WHO consolidated guidelines on tuberculosis

Module 1: Prevention

Infection prevention and control

World Health Organization

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WHO Guideline Steering Group

Work on these guidelines was overseen by Fuad Mirzayev (WHO Global TB Programme), with contributions from members of the WHO Guideline Steering Group – Annabel Baddeley (WHO Global TB Programme), Dennis Falzon (WHO Global TB Programme), Christopher Gilpin (WHO Global TB Programme), Lice González-Angulo (WHO Global TB Programme), Ernesto Jaramillo (WHO Global TB

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List of abbreviations

ACH	air changes per hour
AMR	antimicrobial resistance
CI	confidence interval
DOI	declaration of interest
DR-TB	drug-resistant TB
DST	drug-susceptibility testing
GNI	gross national income
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GUV	germicidal ultraviolet light
HAI	health care-associated infection
HEPA filter	high-efficiency particulate air filter
HIV	human immunodeficiency virus
IEC	information, education and communication
IGRA	interferon-gamma release assay
IPC	infection prevention and control
IRR	incidence rate ratio
LTBI	latent tuberculosis infection
M. tuberculosis	*Mycobacterium tuberculosis*
MDR-TB	multidrug-resistant TB
OR	odds ratio
PICO	population, intervention, comparator and outcome
SDG	Sustainable Development Goal
RR	rate ratio
TB	tuberculosis
TST	tuberculin skin test
USAID	United States Agency for International Development
UVC	ultraviolet light C
UVGI	ultraviolet germicidal irradiation
WHO	World Health Organization

Definitions

General

Antimicrobial resistance (AMR) The loss of effectiveness of any anti-infective medicine, including antiviral, antifungal, antibacterial and antiparasitic medicines.

Grading of Recommendations Assessment, Development and Evaluation (GRADE) An approach to grading in health care that aims to overcome the shortcomings of current grading systems. For further information, see the GRADE website.[1]

General hospital A health care institution providing medical or surgical (or both) treatment and nursing care for sick or injured people.

General population All individuals, without reference to any specific characteristic.

Health care-associated infection (HAI) An infection occurring in a patient during the process of care in a hospital or other health care facility, which was not present or incubating at the time of admission. HAIs can also appear after discharge. They represent the most frequent adverse event associated with patient care.

Health workers All people engaged in actions whose primary intent is to enhance health (as defined in Chapter 1 of *The world health report 2006 – working together for health*[2]).

Household contact of TB patient An individual who is residing or who had resided in the same household as the infectious TB patient.

Infectiousness Probability of tuberculosis (TB) transmission from an individual with TB disease (usually pulmonary TB) to a susceptible individual through aerosols with droplet nuclei containing viable *Mycobacterium tuberculosis* while, for example, coughing, sneezing or talking.

Latent TB infection (LTBI) incidence The number of new persons identified with LTBI within a specified period of time.

LTBI prevalence The number of persons identified with LTBI at a given point in time.

Multimodal strategy Several elements or components (at least three, and usually five[3]) implemented in an integrated way, with the aim of improving an outcome and changing behaviour. Such a strategy includes tools (e.g. bundles and checklists) developed by multidisciplinary teams that take into account local conditions. The five most common components are system change (availability of the appropriate infrastructure and supplies to enable infection prevention and control [IPC] good practices); education and training of health workers and key players (e.g. managers); monitoring of infrastructure, practices, processes and outcomes, and provision of data feedback; reminders or communications in the workplace; and culture change within the establishment or strengthening of a safety climate.[4]

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1 See http://www.gradeworkinggroup.org

2 Health workers, in: The world health report. Geneva: World Health Organization; 2006 (https://www.who.int/whr/2006/06_chap1_en.pdf, accessed 18 December 2018).

3 Evidence-based care bundles. Institute for Healthcare Improvement; (http://www.ihi.org/topics/bundles/Pages/default.aspx, accessed 18 December 2018).

4 Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level. Geneva: World Health Organization; 2016 (http://www.who.int/gpsc/core-components.pdf, accessed 18 December 2018).

TB incidence The number of new and recurrent (relapse) episodes of TB (all forms) occurring in a given year.[5]

TB prevalence The number of TB cases (all forms) at a given point in time.[5]

IPC interventions

Hierarchy of infection prevention and control measures TB prevention and control consists of a combination of measures designed to minimize the risk of *M. tuberculosis* transmission within populations. A three-level hierarchy of controls comprising administrative controls, environmental controls and respiratory protection has been shown to reduce and prevent the risk of transmission and exposure to *M. tuberculosis*.

Administrative controls Administrative controls are the first and most important level of the hierarchy. These are management measures that are intended to reduce the risk of exposure to persons with infectious TB.

Environmental controls The second level of the hierarchy is the use of environmental controls to prevent the spread of infectious droplet nuclei and reduce their concentration.

Respiratory protection controls The third level of the hierarchy is the use of respiratory protection control. It consists of the use of personal protective equipment in situations that pose a high risk of exposure to *M. tuberculosis*.

Mechanical ventilation Ventilation created using an air supply or an exhaust fan (or both), to force air into or out of a room.

Mixed-mode ventilation A ventilation system that combines both mechanical and natural ventilation, providing the opportunity to choose the most appropriate ventilation mode based on the circumstances.

Natural ventilation Use of natural forces to introduce and distribute outdoor air into or out of a building. These forces can be wind pressures, or pressure generated by the density difference between indoor and outdoor air.[6]

Negative pressure mechanical ventilation system A mechanical ventilation system in which the exhaust airflow rate is greater than the supply airflow rate. The room will be at a lower pressure than the surrounding areas.

Positive pressure mechanical ventilation system A mechanical ventilation system in which the supply airflow rate is greater than the exhaust airflow rate. The room will be at a higher pressure than the surrounding areas.

Respiratory hygiene or cough etiquette The practice of covering the mouth and nose during breathing, coughing or sneezing (e.g. wearing a surgical mask or cloth mask, or covering the mouth with tissues or a sleeve, flexed elbow or hand) to reduce the dispersal of respiratory secretions that may contain infectious particles.

Respiratory protection programme A plan of action aimed at accomplishing an effective and sustainable use of particulate respirators by health workers in settings that pose a high risk for *M. tuberculosis* transmission. The plan includes activity details, responsibilities and timelines, and the means or resources that will be used. Examples of activities are policy development; education and training of health workers; respirator fit-testing; selection of respirator models and sizes; budgeting;

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[5] Methods used by WHO to estimate the global burden of TB disease. Geneva: World Health Organization; 2018 (https://www.who.int/tb/publications/global_report/gtbr2018_online_technical_appendix_global_disease_burden_estimation.pdf?ua=1, accessed 18 December 2018).

[6] Atkinson J, Chartier Y, Pessoa-Silva CL, Jensen P, Li Y, Seto W-H, (eds). Natural ventilation for infection control in health care settings. Geneva: World Health Organization; 2009 (https://www.who.int/water_sanitation_health/publications/natural_ventilation.pdf, accessed 18 December 2018).

procurement of respirators; and installation of signage in high-risk areas of a facility for mandatory respirator use, supervision and disposal.

Respiratory separation / isolation Measures aimed at decreasing or eliminating the risk of airborne *M. tuberculosis* transmission from infectious individuals to other persons seeking medical attention in a health care facility and health workers; such methods include use of individual rooms or designated units, or timing of care procedures.

Triage In the context of TB IPC, a simple and preliminary system of interventions for identifying people with TB signs or symptoms among those seeking medical attention in health care facilities. Triage is used to fast-track TB diagnosis and facilitate further separation or other precautions, when necessary, to minimize transmission from infectious patients.

Ventilation Provides outdoor air into a building or a room, and distributes air within the building. The purpose of ventilation in buildings is to provide healthy air for breathing by diluting pollutants originating in the building with clean air, and by providing an airflow rate to change this air at a given rate. Ventilation is also used for odour control, containment control and climatic control (i.e. temperature and relative humidity). Ventilation may also be used to maintain pressure differentials to prevent the spread of contaminants outside of a room or to prevent contaminants from entering a room.

Transmission of M. tuberculosis

Airborne *M. tuberculosis* transmission The spread of aerosolized *M. tuberculosis* caused by the dissemination of droplet nuclei that remain infectious when suspended in air over long distances and time.

Contagious (infectious) TB patient A patient with pulmonary TB disease (confirmed or undetected) who is able to spread infectious droplet nuclei containing viable *M. tuberculosis* while coughing, sneezing, talking or conducting any other respiratory manoeuvres.

Droplet nuclei Dried-out residuals of droplets of less than 5 µm in diameter. Respiratory droplets are generated when a person with pulmonary or laryngeal TB coughs, sneezes, shouts or sings. As respiratory droplets dry, before reaching room surfaces, they can become droplet nuclei, which are small and light enough to float in-room air for long enough to spread within confined spaces.

In contrast to droplet nuclei, droplets are generally more than 5 µm in diameter. Droplets settle faster than droplet nuclei and do not reach the alveoli when inhaled.

Person with presumptive TB A person who presents with symptoms or signs suggestive of active TB disease.

Risk of *M. tuberculosis* transmission The probability of passing *M. tuberculosis* to another individual. This may be influenced by factors such as the frequency of contact with the source person, proximity and duration of contact, use of respiratory protection, environmental factors (e.g. dilution, ventilation and other air disinfection), infectiousness of the source person and immune status of the exposed person.

TB patient An individual diagnosed with active TB disease (pulmonary or extrapulmonary).

TB symptoms General manifestation of active pulmonary TB disease, including cough for longer than 2 weeks, with sputum production (and could have blood at times), chest pains, fatigue, loss of appetite, weight loss, fever and night sweats.

IPC equipment

Air purifier or air cleaner A portable electrical indoor device intended to remove, inactivate or destroy potentially harmful particles from the circulating air.

Germicidal UV light (GUV) GUV is a modern term for UVGI (see UVGI). The word "irradiation" is removed from the abbreviation to help alleviate end-users' fears of ionizing radiation, which GUV does not contain.

GUV fixture or luminaire An apparatus that distributes the GUV energy emitted from one or more sources. It does not include the sources themselves, but does include all the parts necessary for safe and effective operation, with the means for connecting the sources to the electricity supply.[7]

Particulate respirator (N95 or FFP2) A special type of closely fitted face cover that has the capacity to filter particles, to protect the wearer against inhaling infectious droplet nuclei.

The N95 respirator has a filter efficiency level of 95% or more against particulate aerosols free of oil, when tested against 0.3 µm particles. The "N" denotes that the respirator is not resistant to oil, and the "95" refers to a 95% filter efficiency.

The FFP2 respirator has a filter efficiency level of 94% or more against 0.4 µm solid particles, and is tested against both an oil and a non-oil aerosol.

(The performance of N95 respirators is approved by the National Institute for Occupational Safety and Health [NIOSH] of the US Centers for Disease Control and Prevention, and the performance of FFP2 respirators must comply with the essential health and safety requirements set out in European directives; that is, with "Conformité Européene" [CE].)

Recirculated air filtration Ventilation systems used in enclosed spaces, buildings, aircraft and vehicles, through which various proportions of outside air and recirculated air are mixed, conditioned and filtered before being fed into the enclosed space.

Respirator fit test A test protocol conducted to verify that a respirator correctly fits the user, to minimize ambient air leakage into the wearer's respiratory tract. *Qualitative* fit-testing verifies the respirator's fit using test agents, either detected qualitatively by the wearer's sense of taste, smell or involuntary cough (irritant smoke), or measured quantitatively by an instrument. *Quantitative* fit-testing uses ambient aerosols or artificially generated sodium chloride aerosols, and quantitatively measures aerosol concentrations inside and outside the respirator.

Ultraviolet germicidal irradiation (UVGI) The use of ultraviolet light C (UVC) to kill or inactivate microorganisms. UVGI is generated by germicidal lamps, and is capable of killing or inactivating microorganisms that are airborne or on directly irradiated surfaces. Low-pressure mercury-vapour lamps emit UVC.

Upper-room GUV GUV systems that are designed to generate high levels of UVC irradiance above the heads of room occupants, and to minimize UVC exposure in the lower or occupied portion of the room.

Intervention settings

Community setting In the context of health care, a setting (e.g. primary care or other health care facility at community level) where interventions aimed at maintenance, protection and improvement of health status are provided at or near to places of residence.

Congregate settings A mix of institutional (non-health care) settings where people reside in close proximity to each other. Congregate settings range from correctional facilities (prisons and jails), to homeless shelters, refugee camps, army barracks, hospices, dormitories and nursing homes.

Health care facility Any establishment (public or private) that is engaged in direct care of patients on site.

Health care setting A setting where health care is provided (e.g. hospital, outpatient clinic or home).

[7] International lighting vocabulary (CIE S 017/E:2011). International Commission on Illumination; 2011 (http://www.cie.co.at/publications/international-lighting-vocabulary, accessed 18 December 2018).

Inpatient health care setting A health care facility where patients are admitted and assigned a bed while undergoing diagnosis and receiving treatment and care, for at least one overnight stay.

