



Childhood TB and new TB drugs in the WHO European Region

Kigali, Rwanda, 09/10/ 2017

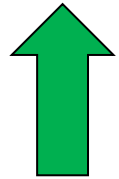
Dr Martin van den Boom, MD, MSc PH, WHO Regional Office for Europe, Joint Tuberculosis, HIV and viral Hepatitis Programme



Key indicators	2011	2015
Approach to drug resistant TB	Small scale pilot projects	Nation-wide integrated programmes
TB notification rate / 100 000	40	36
Drug-susceptible success rate (%)	72	76
MDR-TB detection rate (%)	30	63
MDR-TB treatment coverage (%)	63	Universal access
MDR-TB success rate (%)	48	51

- Full scale programmes
- Less new TB cases per year
- More people successfully treated
- More drug-resistant patients diagnosed
- Universal access to treatment
- Increase in MDR-treatment success rate
- Loss to follow-up among new lab-confirmed TB
- Decrease in drug stock-outs
- Increase in coverage for drug-susceptibility testing
- Improved electronic and individual data surveillance
- Ameliorated awareness and political commitment

Key programmatic achievements in the WHO European Region in at country level



Number of up-to-date childhood TB national clinical and programmatic guidelines



Number of Member States with childhood TB in their Global Fund TB concept notes/Global Fund grants



Number of Member States with childhood TB reflected in their national strategic plans

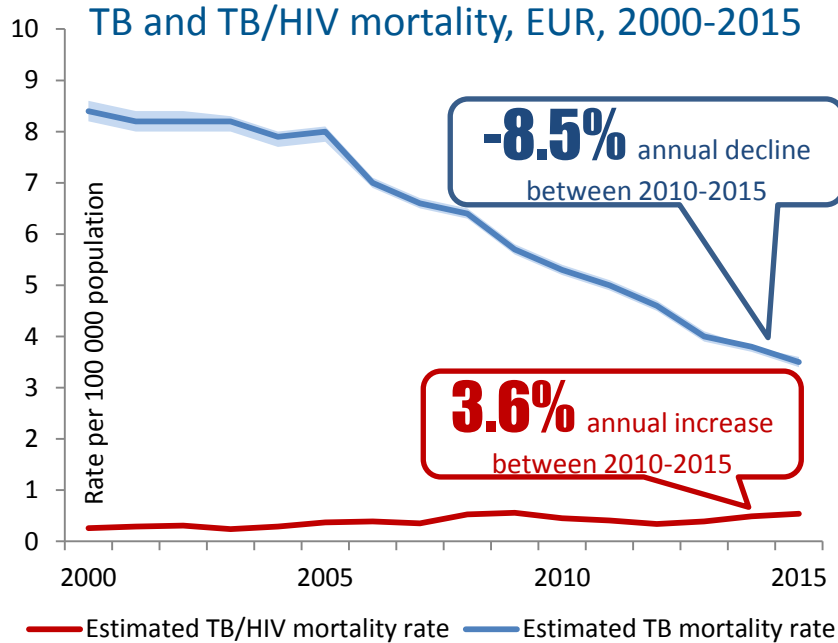


Key strategic directions

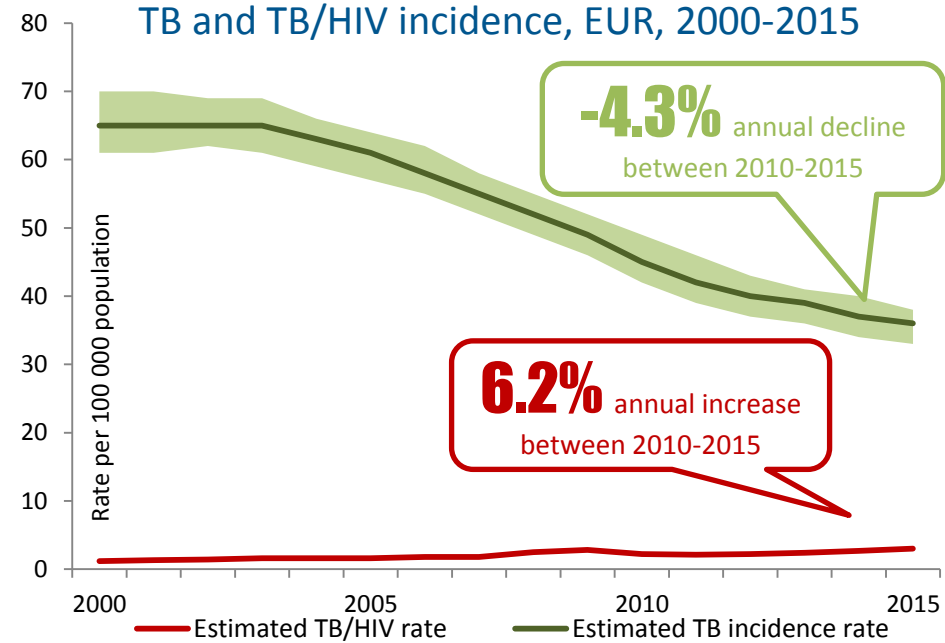


1. Full scale-up of rapid diagnosis
2. Rapid uptake of new medicines
3. Expanding people-centred models of care
4. Shorter and more effective treatment regimens
5. Research for new tools
6. Intersectoral approach to address inequities

Main impact indicators



Impressive decline in TB mortality combined with growing burden of TB/HIV mortality

