Child
& Adolescent
TB Working Group

Report of the

Annual meeting of the Child and Adolescent TB working group
Friday 16 October 2020

Virtual meeting

Introduction

The annual meeting of the Child and Adolescent TB Working Group (CAWG) took place virtually on the Webex platform, on Friday 16 October 2020. The meeting was divided into two sessions of 2.5 hours each, with a two-hour break in between.

The meeting was open to all members of the working group representing a broad range of stakeholders including paediatricians, NTP managers and childhood TB focal points in the NTP, MCH representatives, technical and financial partners, community TB representatives and WHO staff from headquarters, regional and country offices.

The main purpose was to maintain a vibrant child and adolescent TB community, share country experiences in scaling up the response to child and adolescent TB and to discuss next steps to move the agenda forward.

The objectives of the 2020 virtual meeting were:

- To provide an update on the activities of the working group since the last annual meeting on Wednesday 30 October 2019 in Hyderabad, India;
- To give an update of recent WHO policy developments, the update of the guidelines and development of an operational handbook, and review of progress towards UNGA HLM on TB targets for children;
- To share paediatric TB research updates;
- To share recent papers on child and adolescent TB;
- To share findings of systematic reviews on risk of TB after exposure and TB screening approaches in children;
- To share experiences with novel approaches to the diagnosis of TB in children and adolescents; and
- To share experiences and lessons learned in maintaining essential child and adolescent TB services during the COVID-19 pandemic.

A total of **260 registrations** were received, and **192 participants** attended the meeting.

Presentations are available on the working group website hosted by the Stop TB Partnership: http://stoptb.org/wg/dots_expansion/childhoodtb/.

Session 1a: Opening, objectives and update from Chair and Secretariat
Chair: Farhana Amanullah

Welcome and opening address – Tereza Kasaeva, Director WHO Global TB Programme

On behalf of the WHO GTB hosting the Secretariat of the Child and Adolescent TB Working Group, Dr. Tereza Kasaeva warmly welcomed everyone to the 17th annual meeting of the Child and Adolescent TB Working Group.

She was proud to announce that this year's Global TB Report, launched on 14 October, includes better data on TB in children and adolescents (including a better age-break down, with data on adolescents aged 10-19 years, DR-TB among children and treatment outcomes). However, the case detection and prevention gaps remain huge and we need to urgently further scale up our efforts.

Work on paediatric TB drug optimization (PADO) is gaining importance. Just last month many of the working group members participated in the virtual review of the PADO TB 1 priorities. WHO has formalized its Global Accelerator for Paediatric formulations (GAP-f) network under the WHO Science Division. Next month, the Vatican will convene a High-Level Dialogue to Assess Progress on and Intensify Commitment to Scaling Up Diagnosis and Treatment of Paediatric HIV and TB in Children Living with HIV. WHO is looking forward to close continued collaboration with all relevant stakeholders at global, regional and national levels, from public and private sectors, those already engaged in TB to those engaged in the HIV, nutrition and maternal and child health agendas in order to implement the key actions as included in the 2018 Roadmap towards ending TB in children and adolescents and fully aligned with the global targets (reaching at least 3.5 million children with diagnosis, treatment and care & reaching at least 4 million children under age of 5 with preventive treatment by 2022).
Dr. Kasaeva ended by wishing all an interesting meeting and also a fruitful 51st Union conference in which many sessions are organized on ending TB in children and adolescents.

Report from the Chair of the Child and Adolescent TB working group – Farhana Amanullah, Chair, Child and Adolescent TB Working Group

Farhana Amanullah provided an overview of activities since the last annual meeting and of planned activities for the next year, including:

- Progress since UNGA HLM on TB: Roadmap translations into Russian and Spanish; a regional consultation for the EMR, SEAR and WPR regions on Ending TB in children and adolescents, Hanoi, Viet Nam, 26-28 November 2019; a section on children and adolescents in the UNGA HLM progress report and expansion of data reported on children and adolescents in the Global TB report; National TB programme reviews in several TB high burden countries; a consultants training on "What's New in TB and Engagement with the Global Fund"; support to the update of the guidelines on the management of TB in children and adolescents
- Activities in 2019/2020: establishment of the POSEE group (task force under the working group) with development of paediatric budgeting tools integrated into the OneHealth Tool; Implementation working groups meeting; review of Global Fund (GF) applications; participation in the GF Technical Review Panel (TRP)
- Meetings and coordination: annual meeting; core team calls; Paediatric Anti-TB Drug Optimization meeting (PADO-TB) virtual review (22 September 2020); participation in advisory committee for the Union/CDC Centre of Excellence and TB/HIV implementation working group call on paediatric TB/HIV (21 May 2020)
- Webinars on child/adolescent TB and COVID-19: The Union/SSA Centre of Excellence webinar: The Programmatic Management of Paediatric and Adolescent TB in the initial COVID-19 response (3 June 2020); WARN/CARN network on COVID and childhood TB (11 June 2020); Hosted by CAWG and The Union: Maintaining essential child and adolescent TB services during the COVID-19 pandemic: practical solutions and lessons learnt (3 September 2020)
- Planned activities: Regional meeting in the African region (timing depending on COVID-19 situation); support to update of the child and adolescent TB guidelines (expected release date December 2021); Support to development of an operational handbook on the management of child and adolescent TB; Development of updated training materials on child and adolescent TB, in line with guidelines and handbook (in collaboration with The Union); a PADO meeting (PADO-TB2); High Level Dialogue on paediatric HIV and Paediatric TB in children living with HIV hosted

by the Vatican (Rome5), 5-6 November 2020 (virtual); Continue to highlight challenges and opportunities in all relevant fora; Promote research and development; Continue to organize annual meetings of the Child and Adolescent TB working group with regional engagement of all relevant stakeholders; Assist countries to move from single projects to programmatic approaches.

Experiences from a family affected by TB in times of COVID in Brazil – video

This video highlights how delayed evaluation and lack of provision of TB preventive treatment, in this case due to the COVID-19 pandemic, led to a baby getting sick with TB requiring more drugs for treatment and the need for frequent follow up in a health system already challenged by the pandemic. We thank the family for agreeing to share their journey with TB in times of COVID-19 and to the colleagues from Brazil who produced the video: Betina Mendez Alcântara Gabardo, Andrea Rossoni, Tatiane Hirose, Laura Lanzoni, Tony Tahan and Raphael Barbosa from the paediatric infectious diseases clinic in Curitiba, Parana, Brazil. Unfortunately the audio was not working when the video was played.

