



WETENSCHAPPELIJK INSTITUUT  
VOLKSGEZONDHEID  
INSTITUT SCIENTIFIQUE  
DE SANTÉ PUBLIQUE

# TWENTY YEARS OF ANTIBIOTIC RESISTANCE IN NON- INVASIVE *STREPTOCOCCUS PNEUMONIAE* ISOLATED IN BELGIUM (1995 – 2014).

**Vanhoof, R. MD, PhD**  
**Dep. Transmissible & Infectious Diseases**  
**Unit of Antibiotic Research**

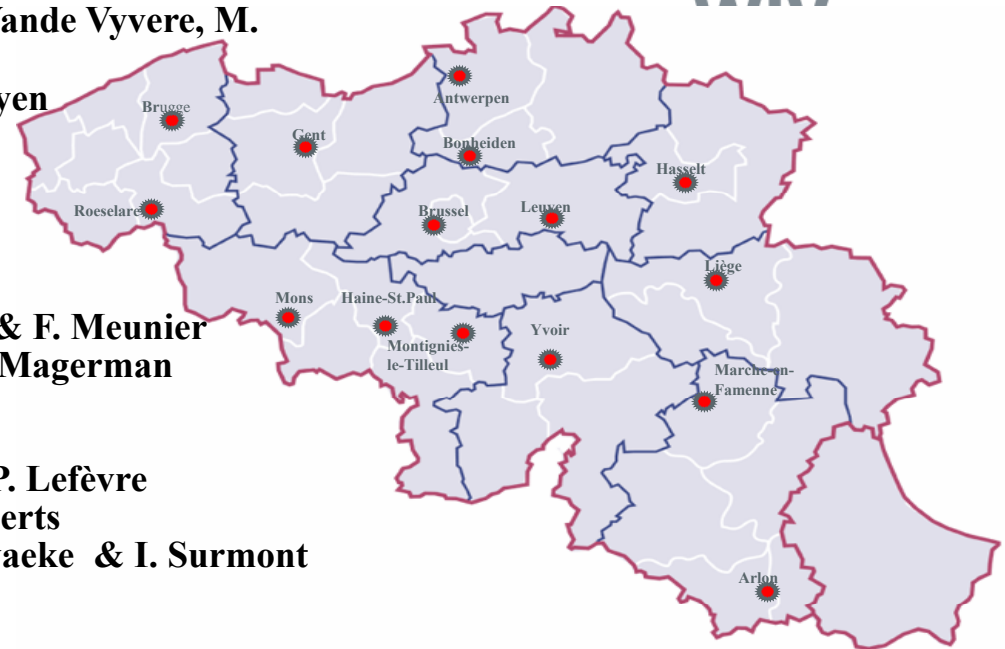
21/05/2015

Brussels, IPH Seminar

✓ Collection of isolates from 1995 to 2014 (n = 5.442)

✓ 15 Participating centres:

- Antwerpen, AZ Stuyvenberg - K. Camps & Vande Vyvere, M.
- Arlon, Cl. St.Joseph - P. & J-B Goffinet.
- Bonheiden, ImeldaZH - J. Frans & R. VanNoyen
- Bousu, CHR Warquignies – I. Philippart
- Brugge, AZ St.Jan – E. Nulens, B.Gordts & H. Van Landuyt
- Brussels, Cebiodi – B. Mulongo & O.Fagnart
- Gent, AZ J.Palfijn – L.Ide & L. VanNimmen
- Haine-St-Paul, Hôp Jolimont – Mukuku Sifa & F. Meunier
- Hasselt, VirgaJesse ZH – R. Cartuyvels & K. Magerman
- Liège, Hôp Citadelle – M. Carpentier
- Leuven, MCH – M. Lontie & B. Van Meensel
- Marche-en-Famenne, Hôp Princesse Paola – P. Lefèvre
- Montigny-le-Tilleul, CHR A.Vésale – D. Govaerts
- Roeselare, H.Haert ZH – E. De Laere, S. Vervaeke & I. Surmont
- Yvoir, CU Mont Godinne – Y. Glupczynski