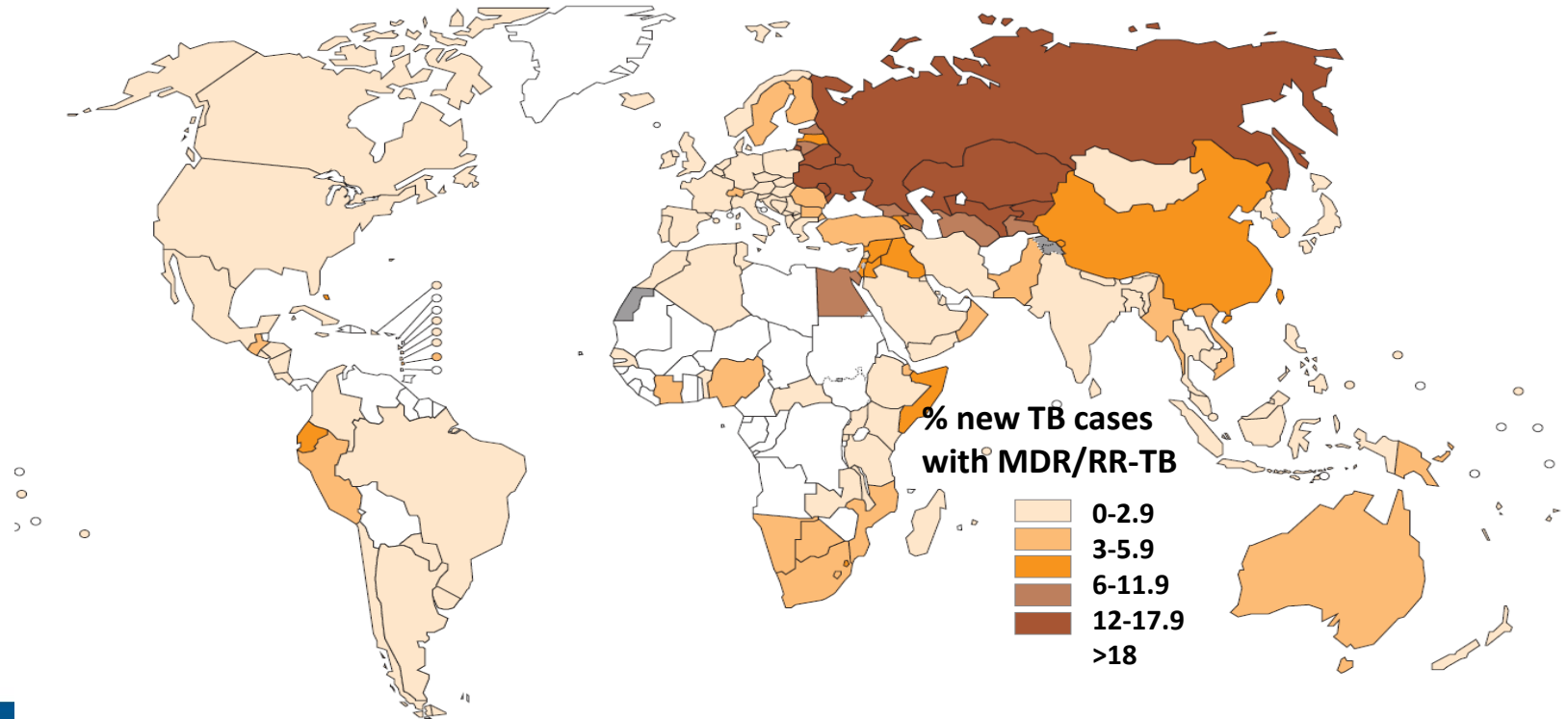


WHO European Region has fastest decline in TB incidence, however ... still growing TB/HIV co-infection

