WHO policy on TB infection control in health-care facilities, congregate settings and households

Annexes (CD-ROM)

Stop TB Department
Epidemic and Pandemic Alert and Response Department
HIV/AIDS Department
Patient Safety Programme

World Health Organization, Geneva, Switzerland
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Introduction

The evidence given in these annexes was derived from systematic reviews and literature searches related to TB infection control measures. The main questions that were considered were:

1) How much TB transmission is there in different settings?

2) What is the effectiveness of triage, separation, cough etiquette and reduction of stay in health-care facilities?

3) What is the effectiveness of ventilation?

4) What is the effectiveness of ultraviolet germicidal irradiation (UVGI)?

5) What is the effectiveness of particulate respirators?

Each evidence profile contains the question in an adapted “PICOT” (population, intervention; comparison, outcome and time) format, the study selection process and a summary of the main results. The outcome that was considered for each question was the decrease in TB incidence (both drug-susceptible and drug-resistant TB), where:

- **TB incidence** was specified as the incidence of TB cases (new and recurrent) or TB infection, measured with cutaneous test or gamma interferon assays, or TB prevalence derived measures
- **decrease in TB incidence** was measured in patients (differentiating between HIV and non-HIV infected) and health workers (differentiating between HIV and non-HIV infected).

The GRADE system was used to determine the quality of the collected evidence. This system considers factors such as study design, quality, consistency, directness and precision.

Annex 1

Quantification of TB transmission in selected settings

A1.1 Question

Table A1.1

<table>
<thead>
<tr>
<th>Question or intervention</th>
<th>Outcome</th>
<th>Setting</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantification of TB transmission in selected settings</td>
<td>TB incidence</td>
<td>Any ward TB ward MDR ward Outpatient Household Congregate a</td>
<td>Patients (HIV positive and all patients) HWS (HIV positive and all HWs)</td>
</tr>
</tbody>
</table>

HW, health worker; HIV, human immunodeficiency virus; MDR, multidrug resistant; TB, tuberculosis

a Congregate settings include prisons, homeless shelters, army barracks and nursing homes.

A1.2 Study selection process

- Health workers
  - TB infection incidence in low- and middle-income countries (LMICs – using the World Bank ranking) (10 studies, 7 from 1 systematic review (1) [see Section 1.5.1] and 3 independent reviews)
  - TB infection incidence in high-income countries (HICs – World Bank ranking) (35 studies, 33 from 2 systematic reviews (2,3) [see Section 1.5.1] and 2 independent reviews)
  - TB incidence in LMICs (22 studies, 20 from 1 systematic review (1) [see Section 1.5.1] and 2 independent reviews)
  - TB incidence in HICs (14 studies, 12 from 1 systematic review (3) [see Section 1.5.1] and 2 independent reviews)

- Inpatients in health-care facilities
  - TB infection and TB incidence (10 studies independent review, data only from HICs)

- Congregate settings contacts
  - TB infection incidence (9 studies independent review, data only from HICs)
  - TB incidence (17 studies independent review, data only from HICs)

- Household contacts
  - TB infection or TB incidence in HICs (14 studies independent review)
A1.3 Summary of evidence

Table A1.2 shows that the incidence of latent TB infection (LTBI) and TB disease among health workers in health-care facilities exceeds the incidence among the general population or among health workers not exposed to health-care facilities. Likewise, the incidence of LTBI and TB among individuals in congregate settings, such as prisons (for which evidence was readily available), and incidence of LTBI and TB among contacts in household settings, exceed the incidence among the general population.

Table A1.2 Pooled estimates (reference general population)

<table>
<thead>
<tr>
<th>Population</th>
<th>Outcome</th>
<th>Settings</th>
<th>Risk ratio&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health workers</td>
<td>LTBI</td>
<td>High income</td>
<td>10.06</td>
</tr>
<tr>
<td></td>
<td>LTBI</td>
<td>Low income</td>
<td>5.77</td>
</tr>
<tr>
<td></td>
<td>TB</td>
<td>Low income</td>
<td>5.71</td>
</tr>
<tr>
<td></td>
<td>TB</td>
<td>High income</td>
<td>1.99</td>
</tr>
<tr>
<td>Congregate (mostly prisons)</td>
<td>LTBI</td>
<td>High income</td>
<td>2.74</td>
</tr>
<tr>
<td></td>
<td>TB</td>
<td>High income</td>
<td>21.41</td>
</tr>
<tr>
<td>Household</td>
<td>LTBI and TB</td>
<td>High income</td>
<td>3.19</td>
</tr>
</tbody>
</table>

LTBI, latent TB infection; TB, tuberculosis
<sup>a</sup> Estimates were computed from studies reported in the GRADE profiles tables

A1.4 GRADE profiles

Table A1.3 Health-care facilities – quality assessment

<table>
<thead>
<tr>
<th>No. studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTBI incidence among HWs in high-income countries</td>
<td>32 Observational study</td>
<td>No serious limitations</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Very strong association&lt;sup&gt;a&lt;/sup&gt;</td>
<td>HIGH</td>
</tr>
<tr>
<td>LTBI incidence among HWs in low to middle-income countries</td>
<td>10 Observational study</td>
<td>No serious limitations</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Very strong association</td>
<td>HIGH</td>
</tr>
<tr>
<td>TB incidence among HWs in high-income countries</td>
<td>14 Observational study</td>
<td>No serious limitations</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Very strong association&lt;sup&gt;b&lt;/sup&gt;</td>
<td>HIGH</td>
</tr>
<tr>
<td>TB incidence among HWs in low to middle-income countries</td>
<td>22 Observational study</td>
<td>No serious limitations</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Very strong association&lt;sup&gt;c&lt;/sup&gt;</td>
<td>HIGH</td>
</tr>
</tbody>
</table>