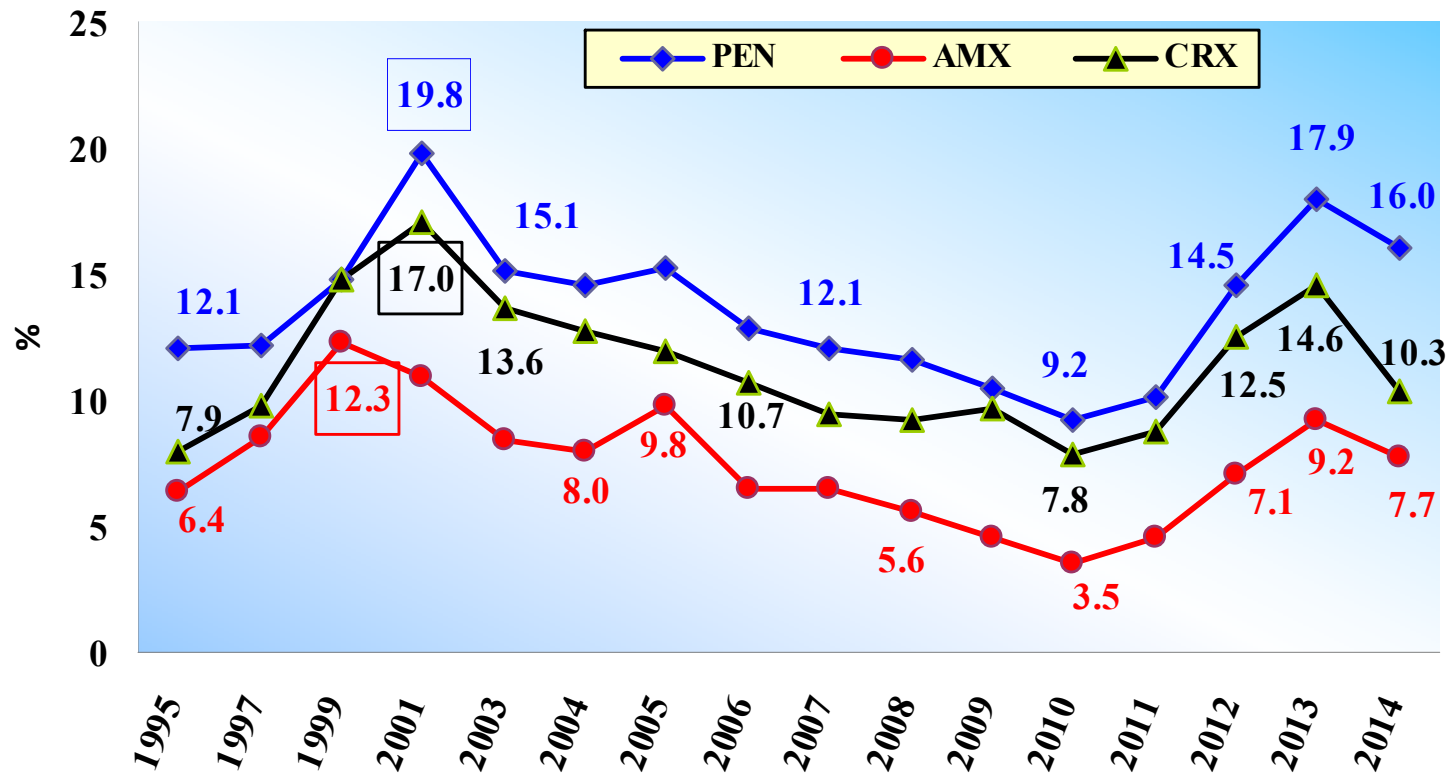


✓ MIC by Microdilution (**EUCAST**) :

- Penicillin (PN)
- Amoxicillin (AM)
- Cefuroxime (CR)
- Ciprofloxacin (CI)
- Levofloxacin (LV)
- Moxifloxacin (MX)
- Erythromycin (ER)
- Telithromycin (TL)
- Tetracycline (TC)

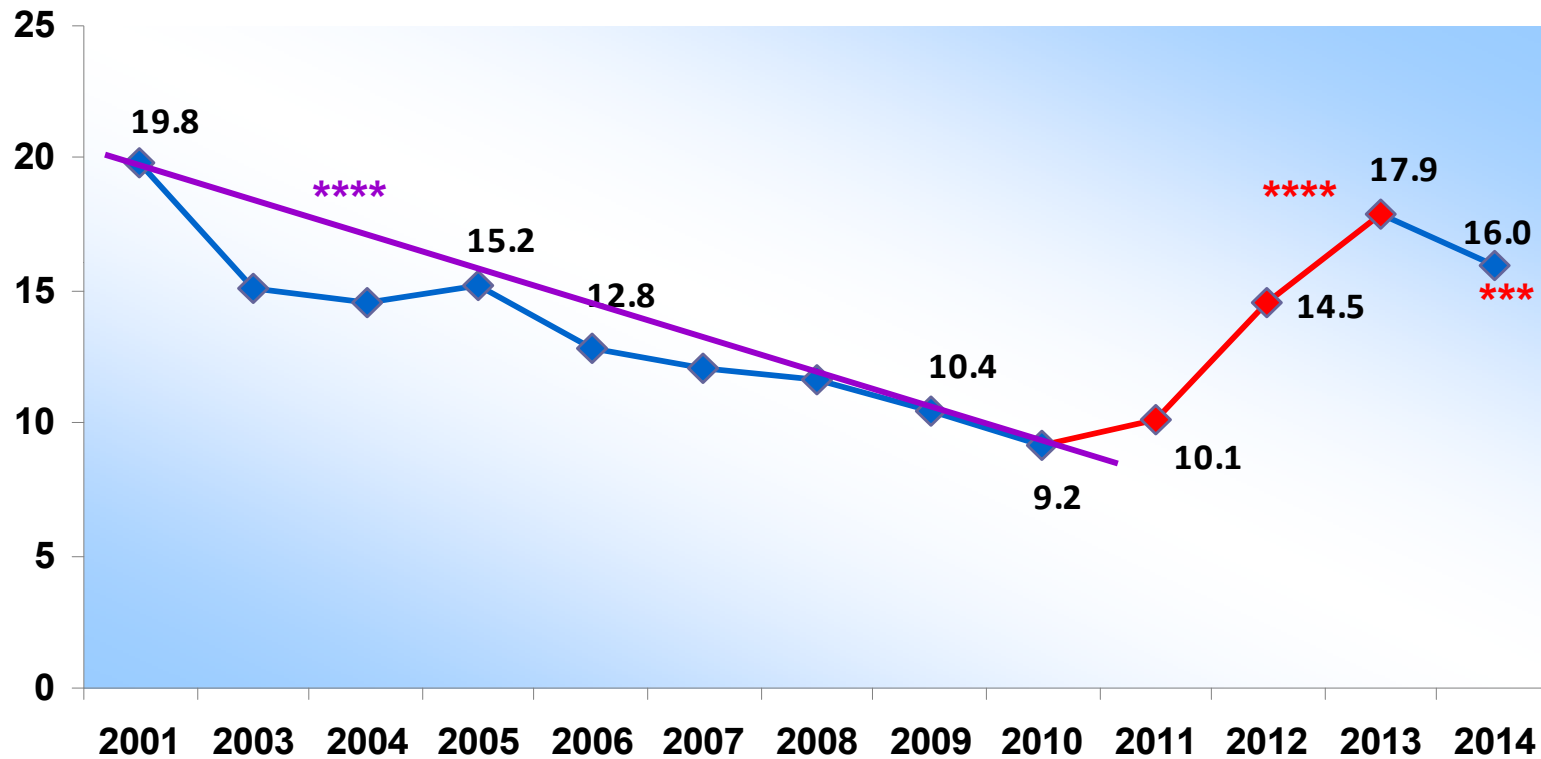
✓ Data on age, origin, sample,  
type of patient (H/A), gender.

