ECDC **GUIDANCE**

Investigation and control of tuberculosis incidents affecting children in congregate settings

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The content of this guidance was developed by the European Centre for Disease Prevention and Control (ECDC) Tuberculosis Programme, with the support of an external *ad hoc* expert panel composed of experts in the different areas of tuberculosis control, paediatric medicine, outbreak investigations and public health communication. These experts included the following individuals: Walter Haas (chair), Sarah Anderson, Ingela Berggren, Ana Maria Correia, Christophe Delacourt, Enrico Girardi, Sytze Keizer, Iris De Schutter, Margaret O'Sullivan, Petri Ruutu and Martina Vasakova.

The development of this guidance was coordinated by Andreas Sandgren and written by an ECDC editorial team consisting of Andreas Sandgren and Marieke J. van der Werf. We also acknowledge the contribution by Guido Maringhini, and the input provided by the ECDC Advisory Forum members.

In the process of developing this guidance document, an assessment of current national practices of investigation and control of TB incidents and verified outbreaks affecting children in congregate settings was performed. The results of the assessment have been incorporated in the background and the specific chapters of this document. The assessment consisted of two literature reviews, a survey and an in-depth interview study carried out under the contract ECDC/2012/3508 by AIPO Ricerche. We would like to acknowledge the work performed under the contract by Giovanni Battista Migliori, Giovanni Sotgiu, Bernadette Bourdin Trunz, Lia D'Ambrosio, Rosella Centis, Richard Godfrey, Marina Tadolini and Giorgio Besozzi.

The *ad hoc* expert panel opinions expressed in this guidance document are the individual professional advice of the members of the panel. The panel of experts is an independent body and does not represent the interests of a commercial body, a Member State, or a professional organisation. The expert opinions expressed in this document should be regarded as independent scientific panel opinions.

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Contents

Abbreviations

DOT	Directly observed treatment
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
ESTC	European Union Standards for Tuberculosis Care
EU	European Union
HIV	Human immunodeficiency virus
IGRA	Interferon gamma release assay
ISTC	International Standards for Tuberculosis Care
LTBI	Latent tuberculosis infection
MDR TB	Multidrug-resistant tuberculosis
M. tuberculosis	*Mycobacterium tuberculosis*
TB	Tuberculosis
TST	Tuberculin skin test
WHO	World Health Organization
XDR TB	Extensively drug-resistant tuberculosis

Definitions

For the purpose of this document the following definitions have been agreed upon by the *ad hoc* expert panel:

TB incident: Exposure to an infectious TB case with the likely occurrence of TB transmission in a specific setting.

Outbreak: An incident with two or more epidemiologically linked cases of active TB disease.

Congregate setting: A setting outside the household where children meet in a habitual manner or share a limited space for an extended period of hours (i.e. schools, kindergartens/day-care centres/nurseries, private day-care services etc.).

Infectious TB case: a case with proof of shedding/excretion of live *M. tuberculosis* bacteria. If the results of the microbiological analysis are pending, adult and adolescent patients with respiratory TB should be considered to be infectious until the microbiological results are available.

Source case: The person who brought the infection to a new setting and infected others.

Contact: A person who has been exposed to another person with infectious TB, by sharing air space with, the so-called source case.

Index case: A person with suspected or confirmed TB disease, who is defined as the initial case detected by the health care system or by the health authorities prompting a contact investigation. The index case is not necessarily the source case. For the purpose of this document, contacts may be children or adults with evidence of prolonged and frequent exposure to the index case in a congregate setting.

Source finding: The investigation undertaken where the aim is to identify the source case, i.e. the case that infected the index case.

Contact investigation: The investigation undertaken where the aim is to identify possible contacts infected by a source case with infectious TB.

Executive summary

The challenge

Young children who are exposed to people with infectious tuberculosis (TB) have an increased risk of developing TB disease if infected with *Mycobacterium tuberculosis*. The risk for children becoming infected following exposure is the highest through close contact with an infectious person (for example in the household) but also in congregate settings such as schools and nurseries. Most children will progress to develop TB disease within one year after being infected, and as such, childhood TB is an indicator of ongoing transmission within a community. Infants and young children are particularly prone to develop severe forms of TB disease and early detection is important for successful treatment. Thus, to rapidly identify the source case of infection and perform contact investigation around the case is essential for interrupting the transmission to avoid additional infected cases. To stop the transmission of *M. tuberculosis* to children is an essential step towards eliminating TB, as infected children will serve as a pool of infection for future generations.

This document focuses on TB transmission potentially taking place in congregate settings where children are present. We referred to this as a TB incident, as only through investigation can it be determined if a verified outbreak with two or more linked cases of TB disease has taken place or not. Tuberculosis incidents in these settings are often challenged by the potentially large scale of the investigations to identify the source case and exposed contacts. As TB incidents affecting children in congregate settings often generate anxiety and publicity, communication requires special attention in the management of these incidents.

Public health guidance

An assessment of current national practices of TB incidents and verified outbreaks affecting children in congregate settings was done towards developing this document. The assessment identified that most EU/EEA Member States often follow similar approaches in the investigation and control of incidents and verified outbreaks. The approaches used are guided by policies or guidelines which are general for generic outbreak management and complemented with TB guidelines for contact investigation.

ECDC aimed to bring the different components of generic outbreak management and TB specific policies and guidelines together, to develop a more comprehensive package of guidance to capture the elements that are specific for TB incidents affecting children in congregate settings. The purpose of this document is to provide the Member States with expert consensus opinions that can aid the development of national policies and guidelines in the topic.

Common practices and expert opinions

This document summarises current common practices and the opinions of the expert panel on good practices for the investigation and control of TB incidents affecting children in congregate settings. As the investigation and control measures of TB incidents cover several sub-topics the document is divided into several chapters and sections related to the specific sub-topics.

The expert panel defines a TB incident as the exposure to an infectious TB case with the likely occurrence of TB transmission including outbreaks in a specific setting. An outbreak is defined as an incident with two or more epidemiologically linked cases of active TB disease. Thus for the purpose of this guidance document the term 'TB incident' is used throughout as it also includes outbreaks.

Even though young children with TB disease are generally not considered to be infectious, they represent an event of recent transmission from someone else in the near environment. Therefore, a case of TB in a child should always stimulate the initiation of both source finding and contact investigation. The investigation should be triggered where an adult with infectious TB is working in/attending a congregate setting; if a child or adolescent with infectious TB attending a congregate setting is detected, and; if there is a child with non-infectious TB (any site of infection) and where no other source has been identified outside of the congregate setting.

The nature of the type of investigation undertaken will depend on the index case. In incidents where the index case is an infectious TB case, contact investigations with the aim of fining infected contacts is the priority. In incidents where the index case is a (non-infectious) child with TB, there is a need to undertake source finding with the aim to find the individual who infected the child, with subsequent contact tracing around the suspected source case. If the source is not found among the household contacts, the source finding investigation should be expanded to congregate settings where the child could possibly have been exposed.

As in any case where rapid action is needed, preparedness and planning is essential for good performance. This is true also for the investigation and control of TB incidents, in order to rapidly stop transmission and prevent disease development. Therefore the expert panel highlights that a TB incident management plan should be written and available at national and local level before a TB incident occurs and it should include a communication plan due to the often high demands of communication around these incidents. The incident management plan should also specify the roles and responsibilities of involved expertise present in the team investigating a TB incident. In the case of TB incidents affecting children, it will be important to consult paediatric expertise to guide the management of infected or sick children as needed.

The principles of screening for TB infection are the same regardless of the age of the index case and contacts and follows what is often named "progressive, concentric circles" or "stone-in-the-pond" principle. Young children are given a higher priority in the contact investigations compared to other contacts of similar exposure due to their greater susceptibility to TB infection and high risk of progression to active TB disease.