HW, health worker; LTBI, latent TB infection; IRR, incidence rate ratio.
<sup>a</sup> Thirteen studies, IRR >5; thirty three studies, IRR >2
<sup>b</sup> Two studies, IRR >5; six studies, IRR >2
<sup>c</sup> Seventeen studies, IRR >5; twenty one studies, IRR >2
Table A1.4  Health-care facilities (patients) – quality assessment

<table>
<thead>
<tr>
<th>No. studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nosocomial transmission of TB or LTBI incidence (patient population)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Observational study</td>
<td>No serious limitations</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Very strong association</td>
<td>HIGH</td>
</tr>
</tbody>
</table>

LTBI, latent TB infection; IRR, incidence rate ratio.

a One study, IRR>5; three studies, IRR>2

Table A1.5  Congregate settings – quality assessment

<table>
<thead>
<tr>
<th>No. studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LTBI incidence among individual in congregate settings</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Observational study</td>
<td>No serious limitations</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Very strong association</td>
<td>HIGH</td>
</tr>
<tr>
<td></td>
<td>TB incidence among individuals in congregate settings</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Observational study</td>
<td>No serious limitations</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Very strong association</td>
<td>HIGH</td>
</tr>
</tbody>
</table>

LTBI, latent TB infection; IRR, incidence rate ratio.

a One study, IRR>5; three studies, IRR>2

b Thirteen studies, IRR>5; fourteen studies, IRR>2

Table A1.6  Household settings – quality assessment

<table>
<thead>
<tr>
<th>No. studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Household transmission of TB or LTBI incidence in high income countries</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Observational study</td>
<td>No serious limitations</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Very strong association</td>
<td>HIGH</td>
</tr>
</tbody>
</table>

LTBI, latent TB infection; IRR, incidence rate ratio

a Four studies, IRR>5; nine studies, IRR>2

A1.5  References

A1.5.1  Systematic reviews


A1.5.2 Latent TB infection incidence among health workers in high-income countries


**A1.5.3 LTBI incidence among health workers in low- to medium-income countries**


**A1.5.4 TB incidence among health workers in high-income countries**


A1.5.5 TB incidence among health workers in low- to medium-income countries


**A1.5.6 Nosocomial transmission of TB or latent TB infection incidence (patient population)**


**A1.5.7 Latent TB infection incidence among individual in congregate settings**


**A1.5.8 TB incidence among individuals in congregate settings**


**A1.5.9 Household transmission of TB or latent TB infection incidence**


ANNEX 2

Triage of people with TB symptoms and separation of infectious cases (Recommendations 8a and 8b)

A2.1 Question

<table>
<thead>
<tr>
<th>Question or intervention</th>
<th>Outcome</th>
<th>Settings</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triage with and without separation versus no intervention</td>
<td>Reduction in TB incidence</td>
<td>Outpatient settings Any ward TB ward MDR ward Congregate settings*</td>
<td>Patients (HIV-positive and all patients) HWs (HIV-positive and all HWs)</td>
</tr>
</tbody>
</table>

HW, health worker; HIV, human immunodeficiency virus; MDR, multidrug resistant; TB, tuberculosis

* Congregate settings include prisons, homeless shelters, army barracks and nursing homes.

A2.2 Study selection process

- 2095 TB infection control citations from 2 databases
- 93 original articles on TB infection control
- 50 articles on triage/physical separation for TB infection control
- 15 articles from which data were extracted after full-text review
- 2002 articles excluded after screening titles
- 43 articles excluded after screening abstracts
- 35 articles excluded due to lack of relevant data or lack of use of Mtb or BCG

BCG, Bacille Calmette Guerin; Mtb, Mycobacterium tuberculosis; TB, tuberculosis
A2.3 Summary of evidence

In total, 15 studies, including 3 (1–3) from LMICs, have been reviewed. The reviewed studies, including three that contained qualitative data only (4–6), support the implementation of triage and physical separation within a set of TB infection control measures. All the studies (2–3) from LMICs reported reduction of TB infection among health workers within a year of introduction of multiple infection control measures. In particular, in two studies (2, 3), the decrease in LTBI incidence was statistically significant; the third study (1) showed a decrease of TB disease among health workers, but this decrease was not statistically significant.

In all studies conducted in HICs (7–15), indicators of nosocomial transmission rapidly declined following the implementation of recommended infection control measures.

Two studies (11, 14) showed that the implementation of the full set of administrative measures reduces transmission of TB to health workers in nosocomial settings. One study showed that reduction of incidence of TB infection among health workers happened after introducing an expanded isolation policy (7). Four studies (11, 13–15) addressed the issue of nosocomial transmission of multidrug-resistant TB (MDR-TB) following introduction of outbreak and administrative control measures. In one study within the HIV ward setting, the exclusive implementation of administrative controls resulted in the complete elimination of MDR-TB transmission among patients (14). However, identification of the key interventions responsible for the decrease in transmission is difficult, because many measures were introduced simultaneously in most facilities.

Overall, the limited evidence available suggests that risk of TB infection can be reduced with simple administrative controls, but this needs to be evaluated in larger, better controlled studies.