# RESISTANCE RATES (%) FOR $\beta$ -LACTAMS



## RESISTANCE RATES FOR $\beta$ -LACTAMS

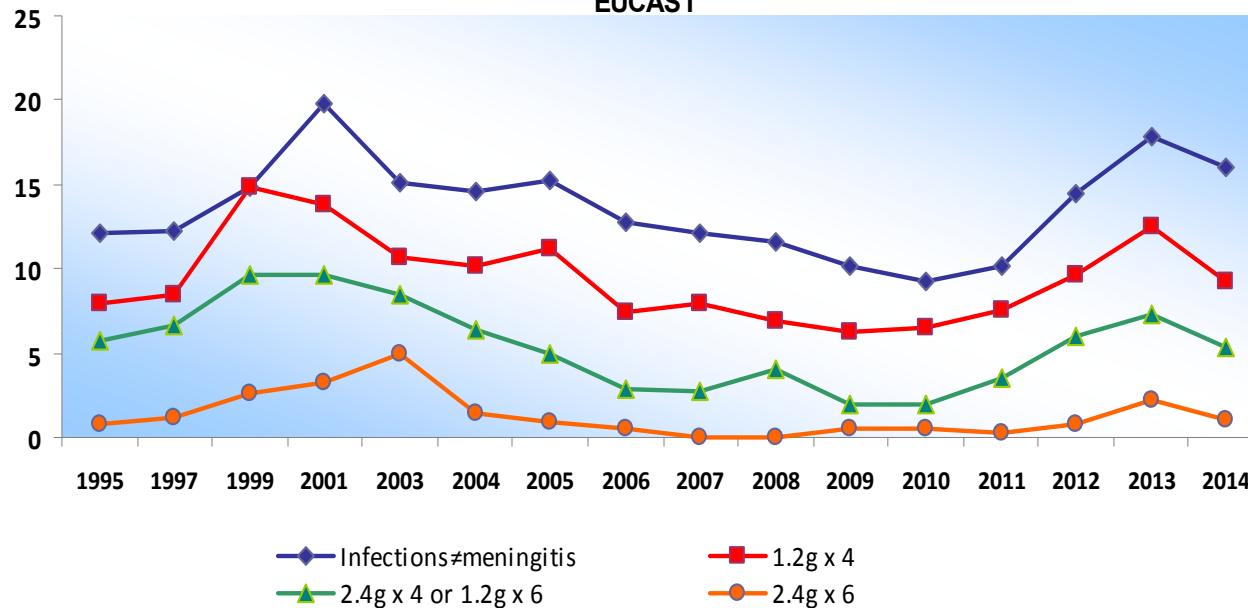
### Evolution of **Penicillin** Non-susceptibility (I+R)



