Original Articles

Isoniazid preventive therapy programmes for healthcare workers in India: Translating evidence into policy

RISHI RAJ, HARI PRASAD, BIKAS K. ARYA, SANGEETA DAS BHATTACHARYA

ABSTRACT

Background. Occupational tuberculosis (TB) among healthcare workers (HCWs) is an important public health issue, especially in India where HCWs are exposed to a high burden of TB and infrastructural infection control procedures are inadequate. We examined the need for implementing isoniazid preventive therapy (IPT) programmes to protect Indian HCWs from occupational TB.

Methods. Bardach's 8-fold path was followed to analyse and formulate the policy for introducing IPT programmes for HCWs in India. The results of surveillance with tuberculin skin testing (TST) and treatment of latent TB infection with isoniazid (INH) for HCWs belonging to two different age groups ($\leq$30 years and >30 years) were compared with each other and with the alternative of maintaining status quo, i.e. no surveillance and no therapy, under various parameters such as the lifetime risks of active TB, deaths due to TB, benefit–risk ratios, cost-savings to the health system and relative risk reductions.

Results. The lifetime risk of TB was found to be higher among HCWs in the age group of $\leq$30 years. IPT for HCWs reduced the lifetime risks of TB and death due to TB in both age groups, with better results in the age group of $\leq$30 years. The relative lifetime risk reduction of active TB was 24.04% for the age group of $\leq$30 years and 19.92% for the age group of >30 years. The relative lifetime risk reduction of death due to TB by administration of IPT was from 13.96% to 19.62% in the two age groups. The benefit–risk ratio of IPT was 11.24 for the age group of $\leq$30 years and 2.88 for the age group of >30 years. IPT was associated with an approximate savings of ₹4000–8000 for each case prevented.

Conclusion. TB is a major occupational hazard for Indian HCWs. The inclusion of IPT programmes in the national policy to combat TB, along with infrastructural infection control measures, can contribute to reduction in workplace TB. IPT programmes for HCWs in the younger age group have better results in terms of prevention of active TB, TB-related mortality and INH-induced hepatitis as compared to the older age group. There is an urgent need for a mechanism of targeted testing and treatment of latent TB infection to minimize the risk of occupational exposure for TB among HCWs in all age groups.

Natl Med J India 2011;24:201–7

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INTRODUCTION

Globally, an estimated 2.2 billion people, i.e. one-third of the world's population, are infected with *Mycobacterium tuberculosis*, and one person is newly infected every second.[1–3] Of the 9.4 million new cases of tuberculosis (TB) reported in 2008, nearly 80% were from 22 high burden countries (as identified by WHO). India accounts for nearly one-fifth of the global incidence of TB with approximately 2 million people developing TB each year. The reported prevalence was 283 per 100 000 in 2008.[4] This large burden of TB among the general population puts healthcare workers (HCWs) in India at an increased risk of contracting the infection through occupational exposure.

The annual incidence of TB in HCWs is much higher in many low- and middle-income (LAMI) countries (69–5780 per 100 000), than in high income countries (HICs) (2–55 per 100 000).[5] The average prevalence of latent TB in HCWs was 63% in LAMI and 24% in HICs.[6] Studies from high burden countries have shown that the risks of latent and active TB among HCWs in high burden countries are higher than those among the general population.[5–8] The annual risk of TB infection (ARI) in HCWs reported from a medical college in India was 4.1%, which was significantly higher than the ARI rate of 1.2% for the general population living in that geographical area.[9,10]

Nosocomial TB in India compromises the health of HCWs, burdens the limited human and financial resources of the healthcare system, and puts additional strain on the economy. Occupational transmission of TB from HCWs to patients can further aggravate the problem.[11] With the emergence of extensively drug-resistant TB and the HIV epidemic in India, there are increased concerns about how to protect HCWs from TB.[12]

Isoniazid (INH) preventive therapy (IPT) is recognized as an important component of TB infection control activities. IPT is also one of the 'I's in WHOs 'Three I's for HIV/TB' (the other two being Infection control for TB and Intensified TB case finding).[13] INH therapy of latent TB infection has been shown to reduce the incidence of active TB by >60%, where adherence could be guaranteed.[14] Successful implementation of infection control and

IPT programmes in health systems have led to a dramatic decline in occupational TB exposure and disease.[15–17] However, there has been little by way of implementation of IPT in India.[9,12] We aimed to translate the best research evidence into policy for IPT programmes for HCWs in the Indian setting.

