

# Evidence Update

Summary of a Cochrane Review

Tuberculosis Series

Do anti-tuberculosis drugs prevent tuberculosis infection in children with HIV?

Fewer children with HIV may get tuberculosis if treated with isoniazid

Researchers from the Cochrane Collaboration conducted a review into the effects of anti-tuberculosis drugs for preventing tuberculosis (TB) infection in HIV-infected children under 13 years. One randomised controlled trial (RCT) of 277 children was identified.

## Why should HIV-infected children be protected against tuberculosis?

HIV infection results in immunosuppression and increases the risk of malnutrition, which further limits the body's ability to fight infections. TB is the most common life-threatening infection among people living with HIV.

The cure rate for TB in HIV-infected children is significantly lower than in children without HIV. Consequently HIV-infected children require a longer treatment period with anti-tuberculosis drugs and therefore a higher pill burden and a greater risk for non-adherence, adverse effects and malnutrition.

## Which anti-tuberculosis drugs can be used to prevent TB in HIV-infected children?

Isoniazid is a drug that is widely used to treat active TB. Research showed that isoniazid is also effective in preventing active tuberculosis infection in adults with HIV and children without HIV. This Cochrane review evaluated whether isoniazid or any other TB drug or combination of drugs, can prevent active TB infection in children with HIV. This is an important public health question especially in countries with high TB and HIV prevalence.

## What does the research say?

One RCT (n=277) conducted in South Africa was included in the review. The RCT was considered to be at low risk of bias. The median length of follow-up was 5.7 months. Compared to placebo, isoniazid was associated with a reduced risk of developing TB (HR 0.28, 95% CI 0.10, 0.77) and of death (HR 0.46, 95% CI 0.22, 0.94) in HIV-infected children, most of whom were not taking antiretroviral therapy.

Few adverse events occurred in both the isoniazid and placebo groups, with a similar incidence across each cohort. There is no long term data on efficacy or adverse effects of the use of isoniazid for the prevention of tuberculosis in HIV-infected children.

## Are the review findings reliable?

The review's search was done in February 2008 and so while up to date when the review was conducted, the review results are now out of date. Two ongoing trials were also identified by the searches. The review was generally well conducted and at low risk of bias.

## Can the research findings be applied to my setting?

The trial was conducted in two tertiary healthcare centres in Cape Town, South Africa. The study included HIV-infected children older than 8 weeks and weighing more than 2.5 kg. Children with chronic diarrhoea were excluded. Isoniazid was given daily or three times per week in doses of 10 mg/kg. All children received cotrimoxazole.

### The effects of using isoniazid to prevent tuberculosis in HIV-infected children

This table provides more detail about what happens when HIV-infected children on cotrimoxazole are also treated with either isoniazid or placebo. These numbers are based on the results of the one included study. The quality of evidence is either ranked as high, moderate, low or very low. As only one relevant study was identified, the quality of the evidence was rated as low. Further research is very likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Outcome	Placebo	Isoniazid	What happens	Quality of evidence
How many children got infected with tuberculosis?	10 per 100	4 per 100	Fewer children with HIV may get tuberculosis with isoniazid	Low
How many children died?	16 per 100	8 per 100	Fewer children with HIV may die of tuberculosis with isoniazid	Low
How many children experienced adverse effects?	6 per 100	4 per 100	Between the groups, there might be little or no difference in the number of children with short term adverse effects	Low

#### More information

##### This summary is based on the following systematic review:

Gray DM, Young T, Cotton M, Zar H. Impact of tuberculosis preventive therapy on tuberculosis and mortality in HIV-infected children. *Cochrane Database of Systematic Reviews* 2009, Issue 1. Art. No.: CD006418. DOI: 10.1002/14651858.CD006418.pub2.

##### What is a systematic review?

A systematic review seeks to answer a well formulated and specific question by identifying, critically appraising, and summarising the results of all relevant trials, published and unpublished, according to pre-stated and transparent methods.

##### What is The Cochrane Collaboration?

The Cochrane Collaboration is an international network of more than 28,000 people from over 100 countries. The collaboration is one of the biggest producers of systematic reviews on the effects of healthcare interventions, and Cochrane Systematic Reviews are recognized internationally as the benchmark for high quality information. The *Cochrane Database of Systematic Reviews* is available from [www.thecochranelibrary.com](http://www.thecochranelibrary.com) and free for eligible countries.

##### How has the quality of evidence been assessed?

The quality of evidence has been assessed using methods developed by the GRADE working group (<http://www.gradeworkinggroup.com>). The GRADE system considers 'quality' to be a judgment of the extent to which we can be confident that the estimates of effect are correct. The level of 'quality' is judged on a 4-point scale. Evidence from randomised controlled studies is initially graded as HIGH and downgraded by one, two or three levels after full consideration of: the risk of bias of the studies, the directness (or applicability) of the evidence, and the consistency and precision of the results.

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

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

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

**Very low:** We are very uncertain about the estimate