# RESISTANCE RATES FOR $\beta$ -LACTAMS

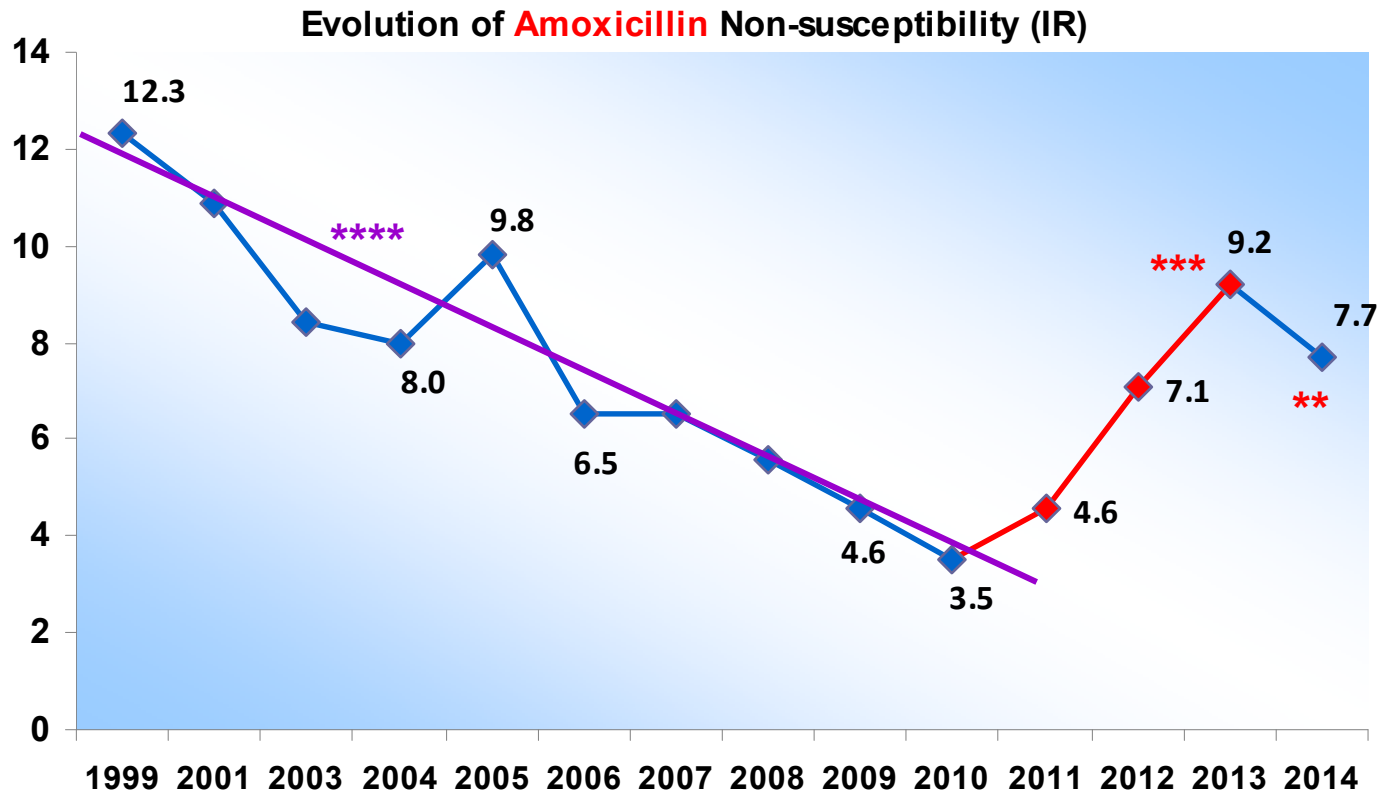


Penicillin Non-susceptibility rates and type of treatment in pneumonia following EUCAST