A2.4 GRADE profiles

Table A2. 1 Triage of people with TB symptoms and separation of infectious cases – quality assessment

<table>
<thead>
<tr>
<th>No. studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triage</td>
<td>Observational studies</td>
<td>No serious limitations</td>
<td>No serious inconsistency</td>
<td>Serious indirectness</td>
<td>No serious imprecision</td>
<td>LOW</td>
</tr>
<tr>
<td>Physical separation</td>
<td>Observational studies</td>
<td>No serious limitation</td>
<td>No serious inconsistency</td>
<td>Serious indirectness</td>
<td>No serious imprecision</td>
<td>LOW</td>
</tr>
</tbody>
</table>

a Indirect intervention – the studies available assess the outcome for several administrative measures implemented concurrently.

A2.5 References


ANNEX 3

Cough etiquette and respiratory hygiene (Recommendation 8c)

A3.1 Question

Table A3.1

<table>
<thead>
<tr>
<th>Question or intervention</th>
<th>Outcome</th>
<th>Settings</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source control interventions (masks, tissues, cough etiquette and respiratory hygiene) versus no intervention</td>
<td>Reduction in TB incidence</td>
<td>Any ward</td>
<td>Patients (HIV positive and all patients)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TB ward</td>
<td>HWs (HIV positive and all HWs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MDR ward</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Outpatient</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Congregate(^{a})</td>
<td></td>
</tr>
</tbody>
</table>

HW, health worker; HIV, human immunodeficiency virus; MDR, multidrug resistant; TB, tuberculosis

\(^{a}\) Congregate settings include prisons, homeless shelters, army barracks and nursing homes.

A3.2 Study selection process

244 TB infection control citations from 2 databases

224 articles excluded after screening titles

20 original articles on TB infection control

10 articles excluded after screening abstracts

10 articles on cough etiquette for TB infection control

4 articles excluded due to lack of relevant data or lack of use of Mtb or BCG

6 articles from which data were extracted after full-text review

BCG, Bacille Calmette Guerin; Mtb, Mycobacterium tuberculosis; TB, tuberculosis
A3.3 Summary of evidence

Two observational studies (1, 2) clearly mention respiratory hygiene among the administrative measures contained in the packages implemented. However, some articles addressed the impact of respiratory hygiene on the reduction of transmission of influenza and pertussis, diseases with transmission dynamics that differ from those of TB (3–6). The few data available from these studies support the implementation of cough etiquette to reduce the transmission of influenza and pertussis. These findings, although not TB related, are used to inform the public health recommendation for the role of cough etiquette for TB infection control.

A3.4 GRADE profile

Table A3.2 Cough etiquette and respiratory hygiene – quality assessment

<table>
<thead>
<tr>
<th>No. studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 a</td>
<td>Observational studies</td>
<td>Serious limitations</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>LOW</td>
</tr>
</tbody>
</table>

* Table generated based on the TB-related papers only (1,2)

A3.5 References


ANNEX 4

Minimizing time spent in health-care facilities (Recommendation 8d)

A4.1 Question

Table A4.1

<table>
<thead>
<tr>
<th>Question or intervention</th>
<th>Outcome</th>
<th>Setting</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimise time spent in health-care facilities versus no intervention</td>
<td>Reduction in TB incidence</td>
<td>Any ward</td>
<td>Patients (HIV positive and all patients)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TB ward</td>
<td>HWs (HIV positive and all HWs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MDR ward</td>
<td></td>
</tr>
</tbody>
</table>

HW, health worker; HIV, human immunodeficiency virus; MDR, multidrug resistant; TB, tuberculosis

A4.2 Summary of evidence

No studies were found that directly assess the contribution of hospital stay to nosocomial TB transmission. Therefore, a GRADE table cannot be generated. There are several studies on cost-effectiveness of ambulatory management versus hospitalization.

A4.3 References


ANNEX 5

Ventilation system: Natural, mixed-mode and mechanical ventilation (Recommendations 10, 10a and 10b)

A5.1 Question

Table A5.1

<table>
<thead>
<tr>
<th>Question or intervention</th>
<th>Outcome</th>
<th>Setting</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation versus no interventions</td>
<td>Reduction in TB incidence</td>
<td>Any ward</td>
<td>Patients (HIV-positive and all patients)</td>
</tr>
<tr>
<td>Mechanical ventilation versus no intervention</td>
<td>Change in ACH</td>
<td>TB ward</td>
<td>HWs (HIV-positive and all HWs)</td>
</tr>
<tr>
<td>Natural or mixed-mode ventilation versus mechanical</td>
<td>Cost or cost-effectiveness</td>
<td>MDR ward</td>
<td></td>
</tr>
<tr>
<td>Single occupancy versus ventilation or mechanical</td>
<td></td>
<td>Outpatient</td>
<td></td>
</tr>
</tbody>
</table>

A5.2 Study selection process

4537 articles excluded after screening titles and abstracts

5334 TB infection control citations from 4 databases

4593 original articles on TB infection control

56 articles on ventilation for TB infection control

9 articles from which data were extracted after full-text review

741 duplicate articles excluded

4537 articles excluded after screening titles and abstracts

47 articles excluded due to lack of relevant data or lack of use of Mtb or BCG

BCG, Bacille Calmette Guerin; Mtb, Mycobacterium tuberculosis; TB, tuberculosis

ACH, air change per hour; HW, health worker; HIV, human immunodeficiency virus; MDR, multidrug resistant; TB, tuberculosis

* Congregate settings include prisons, homeless shelters, army barracks and nursing homes.
A5.3 Summary of evidence

Of the nine included articles (1, 9), three were epidemiologic studies (cohort or cross-sectional designs) (3–5) that looked at tuberculin skin test (TST) conversion rates in health workers; four were modelling studies (1, 6–8) and two described the costs of ventilation interventions (2, 9). No randomized controlled trials studying the effectiveness of ventilation measures were found. One study focused on natural ventilation only (7), the other studies assessed mechanical ventilation. The three epidemiological studies showed a link between ventilation and TST conversion rates: the lower the ventilation, the higher the TST conversion rate in health workers. The factors studied in the nine included articles vary widely.

