87 died

• 112 died

Relative Risk 0.69; 95% confidence intervals 0.52 to 0.92

Steroids for TBM: PICO for systematic review

• Design: systematic review

• Inclusion : ` RCTs

Participants: patients with TB meningitis

• Intervention: steroids

Outcome: death or disability

Figure 1.

Of Any steroid vs. control Of Death Comparison:

Outcome:

Study or sub-category	Treatment n/N	Control n/N			RR (fixed) 95% CI	Weight. %	RR (fixe 95% 0	
O/Toole 1969	6/11	9/12			-	3.73	0.73 [0.39,	1.37]
Girgis 1991	72/145	79/135				35.44	0.85 [0.68,	
Kumaryelu 1994	5/20	7/21		99		2.96	0.75 [0.28,	1.98]
Chatmongkol 1996	5/29	2/30				0.85	2.59 [0.54,	12.29]
Schoeman 1997	4/67	13/67		-	-	5.63	0.31 (0.11,	0.90]
Lardizabal 1998	4/29	6/29		0		2.60	0.67 [0.21,	2.12)
Thwates 2004	87/274	112/271				48.79	0.77 [0.61,	0.96]
Total (95% CI)	575	565				100.00	0.78 [0.67,	0.91)
Total events; 183 (Treatment)	, 228 (Control)				4			
Test for heterogeneity: Chi ² =	5.89, df = 6 (P = 0.44), I2 = 09	4						
Test for overall effect, $Z = 3$.	24 (P = 0.001)			104		708		
			0.01	0.1	1 10	100		

PICO to drive a recommendation









Initiative of Central TB Division Ministry of Health and Family Welfare, Government of India Participants: Adults or children with tuberculous meningitis on tuberculosis (TB) chemotherapy

Settings: Hospital care

Intervention: Any corticosteroid

Comparison: Placebo or no corticosteroid

Outcomes Illustrative comparative risks (95% CI)		Relative effect (95% CI)	Number of participants	Quality of the evidence		
	Placebo	Corticosteroid	(93% CI)	(trials)	(GRADE)	
Follow-up to 2 to 24 months						
Death	41 per 100	31 per 100 (27 to 36)	RR 0.76 (0.66 to 0.87)	1318 (9 trials)	⊕⊕⊕⊕ high ^{1, 2, 3, 4, 5}	
Disabling neurological deficit	8 per 100	7 per 100 (6 to 10)	RR 0.92 (0.71 to 1.20)	1295 (8 trials)	⊕⊕⊖⊝ ^{6,7,8} low	
Follow-up to 5 years						
Death	47 per 100	44 per 100 (37 to 53)	RR 0.93 (0.78 to 1.12)	545 participants (1 trial)	⊕⊕⊕⊝ ^{9,10} moderate	
Disabling neurological deficit	15 per 100	14 per 100 (7 to 25)	RR 0.91 (0.49 to 1.69)	244 (1 trial)	$\bigoplus \ominus \ominus \ominus^{10, 11, 12}$ very low	

^{*}The assumed risk is from the median control group risk across studies. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: confidence interval; RR: risk ratio; TB: tuberculosis.

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Recommendations for use of corticosteroids in EPTB

6.1 In treating tuberculous meningitis in HIV-negative people

Tuberculous meningitis (TBM) is a lifethreatening condition affecting adults and children, which can leave survivors with a range of neurological disabilities. The causes of death and disability in TBM are multifactorial. The main pathological mechanisms are persistent or progressive raised intracranial pressure with or without hydrocephalus, arachnoiditis and involvement of optic nerves or optic chiasma leading to visual deficit, cranial neuropathies and vasculitis of the cerebral blood vessels, leading to stroke.

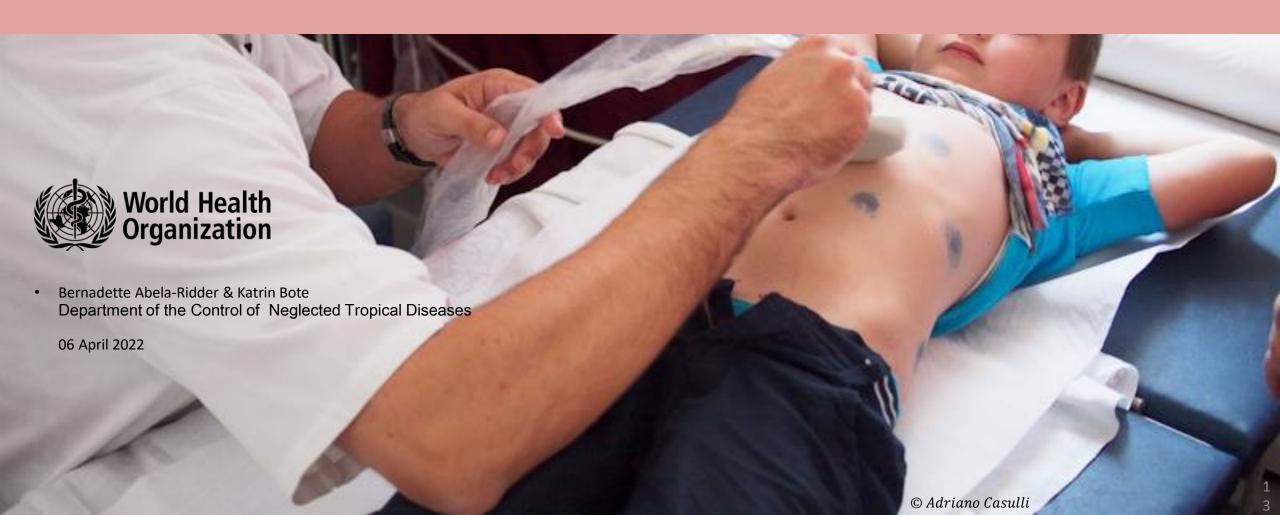
Steroids are thought to reduce inflammation, improve blood flow and reduce cerebral oedema and intracranial pressure. However,