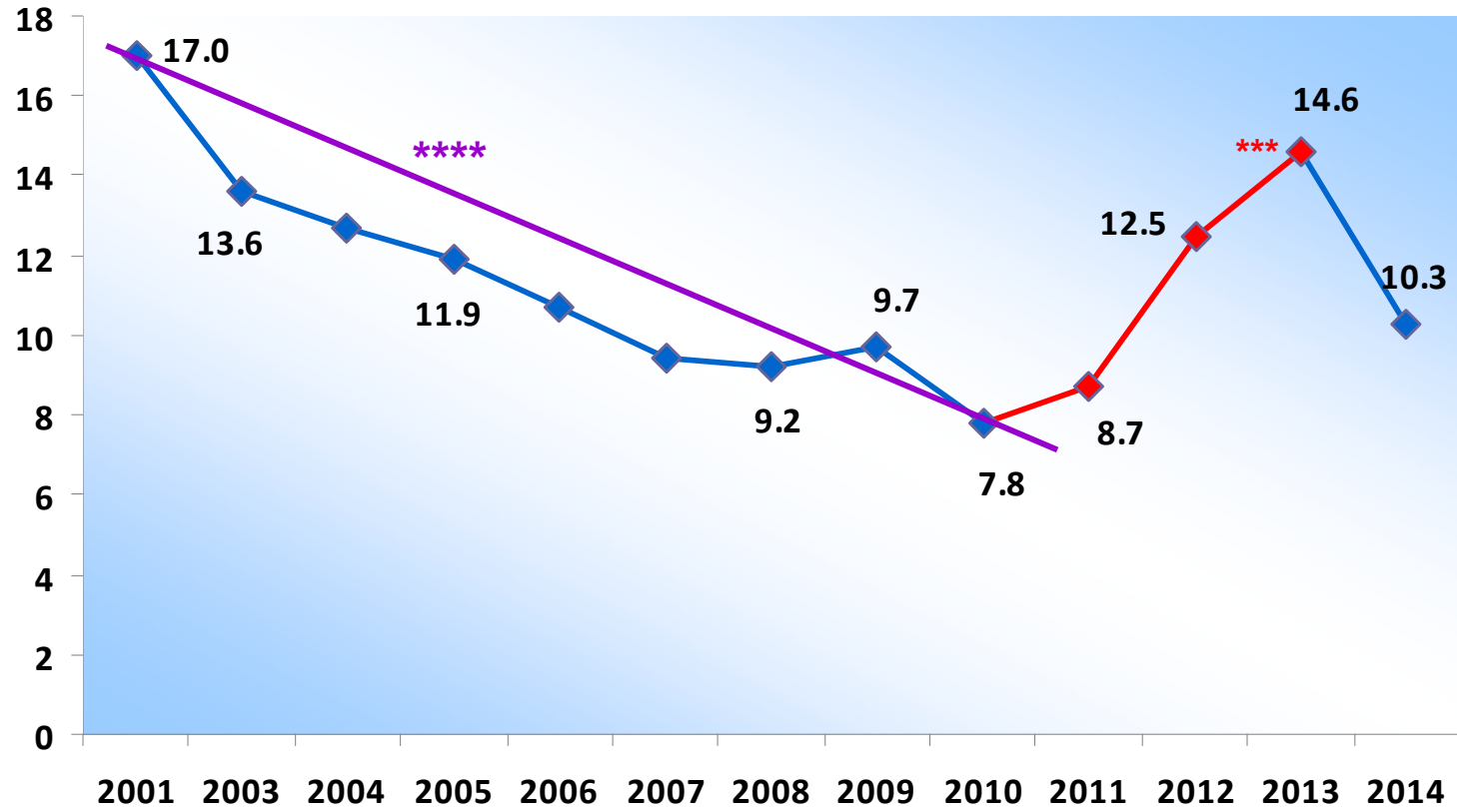
<u>Infection/0 Regimen</u>	<u>Breakpoint</u>	
	S	NS
<u>Infections ≠ meningitis</u>	≤0.06	≥0.12
<u>Pneumonia: 1.2g X 4</u>	≤0.5	≥1
<u>2.4g X 4 or 1.2g X 6</u>	≤1	≥2
<u>2.4g X 6</u>	≤2	≥4

