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Management of child MDR-TB contacts across countries in the WHO European Region: a survey of current practice

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Key Words:	MDR-TB, Paediatric, Preventive treatment, Chemoprophylaxis

Title

Management of child MDR-TB contacts across countries in the WHO European Region: a survey of current practice

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Running head

Management of MDR-TB child contacts in Europe

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Key words

MDR-TB, paediatric, chemoprophylaxis, preventive treatment

Summary

The World Health Organization European Region has one of the highest rates of multidrug-resistant (MDR) tuberculosis (TB) in the world, resulting in many vulnerable children getting exposed each year. Evidence for preventive therapy following MDR-TB exposure is limited and current guidance is conflicting. An online survey was performed to determine clinical practice in this region. Seventy-two clinicians from 25 countries participated. Practices related to screening and decision-making were highly variable. Just over half were providing preventive therapy for MDR-TB-exposed children; the only characteristic associated with provision was practice within the European Union (adjusted odds ratio: 4.07; 95% confidence interval: 1.33-12.5).

Background

Multidrug-resistant (MDR) tuberculosis (TB) is caused by *Mycobacterium tuberculosis* with resistance to isoniazid and rifampicin.[1] In the World Health Organization (WHO) European Region (defined at: http://www.who.int/about/regions/euro/en/) 16% of new TB cases and 48% of retreatment cases were estimated to be MDR-TB in 2015.[2] Over 40,000 cases were notified that year,[2] many of whom had contact with children. Young children are at high risk of progression to TB, including MDR-TB, following exposure.[3,4] MDR-TB treatment is long, expensive and associated with significant adverse events.

There is good evidence for the effectiveness of drug therapy for child contacts of drug-susceptible TB to prevent progression to TB disease.[5] However, the evidence base for the management of child contacts of MDR-TB cases is less robust. National and international guidance is inconsistent and conflicting, with clinicians facing difficult management choices. To date, only limited data exist regarding the current management of paediatric MDR-TB contacts in clinical practice. We therefore aimed to document current practice across different countries in the WHO European Region.

Methods

From March-July 2014 a web-based survey was conducted to explore variations in the management of MDR-TB-exposed children.[6] We developed an online questionnaire in English and Russian capturing the following: respondent characteristics, screening practices, preventive therapy (PT) practices, and follow-up (Supplementary Materials). Participants were asked to define patient groups considered for PT, the PT regimens used and treatment duration. The questionnaire was piloted among five clinical experts within the Paediatric Tuberculosis Network European Trials Group (ptbnet).[7]

A list of clinicians likely to be managing child MDR-TB contacts in the WHO European Region was compiled using the membership lists of ptbnet, the International Union Against Tuberculosis and Lung Disease Childhood TB Working Group, and the Childhood Subgroup of the WHO Stop TB Partnership. Each clinician was sent a personalised email requesting their participation, with the request to forward the invitation to relevant colleagues. Three reminder emails were sent during the study period (Supplementary Materials). To assess factors associated with PT provision, we used a multivariable stepwise logistic regression model. Variables with $p<0.15$ in the univariable analysis were included in the model. Statistical analyses were undertaken using Stata version 14.0 (StataCorp, College Station, U.S.).

Ethics Approval

Under current UK National Research Ethics Service (NRES) regulations, Research Ethics Committee review is not required for research involving healthcare staff recruited as research participants by virtue of their professional role (Governance Arrangements for Research Ethics Committees, paragraph 2.3.13). Participation in the survey was voluntary. Participants were aware that they were participating in research, and that the results may be published.

Results

Of 176 specialists from 44 countries approached, 72 (41%) respondents from 25 countries participated in the survey, including 28 from 6 countries outside the EU/EEA (Figure 1). Of all respondents, 66/72 (92%) had >5 years of experience working with TB; 59/72 (82%) were at senior level and 41/72 (57%) managed ≥3 child MDR-TB contacts a year. To guide the management of the contacts, in addition to clinical history and examination, most respondents used imaging: 42/72 (58%) chest x-rays, 21/72 (29%) both chest x-rays and computer tomography, 4/72 (6%) computer tomography only; the remaining 5/72 (7%) did not routinely use imaging. Nearly half (32/72;44%) stated routinely collecting respiratory specimens in asymptomatic children. Variable combinations of interferon-gamma release assays (IGRA) and skin tests were used to diagnose TB infection: 45/72 (63%) used both IGRA and skin tests, 23/72 (32%) skin tests only, 2/72 (3%) IGRA only and 2/72 (3%) neither. Of the skin tests, the tuberculin skin test (TST) was most frequently used; the Diaskintest (using recombinant CFP-10/ESAT-6; Generium Pharmaceuticals, Moscow) was used by 11 respondents based in the Russian Federation, Belarus, Estonia and Ukraine.