METHODS

We used Eugene Bardach's 8-fold path, an effective step-by-step method of policy analysis to analyse and formulate the policy of introducing IPT programmes for HCWs in India. This model includes the following steps:

1. Define the problem (understand the problem)
2. Assemble the evidence (search for evidence)
3. Construct the alternatives (identify the different policy alternative)
4. Select the criteria (build up a 'criteria' matrix)
5. Project the outcomes (estimate the impact of various policy alternative)
6. Confront the trade-offs (apply evaluative criteria)
7. Decide (weigh the outcomes)
8. Tell your story (advocate the chosen policy).[18,19]

RESULTS

Step 1: Defining the problem

HCWs in India face a high risk of occupational TB exposure: 41% of Indian HCWs have a positive TST as compared to 30% in the general population.[20,21] A recent study from a tertiary medical school hospital in southern India showed a 50% prevalence of latent TB infection among young nursing trainees.[22] The incidence of active TB in Indian HCWs was 208–1260/100 000 in 2004 compared to 168/100 000 in the general population in the same year (WHO Global Tuberculosis Database).[7,8,23] India thus needs to lay down and implement a clear policy to check workplace TB in the healthcare sector.

Step 2: Assembling the evidence

We specifically addressed the following question: Does IPT decrease the incidence of active TB in HCWs with latent TB? Two studies on TST-incorporated TB control programmes, which included IPT as one component, showed a reduction in TST conversion rate among HCWs from 28% to 0% and 9.3% to 2.2%.[24,25] Also, the annual rate of TST conversion was lower in hospitals with TST-incorporated TB control programmes than the national average (0.6% *v.* 1.25%).[26] A Cochrane systematic review for the efficacy of IPT in reducing the incidence of active TB in patients with latent TB,which included 11 high quality randomized control trials of IPT involving 73 375 patients, showed that treatment of latent TB infection with INH is effective in prevention of TB in 60% cases and 1 person is saved from active TB when 35 people completed a 6-month course of INH.[14] The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology developed by the GRADE Working Group was applied to evaluate the robustness of the evidence generated by the Cochrane systematic review (see box).

GRADE: Working Group grades of evidence[27]

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

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

Low quality: 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 quality: We are very uncertain about the estimate.

The GRADE system is a widely adopted systematic approach with considerable flexibility. In cases where consideration of important factors relating to a specific clinical question is needed, the GRADE system allows formulation and modification of recommendations beyond the scope of evidence so that strong recommendations may be made on the basis of low quality evidence.[27] The overall quality of evidence in our case is moderate (Table I).

Step 3: Constructing the alternatives

The density of healthcare personnel in India is 20 per 10 000 population. These data are based on Census estimates of self-reported occupations, which include allopathic and ayurveda, unani, siddha and homoeopathy (AYUSH) doctors, nurses, midwifes, dentists, pharmacists, traditional medical practitioners, faith healers, medical assistants and others.[28] However, these data do not include medical and nursing students, who are equally at high risk of getting infected by *M. tuberculosis*.[7] The total number of students enrolled in medical education in India in 2005–06 was 348 485.[29] For the purposes of our study, we estimated the total HCW population in India to be approximately 2.66 million. This includes students in healthcare disciplines as well.