# RESISTANCE RATES FOR $\beta$ -LACTAMS



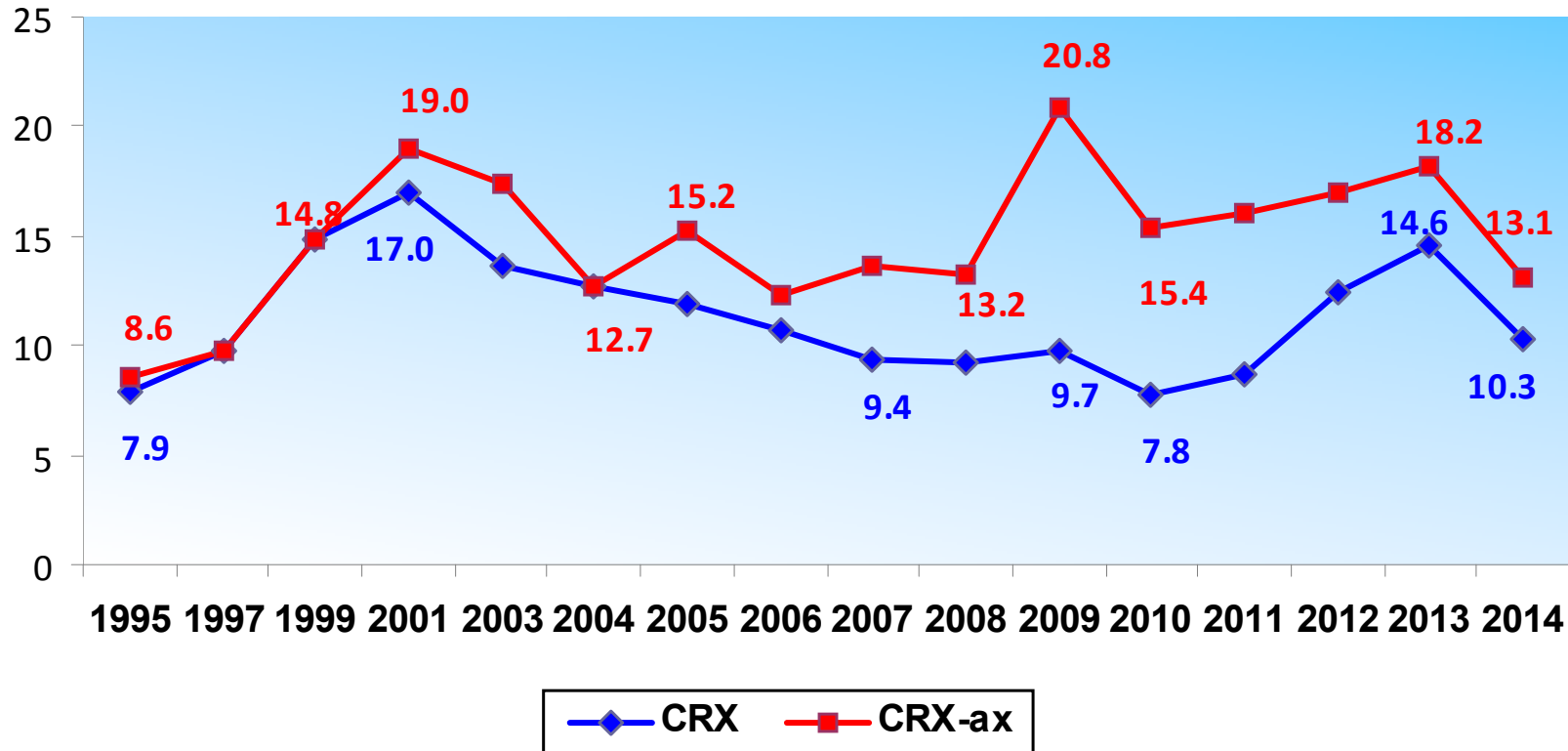
# RESISTANCE RATES FOR $\beta$ -LACTAMS

Evolution of **Cefuroxime** Non-susceptibility (CRX)



## RESISTANCE RATES FOR $\beta$ -LACTAMS

Evolution of non-susceptibility of **CRX** and **CRX-ax** (EUCAST)





# RESISTANCE RATES FOR $\beta$ -LACTAMS



## *S. pneumoniae*: Serotypes

	PCV13	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F
2012	56.9 %					5.9	2.0			9.8		35.3	3.9	
2013	53.0 %		3.0		1.5	1.5			1.5	10.6		16.7	15.2	3.0
2014	40.0 %											30.0	10.0	

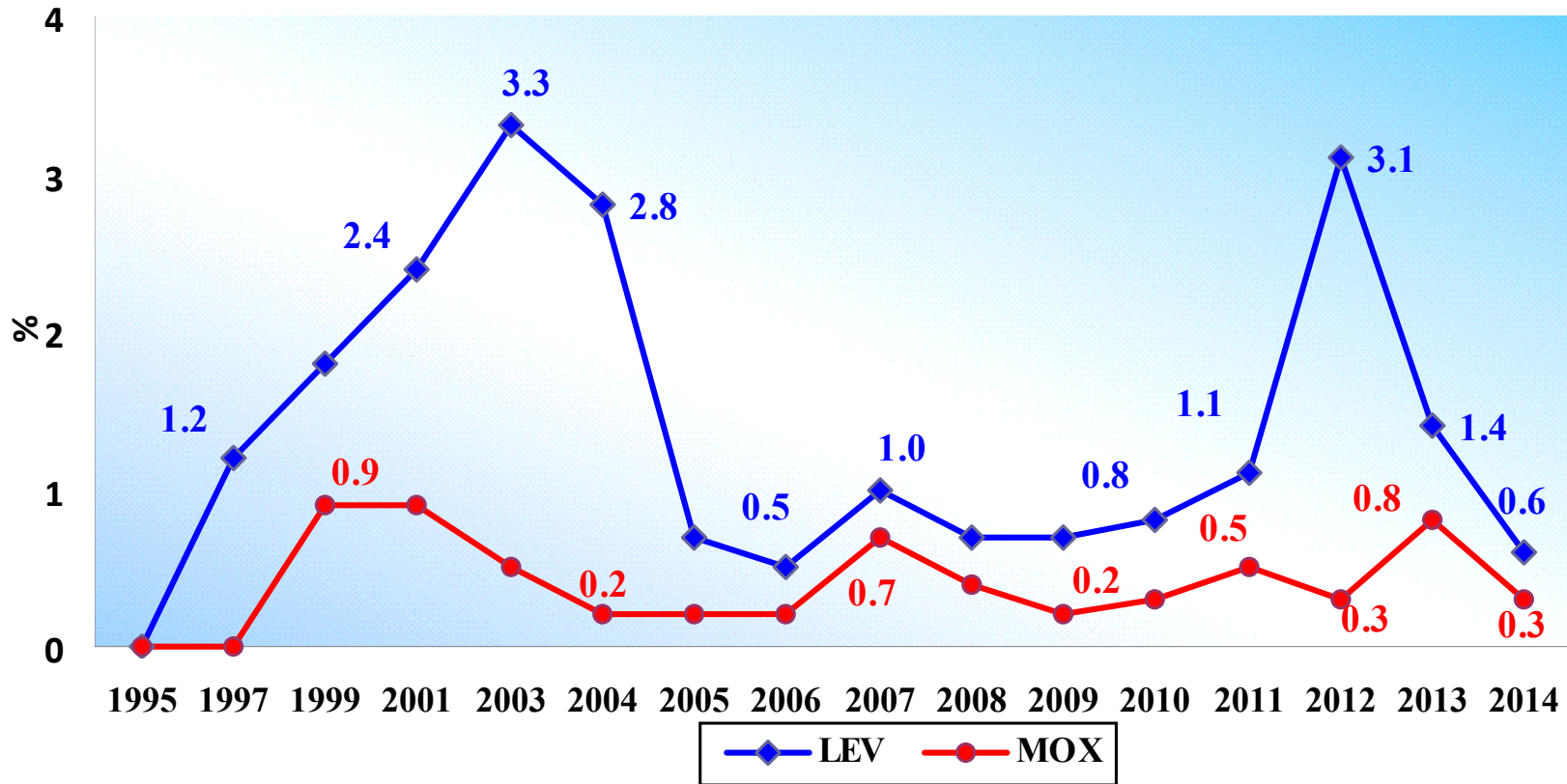
### % PEN-NS in PCV13 isolates from **Adults**

