

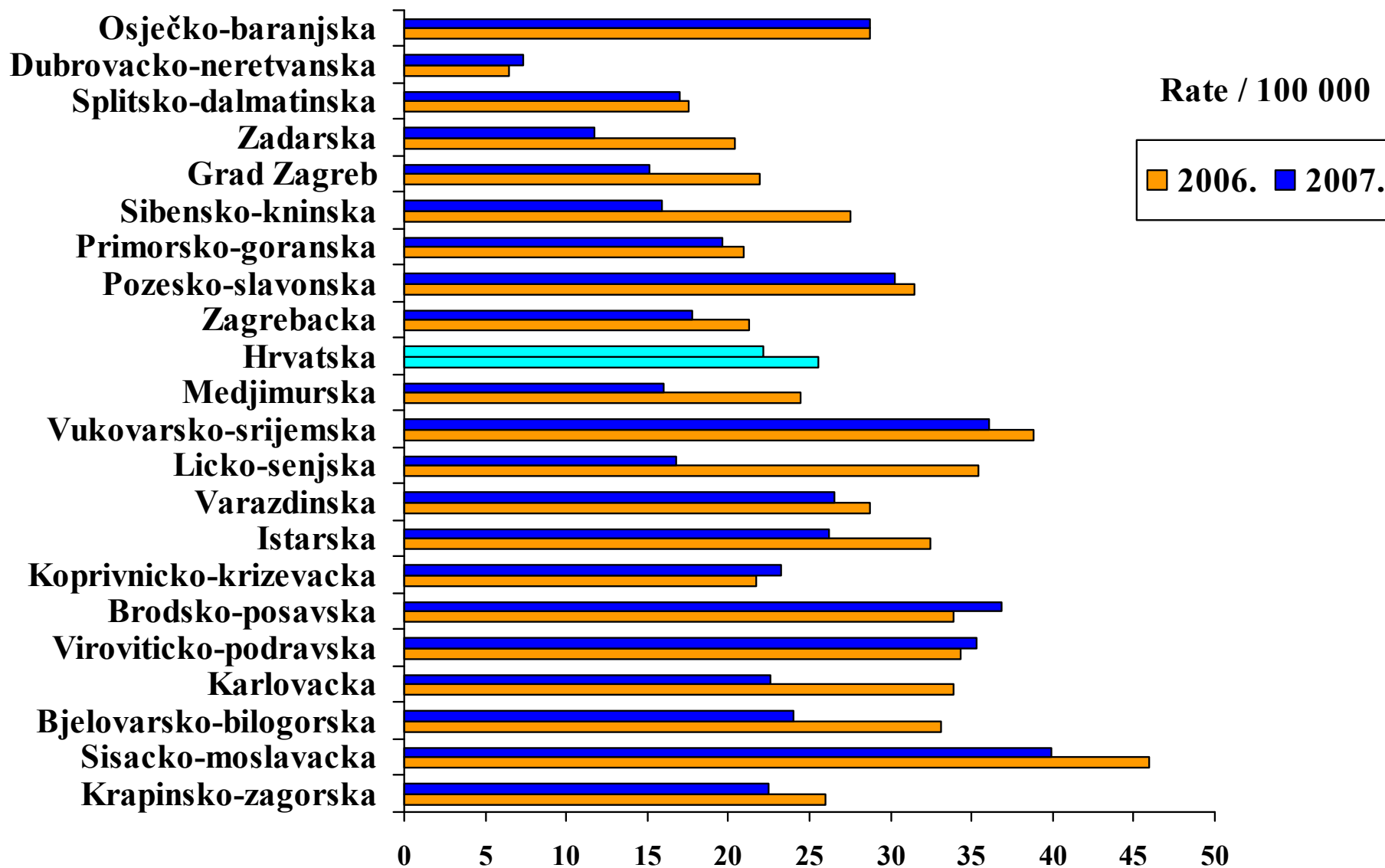
Pokazatelji bakteriološke dijagnostike tuberkuloze u Hrvatskoj

XX stručni sastanak hrvatskih mikobakteriologa

Zagreb, 28. studenoga 2008.

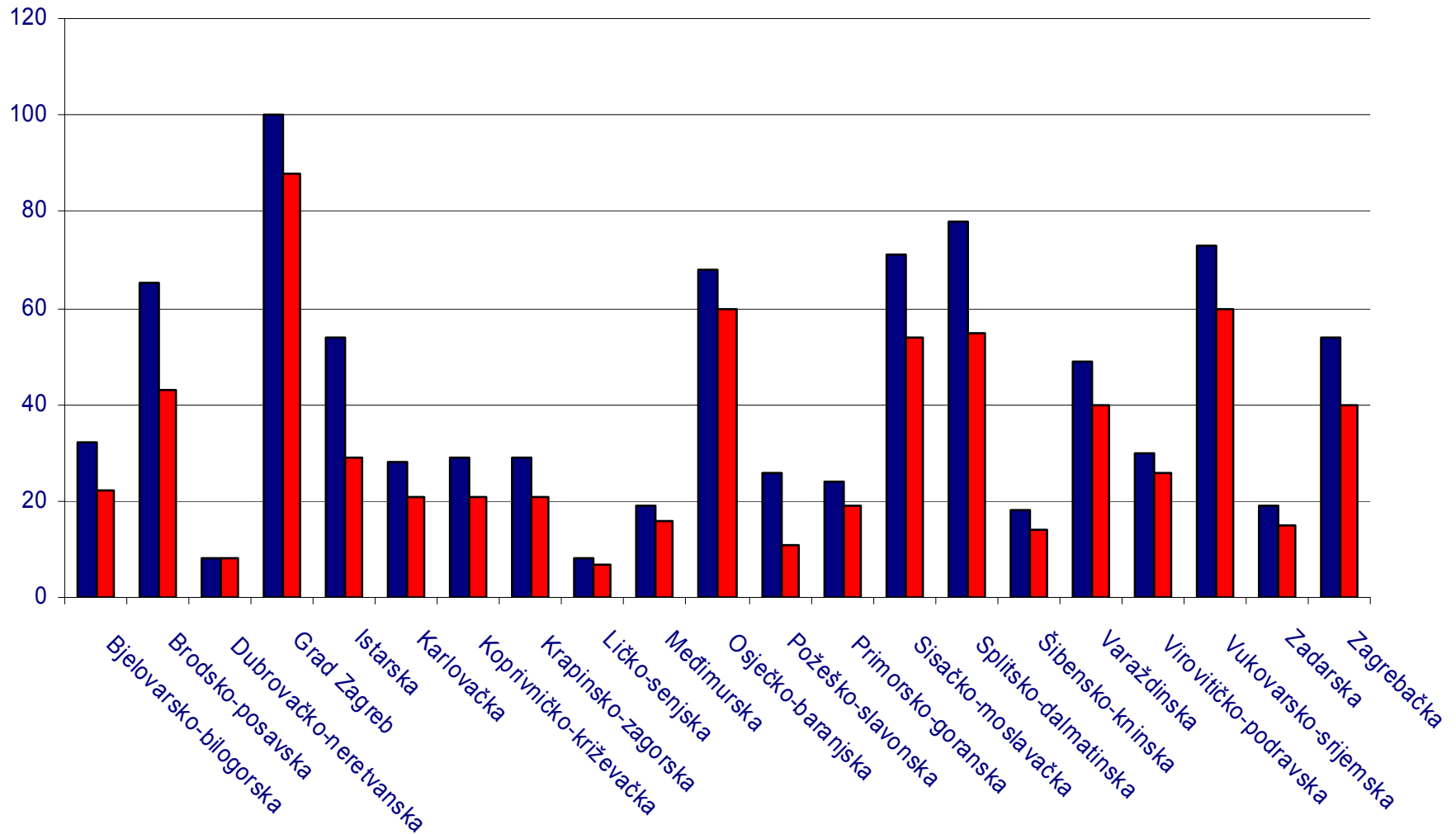


Incidencija tuberkuloze po Županijama, 2006.-2007.