In general, even if the evidence for ventilation is of low quality, studies suggest that these interventions are useful for TB infection control.

A5.4 GRADE profiles

Table A5.2 Natural, mixed-mode and mechanical ventilation for TB infection control – quality assessment

<table>
<thead>
<tr>
<th>No. studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>Observational, modelling, environmental, animal, and cost studies</td>
<td>Serious limitations</td>
<td>Serious</td>
<td>Serious</td>
<td>Serious</td>
<td>LOW</td>
</tr>
</tbody>
</table>

Table A5.3 Key findings from the systematic review on natural and mechanical ventilation

<table>
<thead>
<tr>
<th>Country, type of study, years and reference</th>
<th>Setting and subjects</th>
<th>Type of ventilation</th>
<th>Comparison type</th>
<th>Data without ventilation</th>
<th>Data with ventilation</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa Modelling study (1)</td>
<td>Hospital HWs and patients</td>
<td>Mechanical and natural</td>
<td>Cases of XDR-TB prevented</td>
<td>Mechanical ventilation prevents 12% of XDR-TB cases (range 10–20%)</td>
<td>Improvements to natural ventilation could prevent average of 33% of XDR-TB cases (range 6–35% due to wind patterns)</td>
<td>Mechanical ventilation and HEPA filters can reduce extra 10% of XDR-TB cases (range 20–35%)</td>
</tr>
<tr>
<td>USA 1989–1994 Cost study (2)</td>
<td>5 hospitals, 4 with MDR-TB outbreaks</td>
<td>Nonrecirculated air: $30,000–132,900</td>
<td>Room exhaust fans: $3,500–9,800</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Country, type of study, years and reference</td>
<td>Setting and subjects</td>
<td>Type of ventilation</td>
<td>Comparison type</td>
<td>Data without ventilation</td>
<td>Data with ventilation</td>
<td>Notes</td>
</tr>
<tr>
<td>--------------------------------------------</td>
<td>---------------------</td>
<td>---------------------</td>
<td>----------------</td>
<td>-------------------------</td>
<td>----------------------</td>
<td>-------</td>
</tr>
<tr>
<td>USA Prospective cohort study part of screening program 1993–1996 (3)</td>
<td>ED Hospital staff</td>
<td>Intervention included: 4 isolation rooms (as per CDC standards), 100% non-recirculated air in trauma area, improved ventilation with at least 25% fresh air in ED, laminar flow of air, Plexiglas droplet shields</td>
<td>TST conversion rates over 6-month intervals (10 mm cutoff, 5 TU)</td>
<td>(Baseline) Cycle 1: 451/4547 (8.1%) in other departments, 8/88 (9.1%) in Emergency dept. Cycle 2: 6/50 (12%) for ED, 51/2514 (2%) for OD</td>
<td>Cycle 3 after implementation of all measures: 0/64 (0%) for ED and 36/3000 (1.2%) for OD</td>
<td>Annual incidence of TB disease was 22.1/100,000</td>
</tr>
<tr>
<td>Canada Cross-sectional survey 1992–1995 (4)</td>
<td>17 acute-care hospitals in 4 cities Nurses, physiotherapists, respiratory therapist, orderlies, housekeepers, clerks nonclinical personnel</td>
<td>TST conversion groups (Mantoux, 10 mm cutoff, 5TU)</td>
<td>Inadequate ventilation of nonisolation rooms significantly associated with TST conversion among nursing, housekeeping and respiratory therapy personnel (p&lt;0.001). Inadequate ventilation of bronchoscopy rooms also significantly associated with conversion among respiratory therapists</td>
<td>In multi proportionnal hazards regression, earlier time to conversion significantly associated with ventilation &lt;2ACH in nonisolation rooms (hazard ratio 3.4 (2.1–5.8)) but not with ventilation in respiratory isolation rooms (&lt;6ACH vs &gt;6ACH) 1.02 (0.8–1.3)</td>
<td>Ventilation measured by Smoke tubes and CO₂ release measured by infrared direct reading monitor</td>
<td></td>
</tr>
<tr>
<td>Country, type of study, years and reference</td>
<td>Setting and subjects</td>
<td>Type of ventilation</td>
<td>Comparison type</td>
<td>Data without ventilation</td>
<td>Data with ventilation</td>
<td>Notes</td>
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<tr>
<td>Canada Cross-sectional study (5)</td>
<td>17 acute care hospitals in 4 cities Nurses, pathology and microbiology technicians physiotherapists, respiratory therapist, nonclinical personnel as reference</td>
<td>TST conversion groups (Mantoux, 10 mm cut-off, 5TU)</td>
<td>In converted group, ACH averaged 16.7 In nonconverted group, ACH averaged 32.5 TST conversion significantly associated with lower ventilation (&lt;0.001)</td>
<td>In multivariate analysis, ratio of actual ventilation to minimum recommended (comparing half vs equal) gave OR 1.3 though not significant (CI: 0.9, 1.9)</td>
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<tr>
<td>USA Modelling study using Wells-Riley model (6)</td>
<td>Holding facility Deputy sheriffs</td>
<td>TST conversion rates (Mantoux, 5TU)</td>
<td>At measured ventilation (1763 CFM), 4/37 sheriffs infected; at designed ventilation (4954 CFM), only 1.5/37</td>
<td>62.5% reduction in infection by increasing ventilation by 64%</td>
<td></td>
<td>Annual incidence of TB disease ranged 3–7.3/100,000</td>
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<tr>
<td>Peru Mathematical modelling using Wells-Riley model (7)</td>
<td>8 hospitals including TB wards and clinics (5 built before 1950 and 3 built 1970–1990); susceptible individuals who are exposed</td>
<td>Natural and mechanical ventilation</td>
<td>Median risk of TB transmission (% of individuals infected)</td>
<td>Median risk was 97% for natural-ventilation facilities with windows/doors closed, 33% for natural-ventilation facilities in modern hospitals and 11% in pre-1950 hospitals with windows/doors opened</td>
<td>39% for mechanical-ventilated negative-pressure isolation rooms at 12 ACH</td>
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<tr>
<td>Country, type of study, years and reference</td>
<td>Setting and subjects</td>
<td>Type of ventilation</td>
<td>Comparison type</td>
<td>Data without ventilation</td>
<td>Data with ventilation</td>
<td>Notes</td>
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<tr>
<td>USA Mathematical modeling based on contact investigation (8)</td>
<td>Office building Workers</td>
<td>TST conversion (Mantoux, 10 mm cut-off, 5TU) 4 month intervals</td>
<td>Baseline conversion: 27/67 (40%) Decrease in ventilation by 10 CFM would double infection rate (52/67 or 78%)</td>
<td>Increase of 10cfm would reduce rate by 26.9% (18/67) Increase 20 CFM would reduce to 13/67 (19%)</td>
<td>Further increases in outdoor air ventilation predicted to result in progressively smaller reductions in infection</td>
<td></td>
</tr>
<tr>
<td>USA Life cycle cost analysis for 25 years in 3 cities (9)</td>
<td>Waiting room recirculation: Los Angeles (LA)–$1,707,409 New York (NY)–$1,387,717 Atlanta–$1,718,853</td>
<td>100% exhaust in waiting room: LA–$1,753,471 NY–$1,437,056 Atl–$1,770,116</td>
<td>100% exhaust for entire building: LA–$1,783.45 NY–$1,492.51 Atl–$1,847.92</td>
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</tbody>
</table>