The diagnosis and management of latent TB infection and active TB disease among children should follow existing national and international guidelines. The expert panel however stresses that young children are at increased risk of progression to TB disease if infected, and is a group that benefit the most from chemoprophylaxis and preventive treatment. Provision of chemoprophylaxis and preventive treatment should always follow after an individual risk assessment to evaluate the benefits and potential harm or adverse events of the treatment.

The assessment of current national practices suggests that information on incidents and outbreaks is often not systematically collected and analysed, which leads to a missed opportunity to learn from previous incident and outbreak investigations. The expert panel therefore promotes more analysis of information on TB incidents and outbreaks to evaluate/assess that adequate responses are in place, and to assess lessons learned, in order to improve the investigation and management of future incidents.

Conclusion

With this document, ECDC promotes and encourage Member States to raise the profile of childhood TB in national TB prevention and control strategies and guidelines, taking into consideration that the specific needs of children are important to ensure that all individuals, including children, are getting the highest quality of care.

1 Introduction

1.1 Current situation

The spread of tuberculosis (TB) occurs mainly in settings where prolonged contact between people promotes the transmission from an infectious 'source case' with TB disease to one or several 'contacts'. A main component in containing the spread of TB is to rapidly diagnose and treat infectious TB cases so that the chain of transmission can be interrupted. It is also necessary to trace people who have been in contact with the source case and are likely to have been exposed to infection. Screening of the identified contacts for their infection status allows the detection of latent TB infection (LTBI) or active TB disease. Diagnosing LTBI aims at identifying individuals who would benefit from preventive treatment or follow-up with careful clinical observation, thus reducing the risk of future development of TB disease and promoting early detection.

Children, especially those under the age of five, and adolescents are vulnerable groups that, when infected, are at higher risk of progressing to active TB disease. Childhood TB has long been a relatively overlooked area for TB control, despite the fact that children under the age of 15 years account for over 1 million of the estimated 9 million cases of TB occurring annually in the world [1]. In the European Union/European Economic Area (EU/EEA) Member States, the proportion of overall cases attributable to children under 15 years of age has been reported to be approximately 5% [2].

Given the recent changes in TB epidemiology in low-incidence countries, with a resurgence of cases and a failure in further TB decline, we now observe a renewed emphasis on ensuring correct monitoring, prevention and management of childhood TB. The notion that childhood TB represents a sentinel event of recent transmission, and that infected children represent a potential pool for disease in their adult life, further highlights the need for in depth analysis and knowledge of the epidemiology and control of childhood TB in settings such as the EU/EEA Member States.

When TB occurs among children or staff within congregate settings such as schools and nurseries, this represents an incident where children and staff potentially can be infected. Such incidents generate a great deal of anxiety among parents, children and staff, and there is frequently associated publicity around these incidents. Therefore contact investigations in these settings are delicate. Investigative and management actions may be challenged by the potentially large number of contacts, difficulties in determining the level of exposure, and prioritising whom to screen.

1.2 Scope and purpose of this guidance

ECDC aims to provide EU/EEA Member States with guidance on good practice for the investigation and control of TB incidents affecting children and adolescents aged less than 18 years. The scope of this guidance is intended to be limited to the investigation and control of TB incidents affecting children occurring in congregate settings outside the household, such as schools and nurseries.

This guidance document presents current common practices, evidence and expert opinion regarding good practices for the investigation and control of TB incidents affecting children in congregate settings, in order to provide Member States with support when considering the topic in national TB programmes and/or TB control strategies. It provides Member States with considerations that can aid the development of national documents.

1.3 Document development

Assessment of current practices

In order to provide an overview of current national practices on how TB incidents and verified outbreaks affecting children in congregate settings have been managed, two systematic literature reviews were carried out, supported by the administration of a questionnaire to EU/EEA Member States, whose findings were further integrated by phone interviews. It should be noted that the definition used for the background assessment was different from the one which the expert panel later agreed upon for the purpose of this guidance document. The assessment focused on collecting information on incidents and verified outbreaks with the 'occurrence of at least one case of active TB disease in a child aged 0-14 years, attending a congregate setting for children, which prompted contact investigation and identification of a possible source case'; or, the 'occurrence of an adult active TB index case in a congregate setting for children, which prompted contact investigation for the identification of LTBI and/or active TB disease in children aged 0 to 14 years'.

The literature reviews were developed with the specific aims to: (i) assess the impact of childhood TB incidents and verified outbreaks on the national TB burden; and (ii) describe the evidence on reported practices in the identification and management of TB incidents and verified outbreaks affecting children in the EU/ EEA Member States and selected non EU/EEA low TB incidence countries (i.e. Australia, Canada, United States of America and New Zealand).

In March 2012, ECDC approached all EU/EEA Member States about their willingness to take part in a survey on TB incidents and verified outbreaks affecting children. The majority of the Member States expressed their support and agreed to respond to the survey. A survey was therefore developed and conducted with the aim to identify unpublished data and collect information to gain understanding of: (i) the estimated impact of TB incidents and verified outbreaks affecting children on the overall epidemiological situation of TB among children in the EU/EEA Member States; and (ii) the public health policies, recommendations and current EU/EEA Member States policies, guidelines and practices for the management of TB incidents and verified outbreaks affecting children.

Expert panel

An *ad hoc* expert panel was set-up in order to assess the work of the background assessment, and subsequently express consensus opinions on good practices for triggering investigation and control of TB incidents and outbreaks affecting children. The panel members were identified by ECDC's chief scientist and the TB programme experts by use of the ECDC Expert Directory, by searching the literature for potential experts that publish on related topics, and by professional contacts through the ECDC TB Surveillance and other networks and working groups. The *ad hoc* expert panel was officially appointed by the ECDC director. The experts were selected based on their expertise in the different areas of outbreak investigations, TB control and clinical medicine – including paediatric infectious diseases -, and health communication. The experts were asked to provide opinions based on their professional and scientific merits. The expert opinions expressed are to be considered as personal professional advice of the expert, and the experts are not representing the interests of a commercial body, a Member State or a professional body. The expert opinions expressed should be regarded as independent scientific panel opinions. All members signed a declaration of interest, which was reviewed by the ECDC compliance officer. None of the members of the panel declared any conflicting interests in regard to the discussed topics. The panel was independent from ECDC, which organised, hosted and observed the panel meeting.

Table 1. Members of the independent *ad hoc* expert panel

Name	Affiliation	Country
Walter Haas (CHAIR)	Robert Koch Institute	Germany
Sarah Anderson	Public Health England	UK
Ingela Berggren	Stockholm County Council	Sweden
Ana Maria Correia	Administração Regional de Saúde do Norte	Portugal
Christophe Delacourt	Assistance Publique, Hôpitaux de Paris	France
Enrico Girardi	Istituto Nazionale Malattie Infettive L. Spallanzani	Italy
Sytze Keizer	Amsterdam Municipal Public Health Service	The Netherlands
Iris De Schutter	Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (VUB)	Belgium
Margaret O'Sullivan	Health Service Executive, Ireland	Ireland
Petri Ruutu	National Institute for Health and Welfare	Finland
Martina Vasakova	Thomayer Hospital Prague	Czech Republic

Work process for the expert panel and guidance development

A two-step Delphi process was arranged to collect the opinions of the expert panel. Thereafter, an expert panel meeting was organised in Stockholm, April 2013. Subsequent to the expert panel meeting, a draft of the guidance document was prepared by ECDC and circulated in several rounds to the expert panel from June through September 2013. A complete version was prepared by ECDC in October 2013. The pre-final document was circulated to the ECDC Advisory Forum for input, and after incorporation of some suggestions the final document was approved by the ECDC chief scientist in November 2013. The guidance provided here is based on the evidence available at the time of the expert panel meeting in April 2013. In the event of emergence of new evidence strongly affecting the opinions expressed, this guidance document will be updated in line with the new evidence.

Document format

The main part of the document is the summary of current common practices and the expert opinions on good practices. As the investigation and control measures of TB incidents cover several sub-topics, these have been divided into several chapters and sections. For each section, we present current common practices as derived from the assessment of current national practices, provide the evidence and present a short practise rationale related to the specific sub-topic, followed by the expert opinions formulated as good practices. As the evidence base is very weak for several of the expert opinions expressed, we have also included a chapter on future research needs, as identified by the expert panel, the contractors performing the assessment of practices, and by ECDC.