Of all 72 respondents, 42 (58%) stated they were providing PT to MDR-TB-exposed children. For children with evidence of TB infection, 18/42 (43%) clinicians were providing PT if additional risk factors were present (age <2 or <5 years, HIV-infection or immunocompromise); 24/42 (57%) were treating all TB-infected children. For children without evidence of TB infection, the majority of respondents (26/42;62%) were doing follow-up without PT, 12/42 (29%) were providing PT if risk factors were present, and 4/42 (10%) were treating all contacts. For PT, 31/42 (74%) used regimens tailored to the drug susceptibility pattern of the source case's isolate, 9/42 (21%) used standardised regimens (i.e. independent of susceptibility results), and two used variable approaches depending on situation. Approximately half of the respondents (22/42;52%) were using two-drug regimens, fewer used ≥3 drugs (8/42;19%) or monotherapy (10/42;24%), and the remaining two decided on case by case. Variable combinations of ethambutol, pyrazinamide, high-dose isoniazid and levofloxacin/moxifloxacin were the most commonly reported regimens. Most respondents (30/42;71%) stated treating for 6 or 9 months (50% and 21%, respectively). Most clinicians were following

children up for two years or longer regardless of PT being used or not (30/42;71% and 61/72;85% respectively) (Supplementary Materials).

In the multivariable model the only factor associated with the provision of PT was practice within the EU/EEA (vs. outside the EU/EEA) with an adjusted odds ratio of 4.07 (95% CI: 1.33-12.5; p=0.014; Table 1).

Discussion and Conclusions

The results highlight a wide spectrum of practice in the management of children exposed to MDR-TB in countries of the WHO European Region. Over half of clinicians reported using PT with varying indications and drug regimens. Practices regarding PT differed significantly between clinicians based within the EU/EEA and those based outside. The observed difference between EU/EAA and non-EU countries may be due to a more individualised approach to patient management in EU/EAA countries versus a more programmatic approach in non-EU countries with greater reliance on official national guidelines and WHO recommendations.

In addition to marked heterogeneity regarding provision of PT, our data also indicate high variation in investigations performed in children with MDR-TB contact with somewhat surprisingly high proportion of CT scans and collection of respiratory specimens in asymptomatic children. These findings may be a reflection of the paucity of data to guide standard diagnostic approaches in these children, and indicate that clinicians may have a tendency for more 'aggressive' investigation strategies in MDR-TB contacts.

A key component of the WHO End TB Strategy is the identification and treatment of TB infection,[8] with modelling exercises suggesting that without addressing TB infection it will be impossible to eliminate TB globally.[9] This is as true, if not more so, for MDR-TB as it is for drug-susceptible TB, as a smaller proportion of MDR-TB cases are identified and treated, and outcomes are much poorer. At least three funded trials investigating the treatment of MDR-TB contacts are currently underway, but results are not expected for several years. Observational studies suggest that the use of PT for MDR-TB can be safe and effective,[10] but existing guidelines are highly variable. It is therefore not surprising that current practice across the WHO European Region is so inconsistent, and it appears likely that these inconsistencies will persist until international and national guidelines are harmonised.

The survey was limited to clinicians managing child MDR-TB contacts in the WHO European Region who were identified and responded to the survey. Although we contacted a wide range of clinicians and included flexible answer options, it is likely that not all possible practices were captured. The survey only documents

reported practice, rather than capturing individual patient management. Despite these limitations, the results provide insight into the current management of paediatric MDR-TB contacts in EU/EAA and non-EU, countries and highlight the urgent need for stronger evidence to guide clinical decisions.

Acknowledgements

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Funding

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Conflicts of Interest

All authors – none.

Authors' contributions:

The study was coordinated by JAS. AT, JAS designed the study. All authors piloted and critically appraised the questionnaire. JAS, AT emailed the questionnaire and JAS collated the results. AT and JS undertook the analysis and drafted the paper with input from MT. All authors contributed to the revision of the manuscript and approved the final version.

