Benefits of Screening for Latent Mycobacterium tuberculosis Infection

David N. Rose, MD

Background: The benefits of screening for latent Mycobacterium tuberculosis infection are unknown for most people, because screening has not been studied in clinical trials and preventive therapy has not been tested in all risk groups for whom it is recommended.

Method: A MEDLINE search was performed to determine tuberculosis risk. A Markov model was used to analyze tuberculin skin test screening and preventive therapy for 3-year-old and 30-year-old persons with positive test results. Outcome measures were lifetime and 10-year tuberculosis risk, including spread to others, life expectancy extension, and number needed to screen and number needed to treat to prevent 1 case and 1 death during 10 years.

Results: The benefits of screening and preventive therapy outweigh the risks for all groups tested, although the benefits range from large to small. The number needed to screen to prevent 1 case is 10 to 6888, and the number needed to treat is 2 to 179. Persons with human immunodeficiency virus infection, intravenous drug abuse, or end-stage renal disease treated with transplantation and children exposed to high-risk adults have the highest tuberculosis rates and the lowest number needed to screen and number needed to treat to prevent cases and deaths. The range of risks found in the literature for some risk groups, such as persons with silicosis, leukemia or lymphoma, end-stage renal disease treated with dialysis, or prolonged corticosteroid therapy, is wide and, as a result, the benefits of screening are uncertain.

Conclusions: The benefits of screening and preventive therapy vary widely, although the benefits outweigh the risks for all risk groups. The benefits are large for some risk groups and uncertain for others.

Arch Intern Med. 2000;160:1513-1521
The benefits of screening population groups with unknown tuberculin status and providing preventive therapy for persons with positive tuberculin skin test results were calculated with a Markov model for hypothetical 30-year-old persons. A wide range of groups was analyzed, from tuberculin reactors with the highest epidemiological or medical risks to the general population without risk factors. Children (3 years old) exposed to high-risk adults were also analyzed. The outcomes reflecting a population (public health) perspective were as follows: the 10-year risk of tuberculosis, including secondary and tertiary cases caused by transmission, and the number of persons with unknown tuberculin status needed to screen to identify 1 person with latent infection and to prevent 1 active tuberculosis case and 1 tuberculosis death during 10 years. The outcomes reflecting the individual patient perspective were as follows: lifetime and 10-year risk of tuberculosis; extension of life expectancy as a result of preventive therapy; and the number of persons with positive test results needed to treat to prevent 1 active case and 1 death during 10 years. The number needed to treat (NNT) is a useful measure of treatment outcome, defined as the reciprocal of the absolute risk reduction. The number needed to screen (NNS) is a similar measure that allows comparison of screening interventions.

MODEL

The Markov model begins with population groups that are screened. Screening refers to testing with the tuberculin skin test, 5 purified protein derivative tuberculin units by the Mantoux method, in persons without signs or symptoms of active tuberculosis, and interpretation of the test result by Centers for Disease Control and Prevention guidelines. Persons with positive results of tuberculin tests are offered preventive therapy. Those who take preventive therapy risk a fatal adverse event. All infected persons risk developing fatal or nonfatal tuberculosis, a risk that is decreased by preventive therapy. Whether or not tuberculosis occurs, persons risk death from any cause. In each subsequent year, tuberculin reactors risk developing tuberculosis and all persons risk death from any cause.

The risk of tuberculosis for population groups was assumed to be the product of the prevalence of infection, manifested as positive tuberculin skin test results, and the rate of active disease among those who are infected. The general population without risk factors for tuberculosis was assumed to have a low prevalence of positive tuberculin test results and a low rate of disease among infected persons. Each tuberculin reactor in this group was assumed to have acquired the infection in the remote past.

High-risk tuberculin reactors have either epidemiological or medical risk factors for tuberculosis. Populations with epidemiological risk factors were assumed to have an increased prevalence of infection and to have some tuberculin reactors who were recently infected. Recently infected tuberculin reactors have higher tuberculosis rates than remotely infected tuberculin reactors. Tuberculosis risk for tuberculin reactors with medical conditions was modeled by increasing the rate of active disease relative to that of low-risk tuberculin reactors. Long-term risk for each medical risk group also depends on life expectancy, which was modeled by assuming that annual mortality is the product of the general population mortality rate and the relative risk of mortality. Intravenous drug abusers were assumed to have both epidemiological and medical risk factors for tuberculosis.