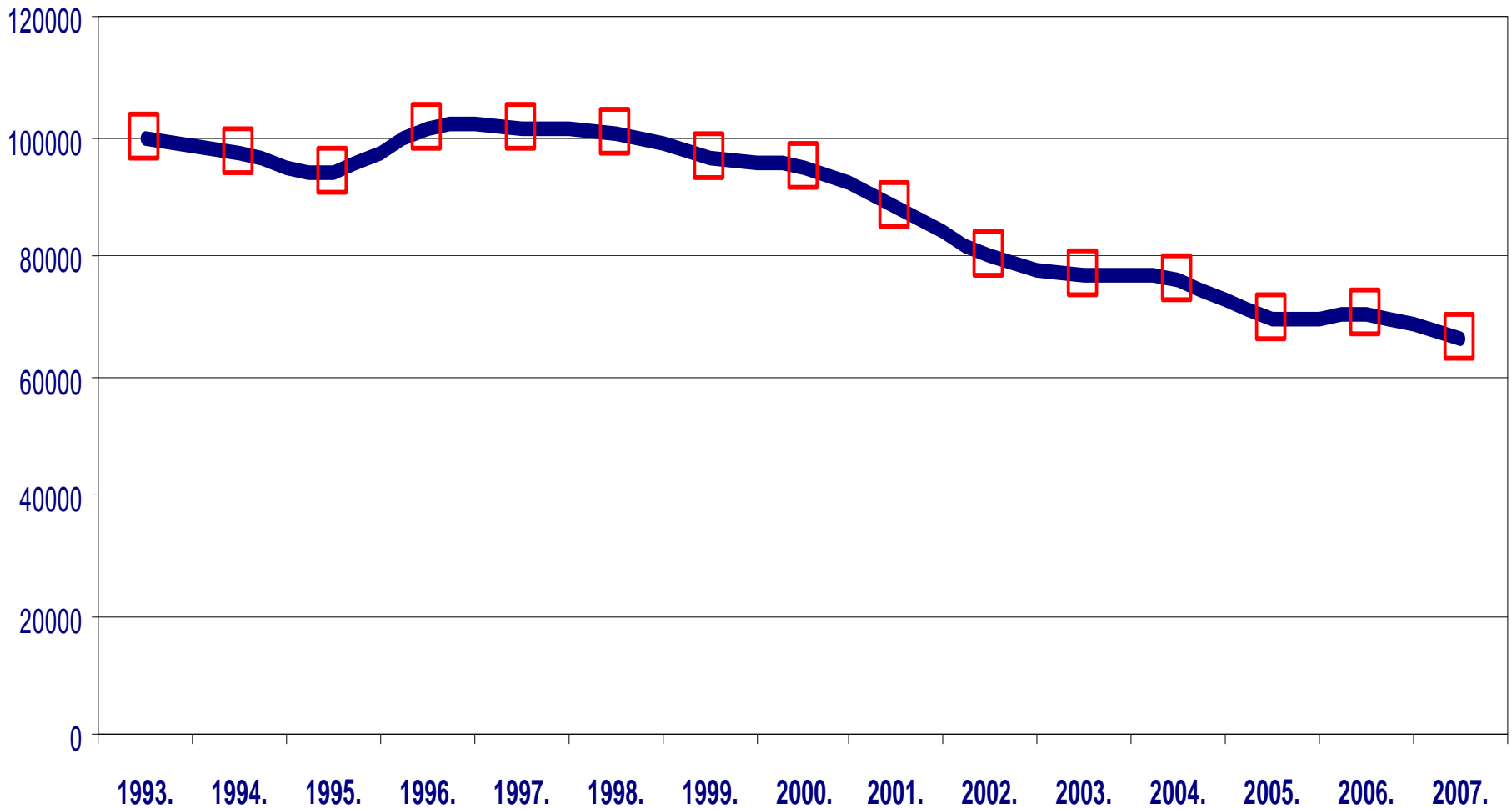


Bakteriološki potvrđena TB

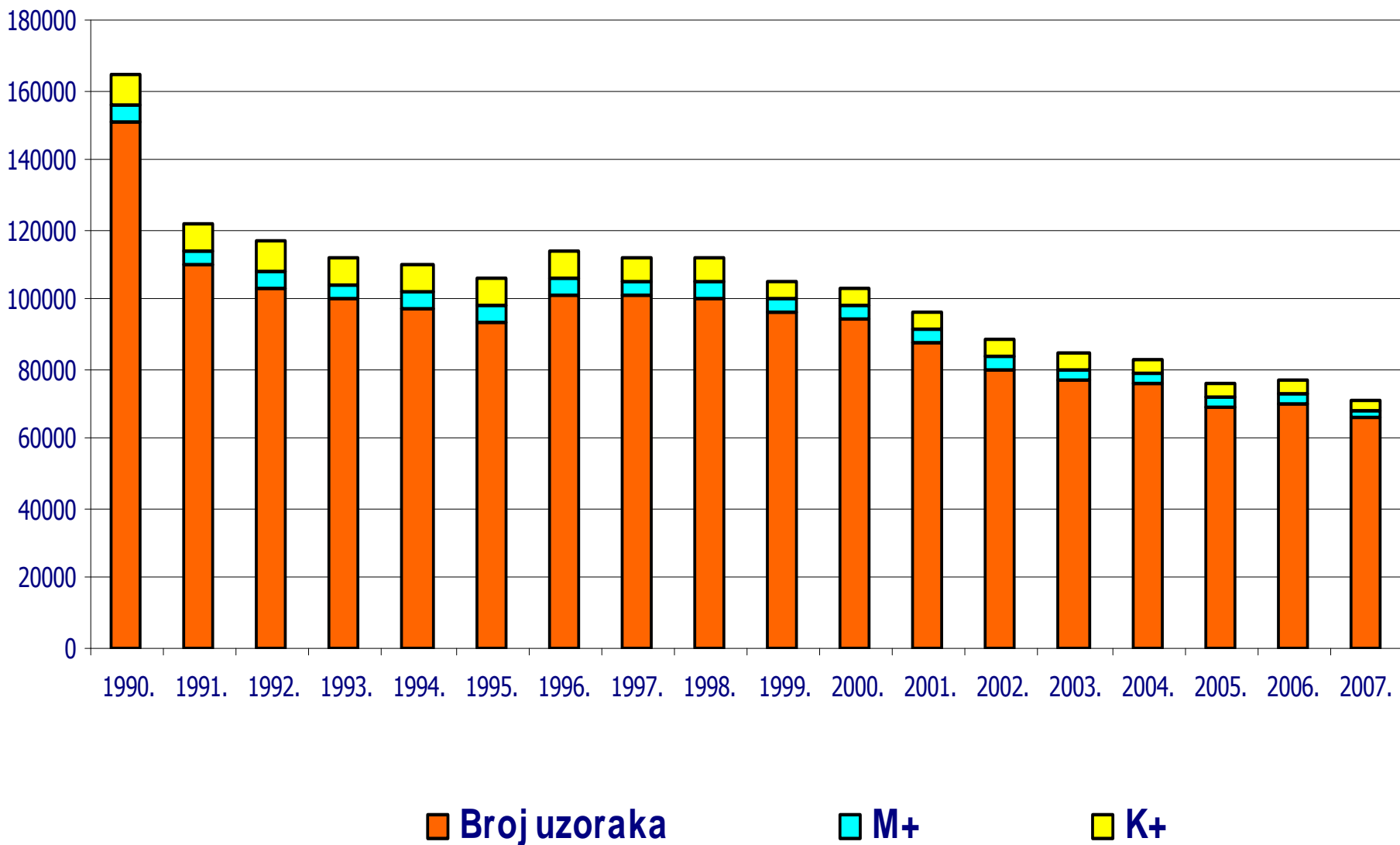
■ Broj oboljelih ■ Broj K+



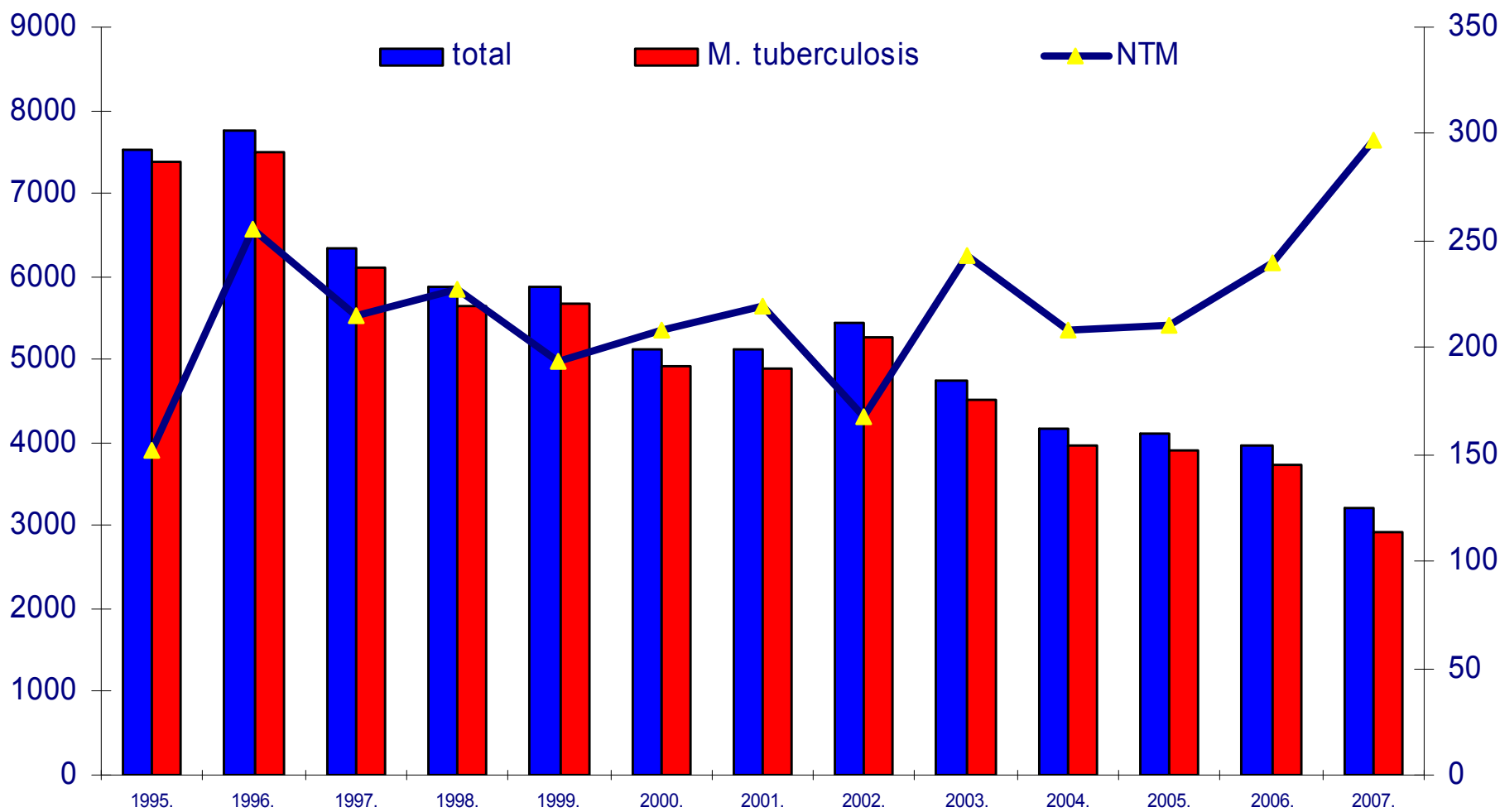
Bakteriološka dijagnostika tuberkuloze u Hrvatskoj



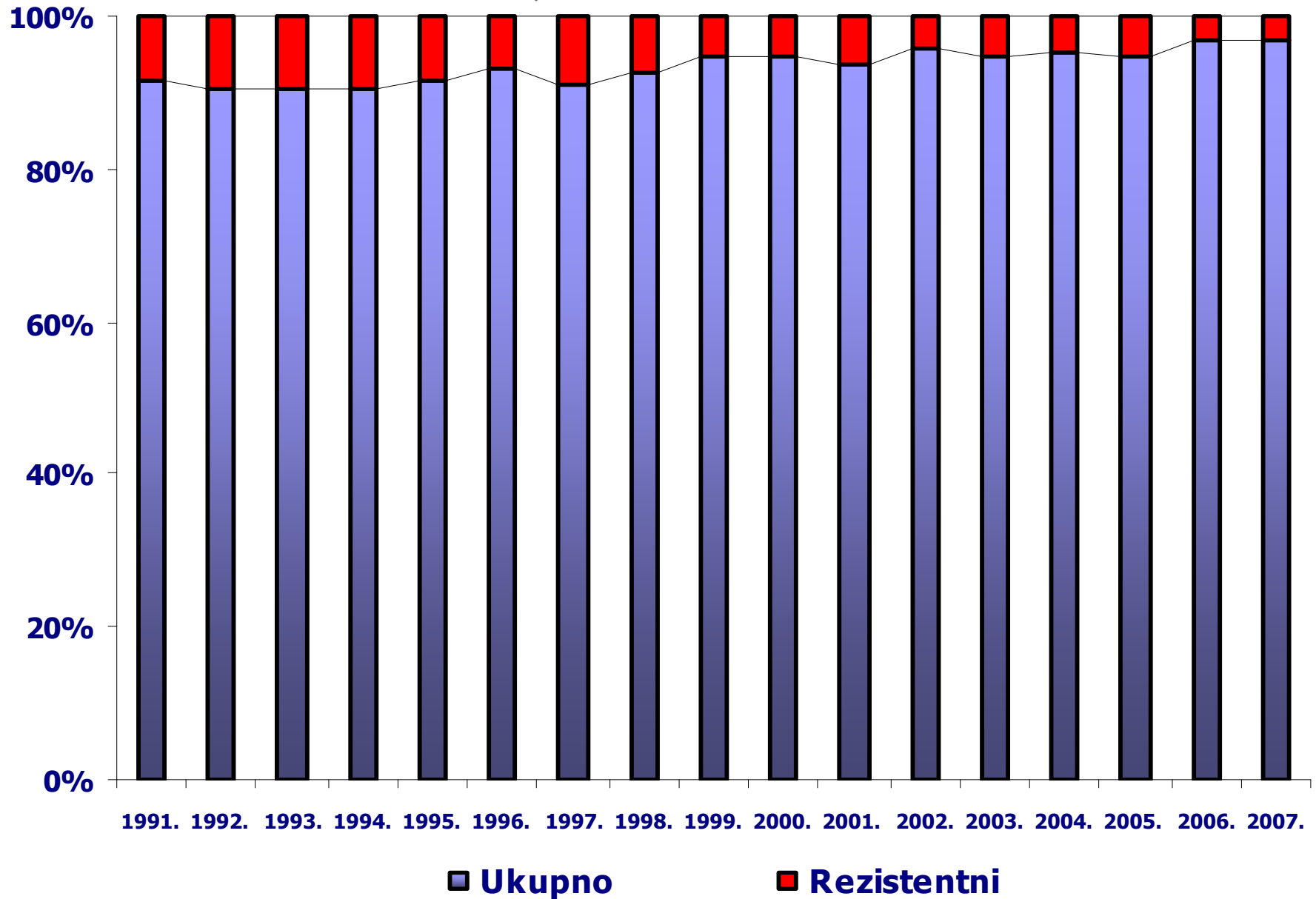
Bakteriološka dijagnostika tuberkuloze, 1990.-2007.



