

South African National Department of Health
Brief Report of NEMLC Limited Review¹
Corticosteroids for the treatment of tuberculous pericarditis
May 2026

Medicine details:

Medicine Class	Corticosteroids	<i>If applicable Please consider therapeutic interchange policy</i>
Medicine/s name -INN: - South African name (if differs from INN)	Prednisone Prednisolone Dexamethasone	http://www.whocc.no/atc_ddd_in dex/
Medicine/s (ATC5):	H02AB07 H02AB06 H02AB02	http://www.whocc.no/atc_ddd_in dex/
Indication (ICD-10 code):	A18.0	https://www.health.gov.za/icd-10-master-industry-table/
SAHPRA Approved	Yes	SAHPRA registered health products database https://medapps.sahpra.org.za:6006/
Dosage form/s	tablet, suspension, injection	
Route of administration/s	Oral, IV injection	
Patient population	Adults and children with and without HIV with tuberculous pericarditis and/or pericardial effusion	
Prevalence and/or incidence of condition	66% of patients with pulmonary TB have signs of pericardial abnormality on echocardiography at the start of anti-TB treatment.[1] 47% of patients have pericardial effusion at TB diagnosis.[1] 12% of patients with pulmonary TB have features of constrictive pericarditis at diagnosis.[1]	<i>May refer to estimates or routine data (DHIS, StatsSA), not necessarily published data.</i>
Level of Care	Hospital level	
Prescriber level	Doctor prescribed	

¹ This template was informed by examples of previous NEMLC limited reviews, input from the Essential Drug Programme Oversight Group and the NEMLC Medicine Review Template which was updated with support through the Evidence-to-Decision (E2D) project which is a collaboration between National Department of Health, the South African Medical Research Council and the University of Stellenbosch.

Current Standard of Care

In adults: Antituberculosis drugs for 6 months. No recommendation regarding use of corticosteroids is provided in the Standard Treatment Guidelines (STGs). National Tuberculosis Management guidelines (2014) recommend the use of corticosteroids in adults with extrapulmonary tuberculosis, including pericarditis.

In children: Antituberculosis drugs for 6 months plus corticosteroids in suspected or proven tuberculous pericarditis.

Executive Summary

- ➔ In sub-Saharan Africa, tuberculous pericarditis is associated with all-cause mortality of 9.1 per 100 person-years (Mayosi, 2014).[2]
- ➔ The current Adult Hospital standard treatment guidelines make no recommendation regarding the use of corticosteroids in people with tuberculous pericarditis. However, National Tuberculosis Management guidelines (2014) recommend the use of corticosteroids in adults with tuberculous pericarditis.
- ➔ The current Paediatric Hospital standard treatment guidelines and Management of Tuberculosis in Children and Adolescents: A Clinical Guideline (2024), while acknowledging the limited evidence in children, recommend the use of corticosteroids in children with tuberculous pericarditis.
- ➔ We conducted an updated rapid systematic review of the evidence for the use of corticosteroids in the management of tuberculous pericarditis in HIV-negative children and adults, as well as in children and adults with HIV (PWH). Only guidelines, systematic reviews with meta-analyses, and randomised controlled trials were included.
- ➔ We identified two clinical practice guidelines:
 - Clinical practice guidelines from WHO (2025) and ATS/CDC/ERS/IDSA (2025) included the same primary studies, but did not stratify results by HIV status, and had not updated recommendations since 2016/2017.
 - The WHO (2025) clinical practice guideline recommended that in patients with tuberculous pericarditis, an initial adjuvant corticosteroid therapy may be used. (Conditional recommendation, very low certainty of evidence)
 - The ATS/CDC/ERS/IDSA (2025) clinical practice guideline suggested that initial adjunctive corticosteroid therapy not be routinely used in patients with tuberculous pericarditis (Conditional recommendation, very low certainty of evidence).
- ➔ We identified three systematic reviews. The most up-to-date and relevant systematic review which stratified results by HIV-status (Wiysonge, 2017), was considered to be of low-quality on AMSTAR2 assessment. Key findings from this review include:
 - In adults without HIV and with tuberculous pericarditis:
 - Corticosteroids probably reduce deaths from pericarditis (RR 0.39 [95% CI 0.19 to 0.80], moderate certainty evidence) and may reduce all-cause deaths (RR 0.80 [95% CI 0.59 to 1.09], low certainty evidence) and the need for repeat pericardiocentesis (RR 0.85 [95% CI 0.70 to 1.04], low certainty evidence).
 - It is uncertain whether corticosteroids have any effect on the incidence of cancer, hospitalisation, development of constrictive pericarditis, or the need for pericardiectomy (very low certainty evidence).
 - In adult PWH with tuberculous pericarditis:
 - Corticosteroids may reduce constrictive pericarditis (RR 0.55 [95% CI 0.26 to 1.16], low certainty evidence) and hospitalization (RR 0.80 [95% CI 0.59 to 1.09], low certainty evidence).
 - Corticosteroids may make little or no difference to the need for repeat pericardiocentesis (RR 1.02 [95% 0.89 to 1.18], low certainty evidence).
 - It is uncertain whether corticosteroids have any effect on deaths from pericarditis, all-cause deaths, the need for pericardiectomy or the development of cancer (very low certainty evidence).
 - These findings are based largely on data from one RCT, in which the majority of PWH with tuberculous pericarditis were not on ART and had CD4 counts ≤ 350 cells/mm³.
- ➔ Two RCTs were identified in the search, both of which were included in the systematic review. However, since the systematic review included only limited safety outcomes, the safety outcomes from the largest RCT were reviewed (Mayosi, 2014). Key findings include:

- More participants in the prednisolone group developed candida and other opportunistic infections than in the placebo group, though this was not statistically significant. - Prednisolone, as compared with placebo, was associated with an increased incidence of cancer (1.05 vs. 0.32 cases per 100 person-years; HR 3.27; 95% CI, 1.07 to 10.03; p = 0.03). This increase was due to a higher incidence of HIV-related cancers in the prednisolone group than in the placebo group (0.73 vs. 0.08 per 100 person-years; HR 9.04; 95% CI, 1.14 to 71.33; p = 0.04), particularly Kaposi's sarcoma and non-Hodgkin's lymphoma. This increase may be related to the co-administration of immunotherapy (<i>M. indicus pranii</i>) in this RCT.
➔ Given the important benefits of reducing death in people without HIV, and in reducing hospitalisation and the development of constrictive pericarditis in PWH, we recommend the use of corticosteroids in adults with tuberculous pericarditis while acknowledging the low certainty evidence. - In PWH, a thorough clinical examination should be performed before starting corticosteroids to exclude HIV-related cancers. - In PWH, antiretroviral therapy should be initiated promptly in accordance with standard treatment guidelines.
➔ No data in children with or without HIV and tuberculous pericarditis were identified. Given the important benefits associated with corticosteroids in adults with tuberculous pericarditis, we suggest using corticosteroids in children with tuberculous pericarditis.

Key Recommendations

Type of ERC recommendation	We recommend against the option and for the alternative (strong)		We suggest not to use the option or to use the alternative (conditional)		We suggest using the option (conditional)		We recommend the option (strong)	
	☐		☐		☒ See recommendation 2		☒ See recommendation 1	
High level summary of conclusions	1. In adults with or without HIV, and with tuberculous pericarditis, we recommend using corticosteroids. 2. In children with or without HIV, and with tuberculous pericarditis, we suggest using corticosteroids.							
NEMLC Ratification	Date		Comments/Recommendation					
	4 June 2026		NEMLC ratified the ERC recommendation as above.					
Therapeutic Interchange Considerations (if applicable)*	If YES:	Alternative medicine/s name (INN)	Alternative/s SAHPRA registered?	Formulation/s	Equipotent dose/ Dose range and dosing interval		If NO, tick box	
							✓	
Trigger for review	Additional clinical trial data or safety signals.							

*Depending on the review and number of products, an annexure may need to be included

Background and rationale

The standard treatment guidelines (STGs) for tuberculosis are being updated and consolidated into a single chapter to outline the various manifestations of TB disease. Currently, the adult hospital and primary healthcare STGs provide no specific guidance for the management of tuberculous pericarditis. Tuberculous pericarditis is an extrapulmonary manifestation of tuberculosis. It is associated with all-cause mortality of 9.1 per 100 person-years in the IMPI trial conducted in sub-Saharan Africa.[2] The paediatric hospital level STGs Chapter 4 – Cardiovascular system recommends antituberculosis drugs for 6 months plus corticosteroids in suspected or proven tuberculous pericarditis (Figure 1). No differential guidance is provided by HIV status.