Three preventive therapy regimens were studied: 6-month and 12-month regimens of isoniazid, 300 mg taken daily, and a 2-month regimen of rifampin, 600 mg, and pyrazinamide, 20 mg/kg of body weight, taken daily. Children were analyzed only with the isoniazid regimens.

Studies documenting risk factors for tuberculosis were identified through a search of MEDLINE and bibliographic references. The assumptions, shown in Table 1, are explained below. All rates were converted to transition probabilities by means of an exponential transformation.

LOW-RISK TUBERCULIN REACTORS

An individual tuberculin reactor’s risk of active tuberculosis over time is not fully known. As a result of the uncertainties, previous decision analyses for low-risk tuberculin reactor differed in the rates used, causing controversy. To accommodate a wide range of risks described in the literature, 2 sets of rates were used, based on the experiences of tuberculosis reactors in large clinical trials of BCG vaccination conducted in the United States and Great Britain. The trials, with a combined 60,000 persons in the control groups, used different methods for enrollment and follow-up. Based on the control groups’ midpoint interval rates, exponentially declining annual rates were calculated. These result in 1.8% and 2.2% lifetime risks of active tuberculosis. (Details of the method are available from the author.)

EPIDEMIOLOGICAL RISK FACTORS FOR TUBERCULOSIS

The prevalences of positive tuberculin skin test results in household contacts of active cases; foreign-born persons

RESULTS

BENEFITS OF SCREENING POPULATION GROUPS WITH UNKNOWN TUBERCULIN STATUS

Children exposed to high-risk adults have 9.1 to 92.8 tuberculosis cases per 1000 persons during 10 years,
from high-prevalence countries; prisoners and employees in high-prevalence prisons; certain low-income, ethnic minority populations; and intravenous drug abusers were taken from observational studies.\textsuperscript{23,26-46,85} Although one third to one half of tuberculosis cases in many cities arise from recent transmission,\textsuperscript{4,43} the proportion of tuberculin reactors who are recent converters is not known. The proportions used here, 10\% to 40\%, are estimates.

Tuberculosis rates of recently infected persons were taken from studies of household contacts of active cases\textsuperscript{23} and of health care workers.\textsuperscript{24} The rates for household contacts with positive tuberculin test results used in this analysis were those of persons with positive tests on first investigation or on testing within 12 months; some may have been remotely infected.\textsuperscript{23} The rates for recent tuberculin converters used in this analysis were those of persons who were tuberculin negative on first testing but tuberculin positive on subsequent testing.\textsuperscript{23,24} Rates in subsequent years were assumed to be the same as the rates of remotely infected tuberculin reactors. Three-year-old children with positive tuberculin test results were assumed to have the tuberculosis rates of recent converters, with the additional risk of an increased rate during adolescence and young adulthood.\textsuperscript{25}

MEDICAL RISK FACTORS FOR TUBERCULOSIS

Persons with medical risk factors, except for intravenous drug abusers,\textsuperscript{85} were assumed to have the same prevalence of positive skin test results as the general population. The relative risk of tuberculosis was taken from observational studies of HIV infection, end-stage renal disease treated with dialysis or transplantation, diabetes mellitus, weight loss of 10\% or greater below ideal body weight, silicosis, prolonged corticosteroid therapy, leukemia and lymphoma, gastrectomy, and intravenous drug abuse.\textsuperscript{*}

TRANSMISSION

The transmission rate of active tuberculosis is uncertain. Although contact investigations in the past 5 decades in this country identified 0.5 to 2.2 infected contacts per active case,\textsuperscript{34,95-97} a modeling study using national data calculated 3.5 new infections from each active case\textsuperscript{87} and a study of Holland from 1921 to 1938 calculated 13 new infections from each active case.\textsuperscript{88} This analysis used the following assumptions to calculate the number of new infections, cases, and deaths during 10 years among contacts of active cases and the next generation of their contacts: each active case results in 3.5 to 13 infections in others; newly infected contacts have the tuberculosis risks of recent converters; half of the infected persons are identified and treated with preventive therapy; and half of the infected persons are children.

MORTALITY

Mortality from active tuberculosis was assumed to be an age-specific rate that is a multiple of general population mortality.\textsuperscript{98} The relative risk, 8.3, was taken from a recent study in the Netherlands.\textsuperscript{98} The mortality rate in the year of active disease, therefore, was assumed to be the product of the general population mortality rate, the relative risk of mortality for the medical condition, and the relative risk of tuberculosis mortality. For example, a 40-year-old person with a chronic disease that doubles the mortality rate who then develops active tuberculosis has a probability of dying that is 16.6 times the general population mortality for persons that age.