No data for stratification of the total HCWs (including students) on the basis of age are currently available for India. Hence, we extrapolated the data from a study conducted to estimate the

TABLE I. GRADE evaluation

Outcome	No. of patients		Relative effect (95% CI)	Quality of evidence (GRADE)	Importance
	Isoniazid	Placebo			
Active tuberculosis	239/40 262	557/33 113	Risk ratio 0.4 (0.31–0.52)	Moderate[1]	Critical
Tuberculosis deaths	3/16 318	10/9396	Risk ratio 0.29 (0.07–1.18)	Moderate [2,3]	Important
Hepatitis	77/13 884	7/6990	–	Moderate [4–6]	Important

1 Serious indirectness: Only one of the 11 trials was conducted in India. No trials assessed outcomes specifically in HCWs.
2 Serious indirectness: None of the trials were from India or other developing nations. No trials assessed outcomes specifically in HCWs.
3 The event rates for death outcomes are very low. The 95% confidence interval (CI) around relative effects is very wide, but the lower limit of 95% CIs indicates high appreciable benefit of INH over placebo. The quality of evidence for imprecision is therefore not downgraded.
4 Inconsistency assessment is not applicable since data are of only one trial.
5 Serious indirectness: Only one trial conducted in 7 European countries reported this outcome; extrapolation of this result to other countries is likely to be unreliable. No trials assessed outcomes specifically in HCWs.
6 No imprecision: Both limits of the 95% CI imply appreciable harm of INH over placebo.

prevalence of latent TB infection in HCWs in a rural medical school hospital of India,[20] which had 76% of HCWs in the age group of ≤30 years and 24% in the age group of >30 years. The rationale behind this classification was that studies from tertiary care hospitals in Vellore and Chandigarh have shown that the age group of ≤30 years is at high risk for occupational TB.[7,8] This group comprises mainly young HCWs including medical students, interns, residents and nursing students.

We considered 3 alternatives to identify the most practical alternative for IPT programmes:

Alternative 1: Active surveillance of healthcare workers ≤30 years of age. All HCWs in the age group of ≤30 years will be screened with TST for latent TB at entry into the workforce. If found positive, a chest X-ray will be done to rule out active TB. TST sceening will be repeated every 2 years, and cases of positive findings will be treated with INH for 6 months.

Alternative 2: Active surveillance of HCWs >30 years of age. All HCWs in the age group of >30 years will be screened with TST for latent TB. If found positive, a chest X-ray will be done to rule out active TB. TST screening will be repeated every 2 years, and cases of positive findings will be treated with INH for 6 months.

Alternative 3: Status quo. No TST will be done and no IPT given for any age group.

We considered the cut-off for TST positivity to be ≥10 mm induration. In people with normal immune function, TST conversion is defined as baseline TST of <10 mm and follow up TST of ≥10 mm, with an increment (absolute increase) of 10 mm.[9]

Step 4: Selecting the criteria

Should preventive treatment with INH be given to HCWs infected with *M. tuberculosis* to prevent reactivation of latent TB? To come to a decision, we applied the following evaluation criteria and their impact on our various policy alternative:

1. Estimated lifetime risk of active TB per 1000 HCWs
2. Estimated lifetime risk of death due to TB per 1000 HCWs
3. Benefit–risk ratio (ratio of the estimated number of cases of TB prevented to the estimated number of hepatitis cases incurred)
4. Estimated total cost of IPT per case of active TB prevented
5. Estimated net savings by IPT per case of active TB prevented in HCWs.

Number needed to treat (NNT). Using a Markovian model of cost-effectiveness analysis of IPT programmes, we derived the NNT to prevent 1 case of TB during the course of a HCWs lifetime, and the NNT to prevent 1 death due to TB for the Indian HCW population with an average TST positivity of 41%.[20,30] In India, exogenous re-infection plays a major role in the development of active TB disease. Our model is therefore based on estimates of the annual risk of latent TB infection (ARI) to provide a quantitative estimate of the relative contribution of exogenous re-infection to the burden of TB. ARI is estimated to be 4.1% for HCWs in India.[5]