Outpatient health care setting A health care facility where patients are undergoing diagnosis and receiving treatment and care but are not admitted for an overnight stay (e.g. an ambulatory clinic or a dispensary).

Settings with a high risk of M. tuberculosis transmission A setting where individuals with undetected or undiagnosed active TB, or infectious TB patients are present and there is a high risk of *M. tuberculosis* transmission (see above). TB patients are most infectious when they are untreated (e.g. before diagnosis) or inadequately treated (e.g. undiagnosed drug-resistant TB treated with first-line drugs). Transmission will be increased by aerosol-generating procedures (e.g. bronchoscopy or sputum induction) and by the presence of highly susceptible individuals (e.g. those who are immunocompromised).

Stratification parameters

High burden countries Countries with the highest absolute number of estimated incident cases, and those with the most severe burden in terms of incidence rates per capita. WHO has defined three lists: one for TB, one for MDR-TB and one for TB/HIV.[8]

High TB burden countries The 20 countries with the highest estimated numbers of incident TB cases, plus the 10 countries with the highest estimated TB incidence that are not in the top 20 by absolute number (threshold: >10 000 estimated incident TB cases per year).[8]

High MDR-TB burden countries The 20 countries with the highest estimated numbers of incident MDR-TB cases, plus the 10 countries with the highest estimated MDR-TB incidence that are not in the top 20 by absolute number (threshold: >1000 estimated incident MDR-TB cases per year).[8]

High TB/HIV burden countries The 20 countries with the highest estimated numbers of incident TB/HIV cases, plus the 10 countries with the highest estimated TB/HIV incidence that are not in the top 20 by absolute number (threshold: >10 000 estimated incident TB/HIV cases per year).[8]

High-income countries Defined by the World Bank as countries with a gross national income (GNI) per capita of US$ 12 236 or more in 2016, calculated using the Atlas method.[9]

High TB burden settings Countries or distinct parts of countries characterized by a high burden of TB (TB incidence >100/100 000 population).[10] Low- and middle-income countries usually match this definition.

Low- and middle-income countries Defined by the World Bank as countries with a GNI per capita, calculated using the World Bank Atlas method,[9] of US$ 12 235 in 2016. This group includes low-income countries (GNI per capita <US$ 1005); lower middle-income countries (GNI per capita of between US$ 1006 and US$ 3955) and upper middle-income countries (GNI per capita of between US$ 3956 and US$ 12 235).

Low TB burden settings Countries or distinct parts of countries characterized by a low burden of TB (TB incidence <10/100 000 population).[10] High-income countries usually match this definition.

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[8] Use of high burden country lists for TB by WHO in the post-2015 era. Geneva: World Health Organization; 2015 (https://www.who.int/tb/publications/global_report/high_tb_burdencountrylists2016-2020summary.pdf, accessed 18 December 2018).

[9] The World Bank Atlas method: detailed methodology. Washington, DC: The World Bank; (https://datahelpdesk.worldbank.org/knowledgebase/articles/378832-the-world-bank-atlas-method-detailed-methodology, accessed 18 December 2018).

[10] Clancy L, Rieder HL, Enarson DA, Spinaci S. Tuberculosis elimination in the countries of Europe and other industrialized countries. Eur Respir J. 1991;4(10):1288-95 (https://erj.ersjournals.com/content/4/10/1288, accessed 18 December 2018).

How to use these guidelines

These guidelines have been developed to provide updated, evidence-informed recommendations on tuberculosis (TB) infection prevention and control (IPC) in the context of the global targets of the Sustainable Development Goals (SDGs) and the World Health Organization (WHO) End TB Strategy. The notion and practice of IPC encompasses a set of broader, practical, evidence-based approaches to preventing the community from being harmed by avoidable infections, preventing health care-associated infections (HAI), implementing laboratory biosafety and reducing the spread of antimicrobial resistance (AMR). The IPC concept is used throughout these guidelines – in the context presented here, it refers to a group of interventions aimed at minimizing the risk of Mycobacterium tuberculosis transmission in health care and other settings.

The recommendations given in this document followed an updated assessment of the effect of specific interventions, including extensive deliberation by a Guideline Development Group over the course of 1 year. In view of this, the recommendations described here supersede the 2009 *WHO policy on TB infection control in health care facilities, congregate settings and households*.[11]

The interventions presented here are not new, they replicate those described in earlier WHO guidelines;[11] what is new is the focus on the spectrum of measures as a "package" of interventions. These updated guidelines continue to emphasize the need to implement the hierarchy of infection control as a systematic and complex approach for strengthening IPC and reducing the risk of *M. tuberculosis* transmission. In particular, they draw attention to the core components of IPC[12] as a set of essential elements (i.e. core components) or minimum IPC standards that should be implemented across settings and across the various levels of care, for the effective and efficient functioning of IPC activities and practices.

These guidelines are summarized in three main chapters and a set of web annexes;[13] there is also an Executive Summary that includes a list of the recommendations. The introduction outlines the rationale for developing these guidelines, the objective and the intended audience and also summarize changes in recommendations between the 2009 and 2019 guidelines. Chapter 2 presents the WHO policy recommendations, along with a summary of the evidence, the rationale behind the recommendations and specific implementation considerations for each intervention. Chapter 3 is intended for national authorities and policy-makers to become aware of and to adopt IPC core components for the establishment and effective functioning of IPC programmes and practices. Chapter 4 emphasizes what is needed from current research to better inform future recommendations.

The Web Annex A describes the methods used to develop the guidelines according to WHO standard procedures and a synopsis of the judgements of the Guideline Development Group and outlines the processes for publication and dissemination of the guidelines. Web annexes B, C and D provide GRADE evidence summaries, evidence to decision tables and results of systematic reviews informing this guideline development.

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[11] WHO policy on TB infection control in health-care facilities, congregate settings and households (WHO/HTM/TB/2009.419). Geneva: World Health Organization; 2009 (http://apps.who.int/iris/bitstream/handle/10665/44148/9789241598323_eng.pdf?sequence=1, accessed 18 December 2018).

[12] Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level. Geneva: World Health Organization; 2016 (http://www.who.int/gpsc/core-components.pdf, accessed 18 December 2018).

[13] The annexes include a complete list of participants of the Guideline Development Group meeting, a summary of declarations of interest, a summary of a series of complementary systematic reviews aimed at describing the risk of developing TB infection or progressing to TB disease in specific at-risk populations, and a brief description of the effect of treatment on infectiousness.

As stated earlier, the interventions described under each recommendation are not intended as stand-alone interventions; rather, they are to be implemented as a full IPC package. To properly implement these guidelines, all recommendations should be read alongside the remarks and implementation considerations that follow each recommendation.

Executive summary

Worldwide, tuberculosis (TB) continues to be the most important cause of death from a single infectious microorganism.[14] Although recent decades have witnessed increased efforts in the fight to end TB, fundamental gaps are hampering these efforts, particularly in resource-constrained settings and in settings with a high burden of disease. The World Health Organization (WHO) estimates that close to 54 million TB deaths were averted between 2000 and 2017 because of improved disease prevention and management, and service delivery; nevertheless, up to 10 million people continue to fall ill with TB every year.[14]

One of the targets of the Sustainable Development Goals (SDGs)[15] for the period 2015–2030 is to end the global TB epidemic. In line with this target, the WHO End TB Strategy,[16] approved by the World Health Assembly in 2014, calls for a 90% reduction in TB deaths and an 80% decrease in the TB incidence rate by 2030. The strategy emphasizes the need for prevention across all approaches, including infection prevention and control (IPC) in health care services and other settings where the risk of *Mycobacterium tuberculosis* transmission is high. IPC practices are vital to reduce the risk of *M. tuberculosis* transmission, by reducing the concentration of infectious droplet nuclei in the air and the exposure of susceptible individuals to such aerosols.

Initial WHO recommendations on TB IPC focused primarily on decreasing the risk of transmission in health care facilities in resource-limited settings.[17,18] These initial recommendations were then expanded in 2009 to provide further guidance on the use of specific measures for health care facilities, congregate settings and households.[19] After the 2009 guidelines had been in effect for almost 10 years, the need for an update was anticipated, to provide a revised evidence assessment, reinforcing earlier recommendations and linking to core components of effective IPC programmes overall. The present updated guidelines also stress the importance of implementing IPC measures in a systematic and objective way that prioritizes consideration of the hierarchy of IPC controls. Thus, the interventions described here should not be implemented individually or in a way that dissociates them from other administrative and environmental controls, and personal protection; rather, they must be considered as an integrated package of IPC interventions to prevent *M. tuberculosis* transmission.

These guidelines do not attempt to create a parallel programme exclusively dedicated to TB IPC; instead they, emphasize the importance of building integrated, well-coordinated, multisectoral action towards TB infection control across all levels of care, as well as in non-health care settings

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[14] Global tuberculosis report 2018 (WHO/CDS/TB/2018.20). Geneva: World Health Organization); 2018 (http://apps.who.int/iris/bitstream/handle/10665/274453/9789241565646-eng.pdf?ua=1, accessed 18 December 2018).

[15] The SDGs were adopted by world leaders in September 2015 to end poverty, protect the planet and ensure prosperity for all as part of a new sustainable development agenda. Further information is available at: https://www.un.org/sustainabledevelopment/development-agenda/.

[16] The End TB Strategy provides a global TB strategy framework, and sets the targets to reduce TB deaths by 95%, reduce TB incidence by 90% and prevent affected families facing catastrophic costs due to tuberculosis. Further information is available at: http://www.who.int/tb/strategy/End_TB_Strategy.pdf?ua=1.

[17] Guidelines for the prevention of tuberculosis in health care facilities in resource-limited settings (WHO/CDS/TB/99.269). Geneva: World Health Organization; 1999 (http://www.who.int/tb/publications/who_tb_99_269.pdf?ua=1, accessed 18 December 2018).

[18] Tuberculosis infection-control in the era of expanding HIV care and treatment – addendum to WHO guidelines for the prevention of tuberculosis in health care facilities in resource-limited settings. Geneva: World Health Organization (WHO); 1999 (http://apps.who.int/iris/bitstream/handle/10665/66400/WHO_TB_99.269_ADD_eng.pdf?sequence=2, accessed 18 December 2018).

[19] WHO policy on TB infection control in health-care facilities, congregate settings and households (WHO/HTM/TB/2009.419). Geneva: World Health Organization; 2009 (http://apps.who.int/iris/bitstream/handle/10665/44148/9789241598323_eng.pdf?sequence=1, accessed 18 December 2018).

with a high risk of *M. tuberculosis* transmission. In doing this, as an initial step, these guidelines lay out general recommendations and good practice activities that are crucial for the establishment and effective functioning of all IPC programmes. These core components[20] of IPC programmes form a key part of WHO strategies to prevent current and future threats; strengthen health service resilience; help to prevent conditions such as health care-associated infections, including TB; and combat antimicrobial resistance.

The target audience for these guidelines includes national and subnational policy-makers; frontline health workers; health system managers for TB, HIV and highly-prevalent noncommunicable disease programmes; managers of IPC services in inpatient and outpatient facilities; managers of congregate settings and penitentiary facilities; occupational health officials; and other key TB stakeholders.

The objective of these guidelines is to provide updated, evidence-informed recommendations outlining a public health approach to preventing *M. tuberculosis* transmission within the clinical and programmatic management of TB, and to support countries in their efforts to strengthen or build reliable, resilient and effective IPC programmes to reach the targets of the "End TB Strategy".

This document supersedes the *WHO policy on TB infection control in health care facilities, congregate settings and households* that was published in 2009.[21]

Guideline development methods

These guidelines were developed in accordance with the process described in the *WHO handbook for guideline development*.[22] Confidence in the certainty of the evidence underpinning the recommendations was ascertained using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. The Guideline Development Group, an international group of experts, was convened to advise WHO in this process, to provide input into the scope of these guidelines and to assist the WHO Steering Group in developing the key questions. A total of three background questions and four PICO (population, intervention, comparison and outcome) questions were developed. The guideline development process was informed by systematic evidence reviews, which concluded in seven IPC policy recommendations.

To ensure that these recommendations are correctly understood and applied in practice, additional remarks as well as considerations for implementation are included under each recommendation in the full text of the document. The seven recommendations are presented below.

[20] Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level. Geneva: World Health Organization; 2016 (http://www.who.int/gpsc/core-components.pdf, accessed 18 December 2018).

[21] WHO policy on TB infection control in health-care facilities, congregate settings and households (WHO/HTM/TB/2009.419). Geneva: World Health Organization (WHO); 2009 (http://apps.who.int/iris/bitstream/handle/10665/44148/9789241598323_eng.pdf?sequence=1, accessed 18 December 2018).

[22] WHO handbook for guideline development (second edition). Geneva: World Health Organization (WHO). 2014 (http://apps.who.int/iris/bitstream/10665/145714/1/9789241548960_eng.pdf, accessed 18 December 2018).