BENEFITS AND RISKS OF PREVENTIVE THERAPY

Effectiveness of the isoniazid regimens was taken from a large international clinical trial.\textsuperscript{89} Tuberculin reactors with fibrotic pulmonary lesions were assigned to 12, 24, or 52 weeks of isoniazid therapy or placebo. The tuberculosis rate was reduced by 75\% and 65\% in the 52-week and 24-week isoniazid groups, respectively. Reductions were even greater among the subjects who adhered to the regimens. The 2-month rifampin and pyrazinamide regimen was studied in an international trial of tuberculin reactors with HIV infection.\textsuperscript{14} The tuberculosis rate was not significantly different with this regimen than with 12 months of isoniazid therapy. The rate of fatal isoniazid-associated hepatitis was taken from reviews of adverse events of monitored preventive therapy.\textsuperscript{90,91} Nonfatal adverse reactions to preventive therapy were not considered in this analysis.

CALCULATIONS

Outcomes were calculated with a model written on Microsoft Excel (Microsoft Corp, Redmond, Wash). Each risk group was studied with the 2 tuberculosis risk models, all combinations of the extremes of pertinent risk ranges (Table 1), and the 3 preventive therapy regimens. Children were limited to the isoniazid regimens. Each risk group, therefore, had a series of calculations for each outcome measure. The results are reported as ranges of outcomes.

All persons screened with tuberculin skin tests were assumed to initiate preventive therapy if found to have positive test results. This and other assumptions were tested in a sensitivity analysis.

\*References 47-49, 51-60, 62-64, 67-72, 75-83.

which cause 0.73 to 315.1 tuberculosis cases in others (Table 2). The NNS to identify 1 person with latent \textit{M tuberculosis} infection is 2 to 4, to prevent 1 tuberculosis case it is 10 to 126, and to prevent 1 tuberculosis death it is 2675 to 39743, assuming all persons found to have positive tuberculin test results initiate preventive therapy. Other epidemiological risk groups have fewer cases per cohort and higher NNS to prevent tuberculosis cases. The tuberculosis case-fatality rate for children is low, and therefore the NNS to prevent 1 death is high. Among the medical risk factors for tuberculosis, persons with end-stage renal disease treated with transplantation and persons with HIV infection have the highest numbers of cases per cohort and the lowest NNS to prevent tuberculosis cases and deaths. Intravenous drug abusers have a wide range of cases, including very high numbers, and low NNS to identify infected persons and to prevent cases and deaths. The general population with no risk factors for tuberculosis has a relatively low number of cases per cohort and high NNS to prevent cases and deaths.
Benefits of Preventive Therapy for Persons with Positive Tuberculin Skin Test Results

Tuberculin-positive children exposed to high-risk adults have a 5.0% to 20.1% lifetime risk of developing active tuberculosis and have 37 to 186 cases per 1000 persons during 10 years (Table 3). Preventive therapy extends life expectancy by 0.1 to 0.5 month. The NNT to prevent 1 tuberculosis case during 10 years is 7 to 42, and to prevent 1 tuberculosis death it is 1930 to 14010. Persons with recent conversion from tuberculin test negative to tuberculin test positive have slightly lower lifetime risks but similar 10-year risks. Household contacts of active cases, ethnic minority persons, foreign-born persons, and residents and employees of high-prevalence prisons have moderate to high tuberculosis risks and benefits from preventive therapy. Tuberculin reactors with no additional risk factors have small tuberculosis risks and small or moderate preventive therapy benefits.