A mathematical relation was derived to depict an association between TST positivity and ARI adjusted NNT values by fitting an appropriate curve to the available data using MATLAB® software. A curve based on 'power function' was found to be suitable in terms of goodness of fit with a mean r-squared value approaching 1 (0.99). By extrapolation of the curve corresponding to the ARI value for Indian HCWs (i.e. 4.1%), we obtained the NNT to prevent 1 case of active TB and 1 death from TB for different Indian HCW population age groups (Table II, Figs 1 and 2). The NNT values for the Indian HCW population calculated by our model are considerably greater than that reported for HCWs in the USA for corresponding TST positivity rates, indirectly indicating relatively lower efficacy of IPT in India owing to re-exposures and re-infection. A comparative analysis of NNT values for preventing a case of TB, for preventing 1 TB-related death, TST positivity rates and effectiveness of IPT showed a relatively lower efficacy of 55.6% for HCWs in India. The overall treatment efficacy of IPT can therefore be enhanced by providing wards with good ventilation, especially for multiple-bed hospital wards, separation or segregation of smear-positive TB patients and multidrug resistant (MDR)-TB suspects (TB relapses, failures, contact persons of MDR-TB patients, treatment interruptions), and the use of personal protection measures.

Lifetime risks. The lifetime risks of developing active TB and TB-related deaths are not the same among different age groups. Springett found a comparatively larger mortality due to TB in young adults, and the age generation curves appear to be like a large inverted 'U' with the highest incidence in young adults, 20–30 years of age.[31] Comstock observed that the risk of TB in a birth cohort decreases over time.[32] It has been assumed that the lifetime risk of reactivation TB is 10% in late adolescents and decreases at a rate of 10% per decade.[33] The average lifetime risks of reactivation of TB for an age cohort are calculated from equation 1, and the results for the different age groups are given in Table II.

TABLE II. Average lifetime risk of reactivation tuberculosis (TB) in different age groups

Age group (years)	TST positivity (%)	Average lifetime risk reactivation TB (%)	Estimated NNT to prevent 1 case	Estimated NNT to prevent 1 death
≤30	32	9.59	30	465
>30	70	7.68	25	417
Total	41	8.21	28	449

TST tuberculin skin test NNT number needed to treat

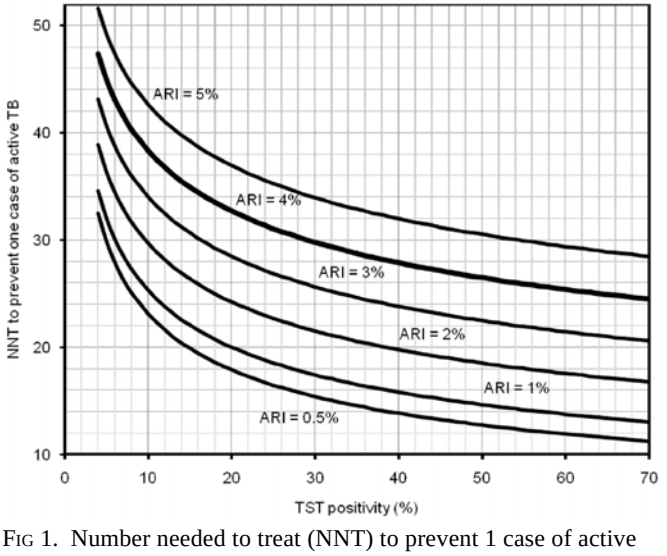

FIG 1. Number needed to treat (NNT) to prevent 1 case of active tuberculosis (TB) compared with tuberculin skin test (TST) positivity. Based on the available literature the annual risk of infection (ARI) for healthcare workers in India is 4.1%

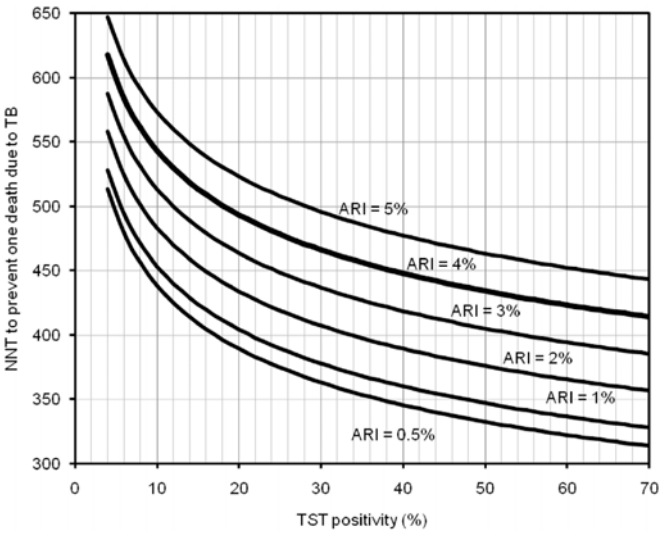

FIG 2. Number needed to treat (NNT) to prevent 1 death due to tuberculosis (TB) compared with tuberculin skin test (TST) positivity. Based on the available literature the annual risk of infection (ARI) for healthcare workers in India is 4.1%

