

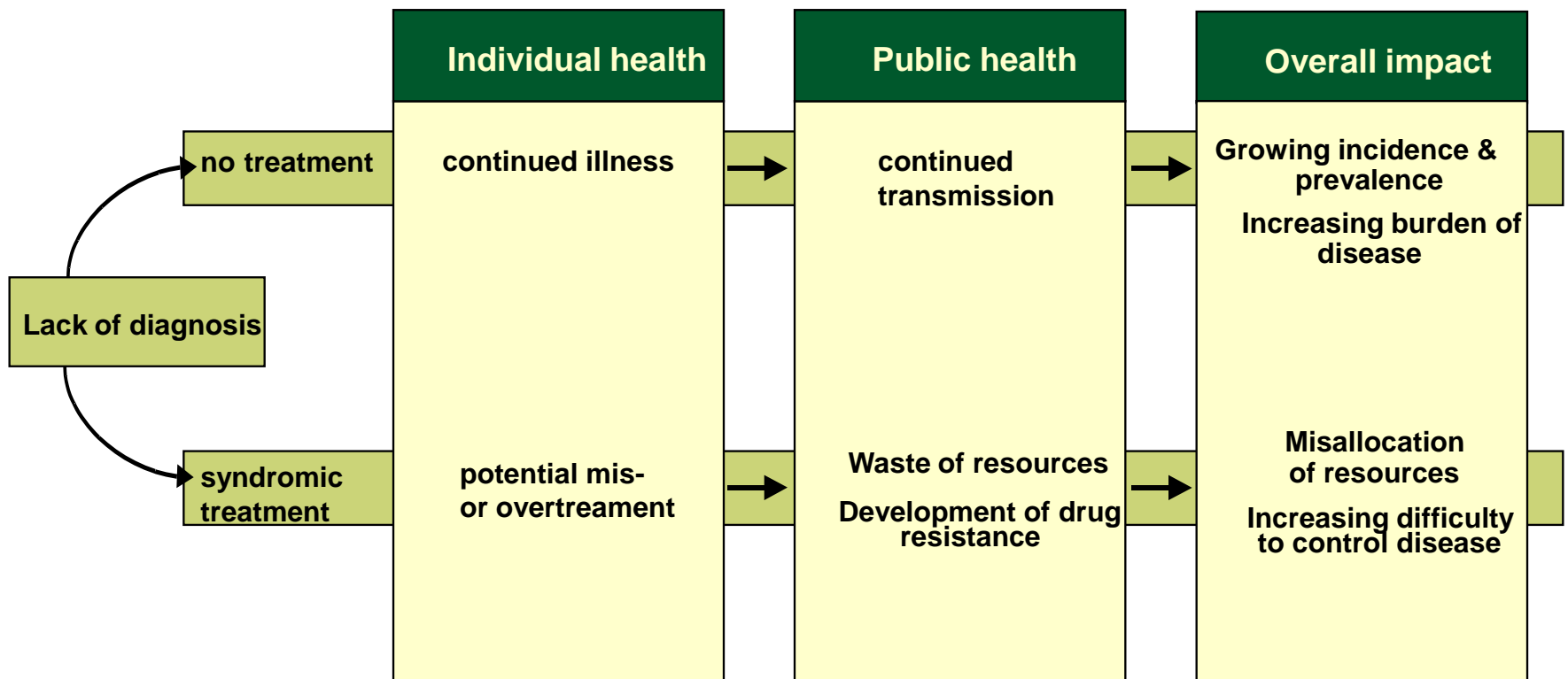


New frontiers: changing diagnostic paradigms

Dr. Giorgio ROSCIGNO, CEO
Foundation for Innovative New Diagnostics
Geneva, Switzerland

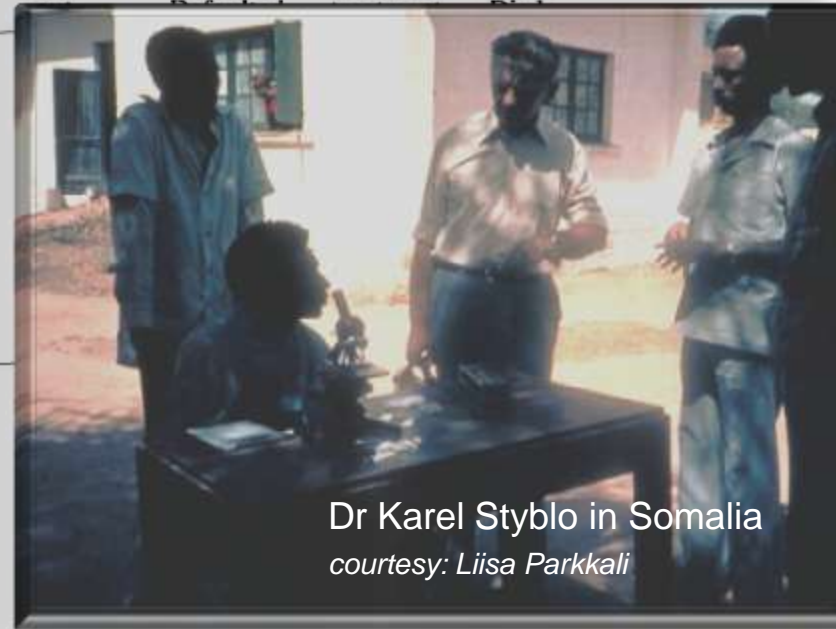
Partnering for better diagnosis for all

Poor diagnosis: Impact on individuals, communities and global health programmes



DOTS (I): origin with Dr Karel Styblo

Year registered	No. assessed	Results (%)			
		Cured	Treatment completed	Transferred	Still on
Standard chemotherapy					
1979	5,418	31	13		
1980	5,867	39	16		
1981	5,527	39	14		
1982	5,498	37	15		
Standard and short-course chemotherapy					
1983	5,825	43	15		
1984	7,172	49	18		
1985	8,034	61	11		