### Table 1. Assumptions Used in the Analysis*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk tuberculin reactors (remotely infected), TB rate, per 1000 persons per y</td>
<td>1.12 × e^{-0.1832n} × 3.84 × e^{-0.0569n–3.84}</td>
</tr>
<tr>
<td>General population, no risk factors for TB, prevalence of infection, %†</td>
<td>Year 1, 19.6; years 2-4, 3.1; years 5-7, 2.4; years 8-10, 0.4 – year 1, 19022,24</td>
</tr>
<tr>
<td>Recent tuberculin converters (recently infected), TB rate, per 1000 persons per y</td>
<td>Age 14, 0.8; age 19 y, 1.8; age 24 y, 0.5†</td>
</tr>
<tr>
<td>Adolescence and young adulthood, TB rate, per 1000 persons per y</td>
<td>25–5012,26–34</td>
</tr>
<tr>
<td>Household contacts of active TB cases, prevalence of infection, %†</td>
<td>Year 1, 11.5; years 2-4, 2.9; years 5-7, 2.0; years 8-10, 0.7†</td>
</tr>
<tr>
<td>Household contacts with positive tuberculin skin tests, TB rate, per 1000 persons per y</td>
<td>27–7013,26</td>
</tr>
<tr>
<td>Certain low-income, ethnic minority populations, prevalence of infection, %†</td>
<td>19–5314,43</td>
</tr>
<tr>
<td>Prisoners and employees in high-prevalence prisons, prevalence of infection, %†</td>
<td>10–2515,46</td>
</tr>
<tr>
<td>Foreign-born persons, prisoners and prison employees, certain low-income, ethnic minority populations, intravenous drug abusers, proportion of tuberculin reactors with recent conversion, %</td>
<td>10–4016</td>
</tr>
<tr>
<td>HIV infection, RR of TB§</td>
<td>9.7–170.312,43</td>
</tr>
<tr>
<td>RR of mortality without TB</td>
<td>36–4517,20</td>
</tr>
<tr>
<td>End-stage renal disease, dialysis, RR of TB§</td>
<td>1.6–1618,58</td>
</tr>
<tr>
<td>Transplantation, RR of TB§</td>
<td>36.6–5019,60</td>
</tr>
<tr>
<td>All renal replacement therapy, RR of mortality without TB</td>
<td>19110,61</td>
</tr>
<tr>
<td>Diabetes mellitus, RR of TB§</td>
<td>2.0–4.111,44</td>
</tr>
<tr>
<td>RR of mortality without TB</td>
<td>1.2–3.412,45</td>
</tr>
<tr>
<td>Weight loss ≥10% below ideal body weight, RR of TB§</td>
<td>1.8–2.116,58</td>
</tr>
<tr>
<td>Silicosis, RR of TB§</td>
<td>1.5–3.218,59</td>
</tr>
<tr>
<td>RR of mortality without TB</td>
<td>1.4–3.019,54</td>
</tr>
<tr>
<td>Prolonged corticosteroid therapy, RR of TB§</td>
<td>1.0–5.115,77</td>
</tr>
<tr>
<td>Leukemia, lymphoma, RR of TB§</td>
<td>1.0–3516,79</td>
</tr>
<tr>
<td>RR of mortality without TB</td>
<td>2.0–5.01</td>
</tr>
<tr>
<td>Gastrectomy, RR of TB§</td>
<td>5.0–6.813,81</td>
</tr>
<tr>
<td>Intravenous drug abuse, RR of TB§</td>
<td>3.2–19.218,82</td>
</tr>
<tr>
<td>RR of mortality without TB</td>
<td>8.6–17.814</td>
</tr>
<tr>
<td>Prevalence of infection, %†</td>
<td>10–2015,60</td>
</tr>
<tr>
<td>Transmission of infection per active case, No.</td>
<td>3.2–1316,67</td>
</tr>
<tr>
<td>TB mortality, relative risk, relative to general population age-specific mortality rate</td>
<td>8.318,88</td>
</tr>
<tr>
<td>Preventive therapy effectiveness, %</td>
<td></td>
</tr>
<tr>
<td>Isoniazid 12-mo regimen</td>
<td>7519</td>
</tr>
<tr>
<td>Isoniazid 6-mo regimen</td>
<td>6518</td>
</tr>
<tr>
<td>Rifampin and pyrazinamide 2-mo regimen</td>
<td>7517</td>
</tr>
<tr>
<td>Preventive therapy adverse event rates, deaths per 1000 persons</td>
<td></td>
</tr>
<tr>
<td>Isoniazid regimens</td>
<td>0.0226,91</td>
</tr>
<tr>
<td>Rifampin and pyrazinamide regimens</td>
<td>017,68</td>
</tr>
</tbody>
</table>

*Assumptions are presented as ranges, except in those cases of singular assumptions. TB indicates tuberculosis; e, base of the natural logarithm; n, number of years after age 3 or 30 years; HIV, human immunodeficiency virus; and RR, rate ratio.†Infections manifested by positive tuberculin skin test results; all general population infections acquired remotely, all recent converters acquired recently, all other populations have a mixture of remote and recent infections.‡Estimate.§Ratio of TB rate among tuberculin reactors in risk group to rate among tuberculin reactors not in risk group.‖Calculated from life expectancy or survival.
SENSITIVITY ANALYSIS

For population groups, the variables that most influence outcomes are the prevalence of positive tuberculin tests, the proportion of tuberculin reactors who initiate preventive therapy, the rate at which tuberculin reactors develop active tuberculosis, and the effectiveness of preventive therapy. Variations in the proportion of tuberculin reactors who are recent converters have moderate effects on outcomes, and variations of the number of secondary and tertiary infections caused by each active case have smaller effects on outcomes.

