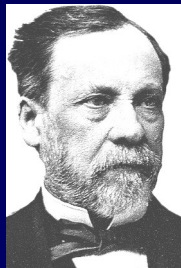


Current trends in **TUBERCULOSIS** epidemiology in **BELGIUM**

Maryse FAUVILLE-DUFAUX



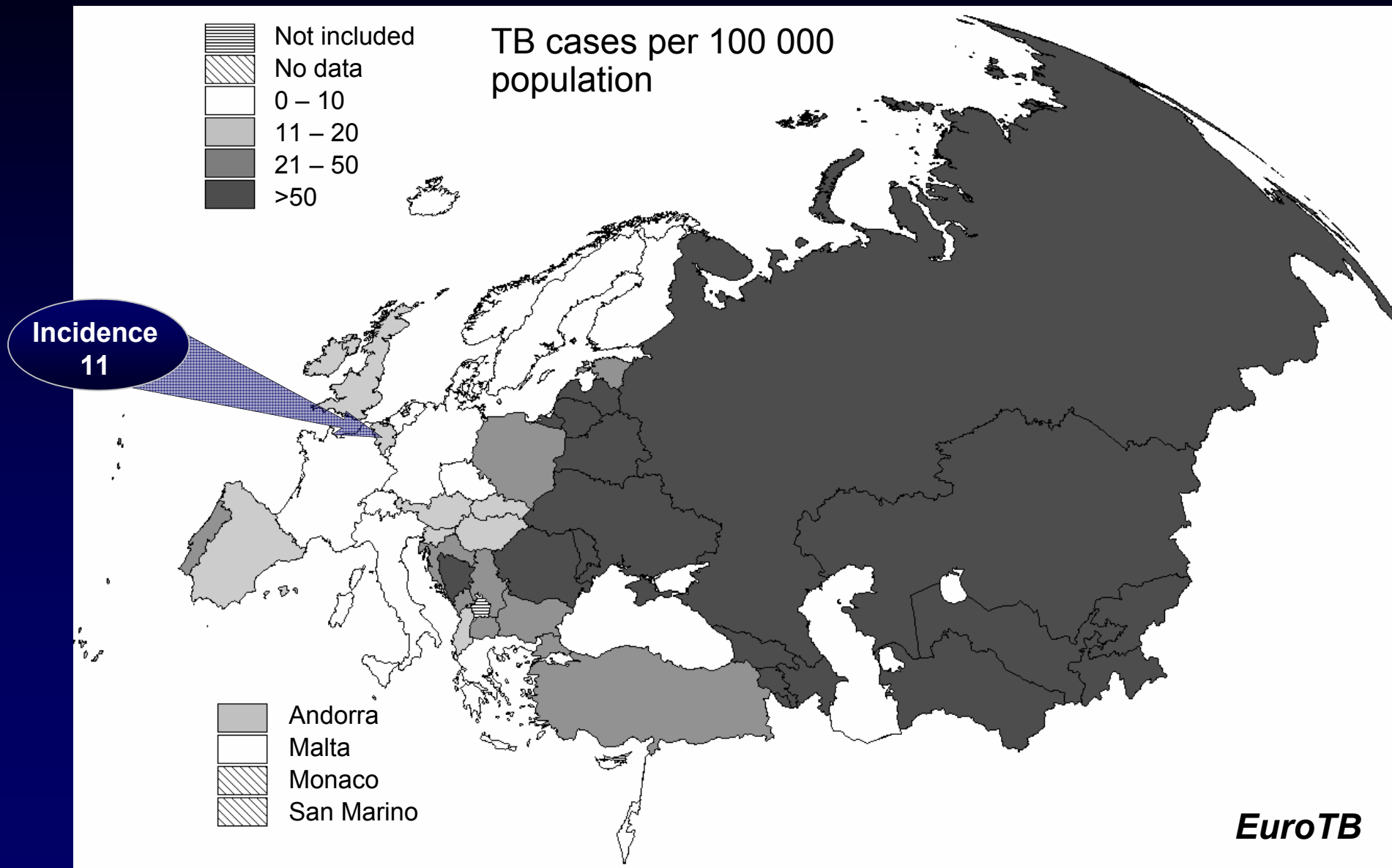
Scientific Institute of Public Health

Pasteur Institute, Brussels

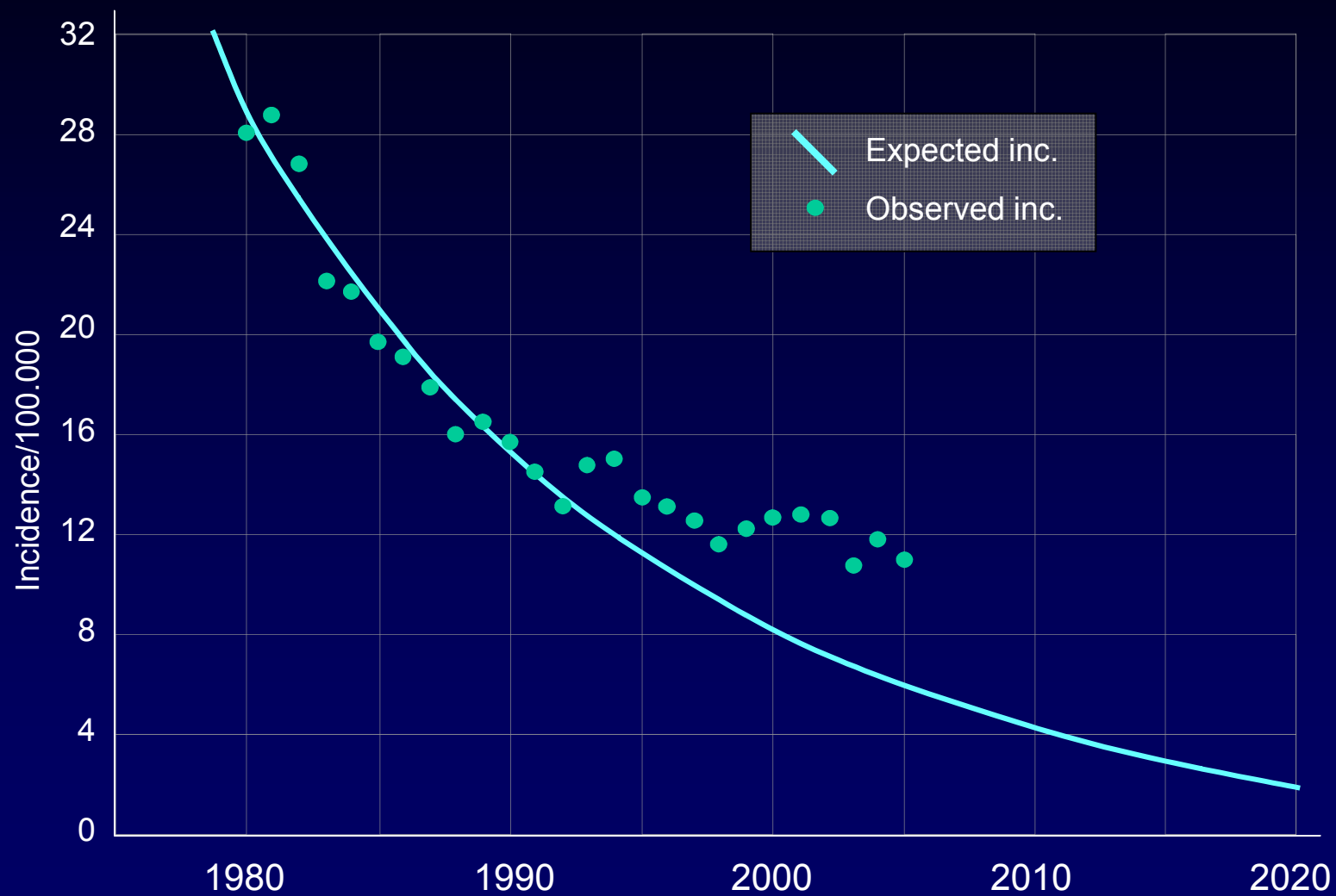
Reference Centre of Mycobacteria