WHO update on new policy recommendations and progress towards UNGA HLM on TB targets – Annemieke Brands and Sabine Verkuijl

The secretariat provided an update on new data, progress towards UNGA HLM on TB targets and new policy recommendations. The presentation included the following:

- Global TB Report: Countries with electronic case-based systems requested to report in age bands 0-4, 5-9, 10-14, 15-19 years (for 2019); Treatment initiation for MDR/RR-TB in children and young adolescents 0-14 years (2018 and 2019); Treatment outcomes in children/young ado's 0-14 years (2018 cohort, mainly treatment success rate); Box 5.3 on "Strengthening data collection for children and adolescents with TB" (Chapter 5, TB diagnosis and treatment, page 79-81) – for details: see the presentation
- Progress against child and adolescent TB related UNGA HLM targets (we should be at 40% of the 2022 target, covering data from 2018 and 2019)
    - Case detection and treatment: 30% (1,040,000) of 3.5m
    - Children started on second-line treatment: 7.8% (8,984) of 115,000
    - Provision of TB preventive treatment (TPT)
        - Contacts <5 initiated on TPT: 20% (782,952) of 4m
        - Contacts ≥5 initiated on TPT: 0.9% (178,051) of 20m
        - PLLIV initiated on TPT: 88% (5.3m) of 6m
- Global TB Report 2020 is available at: https://www.who.int/publications/i/item/global-tuberculosis-report-2020
- TB Preventive treatment guidelines and handbook: **6/9H, 3HP, 3HR (strong recommendations)**, 4R, 1HP (conditional recommendations) alternative options (all disease burden settings and target populations including PLHIV); choice depends on availability of appropriate formulations and considerations for age, safety, drug-drug interactions and adherence; Age limits: 3HP ≥2y; 1HP ≥13y.
    - https://www.who.int/activities/preventing-tb
    - 3RH is the preferred regimen in most situations, using the available dispersible 2-FDC RH 75/50mg (in the absence of a suitable formulation for rifapentine for children), except for children living with HIV on most ART regimens

- Guidelines and handbook on rapid diagnostics for TB detection
    - For childhood TB, the recommendations in these new guidelines are an important milestone, as stool and nasopharyngeal aspirates are now recommended as specimens for the diagnosis of PTB in children. This has important consequences for NTPs and funding applications.
    - The LF-LAM policy was published in 2019 and has been integrated in the 2020 guideline on rapid diagnostics; The policy highlights a distinction between in-patient and out-patient settings. Algorithms for both in and outpatient settings are available and explained in more detail in the operational handbook. It needs to be noted that LF-LAM should be used in conjunction with Xpert MTB/RIF or Xpert Ultra. It should not be used as a replacement or triage test.
        - Guidelines: https://apps.who.int/iris/rest/bitstreams/1284627/retrieve
        - Handbook: https://apps.who.int/iris/rest/bitstreams/1284635/retrieve
- Drug-resistant TB treatment guidelines and handbook: The shorter all oral bedaquiline containing regimen (4–6 Bdq $_{(6\ m)}$-Lfx-Cfz-Z-E-H^{h}-Eto / 5 Lfx-Cfz-Z-E) is recommended for eligible children aged 6 years and above; Longer individualized regimens for those not eligible for shorter regimen above, including children <6y and with EPTB other than TB LN; BPaL may be used under OR conditions in ≥14y in MDR-TB with fluoroquinolone resistance
    - https://www.who.int/activities/tackling-the-drug-resistant-tb-crisis
- WHO has started the process of updating the 2014 guidelines on the management of TB in children; An expansion is planned for a target audience beyond NTPs and to include adolescents (10-19 years); A consolidated document will include new recommendations but also updated recommendations relevant to children and adolescents from other WHO TB, HIV and other guidelines; An accompanying operational handbook will be developed, with practical "how to" guidance on all topics, including those without evidence-based recommendations
    - Call for data issued on 24 July; Emerging scope: Treatment shortening in children with non-severe TB; Diagnostic approaches in (vulnerable) children; Treatment of children with drug-resistant TB with all oral regimens; Models of care for TB prevention, case detection, treatment and care
    - Next steps: Finalization of scope and PICO questions; Commissioning of systematic reviews; Establishment of a Guideline Development Group (GDG); Target date for publication: end 2021.
- Impact of COVID-19 on child and adolescent TB services: Isolation of children with features of respiratory infection; Lockdowns, closed TB facilities, reassignment of staff, leading to delays in TB diagnosis and treatment and increased household exposure to TB; Competing needs for diagnosis of COVID-19 over TB (e.g. GeneXpert); Indirect impact among others: reduced household income, increased poverty, food insecurity, malnutrition, vulnerability to other diseases, missed health checks and vaccinations including BCG vaccination.
    - WHO publications; Information note on TB and COVID; Q&A on TB and COVID; Scientific brief on BCG and COVID; Maintaining essential health services: operational guidance for the COVID-19 context
    - https://www.who.int/teams/global-tuberculosis-programme/covid-19

Session 1b: Paediatric TB research update
Chair: Steve Graham

Study on burden and outcomes of TB meningitis in children at national and sub-national level in South Africa: opportunities for prevention, earlier diagnosis and treatment - Karen Du Preez, Stellenbosch University

Karen du Preez from the Desmond Tutu TB Centre at Stellenbosch University presented on an interdisciplinary and multi-level approach to estimate the disease burden and outcomes of childhood tuberculous meningitis (TBM).

She reminded the audience that paediatric TB surveillance should capture the full spectrum of disease. Young children are at high risk of disseminated forms of TB, such as TBM, which has high morbidity and mortality and often permanent neurological disability: this has substantial economic and social burden on families and public health services.
TBM has non-distinct symptoms, leading to diagnostic delays, advanced presentation and severe morbidity. Early diagnosis and treatment are critical to improve TBM outcomes. However, routine TB surveillance data does not distinguish TBM from other forms of TB.

A new study was introduced, which aims to determine the burden and outcomes of paediatric TBM at a global level, and at a national and sub-national level in South Africa, identifying opportunities for prevention, earlier diagnosis and treatment. Specific research aims include:

- Modelling the global disease burden and attributable mortality of childhood TBM (expected results: 2021)
- Spacio-temporal analyses or reported childhood TBM at national level (South Africa) (expected 2021/2022)
- Prospective observational childhood TBM cohort study at sub-national level (City of Cape Town) (expected 2023/2024).

SHINE trial update – Aarti Avinash Kinikar and Priyanka Raichur, Byramjee Jeejeebhoy Government Medical College, Pune

The main findings of the SHINE trial (Shorter Treatment for Minimal Tuberculosis in Children), a phase III randomised open trial comparing 4 versus 6 months treatment in children (+/- HIV) with smear-negative non-severe TB in Africa and India, were presented by Dr. Aarti Avinash Kinikar and Priyanka Raichur.

The study was designed to include 1200 children less than 16 years, randomised in a 1:1 ratio, with 600 in each arm and then followed up for 72 weeks for the primary outcome assessment. The study used the paediatric dispersible FDCs and the WHO-recommended weight band-dosing. The trial was conducted in 5 sites, 3 in Africa (South Africa, Zambia and Uganda) and 2 in India (Pune and Chennai). It was coordinated by the MRC CTU at University College London, UK.