Equation 1. Average lifetime risk of reactivation TB (%)

$$= \frac{\int_{\text{Lower age limit}}^{\text{Upper age limit}} 10\,(0.9)^{\frac{t-20}{10}}\,dt}{\int_{\text{Lower age limit}}^{\text{Upper age limit}} dt}$$

Studies have shown that 7.8% of people with workplace TB have a lifetime risk of death due to TB.[34] However, HIV infection and drug resistance may increase the risk of death. Equations 2 and 3 below are used to calculate the estimated lifetime risk of active TB and death due to TB, respectively, in HCWs.

Equation 2. Estimated lifetime risk of active TB per 1000 HCWs

$$= \frac{\text{TST positive (\%)} \times \text{Total number of HCWs} \times \text{Life-time risk of reactivation TB (\%)}}{\text{Total HCW population}} \times 1000$$

Equation 3. Estimated lifetime risk of death due to TB per 1000 HCWs

$$= \frac{\text{TST positive (\%)} \times \text{Total number of HCWs} \times \text{Life-time risk of death due to TB (\%)}}{\text{Total HCW population}} \times 1000$$

The estimated number of active cases of TB and deaths due to TB prevented in each alternative is estimated using NNT, prevalence rate of TST positivity and number of HCWs in each category (Equations 4 and 5 below).

Equation 4. Estimated number of active TB cases prevented by IPT for the given group

$$= \frac{\text{TST positive (\%)} \times \text{Number of HCWs in the given group}}{\text{NNT to prevent 1 case of active TB}}$$

Equation 5. Estimated number of TB-related deaths prevented by IPT for the given group

$$= \frac{\text{TST positive (\%)} \times \text{Number of HCWs in the given group}}{\text{NNT to prevent 1 TB related death}}$$

INH-induced hepatitis. INH-induced hepatitis is an important adverse effect of IPT that ranges in severity from asymptomatic elevation of serum transaminases to hepatic failure and death. The morbidity due to drug-induced hepatotoxicity and the consequent interruption in IPT can have deleterious consequences. This concern of hepatotoxicity was the major reason behind choosing 6 months of IPT over 9 or 12 months therapy. In a large eastern European clinical trial, 33 of 6919 persons in the 6 months IPT group developed acute hepatitis compared with 7 of 6990 persons in the control group. However, in this study serum transaminase levels were not measured regularly nor was INH discontinued when signs of hepatotoxicity appeared.[14,35] The number needed to harm (NNH) to cause 1 case of hepatitis with 6 months of IPT calculated from the results of the above trial was 265, i.e. for every 265 patients treated with IPT, 1 adverse hepatitis event will occur beyond those that would have happened under control. In an INH surveillance study among 13 838 patients on IPT, the incidence of hepatitis was uncommon in patients <20 years of age, occurred in 0.3% of patients aged 20–34 years and in 1.75% of patients aged 35–64 years.[36] These risk percentages have been used to estimate the number of drug-induced hepatitis cases for two alternatives in our study. The benefit-to-risk ratio is an important measure for quantifying the balance between advantages and disadvantages of the IPT programmes.[35] The ratio calculated in this study is based upon the assumption that 1case of TB prevented is equal to 1 case of hepatitis caused by INH (Equation 6).

