Main results

7 studies were included; 5 were placebo controlled (4652 patients), and 3 compared isoniazid with rifampin plus pyrazinamide (1 placebo-controlled trial had an active therapy comparison) (2725 patients). When the placebo-controlled trials were pooled, fewer patients who received preventive therapy had active TB than did patients who received placebo (Table). The groups did not differ for mortality (Table). In patients with positive results on tuberculin skin testing (n = 2361), the incidence of TB and mortality were reduced (odds ratio [OR] 0.35, 95% CI 0.21 to 0.59 and OR 0.70, CI 0.50 to 0.98, respectively) among those who received preventive therapy. In patients with negative results (n = 2202), groups did not differ for TB or mortality (OR 0.82, CI 0.51 to 1.31 and OR 1.04, CI 0.86 to 1.28). Adverse drug reactions were seen in more patients who received preventive therapy than in those who received placebo (Table). 1 trial that assessed progression of HIV disease showed no difference between preventive therapy and placebo. 3 trials that compared isoniazid with rifampin plus pyrazinamide showed no difference for active TB or mortality.

ConClusIon

In patients with HIV and a positive result on tuberculin skin testing, preventive therapy reduces the development of active tuberculosis in the short to medium term.

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Preventive therapy vs placebo in patients with HIV who are at risk for tuberculosis (TB)*

<table>
<thead>
<tr>
<th>Outcomes at 15 to 33 mo</th>
<th>Weighted event rates</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preventive therapy</td>
<td>Placebo</td>
<td></td>
</tr>
<tr>
<td>Active TB</td>
<td>3.1%</td>
<td>5.3%</td>
<td>41% (21 to 56)</td>
</tr>
<tr>
<td>Mortality†</td>
<td>22%</td>
<td>21.6%</td>
<td>2% (−18 to 18)</td>
</tr>
<tr>
<td>Adverse drug reaction</td>
<td>4.3%</td>
<td>2.6%</td>
<td>79% (24 to 159)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.
†Random effects used in analysis.

Commentary

This important meta-analysis by Wilkinson of 7 published randomized controlled trials confirms that preventive TB therapy benefits adults with HIV. Only certain patients, however, showed benefit. 2 distinct HIV-patient groups were analyzed: those with a positive result on tuberculin skin testing and anergic patients “at high risk” for TB. The latter group is more heterogeneous than is the former group, and benefit could not be shown (given the period of prophylaxis and follow-up) for this diverse group.

Important ramifications exist for those with HIV and positive results on tuberculin skin testing. Clearly, isoniazid prophylaxis (6 to 12 mo) lowers the incidence of active TB and decreases mortality. It is therefore no longer debatable whether prophylaxis should be offered such patients. The only question is which therapy is most effective? These studies did not have the power to determine whether shorter combination therapy was superior to longer isoniazid prophylaxis. Furthermore, they were not designed to evaluate long-term (> than 3 y) benefits or to compare different durations of single- or multiple-drug regimens. Thus, we do not know whether lifelong prophylaxis is superior to limited-duration prophylaxis. But we do know that adverse drug reactions were more frequent with combination therapy than with monotherapy or placebo.

This meta-analysis showed that providing drug prophylaxis for 22 tuberculin-positive patients with HIV prevents 1 additional active case of TB at 15 to 33 months. This information must be translated into clinical practice.

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