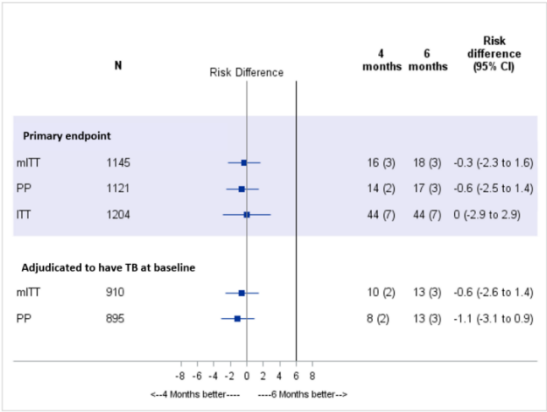
The trial population included children aged 0-16 years weighing 3 kg or more, with no drug resistance, a clinical decision to treat, symptomatic but with non-severe TB, with a smear negative respiratory sample

(GeneXpert MTB+ was allowed), not treated for TB in the previous 2 years and with known HIV status. Non-severe or minimal TB was defined as extra-thoracic lymph node TB or intrathoracic lymph node TB with no airway obstruction or uncomplicated forms of pulmonary TB confined to one lobe with no cavities. The primary efficacy outcome was a composite unfavorable outcome, which included TB treatment failure or TB recurrence or death by 72 weeks or on-treatment loss to follow-up. The primary safety outcome was on-treatment grade 3-5 adverse events.

Results: 1461 children were screened, 257 excluded, 1204 were randomized with 602 in each arm. For the primary analysis population there were 572 children in the 4 months' and 573 in the 6 months' arm.

There was good balance in baseline characteristics across the arms. Children were relatively young (median age around 3.5 years), about 10% HIV positive, all had some symptoms and 14% were bacteriologically confirmed cases. There was good and balanced adherence to the randomised duration at 94% in both arms and 95% retention at week 72 across both arms.

The primary endpoint risk difference is on the same line about "0" (meaning no difference in the arms) with a tight confidence interval, with the upper bound well below the 6% non-inferiority margin - showing that 4 months of treatment is as good as 6 months (see figure on the right). The results were consistent across ITT (intention to treat) and PP (per protocol) analyses and were consistent in the key secondary analysis of those adjudicated to have TB at baseline. There was no difference in adverse events between the 2 arms.



In conclusion:

- The SHINE Trial found that the 4 months treatment was as good as the standard 6 month treatment for children with minimal TB
- There were few unfavourable outcomes in both arms (3% vs 3%)
- The results were consistent across all the analyses performed
- Few treatment related side-effects and similar in both arms
- Two thirds of children with TB could potentially be safely and effectively treated with 4 months of treatment
- Reducing the length of treatment could make treatment easier for children and caregivers, as well as reduce costs to families and the health system
- Guideline and policy makers should consider moving to 4 months of treatment for children with minimal TB

Paediatric TB Prevention Trials: an update – Anneke Hesseling, Stellenbosch University

Coverage of TB preventive treatment (TPT) in eligible child contacts aged below 5 years is still very low, 33% in 2019 (data from 2020 Global TB Report).

Priorities for TPT in children:

- 3HP (3 months of once-weekly isoniazid and rifapentine [RPT]) with or without ARVs:
    - TBTC Study 35: Phase I/II Dose Finding and Safety Study of Rifapentine and Isoniazid in HIV Infected and HIV Uninfected Children with LTBI (FDA IND # 141932); Status: Re-opening after COVID: cohorts 3, 4 (<2 years): enrollment delayed due to nitrosamine impurity: possibly reopening in quarter 1, 2021 (depending on FDA and in-country approval)
    - DOLPHIN study: To assess the safety, tolerability and pharmacokinetics of 3HP among infants, children and adolescents living with HIV taking DTG and 2 NRTIs; Status: in protocol development, results anticipated late 2023
- 1HP (one month of daily isoniazid and rifapentine) with ARVs:
    - IMPAACT P2024: Data on PK and safety of 1 HP in HIV infected and uninfected children (daily RFPT dosing vs. once weekly for 3 HP); PK and safety of 1 HP in HIV+ and HIV children <15 years of age; HIV+ on DTG (rollout, bd) or EVF based regimens; Using Paediatric DTG formulation and adult 150 mg RPT until paediatric formulation available; Timeline: planned to open 2021
- Cross-cutting: RPT formulation
    - Nitrosamine impurities: FDA: https://www.fda.gov/drugs/drug-safety-and-availability/fda-works-mitigate-shortages-rifampin-and-rifapentine-after-manufacturers-find-nitrosamine; WHO: https://extranet.who.int/pqweb/news/nitrosamine-concerns-rifapentine-and-rifampicin; Sanofi: Paediatric formulation development work on hold for several months until impurity issue is resolved; Impact on clinical routine access and trials not clear.
    - Benefit of clear preferred product characteristics (PCC) after resolution of impurity issues: discussed at TB PADO (Paediatric Anti-TB Drug Optimization) virtual review
    - Currently available: 150 mg unscored tablet (non-dispersible), commercial product; Sanofi: Water dispersible FDC tablet: 150 mg RPT/150 mg INH; mango flavoured and dispersible single unscored RPT 100 mg and 20 mg tablets (these are trial formulations, not commercially available)
    - PADO-TB virtual review: reviewed dosing predictions based on unscored versus scored 150 mg RPT tablet; Ideal RPT formulation characteristics include: Strength: 150 mg single formulation, dispersible, scored: 75: 75 mg (“ease of use” as minimum, ideally functional), palatable, long shelf life; modeled PK data can update WHO Expression of Interest (WHO EOI): dispersible, scored 150 mg; Industry: target 1 priority paediatric formulation for WHO PQ once impurity issues resolved: which can serve multiple indications, and durable. A standalone RPT formulation will remove complexity with FDC.
- Drug resistant TB TPT
    - 3 ongoing trials:
        - TB CHAMP: Levofloxacin (novel paediatric dispersible formulation) versus placebo daily for 6 months (children 0-4 years); Status: reopened in July 2020, after pause in accrual due to COVID; interim analyses on track,
        - A5300B/IMPAACT2003B/ PHOENIx (Protecting Households On Exposure to Newly Diagnosed Index Multidrug-Resistant Tuberculosis Patients): delamanid

versus standard dose INH daily for 26 weeks (HIV + children <5 yrs, TST/IGRA + > 5 y); Status: 16 out of 20 sites activated
- V-QUIN: Lfx versus placebo daily for 6 months (adults and adolescents, TST +, small group of children)

Selection of interesting peer-reviewed articles – James Seddon, Imperial College London, Desmond Tutu TB Centre

See pdf copy of the slides presented.