Equation 6. Benefit-to-risk ratio

$$= \frac{\text{Estimated number of TB cases prevented}}{\text{Estimated number of hepatitis cases occurred}}$$

Costs. The cost of treating 1 case of latent TB was estimated to be ₹716 (US$ 15.5), which included the cost of medication for 6 months (₹143.2), clinic visits and management of complications (including screening for liver functions). The cost of medication for treating an active case of TB with directly observed treatment, short course (DOTS) (HRZE for 2 months and HR for 4 months) was estimated to be ₹1015.2. The total cost of treating an active case of TB, including medication cost (₹1015.2), hospitalization, evaluation and treatment of complications, contact tracing, and other costs as needed was estimated to be ₹25 380 (US$ 550). The cost for TST was estimated to be ₹70 (US$ 1.5), which included the operational costs, and a chest X-ray when needed. These cost estimations were done using simple mathematical analyses, based on the assumption that the drug cost is a fraction of the total treatment cost. The medication cost to total treatment cost ratios (0.2 for latent TB and 0.04 for active TB) calculated from published studies from the US were used to calculate total treatment cost estimates for the Indian HCW population.[30,37] The drug costs were calculated in Indian rupees using the *Current Index of Medical Specialties* handbook.[38] The cost estimates for our study analyses were obtained by dividing the calculated drug costs with the individual ratio values described earlier (Equation 7).

Equation 7. Estimated total cost of treatment of a case of active TB/latent TB

$$= \frac{\text{Calculated medication cost (i.e. drug cost)}}{\text{Estimated medication cost to total treatment cost ratio}}$$

The cost estimates for the HCW population of India are significantly lower than those for the HCW population of USA, but are higher than the average cost of DOTS therapy for the

general population in India, possibly because the latter does not include hospitalization, contact tracing and treatment of complications.[30,39] Using the estimated treatment costs of treating latent TB infection and active TB, and considering the figures for TST positivity, HCWs in each category and number of cases of TB prevented in different alternatives, we calculated the cost of IPT per case prevented and the net monetary savings to the health system per case of active TB prevented (Equations 8 and 9).

Equation 8. Cost of IPT per case of active TB prevented in the given alternative

$$= \frac{\text{Number of HCWs in the given group} \times \text{TST positivity (\%)} \times \text{Estimated IPT cost to treat 1 case of latent TB infection}}{\text{Number of cases of active TB prevented in the given alternative}}$$

Equation 9. Net savings per case of active TB prevented in the given alternative

= Estimated cost of treatment of 1 case of active TB – cost of IPT per case of active TB prevented

Step 5: Projecting the outcomes

Without IPT programmes (Alternative 3), the lifetime risk of active TB is 33.98 per 1000 HCWs, and the lifetime risk of death due to TB is 2.65 per 1000 HCWs. Our study indicates that IPT for HCWs in Alternatives 1 and 2 can prevent an estimated 21 742 and 18 013 active TB cases, and 1390 and 998 TB-related deaths, respectively (Table III). The estimated number of INH-induced hepatitis cases among HCWs on IPT is 1935 in the age group of ≤30 years as against 7899 in the age group of >30 years. However, this might be an underestimation because studies from which the data for calculation of cases of hepatitis were taken did not include screening for liver function tests.

Both alternatives considered for IPT were cost-effective. For HCWs ≤30 years of age, the estimated cost of IPT per case of active TB prevented was ₹21 287 and the net savings per case prevented was ₹4073. The net savings in the age group of >30 years were more (Table IV). The above calculations were repeated using a balanced population of 50% in each of the 2 age groups. The cost per case prevented by IPT using the balanced population groups was ₹21 480 and ₹17 900 in the age groups of ≤30 years and >30 years, respectively. The corresponding net savings per case prevented is ₹3900 for the age group of ≤30 years and ₹7480 for the age group of >30 years, which are similar to those observed in our initial calculations. We have used equal treatment costs for both younger and older populations; but in practice, the treatment cost is likely to be substantially more for the older population owing to their increased risk of developing complications such as hepatitis. This could explain the higher savings observed in alternative 2. The minimum compliance needed for obtaining cost-effectiveness in our model is 70%–83%. However, this might be an overestimation because of the restriction of benefits in our model to the cost of treatment of cases of active TB which were prevented by the intervention programme, which in fact forms only a small portion of the total effectiveness. We therefore believe that IPT would be cost-effective even for a lower compliance.

