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Regional workshop on child and adolescent tuberculosis in the WHO European Region

**29–30 January 2020
Copenhagen, Denmark**

ABSTRACT

Against the backdrop of widespread tuberculosis (TB) among vulnerable and marginalized populations, including children and adolescents, and in the context of increasing complexities resulting from HIV coinfection and multidrug-resistant TB (MDR-TB), the WHO Regional Office for Europe convened a workshop of key experts working in the field of both TB and paediatric specialties in the WHO European Region on 29–30 January 2020. Key issues, such as the need for preventing TB in children and adolescents through contact-tracing of TB patients, the availability of child-friendly formulations, the role of the bacille Calmette–Guérin (BCG) vaccine, and the importance of patient and child-centred care, were discussed at length, and practices and experiences were shared. This report summarizes the keynote presentations and ensuing interactions among participants, poster sessions, and panel and group discussions.

Keywords

TUBERCULOSIS – DIAGNOSIS, DRUG THERAPY,
PREVENTION AND CONTROL
TUBERCULOSIS, MULTIDRUG-RESISTANT –
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Acronyms

ART	antiretroviral therapy
BCG	bacille Calmette–Guérin
DR-TB	drug-resistant tuberculosis
DST	drug-susceptibility testing
DS-TB	drug-susceptible tuberculosis
ECDC	European Centre for Disease Prevention and Control
EU	European Union
GDF	Global Drug Facility
GRADE	Grading of Recommendations Assessment, Development and Evaluation (approach)
IFRC	International Federation of Red Cross and Red Crescent
IGRA	interferon gamma release assay (test)
IMCI	Integrated Management of Childhood Illness
LTBI	latent tuberculosis infection
MDR-TB	multidrug-resistant tuberculosis
M/XDR-TB	multidrug and extensively drug-resistant TB
PTB-net	Pediatric Tuberculosis Network European Trials group
SDGs	(United Nations) Sustainable Development Goals
STBP/GDF	Stop TB Partnership and Global Drug Facility
TB	tuberculosis
TPT	TB prevention treatment
TST	tuberculin skin test
UNICEF	United Nations Children’s Fund
XDR-TB	extensively drug-resistant tuberculosis

Executive summary

After decades of relative neglect, the tuberculosis (TB) epidemic in children is back in the spotlight. The goal of zero TB deaths in children has been endorsed by the international TB community, and the United Nations TB high-level meeting political declaration underscores the need to also focus on TB in children and adolescents. Key stakeholders have united in their efforts to make these goals a reality.

The WHO Regional Office for Europe convened a regional workshop on child and adolescent TB in Copenhagen, Denmark on 29–30 January 2020. Its aims were to discuss the implications of the United Nations TB high-level meeting political declaration regarding child and adolescent TB, and to share and plan common and enhanced national strategies to combat current regional childhood TB challenges. The workshop brought together country representatives and experts from 34 countries or territories of the Region, representatives of international partners and colleagues from the WHO Global TB Programme.

Through presentations, poster sessions, panel discussions and group work, several challenges were identified and suggestions for priority actions put forward and discussed. Key themes of the discussions included:

- the necessity of preventing TB in children and adolescents through enhanced contact-tracing of TB patients;
- the availability of child-friendly formulations, especially in European Union countries;
- the role of the bacille Calmette–Guérin (BCG) vaccine in child vaccination programmes;
- the importance of patient- and child-centred care, and transitioning away from institutionalization of children with TB;
- stigma associated with TB in general and for children and adolescents specifically;
- the role of intersectoral actions and initiatives beyond the health-care sector; and
- the need for greater awareness of TB among health-care workers.

Introduction

After decades of relative neglect, the tuberculosis (TB) epidemic in children¹ is back in the spotlight. The goal of zero TB deaths in children has been endorsed by the international TB community, and the United Nations TB high-level meeting political declaration underscores the need to also focus on TB in children and adolescents. Key stakeholders have united in their efforts to make these goals a reality.

Childhood TB can only effectively be addressed by collaboration across health systems and communities. It is critical that childhood TB is prioritized in national health strategies, plans and budgets, and that childhood TB services are well integrated within national health systems, embracing primary health care, paediatric and maternal care services and other mother and child health initiatives. TB is difficult to diagnose in young children and may remain undetected until the onset of serious forms of the disease. Vigilance and early diagnosis are essential to prevent unnecessary suffering and improve treatment outcomes.

TB in adolescents poses additional challenges, as this age group is more prone to the effects of social marginalization, stigma and discrimination. Unnecessary and prolonged hospitalization during the pre-adult life stage has long-lasting consequences for educational attainment, employment opportunities and relationship prospects. This age group is also more likely to experience the psychological and physical consequences of the disease, and some adolescents may also start to exhibit behaviours such as alcohol abuse and smoking. Treatment services therefore must recognize and be attuned to the unique needs of this age group.

The Regional Workshop on Child and Adolescent Tuberculosis in the WHO European Region took place in Copenhagen, Denmark on the 29–30 January 2020. It brought together country representatives and experts from 34 countries or territories of the Region, representatives of international partners (the European Centre for Disease Prevention and Control (ECDC), the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), United Nations Children's Fund (UNICEF), the KNCV TB Foundation, the Global Drug Facility (GDF), Stop TB, TB People, the International Federation of Red Cross and Red Crescent (IFRC) and the Pediatric Tuberculosis Network European Trials group (PTB-net)) and colleagues from the WHO Global TB Programme. Progress made since the previous regional childhood TB meeting held in Copenhagen in December 2017 and major challenges across a range of highly relevant topics in paediatric TB were openly debated at poster sessions and panel and group discussions. Important updates were given on new developments in the diagnosis and treatment of childhood TB and on access to child-friendly drug formulations for TB in the Region. Participants also engaged in group work to identify priorities for action to strengthen national policies.

The objectives of the two-day workshop were to:

- discuss the implications of the United Nations TB high-level meeting political declaration regarding child and adolescent TB, and share and plan common and enhanced national strategies to combat current regional childhood TB challenges;
- follow up on the previous two child and adolescent TB workshops of the WHO European Region in 2015 and 2017;
- update Member States on new WHO global guidelines on multidrug-resistant TB (MDR-TB) and its implications for child and adolescent TB;
- present the newly prepared (2019) expert regional opinion document on childhood MDR-TB; and
- present an update on modified child TB estimate methodology and its implications for the WHO European Region.

¹ All references to TB in children in this document include TB in both children and adolescents.

The expected outcomes from the workshop were that participants would:

- be updated on key changes to, and aspects of, the management and treatment of childhood TB, including the recently published global WHO MDR-TB guidelines and the regional guidance/expert opinion document on childhood TB; and
- define next steps in updating elements of current national strategic plans relevant to childhood TB in line with the global End TB Strategy (1) and the TB action plan for the WHO European Region 2016–2020 (2).

This report summarizes keynote presentations by distinguished experts, country presentations from two selected Member States, and panel and group discussions among participants. The meeting's scope and purpose is shown at Annex 1, the programme at Annex 2 and participants at Annex 3.

Background

TB continues to be an important public health problem in the WHO European Region. Significant challenges, such as widespread TB among vulnerable and marginalized populations (including children and adolescents), increasing HIV coinfection and high rates of MDR-TB, are further hampering efforts to reach the strategic goal to End TB by 2035 and achieve the pre-elimination phase for TB in the Region.

The age-specific challenges for TB prevention and care in children and adolescents are increasingly recognized. Addressing these challenges requires greater focus by national TB programmes and increased public health prioritization. This is as relevant in the WHO European Region as in the rest of the world. The challenges are even more pronounced when addressing the MDR-TB epidemic, as the WHO European Region has the highest proportion of the global MDR-TB burden, being home to 10 of 30 high MDR-TB burden countries.

The full scope of the global and regional problem of TB in children and adolescents is not fully known. In the WHO European Region, more than 7200 children and adolescents under 15 years of age account for about 4% of notified new TB patients (2016 data). In addition to a large undiagnosed MDR-TB disease burden, recent modelling suggests that in the WHO European Region, 14.1% of children with TB were infected with MDR strains, the highest proportion in the world. This represents a vast reservoir of future MDR-TB cases that will contribute to ongoing transmission and propagation of the epidemic.