Session 2a: Developments in diagnosis of TB in children and adolescents
Chair: Moorine Sekadde

Country experiences on implementation of the Simple One Step (SOS) stool method using Xpert MTB/RIF, lessons learned – Edine Tiemersma, KNCV Tuberculosis Foundation Netherlands and Endale Mengesha Goshu, KNCV Tuberculosis Foundation Ethiopia

KNCV Simple One-Step (SOS) stool method:

- As simple as sputum testing with Xpert; Feasible to perform at every GeneXpert site without need for additional materials with only a short training required for Xpert staff
- SOS stool projects in Ethiopia: accuracy and robustness studies (compared to Xpert on nasogastric aspirate samples), small scale implementation studies
    - Preliminary results of accuracy study: 430 children enrolled; 4.7% stool MTB+, 5.4% error/invalid (Xpert) or contaminated (culture)
    - Further fine-tuning of the SOS stool methods underway (looking at storage conditions, optimum incubation/sedimentation time, contact time with sample reagent and amount of stool added to sample reagent)
    - Zonal level implementation experience: in 20 health facilities with high TB case load, baseline TB notification data collected, monitoring of childhood TB case notification rates
    - Take home messages: Difficult to achieve projected sample size due to COVID-19; Logistical issues not to be underestimated (GeneXpert machines need to be upgraded for Ultra cartridge utilization; Continued (re)training needed due to staff rotation); Stool well received by NTP and peripheral labs as alternative specimen for Xpert testing; Children's guardians favor stool much above NGA as specimen for diagnosis of TB; SOS stool method for Xpert seems robust and well accepted
- Conclusions from work on SOS stool method: It can be feasibly implemented at peripheral and district level, with initial close monitoring and trouble shooting (Ethiopia, Indonesia, Vietnam); Training (incl. TOT) can be provided remotely (Vietnam); Head-to-head comparison studies suggest that there is no difference between the three stool processing methods; Currently estimating costs and impact of implementation of this method at peripheral level (modeling study); Can be used for children and adults (living with HIV) (Vietnam, Zambia); Can probably also be combined with other (transport) buffers (Zambia)

- Next steps: Complete studies for further evidence on SOS stool method; Head-to-head comparisons; Gain more experience with pilot implementation projects; Finalize (online) SOS stool tool-box containing training, monitoring and supervision package, General implementation plan and guidance on interpretation of diagnostic test results; In collaboration with WHO to prepare a quick guideline of stool processing methods; Create community of practice.

Emerging experiences with diagnostic approaches in children with HIV, severe pneumonia and malnutrition – Chishala Chabala, University Teaching Hospital, Zambia

The TB-Speed project aims to contribute to the reduction in childhood mortality from TB, with as expected outcome a feasible and cost-effective strategy using innovative diagnosis tools and decentralized approaches improving childhood TB diagnosis in high TB-burden settings. The research project is implemented in Cambodia, Cameroon, Côte d'Ivoire, Mozambique, Sierra Leone, Uganda and Zambia. The study focuses on children with HIV-infection, severe acute malnutrition (SAM), severe pneumonia (who have a high risk of TB disease, of death and of under-diagnosis of TB).

Preliminary results focusing on the feasibility of NPA and stool sample collection and Xpert Ultra testing for TB diagnosis in vulnerable children:

- Pneumonia study: Overall 586 out of 619 children (94.7%) with a valid NPA Ultra result; 476 out of 619 (76.9%) with a valid stool Xpert result
- HIV study: validation of the PAANTHER study TB treatment decision algorithm; 59 out of 65 children (90.8%) with a valid NPA Ultra result; 55 out of 65 (84.6%) with a valid stool Xpert result
- SAM study: 129 out of 137 children (94.2%) with a valid NPA Ultra result; 116 out of 137 (84.7%) with a valid stool Xpert result

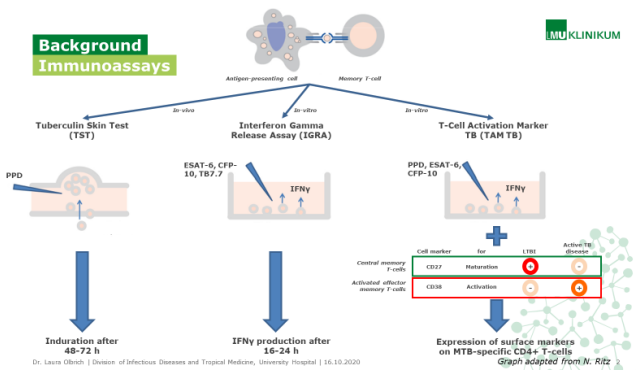
Conclusions:

- High feasibility of NPA sample collection confirmed in highly vulnerable children (> 90% of children with valid Ultra result from NPA)
- High feasibility of stool sample in HIV infected children with presumptive TB and hospitalized children with SAM (but slightly more challenging in children hospitalized with severe pneumonia)
- Feasibility of approaches at lower level of care (District Hospital and PHC) - currently assessed in TB-Speed Decentralization study
- Qualitative assessment on feasibility and acceptability starting - interviews with parents and healthcare workers in the Pneumonia study
- Final study results are expected: TB-Speed Pneumonia: Q4 2021; TB-Speed HIV: Q1 2022; TB-Speed SAM: Q3 2021

T-cell marker-based assays for the diagnosis of tuberculosis in children and adults – Laura Olbrich, University of Munich

Background on immunoassays:

- New test principles (TAM-TB) on blood: 23 cases detected; 8 in addition to culture: + 44% increase in case detection (Geldmacher et al, 2014)
- Preliminary results of TAM-TB evaluation in adults and children (RefuScreen-AIDA-TB): Sensitivity 80.8% (95% CI 70.3 – 88.8%); Specificity 98,2% (95% CI 90.4 – 100.0%); ROC AUC: 0.89 (95% CI: 0.85 – 0.94)



TAM TB:

- Development of commercialized kit
- MEC-CMC pilot study: Prospective evaluation of TAM TB compared to microbiological reference standard (culture, Xpert®): Sensitivity 80%, specificity 84% (Higher Specificity with more stringent classification of unlikely TB)
- RaPaed-AIDA-TB Consortium: Study Design: Diagnostic validation study, 8 new diagnostic tests incl. TAM TB, 1,000 symptomatic children, 20-25% target confirmation rate
    - Preliminary results: TAM-TB performance: all ages, sensitivity (all pos) 56.5% (41.1% - 71.1%); sensitivity (without single Xpert trace) 75.8% (57.7% - 88.9%), specificity 91.7% (77.5% - 98.2%), ROC area 0.74 (0.66 – 0.83); highest sensitivity and specificity in age group 0-1 year

Conclusions:

- TAM TB shows promising performance in a variety of settings, in both children and adults
- Simplified and standardized assay kit developed
- RaPaed-AIDA-TB promising test performance, particularly for infants; Requires laboratory infrastructure, incl. incubation and flow cytometry
- Ongoing evaluation: RaPaed-AIDA-TB, endpoint review is being conducted; ERASE TB (incipient TB, household contacts, initiation of recruitment Q1 2021)

Session 2b: Systematic reviews on the risk of TB after exposure and TB screening in children
Chairs: Lindsay McKenna and Susan Maloney

The risk of TB in children after close exposure: a systematic review and individual-participant meta-analysis – Leo Martinez, Stanford University School of Medicine

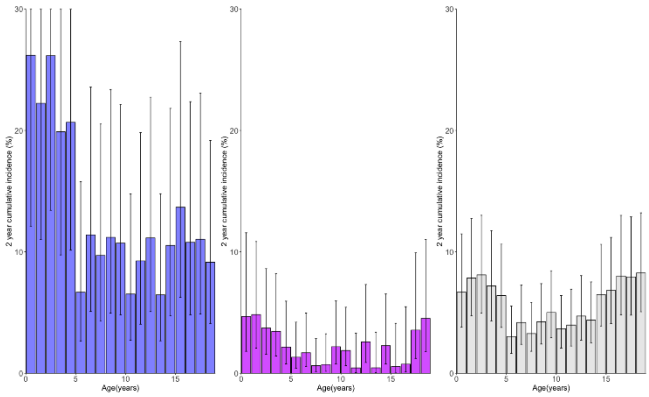
The presentation focused on the risk of TB in children after close exposure and recent infection, specifically describing a recent individual-participant meta-analysis. The majority of knowledge about

paediatric TB is largely through historical data and studies. And, in TB, the older literature is very strong. In 2004, Ben Marais conducted a large review of the historical literature on paediatric TB and summarized important epidemiological concepts from studies performed prior to 1940. One of these is that the risk of developing tuberculosis after recent infection is very high, upwards of 20-50% in the first few years of life.