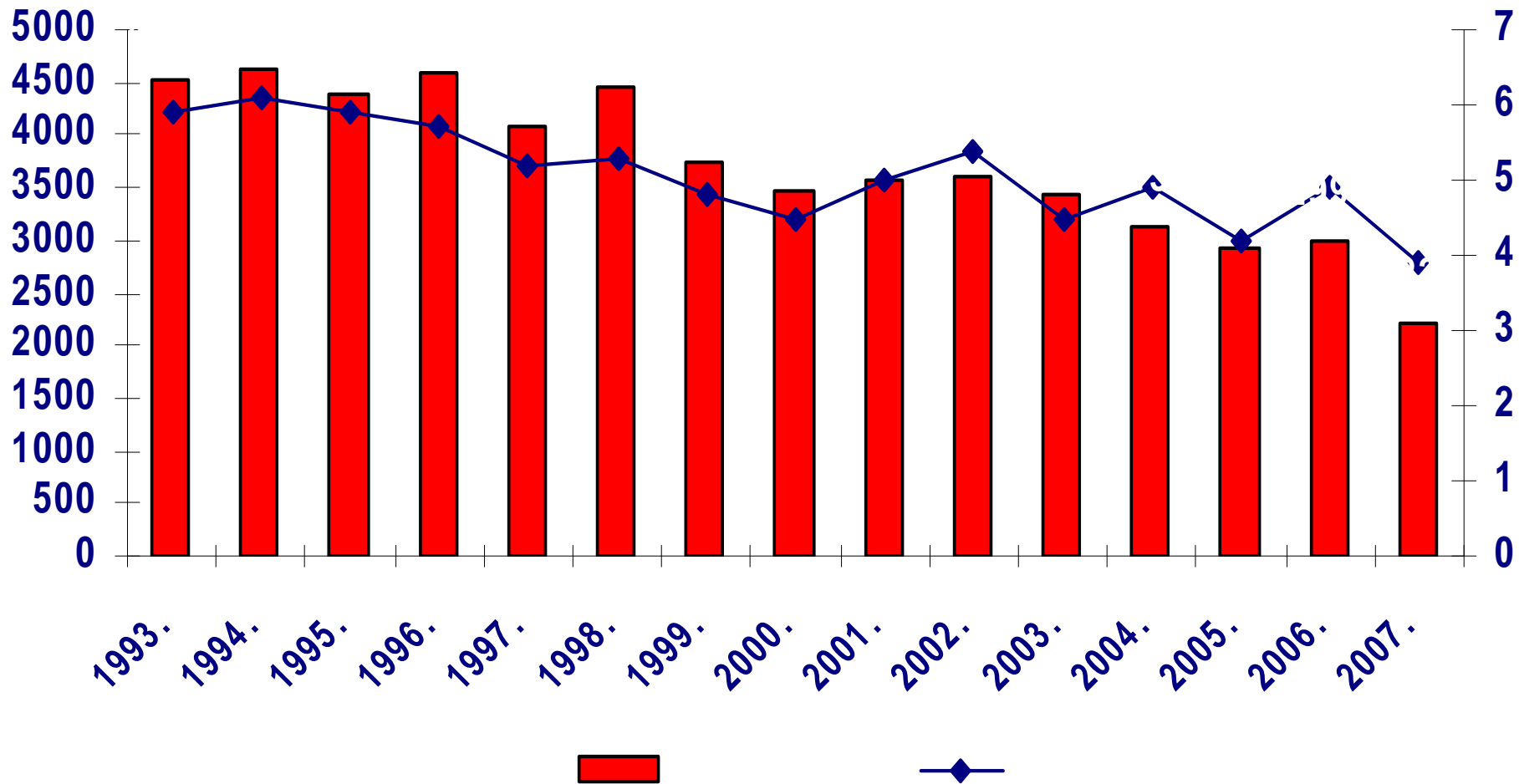
Izolirane mikobakterije, 1995.-2007.