After decades of relative neglect, the childhood TB epidemic is now in the spotlight. TB elimination, as set out by the United Nations Sustainable Development Goals (SDGs) and the End TB Strategy, will only be feasible with dedicated strategies aimed at young people. Child and adolescent TB can only effectively be addressed through collaboration across health systems and communities. To meet the goal of zero TB deaths, it is critical that child and adolescent TB is prioritized in national health strategies, plans and budgets. To this end, it is also crucially important that childhood TB is well integrated with national health systems in, for example, primary health care and paediatric and mother and child health initiatives and services.

Currently, the regional TB action plan covering the period 2016–2020, endorsed at the 65th session of the WHO Regional Committee for Europe in September 2015, is being implemented. The plan is in line with the global End TB Strategy. An analysis of two earlier regional consultations in 2015 and 2017 identified common challenges and revealed that not all Member States featured childhood-specific documents in their national strategic plans. A new expert opinion document on child and adolescent MDR-TB has been prepared to guide and inform Member States on the newest developments in the field. Child and adolescent TB should be considered carefully for inclusion or redevelopment/updating, as it falls into several areas of intervention of the regional TB action plan and links to the three pillars of the global End TB Strategy.

This context requires concerted effort to more effectively combat TB in children and adolescents, one of the most vulnerable patient groups. Strong and well-defined collaboration at international and national levels is important to reduce the burden and suffering of child and adolescent TB.

Day 1. Wednesday 29 January 2020

Opening remarks

Dr Askar Yedilbayev, Team Leader, TB unit, TB, HIV and Viral Hepatitis Programme, WHO Regional Office for Europe; Dr Malgorzata Grzemska, Unit Head, Global TB Programme, TB Vulnerable Populations, Comorbidities and Communities, WHO headquarters; and Dr Martin van den Boom, Technical Officer, TB, HIV and Viral Hepatitis Programme, WHO Regional Office for Europe

Dr Yedilbayev opened the workshop by welcoming all participants and thanking them for their participation. The broad representation from countries, partner organizations, civil society and former TB patients was welcome, as it creates the foundation for rich discussions and sharing of experiences. Participants were encouraged to actively take part in the discussions, share their experiences, and learn from the challenges and opportunities faced by practitioners every day. The importance of eradicating TB among children and adolescents as part of eliminating TB in the WHO European Region was stressed.

Dr Grzemska also gave a warm welcome to the participants. The WHO European Region has made great achievements over the past decades and is on track to reaching several global TB targets. More work is needed in some areas, however, and the Region is well positioned to take on more ambitious targets. It was emphasized that in the area of MDR-TB, the Region is still not on track and more can be achieved if countries within the Region improve in areas such as TB reporting and identifying and treating TB patients efficiently, including children and adolescents.

Dr van den Boom thanked the participants not only for their participation in the workshop, but also for preparing in advance and sharing posters identifying national challenges and successes in combating child and adolescent TB. The objectives and programme of the meeting were introduced, building on evaluations of previous workshops in 2015 and 2017.

Follow up on the previous workshops: what has been achieved, current progress and European expert opinion

Dr Matthias Groeschel, Consultant, TB, HIV and Viral Hepatitis Programme; and Dr Martin van den Boom, Technical Officer, TB, HIV and Viral Hepatitis Programme, WHO Regional Office for Europe

Dr Groeschel and Dr van den Boom put the progress made in TB into a historical context and presented the burden of MDR-TB and the proportion of TB among children in the Region. They highlighted how the roadmap to implement the TB action plan for the WHO European Region 2016–2020 (3) and the political declaration of the United Nations General Assembly High-level Meeting on the fight against Tuberculosis (4) emphasize that attention should also be given to TB in children and adolescents. Despite progress, several challenges persist in childhood TB in the Region, many of which relate to lack of innovations in diagnostics, challenges in the bacteriological diagnosis in young children and research, under- and misdiagnosis of children, the lack of availability of child-friendly formulation and the absence of routine reporting by age and drug-resistance level.

Since the 2017 regional workshop on child and adolescent TB, WHO has provided support to 20 Member States in updating national strategic plans and TB treatment and care guidelines. More than 15 in-country missions have provided countries with technical assistance in the area of child and adolescent TB, and support has been given to ensure inclusion of child and adolescent TB in

applications to the Global Fund. In addition, support through linking and embedding with regional initiatives (the European TB Research Initiative, the European Laboratory Initiative, the regional Green Light Committee, the Technical Advisory Group for TB and the Regional Collaborating Committee on accelerated response to TB, HIV and viral hepatitis) and interdivisional work and projects have been delivered.

Other important developments since the 2017 workshop include the publication by the WHO Regional Office for Europe of *Multidrug-resistant tuberculosis in children and adolescents in the WHO European Region: expert opinion* (5) in 2019, focusing on how to tackle MDR-TB in children and adolescents. The guidance provides an update on recent scientific evidence as well as Region-specific clinical and public health recommendations on child and adolescent MDR-TB. It also includes an epidemiological overview, lists key guideline documents and gives guidance on diagnosis and management of TB, integration of TB prevention and care at primary care level, and vaccination. The fourth edition of The Sentinel Project field guide on MDR-TB in children was published in 2019 (6).

The year in childhood TB review

Dr James Seddon, Senior Lecturer, Imperial College London, United Kingdom, and Stellenbosch University, Cape Town, South Africa

Dr Seddon participated remotely and provided an overview of 15 of the most interesting research publications on child and adolescent TB published in 2019. The number of publications on the topic has increased over the years, and today approximately 1000 peer-reviewed articles on child and adolescent TB are published annually. Based on a Medline search on articles published in 2019, 134 were assessed to be relevant and read in full text. Of these, the 15 articles perceived to be the most relevant, seen from the perspective of Dr Seddon, were presented to the participants (the full list is in Annex 4). The publications covered research on the following topics:

- **TB transmission** outside the household and transmission of TB from adolescents;
- the role of **migration** in TB transmission;
- **stool samples for diagnostics** compared to respiratory samples;
- the use of **ultrasound** compared to X-rays for diagnosis in children;
- the **correct dosage of drugs** for children and the **role of malnutrition**;
- the **feasibility of screening all household contacts** to a confirmed TB case and providing preventive treatment;
- **treatment of MDR-TB** in children and the treatment outcome;
- the role of **BCG vaccine in incidence of TB meningitis** in children and in **overall mortality**; and
- the **non-specific effects of BCG vaccines** over a lifetime, such as reduced incidence of lung cancer in people who received a BCG vaccination at birth.

Dr Seddon presented selected ongoing research projects in childhood TB therapeutics, including:

- implementation studies in western Africa on TB transmission in children (the Transmission Investiguée de la Tuberculose Infantile study);
- studies on rifampin safety and efficacy;
- studies of the effectiveness of treatment for drug-susceptible TB (DS-TB) (the SHINE project);
- a study on optimizing treatment to improve TB meningitis outcomes in children (the TBM Kids study); and
- Various trials on MDR-TB treatment:
 - TB Child Multidrug-resistant Preventive Therapy Trial in South Africa;
 - AIDS Clinical Trials Group trial;
 - the V-QUIN trial; and

- a study on the use of delamanid in treatment of childhood MDR-TB (Otsuks study).

Looking forward, Dr Seddon shared his expectations for what can be achieved in child and adolescent TB over a two-year perspective:

- three-month, once-weekly treatment for all ages of children with TB infection
- evidence for a four-month regimen for treatment of DS-TB disease
- evidence for MDR-TB infection treatment.

His expectations over a four-year perspective were:

- better and shorter regimens for TB meningitis;
- a one-month regimen for DS-TB infection;
- evidence for a six-month all-oral MDR-TB treatment regimen; and
- possibly ultra-short regimens for DS-TB infection and disease using higher dosages of rifampicin.

During the subsequent discussions, several important aspects were raised.