CHAPTER 4	CARDIOVASCULAR SYSTEM
MEDICINE TREATMENT	
If suspected or proven TB pericarditis, give antituberculosis drugs for 6 months plus corticosteroids.	
• Prednisone, oral, for 6 weeks: ○ Week 1: 2 mg/kg/day, ○ Week 2: 1.5 mg/kg/day, ○ Week 3: 1 mg/kg/day, ○ Week 4: 1 mg/kg/day, ○ Week 5: 0.5 mg/kg/day, ○ Week 6: 0.25 mg/kg/day.	
LoE III ^{13,14}	

Figure 1. Paediatric Hospital Level Standard Treatment Guidelines. Chapter 4. Cardiovascular system. Pericardial effusion. (The references for this recommendation are the trials by Mayosi, 2014 and Strang, 1987[2,3])

The National Tuberculosis Management Guidelines (2014) recommend the use of corticosteroids in adults with extrapulmonary tuberculosis, including pericarditis (Figure 2). No differential guidance is provided by HIV status.

7.5.2 Steroids The use of corticosteroids is recommended in extra-pulmonary tuberculosis, particularly for TB meningitis and pericarditis. High dose steroid treatment for 2-4 weeks and the taper off gradually over several weeks depending on clinical progress is recommended. The response to treatment is assessed clinically.
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Figure 2. National Tuberculosis Management Guidelines 2014. Page 42 of 120. Adjunctive treatment.

The largest study on the use of corticosteroids in tuberculous pericarditis was published in 2014, subsequent to the 2014 National Tuberculosis Management Guidelines. Recently, data on the differential effect of steroids in people with and without HIV in the setting of other extrapulmonary manifestations of tuberculosis has emerged. Therefore, in order to update and consolidate the tuberculosis STGs a rapid review of use of corticosteroids in tuberculous pericarditis was undertaken.

Purpose/Objective i.e., PICO question:

PICO 1

Population Subgroups	HIV-negative adults and children with tuberculous pericarditis
Intervention(s)	Corticosteroids (prednisone or prednisolone) plus standard anti-TB treatment
Comparator(s)	Anti-tuberculous treatment (ATT) alone or with placebo
Outcome(s)	Mortality, constrictive pericarditis, adverse events
Study types	Guidelines, systematic reviews with meta-analysis, randomised controlled trials

PICO 2

Population Subgroups	Adults and children living with HIV and tuberculous pericarditis
Intervention(s)	Corticosteroids (prednisone or prednisolone) plus anti-TB treatment
Comparator(s)	Anti-tuberculosis treatment (ATT) alone or with placebo
Outcome(s)	Mortality, constrictive pericarditis, adverse events
Study types	Guidelines, systematic reviews with meta-analysis, randomised controlled trials

Methods

1. Data Sources

Clinical practice guidelines: We searched for relevant clinical practice guidelines from the American Thoracic Society and World Health Organization.

Systematic reviews and randomised controlled trials: We searched PubMed for guidelines, systematic reviews, and randomised controlled trials.

2. Search Strategy

The following search terms were used:

((TB pericarditis) OR (tuberculous pericarditis)) OR (tuberculosis pericarditis)) AND (corticosteroids)
PubMed searches were filtered by guideline, systematic review, meta-analysis and randomised controlled trials.

3. Study selection and eligibility criteria, data extraction and analysis, and evidence synthesis

The study screening, selection and data extraction, analysis and evidence was conducted by 1 reviewer. Evidence was synthesised narratively.

4. Assessment of methodological quality

The most recent and up-to-date systematic review was appraised by one reviewer using AMSTAR.[4]

5. GRADE assessment

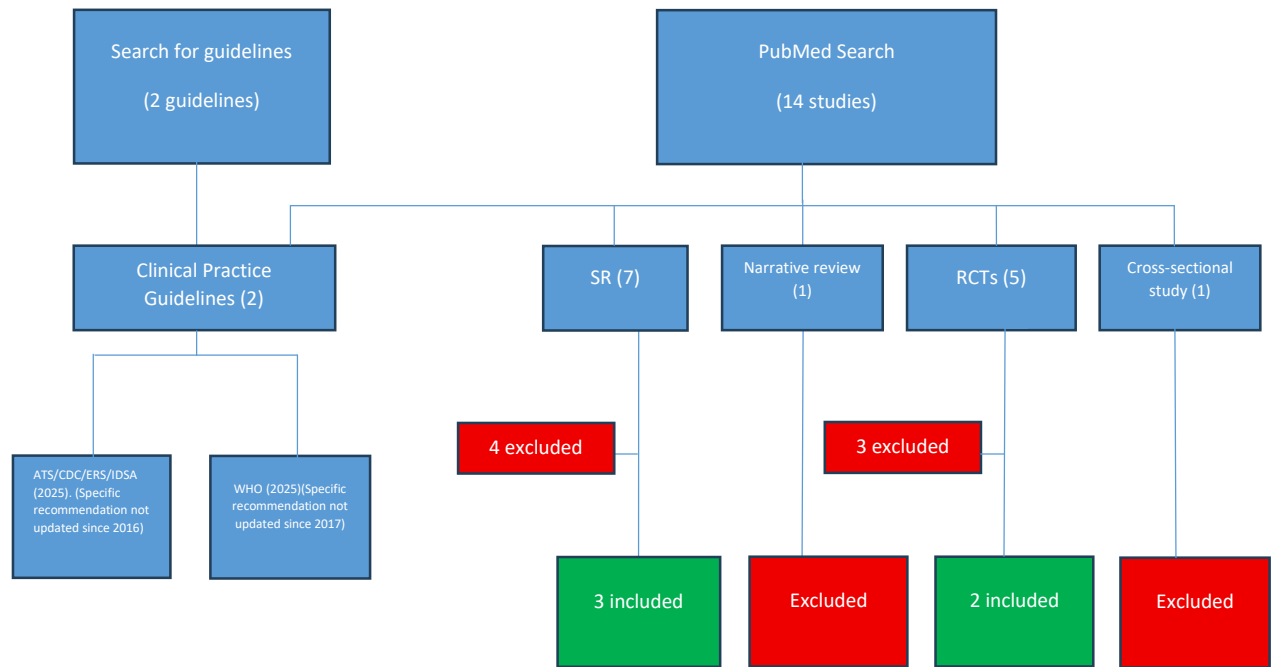
We adopted the GRADE (Grading of Recommendations Assessment, Development and Evaluation) assessment in the systematic review.

Results

1. Result of the search

The search results are illustrated in **Figure 3. Search Flow Chart**. Specific reasons for inclusion or exclusion of studies identified in the search are listed in **Appendix 1**.

Figure 3. Search Flow Chart



Abbreviations: ATS, American Thoracic Society; CDC, Centers for Disease Control and Prevention; ERS, European Respiratory Society; IDSA, Infectious Diseases Society of America; WHO, World Health Organisation; SR, systematic review; RCTs, randomised controlled trials

2. Description of included studies

2.1. Clinical Practice Guidelines

Two clinical practice guidelines were identified. Both clinical practice guidelines had not updated specific recommendations related to corticosteroid use in tuberculous pericarditis since 2016-2017. These guidelines with their respective recommendations are summarised in **Table 1**. Importantly, effect estimates by HIV status are not provided in either guideline's summary of findings tables. Summary of findings tables from the guidelines are included in **Appendix 2**.