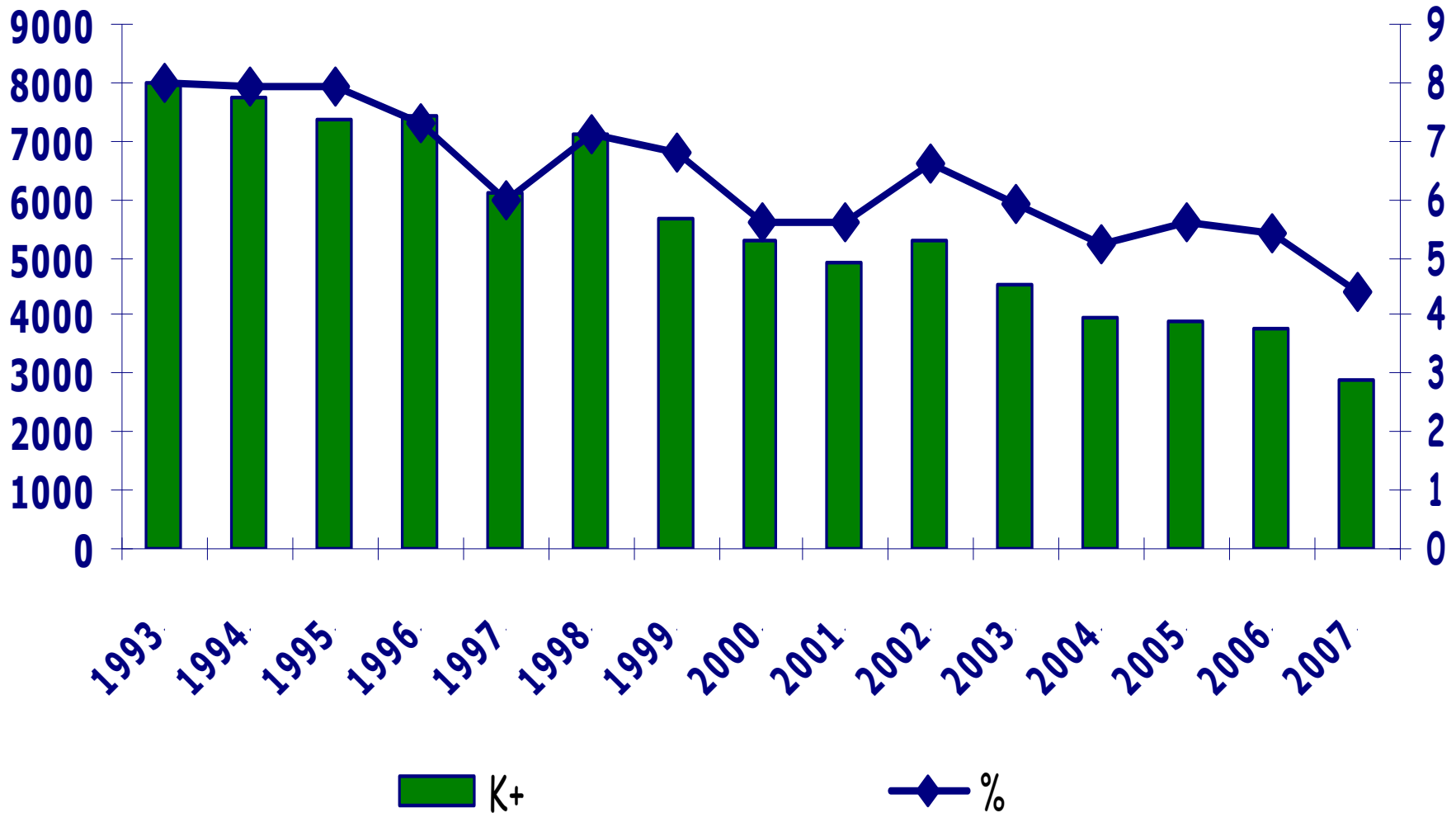
Izolirani sojevi *M. tuberculosis*



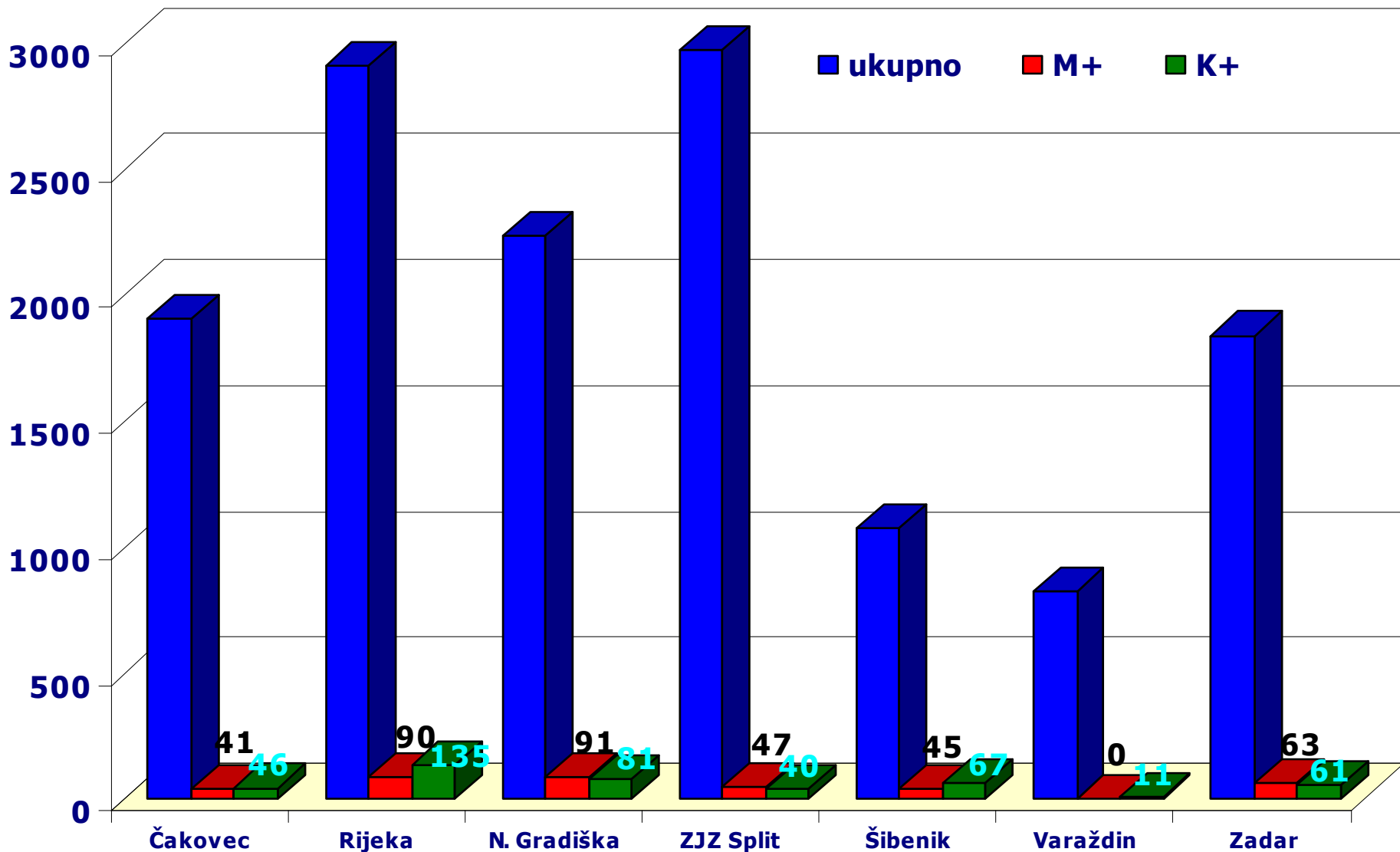
Mikroskopija



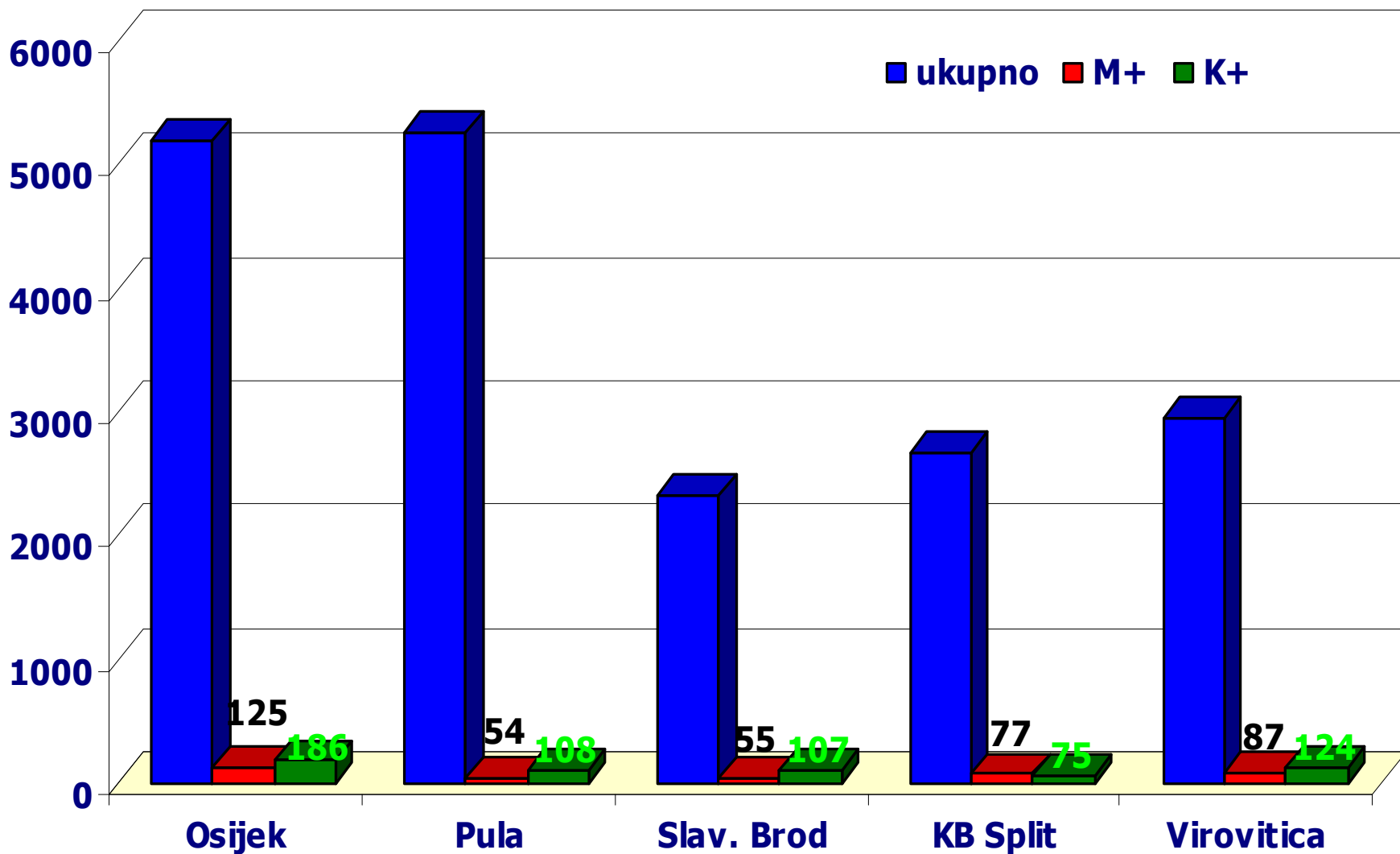
Kultivacija



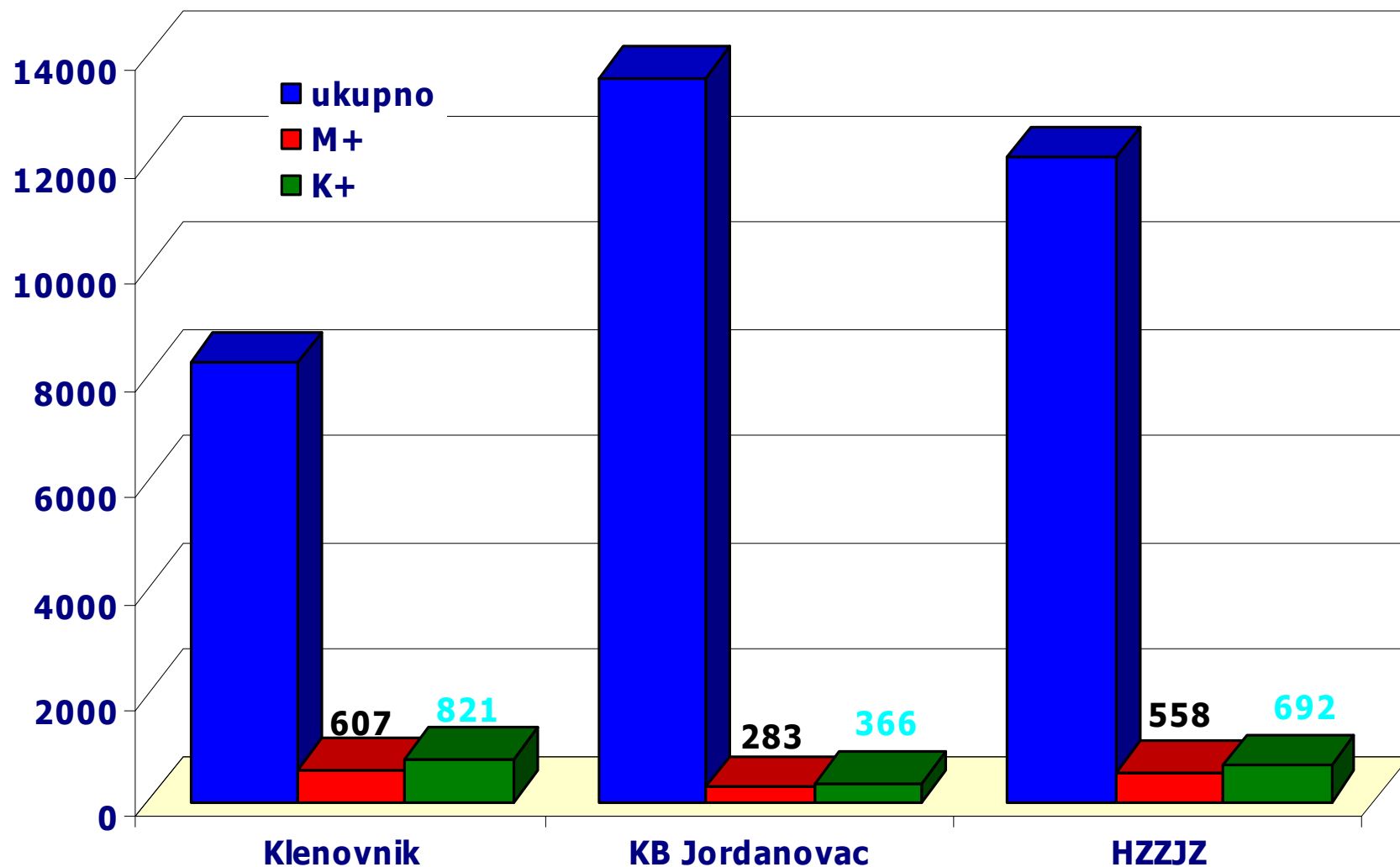
Bakteriološka dijagnostika tuberkuloze u Hrvatskoj



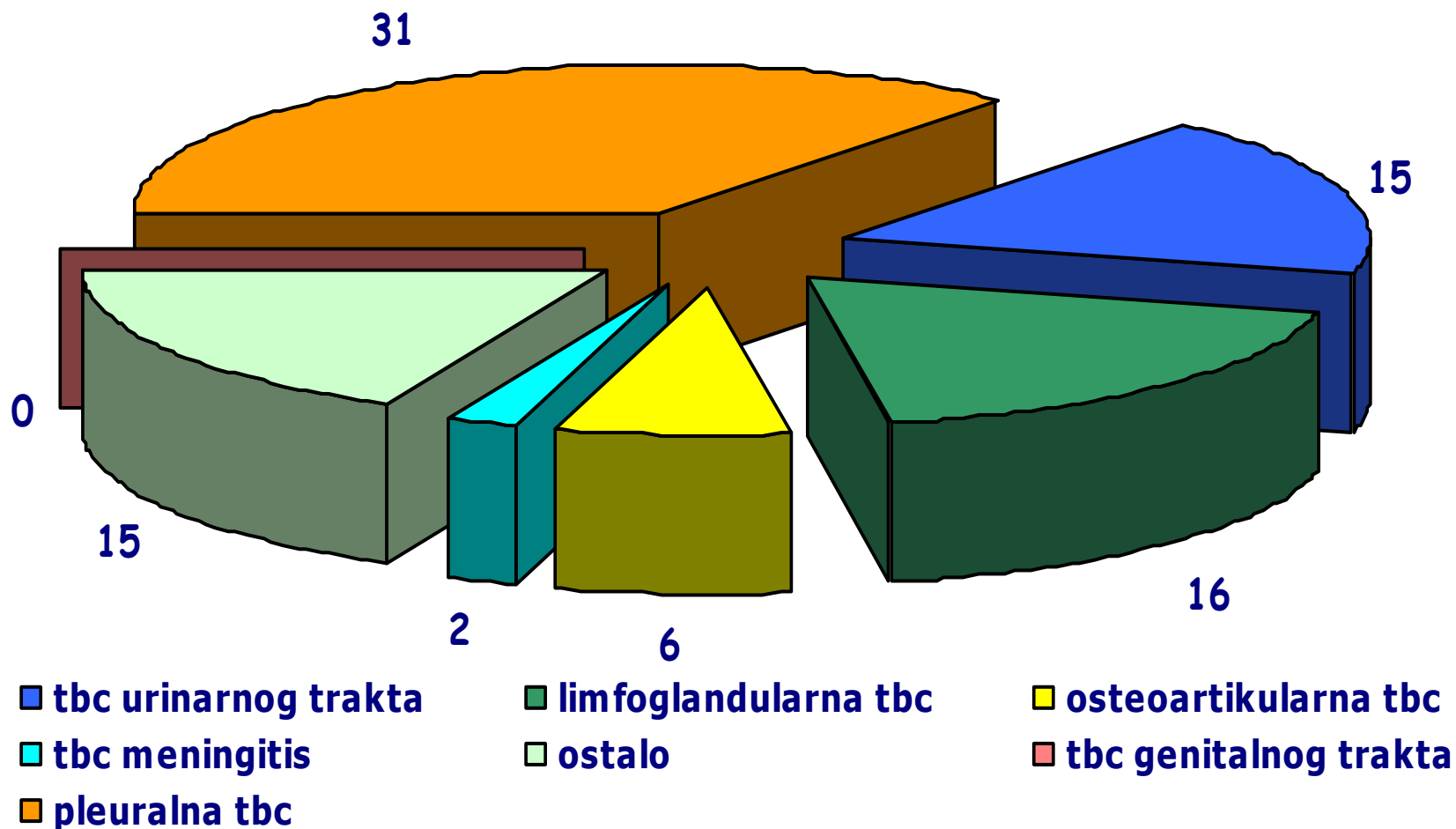
Bakteriološka dijagnostika tuberkuloze u Hrvatskoj



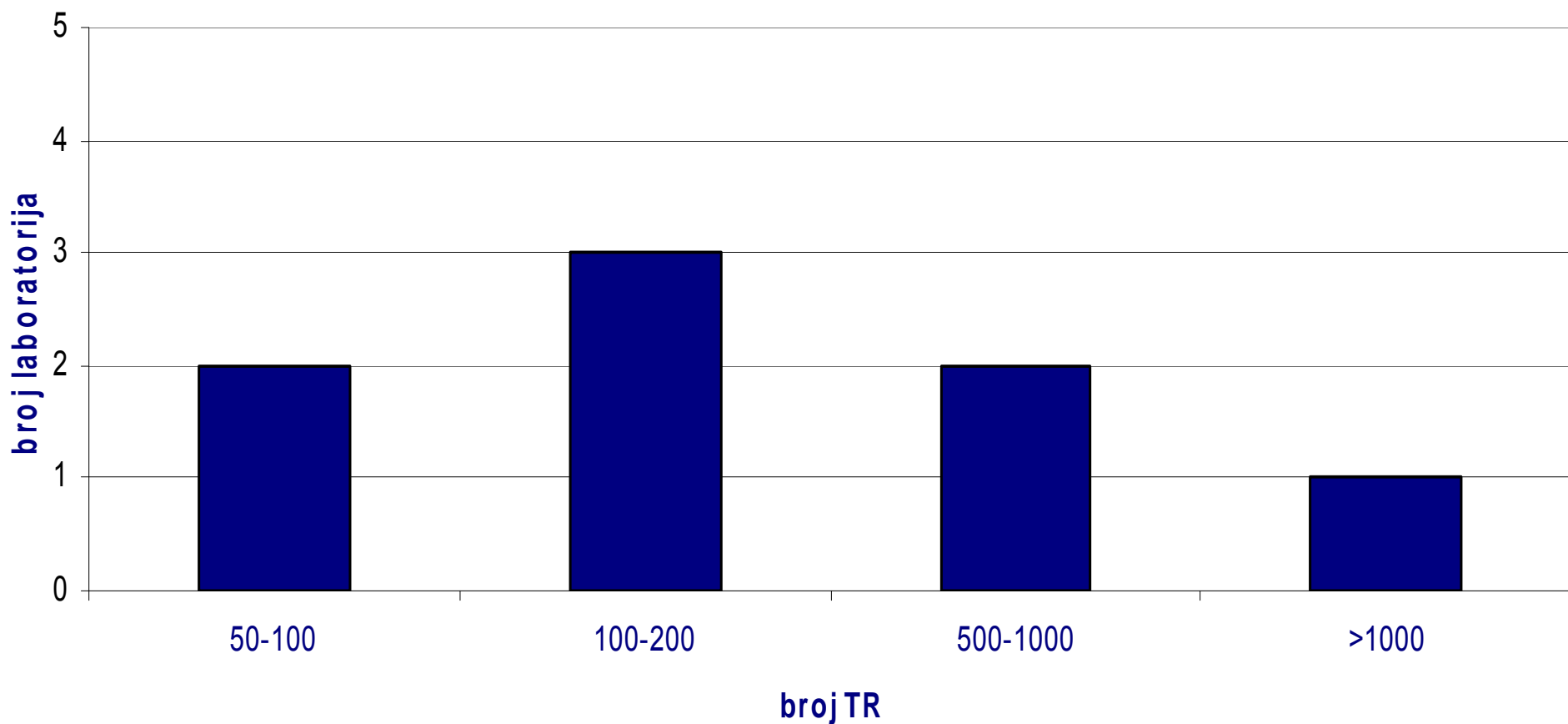
Bakteriološka dijagnostika tuberkuloze u Hrvatskoj