Dr Karel Styblo in Somalia
courtesy: Liisa Parkkali

REVIEWS OF INFECTIOUS DISEASES • VOL. 11, SUPPLEMENT 2 • MARCH-APRIL 1989
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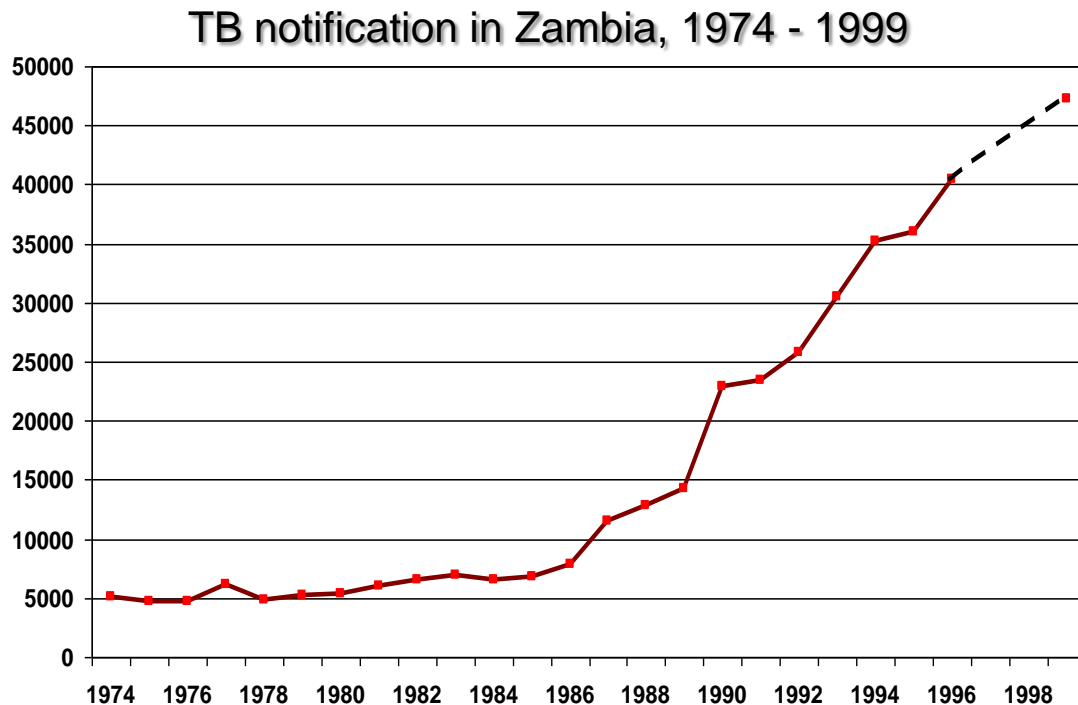
The 5 essential components of the DOTS strategy:

1. Sustained political commitment
2. Quality-assured sputum smear microscopy
3. Direct-observed treatment, short-course
4. Uninterrupted supply of quality-assured anti-TB drugs
5. Recording and reporting system