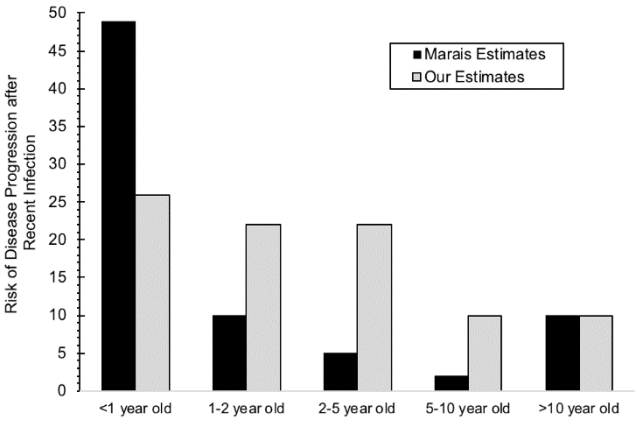
To attempt to re-evaluate the question on the risk of developing TB after recent exposure with contemporary data, all available individual-level data on children with TB exposure from the past 20 years were collected. Contact tracing studies were included to study recently exposed children. The second question was on the individual- and population-level impact of TB preventive treatment in these children.

Systematic review of all contact-tracing studies:

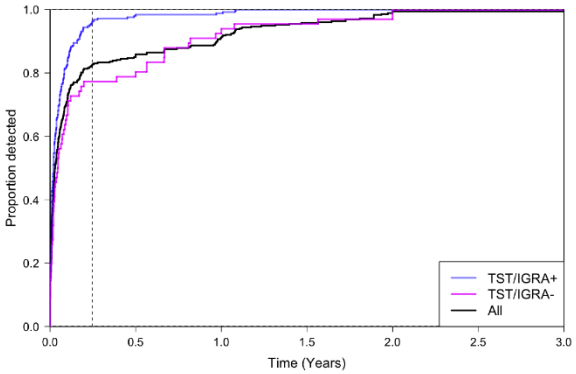
- In all, approximately 137,000 children were evaluated for prevalent disease and 126,000 children were followed for incident disease. These children were followed for over 425,000 person-years.
- Mixed-effects logistic regression models for disease prevalence and parametric survival time models for disease incidence. In order to evaluate preventive therapy, a propensity score analysis was conducted to adjust for cofounding by indication, which may occur if children at higher disease risk were preferentially given preventive therapy.
- Two-year cumulative risk of developing TB among children infected at baseline, uninfected at baseline, and all children. Note: only children who were not on preventive therapy and from prospective cohort studies were included (N.B. including retrospective studies in this analysis would underestimate the true risk of TB in these children, as these often have low TB case ascertainment, especially for children)



    - TB risk is very high in the youngest children with TB infection
    - These contemporary estimates are distinct from the historical estimates before the 1940s. This graph shows direct comparisons of risk of progression by age group. It was found that children are at high risk to develop disease, especially if infected but that the risk was about half the historic estimates in children below 1 but were higher between 1 and 5 years of age and continued to be high throughout childhood and early adolescence.



- Preventive treatment was over 60% protective among all children and was 90% protective among children with a positive baseline test for TB infection.
- Among all children <5 years of age 83% were diagnosed within 90 days. And among children with a baseline positive TST/IGRA 96% were diagnosed within 90 days. The fact that such a high proportion of children with infection develop disease within 90 days of an exposure indicates that we may not be able to reach them fast enough to give them preventive treatment.



Conclusions:

- High-risk in children <5 years old with TB infection
- Adolescent and young adult children should also be prioritized as part of TB control
- Preventive treatment is a highly effective individual-level tool - can we make it more effective as a population-based tool?

Results of a systematic review of TB screening approaches in children – Bryan Vonasek, Baylor College of Medicine

The primary objective of this systematic review was to determine the accuracy of screening tests for pulmonary tuberculosis in children & adolescents in high-risk groups. The WHO defines screening as "Systematic identification of people with suspected active TB, in a predetermined group, using tests, examinations or other procedures that can be applied rapidly."

Index tests used included: One of multiple symptoms (symptom 'clusters'), chest radiography (any abnormality or abnormality suggestive of TB); Xpert MTB/RIF.

Reference standards: Microbiological (MRS): solid or liquid culture, Xpert MTB/RIF, or Xpert Ultra on a respiratory specimen; Composite (CRS): Microbiological confirmation OR Clinically diagnosed pulmonary TB.

Overall 25 studies were included in the review. 13 PICOs were assessed in this review; 4 were presented at the recent TB Screening Guideline Development Group meeting in September 2020.

Findings:

- Index Test: Chest radiography with any abnormality; Reference Standard: composite; Population: children and adolescent close TB contacts
    - 8 studies, 3513 individuals; Prevalences: 2% to 25%; Pooled sensitivity: 0.87 (0.75 to 0.93); Pooled specificity: 0.98 (0.68 to 1.00)
- Index Test: WHO-recommended four-symptom screen; Reference Standard: composite; Population: children and adolescents living with HIV

- 2 studies; 20,926 individuals; 203,135 screens; Prevalences: 3% and 7%; Pooled sensitivity: 0.61 (0.58 to 0.64); Pooled specificity: 0.94 (0.86 to 0.98)

Going forward:

- Ongoing dissemination of findings
- WHO TB Screening guideline update
- Systematic review of TST & IGRA to screen for active TB
- Overall limited research evaluating TB screening in children; future studies should: Use both composite & microbiologic reference standards; Apply the reference standard to all, not just those with positive screens and; Assess sequential and parallel strategies utilizing complementary strategies (e.g. symptom screen followed by CXR)

Session 2c: Impact of COVID-19 on child and adolescent TB services
Chairs: Kobto Ghislain Koura and Anthony Enimil

Impact of COVID-19 on child and adolescent TB services: experiences from Africa – Anthony Enimil, Ghana

General COVID-19 data were presented, comparing South Africa (higher incidence and mortality) with Ghana (lower incidence and mortality). In Ghana, total OPD attendance dropped from close to 800,000 to just over 600,000 in quarter 2, 2020. There was some recovery in July and August 2020. The total number of TB cases diagnosed in Ghana dropped by over 25% in quarter 2, 2020, compared to the same period in 2019. In 2019, the TB case detection gap for children aged below 15 years in Ghana was estimated at 90%. Considering this challenging situation in normal times, the COVID-19 pandemic is likely to further worsen this gap.