ACH, air changes per hour; CDC, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America; CFM, cubic feet per minute; ED, emergency department; HEPA, high-efficiency particulate air; HW, health worker; LA, Los Angeles; MDR, multidrug resistant; NY, New York; OD, outpatient department; TST, tuberculin skin test; TU, tuberculin unit; XDR extensively drug resistant

A5.5 References


Use of ultraviolet germicidal irradiation fixtures
(Recommendation 11)

A6.1 Question

Table A6.1

<table>
<thead>
<tr>
<th>Questions/interventions</th>
<th>Outcome</th>
<th>Setting</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>• UVGI lights versus no intervention</td>
<td>• Reduction in TB incidence</td>
<td>• Any ward</td>
<td>• Patients (HIV-positive and all patients)</td>
</tr>
<tr>
<td>• UVGI lights versus UV lights plus other interventions</td>
<td>• Cost or cost-effectiveness</td>
<td>• TB ward</td>
<td>• HWs (HIV-positive and all HWs)</td>
</tr>
<tr>
<td></td>
<td>• Adverse outcomes</td>
<td>• MDR ward</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Outpatient</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Congregate(^a)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Congregate settings include prisons, homeless shelters, army barracks and nursing homes.

A6.2 Study selection process

- 5334 TB infection control citations from 4 databases
- 4593 original articles on TB infection control
- 70 articles on UVGI for TB infection control
- 11 articles from which data was extracted after full-text review
- 741 duplicate articles excluded
- 4523 articles excluded after screening titles and abstracts
- 59 articles excluded due to lack of relevant data or lack of use of Mtb or BCG

BCG, Bacille Calmette Guerin; Mtb, Mycobacterium tuberculosis; TB, tuberculosis; UVGI, ultraviolet germicidal irradiation
A6.3 Summary of evidence

There is wide variation in the factors studied in the 11 included articles (1–11). Only one is an epidemiologic study that looked at TST conversion rates in health workers showing no major additional benefit (2). However, one well designed animal model study demonstrated that UVGI could reduce TB transmission and disease in guinea pigs (1). All the three laboratory experiments studies showed reduction in bacteria concentration, and absence of tubercles in animals exposed to UVGI (8, 9, 11).

Two are modelling studies (3, 5), another looks at adverse effects (7), and one article describes the costs of the UVGI intervention (4). There are no randomized controlled trials studying the effectiveness of UVGI. However, given the ethical consideration for the conduction of a randomized controlled trial in humans to determine the efficacy of UVGI, results from the animal model study represent the closest proxy to a randomized controlled trial.

There is little evidence on the effectiveness of UVGI as an intervention. However, the available evidence, though weak and indirect, is generally favourable on its use for TB infection control.