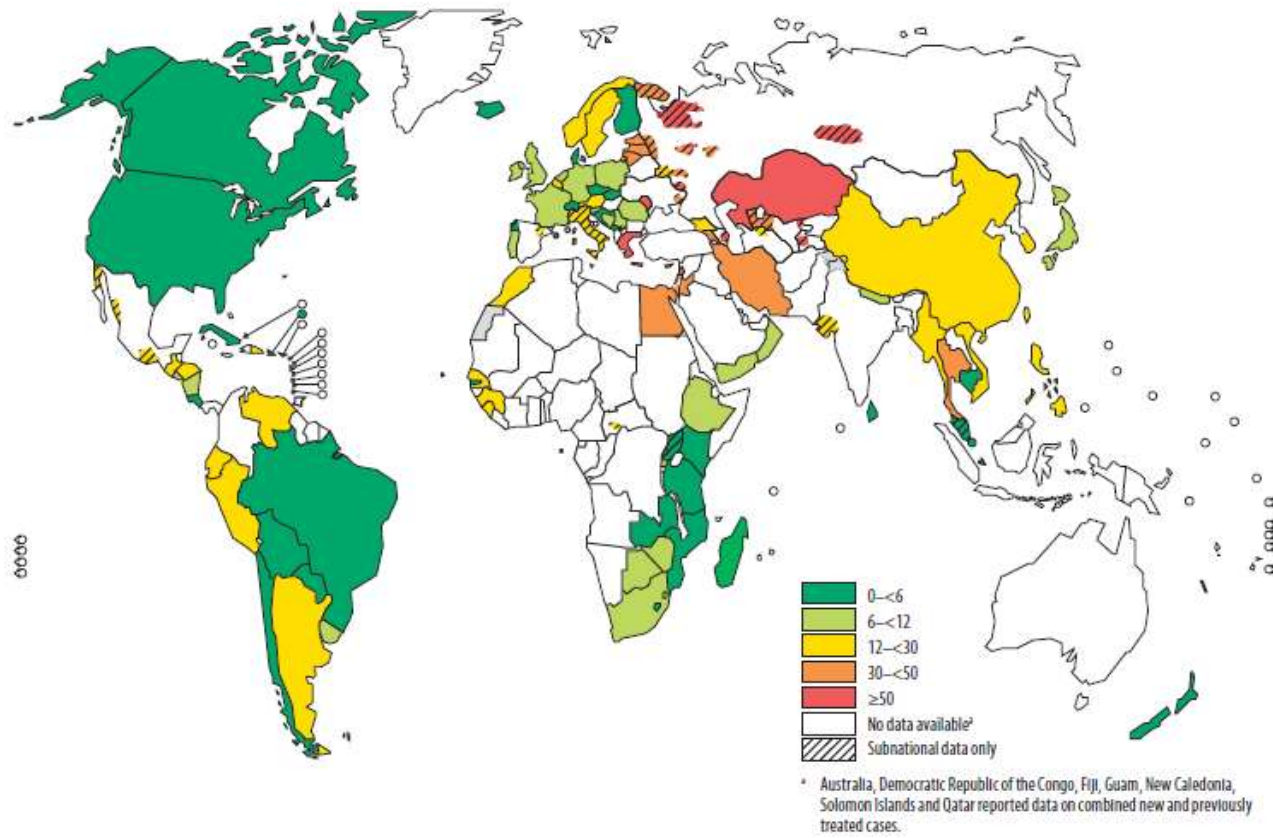
The shortfalls of DOTS (I): HIV

“The impact of HIV on the epidemiological situation of TB is so large that the ***tools available at present for TB control will fail to restrain*** the increase in the incidence of TB caused by HIV infection.”

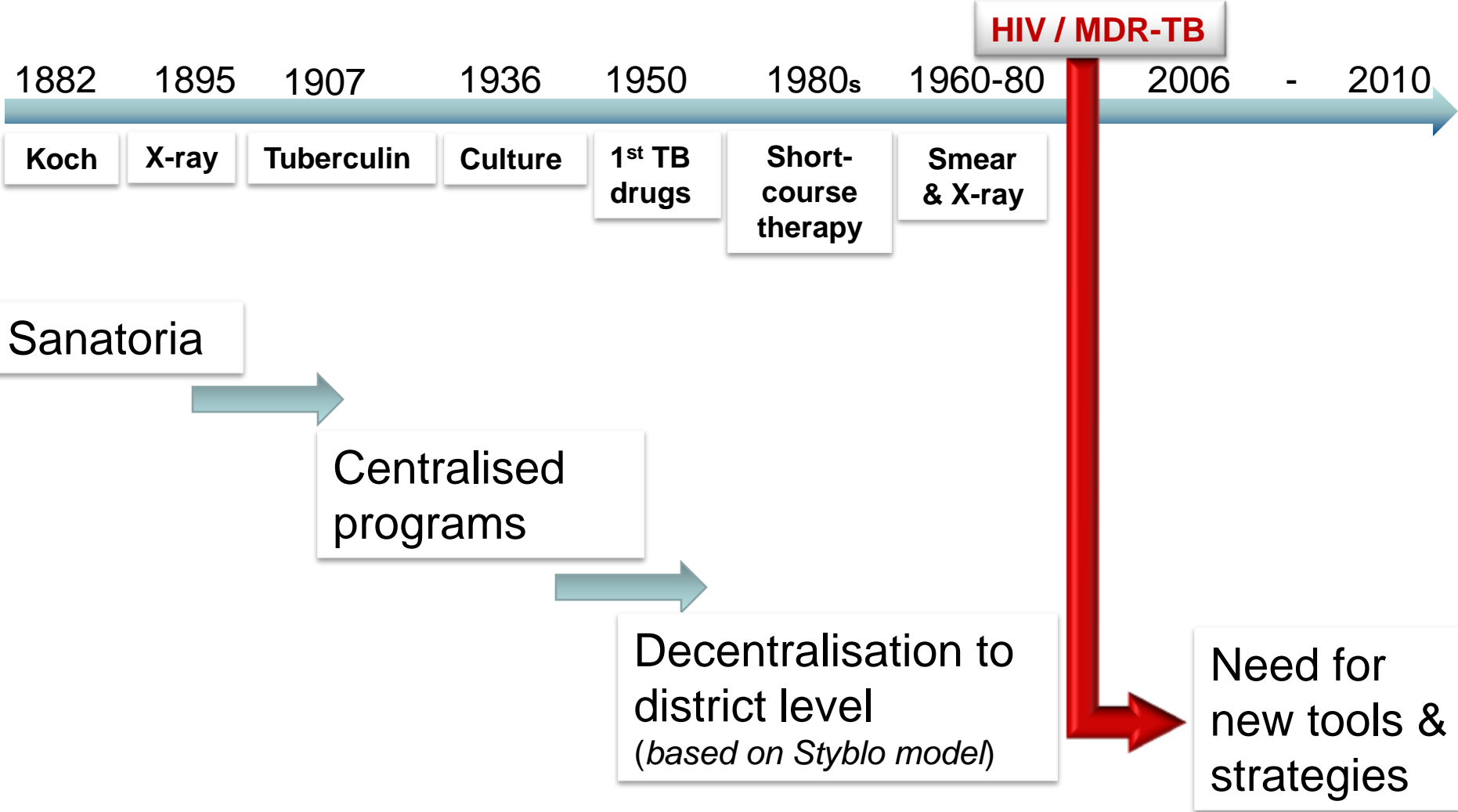
Karel Styblo - *Bull. IUATLD, Vol.65, N 1, March 1990*