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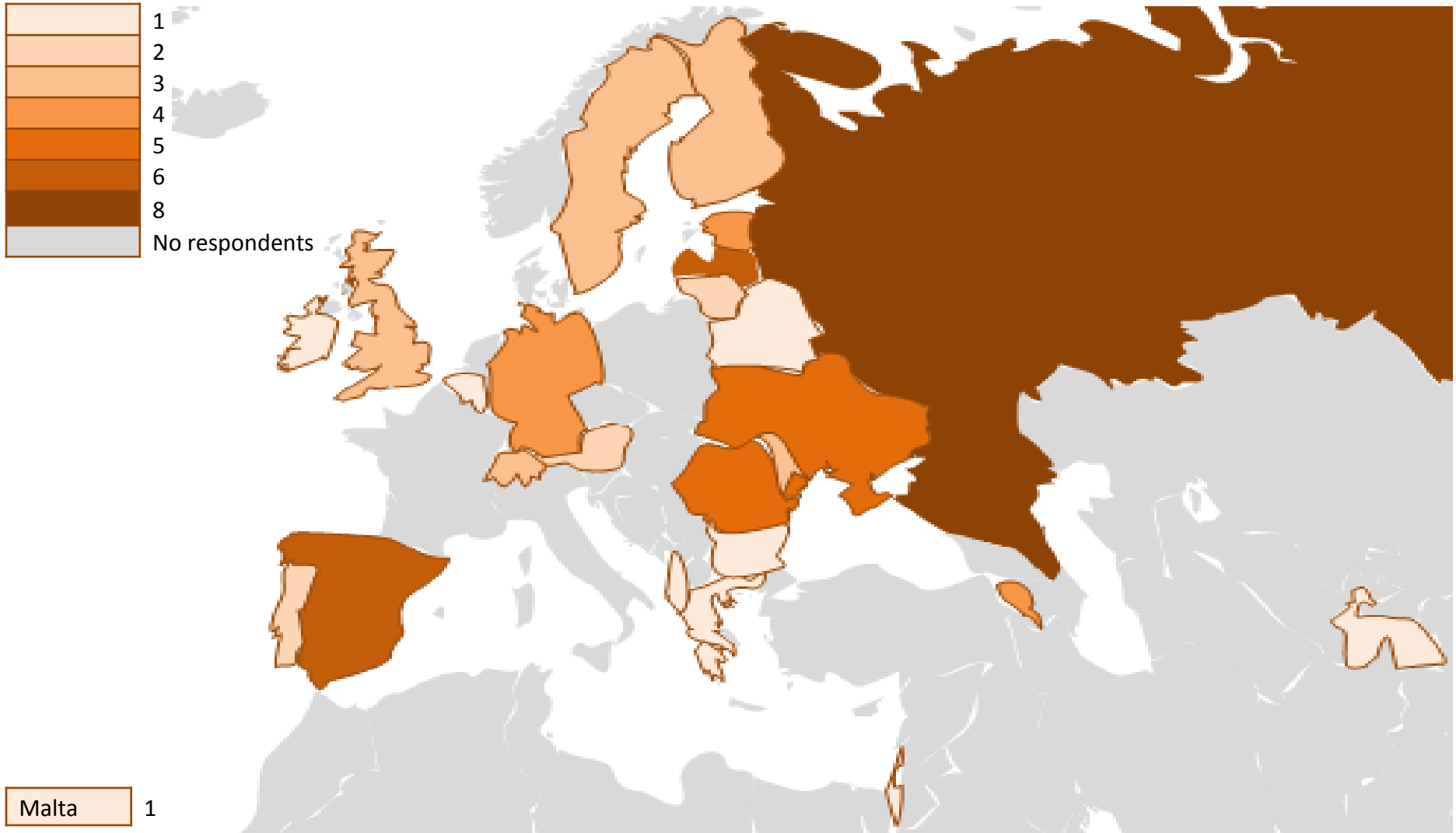
Table 1. Association between respondent characteristics and the provision of preventive therapy (n=72)

		PT given (n)	PT not given (n)	Odds ratio (95% CI)	P value	Adjusted Odds ratio (95% CI)	P value
Experience of treating TB patients	<10 years	13	10	Ref	0.83		
	≥ 10 years	29	20	1.12 (0.41-3.06)			
Specialist TB doctor	No	28	13	Ref	0.05	Ref	0.51
	Yes	14	17	0.38 (0.14-1.04)		0.69 (0.23-2.09)	
Consultant level doctor	No	6	7	Ref	0.33		
	Yes	36	23	1.83 (0.54-6.22)			
Number of MDR-TB child contacts managed per year	<3 per year	19	12	Ref	0.66		
	≥3 per year	23	18	0.81 (0.31-2.10)			
Country of respondent	Outside EU/EEA	10	18	Ref	0.002	Ref	0.014
	Within EU/ EEA	32	12	4.80 (1.59-14.5)		4.07 (1.33-12.5)	

CI: confidence interval; EEA: European Economic Area; MDR-TB: multidrug-resistant tuberculosis; PT: preventive therapy Ref: reference value; TB: tuberculosis.

Figure Legend

Figure 1: Location of practice and number of survey respondents in countries in the World Health Organization European Region. Participating countries: Albania, Armenia, Austria, Belarus, Belgium, Bulgaria, Estonia, Finland, Germany, Greece, Ireland, Israel, Latvia, Lithuania, Malta, Moldova, Portugal, Romania, Russian Federation, Spain, Sweden, Switzerland, Tajikistan, UK, Ukraine


1
2
3
4
5
6
8
No respondents
Malta
1

Supplementary Materials

CONTENTS

I. Screenshots of the English version of the online survey

Child Contacts of MDR-TB

Multidrug-resistant (MDR) tuberculosis (TB) is a growing challenge within Europe with the number of cases rising. For child contacts of drug-susceptible TB, preventive therapy with isoniazid (and/or rifampicin) is an effective therapy to reduce the risk of progression from TB infection to TB disease. However, it is unclear how children exposed to MDR-TB should be managed.