SPF – Public Health

TB notification rates per 100,000 population, European Region, 2005



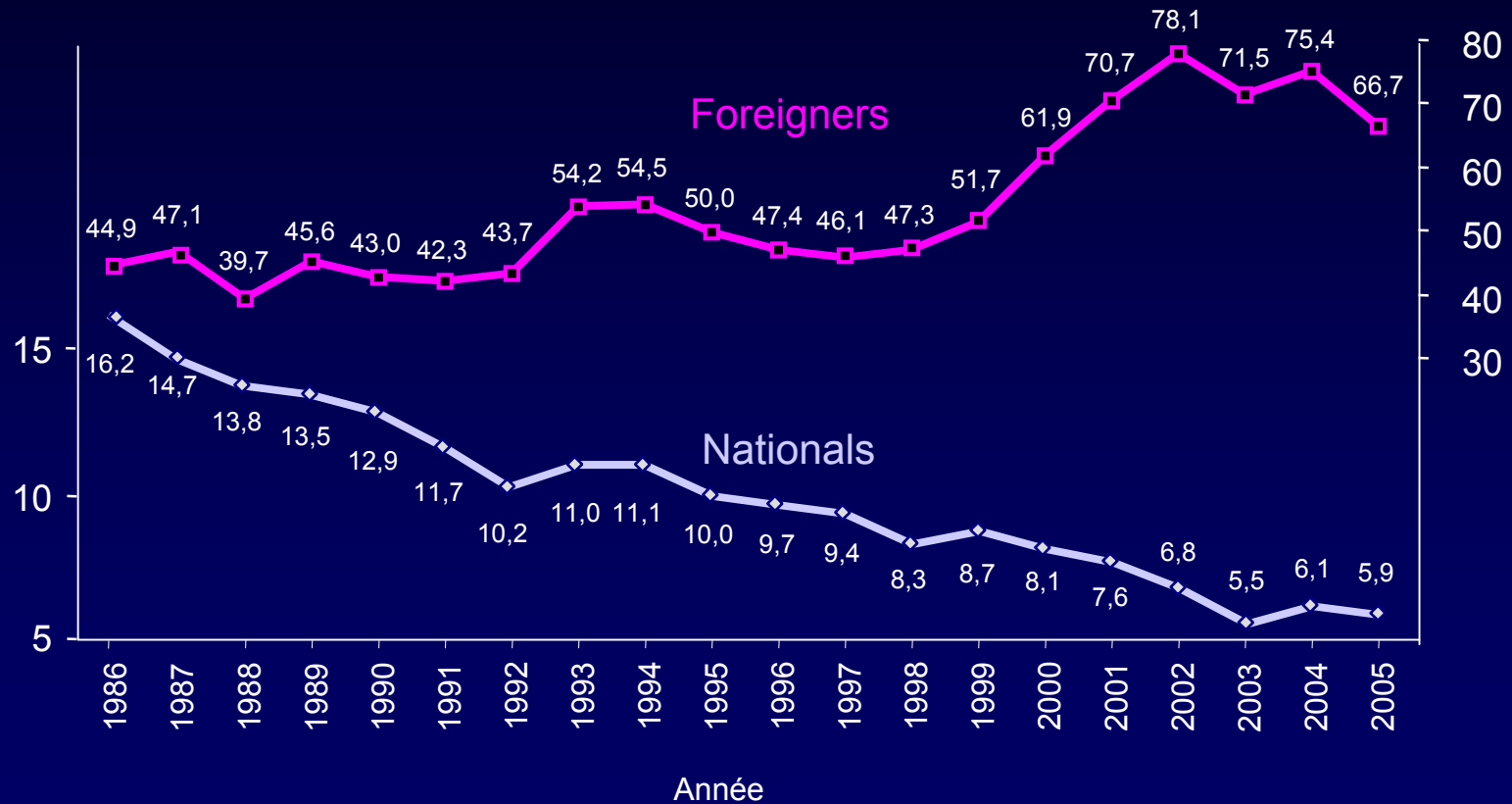
Incidence of tuberculosis in Belgium (1980-2005)



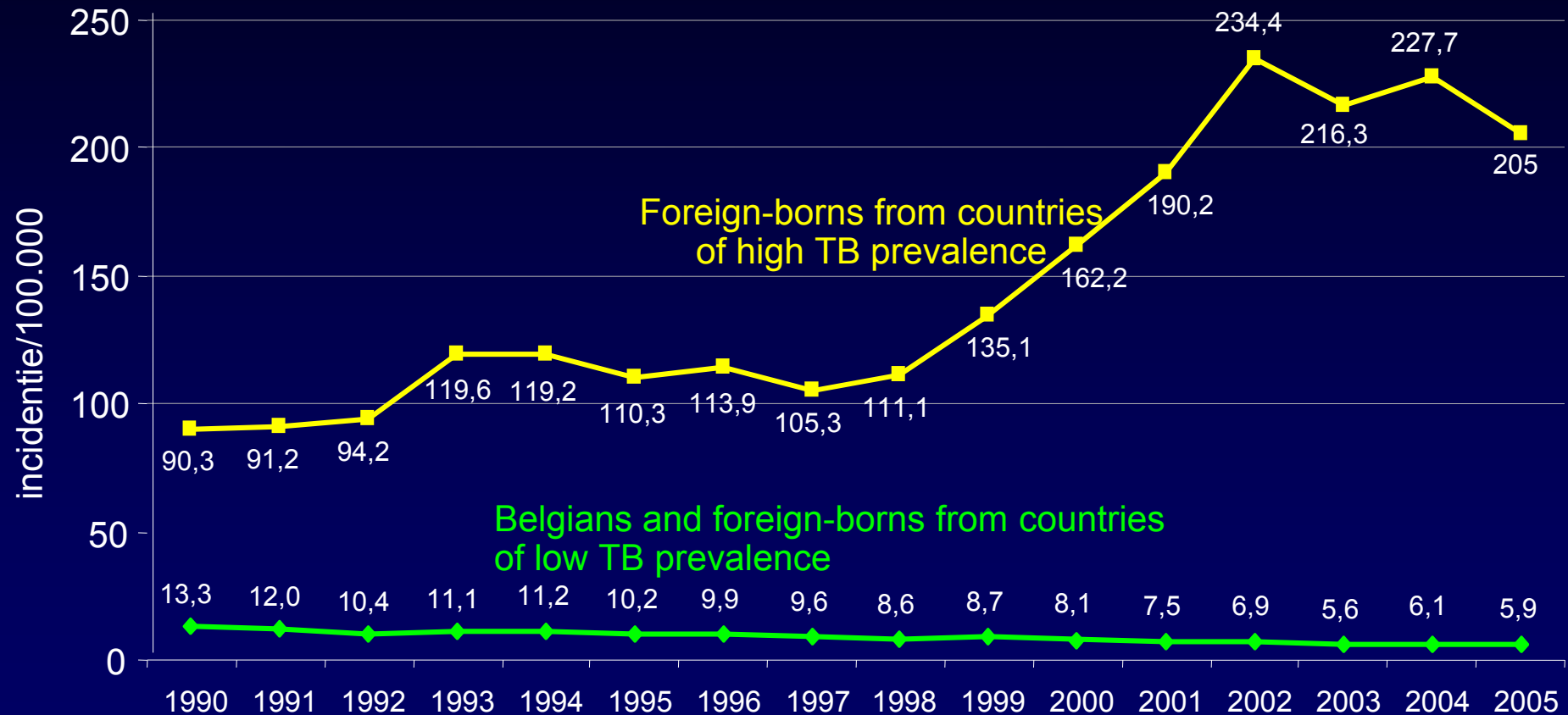
Evolution of TB incidence in Belgium among foreigners and nationals