2 Background

2.1 Childhood TB epidemiology

Estimates from different parts of the world suggest that TB disease among children up to 15 years of age constitute at least 10-20% of the global TB burden [1,3,4].

A comprehensive situational analysis of childhood TB in the EU/EEA in the last decade (2000–2009) showed that 39 695 paediatric TB cases were notified in the EU/EEA, accounting for 4.3% of all notified cases reported overall during that period [5]. During the past decade, the EU/EEA overall paediatric notification rates dropped from 5.5 per 100 000 in 2000 to 4.0 per 100 000 in 2011 [2]. Globally, the diagnosis of TB in children is less frequently confirmed by culture than in adults. This is largely explained by the paucibacillary nature of disease in this age group, higher rates of extra-pulmonary disease than in adults and the difficulty to produce sputum in children below 10 years of age. Clinical and radiological signs of TB on chest x-ray are less specific and pronounced compared to adults. A close link with an index case should always prompt investigation for TB in a child. Overall, during the last decade in the EU/EEA confirmation by culture of paediatric cases has increased from 14.1% in 2000 to 19.2% in 2009 [5]. There is however large variation across the EU/EEA Member States, where certain countries reach above 50% or even 60% culture confirmation of paediatric cases and others confirm only below 10% of the cases.

The study by Sandgren et al. also revealed a poor correlation between childhood TB and overall rates (i.e. low incidence settings revealed disproportionately high or increasing childhood TB notification compared to their overall trends). This poor correlation could be attributable to a number of factors. One hypothesis is that the figures on childhood TB might be particularly sensitive to TB outbreaks due to the small absolute number of cases in contrast to overall epidemiological trends [5].

The finding of increasing numbers of paediatric TB cases clearly highlights the need to pay special attention to transmission of TB to this vulnerable group and to early detection and control of outbreaks affecting children. This is critical to overall TB control and represents an important component towards elimination of the disease in Europe.

2.2 Epidemiology of TB affecting children in congregate settings

Systematic literature reviews, a survey and in-depth interviews were undertaken to provide background information for the development of this guidance document (see Chapter 1.3). The systematic review collected evidence from the literature on published descriptions of TB incidents and verified outbreaks affecting children in congregate settings in the EU/EEA during the period 2004–2011. Ten included articles [6-15] reported on ten different verified outbreaks occurring in five EU/EEA Member States: Ireland (n=1), Italy (n=3), Spain (n=1), Sweden (n=2), and United Kingdom (n=3). The outbreaks occurred either in a primary/junior school (4/10) or in a nursery (4/10), one occurred in a hospital maternity ward (1/10) and one in a secondary school (1/10).

The number of children examined ranged from 29 [13] to 1 340 [6]. The number of children below 15 years of age diagnosed with active TB disease within the outbreaks ranged from a single case [6] in a maternity ward outbreak, to 27 children in a primary school outbreak [15]. The detection rate varied from 0.08% [6] to 38% [13]. Paediatric TB cases detected in these outbreaks accounted for 0.5% [6] to 48.6% [11] of the overall number of reported paediatric TB cases in the respective country for the year of the outbreak. In five of eight studies outbreaks contributed to 10% or less to the overall national burden of paediatric TB.

The number of children below 15 years of age diagnosed with LTBI ranged from nine cases in a primary school outbreak [15] to 118 in a maternity ward outbreak [6]. The LTBI detection rate varied from 6.2% [7] to 34.5% [13]. The number of LTBI cases among children attributable to outbreaks cannot be estimated as most countries do not have national notification data available on LTBI.

To support the data retrieved from the systematic review, a survey was conducted to gain further understanding of the estimated impact of TB outbreaks affecting children on the overall epidemiology of paediatric TB in the EU/EEA. Of the 30 countries invited to participate in the survey, 25 responded to the questionnaire. Sixteen countries had information on verified outbreaks or in some cases also TB incidents, either through notifications in the national surveillance systems or based on unofficial estimates. High variability in number of outbreaks and children affected was observed among the 25 survey responders. While five countries reported no outbreaks, the United Kingdom stood out with 419 events during the period 2004–2011, including both incidents and verified outbreaks.

Ten countries provided information on the number of TB cases among children found by active case finding and potentially attributable to outbreaks. Of these countries, some reported a high percentage of children with TB identified through outbreak investigations, such as 21.7% in Ireland and 19.5% in the Czech Republic. In Norway, no childhood TB cases were identified through outbreak investigation. Overall, 6.1% of the childhood TB cases were attributable to outbreaks.

Only five countries for which there are notification data or estimates for latent TB infection, reported the number of children with LTBI identified in outbreak investigations. In these countries, 0.2 to 44.3% of children with LTBI were identified through outbreak investigations.

Both the systematic review and the survey study give estimates that show the great heterogeneity across different EU/EEA Member States. The core finding of the studies is that the epidemiological information on TB cases and latently infected children detected within outbreak investigations are not sufficiently detailed to allow a precise description of their epidemiological impact within the EU/EEA. There were large uncertainties for both studies. The systematic review is limited by a large under-reporting because of publication bias, as not all outbreaks are published. The survey study is limited by the lack of national notification through routine surveillance of how individual TB cases have been detected. In many Member States detailed information on outbreaks is available on a regional/local level, but not collated at national level.

2.3 Latent tuberculosis infection (LTBI)

Upon exposure and inhalation of airborne droplets containing *Mycobacterium tuberculosis*, a proportion of individuals will be infected and the majority of these develop an immune response that contains the infection. These individuals are asymptomatic but infected. LTBI has been defined as presumptive infection with *M. tuberculosis* complex (usually *M. tuberculosis*), as evidenced by a positive tuberculin skin test (TST) and/or a positive interferon-gamma release assay (IGRA), in the absence of any clinically or radiological signs of disease [16] [17]. Individuals with LTBI are not a source of infection. It is estimated that 5 to 10% of adult immunocompetent individuals with LTBI will develop TB disease during their lifetime. Some groups are at higher risk of progression to TB disease once infected, such as infants, children under five years of age and adolescents [17-22]. The risk of progressing from LTBI to TB disease in these groups is about 20% to 40% depending on age, with the youngest carrying the highest risk of disease progression. The majority of TB disease in children generally develops within the first year after infection. In the event of immunosuppression either induced (e.g. during transplantation; anti-tumour necrosis factor (TNF)-medication) or acquired (e.g. HIV infection), the risk of reactivating TB from LTBI is also increased in adults [23].

2.4 TB disease in children

Children bear severe tuberculosis-related morbidity and mortality and constitute a significant proportion of the disease burden [1,4,5,24,25]. Children, particularly infants under two years of age or immunocompromised (e.g. children with HIV), have the highest risk of developing life-threatening forms of TB disease, including disseminated forms such as TB meningitis or miliary TB [26].

The clinical presentation of TB differs in children from adults. Symptoms and signs are often non-specific and vary from minor to life threatening. The clinical presentation of TB in children can be diverse [27], and can affect basically any organ; however, the most common form of paediatric TB disease is pulmonary TB, and children are more likely to present with primary TB, characterised by pulmonary infiltrates and/or hilar adenopathy [21]. Bacteriological confirmation is difficult to obtain in early disease but the combination of recent household contact, immunologic evidence of TB infection and radiographic signs on the chest allows accurate diagnosis in most cases [21,27,28]. International standards recommend sputum induction, bronchoscopy and nasopharyngeal and gastric lavage in children to obtain samples for culture and drug sensitivity testing [28].

In children with a positive TST, symptoms suggestive of TB, or known contact(s) with an adult TB case, the presence of active TB disease is investigated by clinical examination.