A survey by van der Werf et al. (Int J Tuberc Lung Dis 2012; 16: 426) demonstrated very heterogeneous guidelines throughout Europe and the European Centre for Disease Prevention and Control (ECDC) has suggested two options for the management of child MDR-TB contacts: 1) preventive therapy or 2) close follow-up.

On behalf of the Paediatric Tuberculosis Network European Trials Group (PTBNet) we are carrying out a survey into the management of children exposed to MDR-TB. We are aiming to look at the current practice of how children within Europe are managed following exposure to MDR-TB.

The survey should only take 10 minutes to complete and your personal details will remain completely confidential (it is not essential to even provide them). If you know of other people who may be providing care for children who have been exposed to MDR-TB in Europe, please forward this email to them. This survey will provide important information on current practices within Europe which will inform the management of child MDR-TB contacts in the future.

Terminology

Just to make sure we all mean the same thing PLEASE TAKE A MOMENT to read through the definitions that will be used in this survey, which are taken from a consensus statement of paediatric TB specialists. (J Ped Infect Dis Soc 2013; 2: 100-109)

IGRA: Interferon-gamma release assays (QuantiFERON-TB Gold assays or T-SPOT.TB assay)

TST: Tuberculin skin test (also known as Mantoux test). Consider tests positive as per definition by your national TB programme

Diaskintest: a skin test (alternative to TST), which utilizes specific antigens of M. tuberculosis: CFP10 and ESAT6 instead of tuberculin

MDR-TB: M. tuberculosis strain resistant to at least rifampicin and isoniazid

MDR-TB contact: A child exposed to an infectious MDR-TB source case who, in the last 12 months, has either slept in the same household or had daily interaction with the child

M tuberculosis infection (also termed Latent TB Infection or LTBI): A positive immunological test (TST or IGRA), in the absence of symptoms and physical signs (both acute and chronic), together with no abnormal radiological findings but in combination with being a MDR-TB contact

Preventive therapy: Includes post-exposure prophylaxis (including window period prophylaxis, when prophylaxis is given during the time span between the date of an initial TST with a negative reaction and the date of the follow-up TST), secondary prophylaxis, and treatment of M. tuberculosis infection/LTBI

* Required

Contact Details

Name
(optional)

Your answer

Country *

Choose

City
(optional)

Your answer

Email address
(optional)

Your answer

Professional Details

1. How long have you been working with TB patients? *
(please tick only one box)

- ◯ < 1 year
- ◯ 1-2 years
- ◯ 2-5 years
- ◯ 5-10 years
- ◯ >10 years

2. What is your main area of work *
(please tick only one box)

- ◯ General Paediatric Doctor
- ◯ Paediatric Infectious Diseases Doctor
- ◯ Tuberculosis Doctor (Paediatric)
- ◯ Tuberculosis Doctor (Adult)
- ◯ Paediatric Pulmonary Doctor
- ◯ Adult Pulmonary Doctor
- ◯ Adult Doctor
- ◯ Microbiologist
- ◯ Other : _____

3. What type of doctor are you? *
(please tick only one box)

- ○ Consultant/Attending/Senior
- ○ Middle/Resident/Registrar/Fellow
- ○ Junior/Intern/SHO
- ○ Other : _____

4. Where do you mainly see child contacts of MDR-TB? *
(please tick all boxes that apply)

- ☐ Dedicated Tuberculosis Centre
- ☐ Paediatric Hospital
- ☐ Paediatric Department of General Hospital
- ☐ General Hospital
- ☐ Primary Care/Community Clinic/Polyclinic
- ☐ TB Sanatorium
- ☐ Other: _____

5. How many MDR-TB child contacts have you seen each year on average over the last five years? *
(please tick only one box)

- ○ None
- ○ Infrequently
- ○ 1-2 per year
- ○ 3-5 per year
- ○ 5-10 per year
- ○ >10 per year

Identification and screening of child contacts

6. Following the diagnosis of MDR-TB in an adult, how are child contacts identified? *
(please tick only one box)

- ○ On questioning of the MDR-TB source case
- ○ At a home visit
- ○ Both by questioning and home visit
- ○ Other : _____

7. Who usually refers child contacts to your services? *
(please tick all boxes that apply)

- ☐ Nurses/doctors working in TB programme
- ☐ School nurses
- ☐ Primary care/family doctors
- ☐ Paediatric doctors
- ☐ Adult doctors
- ☐ Self referral
- ☐ Other: _____

8. In an asymptomatic child MDR-TB contact, which tests do you commonly use to make a decision on further management? *
(please tick all boxes that apply)