Summary of recommendations

Administrative controls

Recommendation 1: Triage of people with TB signs and symptoms, or with TB disease, is recommended to reduce *M. tuberculosis* transmission to health workers (including community health workers), persons attending health care facilities or other persons in settings with a high risk of transmission. *(Conditional recommendation based on very low certainty in the estimates of effects)*

Recommendation 2: Respiratory separation / isolation of people with presumed or demonstrated infectious TB is recommended to reduce *M. tuberculosis* transmission to health workers or other persons attending health care facilities. *(Conditional recommendation based on very low certainty in the estimates of effects)*

Recommendation 3: Prompt initiation of effective TB treatment of people with TB disease is recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission. *(Strong recommendation based on very low certainty in the estimates of effects)*

Recommendation 4: Respiratory hygiene (including cough etiquette) in people with presumed or confirmed TB is recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission. *(Strong recommendation based on low certainty in the estimates of effects)*

Environmental controls

Recommendation 5: Upper-room germicidal ultraviolet (GUV) systems are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission. *(Conditional recommendation based on moderate certainty in the estimates of effects)*

Recommendation 6: Ventilation systems (including natural, mixed-mode, mechanical ventilation and recirculated air through high-efficiency particulate air [HEPA] filters) are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission. *(Conditional recommendation based on very low certainty in the estimates of effects)*

Respiratory protection

Recommendation 7: Particulate respirators, within the framework of a respiratory protection programme, are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission. *(Conditional recommendation based on very low certainty in the estimates of effects)*

1. Introduction

With a burden of disease that accounts for more than 10 million new cases per year, of which less than two thirds are reported, tuberculosis (TB) continues to be a major global health threat *(1)*. Although the global number of TB deaths fell by 42% between 2000 and 2017, and the annual decline in the global TB incidence rate is currently 1.5% *(1)*, much action is needed to accelerate progress towards achieving global milestones to end TB *(2)*. TB can affect everyone, but specific population groups have a higher risk of acquiring TB infection and progressing to disease once infected; these groups include people living with HIV infection, health workers and others in settings with a high risk of transmission of *M. tuberculosis*. For instance, global TB data indicate that, in 2017 – out of the 920 000 estimated incident TB cases among people living with HIV – there were an estimated 300 000 deaths[23] from TB in this population. Also, 9299 TB cases among health workers were reported in 60 countries alone, with the notification rate for health care-associated transmission of *Mycobacterium tuberculosis* being twice as high as the rate in the general adult population. In addition, more than a million incident cases were estimated among children (aged <15 years), reflecting ongoing community transmission.

An increasing challenge to public health and to TB prevention is that of transmission of drug-resistant strains of *M. tuberculosis*. Initial evidence suggested reduced transmissibility of resistant strains; however, it is now clear that primary transmission of drug-resistant bacteria (as opposed to acquired resistance) is the dominant mechanism sustaining the global transmission of drug-resistant TB (DR-TB) cases *(3, 4)*.

Interrupting the cycle of *M. tuberculosis* transmission is crucial to achieving global targets to end the TB epidemic. Thus, there is a need to implement interventions to rapidly identify source cases, and impede person-to-person transmission by reducing the concentration of infectious particles in the air and the exposure time of susceptible individuals. These principles form the basis for effective infection prevention and control (IPC).

Initial global recommendations on the implementation of IPC for TB were published between 1999 and 2009 *(5–7)*. The demand for these recommendations stemmed from the resurgence of TB and the various drivers fuelling the epidemic, such as the upsurge in HIV infections, concurrent with disrupted health care systems in low- and middle-income countries, the growing incidence of noncommunicable diseases *(8, 9)* and the emergence of drug-resistant forms of TB. Although the implementation of IPC measures can reduce the risk of *M. tuberculosis* transmission *(10–12)*, IPC practices are not routinely or systematically implemented, despite their potential benefit and impact, especially in settings with limited resources. Also, there has been little progress in the generation of evidence specific to IPC practices in TB – to date, there are no data available to evaluate the progress in implementing IPC measures globally, including in high TB burden settings.

Since the *WHO policy on TB infection control in health care facilities, congregate settings and households* was published in 2009 *(7)*, it has been anticipated that the evidence will need to be reassessed and the guidelines updated.

Fuelled also by user needs, the revised guidelines address important gaps for IPC implementation within the clinical and programmatic management of TB (see the Summary of changes table). These revised guidelines also bring together existing World Health Organization (WHO) recommendations in the context of the overall framework of IPC programmes. Hence, this document incorporates

[23] TB deaths among HIV-positive patients are classified as HIV in the international classification of diseases system (ICD-10).

the recommendations from *Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level*, published by WHO in 2016 *(13)*. The initial development of those core components resulted from requests for support from Member States for strengthening of overall IPC capacity, to achieve resilient health systems, both at the national and at the facility level. Their inclusion in this document provides the basis for adopting specific components that are crucial for the effective functioning of IPC across health care programmes.

Scope of the guidelines

These updated guidelines focus on a package of interventions aimed at reducing the risk of *M. tuberculosis* transmission, and they supersede the 2009 recommendations *(7)*. Overall, the recommendations cover health care and other groups outside the health care system; also, where possible, specific remarks and additional considerations are given, to highlight specific areas or processes required for the implementation of these recommendations within health care facilities and other, non-health care settings such as congregate settings, community settings and households.

These guidelines do not present interventions directed to household settings, given that there was no directly applicable evidence that fulfilled the inclusion criteria for this systematic evaluation of data. However, some considerations pertinent to households are mentioned, where applicable (i.e. respiratory hygiene and respiratory protection) under implementation considerations. Similarly, these guidelines do not cover any aspects related to TB laboratory biosafety because this area of work is addressed elsewhere *(14, 15)*.Another strategy that is critical for reducing the burden of TB disease among individuals exposed to *M. tuberculosis* – preventive treatment – is further described in the 2018 updated and consolidated guidelines for programmatic management of latent TB infection (LTBI) *(16)*.

Objective

The objective of these guidelines is to provide updated, evidence-informed recommendations outlining a public health approach to preventing transmission of *M. tuberculosis* within the clinical and programmatic management of TB, and to support countries in their efforts to strengthen or build reliable, resilient and effective IPC programmes.

We expect these guidelines to form the basis for development of national and subnational policies by Member States. Effective implementation of these guidelines will contribute to achievement of the "End TB Strategy" by contributing towards the reduction in the numbers of TB cases and deaths in the years to come.

Target audience

The recommendations presented here are intended to inform and contextualize TB-specific IPC interventions and activities within national-level and local-level IPC policies and protocols. Therefore, the target audience includes national and subnational policy-makers, including health system managers for TB, HIV and other disease programmes; IPC services; inpatient and outpatient facilities; IPC and quality assurance programmes; associations of affected groups; managers of congregate settings and penitentiary facilities; and occupational health and other relevant stakeholders.

The adoption of these guidelines goes beyond national TB programmes. It requires an interdisciplinary, multisectoral and multilevel approach to ensure the proper implementation of the recommendations in settings where transmission of *M. tuberculosis* is likely to occur.

Guiding principles

- Effective IPC measures are a critical part of the quality of health service delivery to achieve people-centred, integrated universal health coverage.
- These guidelines are based on a public health approach to strengthening the adoption and implementation of evidence-based interventions for IPC, including transmission-based precautions, and the recommendations given here should be considered as the minimum IPC standard.
- Implementing these guidelines requires an understanding of the interdependence of the three-level hierarchy of IPC, giving prominence to the implementation of administrative controls as the basis for reducing the risk of transmission of *M. tuberculosis*.
- The implementation of these recommendations needs to be accompanied by efforts[a] to promote and protect the human rights of all patients, their communities and care providers.

[a] Ethics guidance for the implementation of the End TB strategy (WHO/HTM/TB/2017.07). Geneva: World Health Organization; 2017 (http://apps.who.int/iris/bitstream/handle/10665/254820/9789241512114-eng.pdf?sequence=1, accessed 18 December 2018).

IPC: infection prevention and control.

Summary of changes in the evidence-based recommendations between the 2009 and 2019 guidelines

Setting	WHO policy on TB infection control in health care facilities, congregate settings and households, 2009	WHO guidelines on tuberculosis infection prevention and control, 2019
National and subnational	**Activity 1.** Identify and strengthen a coordinating body for TB infection control, and develop a comprehensive budgeted plan that includes human resource requirements for implementation of TB infection control at all levels. **Activity 2.** Ensure that health facility design, construction, renovation and use are appropriate. **Activity 3.** Conduct surveillance of TB disease among health workers, and conduct assessment at all levels of the health system and in congregate settings. **Activity 4.** Address TB infection control advocacy, communication and social mobilization (ACSM), including engagement of civil society. **Activity 5.** Monitor and evaluate the set of TB infection control measures. **Activity 6.** Enable and conduct operational research.	The Guidelines *Core components of infection prevention and control programmes at the national and acute health care facility level* were adopted in the 2019 update, to integrate 2016 evidence-based and consensus-based recommendations and good practice statements developed by the WHO Department of Service Delivery and Safety. National and subnational activities have also been adopted within the present policy guideline, and have been aligned with the core components, which provide a broader, health systems framework for the implementation of IPC.
Health care facilities	**Control 7.** Implement the set of facility level managerial activities.	Aligned with *Core components of infection prevention and control programmes at the national and acute health care facility level (13).*
	Control 8. (8a) Promptly identify people with TB symptoms (triage), (8b) separate infectious patients, (8c) control the spread of pathogens (cough etiquette and respiratory hygiene) and (8d) minimize time spent in health care facilities.	**Recommendation 1. Triage** Triage of people with TB signs and symptoms, or with TB disease, is recommended to reduce *M. tuberculosis* transmission to health workers, and to persons attending health care facilities or other persons in settings with a high risk of transmission.

Setting	WHO policy on TB infection control in health care facilities, congregate settings and households, 2009	WHO guidelines on tuberculosis infection prevention and control, 2019
Health care facilities		**Recommendation 2. Respiratory separation / isolation** Respiratory separation of people with presumed or demonstrated infectious TB is recommended to reduce *M. tuberculosis* transmission to health workers or other persons attending health care facilities. **Recommendation 3. Prompt initiation of effective treatment** Rapid diagnosis and initiation of effective treatment of people with TB disease is recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care settings or other persons in settings with a high risk of transmission. **Recommendation 4. Respiratory hygiene (including cough etiquette)** Respiratory hygiene (including cough etiquette) in people with presumed or confirmed TB is recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.
	Control 9. Provide a package of prevention and care interventions for health workers, including HIV prevention, antiretroviral therapy and IPT for HIV-positive health workers.	The recommendation on preventive therapy was removed from the current policy as this is addressed in WHO LTBI and HIV policy recommendations.[a,b]
	Control 10. Use ventilation systems: (10a) natural ventilation, (10b) mechanical ventilation.	**Recommendation 6. Ventilation systems** Ventilation systems (including natural, mixed-mode, mechanical ventilation and recirculated air through HEPA filters) are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

Setting	WHO policy on TB infection control in health care facilities, congregate settings and households, 2009	WHO guidelines on tuberculosis infection prevention and control, 2019
Health care facilities	**Control 11.** Use of upper-room or shielded ultraviolet germicidal irradiation fixtures.	**Recommendation 5. Upper-room GUV systems** Upper-room GUV systems are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.
	Control 12. Use of particulate respirators.	**Recommendation 7. Respiratory protection** Within the framework of a respiratory protection programme, particulate respirators are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.
Congregate settings	Extrapolation from recommendations for health care facilities.	The 2019 policy recommendations are expanded to other settings with a high risk of *M. tuberculosis* transmission,[c] where applicable.
Households	No specific recommendations, but a set of principles were outlined.	Remarks or considerations on specific interventions are made where applicable (e.g. respiratory hygiene, ventilation systems and respiratory protection).

GUV: germicidal ultraviolet; HEPA: high-efficiency particulate air; HIV: human immunodeficiency virus; IPC: infection prevention and control; IPT: isoniazid preventive therapy; LTBI: latent TB infection; *M. tuberculosis*: Mycobacterium tuberculosis; TB: tuberculosis; WHO: World Health Organization.

[a] Latent TB infection: updated and consolidated guidelines for programmatic management [WHO/CDS/TB/2018.4]. Geneva: World Health Organization(WHO); 2018 (http://www.who.int/tb/publications/2018/latent-tuberculosis-infection/en/, accessed 19 December 2018).

[b] Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach (second edition). Geneva: World Health Organization; 2016 (http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1, accessed 18 December 2018).

[c] See definition in the Glossary.

2. Recommendations

Evidence summary and rationale

The recommendations given below on TB-specific interventions are not envisioned as stand-alone measures; rather, they are components of a comprehensive hierarchy of controls, which in turn is a component of the overall framework of IPC practices, and depends on the adoption of a multimodal strategy. Thus, the adoption of several elements needs to be integrated. Typically, these elements would include system change (improving equipment availability and infrastructure at the point of care) to facilitate best practice; education and training of health workers and key stakeholders; monitoring of practices, processes and outcomes, and provision of timely feedback; improved communication; and culture change through fostering of a safety climate.

Each recommendation is followed by a summary of the evidence, a rationale for the recommendation and a set of implementation considerations.