There are differences in the risk of being infectious for children, adolescents and small children respectively [21]. The typical transmitter is an adult with cavitary pulmonary tuberculosis, a chronic productive cough and strongly positive sputum smears. These characteristics do however very rarely occur in children, as they are often not capable of producing sputum and frequently have paucibacillary disease [24]. Children are therefore generally not infectious. In addition, due to the lack of force when they cough infectious droplet nuclei are hardly ever expelled. However, transmission from individual children does occur [29-31] . Adolescents are more often infectious since their manifestations of pulmonary TB are more like those seen in adults [19,21].

3 Summary of current practice and evidence and panel opinions on good practice

3.1 Triggers and scope of a TB incident investigation

3.1.1 Triggers for the investigation of TB incidents affecting children in congregate settings

Current practice, evidence and practice rationale

The consideration to investigate a TB incident in a congregate setting should be the notification and a subsequent risk assessment of any case of active TB disease in this setting. The notification of a TB incident will follow the existing alert and notification practices and legal requirements of the country.

Common practice in incident investigations calls for a cost-effective approach for the risk assessment and to only consider bacteriologically positive cases as index cases and as a trigger for further investigation. From the assessment of current national practices it appears –despite the heterogeneity of findings- that a more cautious approach is often implemented in the case of TB incidents that affect children. The assessment showed that the trigger for extensive investigations is equally divided between adult bacteriologically positive cases and children diagnosed with TB. However, when the source case is identified this can most often be attributed to an infectious adult case.

As young children are at an increased risk of rapid progression from TB infection to disease, the TB incident investigations are also frequently triggered by bacteriologically negative adults or children. To balance this cautious approach, both the high risk of children to develop TB and the cost-effectiveness of the approach should be taken into consideration. An individual risk assessment should always be performed by a team of experienced clinical and public health experts, taking into consideration the characteristics of the index case and of the setting in which the incident occurs.

Young children with TB disease are generally not considered to be infectious. They represent an event of recent transmission from someone else in the near environment. Therefore, a case of paediatric TB should always stimulate the initiation of both source finding and contact investigation.

The expert panel decided that the following index cases should be the triggers for initiating an investigation of a TB incident affecting children in a congregate setting:

Expert opinions

- An adult with infectious TB working in/attending a congregate setting.
- A child with infectious TB attending a congregate setting.
- A child with non-infectious TB (any site of infection) and where no other source has been identified outside of the congregate setting.

3.1.2 Persons to be investigated/ screened during the investigation of TB incidents affecting children in congregate settings

Current practice, evidence and practice rationale

The 'source case' is the individual who brought the infection to the setting and infected others. A 'contact' is someone who has been exposed to a person with infectious TB, by sharing air space with, the so-called source case. The probability of being infected upon exposure increases with the duration and closeness of contact as well as the infectiousness of the source case. The susceptibility of the exposed individual does then determine whether disease will develop after infection. The 'index case' is a person with suspected or confirmed TB disease, who is defined as the initial case detected by the healthcare system or by the health authorities prompting a contact investigation. The index case is not necessarily the source case. For the purpose of this document, contacts may be children or adults with evidence of prolonged and frequent exposure to the index case in a congregate setting.

Incident investigations can include two different types of contact investigation and in children both are undertaken, usually: 'source finding', in which the aim is to identify the source case, i.e. the case that infected the index case; and 'contact investigation', in which the aim is to identify possible contacts infected by a source case. It should be taken into consideration that the source case might have left the congregate setting, and if relevant, the investigation should also include individuals that have attended/worked in the congregate setting in the past.

The nature of the type of investigation undertaken will depend on the index case. In incidents where the index case is an infectious TB case, contact investigations with the aim to find infected contacts is the priority. In incidents where the index case is a (non-infectious) child with TB, there is a need to undertake source finding with

the aim to find the individual who infected the child, with subsequent contact tracing around the suspected source case. If the source is not found among the household contacts, the source finding investigation should be expanded to congregate settings where the child could possibly have been exposed.

The number of children investigated within the context of a TB incident in congregate settings appears to be larger than what is usually reported for other types of active case finding investigations (e.g. household contact investigations). However, these operational and logistical challenges appear to be justified given the proportion of childhood TB cases attributed to outbreaks reported in the systematic review conducted in preparation of this document.

From the perspective of TB elimination, all TB cases and latently infected individuals are relevant, thus all subjects with potential extensive exposure to the index case should be considered of interest and duly investigated. It is important to realise – and this is clear from both the literature review and survey performed– that TB incidents affecting children require comprehensive investigation and should always include both contact investigation to identify possible contacts infected by an infectious adult or paediatric case, and the more cumbersome exercise to identify the source case of infection when the index case is a child (and the source is unknown).

For these two types of investigations of TB incidents in congregate settings, the expert panel found it of relevance to emphasise the following:

Expert opinions

- **Contact investigation/ screening:**
  All individuals working/attending the congregate setting should be considered. Based on an individual risk assessment, priority should be given to the contacts with the most extensive exposure to the index case (according to the stone-in-the-pond principle, see further 3.3.2) and the highest risk for progression to disease (i.e. the very young children, and immunocompromised individuals).
- **Source finding:**
  All individuals working/attending the congregate setting should be considered (if a source has not been identified outside the setting). Based on an individual risk assessment, priority should be given to the individuals with closest contact and the highest risk of transmitting the disease to the index case (usually adults and adolescents).

3.2 Preparedness, planning and responsibilities

3.2.1 Incident management plan for TB incidents affecting children in congregate settings

Current practice, evidence and practice rationale

Preparedness and planning are of utmost importance for preventing infectious disease transmission and managing outbreak events when there is a need for rapid action. As the investigation of TB incidents in congregate settings such as schools are challenged by the potentially large number of contacts, the management of such complex investigations will be greatly facilitated by having plans available. Tuberculosis incidents in congregate settings often generate publicity and anxiety among those affected, therefore communication preparedness is essential.

The expert panel chose to focus on the essential aspects of an incident management plan which would be of particular relevance to TB incidents affecting children, so as not to repeat the full content of a regular outbreak management plan. On the advice of the expert panel, a template for an incident management plan is proposed in Appendix 1. The purpose of the template is to provide a practical example that can be adapted to the specific requirements and needs of the country in order to develop a national incident management plan.

Expert opinions

- A TB incident management plan should be written and available at national and local level before a TB incident occurs and should include a communication plan. A template TB incident management plan is propsed in Appendix 1, which incorporate generic components of the investigation and control of TB incidents.

3.2.2 Responsibilities for initiating the investigation of a TB incident affecting children in congregate settings

Current practice, evidence and practice rationale

The assessment of current national practices does not highlight any particular advantages regarding what level (local/regional/national) holds responsibility for TB incident identification and management. Clearly assigned responsibility for reacting to TB incidents should facilitate the investigation and control in the congregate setting, implementation of measures, and follow-up of cases according to existing guidelines. In several countries a central level institution remains important for national level surveillance of TB incidents affecting children in congregate settings and can facilitate certain aspects of the incident management.

Expert opinions

- Any health professional diagnosing TB in a person working/attending a congregate setting for children should alert the competent health authority having jurisdiction over the location of the incident, and initiate an investigation, as defined in the national legislation.

3.2.3 Roles and expertise in the team investigating a TB incident affecting children in congregate settings

Current practice, evidence and practice rationale

The roles should be defined by national and local guidance, in order to ensure a complete coverage of all the incident investigation and management components.

Expert opinions

The composition of the incident management team should be adapted to the specific situation. The following experts should always be available either within the TB incident team or by way of consultation/ information:

Core members of the TB incident team:

- Specialist in public health (TB/ infectious disease), usually of the competent health authority
- Consultant paediatric expertise (TB/ infectious disease expertise)
- Consultant adult expertise (TB/pulmonology/infectious disease expertise)
- TB Nurse/ (or a nurse with expertise in TB contact investigation)

People to be consulted/informed should include:

- Consultant microbiology expertise
- Communication expertise/manager/spokesperson (for large incident investigations in particular)
- Surveillance expertise/epidemiology expertise
- Representative from the congregate setting
- Municipality representative
- Others as may be appropriate to the particular incident

3.3 Investigation and control of a TB incident

3.3.1 Steps to consider in the investigation and control of a TB incident affecting children in congregate settings

Current practice, evidence and practice rationale

Interventions for the investigation and control of a TB incident should be conducted in line with existing national guidelines and recommendations. There are certain aspects that are of particular importance in investigations of incidents involving children that might not be included in recommendations on outbreak management in general.