For persons with positive tuberculin test results who take preventive therapy, the variables that most influence outcomes are the rate of developing active tuberculosis and the effectiveness of preventive therapy. Varia-
tions in life expectancy have relatively small effects on tuberculosis rates but larger effects on the 10-year tuberculosis mortality rate. Variations in the rate of adverse events caused by preventive therapy have a minimal effect on outcomes.

The 3 preventive therapy regimens result in similar outcomes for all but the highest-risk groups, such as persons with HIV infection or end-stage renal disease. For example, tuberculin reactors with diabetes have, on average, 0.7-month life expectancy extension with the 2-month rifampin and pyrazinamide regimen and 0.6 month with the 6-month isoniazid regimen. In contrast, tuberculin reactors with HIV infection have, on average, 22.5-month life expectancy extension with the 2-month rifampin and pyrazinamide regimen and 18.2 months with the 6-month isoniazid regimen.

The isoniazid fatal toxic effect rate must be greater than 0.023% for the risks of the 6-month isoniazid regimen to outweigh the benefits for tuberculin reactors with no additional risk factors, 11 times the base-case rate. The threshold rate for persons with end-stage renal disease treated with dialysis is 1.7%, and for persons with HIV infection it is 15.2%.

The analysis was performed for 55-year-old tuberculin reactors with the additional assumption that the isoniazid-containing regimens have a fatal toxic effect rate of 0.001%, 5 times the base-case rate. The lifetime risk of tuberculosis is less but the tuberculosis case-fatality rate is greater for these persons than for 30-year-old tuberculin reactors. The benefits of preventive therapy are not very different for the 2 age groups. Foreign-born 55-year-old tuberculin reactors have a 1.4% to 18.6% lifetime risk of tuberculosis and have 8 to 184 cases per 1000 persons during 10 years; preventive therapy extends life expectancy by 0.3 to 2.7 months; the NNT to prevent 1 case is 7 to 184, and to prevent 1 death it is 126 to 2228, fewer than for 30-year-old persons.

**COMMENT**

Although all analyzed groups with unknown tuberculin status benefit from screening and all persons with positive tuberculin tests benefit from preventive therapy, the benefits range from large to small. Persons with HIV infection, intravenous drug abuse, or end-stage renal disease treated with transplantation have the greatest benefits, as indicated by all outcome measures of the analysis. Consistent with the current recommendation not to screen the general population without risk factors for tuberculosis,¹ the benefits of screening and preventive therapy for this group are small. For other risk groups, the magnitude of benefit depends on the outcome measure used. Children exposed to high-risk adults have small benefits by some measures but large benefits by other measures. Furthermore, the range of risks found in the literature for some risk groups is wide, and as a result the benefits of screening are uncertain. Some persons with epidemiological risk factors for having latent M tuberculosis infection, such as ethnic minorities, foreign born, or prisoners, may benefit greatly from screening if the risk of active disease in the years just after infection is very high, as shown in some studies²³ but not in others.²⁵ Persons with silicosis, leukemia or lymphoma, end-stage renal disease treated with dialysis, or prolonged corticosteroid therapy may benefit greatly from preventive therapy if the relative risk of developing disease during their lifetimes is high, as shown in some studies²¹,²⁷,⁶⁹,⁷⁰,⁷⁷,⁷⁹ but not in others.⁸⁰,⁷¹,⁷²,⁷⁵,⁷⁶,⁷⁸

This analysis also leads to 4 additional significant conclusions about screening and preventive therapy. First, the benefits of screening are reduced if persons with positive tests do not initiate preventive therapy. Screening efficiency therefore increases if it is limited to persons who intend to initiate preventive therapy if found to be tuberculin positive. Second, for most tuberculin reactors, the choice of preventive therapy regimen makes little difference in the extent of benefit. For the highest risk groups, however, the smaller benefit of the 6-month isoniazid regimen may be clinically important. Third, although the benefits of preventive therapy are small for many tuberculin reactors, their isoniazid fatal toxic effect rate is far smaller. For low-risk tuberculin reactors, the isoniazid fatal toxic effect rate must be 11 times greater than the observed rate⁰⁰.⁹⁰ to justify not using isoniazid, and the threshold toxic effect rate for higher-risk tuberculin reactors is even greater. Fourth, the benefits of screening and preventive therapy are not substantially different for 55-year-old persons than for 30-year-old persons, even if the isoniazid toxic effect rate is higher for older persons.