2.1 Administrative controls

A set of administrative controls is the first and most important component of any IPC strategy. These key measures comprise specific interventions aimed at reducing exposure and therefore reducing transmission of *M. tuberculosis*. They include *triage* and *patient separation systems* (i.e. management of patient flows to promptly identify and separate presumptive TB cases), *prompt initiation of effective treatment* and *respiratory hygiene*.

Recommendation 1. Triage

Triage of people with TB signs and symptoms, or with TB disease, is recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

(Conditional recommendation based on very low certainty in the estimates of effects)

Evidence and justification

Recent decades have seen the accumulation of a substantial body of evidence on TB treatment and care. However, research in the area of TB IPC has been rather limited – reflected in the number of studies collected to inform this and the other recommendations included here. Looking at the effect of triage on the incidence of LTBI and TB disease among health workers, the systematic search *(17)* yielded 15 observational studies from secondary and tertiary health care facilities, of which 73% were carried out in low TB burden settings. A total of six studies measuring the effect of triage on the incidence of LTBI alone among health workers in all settings were included in the analysis *(18–23)*.

Given the significant heterogeneity among the studies, only crude estimates were assessed by the Guideline Development Group and are described in this document. Estimates of effect showed an absolute risk reduction of 6% for LTBI incidence among health workers in all settings (n=6). When disaggregating by burden of disease, a 3% absolute risk reduction in LTBI was observed among

health workers in low TB burden settings (*n*=5), compared with a 1.7% reduction in high TB burden settings (*n*=1). Three additional studies – one in low TB burden and two in high TB burden settings – were further assessed to determine the effect of triage on the incidence of TB disease among health workers *(24–26)*. Estimates of reduction of TB incidence in high TB burden settings, calculated from crude pooled data, seemed to indicate very slight or no reduction in TB incidence (crude incidence rate ratio [IRR]: 0.98) among health workers after the implementation of triage within a set of composite IPC measures. The only study in which triage was implemented with no other interventions in a low TB burden setting *(26)* reported an incidence rate of 78 episodes of TB disease among health workers in 38 331 person-years in the control group (before the intervention was implemented), and 12 episodes in 18 229 person-years after the implementation of triage (crude IRR: 0.32, after versus before) (see Web Annex D for further information).[24]

Although there were scant data from which to assess the impact of triage on prevention of TB infection among non-health care staff (i.e. other persons attending health care settings), two studies from low TB burden countries provided information about the effect of this measure in reducing the incidence of TB disease among this population *(27, 28)*. These studies seemed to indicate that there is a 12.6% absolute risk reduction (crude estimate combining data from two studies) in the number of active TB disease cases in persons attending health care settings with the use of triage (in combination with other IPC measures) compared with similar populations in settings where triage was not implemented.

The analysis presented here had some limitations; namely, the scarcity of studies measuring the effect of TB-specific IPC interventions, and issues with the methodology of the studies and the quality of the data. A major challenge encountered during the evidence assessment was that a wide range of IPC activities were typically undertaken as part of composite interventions, making it impossible to determine the effects of individual components. All the included studies apart from one *(26)* presented a combination of measures that were implemented either simultaneously or sequentially.

Owing to the heterogeneity of studies identified in this systematic review, meta-analysis was not performed, and the analysis was restricted to the use of crude estimates and narrative summaries for some outcomes. In turn, this limited the possibility of exploring the effect of potential confounders or evaluating the impact of targeting specific risk factors in these analyses. The heterogeneous nature of the included studies (e.g. lack of standardization, use of composite interventions and outcome measurements) led the Guideline Development Group to downgrade all evidence by two levels, based on *indirectness* arising from several sources, and limitations leading to serious *inconsistency* and *risk of bias* (see Web Annex C).

Another major source of indirectness was the interpretation or definition of the term *triage*, and whether measures were standardized and implemented systematically throughout a specific setting, or were applicable only to a perceived at-risk population *(19–22, 29, 30)*. For instance, some studies triaged HIV-positive individuals, and people experiencing homelessness who were presenting to health care facilities with pneumonia or evidence of TB, whereas others described triage as a set of measures that included the prioritization of patients with cough for more than 2 weeks (regardless of perceived risk) and the rapid collection of respiratory specimens or the routine screening of all new admissions with chest X-rays. An additional consideration in the quality assessment was that of applicability or generalizability of the results. Three quarters of studies included for the evaluation of triage systems were conducted in low TB burden settings – 60% were carried out in the United States of America (USA) alone.

The panel also discussed the potential introduction of inconsistency and bias in the pooled results. Variability in results could be expected because the methods used to measure outcomes varied from study to study; for example, in measuring TB infection, it was not always clear whether a single

[24] Substantial heterogeneity was observed in these studies.

tuberculin skin test (TST) or two-step testing[25] was used. Also, false readings were possible if readers were insufficiently skilled.

The observational studies identified through the systematic search were, by design, single group comparisons, often in a single health facility. The studies were before-and-after (*n*=7), during-and-after (*n*=4) and cross-sectional (*n*=1). Before-and-after and during-and-after studies are the simplest ways to evaluate the effect of an intervention in a particular population; however, the panel acknowledged that comparing outcomes before-and-after implementation of a particular intervention introduced serious risk of bias, in addition to the effect of unidentified confounders, mainly due to lack of randomization. These designs cannot control for contemporaneous changes in case mix, background changes in the incidence in the general population, referral patterns or other elements of care. Often, such studies are of too short a duration to determine whether the intervention and its apparent effect are sustainable over time and across all settings.

The analysis was further constrained by the limited data from high TB burden settings; only three studies – from Brazil (four general hospitals), Thailand (one referral hospital) and Malawi (40 hospitals) – were identified and included in the systematic search *(18, 24, 25)*. No data on the use of triage in primary health care facilities were available.

Despite the lack of direct data, the Guideline Development Group advised that rapid triage systems – covering all health workers and other persons attending health care settings – be recommended in all health care facilities, regardless of the level of care. Although this recommendation was based on very low certainty in the evidence, a strong priority was assigned to this intervention given that, if properly and systematically implemented alongside other recommended IPC interventions, it is unlikely that harm would accrue from this intervention.

Implementation considerations

The effective implementation of this recommendation and the other recommendations in these guidelines relies on the understanding that interventions within the three-level hierarchy of IPC should not be prioritized individually or implemented separately, but must be considered as an integrated package of IPC interventions.

Implementation of any triage system needs to be focused on fast-tracking of presumed TB cases and on minimizing time in the facility.

Consultation and ongoing dialogue with both health care staff and patients should be considered, to provide feedback that could facilitate the implementation of the recommendation without contributing to stigma or alienation of patients. The considerations outlined below should guide the implementation of the recommendations.

Settings and target population

The recommendation on the implementation of triage of people with TB signs and symptoms as a means of reducing *M. tuberculosis* transmission to health workers or other persons attending relevant facilities applies explicitly to health care settings. Although the scope of the review was limited to such settings, the Guideline Development Group recognized that it is vital to implement triage in other settings with a high risk of *M. tuberculosis* transmission where persons with presumed TB may congregate (e.g. long-term care and correctional facilities), regardless of the burden of TB disease.

In addition, community health workers are key to promptly identifying presumptive TB cases at the community level and making use of referral systems, to fast-track TB diagnosis and facilitate the

[25] In some persons who are infected with *M. tuberculosis*, the ability to react to tuberculin may wane over time. When given years after infection, the TST may have a false-negative reaction. However, false-positive reactions may also result due to recent vaccination with bacille Calmette-Guérin (BCG) or a boosted reaction to subsequent Mantoux skin tests.

implementation of other interventions. Community health workers could help to improve the early detection of TB cases, and reduce the risk of transmission in the community in general.

Resources

The effective implementation of triage goes beyond the minimal infrastructure requirements (e.g. conditions for fast-tracking of patients with presumed TB, rapid diagnosis, respiratory separation, use of data-recording tools for documentation, and analysis of data for developing or changing evidence-based policies). The implementation needs to prioritize the availability, education, sensitization and continuous training of health care providers and others working in settings with a high risk of *M. tuberculosis* transmission.

Subgroup considerations

In line with current guidelines on screening for active TB disease, people living with HIV should be systematically screened for active TB at each visit to a health care facility *(31, 32)*. Similarly, routine HIV testing should be offered to all patients with presumptive and diagnosed TB, especially in high HIV burden settings *(33)*.

Triage systems may be part of collaborative activities established to prevent and identify TB across other disease programmes (e.g. diabetes and conditions that increase the risk of LTBI or TB disease).

Recommendation 2. Respiratory separation / isolation

Respiratory separation / isolation of people with presumed or demonstrated infectious TB is recommended to reduce *M. tuberculosis* transmission to health workers or other persons attending health care facilities.

(Conditional recommendation based on very low certainty in the estimates of effects)

Remark

Health care systems must implement available *patient care and support* measures (including decentralized models of care,[a,b,c] if applicable) before resorting to isolation of any person.

[a] WHO treatment guidelines for drug-resistant tuberculosis, 2016 update. October 2016 revision (WHO/HTM/TB/2016.04). Geneva: World Health Organization; 2016 (http://apps.who.int/iris/bitstream/10665/250125/1/9789241549639-eng.pdf, accessed 18 December 2018).

[b] Guidelines for treatment of drug-susceptible tuberculosis and patient care, 2017 update (WHO/HTM/TB/2017.05). Geneva: World Health Organization; 2017 (http://apps.who.int/iris/bitstream/10665/255052/1/9789241550000-eng.pdf?ua=1, accessed 18 December 2018).

[c] Ethics guidance for the implementation of the End TB strategy (WHO/HTM/TB/2017.07). Geneva: World Health Organization; 2017 (http://apps.who.int/iris/bitstream/handle/10665/254820/9789241512114-eng.pdf?sequence=1, accessed 18 December 2018).

Evidence and justification

The systematic search yielded 24 observational studies reporting assessment of the use of respiratory separation or isolation of persons with presumed TB, or with patients demonstrated to have infectious TB. As mentioned for Recommendation 1, the Guideline Development Group identified serious limitations with the studies reporting on the impact of administrative measures for TB prevention and control. In the case of respiratory separation measures, sources of indirectness included the use of composite interventions, and variability on how the intervention[26] was implemented. For the latter, for instance, some facilities made use of negative pressure isolation rooms with high-efficiency

[26] Some studies reported the use of specific respiratory measures when separating sources of infection whereas others referred to strict isolation procedures specific to acid-fast bacilli (AFB).

particulate air (HEPA) filtration, whereas others described isolation rooms designed to provide six or more air changes per hour (ACH) or simpler features.

Among the studies identified, about one third (*n*=7) were excluded from the summary because data were not reported in a format suitable for aggregation *(29, 30, 34–38)*. Of the selected studies (*n*=17), 15 were included in the summary analysis (crude summaries of findings) of outcomes related to LTBI and TB disease among health workers *(11, 18–25, 39–44)*; only two additional included studies measured the burden of TB disease among non-health workers; that is, other persons attending health care services *(27, 28)* (see Web Annex B).

Results in this systematic review were indicative of an absolute risk reduction of 2% in health workers when persons with presumed TB and confirmed TB patients underwent respiratory separation or isolation. When data were disaggregated by TB burden (low versus high), there was a relatively small reduction in risk of acquiring LTBI when respiratory separation or isolation was implemented, but no significant differences in absolute risk reductions were observed between low and high TB burden settings (1.6% versus 1.9%). In relation to the studies measuring the effect of respiratory separation or isolation on reducing TB incidence among health workers, two studies conducted in secondary and tertiary care facilities in high TB burden settings seemed to show a slight or no reduction in TB incidence among health workers when isolation was implemented. Both of these studies implemented isolation, together with a number of other administrative, environmental and protective infection control measures. In an additional study reporting on the use of isolation (an infection control audit at 121 primary health care facilities in South Africa), the authors reported slightly increased odds of developing smear-positive TB (unadjusted odds ratio [OR]: 1.09; 95% confidence interval [CI] 0.99–1.19) in health workers for a unit increase in the administrative audit tool score, where a higher score equates to better administrative control measures *(11)*.

In this systematic review, estimates of LTBI incidence could not be captured for other persons (e.g. non-health workers) attending health care facilities. However, data from two studies from low TB burden settings were available *(27, 28)*. Estimates of TB disease in the observed groups in these studies seemed to indicate that the risk of developing active TB disease in persons attending secondary or tertiary level facilities was reduced by 12.6% when presumed or confirmed TB cases underwent respiratory separation *(27, 28)*. However, in both these studies, the sample size and the number of outcomes were small (45/306 TB cases before and 5/237 after the intervention); also, the intervention was implemented in combination with other IPC measures.

Evaluated studies seemed to indicate the positive effect of respiratory separation in reducing the risk of acquiring LTBI or of developing active TB disease, particularly in individuals attending health care settings (e.g. non-health workers). However, in this review, isolation of TB patients seemed to have an inconspicuous effect or no effect on the risk of active TB disease among health workers, as indicated earlier.