- Research on the **role of prevention and interventions in the education sector**: to Dr Seddon's knowledge, no research is being done on widespread prevention using schools and kindergartens as entry points, but it is an interesting question that should be further explored, in addition to using, for example, nutrition centres and HIV clinics as entry points for prevention and detection.
- The **effects of changing BCG vaccination policies**: Portugal shared experience in limiting the BCG vaccine to at-risk groups and subsequently observing an increase in the incidence of TB meningitis. This led to discussion on the awareness of health-care personnel of uncommon health conditions. In addition, it was underscored that the BCG vaccine should be provided to children of HIV-positive mothers.
- The prospect of **firmer recommendations from WHO on MDR-TB preventive treatment**: it was emphasized that WHO has recommendations on MDR-TB prevention which, although based on observational data, have a strong evidence base. More clinical-trial data is needed to enable WHO to give firmer recommendations on the subject.

Discussion points and comments

In a round of discussion, participants deliberated on a selection of the challenges and successes in combating childhood TB presented in the country posters. The discussions were divided into three sections, focusing on challenges in prevention, diagnosis and treatment. Below is a summary of the key challenges raised.

Key challenges in prevention, including MDR-TB prevention

- In general, there is a **lack of attention to the prevention of TB among children**. The focus is often put on the challenges in diagnosis and treatment.
- The **scope of prevention** ranges from no prevention efforts to a preventative drug regimen.
- Some countries **lack knowledge in how to address MDR-TB and XDR-TB prevention** (that is, contacts of patients with MDR/XDR-TB).

- **Hospitalizing children** who are TB contacts as a preventive measure is still practised in a number of countries in eastern Europe and central Asia. This practice is not in line with WHO recommendations and should be phased out immediately.
- The proportion of children with active MDR-TB is high. Most are infected through close contacts, which underscores the importance of **preventing MDR-TB transmission to contacts**.
- In low-burden countries like the United Kingdom, **expert forums for the discussion of MDR-TB cases** allow physicians to access the necessary advice on how to prevent transmission to child contacts.
- WHO reminded participants of the target from the United Nations political declaration of having 4 million children under 5 on preventive treatment by 2022. If the WHO European Region is to contribute to reaching this target, countries need to **step up preventive measures and improve reporting on these efforts**.
- WHO is happy to provide **support and guidance to countries** that would like to improve or expand their efforts in MDR-TB prevention among children.

Key challenges in diagnosis

- **Bacteriological confirmation** of TB in young children is a key challenge across the Region.
- The challenges in the need for bacteriological confirmation of TB leads to challenges in **reporting to registries**.
- The WHO recommendations on treatment of paediatric TB state that clinical diagnosis is enough to initiate treatment. **New WHO guidelines on diagnostics** are expected to be published in spring 2020.
- There is a need for good **latent TB infection (LTBI) registries**, including for LTBI among children and adolescents.

Key challenges in treatment, including drug supply

- By far the biggest challenges in treatment of TB in children in European Union (EU) countries is the **lack of child-friendly formulations** suitable for the youngest children.
- **The GDF** has these child-friendly formulations available, but political and administrative obstacles prevent EU countries from taking the necessary steps to make the formulations available. In addition, the market for child-friendly formulations within the EU is too small for pharmaceutical companies to officially register these drugs following the necessary regulatory procedures.
- Bulgaria has been able to acquire child-friendly formulations through the GDF via a Global Fund grant. It remains uncertain if they will be able to continue acquiring the drugs from the GDF through government, rather than Global Fund, funds.
- WHO and the GDF are exploring measures to make the drugs available and are collaborating with colleagues in the WHO Essential Medicines and Health Products department. An option being explored is to label the drugs as orphan drugs, which would allow for lower registration fees. A meeting in April 2020 in the Vatican with the United States Food and Drug Administration, the European Medicines Agency, chief executive officers of drug manufacturers, leaders and others provides an opportunity to bring attention to the problem.
- An additional **challenge in low-burden countries** relates to issues around having sufficient allocation of resources, despite countries in general not lacking resources. The very low number of children and adolescents with TB makes it difficult to persuade decision-makers to allocate the necessary resources.
- A key challenge in several Member States of the Region relates to **the long-term hospitalization of children** and the **lack of child-friendly and patient-centred care**.

- The treatment of **TB in children of migrant workers** was mentioned as a challenge in terms of ensuring continuation of treatment and information on treatment outcomes.
- Challenges in treatment that are not associated with medical care, such as **education, stigma** and **access to health care**, were underscored as being important to address.

WHO policy update on prevention, diagnosis and treatment of TB in children and adolescents

Ms Annemieke Brands, Technical Officer, Global TB Programme, WHO headquarters

Ms Brands presented a WHO policy update on prevention, diagnosis and treatment of TB in children and adolescents. The key messages were:

- children usually tolerate second-line treatment well;
- TB in children is often paucibacillary (sputum-smear and/or Xpert-negative) and less severe, with better treatment outcomes than are seen in adults;
- children should benefit from shorter, safer, effective and tolerable (injectable-free) regimens for MDR-TB;
- long-term hospitalization may impact on development and education, so unnecessary hospitalization should be avoided; and
- age-disaggregated data are not routinely reported, making the extent of MDR-TB among children and adolescents uncertain.

Quick facts on TB in children and adolescents

- Globally, at least 1.12 million children (under 15 years of age) become ill with TB every year (581 000 boys and 538 000 girls in 2018); 47% are under 5 years.
- Children represent approximately 11% of all TB cases, with a higher proportion (15%) in high-burden countries.
- In 2018, 205 000 children died of TB (560 children per day), including 32 000 TB deaths (16%) among children who were living with HIV.
- Eighteen per cent of children with TB died, compared to 15% overall in the number of people with TB who died in 2018.
- Researchers estimate that 67 million children are infected with TB (7.5 million every year) and are therefore at risk of developing disease in the future.
- Researchers estimate that 25 000 children develop MDR-TB every year.
- Data on TB among adolescents (10–19 years) cannot easily be analysed, as countries report by 0–4 and 5–14 years (children) and 15–24.

Sources: WHO (7); Dodd et al. (8).

Key challenges in TB in children remain both a case-detection gap and a prevention gap. Overall, 54% of children below 15 years are missed (63% of children under 5 and 46% aged between 5 and 14) compared with 33% of people aged over 15 years. This is due to a combination of underdiagnosis and underreporting. In prevention, 72.5% of the 1.3 million eligible household contacts under 5 years of age did not access TB preventive treatment. The political declaration of the United Nations TB high-level meeting in 2018 addresses these challenges and sets targets for:

- 40 million people with TB to be reached with care during the period 2018–2023, including 3.5 million children and 1.5 million people with drug-resistant TB (DR-TB), and 115 000 children with DR-TB; and
- at least 30 million people to be reached with TB prevention services during the period 2018–2023, including 4 million children under 5 years, 20 million other household contacts and 6 million people living with HIV (including children).

The roadmap towards ending TB in children and adolescents (9) addresses persistent challenges and missed opportunities with 10 key actions. The roadmap is calling for high-level political will, strong leadership and accountability to address TB in children and adolescents.

Since the 2017 regional meeting on childhood TB in the WHO European Region, WHO has published a range of updates to policies on TB in children.

- A WHO position paper on BCG was published in February 2018. Updates include:
 - in settings with high TB burden, a single dose should be given to all healthy neonates at birth or at the earliest opportunity thereafter; countries with low incidence of TB or leprosy may choose selectively to vaccinate high-risk neonates;
 - BCG can safely be co-administered with other routine vaccines, including the hepatitis B birth dose;
 - revaccination is not recommended even if the tuberculin skin test (TST) or interferon gamma release assay (IGRA) test is negative;
 - BCG is recommended for unvaccinated, TST- or IGRA-negative schoolchildren coming from/moving to high-incidence/burden settings and older groups at risk through occupational exposure;
 - children who are HIV infected should not receive BCG vaccination, but HIV-infected individuals, including children, who are receiving antiretroviral therapy (ART), are clinically well and immunologically stable should be vaccinated;
 - BCG vaccination for neonates with HIV infection should be delayed until ART has been started and the neonates are immunologically stable; and
 - asymptomatic neonates born to mothers with bacteriologically-confirmed pulmonary TB should receive preventive treatment (after exclusion of TB disease); if the infant remains asymptomatic on follow up without immunological evidence of TB and is HIV-negative, BCG vaccination should be provided using a normal infant dose (after completion of preventive treatment).
- Programmatic management of LTBI 2018 was updated, with more testing and treatment options to come out early in 2020 along with an implementation guide:
 - expanding the number of groups prioritized for LTBI testing and treatment – apart from all people living with HIV and children under 5 years, additional high-risk groups are HIV-negative children of 5 years and under, adolescents and adults who are contacts of TB patients, and contacts of patients with MDR-TB;
 - expanding testing options in all countries (TST or IGRA); active TB should always be ruled out before prescribing preventive treatment (LTBI testing is not a requirement for initiating TB prevention treatment (TPT) in people living with HIV or child contacts under 5 years);
 - expanding preventive treatment options with new shorter regimens as alternatives to 6H² (3HP³ for adults and children, and 3RH⁴ for children and adolescents under 15 years) should address concerns about giving monotherapy and facilitate adherence;
 - in countries with a high TB incidence, children aged 5 years and above, adolescents and adults who are household contacts of people with bacteriologically-confirmed pulmonary TB who are found not to have active TB by an appropriate clinical evaluation or according to national guidelines may be given TB preventive treatment (this is a conditional recommendation, with low-quality evidence);

² Six months of daily isoniazid.