Table 1. Summary of the recommendations from clinical practice guidelines identified

Guideline	Recommendation	Justification	Subgroup considerations	Studies included in the systematic review	Outcomes considered
WHO Consolidated guidelines on tuberculosis. Module 4: Treatment and care. 2025.	In patients with tuberculous pericarditis, an initial adjuvant corticosteroid therapy <u>may be used</u>. (Conditional recommendation, very low certainty of evidence) This recommendation was first put forward in the guidelines update of 2017. They are copied without modification into this consolidated document and appear exactly as in the 2017 guidelines.	In patients with tuberculous pericarditis, evidence from studies in the systematic review showed a benefit to steroid treatment with regard to death, constrictive pericarditis and treatment adherence. When the studies were considered individually, the largest (1400 patients) and most recent study – the IMPI study – showed no benefit with steroids. However, a complicating factor in these findings is HIV infection. In the IMPI study, 67% of subjects were HIV-positive and only 14% were on ART. This raises the question as to whether immunosuppressed patients may have had a different benefit from steroids when compared to HIV-negative people or persons living with HIV who are on ART. In the IMPI study, a supplemental analysis was done of the HIV-negative patients only and a small mortality benefit was shown with steroid treatment. However, the relationship between HIV infection and steroids is complex. In another smaller study of 58 subjects, all of whom were HIV-positive, steroids were found to reduce mortality. It is of note that the other studies in the review did not address HIV and mortality. The panel considered that the benefit in preventing constrictive pericarditis outweighed the potential harms of corticosteroid therapy.	With regard to the use of steroids in tuberculous pericarditis, in one study an increase in HIV-related cancers (non-Hodgkins' lymphoma and Kaposi sarcoma) was observed. However, this increase appears to be caused by co-administration of immunotherapy (<i>M. indicus pranii</i>).	Strang et al. 1987 Strang et al. 1988 Hakim Et Al. 2000 Mayosi et al. 2014 Reuter et al. 2006	Mortality (5 studies) Treatment adherence (2 studies) Constrictive pericarditis (3 studies)
Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis, 2016. Update on the Treatment of Drug-Susceptible and Drug-Resistant Tuberculosis. An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline, 2025.	We suggest initial adjuvant corticosteroid therapy <u>not be</u> routinely used in patients with tuberculous pericarditis (Conditional recommendation; very low certainty of evidence).	Based on small studies that have shown mortality and morbidity benefits, corticosteroids have previously been universally recommended in combination with a standard 6-month regimen for treating tuberculous pericarditis; however, a recent placebo-controlled randomized clinical trial with 1400 participants did not find a difference in the combined primary endpoint of the trial, which included mortality, cardiac tamponade, or constrictive pericarditis, between patients treated with adjuvant corticosteroids vs placebo. A subgroup analysis, however, did suggest a benefit in preventing constrictive pericarditis. Similarly, a systematic review conducted to obtain evidence in support of this guideline did not find a statistically significant benefit in terms of mortality or constrictive pericarditis from the use of corticosteroids. Therefore, we suggest that adjuvant corticosteroids should not be used routinely in the treatment of patients with pericardial tuberculosis.	However, selective use of corticosteroids in patients who are at the highest risk for inflammatory complications might be appropriate. Such patients might include those with large pericardial effusions, those with high levels of inflammatory cells or markers in pericardial fluid, or those with early signs of constriction.	Strang et al. 1987 Strang et al. 1988 Hakim Et Al. 2000 Mayosi et al. 2014 Reuter et al. 2006	Mortality (5 studies) Treatment adherence (2 studies) Constrictive pericarditis (3 studies)

2.2. Systematic reviews

Three systematic reviews were identified in the search (**Table 2**). The Cochrane systematic review by Wiysonge, 2017 was considered to be the most up-to-date and relevant as analyses presented are stratified by HIV status.

Table 2. Characteristics of systematic reviews identified

Systematic review	Year Published	Studies included	Subgroup analysis by HIV status	Comment
George et al.[5]	2018	Strang, 1987 Strang, 1988 Hakim, 2000 Mayosi, 2014 Reuter, 2006	No	
Wiysonge et al.[6]	2017 (reviewed in 2019 and considered up-to-date with respect to intervention of corticosteroids)	Schrire, 1959 Hakim, 2000 Strang, 2004a (10-year follow-up study of Strang 1987) Strang, 2004b (10-year follow-up study of Strang 1988) Reuter, 2006 Mayosi, 2014	Yes	Most up-to-date and relevant AMSTAR quality appraisal: Low-quality (Appendix 3)
Ntsekhe et al. [7]	2003	Schrire, 1959 Strang, 1987 Strang, 1988 Hakim, 2000	Yes	

2.2.1. Wiysonge, 2017[6]

This is an update of an earlier Cochrane systematic review published in 2002. This systematic review included seven randomised controlled trials (RCTs) or quasi-RCTs, all from sub-Saharan Africa, including the largest RCT conducted to date. Six trials comprising 1926 participants evaluated corticosteroids in tuberculous pericarditis.[2,8-11] Characteristics of these studies are summarised in **Table 3**. Four trials, comprising 1841 participants, were considered to be at low risk of bias. Three trials, comprising 118 participants, were considered to be at high risk of bias (**Figure 4**). Five trials enrolled participants with tuberculous pericardial effusion and one trial enrolled participants with tuberculous pericardial constriction. The corticosteroids evaluated included cortisone (1 trial), prednisone and triamcinolone hexacetonide (1 trial), and prednisolone (4 trials). The length of follow-up across trials ranged from 1 to 10 years. Only 2 trials included adults and children, with only 7 participants < 15 years included in the systematic review.[8]

In the systematic review, analyses were stratified by HIV status. Data on HIV status were not available in three trials that were conducted in South Africa before the onset of the HIV epidemic.[8,9] The participants in these trials were assumed to be HIV negative for the purposes of the systematic review. One trial enrolled only people with HIV (PWH).[10] Two trials enrolled both PWH and HIV-negative people. [2,11] More than half of all participants included in the systematic review were PWH (1018/1926, 52.9%), however only 19.9% were on antiretroviral therapy at enrolment. In the largest trial included in the systematic review, which comprised 939 PWH, baseline CD4 was available for 633 of 939 participants (67.4%). In these participants, the median CD4 count was 144 cells/mm³; 103 participants (16.3%) had a CD4 count < 50 cells/mm³; 295 participants (46.6%) had a CD4 count between 50 and 199 cells/mm³, 144 participants (22.7%) had a CD4 count between 200 to 350 cells/mm³, and 91 participants (14.4%) had CD4 cell counts > 350 cells/mm³. [12]

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Hakim 2000	+	+	+	+	+	?	+
Liebenberg 2016	+	+	?	+	-	?	+
Mayosi 2014	+	+	+	+	+	+	+
Reuter 2006	?	-	+	?	-	?	+
Schrire 1959	-	-	-	-	?	?	+
Strang 2004a	+	+	+	+	+	?	+
Strang 2004b	+	+	+	+	+	?	+

Figure 4. Risk of bias summary from systematic review

(Note: The study by Liebenberg 2016 included in Figure 4 below is relevant to a different research question with colchicine as the intervention)

Table 3. Summary of studies included in Wiysonge, 2017

Study and Location	Methods	Participants	Interventions	Outcomes
Schire 1959 Cape Town, South Africa	Alternate allocation of 28 participants to adjuvant steroids or no steroids	28 adult participants with pericardial effusion who were on antituberculous chemotherapy for suspected tuberculous pericarditis. The trial authors did not provide the characteristics of the included participants, and did not specify the antituberculous drugs used. No participants with HIV. Definite TB: Not reported	Intervention • Cortisone with a loading dose of 300 mg and maintenance dose of 100 mg daily for several weeks was prescribed for 14 participants. - At a later date, prednisolone 60 mg/day with a maintenance dose of 20 mg was substituted. Control • No corticosteroids. The trial authors did not specify the length of follow-up.	Constriction requiring pericardiectomy
Hakim 2000 Harare, Zimbabwe	Computer-generated randomization list Double blind placebo controlled trial	58 HIV-positive adults with pericardial effusion who were on antituberculous chemotherapy for suspected tuberculous pericarditis. Inclusion criteria: (a) age 18 to 55 years; (b) residence in Harare city to ensure good follow up; (c) HIV seropositive; (d) no diagnosis of tuberculosis within the past two years; (e) large pericardial effusion on echocardiography (> 1 cm anteriorly and > 1 cm posteriorly; and (f) pericardial aspirate with > 50% lymphocytes and protein content > 30 g/L. Exclusion criteria: (a) antituberculous treatment started more than 48 hours before recruitment; (b) corticosteroid treatment within previous one month; (c) presence of Kaposi's sarcoma or any other malignancy; (d) coexisting life threatening disease; (e) bacterial pneumonia; (f) pregnancy; (g) cavitating pulmonary tuberculosis; and (h) other causes of pericardial effusion. All patients received a standard short course anti tuberculous regimen in accordance with national guidelines. This included rifampicin, isoniazid, pyrazinamide, and ethambutol for two months, followed by rifampicin and isoniazid for a further four months in standard doses. 0 participants on ART Definite TB: 38%	Intervention • Prednisolone for the first 6 weeks of antituberculous chemotherapy. • Dose for adults: 60 mg for the first week and tapering by 10 mg every week. Control • Placebo.	Primary outcomes • Death. • Resolution of pericardial effusion. Secondary outcomes • Resolution of pretreatment symptoms and signs, and ECG changes. • Corticosteroid-related adverse effects.