The recommendation given here was set as conditional, based on the limitations of the data (small estimates of effect and large variance), and the various factors that national authorities need to take into account to ensure that TB-specific IPC measures are properly implemented. The comprehensive and effective implementation of IPC measures relies on the measures being implemented as a package. Also, health care authorities need to consider the value that patients place on the interventions, especially because of social alienation, stigma and financial impact. The Guideline Development Group argued that although respiratory separation or isolation measures are commonly used in various settings as basic measures in IPC practices, current evidence suggests that such measures alone are insufficient to help reduce the risk of transmission, especially among high-risk populations.

The Guideline Development Group emphasized that the risk of transmission of airborne pathogens can increase as a result of inadequate infrastructure of health care facilities, inconsistent use of personal protective equipment such as respirators by health workers, and staff shortages, coupled with lack of knowledge of basic IPC. The panel expressed concerns about the notion of separation

of patients without the implementation of treatment and proper airborne precautions, including airborne precaution protocols. Also, the panel emphasized that success in reducing transmission would depend on how well the interventions were implemented and what standards were followed by those implementing the interventions.

Implementation considerations

It is critical that national health authorities and public health policy-makers consider these recommendations in the context of the burden of disease; the strengths and weaknesses of health systems; and the availability of financial, human and other essential resources. Additionally, they should be aware that the data assessment and conclusions reached by the Guideline Development Group supported the implementation of respiratory separation in certain circumstances (provided that rapid initiation of effective anti-TB treatment is in place), and other measures to prevent or reduce *M. tuberculosis* transmission.

Current recommendations on models of care for all TB patients – including the management of cases with DR-TB, and recommendations on patient care and support – have been described elsewhere *(45–47)*. A decentralized[27] model of care is recommended over a centralized model for TB patients (including those on DR-TB treatment). However, this model of patient care may not be appropriate for patients for whom treatment adherence is of concern, severely ill patients with extremely infectious forms of the disease or serious comorbidities, or cases where there are important barriers to accessing other forms of ambulatory care (e.g. outpatient or community-based care). In such situations, an individual risk assessment should be considered; this assessment should follow a human rights-based approach to TB, balancing the potential risks and benefits of the proposed interventions (i.e. respiratory separation or isolation) to the patient with the potential risks and benefits to health workers and the community in general.

Health care systems must implement available patient care and support measures before resorting to isolation of any person. In situations where isolation is required, this should be decided in consultation with the patient, and carried out in medically appropriate settings.

The Guideline Development Group did not address the use of involuntary hospitalization and incarceration of TB cases.

For the adequate implementation of isolation, it is important that health care authorities and those implementing the interventions consider the rights and freedoms of TB patients, balancing such individual liberties with the advancement of the common good *(47)*.

The use of respiratory isolation or separation measures for TB patients can present several challenges, especially if:

- such measures are not implemented through clear protocols;
- facilities do not meet minimal standards for implementation;
- staff are not trained; and
- the undesirable effects (e.g. perception of alienation) for those affected are not considered.

Appropriate financial resources would be required to provide proper respiratory separation or isolation measures in such a way that the intervention protects the rights of the patient, and does not increase the risk for health workers or other persons attending health care or settings with a high risk of *M. tuberculosis* transmission. In situations where respiratory isolation is not feasible, health care facilities should consider the use of referral systems, in consultation with the patient.

[27] "Decentralized care" was defined as care provided in the local community where the patient lives, by non-specialized or peripheral health centres, by community health workers or nurses, non-specialized doctors, community volunteers or treatment supporters. Care could occur at local venues or at the patient's home or workplace. "Centralized care" was defined as inpatient treatment and care provided solely by specialized DR-TB centres or teams for the duration of the intensive phase of therapy, or until culture or smear conversion *(46)*.

Patients admitted to isolation have higher rates of anxiety and depression than other hospitalized subjects *(48, 49)*. Therefore, it is essential that patients are informed of the rationale for respiratory separation or isolation measures, and that psychological support is provided to patients who are isolated. In addition, health care staff should be trained in the identification of anxiety and depression in TB patients, and the provision of the necessary support. Mental health risk assessments can be conducted to inform isolation decisions, to discuss supportive measures with the patient and their families, and to provide opportunities for the patient to participate in decision-making, as appropriate.

Although evidence on physical separation at home, including specifications of such, was not evaluated in this systematic review, it is important to emphasize current recommendations on decentralized models of care *(46)*. In situations in which patients are considered to be infectious and care is being provided at decentralized facilities (e.g. patient's home), patients and family members providing care should receive clear guidance and indications on IPC, particularly if the TB patient is receiving palliative and end-of-life care.

Settings and target population

The use of respiratory isolation or separation measures applies to health care settings, as well as other settings with a high risk of *M. tuberculosis* transmission (congregate settings where health care services, including hospitalization is provided, such as correctional facilities), regardless of the burden of TB disease in the community.

Initiation and duration of isolation

The systematic review[28] attempted to estimate the effect of effective treatment on the infectiousness of TB cases, to guide the duration of isolation (see Web Annex B). However, the temporal dynamics indicating when effective treatment renders the patient non-infectious could not be ascertained in the present review. Where management policies differ across settings, in some settings individuals with infectious TB are separated at the outset of treatment. However, elsewhere, priority areas of patient care (e.g. treatment supervision, treatment adherence interventions and decentralized models of care) have been recommended. If these measures fail and there is an increased risk of transmission of *M. tuberculosis* to the community, health care authorities can resort to isolating a patient.

In situations in which patients are isolated, de-isolation should be based on the likely infectivity of the individual case and the availability of other supportive systems (in particular, decentralised models of care).

Patients who are isolated for extended periods of time, regardless of disease, have been shown to experience greater levels of anxiety, depression, anger and feelings of imprisonment; this is difficult for patients and their families.

Resources

Health care authorities need to allocate enough resources, based on a needs assessment, to strengthen the implementation of IPC interventions.

Data on the cost of the intervention were not extracted or captured in this systematic review; however, members of the Guideline Development Group discussed the allocation of resources, and noted that this would vary, depending on factors such as existing structures, burden of disease, and respiratory separation or isolation measures (e.g. open-wall concept versus closed-wall isolation rooms).

[28] A systematic review of the literature was conducted to determine how the infectiousness of TB patients (ability to excrete viable bacteria and sustain transmission) changes after starting on effective TB treatment.

Subgroup considerations

The Guideline Development Group did not assess any evidence on the implementation of respiratory separation or isolation measures in children.

Recommendation 3. Prompt initiation of effective treatment

Prompt initiation of effective treatment of people with TB disease is recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care settings or other persons in settings with a high risk of transmission.

(Strong recommendation based on very low certainty in the estimates of effects)

Evidence and justification

Evidence continues to mount that delays in initiation of effective TB treatment increase the probability of onward transmission of the disease *(50, 51)*.

The current systematic review identified four observational studies evaluating how provision of effective treatment (based on TB drug-susceptibility testing [DST]) for TB patients can have an effect on the burden of LTBI among health workers *(19, 20, 40, 42)* (see Web Annex D). The included studies did not assess the incidence of TB disease among health workers. Evaluations in health workers in health care settings where patients rapidly received effective treatment based on DST indicated an absolute risk reduction of 3.4% compared with settings where effective treatment was delayed. The review also identified one retrospective cohort study that evaluated the protective effect of specific IPC measures in other persons attending a New York City hospital *(27)*. Results suggested a reduction of 6.2% in incidence in active TB disease among HIV-positive individuals admitted to the ward, from 19/216 (8.8%) in the period before the intervention to 5/193 (2.6%) after implementation (P = 0.01).

To better inform some of the recommendations outlined within these guidelines, an additional systematic review[29] was undertaken to determine changes to infectiousness once effective anti-TB therapy has been initiated. Considerable variation was noted in the time taken for patients with proven drug-susceptible pulmonary TB receiving appropriate first-line TB treatment to achieve smear and culture conversion (see Web Annex D).

The scope of this systematic review was not to evaluate a particular treatment regimen, but rather to assess the effect on onward transmission of timely administration of effective TB treatment.

TB treatment has a direct effect on survival of TB patients; it also has the potential to indirectly decrease *M. tuberculosis* transmission, provided the treatment is effective (i.e. treatment is appropriate, based on DST results) and administered in a timely manner. In attempting to assess the former, the Guideline Development Group found insufficient data in the systematic review to determine the real impact or effect that administering effective TB treatment has on health workers and on other at-risk groups; however, the panel considered that the desirable effects (i.e. the potential benefits) of the use of treatment outweighed the potential undesirable effects or harms (e.g. adverse events) that could arise from this medical intervention. The rationale for deciding on a strong recommendation in favour of using effective (and timely) TB treatment – based on very low certainty in the evidence – was further informed by discussion of the paradigmatic situations in which a strong recommendation is warranted, despite low certainty in the estimates of effect *(52, 53)*. Members of the Guideline Development Group referenced the first paradigmatic situation, where low certainty evidence suggests a benefit in a life-threatening situation, not only for the patient themselves but to the strong benefit of others who may be exposed to sources of infection, including transmission of resistant strains of *M. tuberculosis*. The

[29] As mentioned above, a systematic review of the literature was conducted to determine how the infectiousness of TB patients (ability to excrete viable bacteria and sustain transmission) changes after starting on effective TB treatment.

Guideline Development Group placed a high value on the benefits of both effective and timely TB treatment at the individual (i.e. patient) level, and the potential reduction in harm (i.e. in transmission) at the community level, given the small incremental cost (or resource use) relative to the benefits. The review, guided by Background question 3 (see Web Annex D), attempted to clarify the period after which TB patients are likely to become less infectious once they have started on effective TB treatment. Bacteriological culture conversion signifies a clear reduction of infectiousness, but does not usually occur during the first weeks of treatment. Many experts believe that reduction in infectiousness takes place much earlier than culture or smear conversion; for example, during the first 2 weeks on effective treatment for drug-susceptible patients. To determine the time point at which patients may not be infectious, four eligible studies were reviewed, with experimental data from animal-based models – using guinea-pigs as sensitive air samplers exposed to air exhausted from dedicated isolation rooms in which human patients with TB were treated. All four studies presented data suggesting that patients on TB treatment are less infectious to guinea-pigs than patients not receiving effective TB treatment, but none of the studies had data indicating the time it takes for a patient receiving effective treatment to become non-infectious to guinea-pigs (see Web annexes B and D to access the data analysis report). The included studies did not effectively capture or stratify data by cavitary disease or cough behaviour.

The Guideline Development Group further emphasized that the estimates of effect of included studies presented a challenge because of the composite nature of interventions on IPC, leading to a high level of indirectness, as presented in selected studies. Other factors (e.g. the applicability of the evidence) were also questioned by the panel. All selected studies were conducted in the USA, during the mid-1990s, principally in HIV wards reporting outbreaks of DR-TB *(19, 20, 27, 40, 42)*.

Implementation considerations

When assessing the evidence, the Guideline Development Group noted that treatment of patients needs to be guided by the use of DST, something that is important for field practitioners and implementers when putting these recommendations into practice. As currently recommended by WHO, universal access[30] to DST for *M. tuberculosis* should be a standard practice in all settings. DR-TB cases treated with first-line regimens are likely to continue to be infectious and propagate ongoing transmission.

National TB programmes must also consider the implementation of other interventions that facilitate treatment adherence, including strengthening of social protection systems for preventing financial hardship; providing nutritional support, and patient and family health education; and implementing decentralized models of care. Instituting this intervention without sufficient support measures may deter patients from continuing treatment.

Resources

Overall, health care infrastructure and available resources will determine access to rapid diagnostics, including DST and, most crucially, sustainable access to anti-TB medication.

Subgroup considerations

Access to effective TB treatment is clearly essential for TB patients to be cured; however, benefits also accrue to the larger community and population in reducing the risk of transmission.

[30] WHO defines universal access to DST as rapid DST for at least rifampicin, and further DST for at least fluoroquinolones and second-line injectable agents in all TB patients with rifampicin resistance *(54)*.

Recommendation 4. Respiratory hygiene (including cough etiquette)

Respiratory hygiene (including cough etiquette) in people with presumed or confirmed TB is recommended to reduce M. tuberculosis transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

(Strong recommendation based on low certainty in the estimates of effects)

Evidence and justification

Respiratory hygiene (including cough etiquette) to reduce the dispersal of respiratory secretions that may contain infectious particles has been used as an additional measure to prevent *M. tuberculosis* transmission. Although there is literature on understanding the dynamics of cough aerosols of *M. tuberculosis*, data for comparing the effectiveness of respiratory hygiene manoeuvres are scarce, especially data on humans. Respiratory hygiene (or hygiene measures) is defined as the practice of covering the mouth and nose during breathing, coughing or sneezing (e.g. wearing a surgical mask or cloth mask, or covering the mouth with tissues, a sleeve, or a flexed elbow or hand, followed by hand hygiene) to reduce the dispersal of airborne respiratory secretions that may contain *M. tuberculosis* bacilli.

The systematic review identified a total of five relevant studies: four before-and-after studies *(18, 24, 25, 28)*, and one animal model measuring the effect of surgical masks used by MDR-TB patients on transmission to guinea-pigs exposed to ward air *(55)* (see Web Annex D). Meta-analysis was precluded because of significant differences between the interventions that were evaluated and potential differences between study populations, which also made it difficult to calculate crude estimates. All studies, apart from the animal study, reported on the effect of composite interventions (i.e. interventions that combine multiple components).