The shortfalls of DOTS (II): MDR-TB



Evolution in TB diagnosis

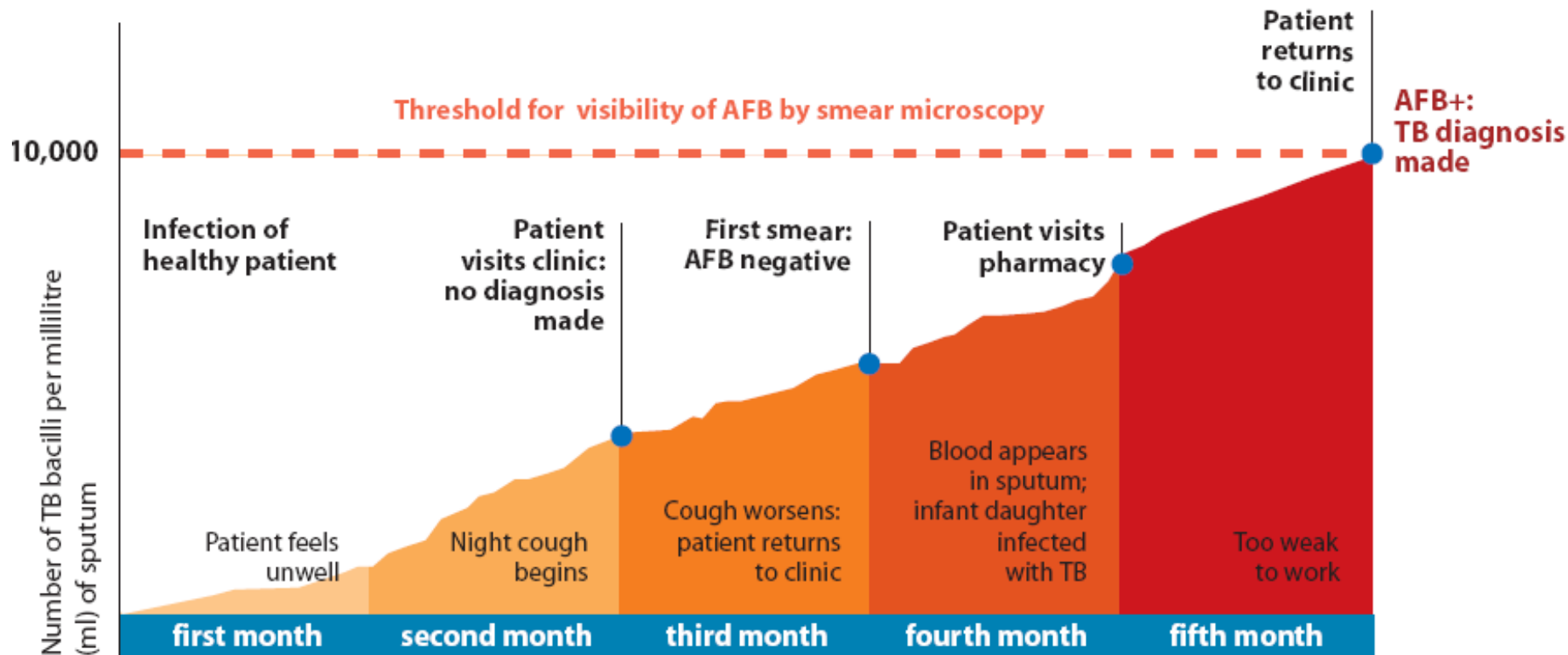


DOTS (II): 6 additional crucial elements in new strategy

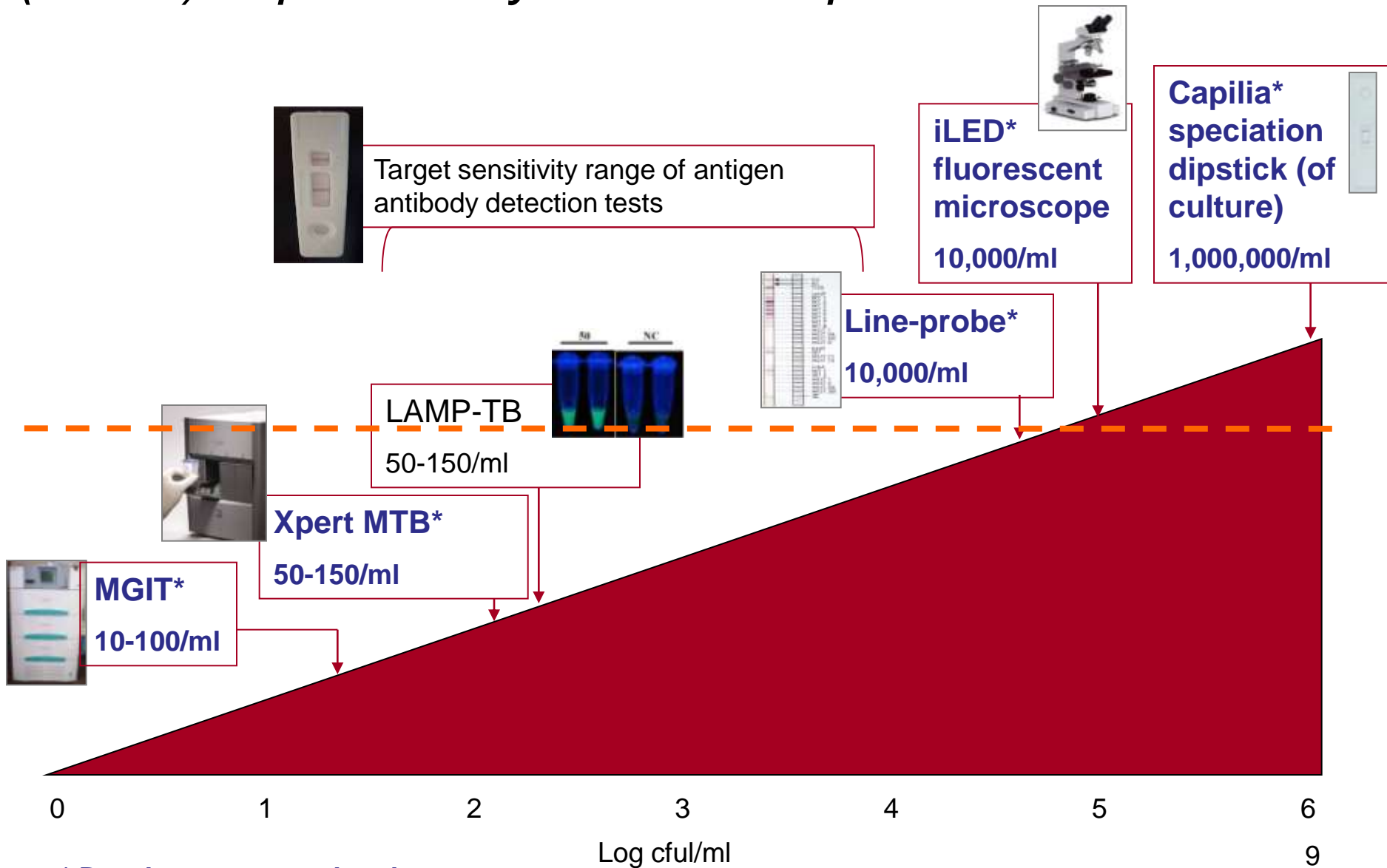
1. Sustaining, improving and accelerating quality DOTS expansion
2. Addressing TB-HIV, MDR-TB and other special challenges
3. Contributing to health system strengthening
4. Engaging all care providers
5. Empowering patients and communities
6. Enabling and promoting research



The slow road to TB diagnosis



Importance of early diagnosis: Sensitivity (cfu/ml) of pulmonary TB tests in portfolio



* Development completed

WHO recommendations 2006-2010

2006	<ul style="list-style-type: none">➤ Smear-positive case definition from 2 to 1 positive smears➤ Screening for TB with 2 instead of 3 smears➤ Conventional FM
2007	<ul style="list-style-type: none">➤ Commercial liquid culture / DST➤ Rapid speciation (MPT64)
2008	<ul style="list-style-type: none">➤ Line probe assay (Rif & INH)
2009	<ul style="list-style-type: none">➤ LED-based FM➤ Non-commercial culture (MODS, CRI, NRA)
2010	<ul style="list-style-type: none">➤ Cartridge-based Automated NAAT: Pending