³ Weekly high-dose rifapentine plus isoniazid for three months.

⁴ Three-month rifampicin and isoniazid treatment.

- the absence of any symptoms of TB and of abnormal chest X-ray findings may be used to rule out active TB disease among HIV-negative household contacts aged 5 years and above and other at-risk groups before preventive treatment (a conditional recommendation, with very low-quality evidence);
- in selected high-risk household contacts of patients with MDR-TB, preventive treatment may be considered based on individualized risk assessment and a sound clinical justification; and
- the evidence base around preventive treatment for contacts of MDR-TB is limited; results of ongoing studies will better inform further recommendations.
- WHO guidelines on TB infection prevention and control were published in 2019 (10), including recommendations on administrative and environmental controls and respiratory protection.
- WHO reviewed the next-generation Xpert MTB/RIF Ultra cartridge in 2017. Following review of the latest evidence, WHO recommendations for the use of Xpert MTB/RIF as the initial diagnostic test for all adults and children with signs and symptoms of TB, and for the testing of selected extrapulmonary specimens (cerebrospinal fluid, lymph node and tissue specimens) now also apply to the Ultra assay.
- WHO consolidated guidelines on drug-resistant tuberculosis treatment were published in 2019 (11) with the following key changes:
 - regrouping of medicines into three categories based on evidence about the balance of effectiveness to safety;
 - the overall approach to designing longer MDR-TB regimens for adults and children is determined by: effectiveness, safety and a preference for oral over injectable agents; the results of drug-susceptibility testing (DST); the reliability of existing DST methods; population drug resistance levels; history of previous use of medicine in a patient; and potential drug–drug interaction(s); and
 - more emphasis on DST, active drug-safety monitoring and management and operational research (modification of shorter regimen encouraged under operational research conditions).

Looking ahead, the following updated guidelines and meetings are planned for 2020:

- an updated version of the WHO guidance on the management of TB in children and adolescents and a comprehensive child and adolescent TB handbook (with implementation guidance in line with new policy recommendations);
- the revision of the 2012 guidelines for systematic screening for TB with updated and consolidated recommendations and implementation guidance for both case-detection and prevention is expected by end 2020;
- dissemination, adaptation and implementation of key actions included in the roadmap towards ending TB in children and adolescents addressing case-detection and prevention gaps;
- support will be provided to TB high-burden and priority countries for programme reviews, national strategic plan development and funding applications, including Paediatric TB Operational and Sustainability Expertise Exchange budgeting tools;
- drug optimization, including follow up to WHO Paediatric Antiretroviral Drug Optimization (February 2019), which prioritized the development of child-friendly single formulations of rifampicin, rifapentine and bedaquiline;
- the annual Child and Adolescent TB Working Group meeting will take place in October 2020; and
- a regional consultation on ending TB in children and adolescents for TB high-burden and priority countries in Africa is planned for late 2020, with a focus on integration.

Epidemiological highlights and update on the WHO European Region, with a focus on childhood TB

Dr Giorgi Kuchukhidze, Technical Officer, TB, HIV and viral Hepatitis Programme, WHO Regional Office for Europe

Dr Kuchukhidze presented epidemiological highlights in childhood TB in the WHO European Region. With a 5% decrease annually, the WHO European Region has the fastest declining TB incidence, but HIV-positive TB incidence is increasing within the Region. Looking at the mortality rate, the Region experiences the fastest decline and is on track to reach the targets of the regional TB action plan. Of the 259 000 cases of TB in 2018, 12 000 were children (4.6%), with a decreasing trend. Of the notified 9000 childhood TB cases, 3000 were under age 5. Contact investigation and LTBI treating practice in children under 5 is reported by 12 of the 53 Member States. Of these, 95% of contacts were screened for TB, 1.2% were found to have active TB, and 42% of those eligible started TB preventive treatment. A key challenge in the Region relates to reporting and disaggregated data.

How are TB incidences modelled? Changes to the current modelling scheme employed by WHO: the importance of solid data-reporting

Dr Pete Dodd, WHO Consultant, Health Economics & Decision Science School of Health & Related Research, University of Sheffield, United Kingdom

Dr Dodd introduced how TB incidences are modelled and the process behind developing global TB estimates. The level of reporting has improved for child TB notification over the past two decades. In general, methods for estimating TB incidences have evolved. They include ad hoc elements but aspire to use available evidence, to be driven by country data where possible and to be transparent, consistent and robust.

The main methods used to model TB incidences are:

- TB prevalence surveys;
- notifications with standard factor adjustments (used by most countries in the WHO European Region);
- inventory studies and notification data; and
- expert opinion and notification data.

For childhood TB estimates, the five main indicators are the proportion of:

1. overall burden found in children
2. treated paediatric cases with a confirmed diagnosis
3. paediatric cases that are sputum smear-positive
4. paediatric cases aged 5 years
5. paediatric cases that are extrapulmonary TB.

Dr Dodd introduced the methods and models for child-specific estimates for TB:

1. simple case-detection ratio;
2. mathematical model;
3. notification adjustment; and
4. a combination of method 1 and method 3, which was used in 2015 and 2016 in the WHO estimate process.

Participants appreciated the introduction to this complex topic. The potential problems of basing targets on TB estimates were discussed. Often there is a political push to use estimates to develop targets, both globally and nationally. Countries can and should alert stakeholders such as

donors if targets are too high or too low. This may be important if a country plan is either over- or under ambitious. A plea was made to countries to use their national data actively to challenge estimates.

Data should be used for patient management but also for issues such as planning, target development and advocacy. More Member States request WHO to provide support in assessing their TB data. Data and information from countries that challenge these models and estimates are always welcomed in the interest of achieving the best estimates in future years.

UNICEF priorities with regards to TB

Dr Ruslan Malyuta, HIV/AIDS and Adolescent Health Officer, UNICEF Regional Office for Europe and Central Asia

Dr Malyuta presented the priorities of UNICEF related to TB in children and adolescents. UNICEF works to increase the focus on TB in children. A key area of concern is the discrepancy between reported and estimated TB cases in children. There is a need to focus on the gap and identify the missing cases.

Using case stories, Dr Malyuta drew attention to the lack of advocacy on behalf of children with TB from both the TB and child-health communities. Childhood TB care is often highly centralized with very limited capacity at district- and lower-level facilities and underutilization of community-based systems. Referral systems tend to be weak and, due to the often-vertical structure of TB programmes, linkages with other child-health providers (both public and private) are also weak.

There is a need to increase capacity and change attitudes at primary health-care level. This implies training of health-care workers working with children, improved curriculums on the signs and symptoms of TB in children and guidance on how to address the challenges of diagnosis and management, especially at primary- and secondary-care levels, where most children present with TB.

Adolescent TB is also often a neglected issue with additional management challenges that are particular to that age group – especially if an adolescent is also living with HIV. The challenges in diagnosis are less relevant than for small children, but challenges nevertheless exist in adherence-promoting interventions. These are well established in, for instance, HIV and diabetes, but completely absent for TB in adolescents. There is therefore a need for better adherence support for adolescents with TB, including adolescent-friendly services and alignment with outreach activities that are not limited to only one venue.