A reduction in the incidence of LTBI was observed in two of the included studies (a reduction in TST conversions in the intervention group compared with the control group). One study showed a reduction of between 4.1 and 12.4 TST conversions per 1000 person-months among health workers *(18)*; the second study indicated that the use of surgical masks by people with presumed or confirmed TB was associated with 14.8% risk reduction in incident TB infection among health workers *(24)*. Estimates from the two studies in which TB disease was measured showed a slight or no reduction in TB incidence in health workers after surgical masks were used by patients; the assessment of the effect of respiratory hygiene on the development of active TB disease in health workers showed a reduction in incident TB of 0.29 cases per 100 person-years in one study *(24)* and of 0.5% in another *(25)*.

Two additional studies assessed the impact of surgical masks used by patients on the burden of TB infection and disease among other persons attending health care settings *(28, 55)*. A prospective cohort study using an animal model evaluated the role of respiratory hygiene in reducing transmission of *M. tuberculosis* in settings with a high risk of *M. tuberculosis* transmission. A retrospective study assessed the effect of implementing IPC measures on transmission during an MDR-TB outbreak, in an HIV ward in Italy *(28)*. The prospective cohort study quantified the effect of surgical masks (worn by MDR-TB patients) on incident infection among pathogen-free guinea-pigs exposed to ward air *(55)*. The study found that 76.6% of animals exposed to air from patients not wearing surgical masks (the control group) became infected with *M. tuberculosis*. In contrast, only 40% of animals exposed to exhaust air from patients wearing masks (the intervention group) acquired infection.[31] The effect of the intervention in animals was extrapolated to a representative control population derived from nine

[31] The methods used to infect guinea-pigs result in high levels of exposure, compared with typical exposure in human populations. Consequently, the absolute proportion of animals with infection is expected to be higher in experimental animal studies than in human studies. To compare the findings in animals with those in humans, the absolute risk difference in a human population was estimated by applying the relative risk in animals to a typical population (based on the average infection incidence in nine studies). Therefore, both the expected absolute risk difference in humans and the relative risk in guinea-pigs are presented for animal studies.

studies where outcomes were measured in humans. Based on this calculation, the intervention would be expected to reduce the incidence of infection from 6.5% in the control group to 3.4% with the intervention – an expected absolute risk reduction of 3.1%. This represents a relative risk reduction of 47.8%. The retrospective outbreak investigation found that no patients developed MDR-TB after IPC measures were fully implemented.

Despite the low certainty in the evidence, the recommendation given here was set as a strong recommendation. As per the five paradigmatic situations offered by the GRADE methodology, this discordance was justified given the potential for preventing a life-threatening or catastrophic situation that could occur in the event that health care or non-health care individuals develop TB infection and progress to active disease. The Guideline Development Group stressed that, despite limited evidence on the impact of respiratory hygiene (e.g. surgical masks worn by infectious TB patients, and cough etiquette) in settings of interest, the use of this measure as part of a composite intervention can help to reduce transmission of *M. tuberculosis*. Such an effect was pronounced in the animal model included in this systematic review, which allowed a more direct assessment of the intervention.

In evaluating the evidence, Guideline Development Group members were concerned that the study using the animal model had been considered of low quality, owing to serious concerns about the indirectness of the data. Panel members argued that animal studies could provide a valid indication of the effectiveness of an intervention. In particular, guinea-pigs are more susceptible to acquiring TB infection than other models, and may show progression of the disease that displays many features of TB in humans. Members of the panel argued that the guinea-pig model of *M. tuberculosis* infection has been used as a valuable tool to understand and describe TB disease mechanisms, as well as its role in determining the effect of specific interventions; hence, if well-conducted, this model can generate high-quality evidence. However, because of the failure to randomize animals to a particular group, the panel argued that the certainty of the evidence should be downgraded by one level due to indirectness (see Web Annex C). A growing body of evidence now suggests that failure to randomize and to employ blind outcome assessment contributes to exaggerated effect sizes in animal studies across a wide range of disease areas; it also fails to provide the foundations for extrapolating animal research findings to humans *(56, 57)*.

The Guideline Development Group noted the limits and limitations of existing data; in particular, the group recognized the lack of data evaluating the effectiveness of other face covers (e.g. covering the mouth and nose with a cloth mask, tissues, a sleeve or a flexed elbow).

Overall, the Guideline Development Group reflected on the reasonable assumption that coughing is an important driving force for transmission of *M. tuberculosis*, and therefore supported a strong recommendation in favour of the use of respiratory hygiene to reduce the release of infectious airborne particles into the environment. The group also emphasized the feasibility of wearing surgical masks.

Implementation considerations

Settings and target population

The use of respiratory hygiene measures applies to individuals with confirmed or presumed TB in all health care settings, as well as to such individuals in other settings with a high risk of *M. tuberculosis* transmission (including households and non-health care congregate settings such as correctional facilities, and refugee and asylum centres), independent of the burden of TB disease in the community and the level of care of the facility (i.e. primary, secondary or tertiary).

Respiratory hygiene must be implemented at all times. The use of surgical masks, in particular, is of utmost importance in waiting rooms, during patient transport and in any situation which can lead to temporary exposure to *M. tuberculosis* (e.g. in physician offices).

Resources

TB continues to be highly stigmatized, with TB patients and their families experiencing considerable discrimination. In some settings, the use of surgical masks by patients may perpetuate social stigma and local misconceptions about TB *(58)*. Thus, the Guideline Development Group emphasized the need to:

- consider health education to key stakeholders – including patients' families, community members and health workers – to better understand the prevailing causes of discrimination and to implement targeted health education programmes;
- institute effective health counselling for patients as part of a comprehensive package of interventions within social protection systems;
- institute respiratory hygiene (including cough etiquette) as a standard practice for coughing patients; and
- provide "how to" information on wearing of surgical masks, during sensitization and educational activities with both patients and health workers.

Surgical masks are part of the standard medical supplies procured by health care facilities. Hence, the provision of surgical masks to patients and a related education programme may incur minimal additional costs, in health care as well as in non-health care settings (e.g. correctional facilities, and refugee and asylum centres).

National authorities will need to consider the additional costs of providing surgical masks to inpatients as well as to those eligible for home isolation, and those under palliative and end-of-life care.

Subgroup considerations

Childhood TB is often paucibacillary, and likely to contribute little to transmission *(59–62)*. The Guideline Development Group acknowledged that use of surgical masks in paediatric TB patients can have a negative psychosocial impact on children and families *(63)*; nevertheless, children should be provided with masks until they are initiated in effective treatment to ensure that they are non-infectious.

The use of surgical masks may be poorly tolerated in severely ill patients. Therefore, health care authorities need to ensure the proper implementation of interventions within the hierarchy of controls for preventing *M. tuberculosis* transmission.

2.2 Environmental controls

To reduce the risk of transmission of *M. tuberculosis*, air can be made less infectious through the use of three principles: dilution, filtration and disinfection. Environmental controls are aimed at reducing the concentration of infectious droplet nuclei in the air. This is achieved by using special ventilation systems to maximize airflow rates or filtration, or by using germicidal ultraviolet (GUV) systems to disinfect the air. Ventilation systems can also be used to control the direction of airflow to reduce the spread of infection; for example, through the use of exhaust fans to generate negative pressure gradients. Environmental controls are used in combination with other IPC measures to help prevent the spread of *M. tuberculosis*.

Recommendation 5. Upper-room germicidal ultraviolet systems

Upper-room germicidal ultraviolet (GUV) systems are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

(Conditional recommendation based on moderate certainty in the estimates of effects)

Evidence and justification

A systematic review assessing the effectiveness of GUV systems yielded a total of five included studies, of which three evaluated IPC interventions involving health workers *(20, 24, 64)* (see Web Annex D). Meta-analysis could not be performed, owing to differences in outcome measurement, and heterogeneity among the interventions.

One of the studies identified *(64)* suggested that the use of composite interventions, including placement of GUV light fixtures or luminaires in patient rooms and common areas, was associated with an 8.8% reduction in TST conversion among health workers. Another study evaluated whether use of GUV systems within TB laboratory units could substantially reduce the incidence of TB infection in health workers *(24)*. This study determined that the implementation of this intervention could contribute to an absolute risk reduction for LTBI of 14.8% among this population, and a reduction in the number of TB cases among health workers of 0.29 cases per 100 person-years. The third study was a retrospective cohort study that evaluated the effect of interventions to prevent *M. tuberculosis* transmission in health care facilities over a 10-year period *(20)*. The authors concluded that the use of mechanical ventilation, in combination with other environmental controls (including the use of GUV), was associated with a 4.1% reduction in TST conversion among health care staff.

The effectiveness of upper-room GUV systems in reducing LTBI and active TB disease in other persons attending health care settings or in settings with a high risk of *M. tuberculosis* transmission was also evaluated through the extrapolation of data from two studies in which infection was measured in animals, again using guinea-pigs as air samplers to measure the quantity of TB in the air *(65, 66)*. Both studies showed reduced rates of LTBI among guinea-pigs following GUV irradiation, compared with no irradiation of the air *(65, 66)*. The model evaluated in South Africa *(65)* demonstrated that 64.4% of the guinea-pigs in the control group compared with 17.7% of animals in the intervention group developed LTBI. The effect of the intervention in animals was extrapolated to a representative control population derived from nine studies where outcomes were measured in humans. Based on this calculation, the intervention would be expected to reduce the incidence of infection from 6.5% in the control group to 1.8% with the intervention – an expected absolute risk reduction of 4.7%. This represents a relative risk reduction of 72.4%. In the experimental model conducted in Peru *(66)*, 34.8% of animals in the control group developed LTBI compared with 9.4% of animals in the intervention group breathing ward air when the UV lights were turned on in the ward. When extrapolated to the same control population, the intervention would be expected to reduce the incidence of infection from 6.5% to 1.8%, a relative risk reduction for TB infection of 72.9%.[32]

There is a growing body of evidence supporting the use of upper-room GUV systems as an effective intervention. The Guideline Development Group placed high value on the benefits presented in the included studies, and considered the evidence to be of moderate certainty for each of the comparisons. The group also acknowledged that – owing to the composite manner in which these IPC measures were implemented in the non-animal studies – it was difficult to discern the magnitude of effect associated with the use of upper-room GUV systems. Some members of the Guideline Development Group considered that the evidence warranted a strong recommendation; however, most of the group voted for the conditional recommendation (voting results: 5 for strong in favour, 11 for conditional in favour, 2 abstentions and 2 absentees). In making this recommendation, the panel emphasized that the effectiveness of such devices in destroying infectious agents would depend not only on the specifications of GUV fixtures themselves, but also on the appropriate selection of areas in which to install the devices, the quality of installation and maintenance, the duration of exposure to UV light (i.e. total exposure time) and the adequacy of air mixing.

[32] The methods used to infect guinea-pigs result in high levels of exposure, compared to with typical exposure in human populations. Consequently, the absolute proportion of animals with infection is expected to be higher in experimental animal studies than in human studies. In order to compare the findings in animals to with those in humans, the absolute risk difference in a human population was estimated by applying the relative risk in animals to a typical population (based upon the average infection incidence in nine studies). Therefore, both the expected absolute risk difference in humans and relative risk in guinea -pigs are presented for animal studies.

Additionally, the panel recognized that the published observational studies in humans raised questions about the applicability of the intervention. For instance, GUV systems were implemented differently in different settings, with variation in unit types, in whether the system was used in conjunction with air-mixing devices and so on.

Implementation considerations

This recommendation is applicable for health care facilities as well as other congregate spaces with a high risk of *M. tuberculosis* transmission. In such settings, upper-room GUV systems should be implemented as part of a standard of care. The Guideline Development Group recognized that, because of cost considerations, the implementation of this intervention may not be feasible in all settings. Low- and middle-income countries that do not have the infrastructure or capacity to fully adopt this recommendation are advised to identify areas of higher risk of transmission, and prioritize the application of this intervention accordingly.

Success in the implementation of this intervention depends on appropriate installation, quality control and maintenance, to ensure that air disinfection occurs without adverse effects. Exceeding the threshold limit value[33] can lead to overexposure,[34] resulting in painful eye and skin irritation; hence, GUV systems must be monitored to ensure that optimal UV dose levels are achieved within a permissible limit of irradiance.

The IPC measures included in these guidelines should not be considered as individual interventions, but rather as a package. The Guideline Development Group recognized the role of upper-room GUV systems, but acknowledged that overreliance on these units as a single measure for IPC – especially without testing, maintenance and validation – may actually increase the risk of exposure to *M. tuberculosis*, defeating the purpose of such systems.

Upper-room GUV systems rely on air mixing between the upper and lower parts of a room. Thus, when implementing this intervention it is essential to consider factors that may affect the vertical air movement and transport of the infectious microorganisms to the upper portion of the room (e.g. use of simple fans to facilitate air movement in a room, temperature differential between the supply air and room air, mechanical ventilation rate and velocity of air out of ventilation diffusers).