A changing landscape

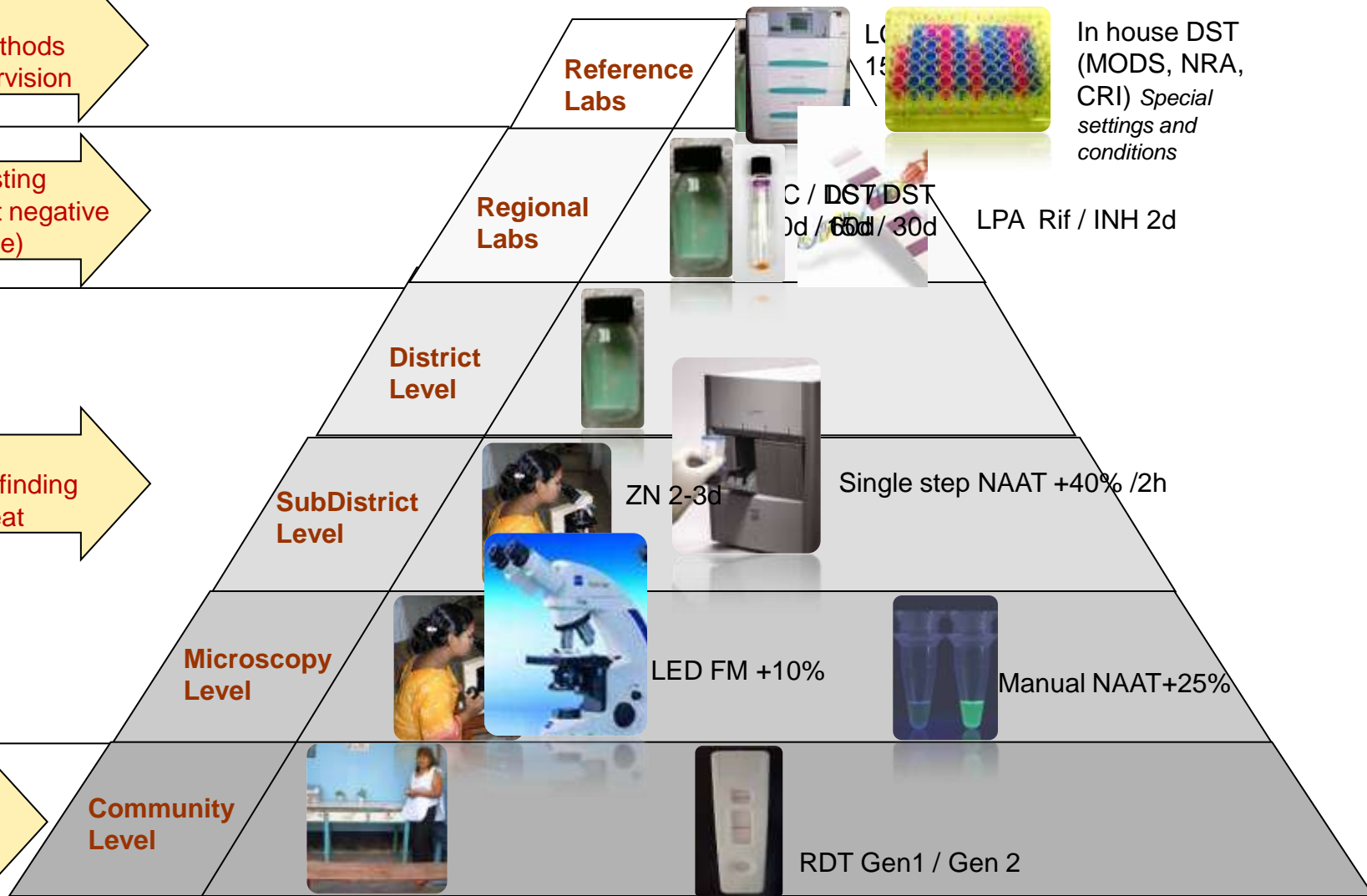
Expected 2012 (Gen 1) / 2014 (Gen 2)

- Surveillance
- Reference methods
- Network supervision

- Resolution testing (screening-test negative drug resistance)

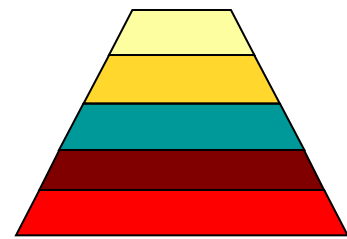
- Screening
- Passive case finding
- Detect and treat

- Clinical Screening
- Primary care

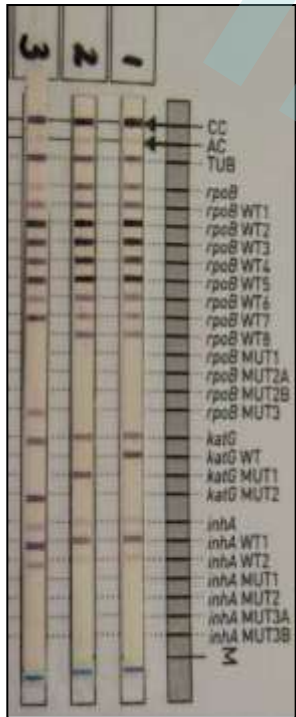


Decentralization of molecular diagnostics

Less complexity, more robustness

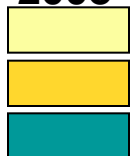


1st generation
MDR



LPA

2008

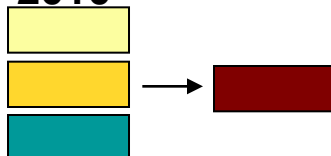


2nd generation
automated MDR

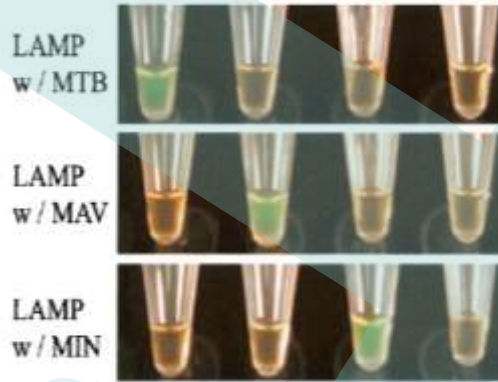


Automated NAAT

2010



1st generation
manual detection



LAMP

2011

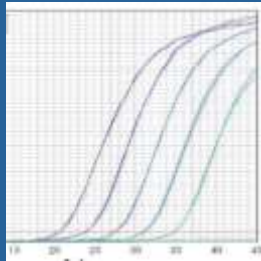


POC test

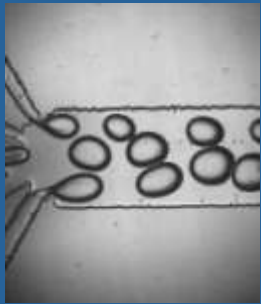
2013



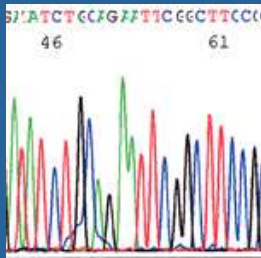
Integration of technologies lead to breakthrough in 2010