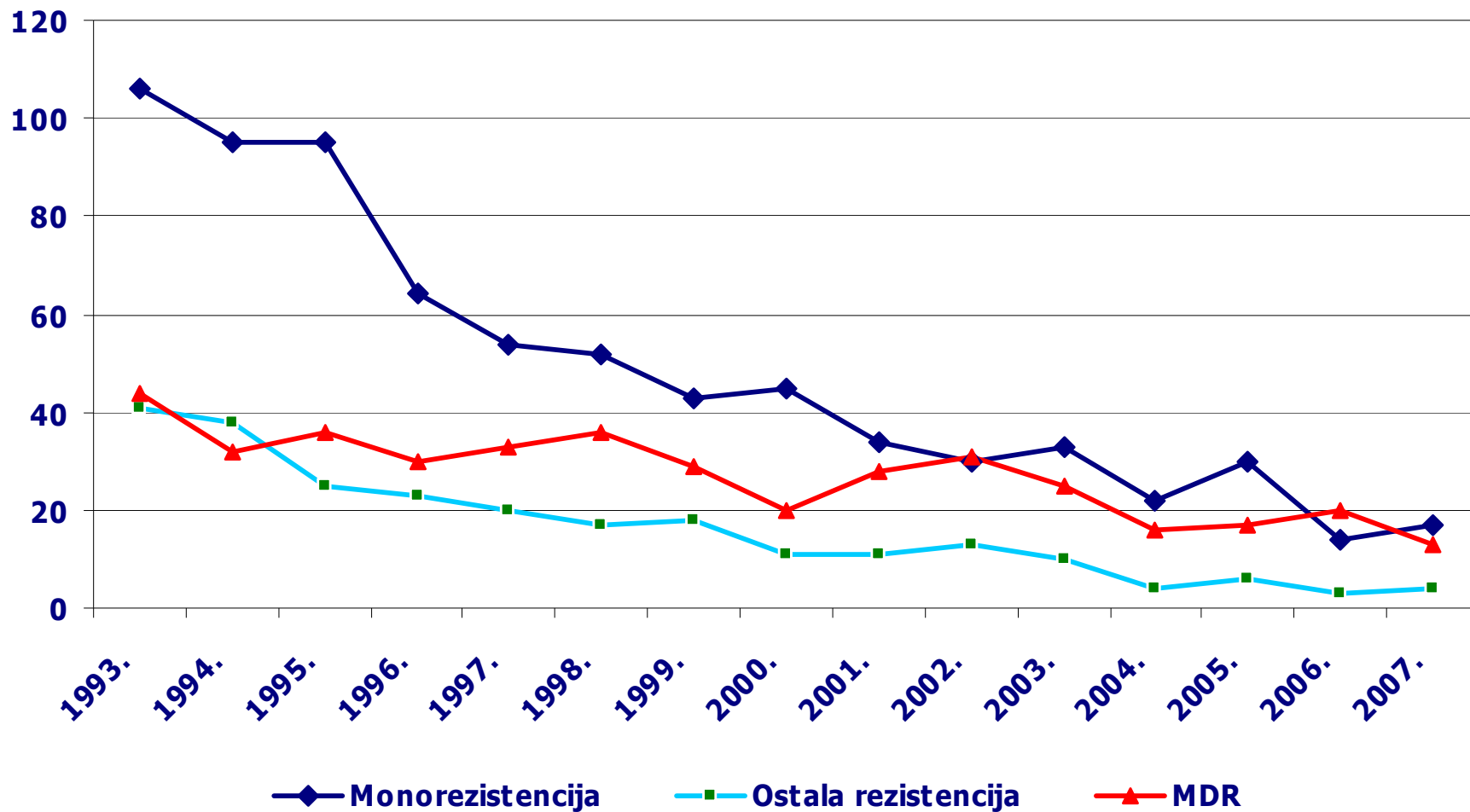
Izvanplućna tuberkuloza u Hrvatskoj, 2007. godina



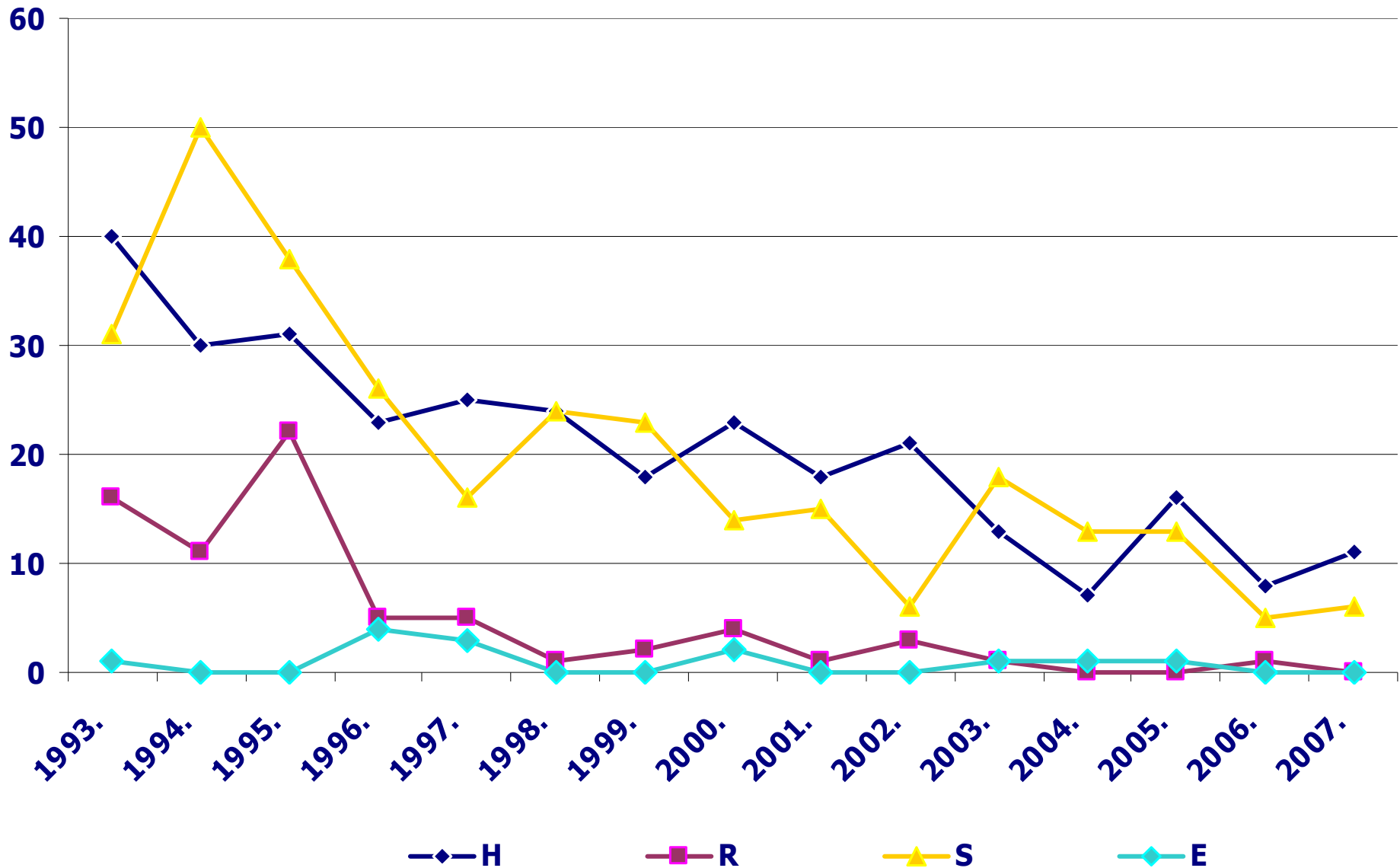
Broj testova osjetljivosti po laboratorijima, 2007. g.



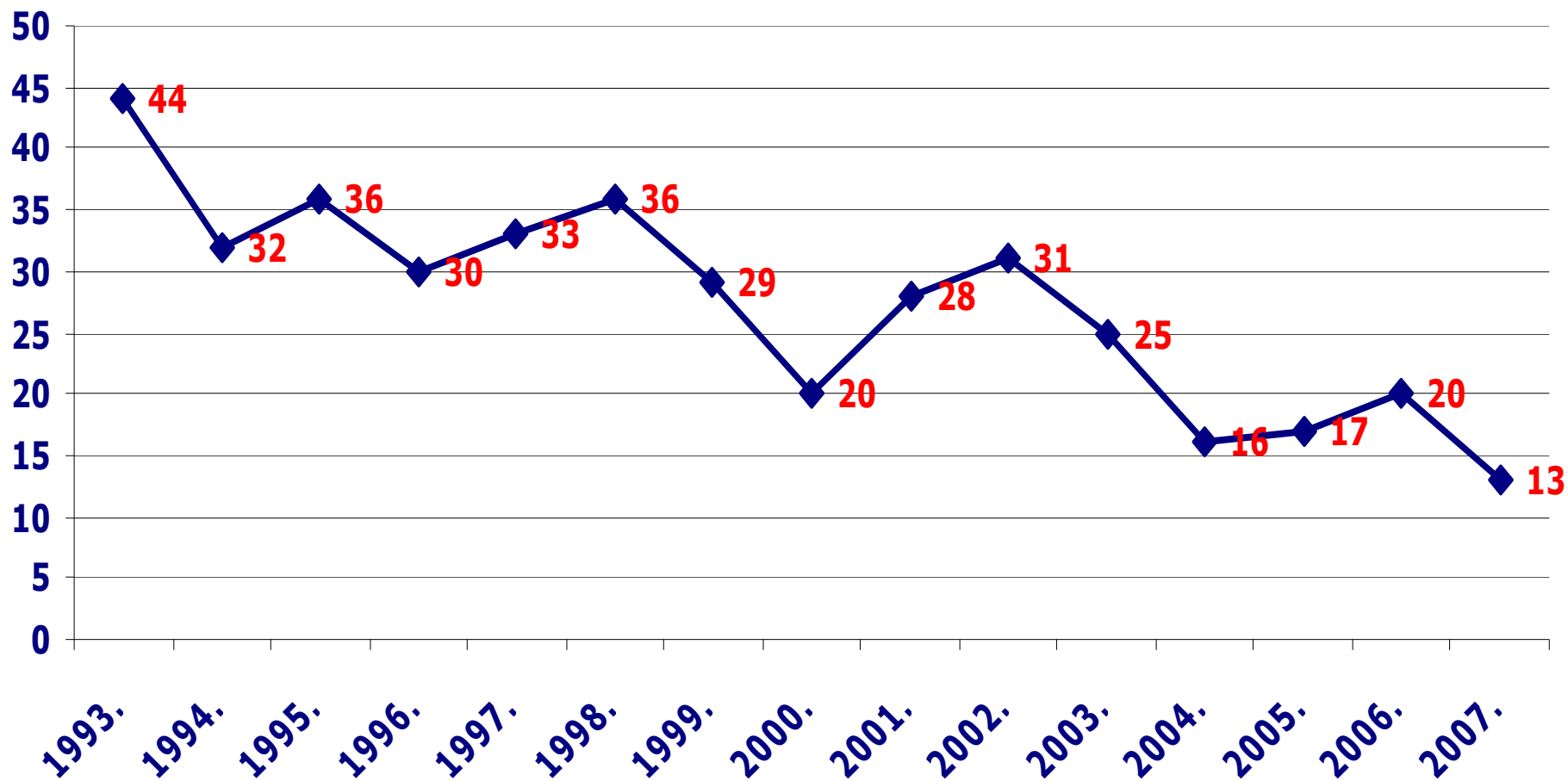
Trend rezistencije na antituberkulotike, 1993.-2007.