Study and Location	Methods	Participants	Interventions	Outcomes
Strang 2004a Umtata, South Africa (Follow-up of Strang, 1987)	Central randomization Double blind placebo- controlled study	143 participants with suspected tuberculous constrictive pericarditis aged 5 years and older. Only 2 participants were younger than 15 years of age. The participants in the treatment and control groups were well-matched in terms of clinical characteristics and completion of antituberculous chemotherapy. Those consenting to take part were all prescribed the same 6-month standard antituberculosis regimen of streptomycin, isoniazid, rifampicin, and pyrazinamide daily for 14 weeks as an in-patient, followed by isoniazid and rifampicin daily up to 6 months. Assumed no participants with HIV. Definite TB: 10%	Intervention • Prednisolone for the first 11 weeks of antituberculous chemotherapy. The dose for children aged 5 to 9 years was 30 mg daily for weeks 1 to 4; 15 mg daily for weeks 5 to 8; 7.5 mg daily for weeks 9 to 10; and 2.5 mg daily for week 11. Regarding children aged 10 to 14 years, the dose was 45 mg for weeks 1 to 4; 22.5 mg for weeks 5 to 8; 7.5 mg for weeks 9 to 10; and 2.5 mg for week 11. The dose for adults was 60 mg for the first 4 weeks; 30 mg for weeks 5 to 8; 15 mg for weeks 9 to 10; and 5 mg for week 1. Control • Matching placebo.	• Death. • Death from pericarditis. • Favourable clinical status at 24 months. • Pericardiectomy.
Strang 2004b Umtata, South Africa (Follow-up of Strang, 1988)	Central randomization Double blind placebo- controlled study Factorial design	240 participants aged 5 years or more diagnosed as having active tuberculous pericardial effusion. Only 5 participants were younger than 15 years of age. The participants in the treatment and control groups were well-matched in terms of their clinical characteristics and completion of antituberculous chemotherapy. Those consenting to take part were all prescribed the same 6-month standard antituberculosis regimen of streptomycin, isoniazid, rifampicin, and pyrazinamide daily for 14 weeks as an in-patient, followed by isoniazid and rifampicin daily up to 6 months. Assumed no participants with HIV. Definite TB: 60%	Intervention 1 • Complete open surgical drainage on admission. Control 1 • No open drainage. Intervention 2 • Prednisolone for the first 11 weeks of antituberculous chemotherapy. The dose for children aged 5 to 9 years was 30 mg daily for weeks 1 to 4; 15 mg daily for weeks 5 to 8; 7.5 mg daily for weeks 9 to 10; and 2.5 mg daily for week 11. Regarding children aged 10 to 14 years, the dose was 45 mg for weeks 1 to 4; 22.5 mg for weeks 5 to 8; 7.5 mg for weeks 9 to 10; and 2.5 mg for week 11. The dose for adults was 60 mg for the first 4 weeks; 30 mg for weeks 5 to 8; 15 mg for weeks 9 to 10; and 5 mg for week 1. Control 2 • Matching placebo.	• Death. • Death from pericarditis. • Favourable clinical status at 24 months. • Tamponade requiring pericardiocentesis. • Constriction. • Pericardiectomy.

Study and Location	Methods	Participants	Interventions	Outcomes
Reuter 2006 Cape Town, South Africa	Computer-generated randomization list Double-blind placebo-controlled study	57 participants, aged 17 to 66 years, with large pericardial effusions on echocardiography, pericardial aspirate with protein content > 30 g/L, and pericardial fluid adenosine deaminase (ADA) activity > 35 U/L; 23 females and 34 males; 40 had microbiological or histological evidence of TB or both, and 17 patients were diagnosed by clinical and supportive laboratory data. 21 (37.0%) were HIV-positive. No PWH were on ART. A standard short-course anti-tuberculous regimen was initiated according to national guidelines, namely a combination of rifampicin, isoniazid, pyrazinamide and ethambutol for two months, followed by rifampicin and isoniazid for a further four months. Patients were discharged on anti-tuberculous therapy and pyridoxine, with or without adjunctive prednisone. HIV-positive patients also received daily oral cotrimoxazole; due to the prevailing national policy at the time of this study, none of these patients received antiretroviral therapy. Definite TB: not reported	Intervention 1 • 200 mg (5 mL) intrapericardial triamcinolone hexacetone. Triamcinolone was injected directly into the pericardium just prior to the removal of the indwelling catheter. Due to limited resources, an oral placebo was not used in conjunction with the intrapericardial triamcinolone. 17 participants were in this arm, 6 (35%) were HIV-positive. Intervention 2 • Oral prednisone plus intrapericardial placebo (5 mL 0.9% saline solution). Oral prednisone was started at 60 mg/day for 4 weeks, followed by 30 mg/day for 4 weeks, 15 mg/day for 2 weeks and 5 mg/day for 1 week. There were 16 participants in this arm, 9 (56%) were HIV-positive. Control • Placebo (5 mL intrapericardial 0.9% saline). 24 participants were included in this arm, and 6 (25%) were HIV-positive. We excluded data from the intrapericardial triamcinolone arm from this review.	Primary outcome • All-cause mortality. Secondary outcomes • Death attributed to pericarditis. • Disability related to pericardial disease at 1 year (defined as a history of restricted physical activity using New York Heart Association functional classification.) • Effusive constriction. • Fibrous constrictive pericarditis requiring pericardiectomy.

Study and Location	Methods	Participants	Interventions	Outcomes
Mayosi 2014 Multiple sites in South Africa, Mozambique, Malawi, Uganda, Sierra Leone, Zimbabwe, Kenya, and Nigeria	Computer-generated randomization list Double-blind placebo-controlled 2x2 factorial study	1400 participants (67% HIV-positive) 18 years of age or older, evidence of definite or probable tuberculous pericarditis, and had begun antituberculous treatment less than 1 week before enrolment. 83% of participants had pericardial effusion. 17% had constriction. 22% of PWH were on ART. Trial participants received antimicrobial treatment for tuberculosis and antiretroviral treatment for HIV according to World Health Organization (WHO) guidelines; management during the trial was revised as recommended treatment practices evolved. Definite TB: 17%	Intervention 1 • Prednisolone for 6 weeks at a dose of 120 mg per day in the first week, 90 mg per day in the second week, 60 mg per day in the 3rd week, 30 mg per day in the 4th week, 15 mg per day in the 5th week, and 5 mg per day in the 6th week. Control 1 • Identical placebo for 6 weeks at a dose of 120 mg per day in the 1st week, 90 mg per day in the 2nd week, 60 mg per day in the 3rd week, 30 mg per day in the 4th week, 15 mg per day in the 5th week, and 5 mg per day in the 6th week Intervention 2 • M. indicus pranii preparation (CADI-Mw injection, Cadila Pharmaceuticals) in 5 doses: at the time of enrolment and at 2 weeks, 4 weeks, 6 weeks, and 3 months. The 1st dose was given as 2 injections of 0.1 mL (containing 0.5 Å~ 109 organisms) in each deltoid region of the upper arm; the 4 subsequent doses were given as a single injection of 0.1 mL. Control 2 • Identical placebo in 5 doses: at the time of enrolment and at 2 weeks, 4 weeks, 6 weeks, and 3 months. The 1st dose was given as 2 injections of 0.1 mL in each deltoid region of the upper arm; the 4 subsequent doses were given as a single injection of 0.1 mL.	Primary outcome • Composite of death or 1st occurrence of cardiac tamponade requiring pericardiocentesis or constrictive pericarditis. Secondary outcomes • Individual components of the primary outcome. • Hospitalization. Safety outcomes • Opportunistic infections. • Cancer. • CD4+ T-lymphocyte cell count (measure of immunosuppression) and immune reconstitution inflammatory syndrome (in HIV-positive).

2.3 Randomised controlled trials (RCTs)

Two RCTs were identified in the search.[2,8] Both studies were included in the Wiysonge(2017) systematic review and the effectiveness results for these two studies are not discussed further. Since the identified systematic review included only limited safety outcomes, the safety outcomes from the largest RCT are included.

The largest RCT was the IMPI trial, which utilised a 2 x 2 factorial double-blind design and was conducted in multiple centres across Sub-Saharan Africa.[2] The study enrolled 1400 adults with definite or probable tuberculous pericarditis to receive either prednisolone (n = 706) or placebo (n = 694) for 6 weeks, and either *M.indicus prannii* immunotherapy or placebo, in addition to standard anti-tuberculous therapy. The primary outcome was a composite of death or the first episode of cardiac tamponade requiring pericardiocentesis or constrictive pericarditis. Two thirds of participants were PWH, and across study arms <15% of PWH were on antiretroviral medication at randomisation. In the Wiysonge (2017) systematic review the IMPI trial was assessed to be at low risk of bias.