Best practices suggest a demand for clear definitions, clear roles and responsibilities, involvement of a specialised team and availability of guidelines for development and implementation of an incident management plan. They are central for successful investigation of TB incidents and outbreaks affecting children.

The assessment of current national practices has highlighted several key steps in the management of TB incidents; however studies and reports measuring the impact of such steps in terms of TB prevention and cost-effectiveness are lacking.

Expert opinions

TB incidents differ in size and complexity. The steps below should be considered in addition to a generic national incident management plan:

- Verification of the alert of a potential TB incident.
- Early preliminary evaluation of the verified TB incident.
- On-site evaluation of the situation
- Identification of the incident management team and assignment of responsibilities.
- Agreement on clear referral pathways with contact details for those to be consulted.
- Assessment and prioritisation of required resources
- Assessment of practicalities of conducting the investigation (including location/s for screening).
- Immediate initiation of screening to ensure early detection of both LTBI and TB cases.
- Simultaneous contact investigation for transmission from index case and for source finding (where source unknown).
- Prioritisation of children for screening based on risk assessment stratified by cumulative exposure and risk of disease progression.
- Initiation of proactive, on-going communication with relevant stakeholders.
- Implementation and monitoring of control measures.
- Management of all active TB and LTBI cases.
- Systematic collection and documentation to allow evaluation and reporting of the TB incident.

3.3.2 Criteria for prioritisation of children to be screened for active TB and LTBI in TB incidents affecting children in congregate settings

Current practice, evidence and practice rationale

There has been a European consensus statement which can help to guide national practices [16,32]. However, a review of the national guidelines and recommendations for contact screening in Europe showed that among existing national guidelines, the criteria for the selection of contacts, the screening process, and the prescription of preventive treatment for LTBI differ [32].

The principles of screening for TB infection are the same regardless of the age of the index case and contacts. After the infectiousness of the index case is established, contacts in the context of a childhood TB incident are commonly traced through what is often named the "progressive, concentric circles" or "stone-in-the-pond" principle [33,34].

The "stone-in-the-pond" principle in practice starts with screening of a restricted number of close contacts. The investigations are extended further if there is evidence of active transmission of infection. The principle gives priority in the assessment according to the highest risk of exposure and the susceptibility of the contact. It also takes into consideration how far to expand contact investigations by assessing whether the expected group prevalence of infection is similar to the observed. If the observed group prevalence of infection is higher than the expected, the contact investigation needs to be expanded.

If young children are among the contacts in given TB incidents, they require a higher priority in the contact investigations compared to contacts of similar exposure due to their greater susceptibility to TB infection and high risk of progression to active TB disease and, especially in children below 2 years of age, to severe or generalised disease. For this reason children below 2 years, and in some European countries below 5 years, are given the highest priority for rapid investigation, independent of the time of exposure to the source case; adolescents are also given higher priority due to increased risk of disease [19-22]. These young children are also given the highest priority for chemoprophylaxis and preventive treatment, even before the presence/absence of infection has been established [16,17,35].

General contact investigation and infection screening guidelines can also be used in the case of MDR TB and XDR TB. Expert opinions and a summary of evidence on the management of contacts of MDR TB and XDR TB patients are provided in another ECDC guidance document [36].

Expert opinions

Criteria 1: Infectivity of the index case

- Evidence of transmission in the household.
- The index case is an adult or adolescent.
- Presence and severity of symptoms/signs compatible with infectious respiratory TB (predictors for infectivity: Acid-fast bacilli positive (PCR-confirmed for *M. tuberculosis*), cavitation, cough, duration of cough.)

Criteria 2: Individual risk factors for rapid progression of disease in potential contacts:

- Age (children less than 5 years, particularly <2 years, have the highest risk of progression; next in priority are adolescents).
- Immunosuppression, including natural/primary (e.g. HIV), disease associated (e.g. malignant hematologic disease), or iatrogenic (TNF-alpha-inhibitors, cytotoxic agents, high-dose or long-term corticosteroids).

Criteria 3: Risk of exposure:

- Through "progressive circles" or "stone-in-the-pond principle": Closest/longest cumulative contact to the index case (re-evaluate if another source case has been identified).
- All children/staff exposed to the index case, especially those with prolonged and repeated exposure.
- Environmental factors such as room size and ventilation should be taken into consideration.

The following are criteria that can be used for prioritisation of children to be screened, these are not mutually exclusive.

3.3.3 Diagnosis of LTBI and active TB in children

Current practice, evidence and practice rationale

Although the diagnosis of LTBI and TB disease in children can be a challenge and forms a clinical continuum, it is certainly feasible with the use of currently available diagnostic tools. LTBI or active TB disease should be suspected in any child with TST and/or IGRA positive results and interpreted in light of: (i) age of the child; (ii) closeness to the index case or source case, if identified; (iii) country of origin of the child, and; (iv) previous BCG vaccination or previous TST/IGRA result, and; (v) the local epidemiological situation. The use, combination and interpretation of these tools and approaches to diagnose infection should be in line with prevailing national and international guidelines.

Several aspects are of importance in the diagnostic process. This includes clinical and radiological examinations and proper use of diagnostic tools (such as making use of rapid molecular methods for the confirmation of disease and for drug susceptibility testing in addition to smear microscopy and culture confirmation). The use of the right specimens (such as gastric aspirates, broncho-alveolar lavage, or induced sputum in children below ten years of age) is also important for the diagnosis.

Expert opinions

Active TB should be diagnosed:

- In line with international or national recommendations.
- In consultation with an expert in paediatric TB, preferably a paediatrician with TB/infectious disease expertise.

Latent TB infection should be diagnosed:

- In line with international and national recommendations.
  [Note: Currently there is varying evidence on the positive predictive value of IGRA for LTBI diagnosis among children <5 years.]
- In consultation with an expert in paediatric TB.
- The intention to treat, when LTBI is diagnosed, should be a guiding principle: all infected subjects should be offered appropriate therapy, unless contraindicated.
- An expert in paediatric TB, preferably a paediatrician with TB/infectious disease expertise (and with MDR TB experience) should be consulted where the suspected source case has MDR TB.

3.3.4 Management of children with active TB disease

Current practice, evidence and practice rationale

Children affected by TB are treated according to national guidelines and taking into account WHO/international recommended guidelines, regimens and directly observed treatment (DOT), as well as the European Union Standards for Tuberculosis Care (ESTC) [37].

Expert opinions

- Children with active TB disease should be managed in line with international or national recommendations and the European Union Standards for Tuberculosis Care.
- Preferably a paediatrician with TB/infectious disease expertise should supervise/ be consulted in the management of a child with active TB disease.

3.3.5 Management of children with LTBI

Current practice, evidence and practice rationale

Young children are at increased risk of progression to TB disease if infected and, according to available evidence, constitute a group that benefits the most from chemoprophylaxis[1] and preventive treatment [35]. However, there is no recent meta-analysis of chemoprophylaxis or preventive treatment for children in general. A Cochrane review from 2011 concluded that chemoprophylaxis and preventive treatment has the potential to play a major public health role by reducing TB incidence and mortality in HIV-infected children. There are not yet, however, enough studies in the general paediatric population to provide specific guidance on duration etc. [38]. As some examples, isoniazid for 6 or 9 months is the international standard regimen. Isoniazid/rifampicin for 3 months is the most frequently recommended or used alternative regimen, followed by a regimen using rifampicin for 4 months [17,39,40], but other national regimens is in practise or under evaluation.