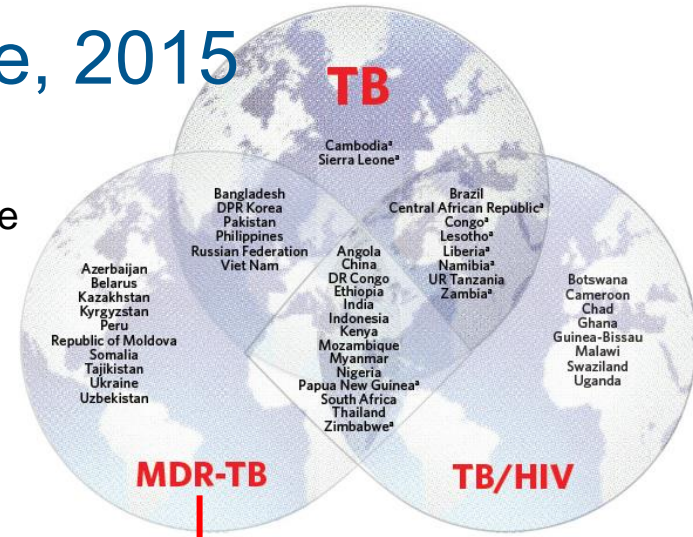
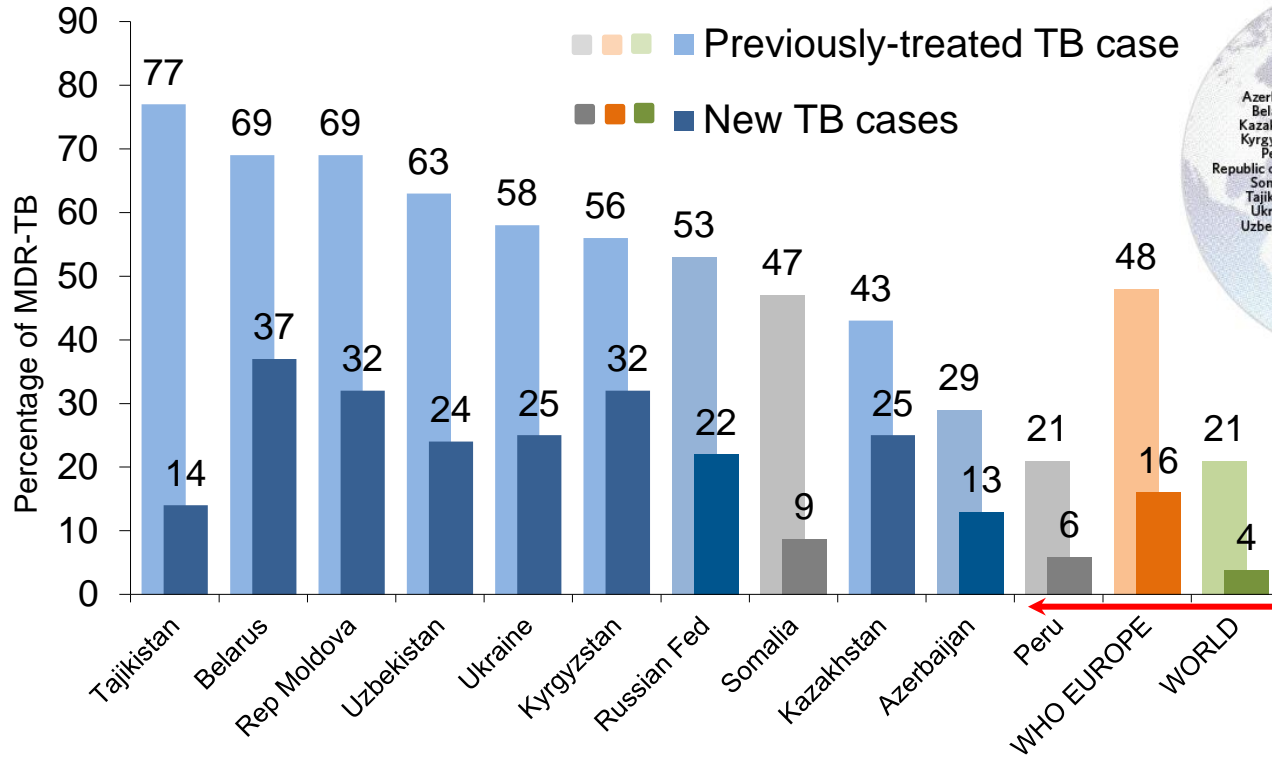
Drug-resistant TB is in every country

Globally: 480,000 new cases of MDR-TB in 2015

+ 100,000 new cases of rifampicin-resistant TB (RR-TB) needing MDR-TB treatment



Multidrug resistant TB, WHO/Europe, 2015



1 of 6 new TB cases in the Region found with MDR-TB



1 of 2 retreated TB cases in the Region found with MDR-TB



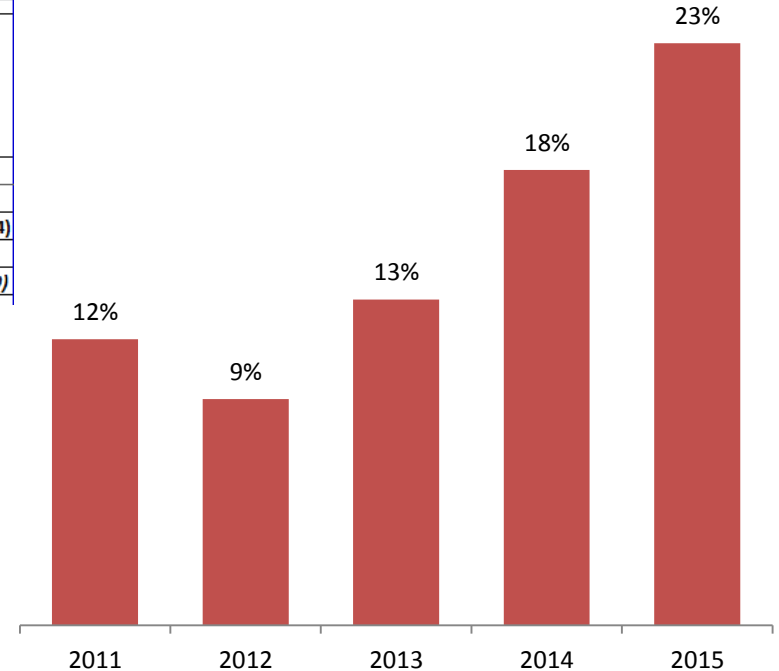
Global tuberculosis control: WHO report 2016. Geneva: WHO, 2016 (WHO/HTM/TB/2016.13)

In 2015 about one in four MDR-TB patients have XDR-TB

Percentage of XDR-TB among detected MDR-TB cases, WHO European Region, 2015

Table 14. XDR TB cases among all laboratory-confirmed MDR TB cases, European Region, 2015

	TB cases with FLD DST ^a		MDR TB among all TB cases ^b		MDR TB with SLD ^c		XDR TB	
	N	%	N	%	N	%	N	%
Total European Region	69 814		10 490	(15.0)	9 165	(87.4)	2 149	(23.4)
<i>Subtotal 18 HPC</i>	<i>47 915</i>		<i>10 017</i>	<i>(20.9)</i>	<i>8 780</i>	<i>(87.7)</i>	<i>2 100</i>	<i>(23.9)</i>