- [ ] IGRA
- [ ] TST
- [ ] Diaskintest
- [ ] Chest x-ray
- [ ] CT scan
- [ ] Gastric washings to send for microbiological tests
- [ ] Sputum to send for microbiological tests
- [ ] Induced sputum to send for microbiological tests
- [ ] Broncholalveolar lavage to send for microbiological tests
- [ ] None of the above
- [ ] Other: _____

Deciding on the management of child contacts

9. With regards TST/IGRA, in which circumstances do you give preventive therapy for child MDR-TB contacts? *
(please tick only one box)

- ◯ I do not give preventive therapy
- ◯ I do not use TST or IGRA to make decisions about preventive therapy
- ◯ Positive TST alone
- ◯ Positive IGRA alone
- ◯ Both TST and IGRA have to be positive
- ◯ Either TST or IGRA has to be positive
- ◯ Other : _____

10. For child MDR-TB contacts with evidence of M. tuberculosis infection (based on positive TST and/or IGRA), who do you give preventive therapy? *
(please tick only one box)

- ◯ I do not use preventive therapy
- ◯ I do not use IGRA/TST to make a decision about preventive therapy
- ◯ Children <1 year only
- ◯ Children <2 years only
- ◯ Children <5 years only
- ◯ All children (<16 years)
- ◯ Children with immunosuppression/immunodeficiency
- ◯ Other : _____

11. Do you ever start preventive therapy in child MDR-TB contacts who do not have evidence of M. tuberculosis infection? *

(please tick only one box)

- ◯ I do not use preventive therapy
- ◯ I do not use IGRA/TST to make a decision about preventive therapy
- ◯ I do not use preventive therapy unless there is evidence of M. tuberculosis infection (based on a positive TST and/or IGRA)
- ◯ Yes, routinely in all children <1 year
- ◯ Yes, routinely in all children <2 years
- ◯ Yes, routinely in all children <5 years
- ◯ Yes, routinely in all children (<16 years)
- ◯ Yes, routinely in all children with immunosuppression
- ◯ Other : _____

12. If you start preventive therapy in children with negative TST/IGRA tests initially, do you ever repeat the tests? *

(Please tick only one box)

- ◯ I do not use preventive therapy
- ◯ I do not use these tests
- ◯ Yes, I repeat TST at 6-12 weeks and stop therapy if it is negative
- ◯ Yes, I repeat the IGRA at 6-12 weeks and stop therapy if it is negative
- ◯ Yes, I repeat both TST and IGRA at 6-12 weeks and stop therapy if both are negative
- ◯ No, if I start preventive therapy, I give a full treatment course
- ◯ Other : _____

13. What regimen do you use for preventive therapy in child MDR-TB contacts? *

(pleaes tick only one box)

- ◯ I do not use preventive therapy
- ◯ I use a standard regimen for all MDR-TB contacts with one drug
- ◯ I use a standard regimen for all MDR-TB contacts with two drugs
- ◯ I use a standard regimen for all MDR-TB contacts with more than two drugs
- ◯ I use a regimen based on the drug susceptibility test (DST) profile of the source case with one drug
- ◯ I use a regimen based on the drug susceptibility test (DST) profile of the source case with two drugs
- ◯ I use a regimen based on the drug susceptibility test (DST) profile of the source case with more than two drugs
- ◯ Other : _____

Standardised Regimens

14. If you use a standard regimen for MDR-TB preventive therapy, which drugs do you use? *
(please tick all boxes that apply)

- [ ] Standard dose isoniazid (5-10mg/kg)
- [ ] High dose isoniazid (15-20mg/kg)
- [ ] Ethambutol
- [ ] Pyrazinamide
- [ ] Ofloxacin
- [ ] Ciprofloxacin
- [ ] Levofloxacin
- [ ] Moxifloxacin
- [ ] Gatifloxacin
- [ ] Ethionamide/prothionamide
- [ ] Cycloserine/terizidone
- [ ] PAS
- [ ] Linezolid
- [ ] Other: _____

Tailored Regimens

15. If you use a regimen tailored to the drug susceptibility test (DST) profile of the source case which drugs do you sometimes use? *

(please tick all boxes that apply)

- [ ] Standard dose isoniazid (5-10mg/kg)
- [ ] High dose isoniazid (15-20mg/kg)
- [ ] Ethambutol
- [ ] Pyrazinamide
- [ ] Ofloxacin
- [ ] Ciprofloxacin
- [ ] Levofloxacin
- [ ] Moxifloxacin
- [ ] Gatifloxacin
- [ ] Ethionamide/prothionamide
- [ ] Cycloserine/terizidone
- [ ] PAS
- [ ] Linezolid
- [ ] Other: _____

Preventive Therapy

16. How long do you generally treat children with preventive therapy after exposure to MDR-TB? *
(please record duration in months)

- ○ 3 months
- ○ 4 months
- ○ 6 months
- ○ 9 months
- ○ 12 months
- ○ 18 months
- ○ 24 months
- ○ Other : _____