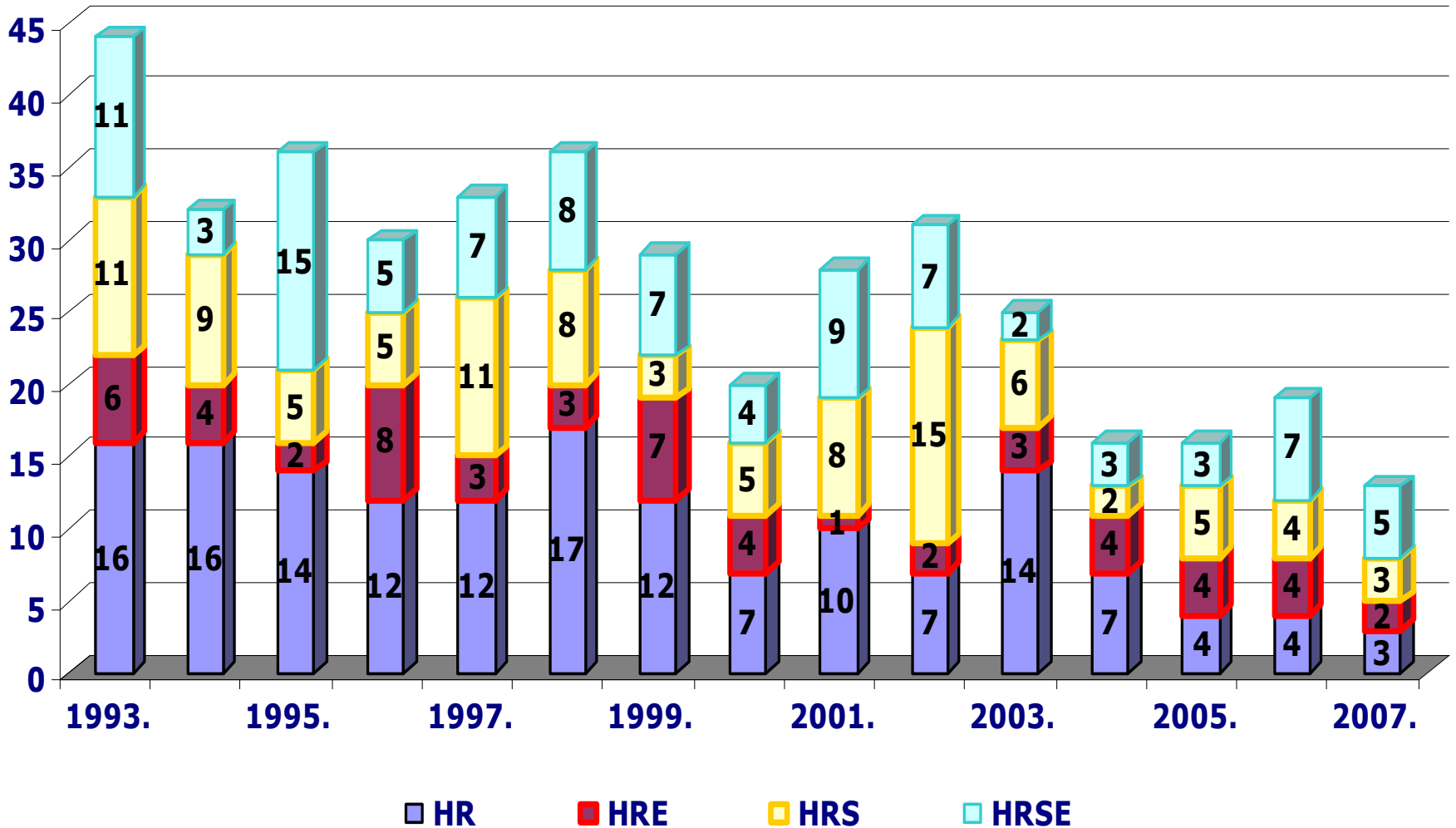
Monorezistencija – trend



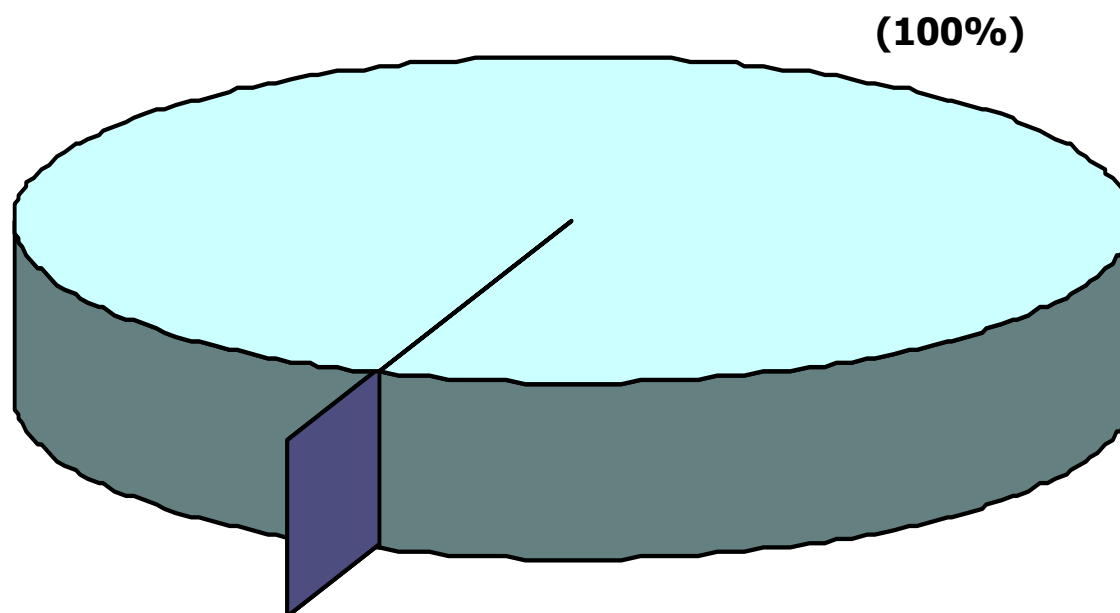
MDR u Hrvatskoj



MDR



Oblici rezistentne tuberkuloze



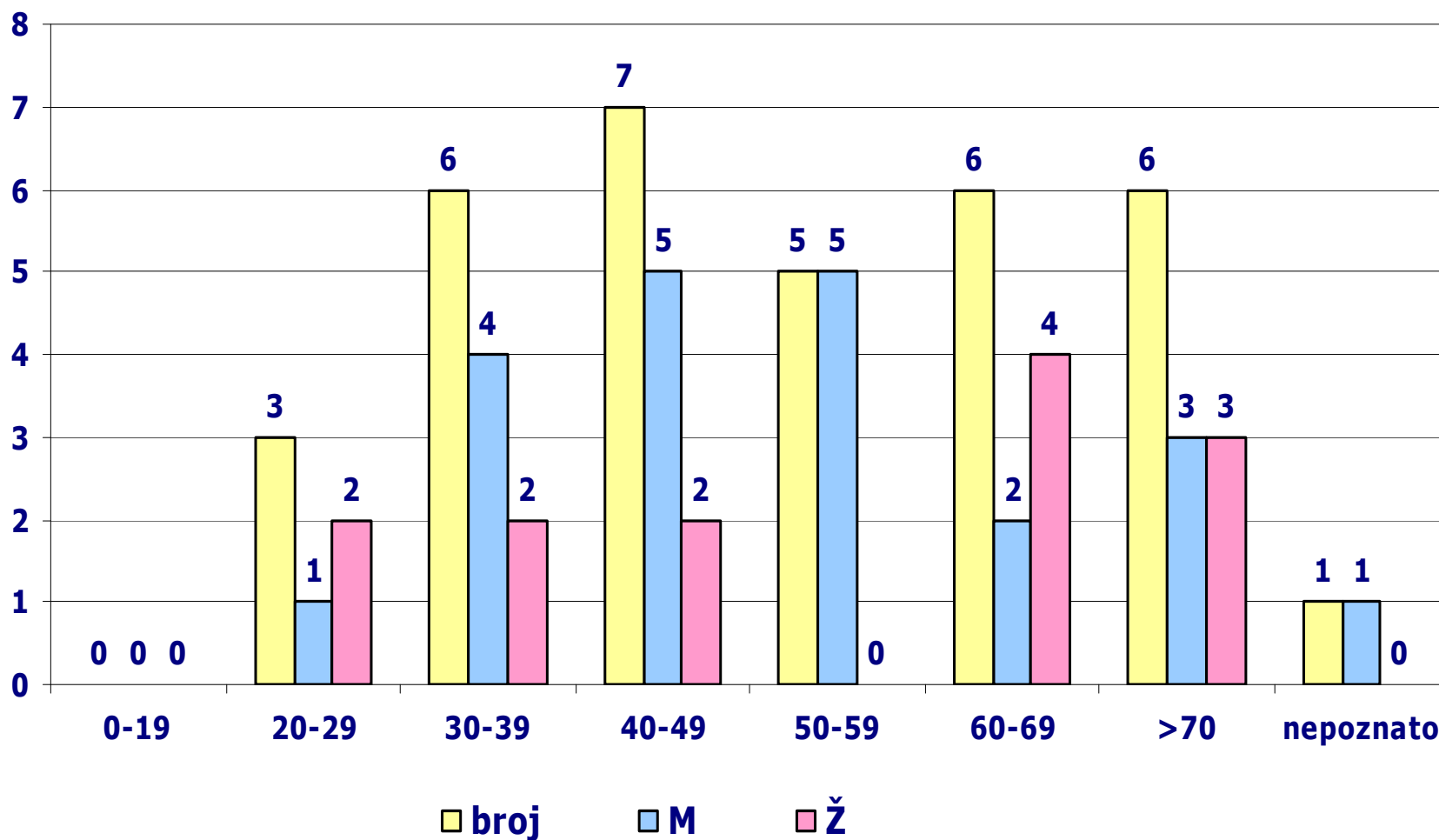
■ tbc urinarog trakta

■ tbc pleure

■ I-g tbc

■ tbc pluća

Rezistentni BK+ bolesnici u 2007. godini



Rezultati upitnika:

1. Obrada uzoraka dnevno 13/15 da
2. Javljanje pozitivnih mikroskopa 13/15 unutar 24h
3. Javljanje pozitivne kulture 9/14 unutar 14 dana
4. Tekuće podloge 12/15 da
5. Tekuće podloge – svi uzorci 7/15 da
6. Tekuće podloge - vrste uzoraka 1 lab. svi zaprimljeni 1. uzorci,
3 lab. svi uzorci osim sp. i
7. Očitavanje tekućih podloga 10/12^{aspirata} ručno
8. Ručno očitavanje 5/12 dnevno
3/12 2xtjedno
3/12 tjedno

Rod *Mycobacterium* (>135 vrsta)

- *M. tuberculosis* complex
- *M. leprae*
- Netuberkulozne mikobakterije (NTM)

NTM - izvor infekcije

- ❑ kućna prašina
- ❑ zemlja
- ❑ voda i vodeni aerosol
- ❑ ptice (*M. avium*, *M. xenopi*)
- ❑ domaće životinje (*M. intracellularae*)
- ❑ dijelovi cigareta — duhan, filter, papir

Hipoteza rasta prevalencije NTM:

- ❑ češća uporaba tuševa nego kupanja
- ❑ starenje populacije

OSOBITOSTI NTM (1)

- ne prijavljuju se epidemiološkoj službi
- prijenos s čovjeka na čovjeka je rijedak
- perzistiraju u protozoima i amebama
- različita geografska rasprostranjenost
- multirezistencija
- > od 3 nove vrste na godinu
- > 60% su opisane u posljednjih 15 godina

OSOBITOSTI (2) –

uzročnici

Različita patogenost pojedinih vrsta NTM

M. tuberculosis complex

- (100%)
- *M. kansasii*
 - (50%)
- *MAC / M. xenopi / M. fortuitum / chelonae / abscessus*
 - (20-25%)
- *M. gordonae*
 - (0?)

Mikobakterioze

- plućne infekcije
- limfoglandularne infekcije
- kožne infekcije
- osteo-artikularne infekcije
- diseminirane infekcije
- sepsa

Epidemiologija mikobakterioza

- Industrijske zemlje: 1-2/100 000
- SAD: do 14/100 000
- HR: 0.07-0.5/100 000

Epidemiologija NTM Ontario, 1997.- 2003.