An example of intersectoral action: United Nations Common Position on Ending HIV, TB and Viral Hepatitis through Intersectoral Action

Dr Assia Brandrup Lukanow, WHO Regional Office for Europe

Dr Brandrup Lukanow presented the United Nations Common Position on Ending HIV, TB and Viral Hepatitis through Intersectoral Action (12) and the need to tackle TB from sectors other than the health sector, as the cause of the problem to a large extent is outside the scope of the health sector. Health literacy plays an important role in this regard, as it is a prerequisite to making healthy choices to protect self, partners and others from the three epidemics. Health literacy can be acquired throughout life, including during childhood years. Using a settings approach to

strengthen health literacy, including kindergartens and schools, is relevant for child and adolescent TB and plays a role in broader SDG discussions.

The new Global Fund cycle and priorities for childhood TB

Dr Daisy Lekhura, TB Advisor, Global Fund to Fight AIDS, Tuberculosis and Malaria

Dr Lekhura introduced the new Global Fund cycle and the fund's priorities for childhood TB. At the sixth Replenishment Conference, donors pledged US\$ 14.02 billion for the next three years. This is the largest amount ever raised for a multilateral health organization, and the largest amount by the Global Fund. The funds have been allocated and countries have received allocation letters.

In the new cycle, packaging TB services and elaborating the strategic focus within the package has been important. Patients are at the centre and finding missing cases – including children – is a priority. Elaborating the strategic focus within the package includes engaging with the public and private sectors, and including and integrating communities to address TB case-finding, care, monitoring and prevention. Improving programme quality and efficiency and integrating services are other priorities.

Dr Lekhura gave an update on the new TB modular framework and the key elements related to paediatric TB in the application material. Different application resources (13) have been developed for the new funding cycle, including handbooks, frequently asked questions and brochures. A TB information note is available in English, French and Spanish and addresses in different parts TB diagnosis, prevention and care in children (including maternal–child health and services integration) and links to the paediatric roadmap and several technical guidelines and documents.

Key changes are made in the TB Modular Framework (related to paediatric TB) to focus more on TB in children:

- focus on a cross-cutting systems approach, including provision of integrated and people-centred services at community and primary health-care levels;
- new interventions under the three core modules (TB Care and Prevention, TB/HIV and MDR-TB) for key populations – children, miners and mining communities and mobile populations (refugees, migrants and internally displaced people);
- revised indicators related to TB preventive therapy and new indicators for human rights and gender-related barriers to TB services, aligned with the latest technical guidance; and
- additional indicator disaggregation (by age, gender and HIV status).

The priorities for 2020–2022 are:

- finding the “missing millions” with TB and DR-TB and treating them (including children);
- strengthening health systems, including laboratory services (using more sensitive screening and diagnostic/DST tools);
- accelerating transition to all-oral regimens for treatment of DR-TB, in line with international recommendations;
- enhancing the engagement of private providers and communities in TB care and scaling-up innovative approaches;
- addressing comorbidities, including TB/HIV and diabetes mellitus;
- addressing TB among high-risk and vulnerable populations, including children, migrant/mobile populations, miners and slum dwellers; and
- scaling-up TB prevention, also among children.

New interventions under TB care and prevention, TB/HIV and MDR-TB modules in children include three modules:

- TB;
- DR-TB case-finding: diagnosis, treatment and prevention interventions specifically targeted at children; and
- TB/HIV collaborative activities: HIV testing, TB screening and case-finding, and treatment and prevention interventions specifically targeted at children with HIV.

Update on Stop TB Partnership/GDF approach to fighting childhood TB

Dr Ramón H. Crespo, Knowledge and Project Management Officer, Stop TB Partnership

Dr Crespo gave an update on the Stop TB Partnership and GDF (STBP/GDF) approach to fighting childhood TB. STBP/GDF has worked (and continues to work) with partners to ensure global availability and sustainability of the tools needed to diagnose and treat all forms of TB in children, particularly for DR-TB. STBP/GDF can support the introduction of these tools from a procurement and supply-management perspective. GDF's coordination capacity and expertise aims to ensure access to TB commodities, and its services are available to all countries. GDF works to ensure access to child-friendly TB treatments and an uninterrupted supply of quality-assured, affordable TB commodities.

Dr Crespo introduced the GDF TB Medicines Dashboard, specifically the Paediatric DR-TB Medicines dashboard (14), which gives an overview of the drugs recommended and their availability.

In efforts to introduce child-friendly formulations, 93 countries (nine in the WHO European Region) have since 2016 procured child-friendly formulations to treat DS-TB, with 961 000 treatments procured (6722 in countries of the Region). Since 2018, 56 countries (10 in the Region) have procured child-friendly formulations to treat DR-TB, with 1100 treatments (384 in countries of the Region).

GDF has negotiated substantial price reductions of 30–85%, making it more affordable for countries.

Global challenges in ensuring access to child-friendly formulations relate to the relatively small markets for many of these products, and countries procuring with non-donor funds may face difficulties in access. Specifically for countries in the EU, child-friendly drug formulations are not yet registered and therefore not available to purchase.

All countries are encouraged to utilize GDF's services, as pooled procurement supports small-market stability. GDF also offers tailored country support when ordering with national funds.

Panel discussion 1: what are the next steps in prioritizing children and adolescents in the WHO European Region TB elimination agenda?

Representatives of the Child Health Programme, WHO Regional Office for Europe, the civil society organization TB People in Ukraine, the TB unit of the WHO Regional Office for Europe and WHO headquarters

Representatives from the WHO Regional Office for Europe and WHO headquarters and a representative from the civil society organization TB People in Ukraine discussed next steps in prioritizing children and adolescents in the WHO European Region TB elimination agenda.

Dr Olya Klymenko, head of TB People in Ukraine, shared her very personal experiences of being a TB patient and the mother of a child on preventive treatment. She shared the frustrations, the uncertainties and the lack of social support throughout the process. The lack of focus on children and the consequences of hospitalization in terms of loss of social contacts and absence of school education signals an urgent need for a more child-friendly and patient-centred approach, not just in medical, but also in social, terms. Dr Klymenko called for more focus on, and funding for, children and adolescents with TB and as contacts of TB patients. There is a need for more research and to build networks that can establish contact between families with children treated for TB. Access to drugs is insufficient, and best practices are needed on how to address social and psychological support for children and adolescents affected by TB. TB People Ukraine has a volunteer programme that works on these issues and helps establish contact between families with children treated for TB. Finally, Dr Klymenko advocated for a focus on patient rights and those of children and their families.

Dr Susanne Carai from the WHO European Programme for Child and Adolescent Health shared some of the activities the programme has been undertaking related to childhood and adolescent TB. One of the main activities has focused on how better to prepare general practitioners to identify and handle TB in children. Specifically, a pocketbook and mobile application (app) for general practitioners working with children and adolescents tries to raise awareness of the symptoms of TB and has a separate chapter on TB in children. The pocketbook will be available in late 2020. Dr Carai also addressed the potential negative effect of hospitalization on the child's development and underscored the firm recommendation of WHO not to treat children with TB in hospitals or sanatoria.

Dr Malgorzata Grzemska from the WHO Global TB Programme also underscored that hospitalization of children is not in agreement with WHO recommendations and should be phased out immediately. What is needed is patient-centred and child-friendly care. It is necessary to look into several different actions, including a regional adaptation of the multisectoral framework and a regional adaptation of the childhood TB roadmap. Not all global recommendations necessarily apply to this Region, so adaptation is necessary. Dr Grzemska also called for an increased focus on the prevention of TB in children and the importance of contact-tracing.

Day 2. Thursday 30 January 2020

Snapshot of child health primary health-care pocketbook for the WHO European Region

Dr Susanne Carai, Programme for Child and Adolescent Health, WHO Regional Office for Europe

Dr Carai presented a child health primary health-care pocketbook for the WHO European Region that will be available in late 2020. She also addressed the problems of hospitalization and institutionalization of children in relation to TB.

A review of the implementation of the Integrated Management of Childhood Illness (IMCI) guidelines in the European Region identified the need for updated primary care guidelines that address the needs of children and adolescents presenting to first-level health facilities. The pocketbook is not yet finalized and inputs are still welcome.