Expert opinions and a summary of evidence on the management of contacts of MDR TB and XDR TB patients are provided in another ECDC guidance document [36]. That guidance document emphasises that the evidence for preventive therapy of MDR TB and XDR TB contacts is very scarce, although for children there are indications of a positive effect of preventive therapy as an alternative to provide information and follow-up with careful clinical observation of the contacts identified to have LTBI [36].

Expert opinions

Chemoprophylaxis[1]:

- Chemoprophylaxis should be given to children in line with national or international guidelines. In particular young children, especially those below 2 years of age, and immunosuppressed children should be treated.
- Exclude active TB disease before initiating chemoprophylaxis.
- Take into account the results of drug susceptibility testing of the suspected source case.
- Ensure proper monitoring of side effects and best possible support to adherence in children provided chemoprophylaxis.
- Educate caregivers about relevant early symptoms and signs of TB, and the need for immediate medical evaluation if symptoms occur.
- Because of lack of evidence, no opinion is provided for the use of chemoprophylaxis when the suspected source case has MDR TB.

LTBI preventive treatment[1]:

- Preventive treatment should be given to children in line with national or international recommendations. In particular young children, especially those below 2 years of age, and immunosuppressed children should be treated.
- Exclude active TB disease before initiating LTBI preventive treatment.
- Take into account the results of drug susceptibility testing of the suspected source case.
- Ensure proper monitoring of side effects and best possible support to adherence in children provided LTBI preventive treatment.
- Because of lack of evidence, no opinion is provided for LTBI preventive treatment when the suspected source case has MDR TB.
- Educate caregivers about relevant early symptoms and signs of TB, and the need for immediate medical evaluation if symptoms occur.
- Educate caregivers about the increased risk of progression to disease when immunosuppressive therapy or an immune compromising conditions is present in a person diagnosed with LTBI.

[1] Chemoprophylaxis is started as soon as possible after exposure of the child, before TST/IGRA results can prove or disprove infection. Chemoprophylaxis is discontinued as soon as infection is disproved. If LTBI however is confirmed (by TST/IGRA 8-12 weeks after exposure) and active TB excluded (by clinical and radiological examinations), it may be continued as preventive treatment. (The terms primary prophylaxis, primary prophylactic treatment and window prophylaxis are also used for the same concept of what we in this document refer to as chemoprophylaxis [16].

3.4 Communication plan

3.4.1 Key requirements for communication around a TB incident affecting children in congregate settings

Current practice, evidence and practice rationale

Information (written and/or verbal) should always be provided at the beginning and end of the TB incident investigation, and in addition as needed. Basic information may be prepared in advance and in different languages according to need. Communication around the incident should be provided by the responsible authority/ies as defined in the specific country/region. From the assessment of current national practices it appears that communication is considered a core activity in all countries. The communication should provide a correct risk interpretation of the event to the affected community and, where necessary, to the public at large.

An explicit communication plan should be part of the national TB incident management plan. In preparation of such a communication plan, the general principles are outlined in the WHO outbreak communication guidelines from 2005 [41].

It is of importance that the communication plan is prepared before an incident or outbreak takes place. This will ensure that the communication is not provided in a state of panic, where initial rushed messages can hamper the incident investigation and the continued communication with involved stakeholders and the public.

The communication should follow some basic principles, in order to build trust. The basic principles that should be ensured are to: be available, embrace openness and transparency; and to provide early, proactive and regular information as needed or requested. As information will need to be provided to a range of stakeholders, the communication should be tailored to recipients. Further, the information provided should be accurate, specific and informative while maintaining patient confidentiality.

Expert opinions

Apart from what is included in the general outbreak communication approach of the WHO outbreak communication guidelines, the expert panel expressed the need to specify certain key considerations for TB incidents affecting children in congregate settings:

To whom:

Stakeholders who should always be communicated with:

- Parents and guardians.
- Representatives, managers, and staff members of the congregate setting.
- All adult and child contacts and the index/ source case, if identified.
- All relevant health practitioners.
- Other relevant authorities.

Stakeholders who should be communicated with as needed:

- Media/general public.
- Other groups that require consideration (such as other professional groups, other child congregate settings etc.).

How:

- Explain to the index case or parents/ guardians of the index case (as appropriate) what needs to happen.
- Provide information/advice material for the parents/guardians. Before screening, written consent of the parents/guardians should be obtained.
- Provide media briefings/statements/interviews as required.
- Have face to face meetings with parents/carers, students, as well as staff and management from the congregate setting, as needed.
- Provide detailed written information to the stakeholders in the congregate setting on what will happen.
- Provide written updates for stakeholders in the congregate setting on the process and progress of the investigation.
- Consider the development of web and social media material.
- Consider a dedicated helpline.
- Provide contact details of all stakeholders in the congregate setting for further information.
- Develop written information material on TB.

Content:

- Explanation of TB infection and TB disease.
- Explanation of what is being done why, where, when, how and by whom.
- Basic information on investigation principles, information on planning of investigation (e.g. process of risk assessment, screening, preventive treatment etc.). It is helpful to include a set of Frequently Asked Questions.
- Importance of patient confidentiality and support.
- Explanation/ reassurance regarding concerns related to TB infectivity/ risk.

3.5 Incident/outbreak documentation and evaluation

3.5.1 Capturing of information on incidents/ outbreaks affecting children in congregate settings in (national) TB surveillance systems

Current practice, evidence and practice rationale

It is helpful if national and local surveillance systems allow the discrimination of those active TB cases identified through, and attributable to, TB incidents in congregate settings. Where available, this allows for the analysis of the contribution of incident-associated cases to national TB notification rates. This would allow for an evaluation of incident management practices and would be of value in estimating resource allocations for future incidents.

Expert opinions

The following information or sources of data would be of value, to allow for a complete capture by surveillance systems of information on incidents that have occurred:

- Document active TB cases with epidemiological links to congregate settings.
- Include information on: if and how the source case was identified (only for children), rationale of case finding, and type of setting.
- Link molecular typing data with epidemiological data. It should be noted that molecular typing data are not routinely available in all countries. In addition, molecular typing data are usually available much later than case notification data.
- Include data on whether there is an epidemiological link to previous incidents involving a congregate setting.
- Use a standardised template for the outbreak report to ensure that all relevant data are captured.
- Link published incident investigation reports to complement notification data.
- Build a national database on the characteristics of occurring incidents.

3.5.2 Evaluation of national epidemiological impact of TB incidents affecting children in congregate settings

Current practice, evidence and practice rationale

By annual analysis of surveillance data it will be possible to assess the contribution of incident related childhood TB cases to overall childhood TB notifications. This would allow a proper assessment of childhood TB trends and monitor magnitude and frequency of outbreaks. In countries with reliable surveillance information, outbreak-related cases may represent a substantial proportion of the national burden; this information allows proper interpretation of occasional spikes in childhood TB notifications at national level.

Expert opinions

Evaluation of the national impact of TB incidents affecting children in congregate settings can be accomplished by:

- Estimating the associated TB disease burden.
- Estimating the associated LTBI burden.

Associated factors might also be examined:

- The outcome of chemoprophylaxis and preventive treatment given, taking into consideration that the level of compliance generally achieved can vary.
- Resources required to respond to the incidents.

Systematically collecting information on TB incidents affords the opportunity to evaluate/assess that adequate responses are in place, and to assess lessons learned, in order to improve the investigation and management of future incidents.

3.5.3 Documentation and reporting of TB incidents and outbreaks affecting children in congregate settings

Current practice, evidence and practice rationale

As shown from the assessment of current national practices, there is an underreporting of outbreaks and especially of incidents where no additional TB cases were identified, and thus confirmed not to be real outbreaks, and therefore there are missed opportunities to learn from previous investigations.

Expert opinions

To encourage and promote sharing of best practices, the expert panel identified the following actions for documentation and reporting to professional audiences:

- Public health and clinical practitioners should be encouraged and supported to publish their work related to outbreak investigations.
- Outbreaks should be documented and reported or published in peer-reviewed journals, bulletins or other professional fora to allow for wide dissemination of experiences and outcomes.
- Outbreak investigation reports should be used as training material for health practitioners.