Settings and target population

Upper-room GUV systems are suitable for all settings with a high risk of *M. tuberculosis* transmission, but particularly for those that have a significant burden of DR-TB.

In biological chamber studies, the effectiveness of upper-room GUV systems has been reported to decrease as humidity increases above 50–60% *(67)*. However, an evaluation of the efficacy of GUV for preventing transmission of *M. tuberculosis* using a guinea-pig air-sampling model demonstrated a protective effect in a setting where relative humidity was above 70% *(66)*. Additional considerations may be necessary in settings with high humidity (>70%), and the installation of systems with greater upper-room irradiance levels needs careful consideration.

Upper-room GUV systems are not feasible for use in household settings.

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[33] The American Conference of Governmental Industrial Hygienists (ACGIH) Committee on Physical Agents has established a threshold limit value for short-wavelength UV (UV-C) light exposure to avoid skin and eye injuries.

[34] Air cleansing using GUV systems requires that persons in the treated space be shielded from excessive exposure to the UV radiation. To do so, the fixtures are shielded with louvres or bafflers in order to block radiation below the horizontal plane of the fixtures. Unshielded GUV lamps should be used only in areas that are not occupied, and safety features (e.g. switching device to deactivate the lamps in case the doors are opened) should be installed to ensure that overexposure to UVGI cannot occur.

Resources

Although no cost or cost–effectiveness studies were analysed for this review, the Guideline Development Group recognized the variability in cost of upper-room GUV installations in different settings. The group emphasized that, in the long run, the cost of such systems may be justifiable, given the potential reduction in *M. tuberculosis* transmission (and the reduction in other airborne pathogens). However, the ability to justify this intervention will depend on the setting.

Because upper-room GUV systems rely on effective air mixing, it is necessary to ensure adequate air movement. Also, health care authorities must ensure proper allocation of resources for proper installation, running and maintenance and overall sustainability of this intervention.

Recommendation 6. Ventilation systems

Ventilation systems[a,b] (including natural, mixed-mode, mechanical ventilation, and recirculated air through high-efficiency particulate air [HEPA] filters) are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

(Conditional recommendation based on very low certainty in the estimates of effects)

Remarks

[a] The preference for specific ventilation systems is described under implementation considerations.

[b] The use of portable room-air cleaner appliances is not advised as a system to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

Evidence and justification

This systematic review sought to identify all relevant studies on five ventilation systems: natural ventilation, mechanical ventilation, mixed-mode ventilation, recirculated air filtration and room-air cleaner appliances. The systematic search yielded a total of only 10 observational studies, limited to the use of mechanical and mixed-mode ventilation. Eight of these studies evaluated the effect of using mechanical ventilation among health workers and others attending health care facilities or other settings with a high risk of *M. tuberculosis* transmission; six were before-and-after studies *(19–21, 42, 64, 68)*, one was a cohort study *(18)* and one was a case–control study *(69)* (see Web Annex D). In addition, two studies – a prospective cohort study and a retrospective cohort study – evaluated the role of mixed-mode ventilation in protecting health workers *(24, 44)*.

Although the systematic search only identified applicable data on two ventilation systems (mechanical and mixed-mode ventilation), the Guideline Development Group decided to extrapolate data to other ventilation systems and conduct a comparative analysis, based largely on data extrapolation and partially on expert opinion. The aim was to provide information on the use of technologies and systems that have been used in multiple settings for decades. This exercise allowed the Guideline Development Group to develop recommendations regarding the use of natural, mixed-mode, mechanical ventilation and recirculated air through HEPA filtration.

Given the absence of data on portable air cleaner appliances, the Guideline Development Group discussed the prospect of extrapolating available data to infer the potential effect of such devices on the incidence of LTBI and TB disease. However, given the suboptimal capacity[35] of most portable

[35] The use of portable air cleaners has been intended to be temporary in nature and not a substitute for any other ventilation system. Additionally, in settings where these devices may have been implemented, their use has been intended for small-sized rooms, because such devices do not have the airflow capacity to reach a minimum of 12 ACH. In the presence of more cost-effective alternatives for which there is long-term experience of use, and to avoid countries erroneously considering portable room-air cleaners as an equivalent ventilation system, the Guideline Development Group advised against the use of such devices unless further evidence on their impact becomes available.

room-air cleaners, and consequently their limited capacity to provide the number of room-air exchanges required to decrease or eliminate the airborne infective agents, the panel decided not to extrapolate data from other ventilation systems to these portable devices.

In assessing available evidence, the Guideline Development Group acknowledged that meta-analyses could not be performed because of the heterogeneity between the included studies, and that results[36] of each study should be assessed individually. All but one of the studies *(18)* reported a reduction in incidence of LTBI, ranging from 2.9% to 11.5%. The longitudinal cohort study assessed the effect of negative pressure isolation rooms with HEPA filtration and 20 ACH in two tertiary care level hospitals in Brazil, comparing TST conversion rates among health workers with those in two other hospitals where environmental controls were not implemented in patient-care areas. The incidence of TST conversions was 7.4 per 1000 person-years and 8.1 per 1000 person-years in the two facilities where the measures were applied, compared with 12.2 per 1000 person-years and 19.8 per 1000 person-years in the two hospitals where the measures were not applied.

Studies reporting the use of mixed-mode ventilation showed reductions in the rate of LTBI among health workers when this intervention was implemented *(24, 44)*. However, the Guideline Development Group noted differences between the settings as well as the way in which interventions were implemented. The use of composite interventions, in addition to mechanical ventilation, in these studies can give rise to spurious associations. An association between the implementation of mechanical ventilation and an increase in TST conversions among other persons attending high-transmission risk settings was observed during an outbreak investigation at a university in Canada, suggesting that TB contacts attending class in mechanically ventilated rooms were more likely to be TST-positive than those in naturally ventilated rooms *(68)*. This effect could have been spuriously induced through residual confounding, or poor maintenance of mechanical ventilation systems leading to poorer overall ventilation. Also, naturally ventilated rooms may have had a higher ACH rate than rooms ventilated by mechanical systems.

The Guideline Development Group reviewed the evidence from the systematic reviews and discussed the limitations of included studies. Difficulties included dissecting the individual effect or impact of each intervention, and the lack of published studies regarding other forms of mechanical ventilation that have long been implemented in a variety of settings. Despite the lack of data, the panel was able to extrapolate from published studies to make decisions on specific interventions, such as natural and mixed-mode ventilation, and recirculated air filtration. Due to the limitations in the available evidence (discussed above), members of the Guideline Development Group decided that confidence in the evidence was to be rated "very low" because of concern about indirectness.

The Guideline Development Group further discussed and recognized the effectiveness of ventilation systems in providing sufficient dilution of particles in high-risk settings, and in effectively reducing the concentration of airborne *M. tuberculosis*. Although the panel agreed on the advantages that these systems confer – when properly installed according to room geometry, correctly monitored and properly maintained – there is a potential risk of paradoxically increasing the risk of transmission when systems are poorly implemented or poorly maintained. These factors led the group to emphasize the conditionality of this recommendation.

The results, once extrapolated, were used to compare and rank the various ventilation modes, bearing in mind the balance between desirable and undesirable effects, as well as other values and preferences. The Guideline Development Group considered that, in terms of function, natural, mixed-mode and mechanical ventilation systems can be equivalent, provided that they are properly designed, installed and maintained. The Guideline Development Group placed a high value on the overall benefit of natural ventilation, even though such ventilation depends on outdoor weather conditions and can have undesirable effects, such as variable direction and magnitude of airflow and the risk of contamination of adjacent rooms. The group ranked mechanically ventilated systems (mixed-mode)

[36] The following results, as described here, represent the evaluation of mechanical ventilation systems; where results specific to mixed-mode ventilation are mentioned, this is made clear.

second in the comparative assessment, noting that such systems may inadvertently pose a greater hazard if they are poorly designed or not properly maintained. Although no cost–effectiveness studies evaluating mechanically ventilated and other environmental systems were available, the Guideline Development Group decided that mixed-mode ventilation systems were likely to be more affordable than fully mechanical modes or recirculated air filtration systems. The panel emphasized that while robust or highly specialized systems can reduce the concentration of infectious droplet nuclei in the air and thus prevent transmission, such systems may cause a false sense of reassurance, given the challenges in installation and maintenance, and the likelihood of human error in their implementation. In addition, the panel based their judgement on the assumption that, in resource-limited settings, highly specialized systems (e.g. mechanical ventilation systems and recirculated air through HEPA filters) would have a negative impact on equity and access, because they may not be adopted nationwide, being too expensive to install and maintain properly.

Overall, the preference for ventilation systems in resource-limited settings, based on available evidence of effectiveness and assumptions about financial constraints, was (in order of decreasing preference): (i) natural ventilation; (ii) mixed-mode ventilation; (iii) mechanical ventilation; and (iv) recirculated air with HEPA filtration (see Fig. 1). This order of preference may not be applicable in settings where resources are sufficient to procure and sustain more sophisticated systems, or where climatic conditions impede the use of natural or hybrid (mixed-mode) ventilation systems.

Lastly, given the variability of effectiveness in these systems, the Guideline Development Group continued to emphasize the complementarity of the three-level hierarchy of IPC, with a primary focus on administrative controls.

Fig. 1. Comparative assessment for the use of ventilation systems[a]

	Natural ventilation	Mixed-mode ventilation	Mechanical ventilation	Recirculated air with filtration
Balance of effects	★★★★☆	★★★★☆	★★★★☆	★★★☆☆
Resources required	★★★★☆	★★★☆☆	★☆☆☆☆	★★☆☆☆
Cost effectiveness	★★★★★	☆☆☆☆☆	☆☆☆☆☆	☆☆☆☆☆
Equity	★★★★☆	★★★☆☆	★★☆☆☆	★★☆☆☆
Acceptability	★★★★★	★★★★☆	★★★★☆	★★★★☆
Feasibility	★★★★☆	★★★☆☆	★★☆☆☆	★☆☆☆☆

[a] Comparative assessment using a Likert-type model for comparison of interventions through the Grading of Recommendations Assessment, Development and Evaluation (GRADE) GRADEpro Guideline Development Tool (GDT) software. All the items in this scale use the five-point answer format, where the lower number of qualifiers (stars) indicates the least preferred system, based on data extrapolation and on individual judgements and perceptions of each member of the Guideline Development Group on feasibility, resources required and other criteria.

Implementation considerations

The decision on which system to use – natural ventilation, mixed-mode ventilation, mechanical ventilation or recirculated air with HEPA filtration – depends heavily on the needs of a particular setting,

climate, cost–effectiveness assessment and sustainability of resources to ensure proper design and continued adoption of rigorous standards and maintenance.

The use of poorly designed or poorly maintained ventilation systems, leading to inadequate airflow, can result in health care-associated transmission of *M. tuberculosis*. Inadequate ventilation also increases the risk of transmission in other non-health care congregate settings such as correctional facilities, and refugee and asylum centres.

Programmes need to ensure the sustained use of ventilation systems that can provide sufficient dilution and removal of infectious particles. This can be achieved through proper commissioning of ventilation systems.

Settings and target population

Natural ventilation is the preferred ventilation system in resource-limited settings where there is high risk of *M. tuberculosis* transmission. However, the use of mixed-mode ventilation, mechanical ventilation or HEPA filters may be more appropriate in settings where natural ventilation is not suitable because of the climate (e.g. in cold climates) or other constraints. Natural ventilation is also the preferred system in settings with no constant electricity supply.

Resources

The effective implementation and functioning of ventilation systems requires allocation of sufficient resources to:

- conduct risk assessments to assess the direction of airflow or to relocate TB wards to the upper floors of buildings or downwind of non-TB wards; and
- install and maintain such systems in many health care and non-health care congregate settings.

The planning of and budgeting for ventilation systems also needs to consider the costs of regular assessment of ventilation performance and of maintenance (or upgrades for mechanical ventilation systems).

As mentioned earlier, the systematic search did not yield any studies evaluating the effectiveness of portable in-room air cleaner appliances. The Guideline Development Group noted that most portable in-room air cleaner appliances enable too few ACH to adequately reduce the risk of transmission. Hence, the group opted to add a specific remark against the use of these devices until further evidence becomes available.

2.3 Respiratory protection

Respiratory protection controls are designed to further reduce the risk of exposure to *M. tuberculosis* (and other airborne pathogens) for health workers in special areas and circumstances. The recommendations given here are aimed at strengthening these controls, and preventing the inadequate implementation of respiratory protection programmes that may lead to a false sense of security and therefore increase the risk to health care staff.

Recommendation 7. Respiratory protection

Particulate respirators, within the framework of a respiratory protection programme, are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

(Conditional recommendation based on very low certainty in the estimates of effects)

Evidence and justification

A systematic review assessing the effectiveness of respiratory protection in reducing the risk of *M. tuberculosis* transmission yielded a total of nine studies *(18, 20, 22, 24, 29, 30, 35, 42, 64)* (see Web Annex D). It was not possible to use meta-analysis, owing to the considerable heterogeneity between the interventions in the included studies. Most included studies found a reduction in the TST conversion rate with the use of particulate respirators by health workers, suggesting a reduction in the number of new TB infections. The magnitude of the effect varied considerably between the studies, but only one observational study indicated that respiratory protection did not reduce the incidence of LTBI – in this study, the reduction in the number of infections among health workers primarily occurred before the introduction of particulate respirators *(22)*.