The pocketbook aims to be a practical tool for primary providers of care for children and adolescents. It establishes standards of care as the basis for benefits packages within the context of universal health coverage and skills and competencies for primary care providers for children and adolescents (the development of university curricula). The pocketbook will be used by WHO in supporting countries to develop national adaptations and promote evidence-based care. It consists of eight major sections:

1. principles of providing care from birth through adolescence
2. health promotion and prevention
3. newborn health
4. the child or adolescent presenting with a specific complaint (such as a cough)
5. the child or adolescent who might have a specific disease or conditions (such as TB)
6. the child or adolescent with long-term care needs
7. adolescent health
8. emergencies and injuries.

Sections 4 and 5 are particularly relevant to TB in children and adolescents. The pocketbook also features a chapter on TB that contains general information on diagnosis, treatment, public health measures and effective communication techniques.

The WHO pocketbook on hospital care for children (15), which is very widely distributed and available online to download, was used as the starting point. The A6-size guidelines are based on the available evidence and focus on inpatient management of the major causes of childhood mortality, including pneumonia, diarrhoea, severe malnutrition, malaria and TB. An editorial group of physicians and health-care experts in child and adolescent care have drafted the chapters and identified and addressed evidence gaps. It is based on existing GRADE guidelines⁵ and the next steps is to have external peer review and field testing. Participants were invited to participate in the external peer-review process.

⁵ The Grading of Recommendations Assessment, Development and Evaluation (GRADE) is an approach to grading quality (or certainty) of evidence and strength of recommendations that is now considered the standard in guideline development.

On the inappropriate hospitalization and institutionalization of children in relation to TB, Dr Carai repeated the statement of the WHO ethics guidance for the implementation of the End TB Strategy:

The significant harms caused from institutionalization, hospitalization, confinement or isolation of infectious and non-infectious children do not compensate for the potential benefits.

In some eastern European and central Asian countries, children with suspected TB are routinely institutionalized in sanatoria for extended periods of time, some even mandatorily. Placement in a sanatorium negatively affects a child's education, family and personal relationships. Hospitalization should occur only in exceptional cases where treatment can only be provided in a hospital.

A desk review was carried out to assess country practices in relation to hospitalization and institutionalization of children in paediatric TB sanatoria. Eleven countries were identified as having paediatric TB sanatoria and were contacted for further information. Responses were received from five: Armenia, Belarus, Georgia, the Russian Federation and Ukraine. In three countries (Belarus, the Russian Federation and Ukraine), children are placed in sanatoria for latent TB, active TB, contact with TB patients and rehabilitation after TB cure. Georgia and Armenia have discontinued the practice of placing children in paediatric TB sanatoria. The desk review found that the length of stay was up to nine months, and that the cost of staying in a TB sanatorium ranges from US\$ 12 per child per day to US\$ 25.

Panel discussion 2: partners' priorities for child and adolescent TB prevention and care in the WHO European Region

The second panel discussion included representatives from ECDC, IFRC, UNICEF, the KNVC Tuberculosis Foundation, GDF and PTB-net, who presented and discussed priorities for child and adolescent TB prevention and care in the WHO European Region.

Dr Crespo, representing the GDF, called for ensuring that the tools needed to treat and prevent TB in children are accessible and affordable. Seen from the pharmaceutical sector, TB is a small market and there is not always sufficient incentive to develop new drugs, especially for DR-TB in children, as it is still rare. This presents a challenge in securing access to child-friendly formulations. GDF is trying to develop tools to ensure that medicines are available. There is a need to further engage with countries and partners. GDF can help procure medicine for any country in the world, but the EU has very strict regulations. Bulgaria and other countries are trying to get around these regulations; the GDF can support the efforts, but not solve the underlying problem. GDF's priority is for better diagnostics for TB in children to be developed.

Dr Senia Rosales-Klitz, representing the ECDC, said that a key priority for the ECDC is to ensure reliable TB data from EU Member States and to conduct relevant analyses of data. Case-based reported data have shown a gap in adolescent data and there is need to disaggregate in age groups of 12–14 and 15–19. To do this, the support of the Member States is necessary. ECDC and WHO can on request conduct coordinated country visits to assist in a deeper analysis. The initiative for such assistance, however, must come from Member States.

Dr Connie Erkens, representing the KNCV Tuberculosis Foundation, reminded participants of KNCV's offer to provide technical assistance for national TB programmes. The focus is on introducing innovative steps to achieve the SDGs. KNCV is currently working with partners on the problem of childhood TB diagnosis by developing new diagnostic tests. Another priority relates to introducing new treatment regimens for children. In addition, stigma is an area KNCV works on not just for children, but also for adults. Work with countries on how to counter this is ongoing and a number of tools to address stigma at different levels (public, patient and health

system) has been developed. Recommendations on how to deal with LTBI and contact investigation, based on experience in the Netherlands, have been translated for low-burden countries. KNCV has a strong research agenda and supports countries in operational research in areas such as digital health solutions.

Dr Lasha Gogvadze, representing the IFRC, presented work on supporting awareness, literacy, social aspects, mother and child care, and stigma for people with TB as key priorities. Health inequality in providing health care at home is another area of work. The use of the many volunteers, especially young people, is an important area of work that includes collaboration with, and support from, civil society organizations.

Dr Malyuta, representing UNICEF, highlighted community health and primary health care, including prevention as key priorities in the work on child and adolescent TB in the WHO European Region. There is a need to increase attention on childhood TB and child rights. This includes strengthened strategic communication with health-care and primary health-care workers. Another aim is to strengthen the TB component within the scope of IMCI.

Dr Folke Brinkmann, representing PTB-net, invited interested parties to join the network, which consists mostly of paediatricians and researchers but is open to everyone. It has no funding but brings together experience from people who work with TB in practice, with the objective of transferring knowledge across institutions. Key priorities are to improve knowledge of childhood TB through an online database with real cases, and improve the care of TB in children, including ensuring better home-centred care. Priority areas also include conducting research projects and supporting the work of developing better case definitions for MDR-TB in children.

During the subsequent discussions, participants expressed positive interest in the PTB-net network. The opportunity to discuss cases gives rise to new perspectives and makes, for instance, **differences in treatment approaches** across subregions and countries clear. The challenge of the **stigma of TB in adolescents** was also discussed. Much has been achieved in overcoming HIV stigma among adolescents, but in many central Asian countries, TB is still associated with stigma and taboo. A United Nations Development Programme project on identifying legal rules and regulations that express underlying stigma against TB was mentioned as an important approach to tackling stigma. The value of **integrated diagnostics** was discussed and the importance of coordinating laboratory diagnostics of TB, HIV and viral hepatitis, as advocated by the European Laboratory Initiative, was stressed. Finally, the challenges associated with the **availability of child-friendly formulations in EU countries** was discussed. It was suggested that a joint advocacy paper addressed to the relevant parties and ministers of EU Member States should be developed. GDF expressed their availability to assist and encouraged all stakeholders and Member States to advocate for the topic to maximize the effect.

Country presentations – three top challenges in paediatric TB

Belarus and the use of new drugs for children with DR-TB

Dr Dmitry Jhurkin, Deputy Director of the Belarus National Scientific and Practical Centre for Pulmonology and TB, presented the experiences of Belarus with using new drugs for children with DR-TB.

Existing guidelines on drugs for children with DR-TB are partly based on the experiences of Belarus, which have published in articles in the *American Journal of Respiratory and Critical*

Care Medicine (volume 195, number 10, 15 May 2017) and *Emerging Infectious Diseases* (volume 23, number 10, October 2017).

The incidence of TB among adults has been falling over the past decade, from 45.4/100 000 in 2008 to 18.6/100 000 in 2019. The incidence among children has also declined, from 4.5/100 000 in 2008 to 1.2/100 000 in 2019. In 2019, 23 children aged 0–17 were diagnosed with TB (eight cases among the 0–4 years group and 15 among the 15–17 years group). The DR-TB proportion in children and adolescents in 2019 was 17.4%.

Dr Jhurkin presented diagnostic findings and comorbidity for the TB cases as well as adverse events experienced by patients. Two clinical cases were described as examples.