4 Future research needs

There is a need for further research in this area. The following research priorities were identified by ECDC and the expert panel:

- To define the real burden of TB incidents affecting children in congregate settings
- To develop new, more reliable diagnostic methods to identify LTBI and TB disease, especially in very young children
- To develop a better tool that would allow the identification of infected persons at risk of progressing to TB disease
- To study the cost effectiveness of different strategies for contact investigation
- To study the effectiveness and cost effectiveness of chemoprophylaxis and preventive treatment
- To build evidence on how to manage child contacts to MDR TB patients, including effectiveness of chemoprophylaxis and preventive treatment, and effectiveness of specific drug regimens.

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Appendix I

Template for a TB incident management plan

Background

In the work of defining what should be part of a TB incident management plan (IMP), and while coming to a consensus on the parts of investigation and control of a TB incident, the *ad hoc* scientific panel identified the opportunity to develop a template for a TB incident management plan specifically for TB incidents affecting children in congregate settings.

The following template should be considered as a possible outline against which national incident management plans could be developed, and is complementary to existing national guidelines and general outbreak management plans. The template is not intended to be a comprehensive and definitive incident management plan, but to reflect the key issues, without expanding on all potential considerations, to be taken into account.

For each chapter/element of the template, the rationale is given explaining in brief what the purpose of each chapter/element is. This provides the authors of the national IMPs with a general idea of what should be covered for each element/section of the IMP.

The creation of a national IMP should take into consideration some basic concepts. The plan should:

- Emphasise the importance of timely and efficient investigation to ensure early detection of both LTBI and TB cases, particularly in young children.
- Provide a plan for allocation/ prioritisation of resources to the TB incident/ congregate setting.
- Give clear allocation of responsibilities within the TB incident team and between health authorities.
- Specify the expertise needed within the TB incident team.
- Outline when there is a need for consultation of regional/national health authorities.
- Recommend a visit to the congregate setting.
- Recommend a systematic risk assessment of children (i.e. taking into account degree of exposure and risk for progression to TB disease).
- Provide a plan for the steps included in the investigation and control of the TB incident should be managed.
- Provide a plan for early, transparent and comprehensive communication.
- Provide a plan for systematic collection and documentation of information on the TB incident.

Elements to cover in a TB incident management plan

1 Objective of IMP

The rationale for this chapter is to set the specific objective the incident management plan has, namely to be specific for TB incidents affecting children in congregate settings. The purpose of the IMP is to ensure timely and efficient investigation to detect both LTBI and TB cases in order to treat and follow up appropriately, and to stop further spread of infection during a TB incident affecting children in a congregate setting.

2 Implementation of IMP

The rationale for this chapter is to outline the process by which the IMP should be practically implemented and to provide details related to how to monitor the progress of the implementation of the IMP.

3 Definition of incident

The rationale for this chapter is to provide a specific definition of a TB incident affecting children in congregate settings.

4 Roles and responsibilities

The rationale for this chapter is to specify the expertise needed within the TB incident team and to clearly allocate responsibilities within the TB incident team and between health authorities for the management of TB incidents affecting children in congregate settings. The description of roles and responsibilities should follow those of the national and regional/local jurisdiction for which the IMP is written. Preferably a detailed list of roles and the corresponding responsibilities should be described. General functions/expertise which are suggested to be available/ensured are outlined in Chapter 3.2.3 of this guidance document.

5 Steps in incident investigation and control

The rationale for this chapter is to establish the chronological order of procedures for the investigation and control of a TB incident affecting children in congregate settings. For each subheading, the intention is to describe the importance of each element and to provide the details of how each procedure should be managed according to the national guidelines, as well as taking into account international guidelines, standards and best practices. Below is a suggestion for the chronological order of procedures. The steps outlined in Chapter 3.3.1 of this guidance document may prove useful when determining which elements to be covered here.

- Source finding
- Contact investigation
- Identification of LTBI and TB cases
  - Screening and diagnosis of cases with LTBI
  - Screening and diagnosis of cases with TB disease
- Individual risk assessments
- Implementation of control measures
  - Exclusion of infectious cases from the setting
  - Treatment of active TB cases
  - Chemotherapy/preventive therapy to LTBI cases

6 Communication

The rationale for this chapter is to provide details of communication requirements in a TB incident in order to provide early, transparent and comprehensive communication to all relevant stakeholders affected by the actions taken in the congregate setting.

7 Training

The rationale for this chapter is to fully provide a scheme for the development of educational knowledge for all health care workers and stakeholders involved in the investigation of TB incidents affecting children in congregate settings.

8 Documentation and evaluation

The rationale for this chapter is to provide a description of requirements for the documentation, monitoring and reporting of TB incidents affecting children in congregate settings, as well as the process to evaluate the response connected to the investigations of these TB incidents and to implement lessons learned.

- Document, monitor and report on the results
- Evaluate effectiveness of procedures and process
- Implement lessons learned.

Appendix II

Summary of expert opinions

Area/ Topic	Expert opinion
3.1.1 Triggers for the investigation of TB incidents affecting children in congregate settings	• An adult with infectious TB working in/attending a congregate setting. • A child with infectious TB attending a congregate setting. • A child with non-infectious TB (any site of infection) and where no other source has been identified outside of the congregate setting.
3.1.2 Persons to be investigated/ screened during the investigation of TB incidents affecting children in congregate settings	Contact investigation/ screening: All individuals working/attending the congregate setting should be considered. Based on an individual risk assessment, priority should be given to the contacts with the most extensive exposure to the index case (according to the stone-in-the-pond principle, see 3.3.2) and the highest risk for progression to disease (i.e. the very young children, and immunocompromised individuals). Source finding: All individuals working/attending the congregate setting should be considered (if a source has not been identified outside the setting). Based on an individual risk assessment, priority should be given to the individuals with closest contact and the highest risk of transmitting the disease to the index case (usually adults and adolescents).
3.2.1 Incident management plan for TB incidents affecting children in congregate settings	A TB incident management plan should be written and available at national and local level before a TB incident occurs and should include a communication plan. A template TB incident management plan is propsed in Appendix 1, which incorporates generic components of the investigation and control of TB incidents.
3.2.2 Responsibilities for initiating the investigation of a TB incident affecting children in congregate settings	Any health professional diagnosing TB in a person working/attending a congregate setting for children should alert the competent health authority having jurisdiction over the location of the incident, and initiate an investigation, as defined in the national legislation.
3.2.3 Roles and expertise in the team investigating a TB incident affecting children in congregate settings	The composition of the incident management team should be adapted to the specific situation. The following experts should always be available either within the TB incident team or by way of consultation/ information: Core members of the TB incident team: • Specialist in public health (TB/ infectious disease), usually of the competent health authority • Consultant paediatric expertise (TB/ infectious disease expertise) • Consultant adult expertise (TB/pulmonology/infectious disease expertise) • TB Nurse/ (or a nurse with expertise in TB contact investigation) People to be consulted/informed should include: • Consultant microbiology expertise • Communication expertise/manager/spokesperson (for large incident investigations in particular) • Surveillance expertise/epidemiology expertise • Representative from the congregate setting • Municipality representative • Others as may be appropriate to the particular incident
3.3.1 Steps to consider in the investigation and control of a TB incident affecting children in congregate settings	TB incidents differ in size and complexity. The steps below should be considered in addition to a generic national incident management plan: • Verification of the alert of a potential TB incident. • Early preliminary evaluation of the verified TB incident. • On-site evaluation of the situation • Identification of the incident management team and assignment of responsibilities. • Agreement on clear referral pathways with contact details for those to be consulted. • Assessment and prioritisation of required resources • Assessment of practicalities of conducting the investigation (including location/s for screening). • Immediate initiation of screening to ensure early detection of both LTBI and TB cases. • Simultaneous contact investigation for transmission from index case and for source finding (where source unknown). • Prioritisation of children for screening based on risk assessment stratified by cumulative exposure and risk of disease progression. • Initiation of proactive, on-going communication with relevant stakeholders. • Implementation and monitoring of control measures. • Management of all active TB and LTBI cases. • Systematic collection and documentation to allow evaluation and reporting of the TB incident.