A6.4 GRADE profiles

Table A6.2 UVGI for TB infection control – quality assessment

<table>
<thead>
<tr>
<th>No. studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Observational, modelling, environmental, animal and cost studies</td>
<td>Serious limitations</td>
<td>Serious</td>
<td>Serious</td>
<td>Serious</td>
<td>LOW</td>
</tr>
</tbody>
</table>

Table A6.3 Key findings from the systematic reviews of ultraviolet germicidal irradiation (UVGI) fixtures

<table>
<thead>
<tr>
<th>Country, type of study, years and reference</th>
<th>Setting and subjects</th>
<th>Type of UVGI</th>
<th>Comparison type</th>
<th>Data without UVGI</th>
<th>Data with UVGI</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peru Animal study (1)</td>
<td>Three wards Guinea pigs</td>
<td>Upper room</td>
<td>TST conversion and detection of TB disease</td>
<td>106 tuberculin-positives in the control group, 43 in the group protected by ionizers, and 29 in the group only exposed to ward air when UV lights were switched on (P &lt;0.0001). Tuberculosis transmission was reduced by 58% by ionizers (log-rank 27; P &lt;0.0001) and by 72% by UV lights (log-rank 46; P &lt;0.0001).</td>
<td>There was autopsy or organ culture evidence of tuberculosis disease in 26 control group animals, compared with 11 in those protected by ionizers (log-rank 3.7; P = 0.055) and 11 in those protected by UV lights (log-rank 5.4; P = 0.02).</td>
<td></td>
</tr>
<tr>
<td>USA Cross-sectional survey 1991–1993 (2)</td>
<td>Hospital HWs, hospital employees</td>
<td>Upper room</td>
<td>TST conversion rates</td>
<td>30/145 (20.7%) baseline conversion rate with several IC measures</td>
<td>Starting from 7/219 (3.2%); changed to 14/227 (6.2%) for first 6 months, then to 4% for next 6 months</td>
<td>TST with 10 mm cut off at 6-month intervals</td>
</tr>
<tr>
<td>Country, type of study, years and reference</td>
<td>Setting and subjects</td>
<td>Type of UVGI</td>
<td>Comparison type</td>
<td>Data without UVGI</td>
<td>Data with UVGI</td>
<td>Notes</td>
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</tr>
<tr>
<td>Italy Prediction modeling (3)</td>
<td>Hospital, HIV wards HWs, hospital employees</td>
<td>N/A</td>
<td>TST conversion rates for 4 types of high-risk procedure</td>
<td>GV: 34.3–99.9% GV+SM: 22.3–98.1% GV+DMR: 5.9–61.5% GV+HM: 1.3–17.9%</td>
<td>GV+UV: 5.8–90% GV+SM+UV: 3.5–42.8% GV+DMR+UV: 0.9–12.6% GV+HM+UV: 0.2–2.8%</td>
<td></td>
</tr>
<tr>
<td>USA Cost study 1989–94 (4)</td>
<td>Upper room, in ventilation duct</td>
<td>Cost</td>
<td>Wall mounted: $84,000 for 12 fixtures, $93,000 for 8 fixtures at another hospital</td>
<td>In ventilation system: $61,400 for 12 fixtures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA Risk analysis Hypothetical modeling (5)</td>
<td>Hospital</td>
<td>Upper room</td>
<td>TB risk, mean annual new infection rate, cost effectiveness</td>
<td>UVGI reduced TB risk by 1.6-fold in low-risk setting UVGI reduced mean infection rate from 2.2 to 1.3 per year at low irradiance</td>
<td>UVGI reduced TB risk by 4.1-fold in high-risk setting; UVGI reduced mean infection rate from 2.2 to 0.6 per year at high irradiance</td>
<td>Mean cost effectiveness ranged from $133 per TST conversion saved in high-risk setting to $1017 per TST conversion saved in low-risk setting</td>
</tr>
<tr>
<td>Canada cross-sectional survey 1997–98 (6)</td>
<td>Hospital</td>
<td>Upper room, portable device</td>
<td>ACH measured by proxy, not directly</td>
<td>2.0 w/o UV 3.1 for upper-room UV 2.2 for UV + unmixed air</td>
<td>4.0 with UV 7.7 for portable UV 4.5 for UV + mixed air</td>
<td>All P&lt;.05 Measured other bacteria in air, did not include Mtb</td>
</tr>
<tr>
<td>USA Double-blind, placebo-controlled field trial, not randomized 1997–2004 (7)</td>
<td>Homeless shelter Shelter staff</td>
<td>Upper room</td>
<td>Adverse effects</td>
<td>223/3611(6%) interviews reported skin or eye symptoms</td>
<td>95 cases entirely during active UV period, 36 during placebo, 36 uncertain (Chi-square P = 0.4)</td>
<td></td>
</tr>
</tbody>
</table>
A6.5 References


Use of particulate respirators for health workers (Recommendation 12)

A7.1 Question

Table A7.1

<table>
<thead>
<tr>
<th>Question/interventions</th>
<th>Outcome</th>
<th>Settings</th>
<th>Population</th>
<th>Special situations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respirators (N95 or equivalent) versus no intervention</td>
<td>Reduction in TB incidence</td>
<td>Any ward, TB ward, MDR ward, Outpatient</td>
<td>HWs (HIV-positive and all HWs)</td>
<td>Procedures involving aerosol versus other procedures</td>
</tr>
<tr>
<td>Fit test versus fit check and/or training</td>
<td>Proper use of the respirator</td>
<td>Any ward, TB ward, MDR ward, Outpatient</td>
<td>HWs (HIV-positive and all HWs)</td>
<td></td>
</tr>
</tbody>
</table>