17. How is preventive therapy delivered to the child? *
(please tick all boxes that apply)

- ☐ The child is admitted to hospital during preventive therapy
- ☐ The child is admitted to a sanatorium during preventive therapy
- ☐ The child is taken daily to a clinic and drug ingestion is observed
- ☐ A health worker goes to the house of the child and observes the drug ingestion
- ☐ The parents give the preventive therapy
- ☐ Other: _____

Follow up

18. For children on preventive therapy after MDR-TB exposure, at which time points do you follow them up? *
(tick ALL TIMEPOINTS that apply)

- [ ] I do not give preventive therapy
- [ ] I give preventive therapy but do not do follow them up (discharge)
- [ ] By one month
- [ ] At two months
- [ ] At three months
- [ ] At four months
- [ ] At six months
- [ ] At nine months
- [ ] At twelve months
- [ ] When clinically indicated
- [ ] Other: _____

19. For children exposed to MDR-TB and NOT placed on preventive therapy at which time points do you follow them up? *
(tick ALL TIMEPOINTS that apply)

- [ ] I do not do follow them up
- [ ] By one month
- [ ] At two months
- [ ] At three months
- [ ] At four months
- [ ] At six months
- [ ] At nine months
- [ ] At twelve months
- [ ] When clinically indicated
- [ ] Other: _____

20. If you do chest x-rays for children on preventive therapy, at which time points do you do them? *
(tick ALL TIMEPOINTS that apply)

- [ ] I do not give preventive therapy
- [ ] I give preventive therapy but do not do follow up chest x-rays
- [ ] By one month
- [ ] At two months
- [ ] At three months
- [ ] At four months
- [ ] At six months
- [ ] At nine months
- [ ] At twelve months
- [ ] When clinically indicated
- [ ] Other: _____

21. If you do chest x-rays for children NOT on preventive therapy, at which time points do you do them? *
(tick ALL TIMEPOINTS that apply)

- [ ] I do not do chest x-rays
- [ ] By one month
- [ ] At two months
- [ ] At three months
- [ ] At four months
- [ ] At six months
- [ ] At nine months
- [ ] At twelve months
- [ ] When clinically indicated
- [ ] Other: _____

22. For children on preventive therapy after exposure to MDR-TB, how long do you routinely follow them up for? *
(please tick only one box)

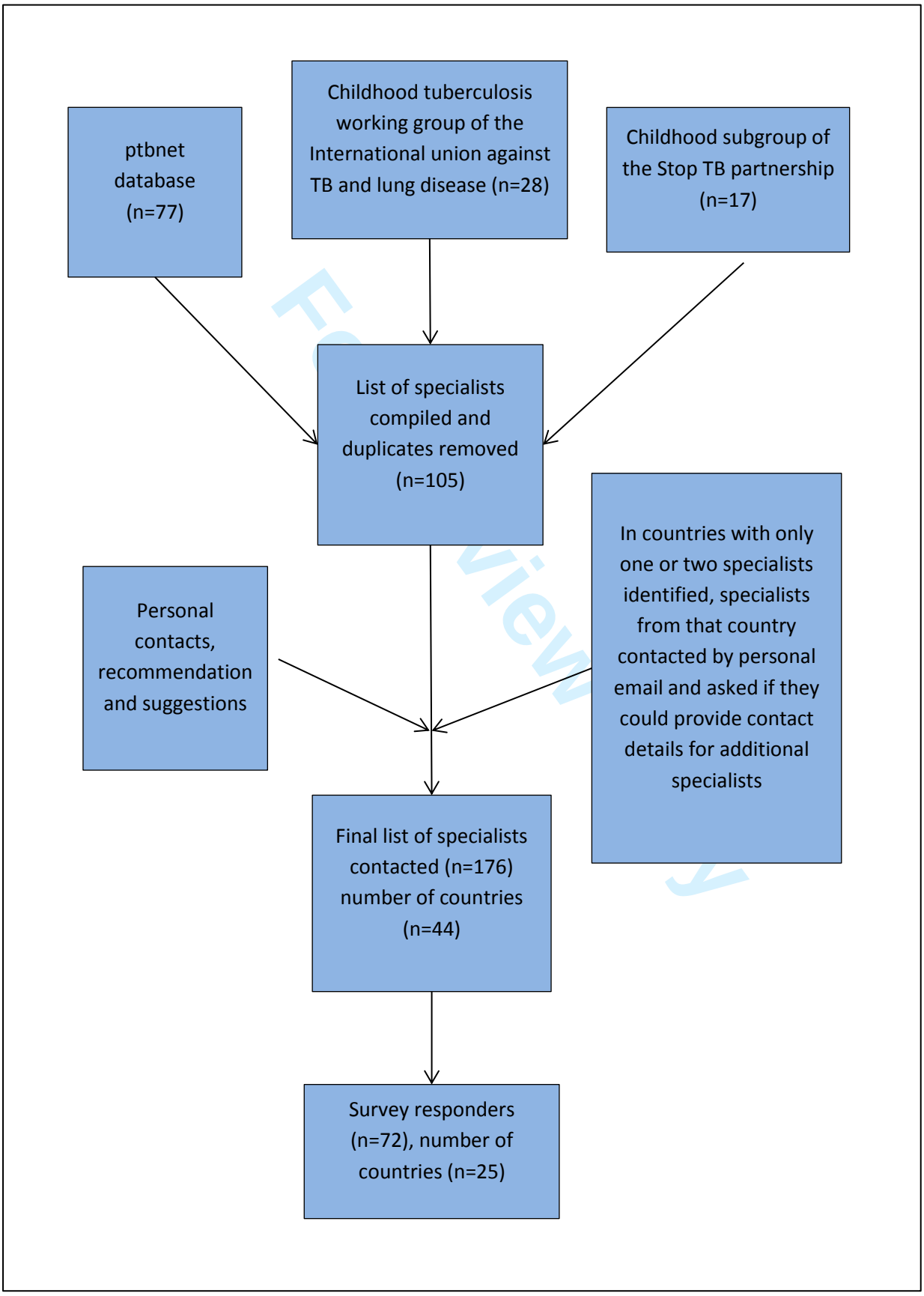
- ( ) I do not use preventive therapy
- ( ) Until preventive therapy is completed
- ( ) Until 3 months after preventive therapy is completed
- ( ) Until 6 months after preventive therapy is completed
- ( ) Until 12 months after preventive therapy is completed
- ( ) Until 2 years after preventive therapy is completed
- ( ) >2 years after preventive therapy is completed
- ( ) Other : _____