the risks associated with steroids include immunosuppression, which is a major concern in the context of an infectious disease, GI bleeding, hyperglycaemia and hypertension, among others. Several randomized controlled trials have been conducted on the effect of corticosteroids in managing TBM. The conclusions from these trials, seen individually, appear inconsistent. One trial (Thwaites G.E., 2004) showed that dexamethasone increases survival rate, but it also raised two questions; do patients who survive because of dexamethasone therapy tend to be left with severe disability, and are there differential effects among subgroups of patients with different degrees of disease severity?

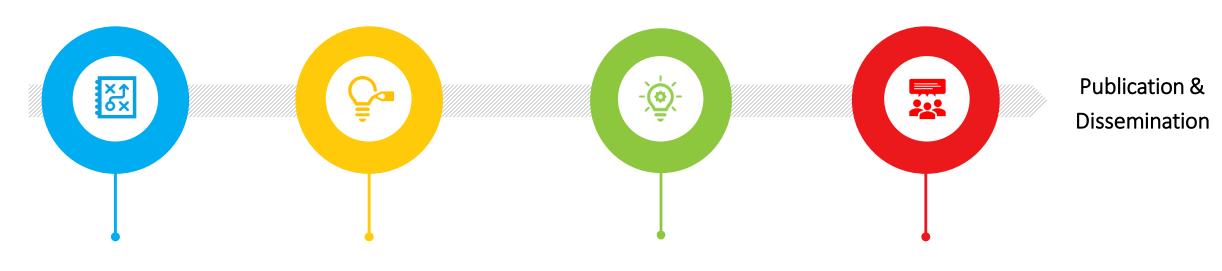
The guideline group reviewed evidence from the updated Cochrane review "Corticosteroids for managing tuberculous meningitis" (Prasad, 2016).

Recommendation	Steroids are recommended for TBM in HIV-negative people. Duration of steroid treatment should be for at least 4 weeks, with tapering as appropriate.
Strength of recommendation	Strong
Evidence	Corticosteroids reduce death from TBM from 41 per 100 people to 31 (27 to 36) per 100 people (nine studies, 1318 participants, high quality evidence). These studies were conducted in a variety of settings, and only one included HIV-positive people (n = 98).
	Disabling neurological deficit is not common in survivors, and steroids may have little or no effect on this outcome (RR 0.92, 95% CI 0.71 to 1.20; eight trials, 1295 participants, low quality evidence).
Panel's view on advantages of using steroids	Reduced mortality from TBM

First Meeting of the Guideline Development Group for treatment of patients with cystic echinococcosis



Guideline Development Overview



Planning

- Priority setting
- Planning Proposal
- Groups and Teams
- PICO questions

Systematic Review

- GRADE
- Evidence to Decision Framework

Recommendations

- Clear and precise
- Accompanied by a rational

Review

- Finalizing guideline
- Submission

WHO Guideline Development Cystic Echinococcosis

Evidence Summaries

17 August 2022

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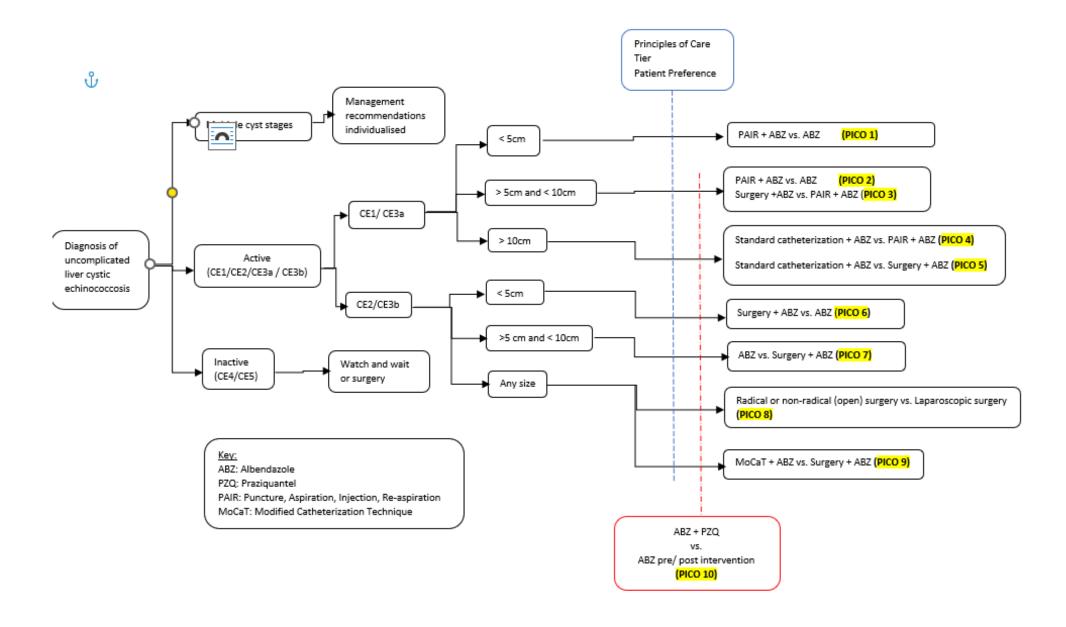
Systematic Review production and management team

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