/100 000
nationals

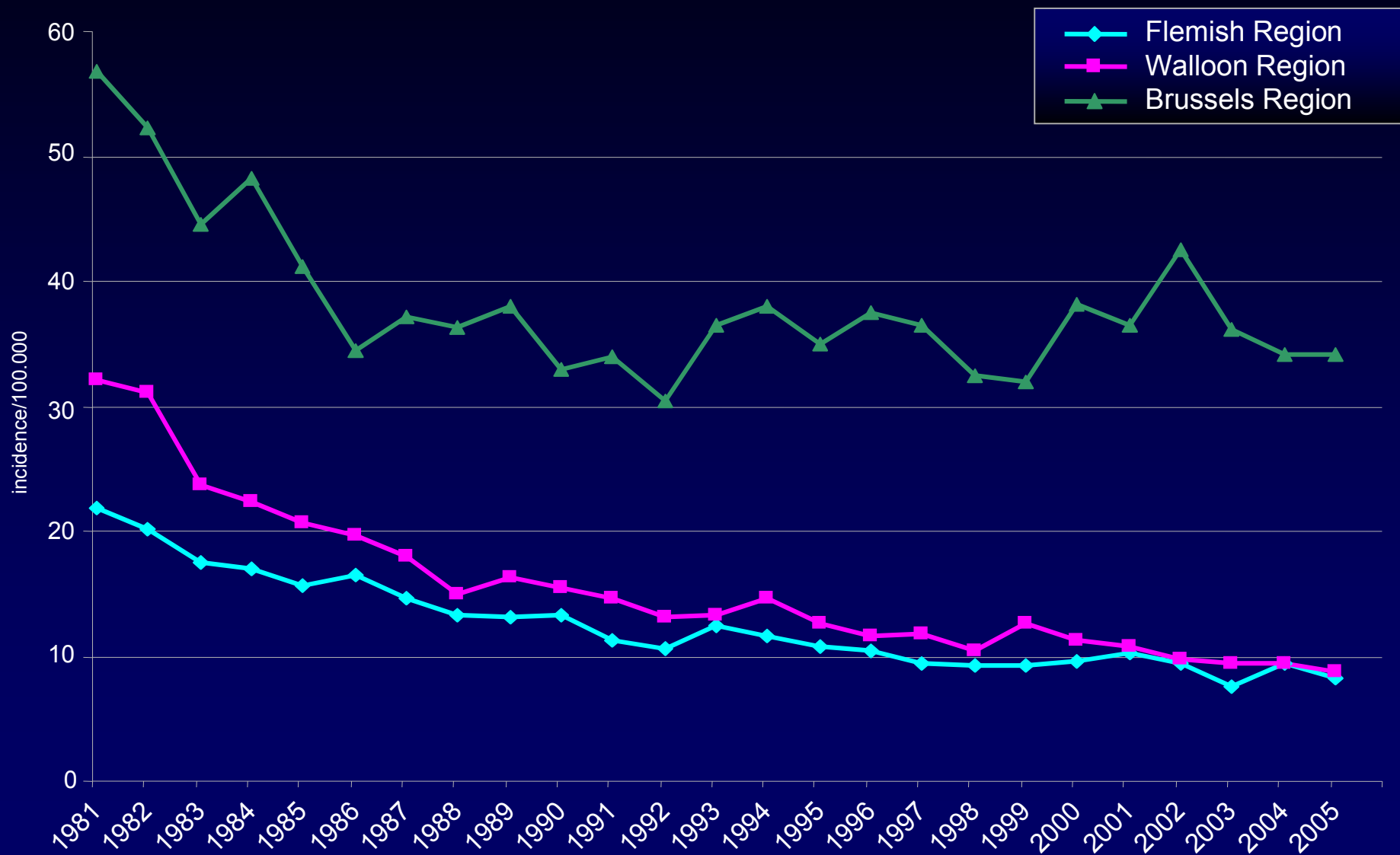
/100 000
foreigners



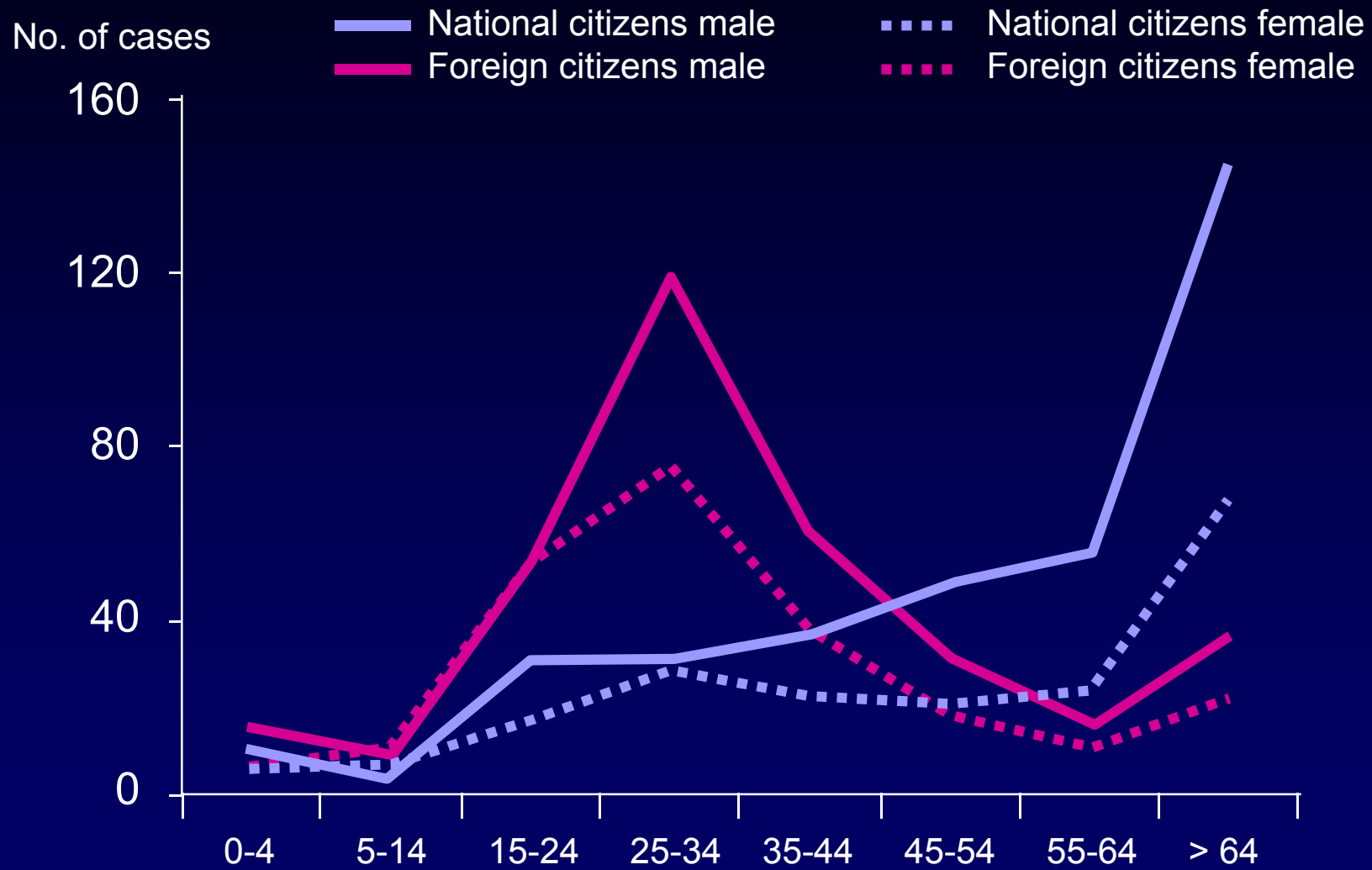
Evolution of TB incidence according to patient's origine (Belgium 1990 - 2005)