On in five TB had MDR-TB

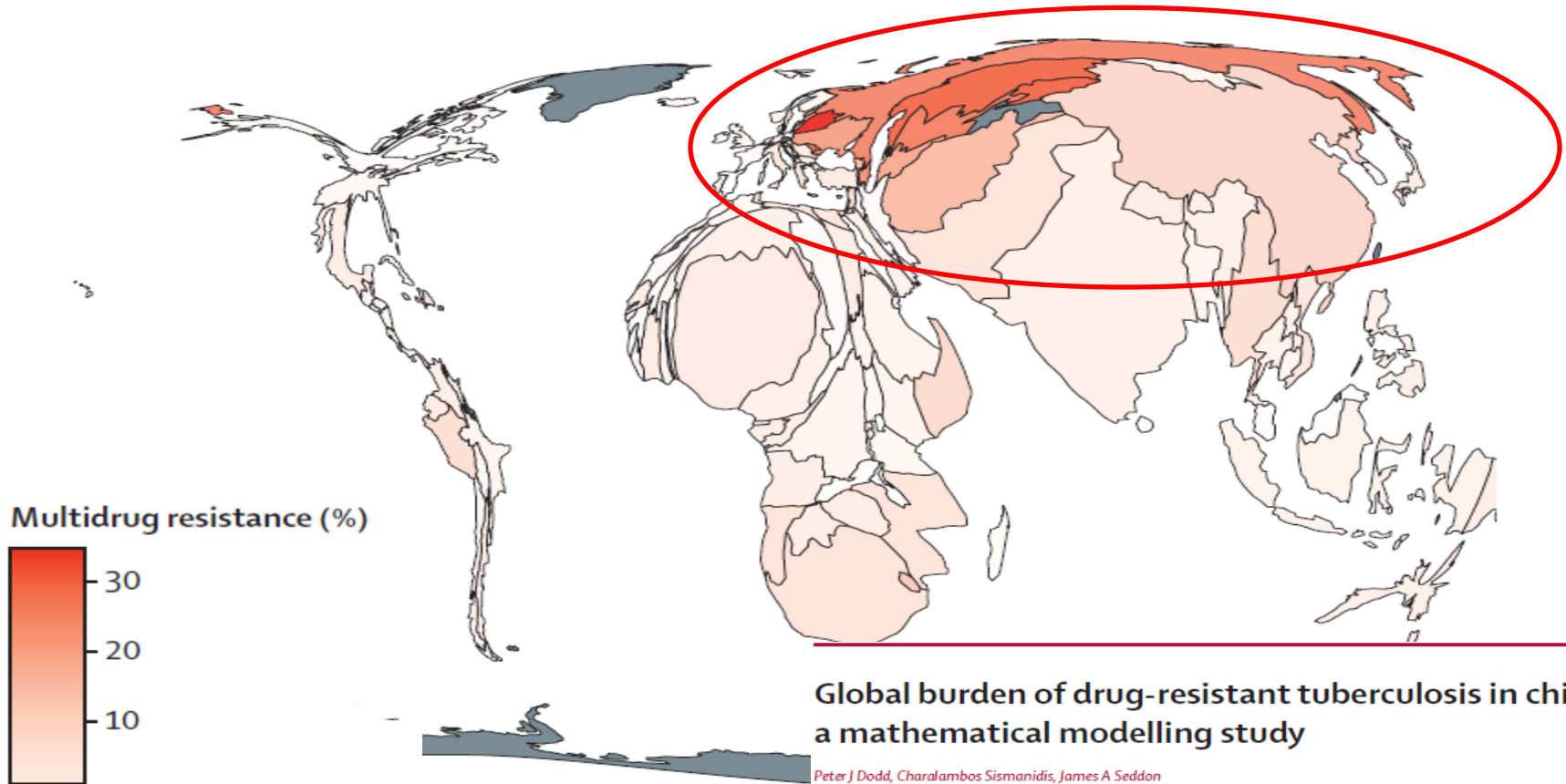
One in four MDR-TB patients had XDR-TB

XDR-TB is more difficult to treat than MDR-TB

Source: WHO Europe / ECDC. Tuberculosis surveillance and monitoring in Europe 2017

MDR-TB in children: incidence (size) and proportion (colour)