Real-Time PCR



Microfluidics



TB DNA sequence

- Molecular beacons
- RT PCR
- Resistance-associated mutations
- Fluorimetric probes
- Microfluidics
- Sonic bacterial lysis



Introducing high tech in low tech settings



Automated Sample Prep,
Amplification and Detection

<120 minutes

A technology platform:

- TB & Rif Resistance
- Potential for HIV viral load
- Potential for HPV STD

Major advantages in workflow

- fully automated with 1-step external sample preparation
- time-to-result 1 1/2 h (walk away test)
- throughput: up to 16 tests / module / run
- no bio-safety cabinet
- closed system (no contamination risk)

Performance

- specific for MTB
- sensitivity close to culture
- detection of rif-resistance via rpoB gene

GeneXpert as a scalable platform

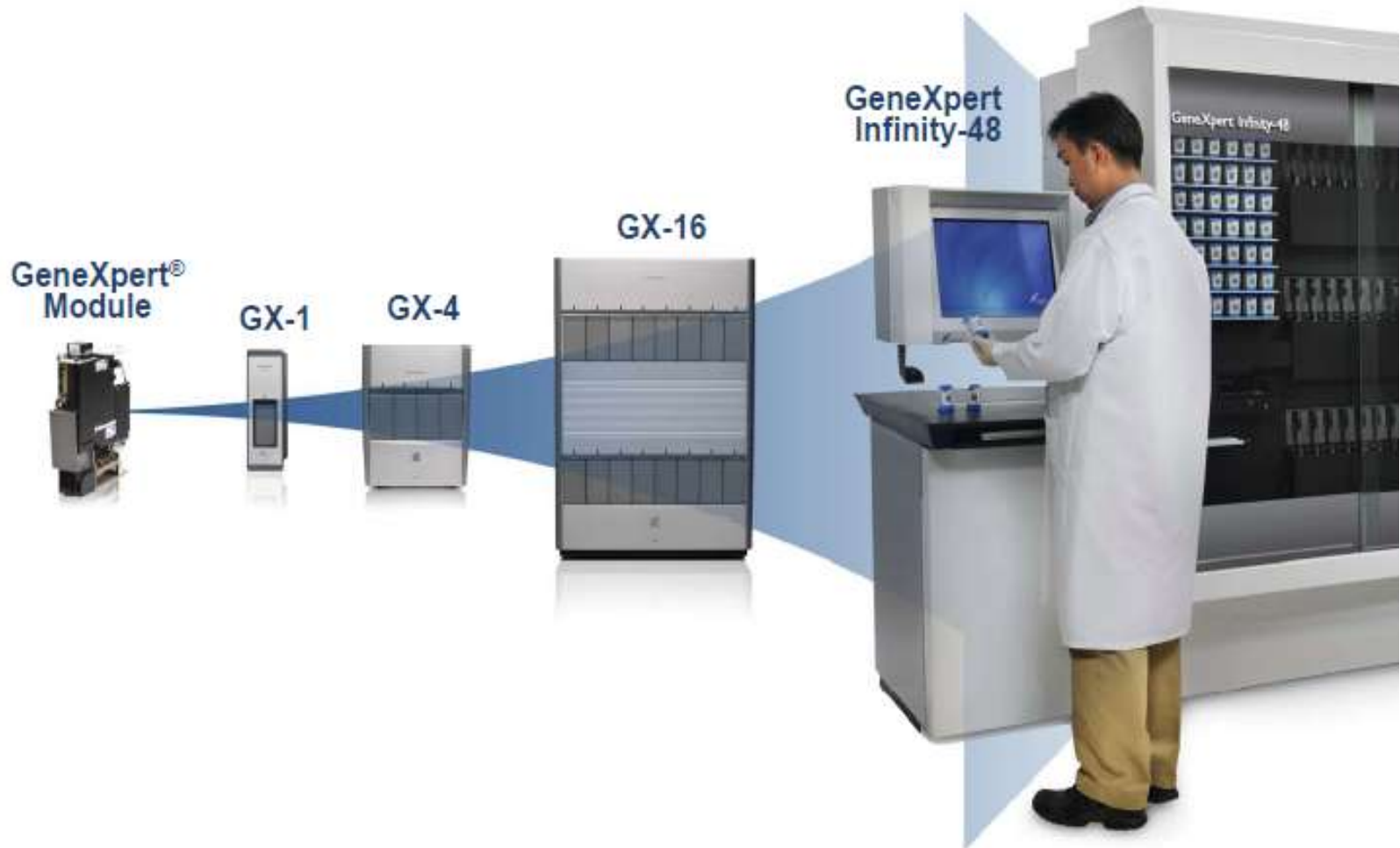


Table 34: Existing test cartridges on the GeneXpert platform

Staphylococcus aureus colonization

Vancomycin resistance

Clostridium difficile

MRSA from tissue or blood