3. Effectiveness and/or safety results

3.1 PICO 1: Corticosteroids plus standard anti-tuberculous treatment compared to anti-tuberculous treatment alone or with placebo in HIV-negative adults with tuberculous pericarditis

Table 4. Summary of findings table for HIV-negative people from Wiysonge, 2017

Summary of findings for the main comparison. Corticosteroids for tuberculous pericarditis in HIV-negative people						
Population: HIV-negative people with tuberculous pericarditis Settings: any setting Intervention: corticosteroids Comparison: placebo						
Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	Number of participants (trials)	Certainty of the evidence (GRADE)	Comments
	Placebo	Steroids				
Death from all causes	22 per 100	18 per 100 (13 to 24)	RR 0.80 (0.59 to 1.09)	660 (4 trials)	⊕⊕⊕⊕ low ^{1,2}	Steroids may reduce the risk of deaths from all causes among HIV-negative people.
Death from pericarditis	8 per 100	3 per 100 (1 to 6)	RR 0.39 (0.19 to 0.80)	660 (4 trials)	⊕⊕⊕⊕ moderate ²	Steroids probably reduce the risk of deaths from pericarditis among HIV-negative people.
Constrictive pericarditis	10 per 100	7 per 100 (3 to 15)	RR 0.72 (0.34 to 1.55)	281 (2 trials)	⊕⊕⊕⊕ very low ^{2,3,4}	It is uncertain whether steroids have an effect on the risk of constriction among HIV-negative people.
Repeat pericardiocentesis	40 per 100	34 per 100 (28 to 41)	RR 0.85 (0.70 to 1.04)	492 (2 trials)	⊕⊕⊕⊕ low ^{1,4}	Steroids may reduce the risk of repeat drainage of the pericardium among HIV-negative people.
Cancer	1 per 100	1 per 100 (0 to 12)	RR 0.85 (0.05 to 13.80)	256 (1 trial)	⊕⊕⊕⊕ very low ^{3,5}	It is uncertain whether steroids have an effect on the risk of cancer among HIV-negative people.
Abbreviations: CI: confidence interval; RR: risk ratio.						
GRADE Working Group grades of evidence High certainty: further research is very unlikely to change our confidence in the estimate of effect. Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low certainty: we are very uncertain about the estimate.						

¹We downgraded by 1 for imprecision: the CI ranges from a large clinical benefit to a small increase in harm.

²We downgraded by 1 for study limitations: one trial was at high risk of bias.

³We downgraded by 2 for imprecision: the CI ranges from clinically important benefits to a large increase in harm.

⁴We downgraded by 1 for selective reporting: data were only reported by 2 of the 4 trials that recruited HIV-negative people.

⁵We downgraded by 1 for selective reporting: data were only reported by 1 of the 4 trials that recruited HIV-negative people.

In addition, only 1 trial reported on hospitalisation. It is uncertain whether corticosteroids reduced the risk of hospitalisation in people without HIV (RR 0.98, 95% CI 0.57 to 1.70, 256 participants, 1 trial, very low certainty evidence).

The effects of corticosteroids on risk of pericardiectomy in people without HIV is also uncertain (RR 0.91, 95% CI 0.58 to 1.41; 432 participants; 4 trials; very low certainty evidence).

3.2 PICO 2: Corticosteroids plus standard anti-tuberculous treatment compared to anti-tuberculous treatment alone or with placebo in adults with HIV and tuberculous pericarditis

Table 5. Summary of findings table for PWH from Wiysonge, 2017

Summary of findings 2. Corticosteroids for tuberculous pericarditis in HIV-positive people

Population: HIV-positive people with tuberculous pericarditis. Most patients (80%) not on antiretroviral drugs

Settings: any setting

Intervention: corticosteroids

Comparison: placebo

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	Number of participants (trials)	Certainty of the evidence (GRADE)	Comments
	Placebo	Corticosteroids				
Death from all causes	17 per 100	15 per 100 (6 to 40)	RR 0.91 (0.34 to 2.42)	575 (3 trials)	⊕⊕⊕⊕ very low ^{1,2}	It is uncertain whether steroids have an effect on the risk of deaths from all causes among people living with HIV.
Death from pericarditis	4 per 100	4 per 100 (2 to 10)	RR 1.07 (0.46 to 2.54)	517 (2 trials)	⊕⊕⊕⊕ very low ^{1,3}	It is uncertain whether steroids have an effect on the risk of deaths from pericarditis among people living with HIV.
Constrictive pericarditis	6 per 100	4 per 100 (2 to 7)	RR 0.55 (0.26 to 1.16)	575 (3 trials)	⊕⊕⊕⊕ low ¹	Steroids may reduce the risk of developing constriction among people living with HIV.
Repeat pericardiocentesis	60 per 100	61 per 100 (53 to 71)	RR 1.02 (0.89 to 1.18)	517 (2 trials)	⊕⊕⊕⊕ low ^{3,5}	Steroids may have little or no effect on the risk of repeat pericardiocentesis among people living with HIV.
Cancer	1 per 100	1 per 100 (0 to 8)	RR 1.62 (0.27 to 9.77)	502 (1 trial)	⊕⊕⊕⊕ very low ^{1,3}	It is uncertain whether steroids have an effect on the risk of cancer among people living with HIV.

Abbreviations: CI: confidence interval; RR: risk ratio.

GRADE Working Group grades of evidence

High certainty: further research is very unlikely to change our confidence in the estimate of effect.

Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low certainty: we are very uncertain about the estimate.

¹We downgraded by 2 for imprecision: the CI ranges from substantial clinical benefits to substantial harm.

²We downgraded by 1 for unexplained heterogeneity ($\text{Chi}^2 = 3.82$, $\text{df} = 1$ ($P = 0.05$); I^2 statistic = 74%).

³We downgraded by 1 for selective reporting: only 2 of the 3 studies that recruited HIV-positive people reported data.

⁴We downgraded by 1 for study limitations: 1 study had a high risk of bias.

⁵We downgraded by 1 for imprecision: the CI ranges from a small beneficial effect to clinically important harms.

Corticosteroids may reduce the risk of hospitalisation in PWH (RR 0.80, 95% CI 0.59 to 1.09; 502 participants, 1 trial, low certainty evidence).

It is uncertain whether corticosteroids have an effect on risk of pericardiectomy in PWH (RR 2.10, 95% CI 0.10 to 44.40; 15 participants, 1 trial, very low certainty evidence)

It is uncertain whether corticosteroids have an effect on the risk of opportunistic infections in PWH (RR 0.95, 95% CI 0.61 to 1.48; 517 participants, 2 trials, very low certainty evidence).

The IMPI trial, which contributed to the majority of participants with HIV in the Wiysonge 2017 systematic review, included a subgroup analyses of the effect of prednisolone on the primary composite outcome by CD4 count (**Figure 5**).

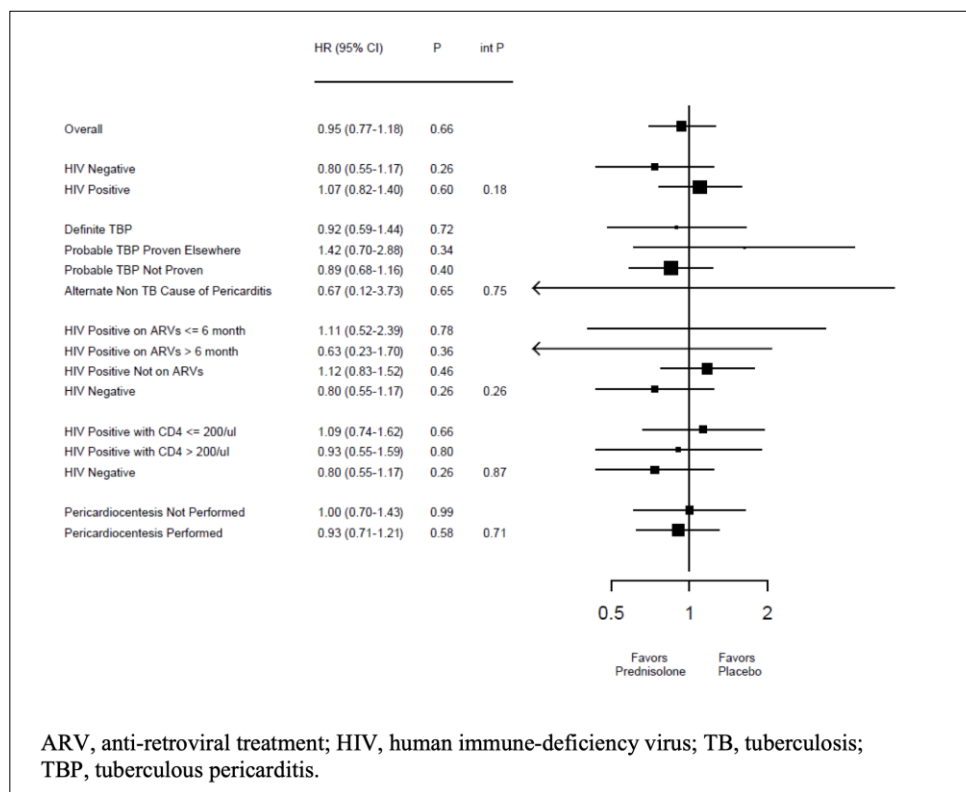


Figure 5. Forest Plot of Effect on Primary Composite Outcome by Key Subgroups for the Prednisolone Comparison from Mayosi, 2014