(Marras et al. Thorax 2007)

- prevalencija 4 najčešće NTM:
 - 1997. – 9.1/100 000
 - 2003. – 14.1/100 000 ($p < 0.0001$)
- godišnji prosjek 8.4%
- učestalost otkrivanja NTM veća nego TB

Mikobakterije – Mayo klinika, 11/2005. – 03/2006.
n=1379

- *Mycobacterium avium/intracellulare* 42%
- *M. gordonae* 19%
- *M. chelonae/M. abscessus* 12%
- *M. tuberculosis* 10%

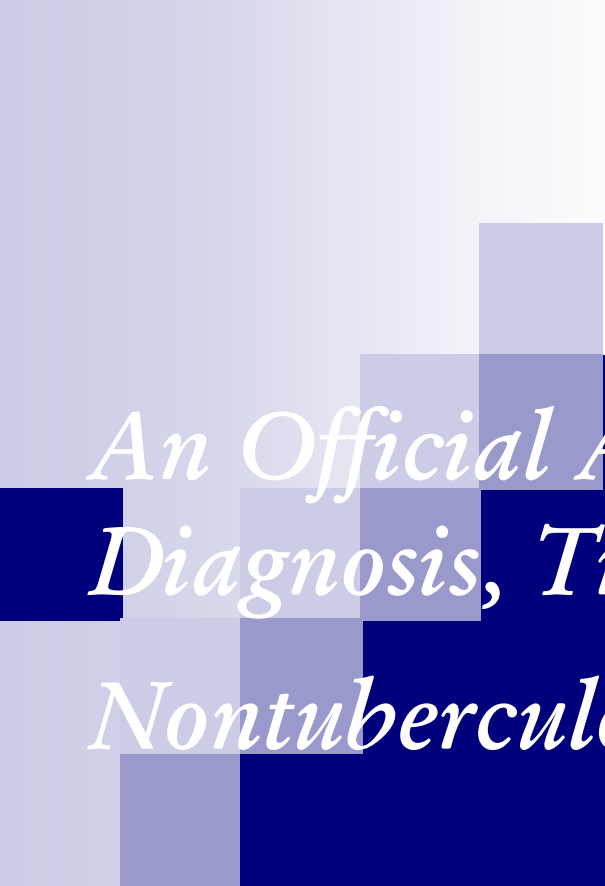
Netuberkulozne mikobakterije

- klinički sindromi

- **plućne infekcije** (94% u 3 klinička oblika: fibrodnodularni, fibronodularni s bronhijektazijama, hipersenzitivni pneumonitis)
- limfoglandularne infekcije
- kožne infekcije
- osteo-artikularne infekcije
- diseminirane infekcije te sepsa

Opći kriteriji za dijagnozu mikobakterioza

- o izolacija NTM
- o klinička slika
- o rtg nalaz
- o odsustvo drugog patogenog
uzročnika



*An Official ATS/DSA Statement:
Diagnosis, Treatment and Prevention of
Nontuberculous Mycobacterial Diseases*

American Journal of Respiratory and Critical Care
Medicine 2007; 175: 367-416

MIKROBIOLOŠKI KRITERIJI MIKOBAKTERIOZA

PREMA AMERIČKOM TORAKALNOM DRUŠTVU, 1997

A. 3 SPUTUMA/ASP. BRONHA

1. 3 M 0 / 3K +
2. 1 M + / 2K +

B. 1 ASPIRAT BRONHA

1. 1K + / 1 M + s velikim brojem bacila

C. NEMA SPUTUMA/ASP. BRONHA

1. K + iz transbronh. aspirata ili biopsije pluća
2. 1 K + u malom broju bacila / histološki nalaz granulomatozne upale

MIKROBIOLOŠKI KRITERIJI

PREMA AMERIČKOM TORAKALNOM DRUŠTVU, 2007

- 3 sputuma
- 2 pozitivne kulture
- 1 bronhalni aspirat ili lavat
- 1 pozitivna kultura, bez obzira na mikroskopski nalaz
- uzorak tkiva
- podudarnost histopatološkog nalaza i (+) kulture
- podudarnost histopatološkog nalaza i (+) sputuma ili bronhalnog lavata u kulturi



Mikrobiološki kriteriji za plućne mikobakterioze

1 izolat NTM iz bronhalnog lavata ili 2 pozitivna
sputuma

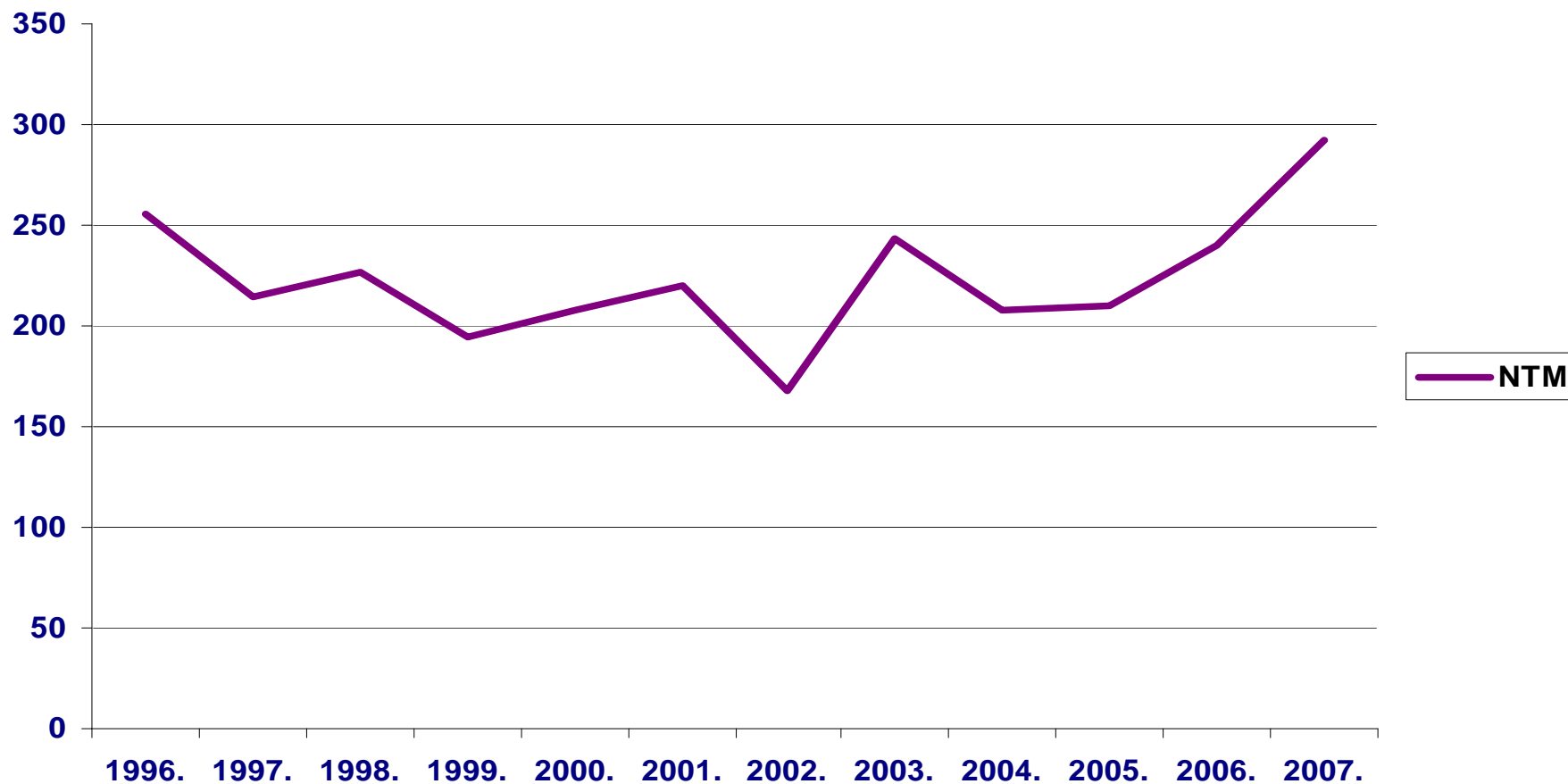


**Liječiti ili ne liječiti
mikobakterioze?**

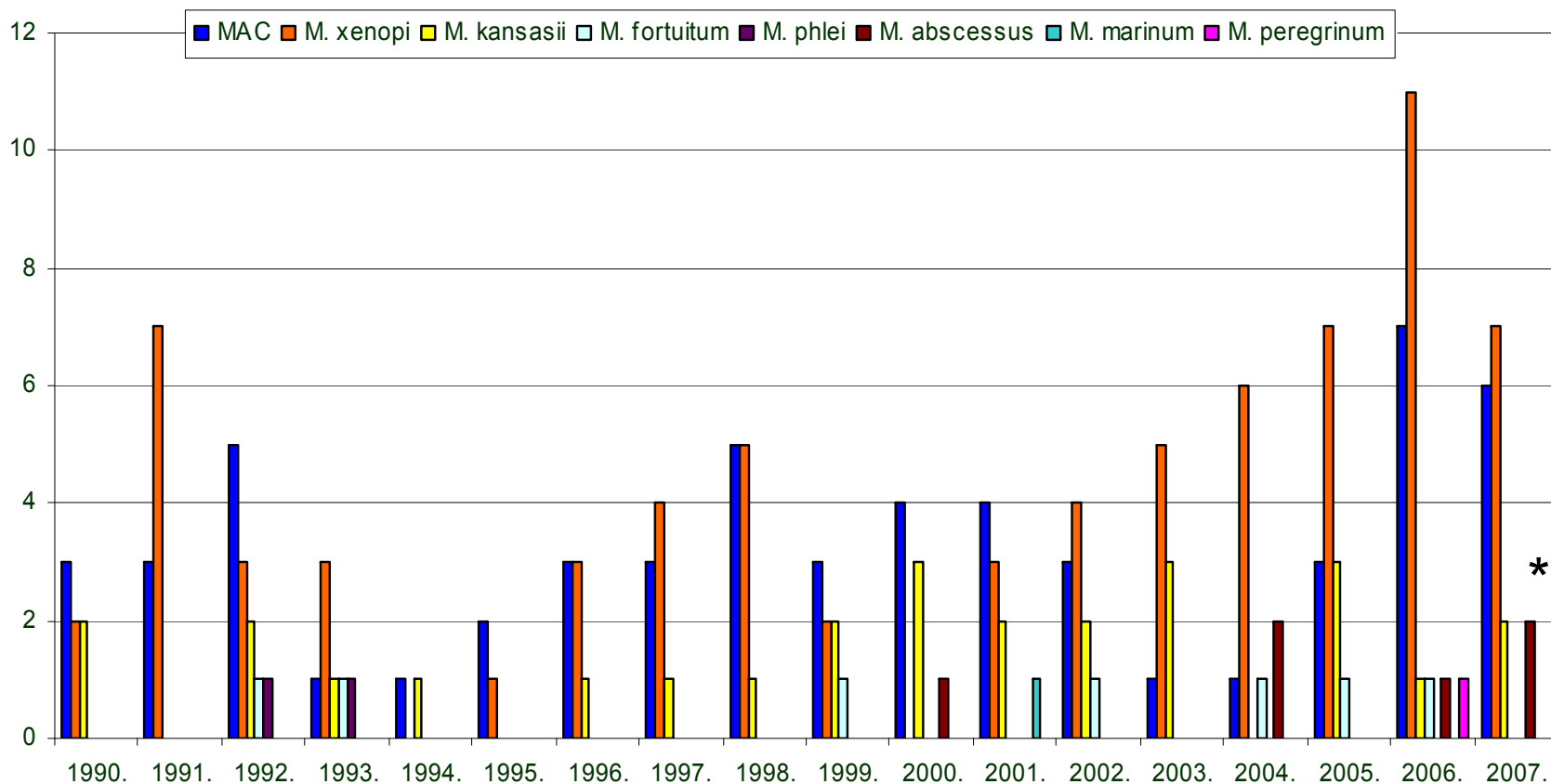
NTM za koje ne postoji korelacija između in vitro testa osjetljivosti i in vivo odgovora

- *M. xenopi*
- *M. abscessus*
- *M. scrofulaceum*
- *M. malmoense*
- *M. simiae*
- *M. immunogenum*
- Etc.

Izolati NTM u Hrvatskoj, 1996. – 2007.