Step 6: Confronting the trade-offs

Implementing an IPT programme reduces the lifetime risk of active TB and death due to TB in HCWs in alternatives 1 and 2. In alternative 1, the reduction in relative lifetime risk of active TB

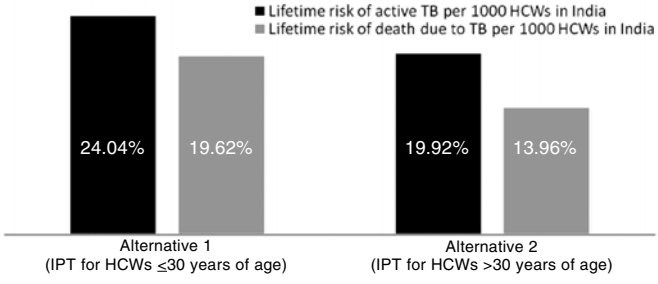

FIG 3. Relative risk reduction of active TB and TB-related mortality in healthcare workers (HCWs)

TABLE III. Risk of active tuberculosis (TB), TB-related mortality and isoniazid-induced hepatitis in healthcare workers (HCWs)

Alternative	Estimated number of			Benefit-to-risk ratio (a/b)	Estimated lifetime risk of	
	active TB prevented (a)	deaths due to TB prevented	hepatitis cases incurred (b)		active TB per 1000 HCWs in India	death due to TB per 1000 HCWs in India
1: IPT for TST positive cases in HCWs ≤30 years of age	21 742	1390	1935	11.24	25.81	2.13
2: IPT for TST positive cases in HCWs >30 years of age	18 013	998	7899	2.28	27.21	2.28
3. Status quo: no TST and no IPT	—	—	—	—	33.98	2.65

IPT isoniazid preventive therapy TST tuberculin skin test

TABLE IV. Cost of isoniazid preventive therapy (IPT) and net savings for the health system in Indian rupees

Alternative	Estimated total cost of IPT	Estimated cost of IPT per case prevented	Estimated total savings by IPT	Estimated net savings per case prevented
1: IPT for TST positive cases in HCWs ≤30 years of age	462 822 400	21 287	88 555 166	4073
2: IPT for TST positive cases in HCWs >30 years of age	320 768 000	17 807	136 420 022	7573

TST tuberculin skin test

is 24.04% compared with a risk reduction of 19.92% in alternative 2. The relative lifetime risk reduction of death due to TB is 19.62% in alternative 1 and 13.96% in alternative 2 (Fig. 3). The total savings realized by the health system by implementation of IPT is approximately ₹89 million for alternative 1 and ₹136 million for alternative 2 (Table IV). The benefit-to-risk ratio calculated based on the estimated number of cases of TB prevented and number of INH-induced hepatitis cases incurred is 11.24 for alternative 1 compared with 2.28 for alternative 2, indicating that IPT is well tolerated and the benefits exceed harm in HCWs in the younger age group (Table III).

The emerging patterns of antimicrobial resistance of *M. tuberculosis* threaten the success of IPT programmes, because individuals infected with INH monoresistant strains would have no real benefit from IPT. We believe that it would still be prudent to implement IPT programmes, since INH-sensitive TB comprises up to 95% of the total cases of TB in India.[40] Second, multidrug-resistant (MDR)-TB generally has limited transmission and is not naturally dominant.[41] Recent reports show that programmes that couple IPT with effective management of drug-resistant TB can achieve better outcomes than programmes that use alternative drug regimens to prevent progression of either drug-sensitive or resistant latent infections. Also, it has been shown earlier that IPT is unlikely to cause drug resistance among individuals who are latently infected with a drug-sensitive strain of TB.[42]

Step 7: Deciding

HCWs in India have a higher burden of TB infection than that of the general population. HCWs with latent TB infection are at risk of developing active disease in the future and this is particularly high among HCWs in a younger age group. Regular TST and treatment of latent TB infection with INH for those who test positive benefits HCWs by reducing their lifetime risk of developing active TB and death due to TB, and is also associated with cost-savings to the health system. We therefore strongly recommend the adoption of a well-defined policy for HCWs in India for TST on entry and repeat TST at regular intervals, followed by treatment of latent TB infection with INH if needed. It must be stressed here, however, that the IPT programmes need to be carried out in conjunction with broader TB infection control programmes.[13] In other words, infection control including administrative and engineering controls and respiratory protection, should be accorded high priority in all such programmes. Every effort must be made to reduce exposure to TB in healthcare settings, and to intensify case finding and ensure treatment completion.