3.3 Safety Outcomes from Mayosi, 2014[2]

Table 6. Effects of prednisolone on Safety Outcomes from Mayosi, 2014

Outcome	Prednisolone (N = 706)		Placebo (N = 694)		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	no. of events/100 person-yr	no. of patients (%)	no. of events/100 person-yr		
Opportunistic infection	78 (11.0)	6.89	68 (9.8)	5.91	1.16 (0.84–1.61)	0.36
Candida infection	54 (7.6)	4.68	36 (5.2)	3.01	1.52 (1.00–2.32)	0.05
Cancer	13 (1.8)	1.05	4 (0.6)	0.32	3.27 (1.07–10.03)	0.03
HIV-related cancer	9 (1.3)	0.73	1 (0.1)	0.08	9.04 (1.14–71.33)	0.04
Immune reconstitution disease	2 (0.3)	0.16	1 (0.1)	0.08	2.02 (0.18–22.28)	0.56

More participants in the prednisolone group developed candida and other opportunistic infections than in the placebo group, though this was not statistically significant. There were very few cases of immune reconstitution inflammatory syndrome (IRIS) in the trial overall, 2 cases of IRIS occurred in the prednisolone group and 1 in the placebo group. Prednisolone, as compared with placebo, was associated with an increased incidence of cancer (1.05 vs. 0.32 cases per 100 person-years; HR 3.27; 95% CI, 1.07 to 10.03; $p = 0.03$). This increase was due to a higher incidence of HIV-related cancers in the prednisolone group than in the placebo group (0.73 vs. 0.08 per 100 person-years; HR 9.04; 95% CI, 1.14 to 71.33; $p = 0.04$). The various cancers are summarised in **Table 7**. Nine of

the 13 cases of cancer in the prednisolone group occurred in participants who also received *M. indicus pranii*. Kaplan-Meier estimates of time to cancer occurrence for all four comparisons in the trial are shown in **Figure 6**. It should be noted that based on the suggestion of a clinical interaction between prednisolone and *M. indicus pranii* on cancer incidence, in the Wiysonge 2017 systematic review for the outcome of cancer, only data from the group that took 1 active intervention (i.e. prednisolone and placebo) were included, and data from the group that received both interventions was excluded.

Table 7. Causes of Malignancy Prednisolone vs. Placebo

Cause of malignancy	Prednisolone 706/1400		Placebo 649/1400		P value*
	n	%	n	%	
All malignancies (Patient could have multiple malignancies)	13	1.8	4	0.6	0.05
Kaposi	7	1.0	1	0.1	0.07
Non Hodgkin's lymphoma	2	0.3	0	0.0	0.50
Gastric / colon cancer	1	0.1	0	0.0	>0.99
Progression of pre-existing malignancy	1	0.1	1	0.1	>0.99
Other	2	0.3	2	0.3	>0.99

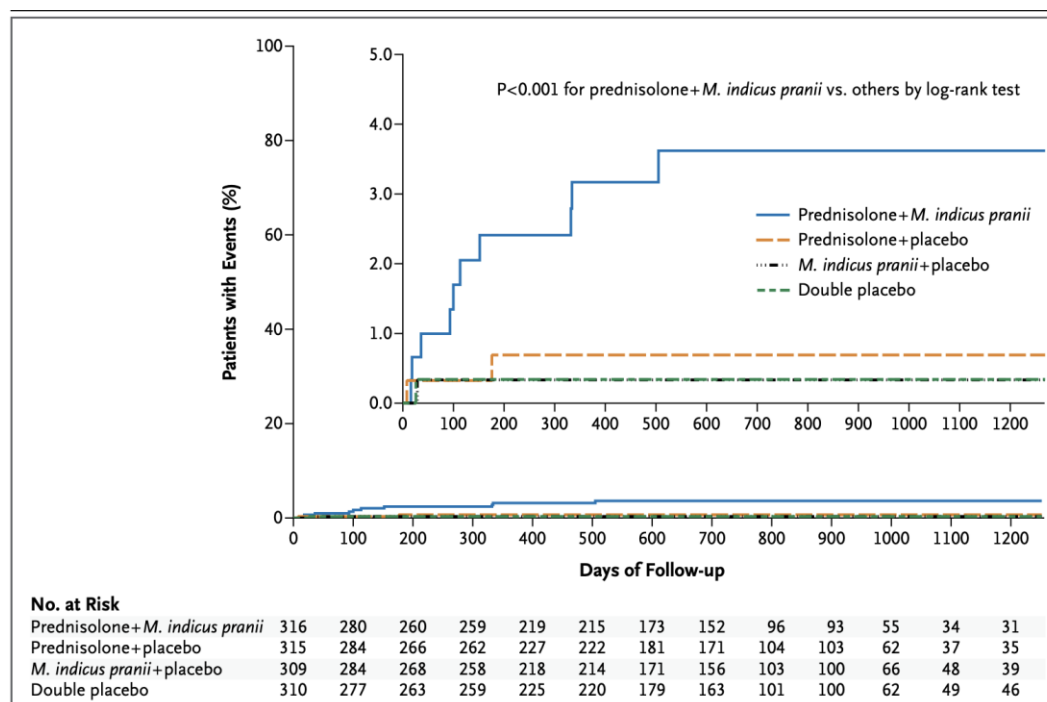


Figure 6. Time to cancer occurrence by study arm from Mayosi, 2014

Costs

The management of TB pericarditis will be a new STG addition to the Adult Hospital publication. As the national TB guidelines recommend the use of corticosteroids in TB pericarditis, we anticipate a minimal incremental budget impact with this recommendation. Costs have been calculated using the oral prednisone dose regimen from Mayosi (2014) RCT as this includes the largest patient cohort. Equivalent doses of dexamethasone IV for patients unable to take oral therapy, were obtained using the online steroid conversion calculator: https://www.mdcalc.com/calc/2040/steroid-conversion-calculator?drug_dosage=90

Table 8. Direct cost of corticosteroids in the treatment of tuberculous pericarditis in adults

TB PERICARDITIS - cost of corticosteroids as adjunctive therapy (ADULTS)					
Dexamethasone IV					
STG dosing guidance		Formulation	Price per ampoule (Rands)	Equivalent number of amps per week	Cost per week (Rands)
Week 1	18mg	4mg/mL as 1mL inj	6,83	35	239,05
Week 2	13,5mg			28	191,24
Week 3	9mg			21	143,43
Week 4	4,5mg			14	95,62
Week 5	2,3mg			7	47,81
Week 6	0,8mg			7	47,81
Cost per course					R764,96
Prednisone oral					
STG dosing guidance		Formulation	Price per tablet (Rands)	Equivalent number of tablets per day	Cost per week (Rands)
Week 1	120mg/day	5mg tablet	0,19	24	31,92
Week 2	90mg/day			18	23,94
Week 3	60mg/day			12	15,96
Week 4	30mg/day			6	7,98
Week 5	15mg/day			3	3,99
Week 6	5mg/day			1	1,33
Cost per course					R85,12
Notes:					
1. Dexamethasone dose conversion based on equivalent dose of oral prednisone using Mayosi 2014 regimen https://www.mdcalc.com/calc/2040/steroid-conversion-					
2. Doses rounded to nearest ampoule/tablet					
3. Prices based on MHPL (Feb 2026)					
4. Where dose ranges recommended - max dose applied for costing					
5. For prednisone, ave price per tablet applied as multiple products on tender					

As the use of adjunctive corticosteroids is already included in the paediatric STGs as standard of care, there is no anticipated incremental budget impact associated with this recommendation (**Table 9**).