Group B *Streptococcus*

Enteroviral meningitis

Coagulation disorders

Anthrax

Bordetella pertussis

Bordetella parapertussis

HSV Type 1

HSV Type 2

RSV Type A

RSV Type B

Norovirus GI





Norovirus GII

Flu A

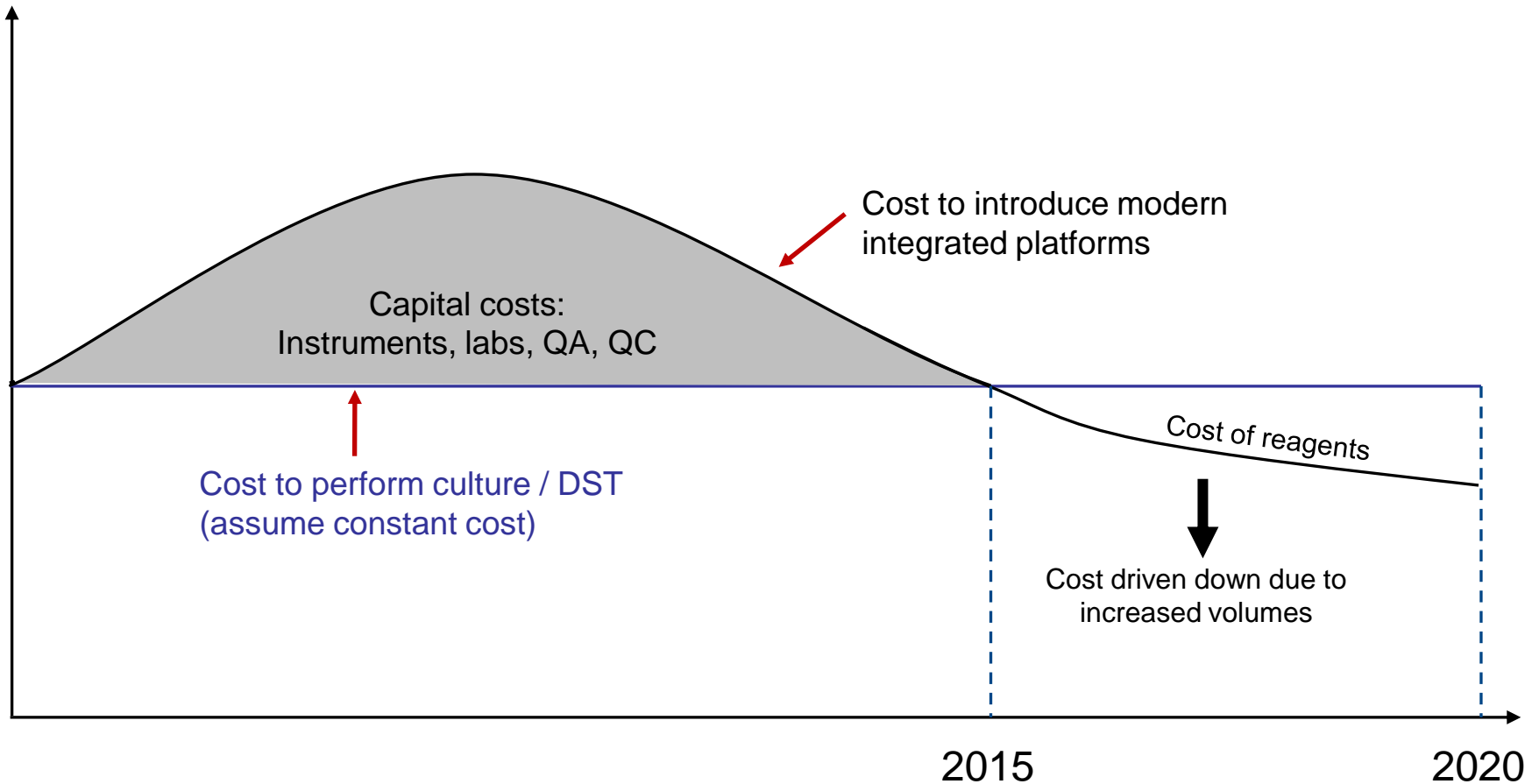
Flu B

Leukemia (BCR-ABL)

Expanding technology platform=increased cost-effectiveness

Technology platform	“Menu”
Regional Laboratories (line probe assay)	 <ol style="list-style-type: none">1. TB Rif / INH2. TB Fluoroquinolones/Inject Aminoglycosides3. EID/HIV
District/Subdistrict Laboratories (automated NAAT)	 <ol style="list-style-type: none">1. TB Rif2. TB Fluoroquinolones/Inject Aminoglycosides3. STDs4. Viral load HIV5. Others: Hepatitis B/C
Microscopy Centres (manual NAAT)	 <ol style="list-style-type: none">1. TB2. Malaria3. HAT4. EID/HIV
Microscopy Centres (LED microscopy)	 <ol style="list-style-type: none">1. TB2. HAT3. Malaria

Decreasing cost of new technologies over time



Thank you!