P Dodd et al. Lancet ID 2016

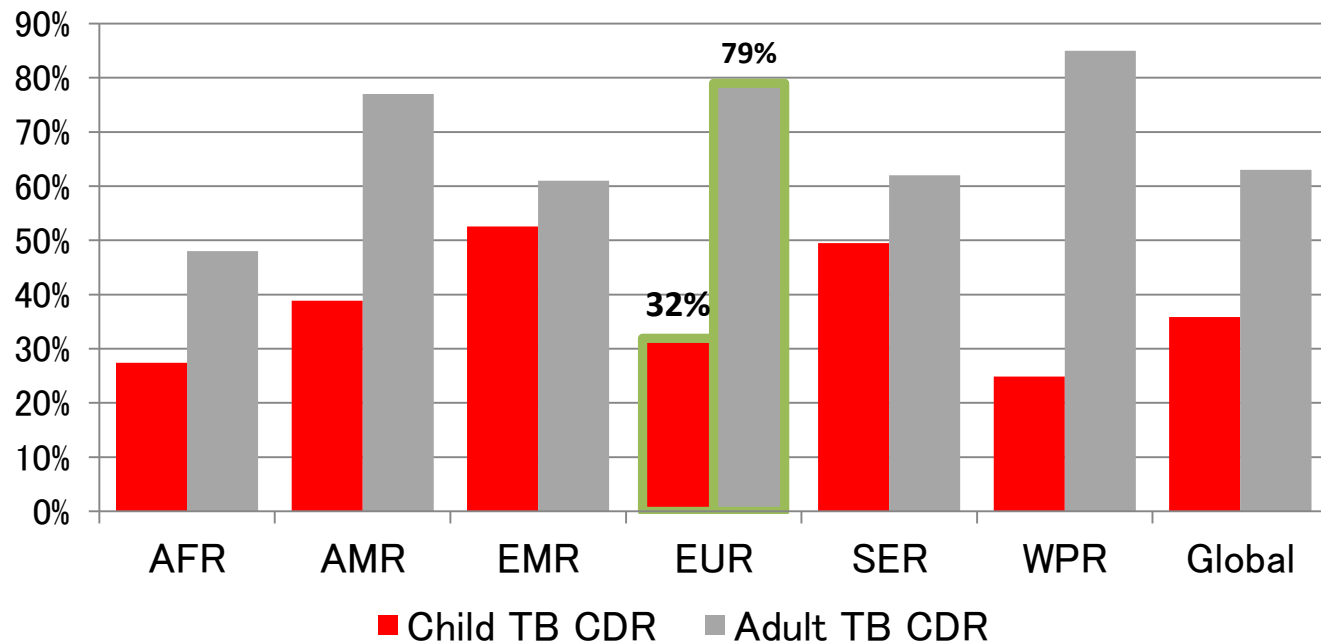


**Global burden of drug-resistant tuberculosis in children:
a mathematical modelling study**

Peter J Dodd, Charalambos Sismanidis, James A Seddon

Comparison of TB case detection rate in adults and children by WHO Regions, 2014

Of estimated
~30,000 child TB
cases only
~10,000 are
detected by
health systems in
WHO European
Region, TX
success >85%



Shift TB care to more people-centredness

Governance	<ul style="list-style-type: none">- Large variation in public spending on health- Serious inefficiencies in health systems- Weak coordination across sectors
Service delivery	<ul style="list-style-type: none">- Overinvestment in secondary and tertiary (hospital-based) care- Underinvestment in outpatient and primary health care
Health financing	<ul style="list-style-type: none">- Payment mechanisms that do not facilitate reconfiguration of existing services or collaboration across the health system
Pharmaceuticals Human resources	<ul style="list-style-type: none">- Insufficient access to M/XDR-TB drugs- Primary health care workers not sufficiently trained

Methodology

22 regional GLC mission reports from 15 sites were analyzed against elements needed to be addressed for introduction of new TB drugs (*Bdq and Dlm*), as per the **Policy Implementation Package**

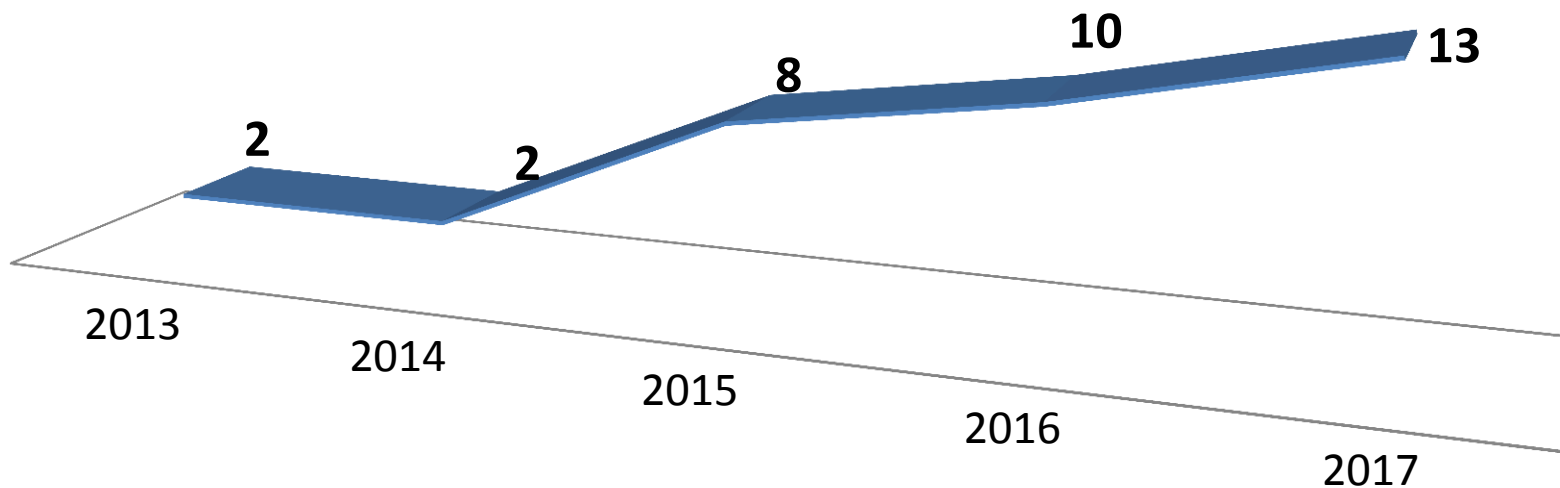
**POLICY
IMPLEMENTATION
PACKAGE**
FOR NEW TB DRUG
INTRODUCTION



Year of the assessment	Armenia	Azerbaijan	Belarus	Georgia	Kazakhstan	Serbia (UN AT Kosovo)	Kyrgyzstan	FYR Macedonia	Moldova	Romania	Republic of Moldova (Transnistria)	Tajikistan	Turkmenistan	Ukraine	Uzbekistan
2016															
2017															