Evolution of TB incidence in the 3 Belgian Regions from 1981 to 2005



Tuberculosis cases by origin, age group and sex, 2005



Tuberculosis case notification, 2005

Total number of cases	1 144	
Notification rate per 100 000	11.0	
Sex ratio (M:F)	1.6	
Median age-group, nationals	55-64 yrs	
Median age-group, non-nationals	25-34 yrs	
Foreign citizens	581	(50.8%)
New (not previously diagnosed)	878	(76.7%)
Culture positive	849	(74.2%)
Pulmonary	835	(73.0%)
of which smear positive*	401	(48.0%)
HIV positive TB cases	52	(4.5%)

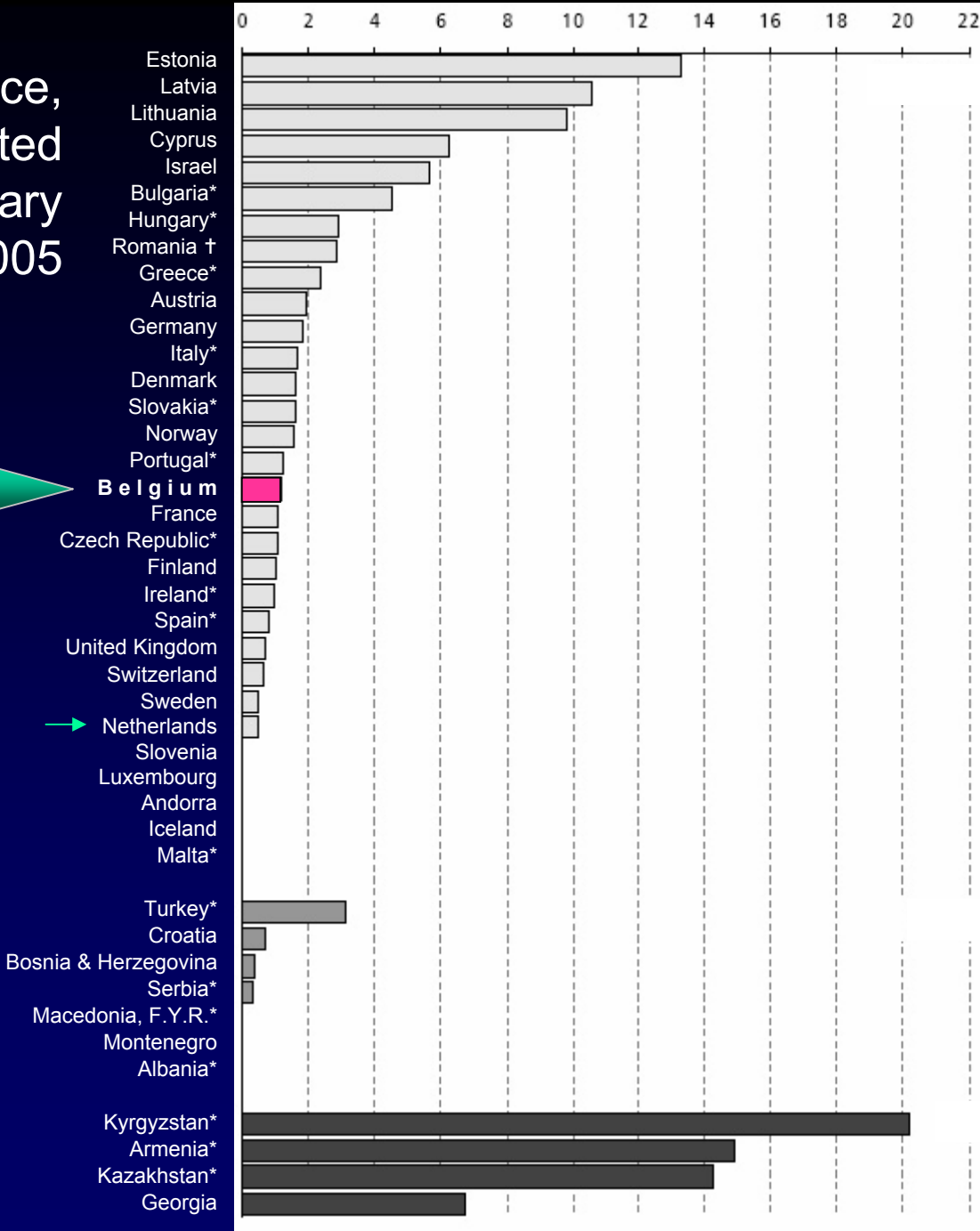
*Including smear of specimens other than sputum

Drug Resistance in Belgium, 2005 among the 849 culture positive patients

	All TB cases	Previously untreated
Cases with DST results	768 (90.0%)	569
Cases resistant to isoniazid	42 (5.5%)	29 (4.9%)
Cases resistant to rifampicin	13 (1.7%)	9 (1.5%)
MDR cases	11 (1.4%)	7 (1.2%)
Cases resistant to ethambutol	14 (1.8%)	8 (1.3%)