During three weeks of national lockdown, TB clinics were closed with follow-up visits disrupted; Medication centers were opened but could not communicate appropriately and transportation (vehicles) to hospitals for medication were not available in cities that were locked down.

After the lockdown ended, hospitals opened but mainly to essential services. Some adolescents were not sure if their care was essential and stayed home. Medication centers continued their services, yet emphasis was on staying home which seem to be preferred option for some adolescents. Transport services resumed but the transport fee was a deterrent for some. There were also administrative challenges, for example staff cohort to manage emergency and therefore all out-patient clinics were suspended. Enablers packages including nutritional and transport support during treatment were also suspended. There was no structured system to track adolescents who needed to refill their medication.

Suggestions to prevent future challenges during similar situations included:

- Electronic database of clients (adolescents in care) with scheduled visits, and drug refill dates
- Alert system/reminders with specific instructions on where to pick medication
- Arranging for WhatsApp or telephonic consultations with clinicians on wellbeing of adolescents with chronic infectious diseases

In summary, it is important to keep engaging the adolescents with chronic diseases. Lessons from COVID-19 must enable us to develop functional models in consultation with adolescents with TB/HIV on how best establish continuum of care during natural disasters and outbreaks.

Impact of COVID-19 on child and adolescent TB services: experiences from the Americas – Celia Martinez, PAHO Child and Adolescent TB Working Group

The impact of COVID-19 on Latin America and the Caribbean (LAC) has been severe in terms of health, economic and social/humanitarian impacts. LAC has seen the highest numbers of absolute and per capita cases worldwide, fragmented and unequal health systems, with low participation in health insurance plans and lack of access to quality health care and information on health, especially serious in rural areas including indigenous people.

The pandemic is exacerbating existing food insecurity caused by environmentally driven food shortages, political turmoil, and dwindling purchasing power. Latin America and the Caribbean has seen an almost three-fold rise in the number of people requiring food assistance. The number of people experiencing acute food insecurity could increase by 11.7 million to 16.0 million people in 2020 because of the pandemic. The Gini index (a measure of statistical dispersion intended to represent the income inequality or wealth inequality within a nation or any other group of people)[1] is expected to increase with the pandemic by between 1.1% and 7.8% in several countries in the region.

The operation of TB services in the Americas has been severely affected through:

- Limited access to services: outpatient services were partially interrupted. These disruptions have affected all types of care for people with TB.
- Health Services: routine health services were reorganized or interrupted and many stopped providing care to people in detection or treatment for TB.
- Diagnosis: interrupted or stopped because of lack of a BSC II and/or adequate PPE to following the recommended biosafety measures.
- Treatment and care: TB health services were reorganized or interrupted, and many stopped providing treatment.
- Health care workers: Decrease in the workforce, many of the health workers who usually provide TB care were reassigned to the COVID-19 response.
- Other factors: Fear of the population to attend the consultation, due to the probable transmission of COVID-19 in the health services.

As a result, case notifications for TB have dropped in most LAC countries, including in children and adolescents. There have also been significant drops in the % of TB cases with known HIV status, provision of TPT, and contact investigation implementation.

PAHO has issued information notes, recommendations, social media campaigns, operational guidelines and communication materials. Ministries of Health provided technical assistance to health services and local TB programs, and established a strong coalition with civil society organizations, scientific societies, Indigenous Health sector, Parliamentary Front and communities, to monitor the access to and continuity

[1] https://en.wikipedia.org/wiki/Gini_coefficient

of essential health services for TB, hold coordination meetings with laboratories and provide psychosocial support for patients with DR-TB and at risk of loss of follow up.

Conclusions:

- Countries including NTPs have made numerous efforts to continue the fight against TB in the context of the pandemic.
- TB capacity building contributes to the response to the COVID-19 pandemic, mainly in relation to search and contact tracing, home and community-based care, as well as in surveillance and monitoring systems for TB.
- The actions incorporated to address Covid-19 can also benefit TB programs, especially in relation to infection control and telemedicine.
- To ensure countries' economic recovery, comprehensive welfare and inclusive social protection systems are necessary.

Community perspectives on COVID and TB – Rahab Mwaniki, KANCO Kenya

Unfortunately, Rahab Mwaniki had trouble connecting to the meeting. Her presentation is available on the working group website.

Discussions (summary of questions and answers submitted through the chat function)

Selected questions answered through the chat function during the meeting are listed below. For the live question and answer sessions, please refer to the recording available on the working group webpage.

Questions	Answers
SHINE trial:	
Were both culture negative and positive included?	Yes, any culture results as well as both Xpert positive and negative. Smear positive children were excluded.
Were the doses of INH and Rif the same across both arms?	The isoniazid and rifampicin doses by weight were same in both arms – the difference was the duration of treatment
Prevention	
What are the groups' thoughts on the FDA letter regarding Rifapentine impurity and the following precautionary measure by Sanofi? How will this affect countries? The nitrosamine impurity may be an issue for rifampicin as well -- is WHO planning to put out an informational note to help programs/patients weigh risk benefit of nitrosamine impurity exposure?	Yes, it also affects rifampicin - but it may be different for the different rifamycins. Also, there are many manufacturers making rifampicin, as opposed to just 2 for rifapentine, although if the impurity is at the API source, then there are also only 2 manufacturers for rifampicin. The USFDA note did implicate rifampicin supplies to the US. But there are many more affected globally. WHO PQ Medicines also launched a call for review of nitrosamines for all API and medicines applications (please refer to https://extranet.who.int/prequal/news/manufacturers-conduct-risk-assessments-impurities), similar to what was done by US FDA, EU and elsewhere. WHO also issued a note about nitrosamine impurity in rifapentine in July (https://extranet.who.int/prequal/news/nitrosamine-concerns-priftin-rifapentine). WHO is currently working