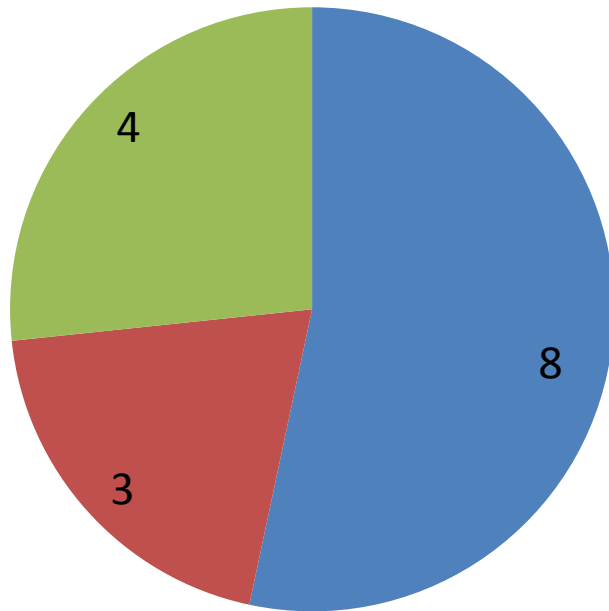
Out of 15 countries assessed, 13 introduced Bdq and/or Dlm

Number of countries that introduced new TB drugs



National implementation plan for introduction of new TB drugs

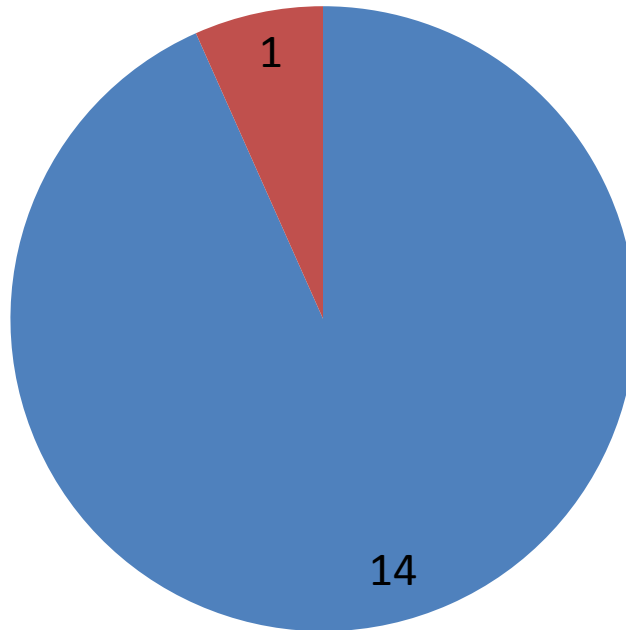
Availability of the National Implementation Plan



- Available in Armenia, Azerbaijan, Belarus, Georgia, Kyrgyzstan, Moldova, Tajikistan, Uzbekistan
- No information on Kazakhstan, Turkmenistan, Ukraine
- Not available in Serbia (UN AT Kosovo), FYR Macedonia, Romania, Moldova (Transnistria)

Minimum requirements for country preparedness and planning: National health context

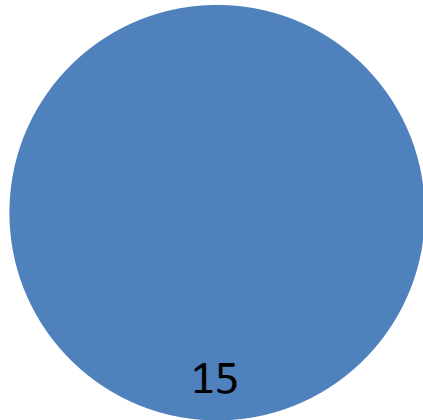
Availability of the National Strategy to fight TB up to 2020



- Available in Azerbaijan, Armenia, Belarus, Georgia, Kazakhstan, Serbia (UN AT Kosovo), Kyrgyzstan, FYR Macedonia, Moldova, Romania, Tajikistan, Turkmenistan, Ukraine, Uzbekistan
- No information on Moldova (Transnistria)

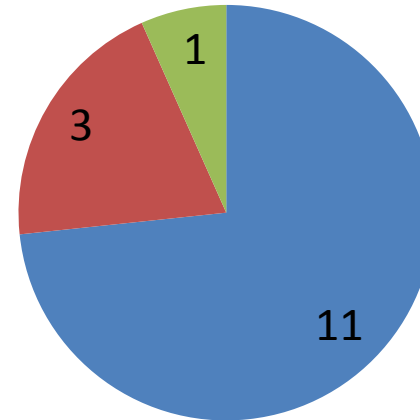
Minimum requirements for country preparedness and planning: Laboratory

Drug susceptibility testing (DST) to first-line drugs (FLD)



- Available in Azerbaijan, Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Serbia (UN AT Kosovo), FYR Macedonia, Moldova, Romania, Moldova (Transnistria), Tajikistan, Turkmenistan, Ukraine, Uzbekistan

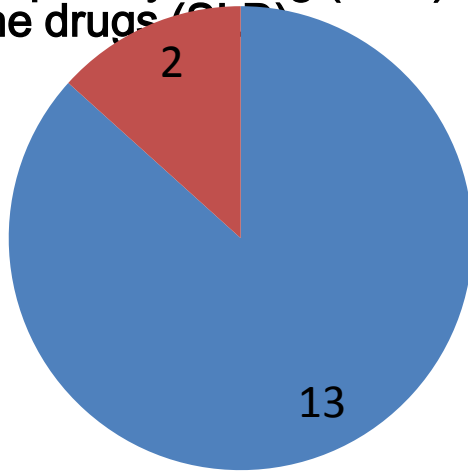
Quality assurance for DST to FLD



- Passed in Azerbaijan, Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, FYR Macedonia, Romania, Tajikistan, Ukraine, Uzbekistan
- No information on Moldova, Moldova (Transnistria), Turkmenistan
- Not passed in Serbia (UN AT Kosovo)