Multidrug resistance, previously untreated TB cases (primary MDR), 2005

1,2% →



EU & West

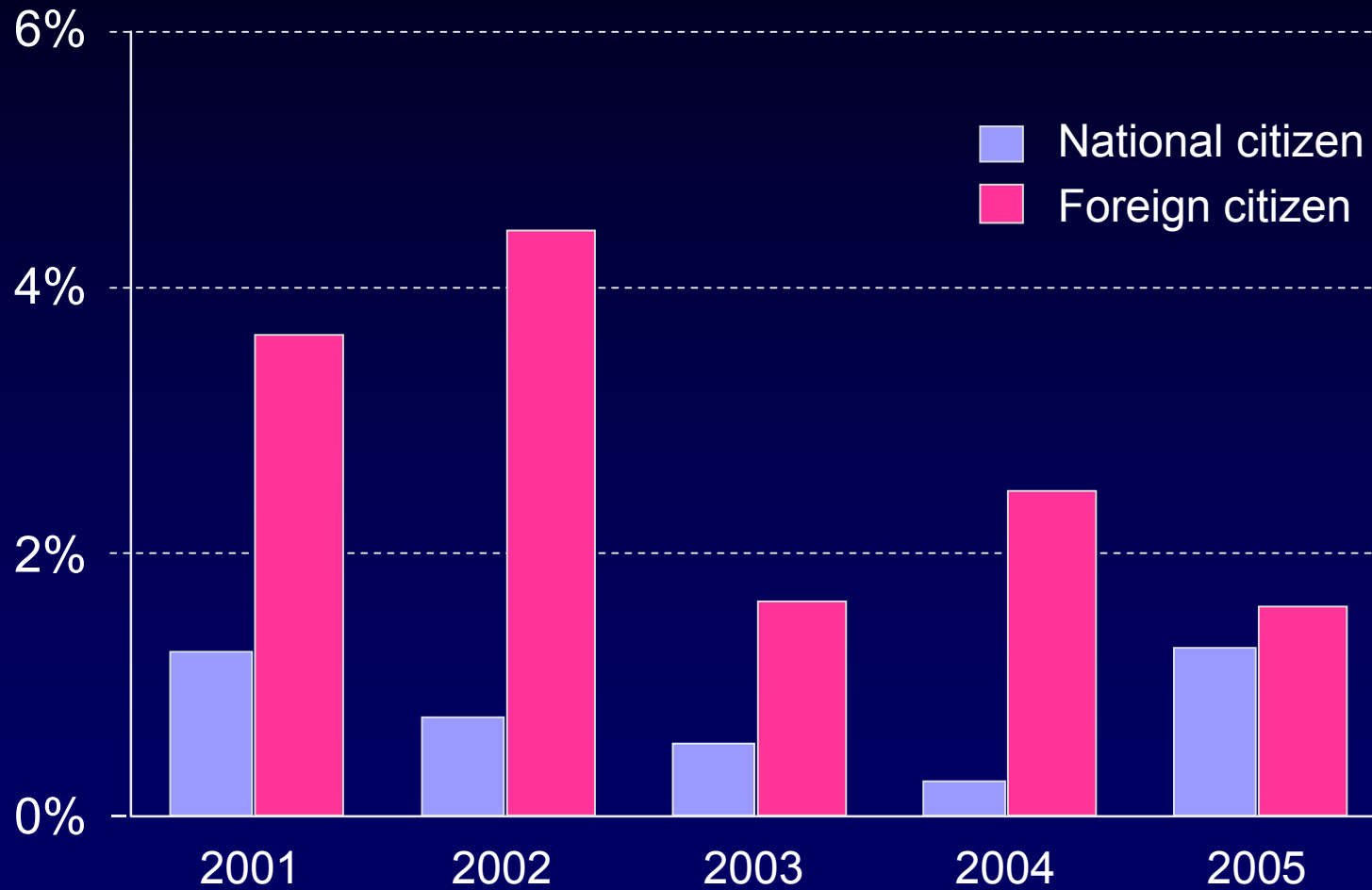
Balkans

East

EuroTB

Combined multidrug resistance, by origin, 2001-2005

% resistance



EuroTB

Structure to fight tuberculosis in Belgium

Clinical diagnosis
and treatment



Private sector

Structure to fight tuberculosis in Belgium

Clinical diagnosis
and treatment



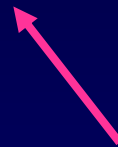
Private sector

LABORATORIES

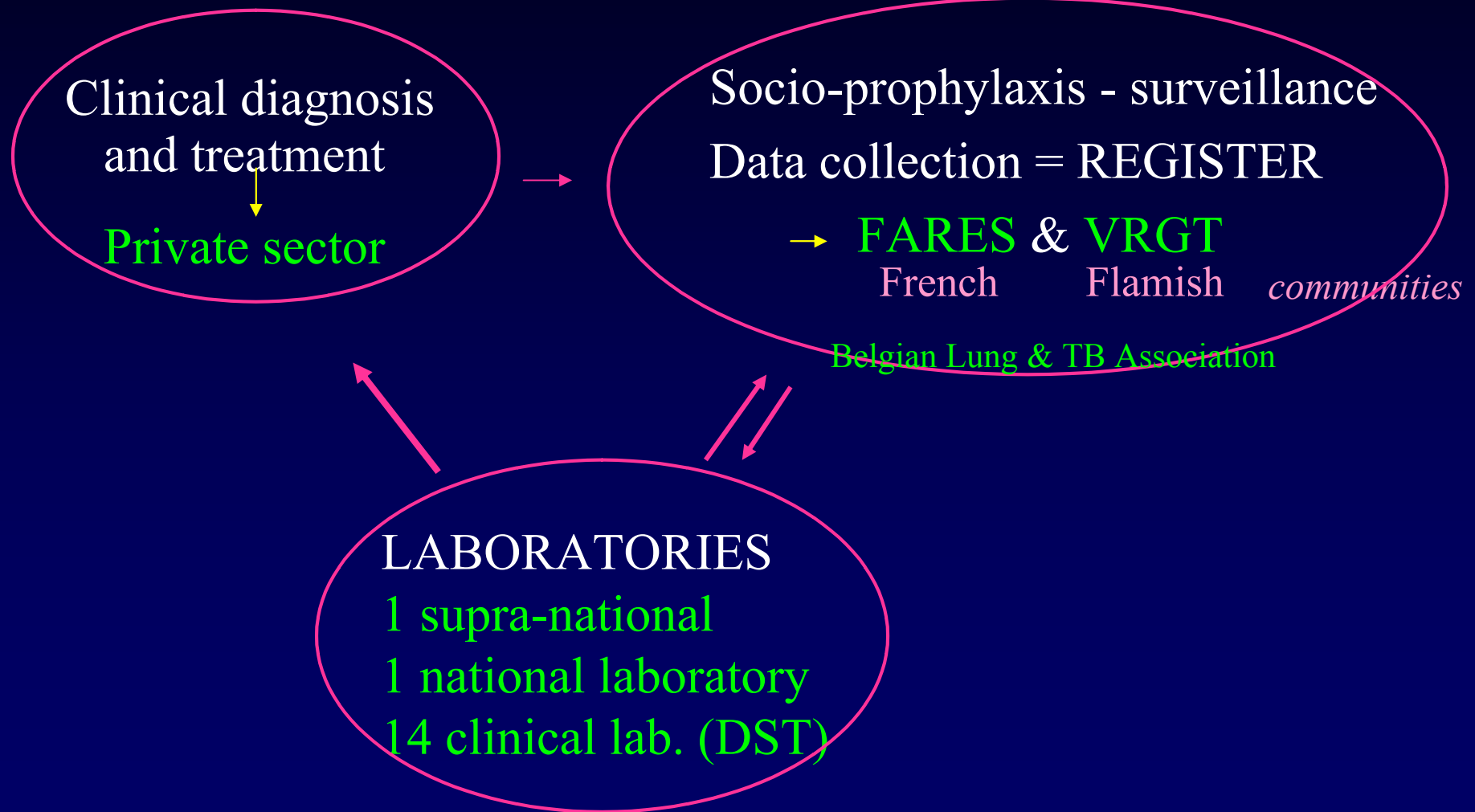
1 supra-national

1 national laboratory

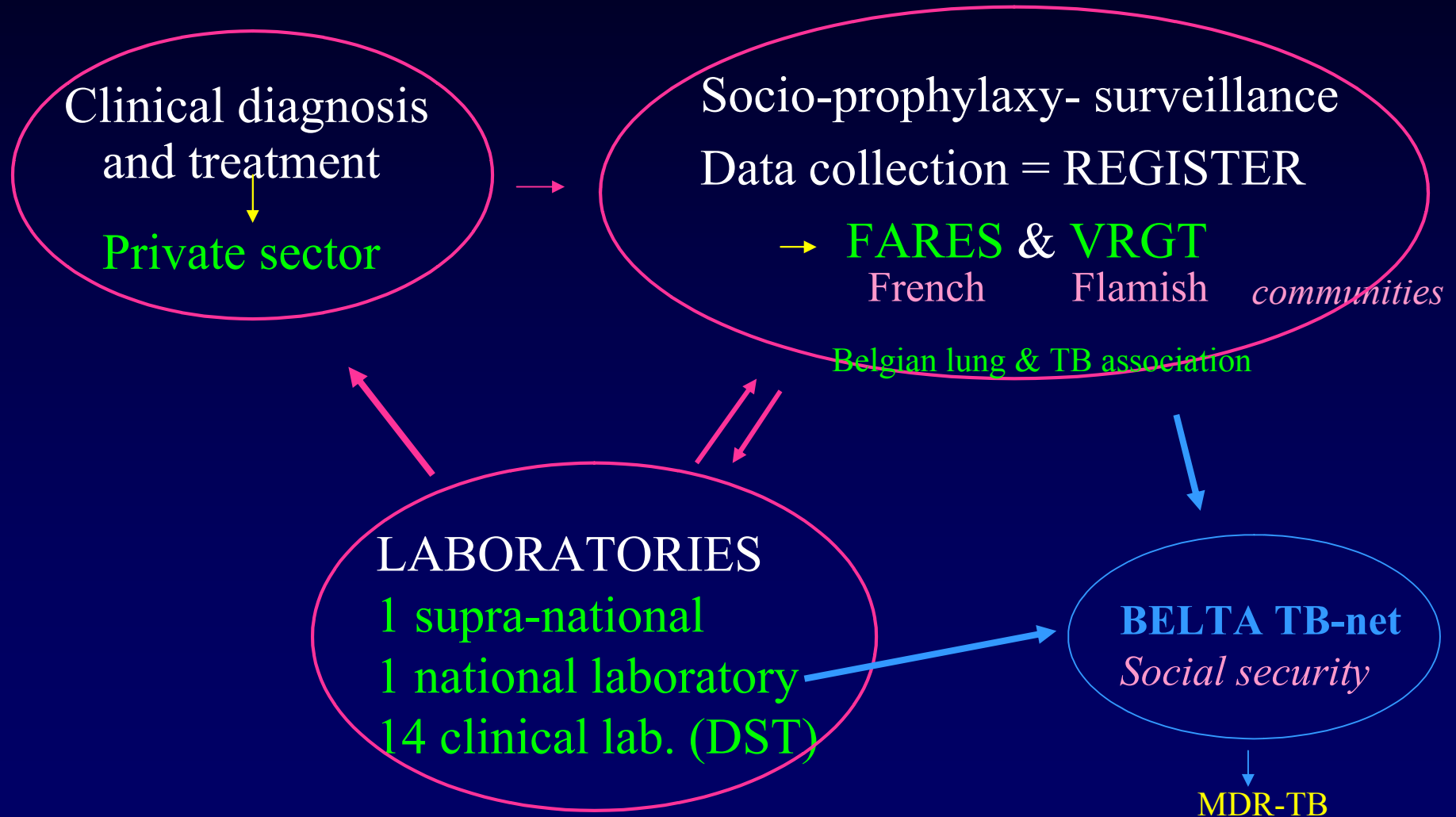
14 clinical lab. (DST)



Structure to fight tuberculosis in Belgium



Structure to fight tuberculosis in Belgium



MDR-TB

BELTA TB-net

Advice for treatment

Free of charge anti TB drugs

Classical epidemiology

Surveillance

National Ref. Laboratory

DST 1st and 2nd line antibiotics

Mutations

Genotyping = molecular
epidemiology

MDR-TB in Belgium 1994-2006

160 multidrug resistant *M. tuberculosis* isolates
obtained from 139 different patients

For 19 patients : series of 2 to 7 isolates (1 isolate per year)

METHODS

1) Susceptibility testing : Proportion method of Canetti on solid medium
Radiometric Bactec
Bactec MGIT 960

2) Resistance confirmation → Detection of mutations

rifampicin : <i>rpoB</i> gene	Inno-Lipa-Rif-TB PCR-sequencing (80bp)		
isoniazid : <i>kat G</i> gene		PCR-sequencing	S315T
	<i>inh A</i> gene promotor	PCR-sequencing	C-15T
pyrazinamid : <i>pncA</i> gene	PCR-sequencing	(720 bp)	

3) Genotyping IS6110 – RFLP (van Embden, 1993)
Spoligotyping (Kamerbeek, 1997)
MIRU – VNTR 24 loci, automated on capillary electrophoresis
system ABI 3100 Avant (Supply 2006)

RESULTS

Among the 139 patients (160 isolates)

- 14 patients = laboratory cross contamination

10 events – 9 laboratories – 6,3 %

- 125 patients = true MDR-TB 1 XDR

+ 3 during treatment

= 87% of all MDR TB cases notified in Belgium
in this 12 years period

RESULTS

- 125 patients = true MDR-TB (1+3 XDR)