Table 9. Direct cost of corticosteroids in the treatment of tuberculous pericarditis in children by weight band (based on current dosing guidance in Paediatric STG)

Assumed weight per patient				10kg			20kg			30kg					
Formulation	Price per pack (Rands)	STG dosing guidance		Dose per week (mg)	Equivalent number of bottles per patient	Cost per course (Rands)	Dose per week (mg)	Equivalent number of bottles per patient	Cost per course (Rands)	Dose per week (mg)	Equivalent number of bottles per patient	Cost per course (Rands)			
15mg/5mL solution (50mL pack) = 150mg per bottle	95,21	Week 1	2mg/kg/day	140	3		280	6		420	9				
		Week 2	1.5mg/kg/day	105			210			315					
		Week 3	1mg/kg/day	70			140			210					
		Week 4	1mg/kg/day	70			140			210					
		Week 5	0.5mg/kg/day	35			70			105					
		Week 6	0.25mg/kg/day	17,5			35			52,5					
				437,5			R285,63		875			R571,26	1312,5		R856,89
Notes:															
1. Based on 3 weight bands (10kg, 20kg and >/=30kg)															
2. Total dose per course rounded to nearest full pack															
3. Prices based on MHPI (Feb 2026)															

Key findings

- In adults without HIV and with tuberculous pericarditis:
 - Corticosteroids probably result in a reduction in deaths from pericarditis (moderate certainty evidence) and may reduce deaths from all causes and the need for repeat pericardiocentesis (low certainty evidence).
 - It is uncertain whether corticosteroids have any effect on the incidence of cancer, hospitalisation, development of constrictive pericarditis, or the need for pericardiectomy.
- In adult PWH not on ART with CD4 counts ≤ 350 cells/mm³ with tuberculous pericarditis:
 - Corticosteroids may reduce constrictive pericarditis and hospitalization (low certainty evidence).
 - Corticosteroids may make little or no difference to the need for repeat pericardiocentesis (low certainty evidence)
 - It is uncertain whether corticosteroids have any effect on deaths from pericarditis, deaths from all causes, the need for pericardiectomy or the development of cancer (very low certainty evidence).
- In the largest RCT conducted to date, key findings relevant to safety outcomes include:
 - More participants in the prednisolone group developed candida and other opportunistic infections than in the placebo group, though this was not statistically significant.
 - Prednisolone, as compared with placebo, was associated with an increased incidence of cancer, particularly HIV-related cancers (Kaposi's sarcoma and non-Hodgkin's lymphoma). This increase may be related to co-administration of immunotherapy (*M. indicus pranii*) in this RCT.
- No data in adult PWH on ART or with higher CD4 cell counts was identified and in these patients the results from adults without HIV may be more applicable.
- No data in children with or without HIV and tuberculous pericarditis was identified.

Conclusion and Recommendation

Given the important benefits of corticosteroids in reducing deaths in adults without HIV, and in reducing hospitalisations and the development of constrictive pericarditis in PWH, we recommend the use of corticosteroids in tuberculous pericarditis, acknowledging the low certainty evidence. In PWH, a thorough clinical examination should be performed before starting corticosteroids to exclude HIV-related cancers and antiretroviral therapy should be initiated promptly in accordance with standard treatment guidelines to mitigate the potential signal of harm observed in the largest RCT.

While no data in children with or without HIV and tuberculous pericarditis was identified, given the important benefits associated with the use of corticosteroids in adults with tuberculous pericarditis, we suggest using corticosteroids in children with tuberculous pericarditis.

Review Team

The following people were involved in this review (alphabetical by surname):

Name	Affiliation(s)	Role and Contribution	Interest declaration
Jessica Taylor (Lead author)	University of Cape Town	Literature search, quality appraisal, data synthesis, drafting report	None
Zahiera Adam	Clinton Health Access Initiative (CHAI) and NDoH	Costing, QA and recommendation	None
Prof Karen Cohen	Division of Clinical Pharmacology, University of Cape Town	QA, expert guidance and recommendation	None
Dr Halima Dawood	Infectious Diseases Unit, Greys Hospital	Expert guidance	None
Dr Jeremy Nel	Division of Infectious Diseases, Department of Medicine, University of the Witwatersrand	QA, expert guidance and recommendation	None

Acknowledgements

Acknowledging members of the South African National Essential Medicines List Committee, its Expert Review Committee and the National Department of health who provided insight and expertise that supported the review.

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Appendix 1: Search results and reasons for exclusion

	Reference	Study Type	Included/Excluded	Reason
1.	Imazio M, Gaita F, LeWinter M. Evaluation and Treatment of Pericarditis: A Systematic Review. JAMA. 2015 Oct 13;314(14):1498-506. doi: 10.1001/jama.2015.12763. Erratum in: JAMA. 2015 Nov 10;314(18):1978. doi: 10.1001/jama.2015.14947. Erratum in: JAMA. 2016 Jan 5;315(1):90. doi: 10.1001/jama.2015.16998. Dosage error in article text. PMID: 26461998.	Systematic review	Excluded	Incorrect population - Not specific to tuberculous pericarditis
2.	López-López JP, Posada-Martínez EL, Saldarriaga C, Wyss F, Ponte-Negretti CI, Alexander B, Miranda-Arboleda AF, Martínez-Sellés M, Baranchuk A; Neglected Tropical Diseases, Other Infectious Diseases Affecting the Heart (the NET-Heart Project). Tuberculosis and the Heart. J Am Heart Assoc. 2021 Apr 6;10(7):e019435. doi: 10.1161/JAHA.120.019435. Epub 2021 Mar 18. PMID: 33733808; PMCID: PMC8174360.	Narrative review	Excluded	Incorrect study type
3.	George IA, Thomas B, Sadhu JS. Systematic review and meta-analysis of adjunctive corticosteroids in the treatment of tuberculous pericarditis. Int J Tuberc Lung Dis. 2018 May 1;22(5):551-556. doi: 10.5588/ijtld.17.0341. PMID: 29663961.	Systematic review	Included	
4.	Wiyongse CS, Ntsekhe M, Thabane L, Volmink J, Majombozi D, Gumedze F, Pandie S, Mayosi BM. Interventions for treating tuberculous pericarditis. Cochrane Database Syst Rev. 2017 Sep 13;9(9):CD000526. doi: 10.1002/14651858.CD000526.pub2. PMID: 28902412; PMCID: PMC5618454.	Systematic review	Included	
5.	Diallo A, Diallo BD, Diallo OH, Carlos-Bolumbu M, Camara M, Sidikiba S. Corticosteroids for reducing tuberculosis mortality in persons living with HIV: a systematic review and meta-analysis using reconstructed individual patient data. BMJ Glob Health. 2025 Aug 14;10(8):e017923. doi: 10.1136/bmjgh-2024-017923. PMID: 40813100; PMCID: PMC12352167	Systematic review	Excluded	Incorrect population – pericardial, meningeal and pleural tuberculosis
6.	Ntsekhe M, Wiyongse C, Volmink JA, Commerford PJ, Mayosi BM. Adjuvant corticosteroids for tuberculous pericarditis: promising, but not proven. QJM. 2003 Aug;96(8):593-9. doi: 10.1093/qjmed/hcg100. PMID: 12897345.	Systematic review	Included	
7.	Mayosi BM, Ntsekhe M, Volmink JA, Commerford PJ. Interventions for treating tuberculous pericarditis. Cochrane Database Syst Rev. 2002;(4):CD000526. doi: 10.1002/14651858.CD000526. Update in: Cochrane Database Syst Rev. 2017 Sep 13;9:CD000526. doi: 10.1002/14651858.CD000526.pub2. PMID: 12519546.	Systematic review	Excluded	2017 update included (Wiyongse et al.)
8.	Mayosi BM, Volmink JA, Commerford PJ. Interventions for treating tuberculous pericarditis. Cochrane Database Syst Rev. 2000;(2):CD000526. doi: 10.1002/14651858.CD000526. Update in: Cochrane Database Syst Rev. 2002;(4):CD000526. doi: 10.1002/14651858.CD000526. PMID: 10796550.	Systematic Review	Excluded	2017 update included (Wiyongse et al.)
9.	Reuter H, Burgess LJ, Louw VJ, Doubell AF. Experience with adjunctive corticosteroids in managing tuberculous pericarditis. Cardiovasc J S Afr. 2006 Sep-Oct;17(5):233-8. PMID: 17117227.	Randomised controlled trial	Excluded	Incorrect intervention/comparison – intrapericardial corticosteroid therapy vs. oral corticosteroid vs. intrapericardial placebo
10.	Strang JI, Nunn AJ, Johnson DA, Casbard A, Gibson DG, Girdling DJ. Management of tuberculous constrictive pericarditis and tuberculous pericardial effusion in Transkei: results at 10 years follow-up. QJM. 2004 Aug;97(8):525-35. doi: 10.1093/qjmed/hch086. PMID: 15256610.	10-year follow-up of 2 randomised controlled trials	Included	.
11.	Mayosi BM, Ntsekhe M, Bosch J, Pogue J, Gumedze F, Badri M, Jung H, Pandie S, Smieja M, Thabane L, Francis V, Thomas KM, Thomas B, Awotedu AA, Magula NP, Naidoo DP, Damasceno A, Banda AC, Mutyaba A, Brown B, Ntuli P, Mntla P, Ntintyane L, Ramjee R, Manga P, Kirenga B, Mondo C, Russell JB, Tsitsi JM, Peters F, Essop MR, Barasa AF, Mijinyawa MS, Sani MU, Olunuga T, Ogah O, Adebiyi A, Aje A, Ansa V, Ojji D, Danbauchi S, Hakim J, Matenga J, Yusuf S. Rationale and design of the Investigation of the Management of Pericarditis (IMPI) trial: a 2 × 2 factorial randomized double-blind multicenter trial of adjunctive prednisolone and Mycobacterium m immunotherapy in tuberculous pericarditis. Am Heart J. 2013 Feb;165(2):109-15.e3. doi: 10.1016/j.ahj.2012.08.006. Epub 2012 Dec 13. PMID: 23351812.	Randomised controlled trial protocol	Excluded	Incorrect study design - protocol
12.	Liebenberg JJ, Dold CJ, Olivier LR. A prospective investigation into the effect of colchicine on tuberculous pericarditis. Cardiovasc J Afr. 2016 Nov/Dec;27(6):350-355. doi: 10.5830/CVJA-2016-035. PMID: 27965998; PMCID: PMC5412665.	Randomised controlled trial	Excluded	Incorrect comparator - colchicine
13.	Mayosi BM, Ntsekhe M, Bosch J, Pandie S, Jung H, Gumedze F, Pogue J, Thabane L, Smieja M, Francis V, Joldersma L, Thomas KM, Thomas B, Awotedu AA, Magula NP, Naidoo DP, Damasceno A, Chitsa Banda A, Brown B, Manga P, Kirenga B, Mondo C, Mntla P, Tsitsi JM, Peters F, Essop MR, Russell JB, Hakim J, Matenga J, Barasa AF, Sani MU, Olunuga T, Ogah O, Ansa V, Aje A, Danbauchi S, Ojji D, Yusuf S; IMPI Trial Investigators. Prednisolone and Mycobacterium indicus pranii in tuberculous pericarditis. N Engl J Med. 2014 Sep 18;371(12):1121-30. doi: 10.1056/NEJMoa1407380. Epub 2014 Sep 1. PMID: 25178809; PMCID: PMC4912834.	Randomised controlled trial	Included	Primary study included in systematic review
14.	Wiyongse CS, Ntsekhe M, Gumedze F, Siwa K, Blackett KN, Commerford PJ, Volmink JA, Mayosi BM. Contemporary use of adjunctive corticosteroids in tuberculous pericarditis. Int J Cardiol. 2008 Mar 14;124(3):388-90. doi: 10.1016/j.ijcard.2006.12.060. Epub 2007 Apr 18. PMID: 17445921.	Cross-sectional study	Excluded	Incorrect study type