	on the measures that applicants to PQ Medicines need to take to mitigate the risk of these impurities whilst ensuring that these TB products are still available for patients. An update is expected shortly on this from PQ Medicines. Note: this was issued on 23 October, see https://extranet.who.int/pqweb/news/nitrosamine-concerns-rifapentine-and-rifampicin
Diagnosis	
It would be interesting to hear the findings from your evaluation of the reasons for the invalid stool testing results. I am also wondering if the other methods experience similar issues with invalid/error results.	1) many of the errors seem to be machine-related, rather than sample-related. We should realize that stool may challenge the Xpert technology much more than sputum does. The KNCV is looking into this. 2) we don't see this in any of our other work, including the head to head studies. Generally the rate is slightly higher than for sputum, but just around 5% for the first sample.
What is the reason for the high positivity with NGA and stool in Vietnam (33%)? What were the enrollment criteria specifically?	Vietnam applies routine implementation, not a study. So though the KNCV Tuberculosis Foundation encourages them to use the stool test on all children and PLHIV with presumptive pulmonary TB, we are dependent on clinicians. Regarding the positivity rate on Xpert stool for children (33%) - there clearly is some selection ongoing. This is because it is an implementation project, not a study, and we can only encourage, not demand, clinicians to request a stool Xpert test for all children with presumptive pulmonary TB.
General question: It will be good to check the types of errors from the different studies and review the possible causes. For the Zambia TB Speed study are we able to provide details of findings by age, for example, the reasons for the 100 children who did not submit a stool sample? Are we able to qualify which age had challenges to submit the stool?	Yes, the KNCV Tuberculosis Foundation is collecting error code for all studies + Vietnam implementation project. (also collect age, sex and some other variables). TB-Speed Zambia had more challenges in obtaining stool samples in children with severe pneumonia, but other components did fairly well. We are conducting qualitative evaluation to understand better the feasibility and acceptance from both the parents and health care provider point of view.
Based on those preliminary findings do you think that a combination of samples should be considered for each child with presumptive TB?	Sample collection was more successful than stool probably because these were hospital-based studies and therefore staff could do the NPA. In the primary health care setting, the stool might be more feasible. We will compare with the results from the decentralisation component of the TB SPEED study. The full results will answer if both samples are needed.
Systematic reviews	
One explanation for the very high rate of disease progression in Ben's review in children <1 year is that children in much of the pre-chemotherapy literature did not receive BCG vaccination which may have been	Agree. Advances in diagnostics have the potential to really help reach these children earlier before they develop TB. Also agree that BCG vaccination may be part of the reason for the very high rates in historical data. BCG vaccination levels were high in our cohorts

most protective in infants. Most of the studies in the IPD SR/MA would have received BCG.	(as they are generally in most countries). Difficult to tease out differences with these estimates with the specific data sources.
What were the BCG status of the children who developed disease? What type of disease- Pulmonary, Extrapulmonary (TBM)? The historical study by Ben showed TBM/Disseminated TB was high among <2 years.	Generally, BCG vaccination was common in these cohorts but heterogeneous depending on the setting. Most TB in children was pulmonary (>90%). Which may confirm the comment about the historical versus contemporary estimates. Very interesting to see estimates of disease progression from more recent data. Agree that BCG vaccination is likely an important factor that can explain the differences between the old and newer data - especially preventing disseminated forms such as TBM in the youngest children. But very interesting to see the relatively higher numbers amongst 5-15 year olds.
Leo, did you look at TB incidence beyond 2 years or where there not enough studies with longer flow up?	We did include studies that followed children for longer than 2 years. Something like 8-10 of the 46 study groups. For some of the analyses we had to restrict the groups to only those with >=2 years of follow-up so that there wasn't differential case ascertainment based on follow-up time.
Presumably most of the studies in Leo's SR were pre-Xpert. As adults are diagnosed earlier, children are likely to be exposed for less time and to less infectious source cases. Would be interesting to see how this changes with more rapid adult diagnostics.	The dataset for the systematic review on risk after exposure was collected from 1998-2018.
Were there data about the timing of the tests for infection (IGRA/TST)? Failure to do a such a test 8-10 weeks after break in contact may partly explain the tendency to disease in the test negative children …	Yes, this is a good question. Most of the tests were done at baseline. Some studies did confirmatory TST tests 8-10 weeks after baseline as well but not all studies did this. Studies with QFT data performed tests at baseline. Only a few studies had incident infection data (which is understandable as expensive).
How sensitive are our symptom screens? We found using cough, fever, weight loss, lethargy (2 or more) were present in almost 60% of all admissions. This will put a strain if all these are potentially to get a CXR, especially because TB contact history is not well documented/assume likely contact already in HBCs?	We weren't able to find a lot of data re symptom screening for the general population, but what we did find (which is what one would expect) is that one-off symptom screening is not accurate. However, a few studies in populations with high TB burden used sequential symptom screening (i.e. only refined symptom screen for those with 2 weeks of persistent cough) and this seems promising. One consideration when assessing the utility of symptom screening is incorporation bias when compared to a composite definition of TB. Most results need to be interpreted with some caution recognizing this bias. Unfortunately, it is hard to have enough numbers to compare against only a microbiological reference standard; and, the microbiological reference standard also is biased towards more severe disease.
How was ”screened positive“ defined in the studies you included? Was presence of only one symptom sufficient to define a child as presumptive TB?	For the analyses of symptom screening we conducted, “positive screens” were defined as presence of one or more symptoms from a set of multiple symptoms

@Bryan do you think this symptom base screening can be used by non-doctor health workers, like is the case for pneumonia screening through the WHO/UNICEF Integrated Management of Child Illnesses (IMCI)?	Absolutely--we have some evidence that fairly simple symptom screening has decent accuracy when used on high-risk populations (e.g. HIV+, TB contacts). However, I'm not sure about how useful symptom screening for TB can be in the general population.

Annex 1: Agenda

FINAL AGENDA

Annual meeting Child and Adolescent TB working group, session 1		**10:00 – 12:30 CEST**
Session 1a: Opening, objectives and update from Chair and Secretariat **Chair: Farhana Amanullah**		
10:00 – 10:10	Welcome and opening address including outline of the meeting	Chair CAWG & Director, WHO GTB
10:10 – 10:30	Report from the Chair of the Child and Adolescent TB working group	Chair, Child and Adolescent TB Working Group
10:30 – 10:35	Experiences from a family affected by TB in times of COVID in Brazil	Video
10:35 – 11:00	WHO update on new policy recommendations and progress towards UNGA HLM on TB targets	Annemieke Brands and Sabine Verkuijl, WHO GTB
Session 1b: Paediatric TB research update **Chair: Ben Marais and Steve Graham**		
11:00 – 11:15	Study on burden and outcomes of TB meningitis in children at national and sub-national level in South Africa: opportunities for prevention, earlier diagnosis and treatment	Karen DuPreez, Stellenbosch University
11:15 – 11:30	SHINE trial update	Aarti Avinash Kinikar and Priyanka Raichur, Byramjee Jeejeebhoy Government Medical College, Pune
11:30 – 11:45	Paediatric TB Prevention Trials: an update	Anneke Hesseling, Stellenbosch University
11:45 – 12:00	Selection of interesting peer-reviewed articles	James Seddon, Imperial College London, Desmond Tutu TB Centre
12:00 – 12:30	*Virtual Discussion: raise your hand or use the chat pod*	*All*
12:30 – 14:30	**Breakfast, Lunch or Dinner Break (depending on your time zone)**	
Annual meeting Child and Adolescent TB working group, session 2		**14:30 – 17:00 CEST**
Session 2a: Developments in diagnosis of TB in children and adolescents **Chair: Lisa Obimbo and Moorine Sekadde**		