23. For children NOT on preventive therapy, how long do you routinely follow them up for? *

(please tick only one box)

- ○ I do not follow them up (discharge)
- ○ I use preventive therapy in all children
- ○ 3 months
- ○ 6 months
- ○ 12 months
- ○ 2 years
- ○ >2 years
- ○ Other : _____

II. Flowchart of the strategy to identify specialists who are likely to manage child contacts of multidrug-resistant tuberculosis cases in Europe



III. Tables: Results of responses to the survey questions

Table 1: Characteristics of respondents to the questionnaire (n=72)

Country of respondent	Albania	1
	Armenia	4
	Austria	2
	Belarus	1
	Belgium	1
	Bulgaria	1
	Estonia	4
	Finland	3
	Germany	4
	Greece	1
	Ireland	1
	Israel	1
	Latvia	6
	Lithuania	2
	Malta	1
	Moldova	3
	Portugal	2
	Romania	5
	Russian Federation	8
	Spain	6
	Sweden	3
	Switzerland	3
	Tajikistan	1
	UK	3
	Ukraine	5
Duration of experience with TB	<1 year	1
	1-2 years	1
	2-5 years	4
	5-10 years	17
	>10 years	49
Type of Doctor	Paediatric Doctor	1
	Paediatric Infectious Diseases Doctor	20
	Paediatric TB Doctor	26
	Adult TB Doctor	6
	Paediatric Respiratory Doctor	11
	Adult Respiratory Doctor	4
	Adult Physician	1
	Other[1]	3
Level of Doctor	Consultant/Attending/Senior	59
	Middle/Resident/Registrar	10
	Junior/Intern	0
	Other[1]	3
Where are child MDR-TB contacts seen?	Dedicated TB centre	40
	Paediatric Hospital	22
	Paediatric part of general hospital	9
	General hospital	1
	Primary care/community clinic/polyclinic	6
	TB sanatorium	4
How many child MDR-TB contacts, on average, do you see a year	Infrequently	18
	1-2 per year	13
	3-5 per year	9
	5-10 per year	12
	>10 per year	20
Language of survey used	English	48
	Russian	24

[1]Researchers/epidemiologists/public health doctors

Table 2: Identification and investigation of child contacts of multidrug-resistant tuberculosis source cases (n=72)