The systematic search also identified four studies in which respirators were used as part of a broader respiratory protection programme. No included studies focused on the implementation of respiratory protection programmes in non-health care congregate settings. The included studies provided heterogeneous results on the effect of such programmes to protect health workers from acquiring TB infection or developing TB disease. The reduction in TST conversion ranged from a 4.3% absolute reduction (with the introduction of particulate respirators and fit-testing as part of a respiratory protection programme) to a 14.8% reduction.

As observed in other interventions, a major limitation in the included studies was the inability to estimate the effect of the individual component of the intervention, because the intervention was introduced as a part of composite IPC measures. For example, the panel noted that determining the impact of respirators alone was impractical, given that respirator use is recommended within the framework of a comprehensive respiratory protection programme.

The Guideline Development Group indicated that the differences in effect estimates could be attributed not only to the variation in the composite interventions in different studies, but also to variations in the characteristics of study populations. The panel also recognized that multiple factors can affect the overall effectiveness of respiratory protection. In essence, the overall pass rate (level of protection) depends on whether respirators have been properly fit-tested and maintained, as well as the adequacy of the training for health care staff and other components of the respiratory protection programme.

Among the nine studies included in this systematic review, only two confirmed the use of formal respirator fit-testing before use of the respirator *(20, 24)*. This means that additional variance in the observed effect in each study could be the result of variable levels of protection caused by respirator face pieces not being tightly fitted, resulting in lower pass rates. The Guideline Development Group rated the quality of the evidence as "very low" owing to concerns about indirectness and serious risk of bias.

Implementation considerations

Health care authorities must ensure proper allocation of resources to strengthen the implementation of TB IPC measures. The Guideline Development Group re-emphasized that the implementation of IPC measures must be adopted as a package of interventions based on a three-level hierarchy of controls.

In line with international standards on occupational safety and health, it is imperative that national health care authorities make use of particulate respirators for health workers only when a respiratory protection programme can be put in place. Attempting to establish one without the other may lead to overreliance on respirators, and give a false sense of protection.

When setting up respiratory protection programmes, health care authorities must also consider the provision of respiratory protection to include community health workers at risk of exposure to individuals with TB.

The panel acknowledged that an important advantage of properly implemented respiratory protection programmes is the appropriate use of particulate respirators and increased compliance among health workers. Effective implementation involves employee education and training activities on the proper use and maintenance (including repair and disposal) of particulate respirators, and periodic audits of practice.

The implementation of respiratory protection for health workers is recommended in health care facilities and other institutions where patients undergo treatment and care. Respiratory IPC measures, including the use of respirators, are also required for family members who are providing close care for patients with TB receiving palliative and end-of-life care.

Resources

Given that the use of particulate respirators is to be implemented within respiratory protection programmes, the necessary resources should be made available to ensure their proper functioning and sustainability. Although the panel emphasized that investment needs would depend on existing infrastructure and service demand, the allocation of resources seemed reasonable when compared with the estimated costs of treating TB in settings with a high risk of *M. tuberculosis* transmission.

Subgroup considerations

Health workers with impaired lung function (e.g. as a result of asthma or chronic obstructive pulmonary disease) may be physically unable to wear a particulate respirator.

Respirators should be worn by all personnel entering high-risk areas, in particular by health workers living with HIV, given the increased risk of developing TB disease if exposed in the workplace.

Settings and target population

The recommendation to use particulate respirators by health workers applies to all health care settings, and to non-health care congregate settings such as correctional facilities. It also applies to other settings where health care services are provided to individuals with presumed and confirmed TB (e.g. refugee and asylum centres).

3. Core components of IPC programmes

The threats posed by epidemics, pandemics and AMR have become increasingly evident as ongoing universal challenges, and they are now recognized as a top priority for action on the global health agenda. Effective IPC is the cornerstone of such action. The *International health regulations* position effective IPC as a key strategy for dealing with public health threats of international concern *(70)*. More recently, the United Nations Sustainable Development Goals (SDGs) highlighted the importance of IPC to safe, effective, high-quality health service delivery and universal health coverage.

In 2016, the WHO Department of Service Delivery and Safety issued a set of guidelines on core components of IPC programmes *(13)*. These core components were founded on earlier recommendations issued in 2009 *(7)*, and work done by the systematic review and evidence-based guidance on organization of hospital infection control programmes (SIGHT) study group *(71)*.

The goal of the 2016 guidelines was to provide the most recent evidence-based recommendations and good practice statements on the core components of IPC programmes that are required at the national level (including various levels within the health care structure) and acute health facility level, with the aim of addressing current and preventing future threats, strengthening health service resilience and helping to combat AMR *(13, 72)*. The 2016 guidelines are also intended to support countries in the development of their own national protocols for IPC and AMR action plans, and to support health care facilities as they develop or strengthen their own approaches to IPC. In the context of *M. tuberculosis* transmission, the importance of these core components lies not only in the potential for building effective and sustainable TB IPC programmes at national and facility levels, but also in the potential to strengthen and integrate TB infection control practices with local and national IPC programmes.

The eight core components combine 11 recommendations and three good practice statements developed in a separate WHO guideline development process. They provide information based on evidence and expert consensus that is necessary to establish an IPC programme. Although the core components are focused on prevention of HAIs, infections with epidemic potential and AMR, their implementation should be included in all IPC programmes, and they should underpin activities aimed at preventing and reducing HAI and AMR, including TB. The core components from the guidelines are given below *(13)*.

Since TB is exclusively transmitted by the airborne route, specific administrative, environmental and personal protection measures for airborne infection should be implemented, in line with evidence-based recommendations provided in the relevant chapters of the guidelines on TB prevention and control.

Core component 1. Infection prevention and control programmes

1a. Health care facility level

The panel recommends that an IPC programme with a dedicated, trained team should be in place in each acute health care facility for the purpose of preventing HAIs and combating AMR through IPC good practices.
(Strong recommendation, very low quality of evidence)

1b. National level

Active, stand-alone, national IPC programmes with clearly defined objectives, functions and activities should be established for the purpose of preventing HAIs and combating AMR through IPC good practices. National IPC programmes should be linked with other relevant national and professional organizations.
(Good practice statement)

Core component 2. National and facility level infection prevention and control guidelines

The panel recommends that evidence-based guidelines should be developed and implemented for the purpose of reducing HAI and AMR. The education and training of relevant health care workers on the guideline recommendations and the monitoring of adherence with guideline recommendations should be undertaken to achieve successful implementation.
(Strong recommendation, very low quality of evidence)

Core component 3. Infection prevention and control education and training

3a. Health care facility level

The panel recommends that IPC education should be in place for all health care workers by utilizing team- and task-based strategies that are participatory and include bedside and simulation training to reduce the risk of HAI and AMR.
(Strong recommendation, very low quality of evidence)

3b. National level

The national IPC programme should support the education and training of the health workforce as one of its core functions.
(Good practice statement)

Core component 4. Health care-associated infection surveillance

4a. Health care facility level

The panel recommends that facility-based HAI surveillance should be performed to guide IPC interventions and detect outbreaks, including AMR surveillance with timely feedback of results to health care workers and stakeholders is essential and should be carried out through national networks. *(Strong recommendation, very low quality of evidence)*

4b. National level

The panel recommends that national HAI surveillance programmes and networks that include mechanisms for timely data feedback and with the potential to be used for benchmarking purposes, should be established to reduce HAI and AMR. *(Strong recommendation, very low quality of evidence)*

Core component 5. Multimodal strategies for implementing infection prevention and control activities

5a. Health care facility level

The panel recommends that IPC activities using multimodal strategies should be implemented to improve practices and reduce HAIs and AMR.
(Strong recommendation, low quality of evidence)

5b. National level

The panel recommends that national IPC programmes should coordinate and facilitate the implementation of IPC activities through multimodal strategies on a nationwide or subnational level. *(Strong recommendation, low quality of evidence)*

Core component 6. Monitoring/audit of IPC practices and feedback and control activities

6a. Health care facility level

The panel recommends that regular monitoring/audit and timely feedback of health care practices, according to IPC standards should be performed to prevent and control HAI and AMR at the health care facility level. Feedback should be provided to all audited persons and relevant staff. *(Strong recommendation, low quality of evidence)*

6b. National level

The panel recommends that a national IPC monitoring and evaluation programme should be established to assess the extent to which standards are being met and activities are being performed according to the programme's goals and objectives. Hand hygiene monitoring with feedback should be considered as a key performance indicator at the national level. *(Strong recommendation, moderate quality of evidence)*

Core component 7. Workload, staffing and bed occupancy at the facility level

The panel recommends that the following elements should be adhered to in order to reduce the risk of HAI and the spread of AMR: (1) bed occupancy should not exceed the standard capacity of the facility; (2) health care worker staffing levels should be adequately assigned according to patient workload.
(Strong recommendation, very low quality of evidence)

Core component 8. Built Environment, materials and equipment for IPC at the facility level

8a. General principles

Patient care activities should be undertaken in a clean and/or hygienic environment that facilitates practices related to the prevention and control of HAI, as well as AMR, including all elements around the WASH infrastructure and services and the availability of appropriate IPC materials and equipment.
(Good practice statement)

8b. Materials, equipment and ergonomics for appropriate hand hygiene

The panel recommends that materials and equipment to perform appropriate hand hygiene should be readily available at the point of care.
(Strong recommendation, very low quality of evidence)

AMR: antimicrobial resistance; HAI: health care-associated infection; IPC: infection prevention and control; WASH: water, sanitation and hygiene.

4. Research priorities

During the guideline development process, the Guideline Development Group identified important knowledge gaps that need to be closed through both primary and secondary research in order to better inform the adoption of current IPC practices and, potentially, of new practices.

The general research gaps listed below are to be prioritized for all IPC interventions:

- *Individual effect of interventions*: Most studies informing these guidelines evaluated the effect of composite measures. Consequently, accurate assessment of the effect of a single component of infection control practices was not possible. The Guideline Development Group suggested that further high-quality prospective research studies (e.g. employing randomized designs) be conducted to evaluate the effect of single interventions.
- *Higher quality studies*: Most of the research evidence informing these recommendations comprised uncontrolled before-and-after studies. This design is considered most useful in demonstrating the immediate impacts of short-term interventions, but is less valuable when evaluating long-term interventions, given that other temporal factors may obscure the effects of an intervention. Modelling studies may improve understanding of the likely effect and cost–effectiveness, if appropriately parameterized. Alternative study designs such as randomized controlled trials should be considered to minimize bias. Further experimental studies where outcomes are measured in animals may also provide useful evidence of the effect of selected interventions on transmission – a particular advantage of these studies being that individual IPC interventions may be studied one at a time.
- *Cost–effectiveness*: Limited evidence is available regarding the cost–effectiveness of IPC measures, other than treatment of TB disease. Information from cost–effectiveness research is required to organize IPC measures at all levels of care and other at-risk settings (e.g. congregate settings) in such a way that benefits can be optimized within available resource constraints, especially in resource-limited and high TB burden areas.
- *Implementation science research*: This form of research provides valuable insights into the feasibility and impact of guidelines in a local context. Countries are encouraged to apply implementation science methodologies to systematically evaluate the introduction of TB IPC standards at both national and subnational levels.
- *Risk assessment settings*: Further research is required to strengthen the understanding of the incidence of *M. tuberculosis* infection and TB disease, including its drug-resistant forms, among health workers and other high-risk populations.

The Guideline Development Group further identified various research priorities for individual interventions, as outlined below.

Triage

- Evaluation of different approaches to triage in general, including triage needs and specific priorities for individuals with comorbidities such as HIV and noncommunicable diseases (e.g. triage strategies in HIV facilities and in noncommunicable disease programmes).

Respiratory isolation

- Evaluation of the appropriate duration of respiratory isolation necessary to minimize the risk of infection to others.

Rapid diagnosis and initiation of effective treatment

- Determination of the effect of treatment on the duration of infectiousness of TB patients.

Respiratory hygiene

- High-quality studies evaluating the effectiveness of surgical masks and other non-mask respiratory hygiene interventions in a clinical setting.

Upper-room GUV systems

- Direct research evidence, including programme data, on the effectiveness of upper-room GUV on outcomes that are important to patients and health workers.
- Further research on safe and effective upper-room GUV dosing by space volume (in cubic feet or metres) to guide implementation.

Ventilation systems

- Effect of different air exchange rates in mechanical ventilation systems on transmission of *M. tuberculosis*.
- Effect of mechanical ventilation modes on microclimate of mechanically ventilated settings.
- High-quality research evaluating the effect of portable room-air cleaners.
- Further research on ventilation parameters for portable room-air cleaners and target product profiles for these devices.

Respiratory protection programmes

- Evaluation of the duration of effectiveness of filtering particulate respirators.

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For further information, please contact:

Global TB Programme
World Health Organization
20, Avenue Appia
CH-1211 Geneva 27
Switzerland
Website: www.who.int/tb

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