In conclusion, the experience of Belarus with treating DR-TB in children and adolescents suggests that:

- patient series will help increase the global knowledge base for paediatric multidrug and extensively drug-resistant TB (M/XDR-TB) patients treated with new drug-containing regimens under programmatic conditions;
- interim results on new drug-containing regimens used in children and adolescents show a good safety profile and excellent treatment outcomes; and
- the experience gained can promote further expansion of this approach for children and adolescents with M/XDR-TB.

The Netherlands and the main challenges in childhood TB

Dr Natasha van't Boveneind, TB Public Health Physician, GGD Haaglanden, presented the main challenges in childhood TB in the Netherlands.

The Netherlands is characterized by low childhood TB case numbers, with the lowest number ever recorded in 2018 (seven cases among those under 5 years; in total, 20 cases among those under 15 years), indicating very low transmission in the country. A challenge of the very low burden is a fear of loss of expertise and alertness about TB in clinical care, leading to problems with case-finding. Between 2005 and 2012, 64% were detected through active case-finding (see Erkens et al. (16)).

The main challenges in diagnosis relates to the general difficulties in diagnosing TB in children under the age of 5 years. In treatment, the lack of child-friendly formulations due to EU regulations presents the biggest challenge. In relation to screening of risks groups, implementation of LTBI screening among asylum seekers under the age of 18 has been difficult to coordinate within the whole asylum procedure. Finally, challenges relate to the coverage of BCG vaccination among eligible risk groups. Some of the children found to have TB were not vaccinated and had visited high-burden countries. A study found that of 100 patients with central nervous system and miliary TB, 33 had been BCG vaccinated and 44 had not (23 (53%) were children under 5 years, 15 (34.1%) were aged 5–14 and six (13.6%) were adolescents).

Another study found that 39% of child TB patients eligible for BCG had not been vaccinated. Work is being done to increase awareness of the BCG vaccine among parents coming from higher-burden countries.

The presentation gave rise to a discussion of the role of BCG vaccination in prevention. In countries where BCG is no longer part of the national vaccine programmes for other than high-risk groups, there is concern that this may lead to an increase in TB meningitis. Problems with shortages of vaccines were also presented as challenges to maintaining sufficient vaccination coverage.

The role of health systems in addressing child and adolescent TB

Dr Ihor Perehinets, Division of Public Health and Health Systems, WHO Regional Office for Europe

Dr Perehinets gave a brief introduction to health system considerations in addressing child and adolescent TB in the WHO European Region. He described health systems as complex dynamic systems and underscored the importance of understanding what the current system looks like in order to improve it for tomorrow. The structure of a system and the perception of a problem like TB as only a biomedical problem and forgetting the human aspect has consequences for how we address it and may result in, for instance, hospitalization of children and adolescents with TB. Dr Perehinets explained how key health system challenges to fighting TB in the WHO European Region relate to issues like governance, service delivery and health financing.

Panel discussion 3: key challenges and how they need to be addressed – innovative solutions for the Region

A short final panel discussion with the participation of Dr Dmitry Jhurkin, Deputy Director the Belarus National Scientific and Practical Centre for Pulmonology and TB, Dr Natasha van't Bovenind, TB Public Health Physician, GGD Haaglanden, the Netherlands, and Dr Perehinets, WHO Regional Office for Europe, gave rise to discussions on the role of TB sanatoria for children, and the need to move towards more ambulatory care and to do so based on a robust and sustainable transition plan. Finally, the need for psychosocial support for TB patients, including infected children and the children of parents with TB, was discussed.

Group work: operationalization of identified challenges and actions

The participants were divided into three groups to discuss common challenges and priorities in their response to child and adolescent TB, with the objectives of collecting ideas and learning from each other.

The group work was divided into two parts. The groups were asked to:

- discuss the three most urgent/critical country-specific **gaps and challenges** in child and adolescent TB prevention, diagnosis and treatment; and
- identify three **priority actions**, defining what, how, who, when and with what funds.

In plenary, each group presented the results of their discussions.

Group 1

Challenges in prevention

- Lack of education and information about the prevention of TB in children and adolescents in the general population.
- Lack of training in TB prevention for health-care workers.
- Stigma, not only towards TB patients, but also towards health-care personnel working in TB, which again leads to challenges in recruiting young doctors and nurses to the field.

Challenges in diagnosis

- Screening migrants for TB.
- LTBI testing and notification – how do we best notify people that they have LTBI, which can be very abstract?
- Outpatient services for testing and diagnostics.

Challenges in treatment

- Access to child-friendly formulations is one of the biggest challenges.
- Tensions between health-care providers and parents of children with TB due to frustrations of not being able to get child-friendly formulations.
- Medicines not being free of charge.
- Intersectoral work with vulnerable groups – how do we engage them in treatment and teach them to understand why they need treatment for LBTI?

Group 2⁶

Challenges in prevention

- Uncertainty over details of local epidemics in children and adolescents and other risk groups.
- Obstacles in introducing LTBI registers.
- Mobile populations in the whole spectrum from prevention to treatment. The challenge is handled differently across the Region and is a problem in almost all countries. Germany, for example, is collaborating with Romania on patients who move between Romania and Germany to ensure they complete their treatment and inform each other about outcomes of treatment to be used for surveillance. The Russian Federation also deals with mobile populations and the related challenges. Labour migrants cannot start work without being screened for TB. Previously, a TB-positive patient had to return to their home country, but patients got lost, so instead they are now put on treatment before being sent back. There is a need for an international system for tracking migrant patients to ensure proper treatment and follow-up.

Challenges in diagnosis

- Lack of awareness of TB both among patients and health-care workers.

Challenges in treatment

- Adherence to treatment.

Group 3⁶

Challenges in prevention

- Lack of appropriate case-finding strategies.
- Lack of awareness and capacity among health-care workers.
- Lack of awareness among parents and caregivers.
- LTBI management and diagnosis.

Challenges in diagnosis and treatment

- Access to imaging diagnostics.
- Delays in sample transportation.
- Lack of clear symptoms of TB in children.

Priority actions from all groups

- Make child-friendly formulations available and accessible in all Member States by:
 - organizing meetings with regulatory authorities and addressing pharmaceutical companies to advocate for the need for making child-friendly formulations available (seek support of EDCD, WHO, the European Medicines Authority and the GDF in preparing for the meeting);

⁶ Listing only challenges not already listed by the other groups.

- engaging ECDC, PTB-net, the TB caucus, GDF and others in developing advocacy papers to find a joint procurement mechanism similar to those developed for other medical conditions;
- collecting and reviewing available data to support the development of an advocacy paper; and
- collecting patient stories to support the advocacy paper.
- Improve information and medical literacy about TB by:
 - informing and addressing the general public, health-care workers and other relevant target groups, such as parents, to improve awareness of TB;
 - using World TB Day to voice the problems of TB in children; and
 - revising the curricula of health-care workers to include more information on, for instance, LTBI.
- Bring attention to the social component of TB, including improving treatment adherence rates through increased social support and campaigns that target parents.
- Progressively scale down unnecessary hospitalization, supported by a solid transition.
- Review national legislation to ensure that TB drugs are adequately addressed.
- Scale-up mobile X-ray use.
- Set up nationwide comprehensive TB/LTBI and other disease registers.
- Develop guidance for TPT in contacts of M/XDR-TB patients
- Ensure support for adherence to TPT.

Closing

Dr Askar Yedilbayev, Team Leader, TB unit, TB, HIV and Viral Hepatitis Programme, WHO Regional Office for Europe; Dr Malgorzata Grzemska, Unit Head, Global TB Programme, TB Vulnerable Populations, Comorbidities and Communities, WHO headquarters

The meeting was closed by Dr Grzemska and Dr Yedilbayev. The number of countries and donors represented and the interactive and valuable discussions were applauded. The workshop clarified the importance of preventing childhood TB through contact-tracing of TB patients, but also stressed the need for more guidance and exchange of experiences on how to do this in practice. It was also clear that there is an urgent need to move away from prolonged institutionalization of children in TB sanatoria and WHO is happy to offer guidance and support on how to transition to patient-centred and child-friendly care. The WHO Regional Office for Europe has the capacity, infrastructure and staff to do better, and this opportunity should not be missed.

It was emphasized that WHO is happy to provide support to the regional research agenda, which also includes TB in children. Any operational research projects in the Region, either ongoing or planned, are welcome to reach out for support.