Our analysis shows that IPT programmes for younger HCWs have the maximum benefit in terms of prevention of active TB and TB-related mortality. Furthermore, we know that nearly 50% of HCWs have latent infection, and 5% of the uninfected workers will be newly infected each year. The results suggest that targeted treatment of young trainees (right from entry into healthcare) merits serious consideration as a means to prevent active TB in HCWs and decrease transmission of *M. tuberculosis* in the health-care sector. In a study conducted in a tertiary hospital in India, acceptance of INH was found to be higher among young trainees and staff nurses; and approximately 61% of the HCWs opted for IPT and completed treatment without any major adverse effects.[20] This does not necessarily imply that TB infection control programmes should focus on only young HCWs. Our study findings suggest that there is an urgent need for a mechanism of targeted testing and treatment of latent TB infection to minimize the risk of occupational exposure for TB among HCWs. Entry level and periodic screening of young HCWs followed by IPT for only those who show conversions will definitely have a long lasting effect in preventing morbidity and mortality due to TB in HCWs.

Step 8: Telling the story

Implementation of a national IPT policy in conjunction with infection control and intensified case finding for HCWs in India to prevent occupational TB is required to support and strengthen India's national TB control efforts.

DISCUSSION

This study is an example of the use of research evidence in the development of public health policies. Concern about the threat of TB to HCWs is long-standing. The shortage of HCWs is widely recognized as a major barrier to reaching those who urgently need anti-TB treatment. It is therefore important that we ask ourselves the question: 'What can we do to care for the health of those who care for the health of others?' There is a pressing need for an evidence-based policy to check occupational TB in healthcare settings. This study shows that IPT programmes for healthcare personnel should be an important part of India's strategy to combat TB. We have also demonstrated how Bardach's 8-fold method has been used to develop a solution concerning cost-effective screening and treatment strategies for HCW at occupational risk of exposure to TB.

WHO has recommended implementation of TB control programmes in all healthcare settings.[13] Currently, the Centers for Disease Control and Prevention (CDC) guidelines recommend that HCWs receive tuberculin testing on entry to the workplace and undergo repeat TST at regular intervals, followed by appropriate treatment of latent TB infection, if necessary.[15] Also, attempts need to be made to implement better TB infection control practices, and the physical and environmental measures recommended by WHO for healthcare facilities.[13]

This analysis has some limitations. The data used for the analysis were derived from compilations of epidemiological and clinical trial data and published cost estimates from India and abroad, and may not be precise. The costs of TB screening and treatment of latent TB infection with INH may vary depending on the delivery setting. Also, personnel costs, training to make sure TST is done and read well, time taken by HCWs to attend TST sessions, etc. were not included in the cost estimates. Since IPT is recommended only for new TST-positive cases, the cost-savings to the health system in subsequent years of IPT programmes is likely to be different. We included one-time cross-section calculations; the results therefore may not reflect longitudinal parameters such as multiple transmission of infection by a case of active TB to others in the population. Another limitation is that we restricted the benefits to the costs of treatment of active disease. Other benefits not included are increased life expectancy and prevention of transmission. The direct benefits of treating TB in HCWs to the health system are likely to be considerably more owing to the increased availability of healthy manpower.

Our primary aim was to gain insight into the impact of IPT programmes on the occupational TB problem in Indian HCWs. We believe that this analysis provides valuable insights for implementing IPT programmes and thereby helps guide decisions concerning prevention of workplace TB among healthcare professionals in India.

ACKNOWLEDGEMENTS

We are grateful to Ranjan Das and Shyam T. from IIT Kharagpur for suggestions and assistance. The initial results of the analysis were presented at the 8th Winter Symposium and 3rd South Asian Regional Symposium on evidence informed health care at South Asian Cochrane Network Centre, Christian Medical College (CMC), Vellore in January 2010.

Conflict of interest: None. We have not been provided with financial support by any external agency, either government or private.

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