14:30 – 14:45	Country experiences on implementation of the Simple One Step (SOS) stool method using Xpert MTB/RIF, lessons learned	Edine Tiemersma, KNCV Netherlands Endale Mengesha Goshu, KNCV Ethiopia
14:45 – 15:00	Emerging experiences with diagnostic approaches in children with HIV, severe pneumonia and malnutrition	Chishala Chabala, University Teaching Hospital, Zambia
15:00 – 15:15	T-cell marker-based assays for the diagnosis of tuberculosis in children and adults	Laura Olbrich, University of Munich
Session 2b: Systematic reviews on the risk of TB after exposure and TB screening in children **Chair: Lindsay McKenna and Susan Maloney**		
15:15 – 15:30	The risk of TB in children after close exposure: a systematic review and individual-participant meta-analysis	Leo Martinez, Stanford University School of Medicine
15:30 – 15:45	Results of a systematic review of TB screening approaches in children	Bryan Vonasek, Baylor College of Medicine
Session 2c: Impact of COVID-19 on child and adolescent TB services **Chair: Kobto Ghislain Koura and Anthony Enimil**		
15:45 – 16:00	Impact of COVID-19 on child and adolescent TB services: experiences from Africa	Anthony Enimil, Ghana
16:00 – 16:15	Impact of COVID-19 on child and adolescent TB services: experiences from the Americas	Celia Martinez, PAHO Child and Adolescent TB Working Group
16:15 – 16:30	Community perspectives on COVID and TB	Rahab Mwaniki, KANCO Kenya
16:30 – 17:00	*Virtual Discussion: raise your hand or use the chat pod*	*All*
17:00	Wrap up, next steps and closure	Secretariat

Annex 2: List of participants

1.	Aarti Kinikar
2.	Agnes Gebhard
3.	Ahmed Bedru Omer
4.	Alberto Roggi
5.	Alex Durena
6.	Alex Kay
7.	Alfrida Silitonga
8.	André Ndongosieme
9.	Andrea Rossoni
10.	Andrew Steenhoff
11.	Andrii Slyzkyi
12.	Angela Crook
13.	Anna Mandalakas
14.	Anna Scardigli
15.	Anna Turkova
16.	Anneke Hesseling
17.	Anne-Marie Demers
18.	Annemieke Brands
19.	Anthony Enimil
20.	Anthony Garcia Prats
21.	Atiar Rahman
22.	Aurelia Vessiere
23.	Babatunde Sanni
24.	Bandana Bhatta
25.	Basant Joshi
26.	Beate Kampmann
27.	Ben Marais
28.	Betina Gabardo
29.	Betty Nsangi
30.	Blessina Kumar
31.	Bryan Vonasek
32.	Bunnet Dim
33.	Celia Martinez de Cuellar
34.	Charlotte Colvin
35.	Charlotte McGowan
36.	Cherise Scott
37.	Chishala Chabala
38.	Christian Lienhardt
39.	Christof Geldmacher
40.	Clemax Sant Anna
41.	Cleotilde How
42.	Corinne Merle
43.	Craig Dalgarno
44.	Daria Szkwarko
45.	Degu Jerene Dare
46.	Dennis Falzon
47.	Diana Gibb
48.	Dillon Wademan
49.	Ebo Krystel Kelly
50.	Edine Tiemersma
51.	Elisa Lopez Varela
52.	Elizabeth Meassick
53.	Ellen Owen-Powell
54.	Enang Oyama
55.	Endale Mengesha
56.	Eric Wobudeya
57.	Esin Nkereuwem
58.	Eveline Klinkenberg
59.	Fajri Gafar
60.	Falokun Temitope
61.	Farai Mavhunga
62.	Farhana Amanullah
63.	Finny Fitry Yani
64.	Galuh Bla
65.	Genevieve Wills
66.	Graeme Hoddinott
67.	Grania Brigden
68.	Gunta Dravniece
69.	Guy Moutembi
70.	H. Simon Schaaf
71.	Helen Mcilleron
72.	Helene Font
73.	Huong Nguyen
74.	Ian Kitai
75.	Immaculate Kathure
76.	Jacquie Oliwa
77.	James Seddon
78.	Jeffrey Starke
79.	Jennifer Furin
80.	Joanna Ehrlich
81.	Joanna Orne-Gliemann
82.	John Baptist Nkuranga
83.	John Paul Dongo
84.	Joseph Kuye
85.	Joy Sarojini Michael

86.	Karen Du Preez
87.	Karen Steingart
88.	Kateryna Gamazina
89.	Kenneth Gunasekera
90.	Kerri Viney
91.	Kobto Koura
92.	Kristen LeBeau
93.	Kristin Kremer
94.	Kyaw Ko Ko Win
95.	Lam Hong Bao Ngoc
96.	Laura Olbrich
97.	Leonardo Martinez
98.	Lina Bergstrom-Randall
99.	Lindsay McKenna
100.	Lisa Adams
101.	Liza Safronova
102.	Loanda Mboyo Aime
103.	Louise Choo
104.	Lulu Muhe
105.	Mags Thomason
106.	Mahfuza Rifat
107.	Malgosia Grzemska
108.	Manoa Razafimanantsoa
109.	Manon Lounnas
110.	Manuele Piccolis
111.	Maria Regina Christian
112.	Marieke van der Zalm
113.	Marilyn Ninan
114.	Marina Tadolini
115.	Mark Cotton
116.	Marta Campos
117.	Martina Casenghi
118.	Martina Penazzato
119.	Maryline Bonnet
120.	Maurice Maina
121.	Megan Palmer
122.	Michael Umoren
123.	Mohammed Bouskraoui
124.	Moorine Penninah Sekadde
125.	Muchammad Fahrul Udin
126.	Munira Khan
127.	Nazir Ismail
128.	Nemes Iriya
129.	Nicola Loffredi

130.	Nicolas Koskas
131.	Nicole Ritz
132.	Nicole Salazar-Austin
133.	Nokulunga Zondo
134.	Nora Fritschi
135.	Norbert Heinrich
136.	Nura Musa Shuaib
137.	Oksana Smetanina
138.	Olena Pavlenko
139.	Olena Diuzheva
140.	Olga Pavlova
141.	Olivier Marcy
142.	Pamela Nabeta
143.	Papy Ndjibu
144.	Patience Edo Opara
145.	Pedro Avedillo
146.	Petra de Haas
147.	Priyanka Raichur
148.	Rachel Dwilow
149.	Rafael López
150.	Rahab Mwaniki
151.	Rajeshwar Dayal
152.	Ramatoulaye Sall
153.	Retno Asih Setyoningrum
154.	Rina Triasih
155.	Robin Basu Roy
156.	Sabine Eva Verkuijl
157.	Sarah Cook-Scalise
158.	Sébastien Morin
159.	Senait Kebede
160.	Senait Kebede
161.	Senia Rosales-Klintz
162.	Seraphine Kaminsa
163.	Shakil Ahmed
164.	Stephanie Wetton
165.	Steve Graham
166.	Susan Hrapcak
167.	Susan Maloney
168.	Susan Purchase
169.	Suvesh Shrestha
170.	T Monique James
171.	Tania Thomas
172.	Tara Devezin
173.	Tereza Kasaeva

174.	Tina Sachs
175.	Tiziana Masini
176.	Tonya Arscott-Mills (plus 2 colleagues)
177.	Toyin Togun
178.	Trinh Duong
179.	Trisasi Lestari
180.	Ufuoma Aduh
181.	Valentina Burzio
182.	Valentina Marchese
183.	Valérie Schwoebel
184.	Varinder Singh
185.	Veronica Mulenga
186.	Vidya Mave
187.	Vijaykumar Edward
188.	Vivian Cox
189.	Yael Hirsch-Moverman
190.	Dial in user (unknown)