67,2 % males

Mean age : 37 ± 16 years old

76,8 % foreign origin

37 % Africa

27 % Asia

26 % Eastern and Central Europe

6,5 % Western Europe

4,3 % Latin America

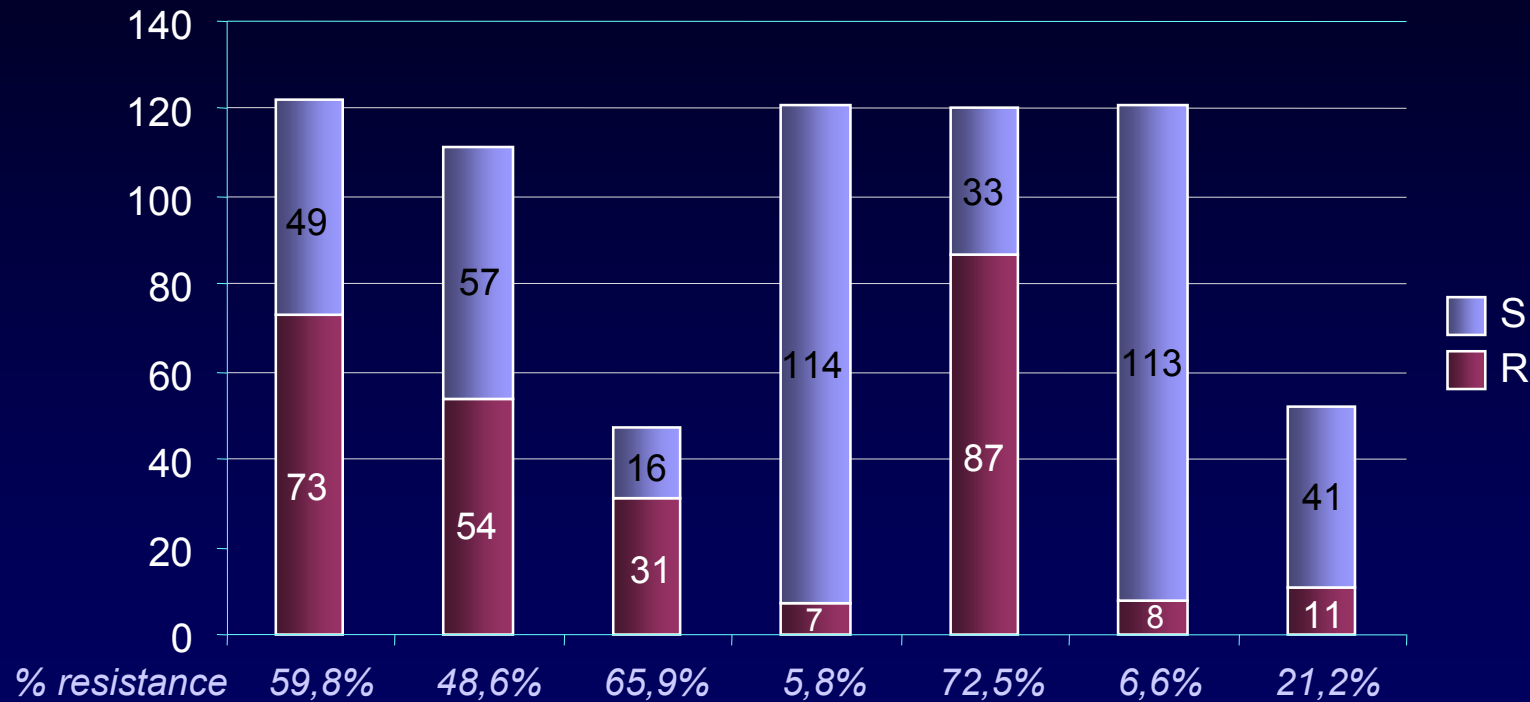
93 % pulmonary disease

75 % smear positive

19 % HIV

Resistance to antituberculous drugs (125 patients)

Nb patients



Ethambutol
Pyrazinamid
Streptomycin
Ofloxacin
Rifabutin
Amikacin
Thioamide

47	SM	Amik
4	R	R
16	S	S
27	R	S

Mutations (125 patients)

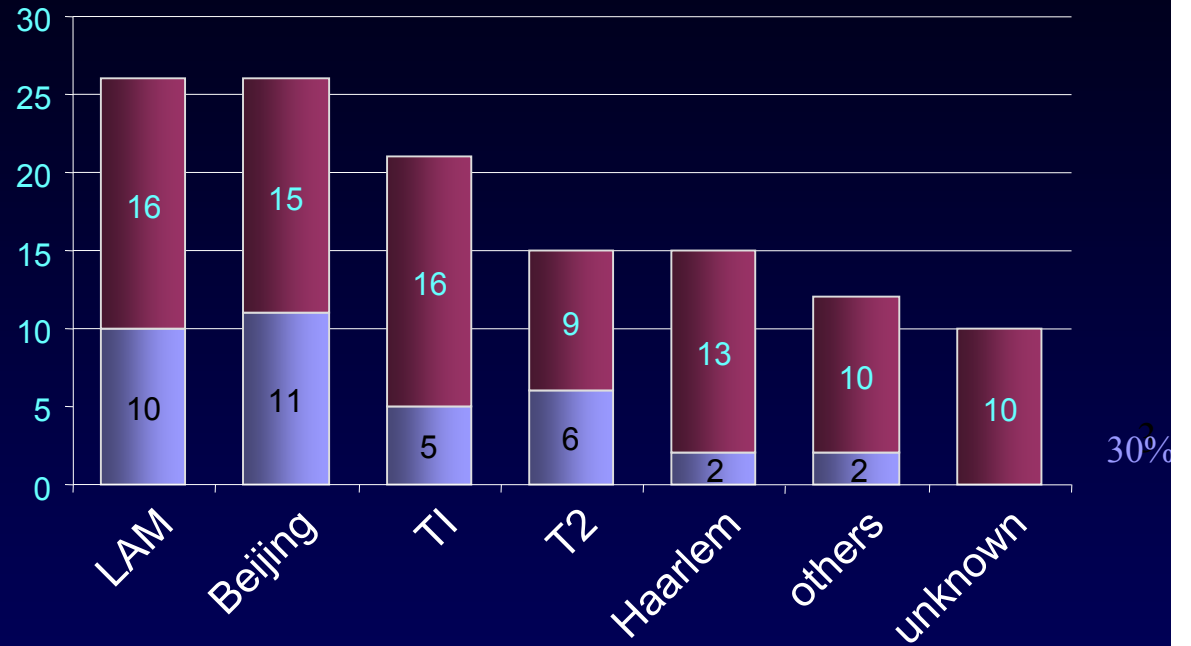
- 96 % in the *rpoB* gene → rifampicin
(80 bp region)
- 84 % in the *katG* → isoniazid
or *inhA* genes
- 78 % of the Z/R isolates → pyrzinamid
in the *pncA* gene

Genotyping (125 patients)

- 89 patients infected by a strain with a single pattern
- 36 patients infected by a strain included in a cluster

Strain-genotype families (125 patients)

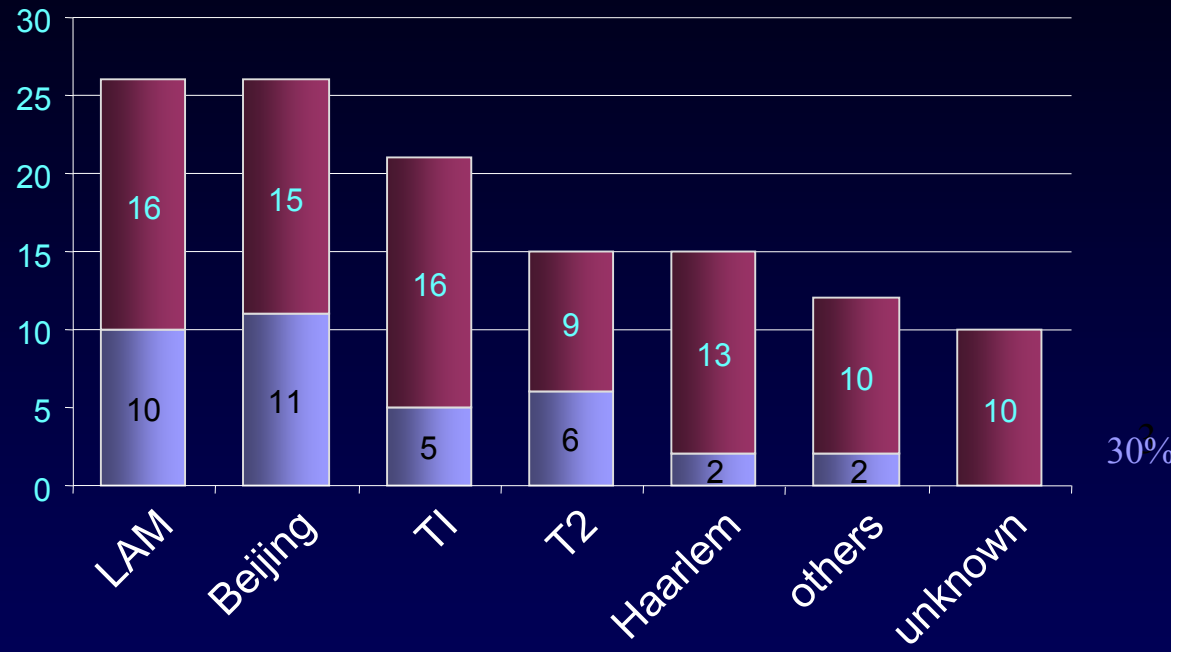
■ 36 patients in clusters
■ 89 patients with single pattern