Appendix 2.

Summary of findings table from WHO Guideline WHO Consolidated guidelines on tuberculosis. Module 4: Treatment and care.

PICO 7

Author(s): Lelia Chaisson

Question: Adjuvant corticosteroids compared with TB treatment without corticosteroids for tuberculous pericarditis

Bibliography: Strang JI et al. Lancet 1987; Strang JI et al. Lancet 1988; Hakim JG et al. Heart 2000; Mayosi BM et al. N Engl J Med 2014; Reuter H et al. Cardiovasc J S Afr. 2006

Quality assessment							Number of patients		Effect			Quality	Importance
Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Adjuvant corticosteroids	TB treatment without corticosteroids	Relative (95% CI)	Absolute (95% CI)			
Death													
5	randomized trials	not serious	serious ¹	serious ²	serious ³	none ⁴	142/897 (15.8%)	142/882 (16.1%)	RR 0.54 (0.23 to 1.26)	74 fewer per 1000 (from 42 more to 124 fewer)	⊕○○○	VERY LOW	CRITICAL
Treatment adherence													
2	randomized trials	serious ⁵	very serious ¹	serious ⁵	not serious	none	744/888 (83.8%)	785/907 (86.5%)	RR 0.91 (0.75 to 1.12)	78 fewer per 1000 (from 104 more to 216 fewer)	⊕○○○	VERY LOW	IMPORTANT
Constrictive pericarditis													
3	randomized trials	not serious	not serious	not serious	very serious ³	none	36/768 (4.7%)	56/747 (7.5%)	RR 0.72 (0.32 to 1.58)	21 fewer per 1000 (from 43 more to 51 fewer)	⊕⊕○○	LOW	IMPORTANT

CI: confidence interval; RR: risk ratio.

1. Inconsistent findings between studies. Death $I^2 = 70\%$; adherence $I^2 = 89\%$. Older studies show larger effects.
2. Although not alone a reason for downgrading (only in context of the concern for publication bias), we considered the older studies not necessarily reflecting the populations seen in practice today.
3. The effects at the ends of the confidence interval would lead to different clinical decisions; in addition, the sample sizes are smaller than the optimal information size.
4. Publication bias is possible – small studies show a large effect. However, these studies are also older, and the enrolled populations may differ, accounting for the difference in the effects.
5. Different definitions of adherence were used by different studies.

Summary of findings table from the *Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis, 2016*.

Evidence profile 14

Date: 05/16/2014

PICO Question 7: Does the use of adjuvant corticosteroids in tuberculous pericarditis provide mortality and morbidity benefits?

Comparison: systemic corticosteroid therapy versus placebo.

Quality assessment							N of patients		Effect		Certainty in the Evidence	Importance
N of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Steroids	placebo	Relative (95% CI)	Absolute (95% CI)		
Death												
5 studies	randomized trials	not serious	very serious ¹	not serious	serious ²	none	142/897 (15.8%)	142/882 (16.1%)	RR 0.54 (0.23 to 1.26)	74 fewer per 1000 (from 42 more to 124 fewer)	 VERY LOW	CRITICAL
Adherence												
2 studies	randomized trials	serious ³	very serious ¹	serious ¹	not serious	none	744/888 (83.8%)	785/907 (86.5%)	RR 0.91 (0.75 to 1.12)	78 fewer per 1000 (from 104 more to 216 fewer)	 VERY LOW	IMPORTANT
Constrictive pericarditis												
3 studies	randomized trials	not serious	not serious	not serious	very serious ²	none	36/768 (4.7%)	56/747 (7.5%)	RR 0.72 (0.32 to 1.58)	21 fewer per 1000 (from 43 more to 51 fewer)	 LOW	IMPORTANT

MD – mean difference, RR – relative risk

Events:

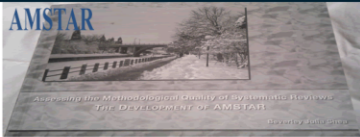
1. Inconsistent findings between studies. Death $I^2 = 70\%$; Adherence $I^2 = 89\%$.
2. The effects at the ends of the confidence interval would lead to different clinical decisions; in addition, the sample sizes are smaller than the optimal information size.
3. Different definitions of adherence were used by different studies.

Evidence Profile References:

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Appendix 3: AMSTAR assessment

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AMSTAR 2 Results

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Article Name: Interventions for treating tuberculous pericarditis (Cochrane Review). 2017

Interventions for treating tuberculous pericarditis (Cochrane Review). 2017 is a Low quality review

1. Did the research questions and inclusion criteria for the review include the components of PICO?	Yes Yes Yes Yes Yes
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	No
3. Did the review authors explain their selection of the study designs for inclusion in the review?	No
4. Did the review authors use a comprehensive literature search strategy?	Yes Yes Yes Yes Yes Yes Yes Yes
5. Did the review authors perform study selection in duplicate?	Yes Yes
6. Did the review authors perform data extraction in duplicate?	Yes Yes
7. Did the review authors provide a list of excluded studies and justify the exclusions?	Yes Yes Yes
8. Did the review authors describe the included studies in adequate detail?	Partial Yes Yes Yes Yes Yes Yes Yes Yes Yes
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	RCT Yes NRSI 0 Yes Yes Yes Yes
10. Did the review authors report on the sources of funding for the studies included in the review?	No
11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	RCT Yes NRSI Yes Yes
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	No
13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	Yes Yes
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	No
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	Yes Yes
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Yes Yes Yes

To cite this tool: Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017 Sep 21;358:j4008.

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