To assess the significance of tuberculosis preventive therapy's benefits, they should be compared with those of other accepted prevention interventions. Wright and Weinstein⁹⁹ tabulated the gains in life expectancy from medical interventions and found that preventive therapies resulted in gains ranging from less than 1 month to 5 years or more. For populations of average risk, they asserted that gains of 1 month "can be considered large." For populations of high risk, they found that many preventive therapies result in gains of 1 year or more. Rembold¹⁰ developed another measure to prioritize screening strategies, the NNS to prevent 1 death. He calculated that the NNS to prevent 1 death in 5 years was 418 for dyslipidemia, 274 to 1307 for hypertension, 1374 for colon cancer, and 2451 for breast cancer among women aged 50 to 59 years. By these measures, the benefits of latent M tuberculosis screening and preventive therapy for most risk groups would be considered small.

However, better measures of the worth of tuberculosis screening and preventive therapy are the NNS and the NNT to prevent 1 case of disease. Because tuberculosis has a low case-fatality rate for most persons, the benefits of screening and preventive therapy are mostly preventing illness, not preventing deaths or extending life expectancy. The NNT incorporates both baseline risk without therapy and risk reduction with therapy and is lower in high-risk than average-risk populations.¹⁸,¹⁰ For example, in clinical trials of statin therapy for hypercholesterolemia, 11 subjects with cardiovascular disease and 42 subjects without cardiovascular disease and similar lipid levels needed to be treated to prevent 1 myocardial
infarction event. In a clinical trial of alendronate sodium therapy for postmenopausal women with low bone mineral density and existing vertebral fractures, 10 subjects with bone mineral density less than 0.59 g/cm² and 30 subjects with bone mineral density of 0.59 g/cm² or higher needed to be treated for 5 years to prevent 1 new clinical fracture.

In hypertension clinical trials, only 18 elderly subjects but 2 to 4 times as many younger subjects needed to be treated to prevent 1 cardiovascular event during 5 years. By these measures, tuberculosis screening and preventive therapy yield moderate or large benefits for most risk groups. The NNT, however, does not fully describe the importance of a treatment effect. Preventive therapy recommendations involve judgments that incorporate not only the NNT, or other measures of the magnitude of treatment effect, but also the seriousness of the disease being prevented, the difficulty of treating the disease if it occurs, and the adverse effects of prophylaxis.

This analysis has several important limitations. Most important, assumptions were based on epidemiological studies of variable quality. Many studies were case series with rate ratios calculated by comparison with historical, general-population tuberculosis rates. Few studies controlled for tuberculin status. Furthermore, tuberculosis risks for some medical conditions, such as HIV infection and diabetes mellitus, may be smaller with current standard treatments. Additionally, the analysis did not factor in the potential effect of drug resistance, which decreases the effectiveness of preventive therapy. Moreover, preventive therapy may result in different effectiveness for some risk groups than for others. Because of these limitations, the benefits found in this analysis must be interpreted as estimates.

The study also did not address nonfatal adverse reactions to preventive therapy, quality of life, or costs. One way to evaluate the worth of an intervention is to compare the NNT with the number needed to harm. Since isoniazid-associated clinical hepatitis occurs in 0.1% to 0.5% of preventive therapy courses, the number needed to harm is 200 to 1000. Less information is available on the rate of adverse reactions to 2 months of rifampin and pyrazinamide therapy. One study of HIV-infected patients reported no significant adverse reactions and another reported 12.5% adverse events, although the regimen was described as safe.

In conclusion, the population groups that should have the highest priority for tuberculosis screening efforts are those that can expect substantial benefits: persons with HIV infection or end-stage renal disease treated with transplantation, intravenous drug abusers, children exposed to high-risk adults, and persons likely to have recent conversion of the tuberculin test. Other population groups studied have smaller benefits from screening and preventive therapy, although the benefits are likely to outweigh the risks, even for the lowest-risk groups. Targeting the highest-risk subgroups and limiting screening to persons who are candidates for preventive therapy may increase the efficiency and benefits. Individual decision making may be enhanced by comparing the NNS and NNT with the number needed to harm.

REFERENCES