Minimum requirements for country preparedness and planning: Laboratory

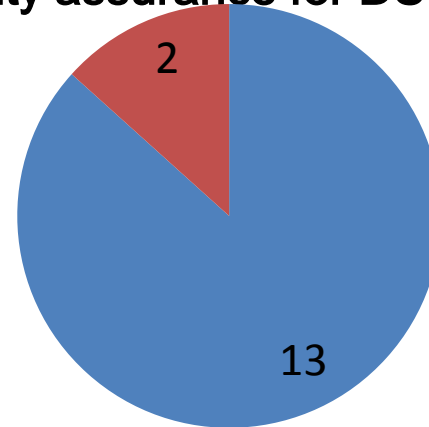
Drug susceptibility testing (DST) to second-line drugs (SLD)



■ Available in Azerbaijan, Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Romania, Moldova (Transnistria), Tajikistan, Turkmenistan, Ukraine, Uzbekistan

■ Not available in Serbia (UN AT Kosovo), FYR Macedonia

Quality assurance for DST to SLD

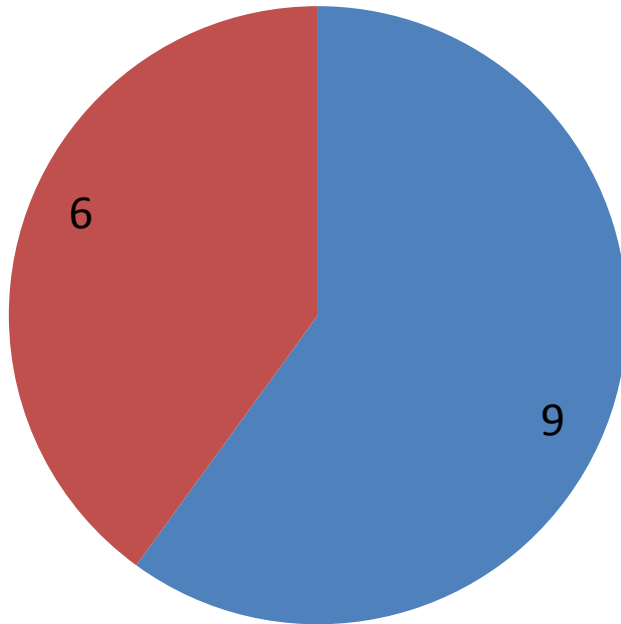


■ Passed in Azerbaijan, Armenia, Belarus, Georgia, Moldova, Kazakhstan, Kyrgyzstan, Romania, Tajikistan, Moldova (Transnistria), Turkmenistan, Uzbekistan, Ukraine

■ Not passed in Serbia (UN AT Kosovo), FYR Macedonia

Minimum requirements for country preparedness and planning: Drug supply and management

Shortage of TB drugs reported during the last 2 years



- No shortage reported in Armenia, Georgia, Kazakhstan, Serbia (UN AT Kosovo), FYR Macedonia, Moldova, Tajikistan, Turkmenistan, Uzbekistan
- Shortage reported by Azerbaijan, Belarus, Kyrgyzstan, Romania, Moldova (Transnistria), Ukraine

Minimum requirements for country preparedness and planning: Drug supply and management

- Registration of Clofazimin (Cfz), Bdq, Dlm is problematic at all countries. Pharmacological companies are not interested to apply for registration, hence, alternative mechanisms should be thought out.
- Bdq and Dlm are imported based on one-time license, mainly because these drugs are still on a clinical trial.
- TB drugs procured with the support from the Global Fund are quality assured. However, drugs procured through local budget, mainly do not hold WHO-prequalification

Country preparedness and planning: Monitoring and evaluation

- All countries use updated WHO definitions for TB (2013 update)
- Some countries still do not have functional electronic TB database and execute paper-based reporting (Azerbaijan, Tajikistan, Turkmenistan, Uzbekistan, Kyrgyzstan)
- Supportive supervisions in majority countries are performed by the National TB Programs, but are heavily relying on the Global Fund support

Children and adolescents – DIm (XDR or “MDR+”)

Pediatric Cohort Characteristics	DIm (n= 17)
Age at admission, years (median, min-max)	16 (13-17,3)
Sex, male	10 (59%)

Treatment outcome	Total (n=17)
Cured	3
Treatment completed	1
Ongoing treatment	13
Died / LTFU / Failure	0
Sputum Culture Conversion at 6 m.	4 / 4 Available data

September 2016

Pediatric patients on DIm reported for	Total (n=17)
Serious AE	3
Outcome of SAE: All resolved w/o dose change	3
Grade 3 QTcF prolongation (> 60 msec or QTcF > 500ms)	0
Non Serious AE	7
Grade 1-2 QTcF prolongation	4

Children and adolescents - Bdq

Experience from MSF and Belarus NTP

- 27 children/adolescents – median age 16 (10-17)
- 65% culture positive at baseline
- 67% presumed or confirmed XDR-TB
- Companion drugs:
 - Mfx (22%), Cfx (96%), Lzd (96%), Imp (15%)
- 100% culture negative after 24w Bdq
- 5 patients had prolonged QTcF – none ceased Bdq

Early diagnosis of all forms of tuberculosis and universal access to drug-susceptibility testing, including the use of rapid tests

The Regional Office, in collaboration with partners, will prepare a guide and *diagnostic algorithms* for expanded and accelerated quality-assured new diagnostic technologies (taking into account paediatric tuberculosis and extrapulmonary tuberculosis diagnostics).