Genotype families		36 clustered patients (29%)		Number of clusters	89 patients with single patterns
26 LAM	21%	10	38%	4	16
26 Beijing	21%	11	42%	3	15
21 T1	17%	5	24%	2	16
15 T2	12%	6	4%	2	9
15 Haarlem	12%	2	13%	1	13
12 others	9%	2	17%	1	10
10 unknown	8%	0	%	0	10

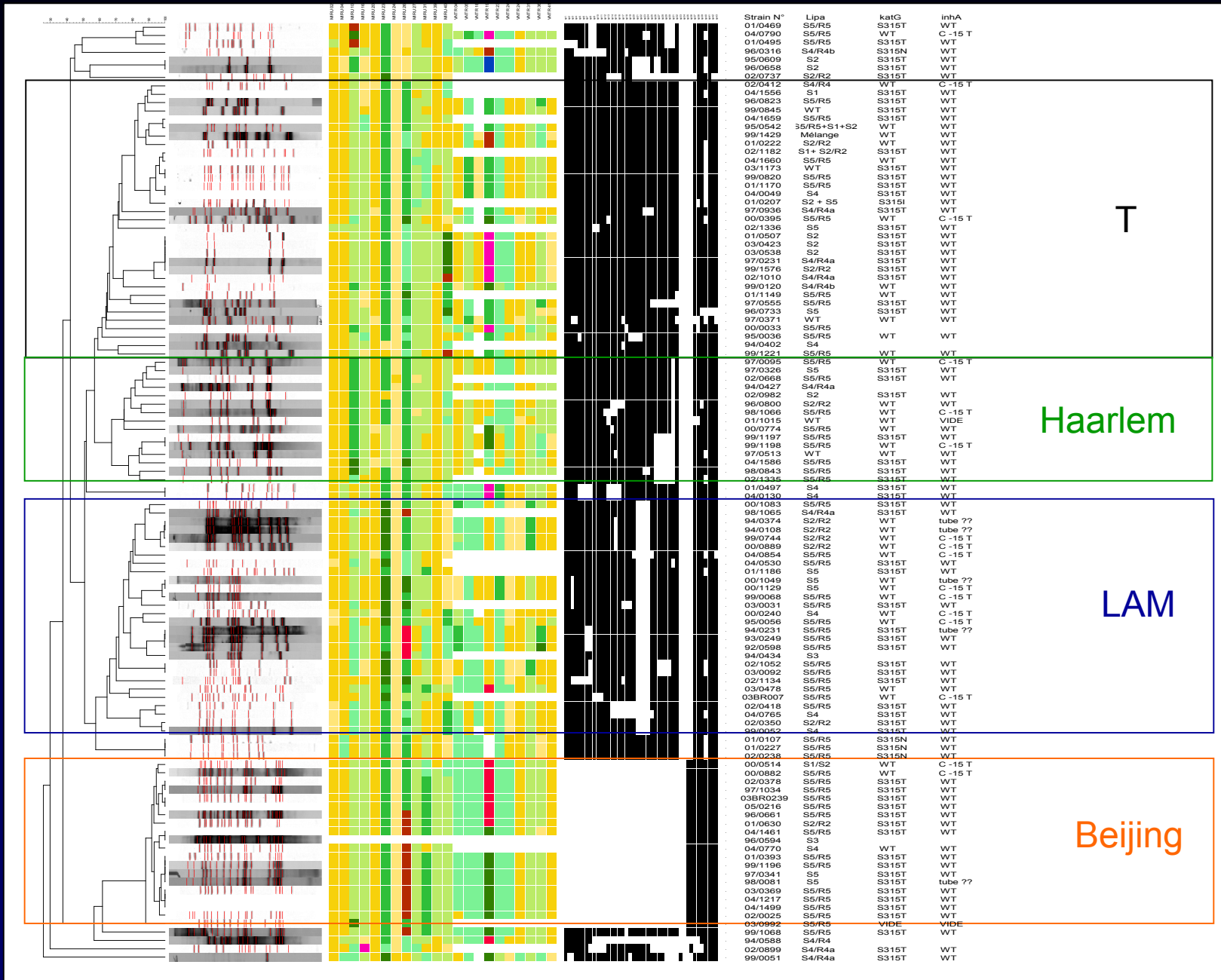
Genotype families (125 patients)

36 patients in clusters
89 patients with single pattern



Link between strain-genotype family and geographic origin of patient

Patterns of MDR TB isolates



IS6110-RFLP

MIRU-VNTR

SPOLIGOTYPING

36 patients
in strain-
clusters

75%
foreigners

Clusters Nr	Genotype family	Nbr patients	Origin	Known link	TB at arrival	
1	Beijing	9	Ex-URSS, Ukraine Georgia, Iran	NO	YES	
2	Beijing	2	Ex-URSS, Armenia	NO	YES	
3	Undef.	2	DR Congo	NO	YES	
4	Undef.	2	DR Congo	NO	YES	
5	LAM	2	DR Congo	YES	Y - N	intrafamilial
6	LAM	2	Burkina-Rwanda	NO	YES	
7	T2	3	RD Congo-Rwanda	NO	YES	
8	Haarlem	2	Turkey-Marroco	NO	YES	
9	LAM	2	Turkey-Belgium	YES		Hospital
10	T1	3	Belgium LIEGE	NO		To be investigated
11	T2	3	China-France-Belgium	YES		Bronchoscope
12	LAM	4	Belgium	YES		Intrafamilial + social contact

Outcome, 125 MDR patients

Cured	67
Still on treatment	17
Treatment interrupted (toxicity)	2
Died	12
Died before treatment	4
Disappeared	15
No information available	8

CONCLUSION

- Incidence of TB in Belgium is stable since 1992 and near to the score of 10/100.000 inhabitants
- TB incidence is higher in large cities like Brussels and Antwerp and high among foreign-born living in Belgium
- Local outbreaks occur
- Multidrug resistant TB is present (1.4 %), some patients cure but other ones disappear
- No transmission from foreign-born to Belgian citizens
- A good structure to control TB is essential as well as a good collaboration between the different public health services and laboratories