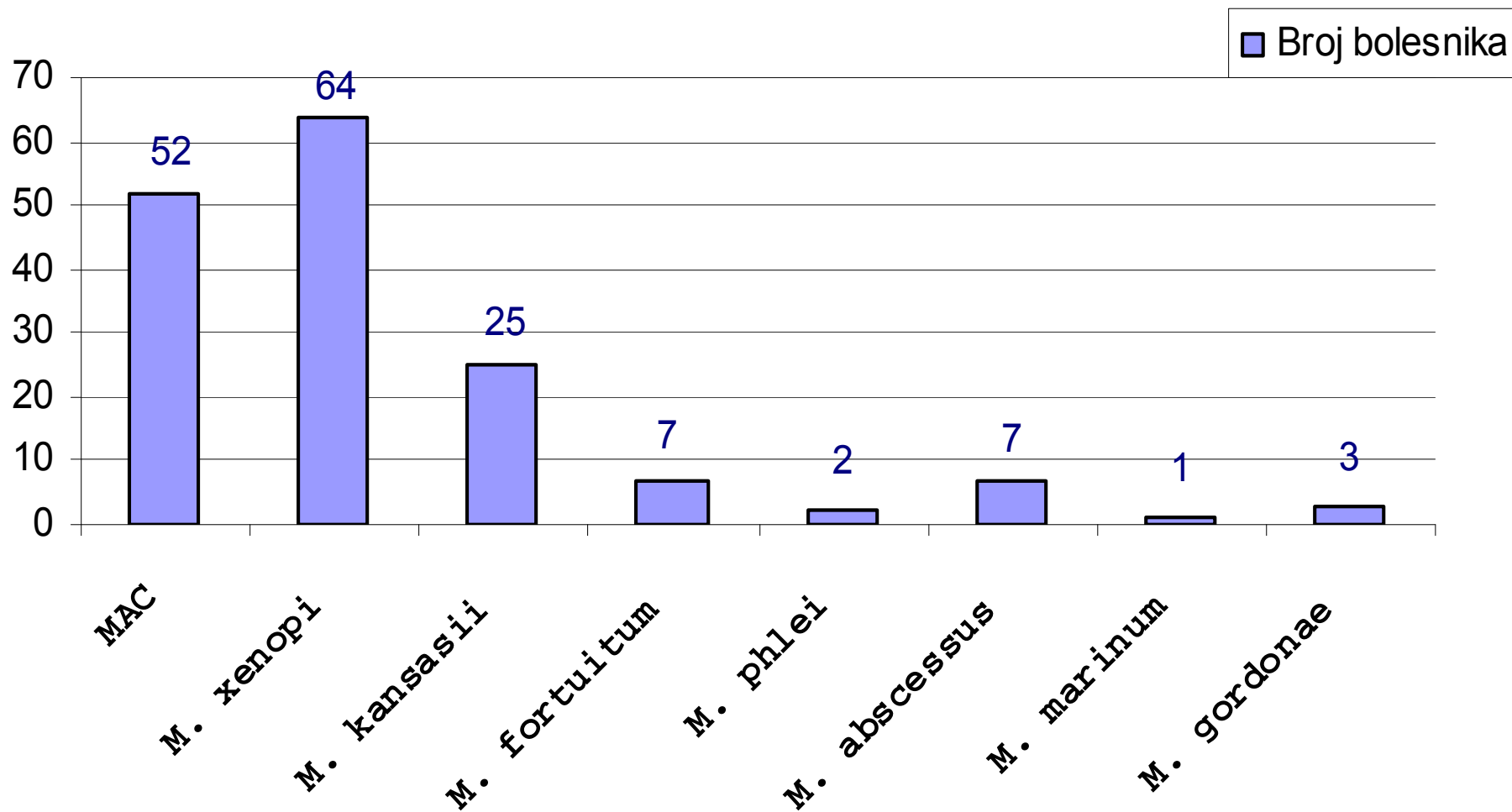


Mikobakterioze, 1990.-2007.



* U 2007. 3 bolesnika s *M. gordonae* !


Bolesnici s mikobakteriozom u Hrvatskoj, 1990.-2007.



OTVORENO PITANJE

Kako naći ravnotežu između „poddijagnosticiranosti“ u progresivnih mikobakterioza i „predijagnosticiranosti“ uz primjenu toksičnih lijekova kod neinficiranih bolesnika?

Odgovor je u timskom pristupu bolesniku !



Pozicija IGRA testova u
dijagnostičkom algoritmu TB?!

Patogeneza tuberkuloze

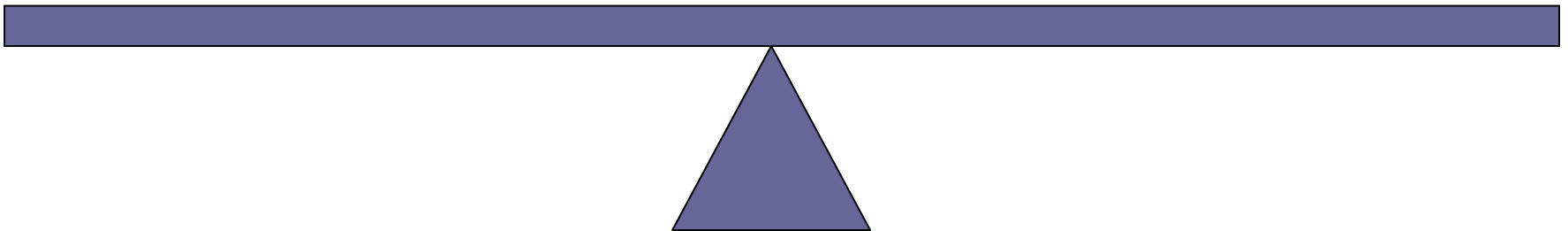


Infekcija

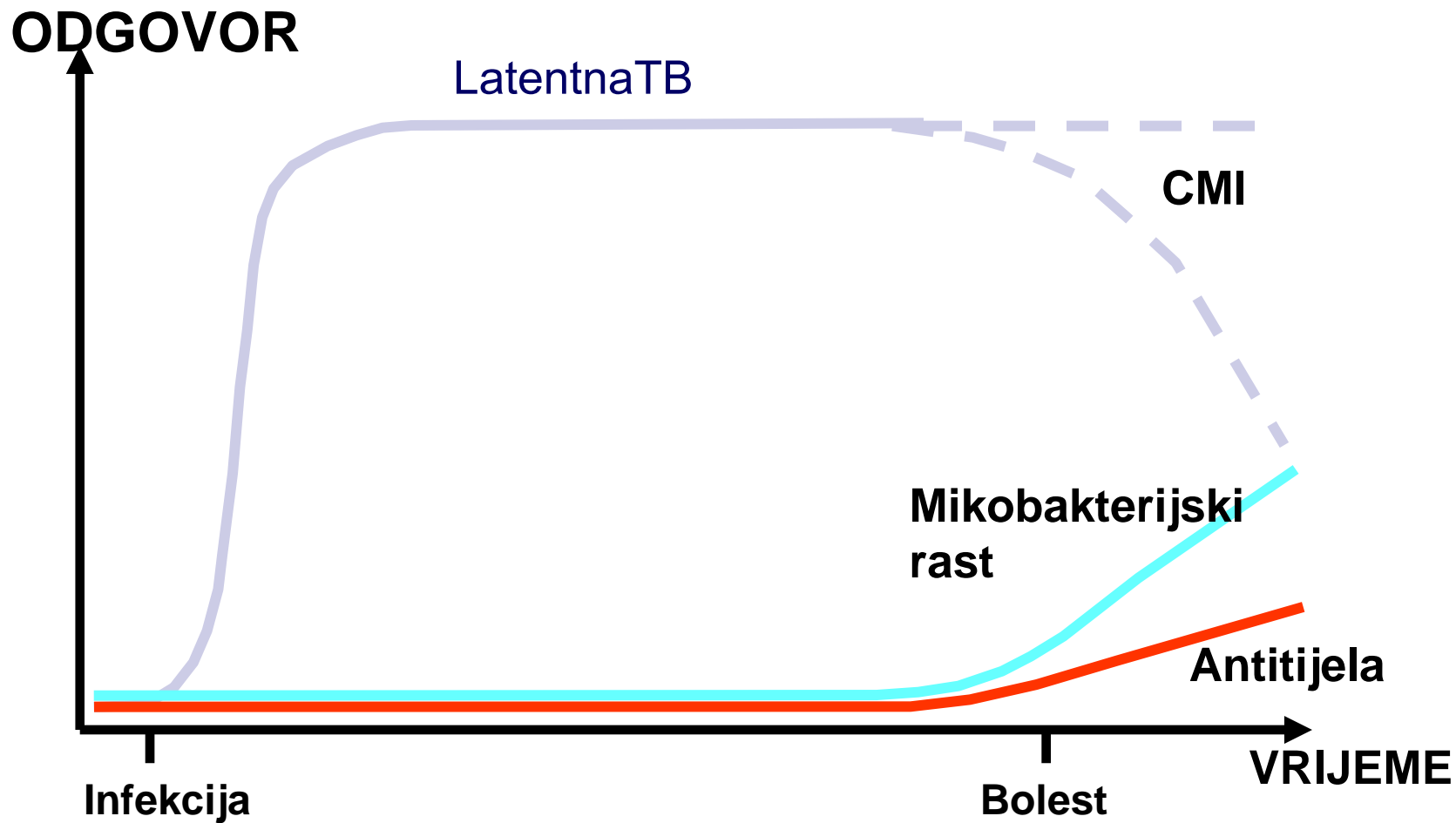
-



Imunitet



Imuni odgovor na TB infekciju i bolest



T-cell responses to the *Mycobacterium tuberculosis*-specific antigens in active tuberculosis patients at the beginning, during, and after antituberculosis treatment

Dominguez J, et al.

T.....

QuantIFERON-TB Gold In-tube, T-SPOT.TB, and TST results in the different groups of TB patients

Groups of patients	Diagnostic tests							
	T-SPOT.TB			QFN-G-IT			TST	
	Positive (%)	Negative (%)	Indet ^a (%)	Positive (%)	Negative (%)	Indet (%)	Positive (%)	Negative (%)
<i>Group 1</i>								
Pulmonary TB confirmed microbiologically (<i>n</i> = 79)	60 (75.9)	16 (20.3)	3 (3.8)	46 (58.2)	31 (39.3)	2 (2.5)	55/58 (94.8)	3/58 (5.2)
At the beginning of treatment (<i>n</i> = 36)	30 (83.3)	4 (11.1)	2 (5.6)	25 (69.4)	10 (27.8)	1 (2.8)	34 (94.4)	2 (5.6)
Smear-positive (<i>n</i> = 19)	14 (73.7)	3 (15.8)	2 (10.5)	14 (73.7)	4 (21.1)	1 (5.2)	17 (89.5)	2 (10.5)
Smear-negative (<i>n</i> = 17)	16 (94.1)	1 (5.9)	0 (0)	11 (64.7)	6 (35.3)	0 (0)	17 (100)	0 (0)
During the treatment (<i>n</i> = 43)	30 (69.8)	12 (27.9)	1 (2.3)	21 (48.8)	21 (48.8)	1 (2.4)	21/22 (95.5)	1/22 (4.5)
<i>Group 2</i>								
Extrapulmonary TB confirmed microbiologically (<i>n</i> = 14)	7 (50)	7 (50)	0 (0)	7 (50)	7 (50)	0 (0)	2/2 (100)	0 (0)
At the beginning of treatment (<i>n</i> = 2)	2 (100)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	2 (100)	0 (0)
During the treatment (<i>n</i> = 12)	5 (41.7)	7 (58.3)	0 (0)	5 (41.7)	7 (58.3)	0 (0)	–	–
<i>Group 3</i>								
Pulmonary TB without microbiological confirmation (<i>n</i> = 10)	8 (80)	2 (20)	0 (0)	7 (70)	3 (30)	0 (0)	10 (100)	0 (0)
At the beginning of treatment (<i>n</i> = 5)	4 (80)	1 (20)	0 (0)	5 (100)	0 (0)	0 (0)	5 (100)	0 (0)
During the treatment (<i>n</i> = 5)	4 (80)	1 (20)	0 (0)	2 (40)	3 (60)	0 (0)	–	–
Extrapulmonary TB not confirmed microbiologically	6 (100)	0 (0)	0 (0)	4 (66.7)	2 (33.3)	0 (0)	4/4 (100)	0 (0)
During treatment (<i>n</i> = 6)								
<i>Group 4</i>								
Healed pulmonary TB after curative treatment (<i>n</i> = 5)	5 (83.3)	1 (16.7)	0 (0)	5 (83.3)	1 (16.7)	0 (0)	5 (83.3)	1 (16.7)

^a Indeterminate result.

TB or not TB?