Following the adult MDR-TB diagnosis, how are child contacts identified?	Questioning MDR-TB source case	40
	Questioning the source case and home visit	30
	Other[1]	2
Who refers child contacts to your services? (more than one answer possible)	Nurses/doctors within the TB programme	54
	School nurses	8
	Primary care/family doctors	26
	Paediatric Doctors	28
	Adult doctors	27
	Self-referral	24
	Other[2]	8
In an asymptomatic child MDR-TB contact, which tests do you commonly use to make a decision on further management? (more than one answer possible)	None	1
	IGRA	47
	TST	67
	Diaskintest	11
	CXR	63
	CT scan	25
	Gastric washings/aspirates	24
	Expectorated sputum	24
	Induced sputum	16
	Broncho-alveolar lavage	12
	Other[3]	5
With regards TST/IGRA, in which circumstances do you give preventive therapy for child MDR-TB contacts?	Never given	30
	TST/IGRA not used to make a decision	1
	TST alone positive	4
	IGRA alone positive	2
	Both TST and IGRA positive	6
	Either TST or IGRA positive	27
	Other[4]	5
For child MDR-TB contacts with evidence of M. tuberculosis infection (based on positive TST and/or IGRA), who do you give preventive therapy?	Never given	30
	Children <2 years	2
	Children <5 years	8
	All children	24
	Children with immunosuppression	10
	Other[5]	5
In which child MDR-TB contacts do you give preventive therapy without evidence of M. tuberculosis infection?	Never given	30
	Preventive therapy only given if evidence of infection	26
	Children <1 year	1
	Children <2 years	5
	Children <5 years	2
	All children	4
	Children with immunosuppression	6
	Other[6]	2
If you start preventive therapy in children with negative TST/IGRA tests initially, do you ever repeat the tests?	Never given	30
	TST is repeated after 2 months	5
	IGRA is repeated after 2 months	2
	Both TST and IGRA are repeated after 2 months	20
	If preventive therapy is started a full course is given	11
	Other[7]	7

[1]Identification through other referral pathways; [2]Public health doctors/researchers; [3]Blood tests for inflammatory markers, full blood count, HIV test; [4]The decision is based on the age of the child; [5]Decision made on a case by case basis; [6]Dependant on BCG status; [7]Depends on clinical circumstances and BCG status

Table 3: Treatment of child contacts of multidrug-resistant tuberculosis source cases (n=72)

What regimen do you use for preventive therapy in child MDR-TB contacts?	Never given	30
	Standard regimen with 1 drug	5
	Standard regimen with 2 drugs	3
	Standard regimen with >2 drugs	1
	Tailored regimen with 1 drug	5
	Tailored regimen with 2 drugs	19
	Tailored regimen with >2 drugs	7
	Other[1]	2
If you use a standard regimen, which drugs do you use?	Standard dose isoniazid	3
	High dose isoniazid	4
	Ethambutol	4
	Pyrazinamide	4
	Levofloxacin	2
	Moxifloxacin	2
If you use a tailored regimen, which drugs do you use?	Standard dose isoniazid	4
	High dose isoniazid	13
	Ethambutol	24
	Pyrazinamide	22
	Ofloxacin	5
	Ciprofloxacin	3
	Levofloxacin	13
	Moxifloxacin	15
	Gatifloxacin	1
	Ethionamide	11
	Cycloserine	6
	PAS	3
	Linezolid	5
How long do you generally treat children with preventive therapy after exposure to MDR-TB?	3 months	4
	6 months	21
	9 months	9
	12 months	3
	18 months	1
	24 months	1
	Other[1]	4
How is preventive therapy delivered to the child?	Child is admitted to hospital	4
	Child is admitted to sanatorium	10
	The child is taken daily to the clinic	5
	A healthcare worker visits the child daily	13
	The parents give the preventive therapy	32
	Other[2]	3

[1]Varies with clinical situation; [2]School supervision/nurse in a children's home

Table 4: Follow up for child contacts of multidrug-resistant tuberculosis source cases (n=72)

For children on preventive therapy at which time points do you follow them up?	No preventive therapy given	30
	By one month	25
	At 2 months	19
	At 3 months	26
	At 4 months	13
	At 6 months	29
	At 9 months	12
	At 12 months	15
	When needed	13
	Other[1]	5
For child MDR-TB contacts NOT on preventive therapy when are they followed up?	No follow up	3
	By one month	16
	At 2 months	20
	At 3 months	40
	At 4 months	2
	At 6 months	45
	At 9 months	11
	At 12 months	28
	When needed	28
	Other[1]	3
If you do chest x-rays for children on preventive therapy, at which time points do you do them?	No preventive therapy given	30
	By one month	1
	At 2 months	3
	At 3 months	17
	At 4 months	1
	At 6 months	19
	At 9 months	2
	At 12 months	14
	When needed	20
	Other[1]	2
If you do chest x-rays for children NOT on preventive therapy, at which time points do you do them?	No chest x-rays done	2
	By one month	8
	At 2 months	5
	At 3 months	27
	At 4 months	0
	At 6 months	39
	At 9 months	5
	At 12 months	29
	When needed	30
	Other[1]	1
For children on preventive therapy after exposure to MDR-TB, how long do you routinely follow them up for?	No preventive therapy given	30
	Until the end of the preventive therapy	2
	Until 3 months after preventive therapy ends	2
	Until 6 months after preventive therapy ends	7
	Until 12 months after preventive therapy ends	1
	Until 2 years after preventive therapy ends	22
	>2 years after preventive therapy ends	8
For children NOT on preventive therapy, how long do you routinely follow them up for?	No follow up	0
	For 3 months	3
	For 6 months	3
	For 12 months	4
	For 2 years	42
	For >2 years	19

[1]Seen daily in sanatorium, seen every month, depends on age of child