Management of latent tuberculosis infection and preventive treatment of persons at high risk, and vaccination against tuberculosis

Member States will ensure that WHO policy *recommendations* on bacillus Calmette-Guérin (*BCG*) *vaccination* for infants are implemented and BCG revaccination is discontinued.

C. Equitable access to quality treatment and continuum of care for all people with tuberculosis, including drug-resistant tuberculosis, and patient support to facilitate treatment adherence

- Member States will ensure that their **tuberculosis and drug-resistant tuberculosis treatment guidelines, including childhood tuberculosis guidelines**, are regularly updated and implemented according to the latest available evidence and WHO recommendations (ongoing activity).
- Member States will develop a *plan for achieving universal access to treatment*, including the treatment of vulnerable populations and **children**, and uninterrupted drug supply (ongoing activity).
- Member States will ensure *the rational, safe and effective introduction of new tuberculosis medicines, including for children*, according to the most recent WHO policy guidance (as soon as possible and not later than 2016)
- Member States will sustain countrywide use of *first-line fixed-dose combination drugs (for adults and children)* and **paediatric** drug formulations in the treatment of drug-susceptible tuberculosis, where possible.

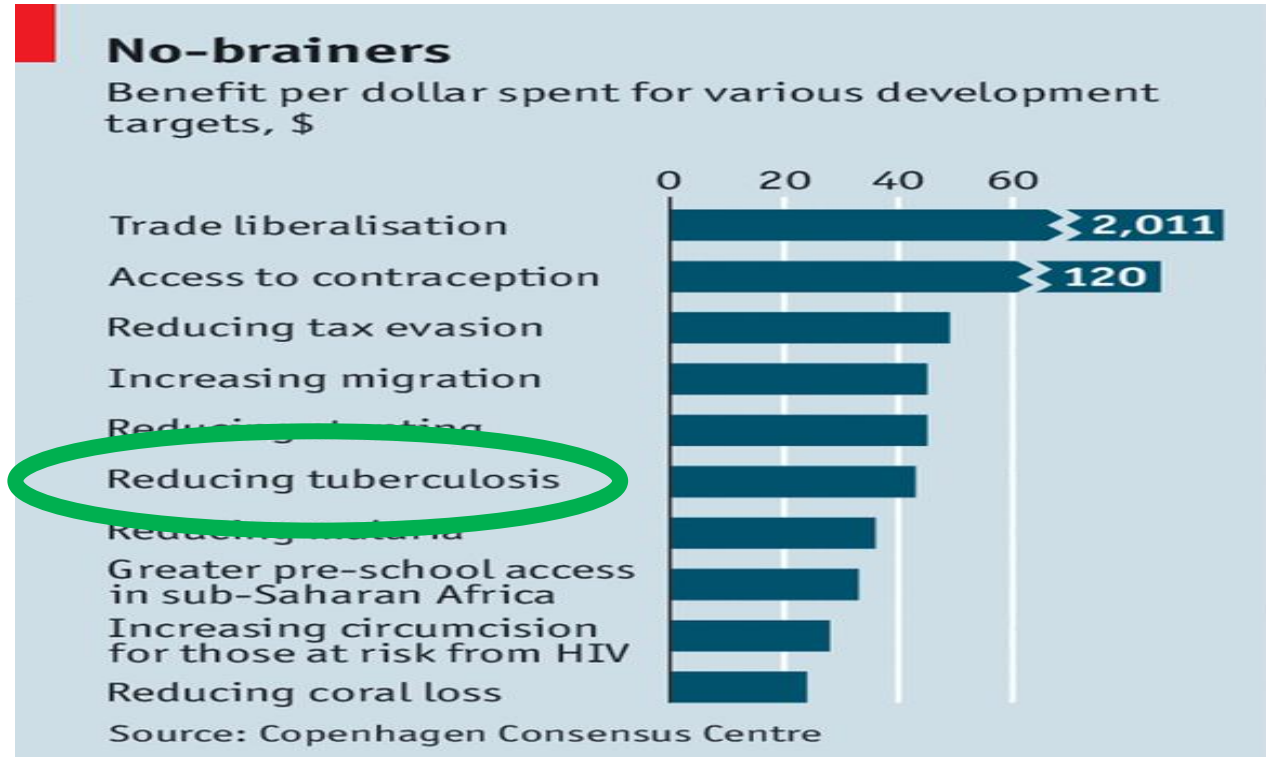
C. Regulatory frameworks for case-based surveillance, strengthening vital registration, quality and rational use of medicines, and pharmacovigilance

The Regional Office will assist Member States in the *development of procedures for the procurement of medical supplies* with an emphasis on quality assurance through *strengthened regulatory authorities* and particular emphasis including, but not limited to, **paediatric** tuberculosis diagnostics and treatment (drug formulations), and limiting the availability of new drugs on the free market (over the counter) without a tuberculosis indicated prescription sale.

The financial reasoning behind TB prevention and care

The Economist - Development - The economics of optimism , Jan 24th 2015 - citing the Copenhagen Consensus Centre

Investing in TB prevention and care: Value for money, the most cost-effective single disease approach investment, 1 USD invested, yields 40 USD return



Political commitment is key

Conclusions

- More (high level) advocacy needed
- Childhood TB to be integrated further within overall TB and beyond, i.e. PHC, pediatrics
- More rapid mechanisms for new drug introductions needed at country levels
- Need for more evidence, partnerships are key
- Capacity building

Acknowledgements

WHO colleagues, especially: Drs Masoud Dara, Malgorzata Grzemska, Ogtay Gozalov and Andrei Dadu

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<http://www.euro.who.int/en/health-topics/communicable-diseases/tuberculosis>

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Thank you
very much for
your
consideration