HW, health worker; HIV, human immunodeficiency virus; MDR, multidrug resistant; TB, tuberculosis

A7.2 Study selection process

5334 TB infection control citations from 4 databases

741 duplicate articles excluded

4593 original articles on TB infection control

4490 articles excluded after screening titles and abstracts

103 articles on masks or respirators for TB infection control

90 articles excluded due to lack of relevant data or lack of use of Mtb or BCG

13 articles from which data were extracted after full-text review

BCG, Bacille Calmette Guerin; Mtb, Mycobacterium tuberculosis
A7.3 Summary of evidence

Of the 13 relevant studies included in the review (1–13), 3 epidemiologic studies (cross-sectional surveys) evaluated TST conversion rates in health workers and showed a decrease in TST conversion in health workers following the introduction of respirators (6, 7, 10). Four articles were modelling studies (2, 3, 7, 12), and four studies described the cost/cost-effectiveness of respirators (2,9,11,13). One study showed low compliance with use of respirators by HWs even if proper training is ensured (4). One study demonstrated that user seal check should not be used as a surrogate for respirator fit testing (5).

A majority of the cost studies determined respirators are expensive and not very cost-effective. There is little evidence on the effectiveness of respirators as an infection control intervention by themselves. However, the available evidence, though weak and indirect, is generally favourable on its use for TB infection control.