Finally, the participants were thanked for their dedication, time, inputs, experiences and for their willingness to collaborate and work together to improve prevention, diagnosis and treatment of TB in children and adolescents.

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Annex 1

SCOPE AND PURPOSE

Background

The age-specific challenges for tuberculosis (TB) prevention and care in children and adolescents are increasingly recognized. However, addressing these challenges still requires greater focus by national TB programmes and increased public health prioritization. This is as relevant in the WHO European Region as in the rest of the world. The challenges are even more pronounced when addressing the multidrug-resistant (MDR)-TB epidemic, as the WHO European Region has by far the highest rates of MDR-TB in the world, being home to 10 of 30 high MDR-TB burden countries.

The full scope of the problem of TB in children and adolescents is not fully known. In the WHO European Region, more than 7200 children and adolescents under 15 years of age account for about 4% of notified new TB patients (2016 data). In addition to a large undiagnosed MDR-TB disease burden, a recent modelling suggested that in the WHO European Region 14.1% of children with TB infection were infected with MDR strains, the highest proportion in the world. This represents a vast reservoir of future MDR-TB cases that will contribute to ongoing transmission and propagation of the epidemic.

After decades of relative neglect, the childhood TB epidemic is now in the spotlight. TB elimination, as set out both by the Sustainable Development Goals and End TB Strategy, will only be feasible with dedicated strategies aimed at the young. Child and adolescent TB can only effectively be addressed with collaboration across health systems and communities. To meet the goal of zero TB deaths, it is critical that child and adolescent TB is prioritized in national health strategies, plans and budgets. To this end, it is also crucially important that childhood TB is well integrated within national health systems, for example, in primary health care, and also in paediatric and mother and child health initiatives and services.

Currently, the regional TB action plan covering the period 2016–2020 endorsed at the 65th session of the WHO Regional Committee for Europe in September 2015 is being implemented. The plan is in line with the global End TB Strategy. An analysis of two earlier regional consultations in 2015 and 2017 has identified common challenges and revealed that still not all Member States feature childhood-specific documents in their national strategic plans. Furthermore, a new expert opinion document on child and adolescent MDR-TB has been prepared to guide and inform Member States on the newest developments in this field. Child and adolescent TB should be carefully considered for inclusion or redevelopment/updating, as it falls into several areas of intervention of the regional TB action plan and links to the three pillars of the global End TB strategy.

This context requires concerted efforts to more effectively combat TB in children and adolescents, one of the most vulnerable patient groups. Strong and well-defined collaboration at international and national levels are important to reduce the burden and suffering of child and adolescent TB.

Objectives

The objectives of the child and adolescent TB Regional workshop are to:

- discuss implications of the United Nations high-level TB meeting political declaration regarding child and adolescent TB, and share and plan common and enhance national strategies to combat the current regional childhood TB challenges;

- follow up on the previous two regional child and adolescent TB workshops of the WHO European Region in 2015 and 2017;
- update Member States on new WHO global guidelines on MDR-TB and its implications for child and adolescent TB;
- present the newly prepared (2019) expert regional opinion document on childhood MDR-TB; and
- present an update on modified child TB estimate methodology and its implications for the WHO European Region

Expected outcomes

The expected outcomes are that:

- participants will be updated on key changes and aspects regarding management and treatment of childhood TB, including the recently published global WHO MDR-TB guidance and the regional guidance/expert opinion document on childhood MDR-TB; and
- next steps in updating elements of current national strategic plans relevant to childhood TB will be defined in line with the global End TB strategy and the regional TB action plan 2016–2020.

Simultaneous translation, Russian/English and English/Russian, will be provided.

Annex 2

PROGRAMME

Day 1. Wednesday 29 January 2020

Time	Topic	Speaker/lead
08:30–09:00	Registration	
09:00–09:15	Opening remarks	Dr Malgorzata Grzemska, Unit Head, Global TB Programme, TB Vulnerable Populations, Comorbidities and Communities, WHO headquarters Dr Askar Yedilbayev, Team Leader, TB unit, Joint TB, HIV and Viral Hepatitis Programme, WHO Regional Office for Europe
09:15–09:25	Presentation of objectives and appointment of event chairs	Dr Martin van den Boom, Technical Officer, TB, HIV and Viral Hepatitis Programme, WHO Regional Office for Europe
09:25–09:45	Follow up on the previous workshops, what has been achieved, current progress, European expert opinion	Dr Matthias Groeschel, Consultant, TB, HIV and Viral Hepatitis Programme
09:45–10:15	The year in childhood TB in review	Dr Martin van den Boom Dr James Seddon, Senior Lecturer, Imperial College London, United Kingdom, and Stellenbosch University, Cape Town, South Africa (presenting via Webex)
10:15–10:30	Discussion	Moderated by Dr Askar Yedilbayev and Dr Martin van den Boom
11:00–12:00	Poster Gallery walk	
12:00–12:45	Discussion	Moderated by facilitators
13:45–14:15	WHO policy update on prevention, diagnosis and treatment of TB in children and adolescents	Ms Annemieke Brands, Technical Officer, Global TB Programme
14:15–14:35	Epidemiological highlights and update on the WHO European Region with a focus on childhood TB	Dr Giorgi Kuchukhidze, Technical Officer, TB, HIV and Viral Hepatitis Programme,

Time	Topic	Speaker/lead
		WHO Regional Office for Europe
14:35–15:00	How are the TB incidences modelled? Changes to the current modelling scheme employed by WHO. The importance of solid data reporting (show some examples how data is missing, i.e. childhood MDR-TB)	Dr Pete Dodd, Health Economics & Decision Science, School of Health & Related Research, University of Sheffield, United Kingdom
15:00–15.30	Discussion	Moderated by session chair(s)
16:00–16:15	UNICEF priorities with regards to TB	Dr Ruslan Malyuta, HIV/AIDS and Adolescent Health Specialist, UNICEF
16:15–16:30	Global Fund to fight Aids, TB and Malaria (GF): Childhood TB priorities	Dr Daisy Lekharu Tuberculosis Advisor, The Global Fund to fight AIDS, Tuberculosis and Malaria (presenting via Webex)
16:30–16:45	Child TB medicines in the European Region	Dr Ramón H. Crespo, Knowledge & Project Management Officer, Global Drug Facility, Stop TB Partnership
16:45–17:30	PANEL 1: what are the next steps in prioritizing children and adolescents in the WHO European Region TB elimination agenda?	Representatives of Child Health Programme, WHO Regional Office for Europe, civil society organization, TB unit of WHO Regional Office for Europe and Dr Malgorzata Grzemska
17:30–17:45	Wrap-up of Day 1	Chaired by Dr Malgorzata Grzemska and Dr Martin van den Boom

Day 2. Thursday 30 January 2020

Time	Topic	Speaker/lead
09:00–09:10	Quick summary of Day 1/presentation of Day 2 agenda/objectives	Dr Martin van den Boom
09:10–09:30	Snapshot of child health primary health care pocketbook for the WHO European Region	Dr Susanne Carai, Child Health programme, WHO Regional Office for Europe
09:30–10:30	PANEL 2: partners' priorities for child and adolescent TB prevention and care in the WHO European Region	Representatives of WHO Regional Office for Europe TB unit, the European

		Centre for Disease Prevention and Control (ECDC), Stop TB Partnership, the International Federation of Red Cross and Red Crescent and the KNCV Tuberculosis Foundation
11:00–11:30	Country presentation – three top challenges	Two national TB programme (NTP) volunteers
11:30–12:30	PANEL 3: i) key challenges; and ii) how they need to be addressed – innovative solutions for the Region	NTP volunteers who presented previously, representative of WHO Regional Office for Europe TB unit and Dr Ihor Perehinets, Technical Advisor, Division of Health Systems and Public Health, WHO Regional Office for Europe
13:30–15:30	Group work: operationalization of identified challenges and action (from panel above)	Operationalization of actions targeting identified challenges and actions including Global Fund, ECDC, and three groups of countries
16:00–16:45	Presentations of group work	
16:45–17:00	Open discussion, wrap-up, next steps, closure	Dr Malgorzata Grzemska, Dr Martin van den Boom

Annex 3

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Annex 4

FIFTEEN TOP ARTICLES ON ADOLESCENT TUBERCULOSIS IN 2019

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The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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