Area/ Topic	Expert opinion
3.3.2 Criteria for prioritisation of children to be screened for active TB and LTBI in TB incidents affecting children in congregate settings	The following are criteria that can be used for prioritisation of children to be screened, these are not mutually exclusive. Criteria 1: Infectivity of the index case • Evidence of transmission in the household. • The index case is an adult or adolescent. • Presence and severity of symptoms/signs compatible with infectious respiratory TB (predictors for infectivity: Acid-fast bacilli positive (PCR-confirmed for M. tuberculosis), cavitation, cough, duration of cough.) Criteria 2: Individual risk factors for rapid progression of disease in potential contacts: • Age (children less than 5 years, particularly <2 years, have the highest risk of progression; next in priority are adolescents). • Immunosuppression, including natural/primary (e.g. HIV), disease associated (e.g. malignant hematologic disease), or iatrogenic (TNF-alpha-inhibitors, cytotoxic agents, high-dose or long-term corticosteroids). Criteria 3: Risk of exposure: • Through "progressive circles" or "stone-in-the-pond principle": Closest/longest cumulative contact to the index case (re-evaluate if another source case has been identified). • All children/staff exposed to the index case, especially those with prolonged and repeated exposure. • Environmental factors such as room size and ventilation should be taken into consideration.
3.3.3 Diagnosis of LTBI and active TB in children	Active TB should be diagnosed: • In line with international or national recommendations. • In consultation with an expert in paediatric TB, preferably a paediatrician with TB/infectious disease expertise. Latent TB infection should be diagnosed: • In line with international and national recommendations. [Note: Currently there is varying evidence on the positive predictive value of IGRA for LTBI diagnosis among children <5 years.] • In consultation with an expert in paediatric TB. • The intention to treat, when LTBI is diagnosed, should be a guiding principle: all infected subjects should be offered appropriate therapy, unless contraindicated. • An expert in paediatric TB, preferably a paediatrician with TB/infectious disease expertise (and with MDR TB experience) should be consulted where the suspected source case has MDR TB.
3.3.4 Management of children with active TB disease	• Children with active TB disease should be managed in line with international or national recommendations and the European Union Standards for Tuberculosis Care. • Preferably a paediatrician with TB/infectious disease expertise should supervise/ be consulted in the management of a child with active TB disease.
3.3.5 Management of children with LTBI	Chemoprophylaxis[1]: • Chemoprophylaxis should be given to children in line with national or international guidelines. In particular young children, especially those below 2 years of age, and immunosuppressed children should be treated. • Exclude active TB disease before initiating chemoprophylaxis. • Take into account the results of drug susceptibility testing of the suspected source case. • Ensure proper monitoring of side effects and best possible support to adherence in children provided chemoprophylaxis. • Educate caregivers about relevant early symptoms and signs of TB, and the need for immediate medical evaluation if symptoms occur. • Because of lack of evidence, no opinion is provided for the use of chemoprophylaxis when the suspected source case has MDR TB. LTBI preventive treatment[1]: • Preventive treatment should be given to children in line with national or international recommendations. In particular young children, especially those below 2 years of age, and immunosuppressed children should be treated. • Exclude active TB disease before initiating LTBI preventive treatment. • Take into account the results of drug susceptibility testing of the suspected source case. • Ensure proper monitoring of side effects and best possible support to adherence in children provided LTBI preventive treatment. • Because of lack of evidence, no opinion is provided for LTBI preventive treatment when the suspected source case has MDR TB. • Educate caregivers about relevant early symptoms and signs of TB, and the need for immediate medical evaluation if symptoms occur. • Educate caregivers about the increased risk of progression to disease when immunosuppressive therapy or an immune compromising conditions is present in a person diagnosed with LTBI. *[1] Chemoprophylaxis is started as soon as possible after exposure of the child, before TST/IGRA results can prove or disprove infection. Chemoprophylaxis is discontinued as soon as infection is disproved. If LTBI however is confirmed (by TST/IGRA 8-12 weeks after exposure) and active TB excluded (by clinical and radiological examinations), it may be continued as preventive treatment. (The terms primary prophylaxis, primary prophylactic treatment and window prophylaxis are also used for the same concept of what we in this document refer to as chemoprophylaxis.*

Area/ Topic	Expert opinion
3.4.1 Key requirements for communication around a TB incident affecting children in congregate settings	Apart from what is included in the general outbreak communication approach of the WHO outbreak communication guidelines, the expert panel expressed the need to specify certain key considerations for TB incidents affecting children in congregate settings: To whom: *Stakeholders who should always be communicated with:* • Parents and guardians. • Representatives, managers, and staff members of the congregate setting. • All adult and child contacts and the index/ source case, if identified. • All relevant health practitioners. • Other relevant authorities. *Stakeholders who should be communicated with as needed:* • Media/general public. • Other groups that require consideration (such as other professional groups, other child congregate settings etc.). How: • Explain to the index case or parents/ guardians of the index case (as appropriate) what needs to happen. • Provide information/advice material for the parents/guardians. Before screening, written consent of the parents/guardians should be obtained. • Provide media briefings/statements/interviews as required. • Have face to face meetings with parents/carers, students, as well as staff and management from the congregate setting, as needed. • Provide detailed written information to the stakeholders in the congregate setting on what will happen. • Provide written updates for stakeholders in the congregate setting on the process and progress of the investigation. • Consider the development of web and social media material. • Consider a dedicated helpline. • Provide contact details of all stakeholders in the congregate setting for further information. • Develop written information material on TB. Content: • Explanation of TB infection and TB disease. • Explanation of what is being done why, where, when, how and by whom. • Basic information on investigation principles, information on planning of investigation (e.g. process of risk assessment, screening, preventive treatment etc.). It is helpful to include a set of Frequently Asked Questions. • Importance of patient confidentiality and support. • Explanation/ reassurance regarding concerns related to TB infectivity/ risk.
3.5.1 Capturing of information on incidents/ outbreaks affecting children in congregate settings in (national) TB surveillance systems	The following information or sources of data would be of value, to allow for a complete capture by surveillance systems of information on incidents that have occurred: • Document active TB cases with epidemiological links to congregate settings. • Include information on: if and how the source case was identified (only for children), rationale of case finding, and type of setting. • Link molecular typing data with epidemiological data. It should be noted that molecular typing data are not routinely available in all countries. In addition, molecular typing data are usually available much later than case notification data. • Include data on whether there is an epidemiological link to previous incidents involving a congregate setting. • Use a standardised template for the outbreak report to ensure that all relevant data are captured. • Link published incident investigation reports to complement notification data. • Build a national database on the characteristics of occurring incidents.
3.5.2 Evaluation of national epidemiological impact of TB incidents affecting children in congregate settings	Evaluation of the national impact of TB incidents affecting children in congregate settings can be accomplished by: • Estimating the associated TB disease burden. • Estimating the associated LTBI burden. Associated factors might also be examined: • The outcome of chemoprophylaxis and preventive treatment given, taking into consideration that the level of compliance generally achieved can vary. • Resources required to respond to the incidents. Systematically collecting information on TB incidents affords the opportunity to evaluate/assess that adequate responses are in place, and to assess lessons learned, in order to improve the investigation and management of future incidents.
3.5.3 Documentation and reporting of TB incidents and outbreaks affecting children in congregate settings	To encourage and promote sharing of best practices, the expert panel identified the following actions for documentation and reporting to professional audiences: • Public health and clinical practitioners should be encouraged and supported to publish their work related to outbreak investigations. • Outbreaks should be documented and reported or published in peer-reviewed journals, bulletins or other professional fora to allow for wide dissemination of experiences and outcomes. • Outbreak investigation reports should be used as training material for health practitioners.