A7.4 GRADE profile

Table A7.2 Respirators for TB infection control – quality assessment

<table>
<thead>
<tr>
<th>No. studies</th>
<th>Design</th>
<th>Limitations</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Quality</th>
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<tbody>
<tr>
<td>13</td>
<td>Observational, modelling, environmental, animal and cost studies</td>
<td>Serious limitations</td>
<td>Serious</td>
<td>Serious</td>
<td>Serious</td>
<td>LOW</td>
</tr>
<tr>
<td>Country, type of study, years and reference</td>
<td>Setting and subjects</td>
<td>Type of mask or respirator</td>
<td>Comparison type</td>
<td>Data with or without mask or respirator</td>
<td>Data with mask or respirator</td>
<td>Notes</td>
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</tr>
<tr>
<td>USA Cost study (1)</td>
<td>Tertiary case hospital HWs</td>
<td>Various</td>
<td>Cost</td>
<td>Simple isolation mask: $1,833 DMR: $1866–28,106 Disposable HEPA respirator: $15,396–114,715 Respirator with replaceable HEPA: $18,614–138,697</td>
<td>Estimated cost of preventing one case of occupational TB Disposable HEPA respirator $631,236 Respirator with replaceable HEPA filter: $5,686,577 Fit testing: $312,422 Fit training: $268,086</td>
<td>Fit testing for 350 new employees per year: $6,124 ($312,422 over 41-year period) Fit training for new employees in year: $5,256 ($268,086 for 41 years)</td>
</tr>
<tr>
<td>USA Modelling study (2)</td>
<td>Hospital HWs</td>
<td>Various</td>
<td>Risk reduction and person-hours to TST conversion</td>
<td>Protection rate versus no respiratory protect (reduce risk fold) • surgical mask 2.4 • disposable dust-mite or dust-fume respirator or disposable HEPA respirator 17.5 • negative pressure cartridge HEPA respirator 45.5 • powered air-purifying respirator 238</td>
<td>Under no UVGI and 6 ACH, 2560 person-hours required for skin-test conversion for no respiratory protection, increases to 6100 hours for surgical mask, 44900 hours for DF/DM mask or disposable HEPA, 116000 hours for negative pressure cartridge HEPA respirator, and 610,000 for powered air-purifying respirator</td>
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<tr>
<td>South Africa Modelling study (3)</td>
<td>Hospital HWs and patients</td>
<td>N95 respirators for staff and mask s for patients</td>
<td>Cases of XDR-TB prevented</td>
<td>Respirator mask use would prevent 2% of XDR cases and 2/3 in staff. 5% of XDR infections averted if patients provided with surgical masks</td>
<td>Enforcement of adherence would increase number of XDR cases averted by average of 1% (range 0–2%)</td>
<td></td>
</tr>
<tr>
<td>Brazil Cross-sectional 2000–01 (4)</td>
<td>Hospital HWs</td>
<td>N95 respirators</td>
<td>Compliance</td>
<td>During high-risk procedures: 20% of patient encounters had HW wear N95 versus 27.8% in non-high-risk procedures (OR = 1.53, P = 0.367) In TB isolation room: 39.5% of patient encounters had HW wear N95 versus 8.7% when patient not isolated (OR = 6.85, p&lt;0.001)</td>
<td>39% of HWs found to have facial-seal leakage (i.e. masks not worn properly); 25.5% of patient encounters had HW wear N95</td>
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<tr>
<td>Country, type of study, years and reference</td>
<td>Setting and subjects</td>
<td>Type of mask or respirator</td>
<td>Comparison type</td>
<td>Data with or without mask or respirator</td>
<td>Data with mask or respirator</td>
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<tr>
<td>Hong Kong Retrospective (5)</td>
<td>Hospital Nurses</td>
<td>N95 and N100</td>
<td>User fit check versus fit testing with Porta-Count reading of 100 as the criterion for a correctly fitte mask</td>
<td>The user seal check wrongly indicated that the mask fitted on 18–31% of occasions</td>
<td>User seal check wrongly indicated that it did not fit on 21–40% of occasions</td>
<td>Results indicate that user seal check should not be used as a surrogate fit test</td>
</tr>
<tr>
<td>USA 1991–1993 cross-sectional (6)</td>
<td>Hospital HWS, hospital employees</td>
<td>Various</td>
<td>TST conversion rates (several IC measures together, including negative-pressure rooms and UV lights)</td>
<td>30/145 (20.7%) baseline conversion rate with Technol shield</td>
<td>Conversion rate at 3.2 then 6.2 (with UV) then 4.0 for particulate respirators 5.8 for dust-mist-fume respirators</td>
<td>TST with 10 mm cut-off at 6-month intervals</td>
</tr>
<tr>
<td>USA Modelling study with modified Wells-Riley (7)</td>
<td>Various</td>
<td>Risk of infection</td>
<td>Risk under moderate exposure category with disposable respirator (leakage 0.2), ACH 6 = 0.042</td>
<td>Risk goes down to 0.021 with a elastomeric half-face respirator (leakage of 0.1)</td>
<td>Risk of infection decreases exponentially with increasing personal respirator protection; relative efficacy of such protection decreases with increased ventilation</td>
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<tr>
<td>Country, type of study, years and reference</td>
<td>Setting and subjects</td>
<td>Type of mask or respirator</td>
<td>Comparison type</td>
<td>Data with or without mask or respirator</td>
<td>Data with mask or respirator</td>
<td>Notes</td>
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<tr>
<td>USA Cross-sectional survey 1992–95 (8)</td>
<td>Hospital HWs</td>
<td>Various</td>
<td>TST conversion rates</td>
<td>For hospitals reporting &gt; 6 patients in 1992: submicron respirator protection (submicron surgical masks, NIOSH-approved disposable particulate respirators: dust mist, DFM and HEPA-filter respirators): TST conversion rate 289/29376 (0.98%) Surgical masks: 497/52648 (0.94%) P = 0.98</td>
<td>For hospitals reporting &gt; 6 patients in 1992 among high-risk HWs (including bronchoscopists and respiratory therapists): Submicron respirator protection: TST conversion rate was 15750 (1.9%) Surgical masks: 19/1183 (1.6%) P = 0.50</td>
<td>Similar analysis for hospitals reporting &lt;6 TB patients/year. No significant differences in HW TST conversion rate between hospital compliant or not compliant with TB infection control measures</td>
</tr>
<tr>
<td>USA Cost study 1994 (9)</td>
<td>Five hospitals HWs</td>
<td>Various</td>
<td>Cost</td>
<td>Total program cost of HW respirator fit-testing program: $8,736–$26,175</td>
<td>Estimate of N95 respirator program cost, assuming single use: $270–422,526</td>
<td>These findings, in contrast to other studies, suggest cost of respirator protection program at most hospitals not excessive</td>
</tr>
<tr>
<td>Brazil Cross-sectional study 1997–99 (10)</td>
<td>Hospital Nurses</td>
<td>Various</td>
<td>TST conversion rates</td>
<td>In relation to use of Technol PFR95 masks, 3168 (68.9%) who reported using them did not convert, as compared to only 278 (25%) who showed tuberculin conversion (RR = 0.3, P = 0.03 CI: 0.09–1.01) In relation to use of surgical masks, 28/68 (42%) who reported using them did not convert, as compared to 6/8 (75%) who showed tuberculin conversion (p = 0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA Cost-effectiveness study (11)</td>
<td>159 veteran affairs hospitals HWs</td>
<td>HEPA respirators</td>
<td>Cost effectiveness</td>
<td>Using HEPA respirators in HWs: Would cost $7 million to prevent 1 case of TB in HW Using HEPA respirators in HWs: Would cost $100 million to save one life</td>
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</tbody>
</table>

**Use of particulate respirators for health workers (Recommendation 12)**
<table>
<thead>
<tr>
<th>Country, type of study, years and reference</th>
<th>Setting and subjects</th>
<th>Type of mask or respirator</th>
<th>Comparison type</th>
<th>Data with or without mask or respirator</th>
<th>Data with mask or respirator</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>USA Modelling study 1992–95 (12)</td>
<td>Various</td>
<td>Various</td>
<td>Cumulative risk of infection</td>
<td>10-year cumulative risk for low-risk scenario: 0.15 (no respirator), 0.067 (surgical mask), 0.0094 (disposable DMF respirator), 0.0033 (elastomeric half-mask HEPA respirator), 0.00064 (HEPA PAPR) Of 1000 HWs, number of expected cases after 10 years: 150, 67, 9, 3, 1 (same order as above)</td>
<td>10-year cumulative risk for high-risk scenario: 0.48 (no respirator), 0.24 (surgical mask), 0.037 (disposable DMF respirator), 0.013 (elastomeric half-mask HEPA respirator), 0.0026 (HEPA PAPR); of 1000 HWs, number of expected cases after 10 years: 480, 240, 37, 13, 3 (same order as above)</td>
<td></td>
</tr>
</tbody>
</table>

A7.5 References


9 Kellerman SE, Tokars JI, Jarvis WR. The costs of healthcare worker respiratory protection and fit-testing programs. *Infection Control and Hospital Epidemiology*, 1998, 19(9):629–634.