2012 79.3 %

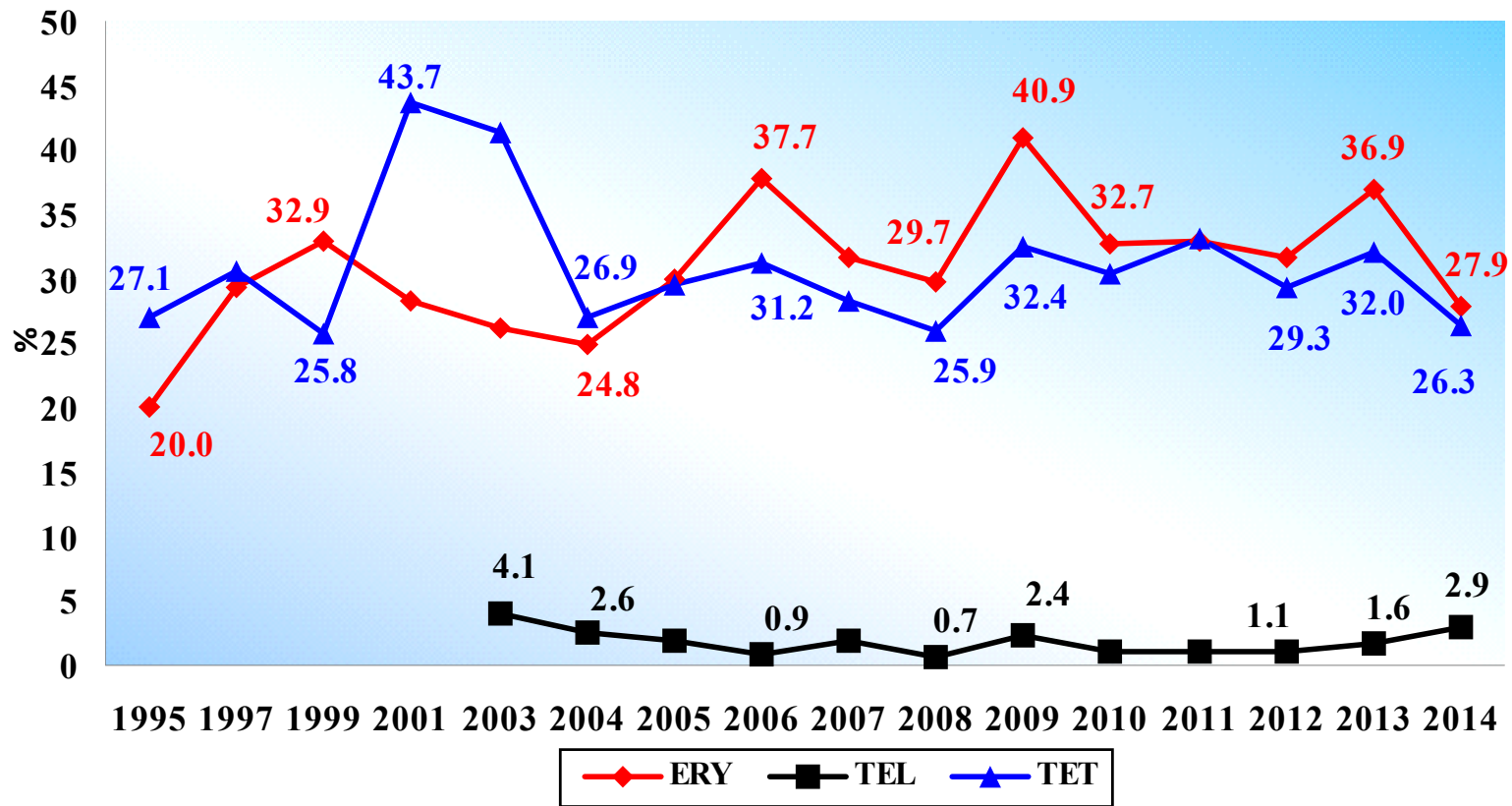
2013 91.4 %

2014 95.0 %

## RESISTANCE RATES (%) FOR FLUOROQUINOLONES

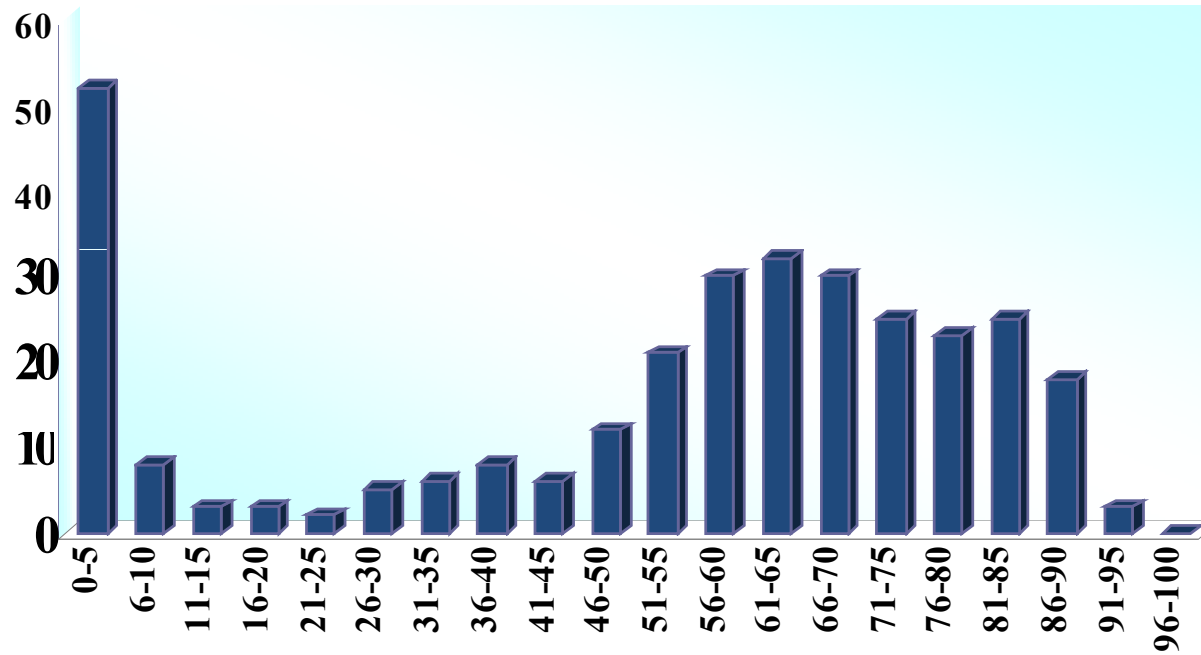


# RESISTANCE RATES (%) FOR MLS & TETRACYCLINE



## RESISTANCE and AGE

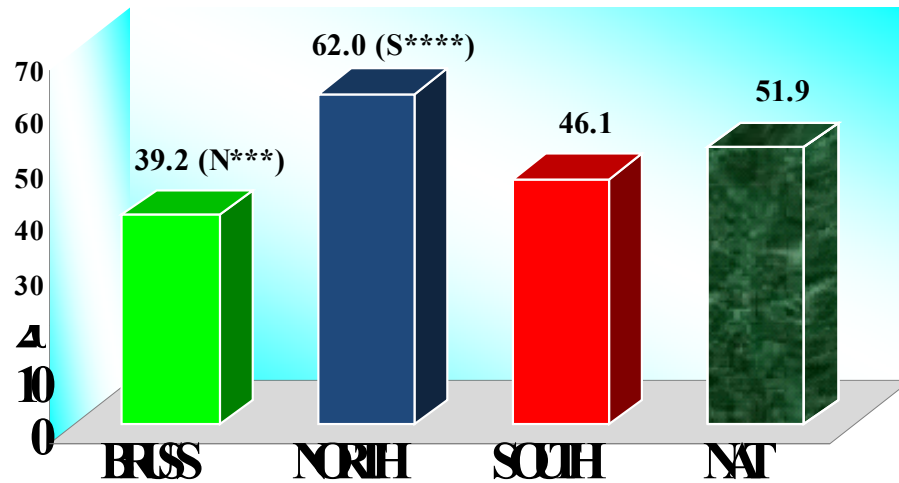
Age Distribution (SP2014)



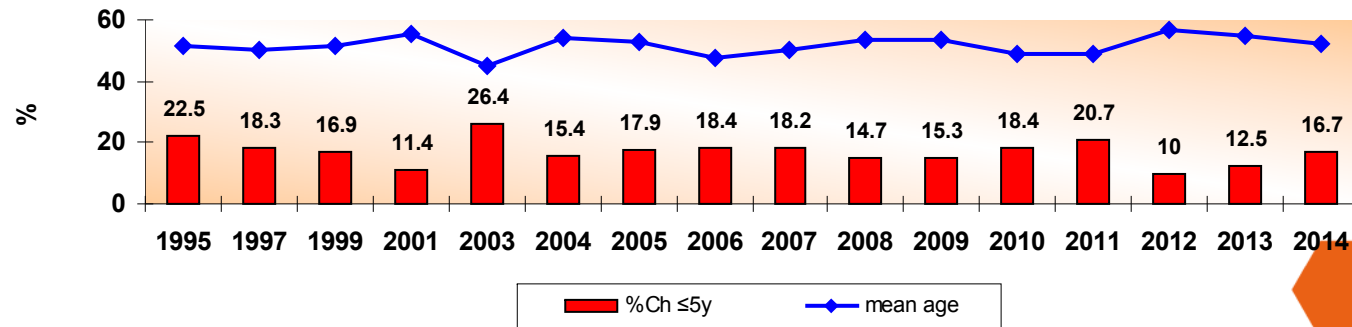
# RESISTANCE and AGE



Mean age by region (SP2014)

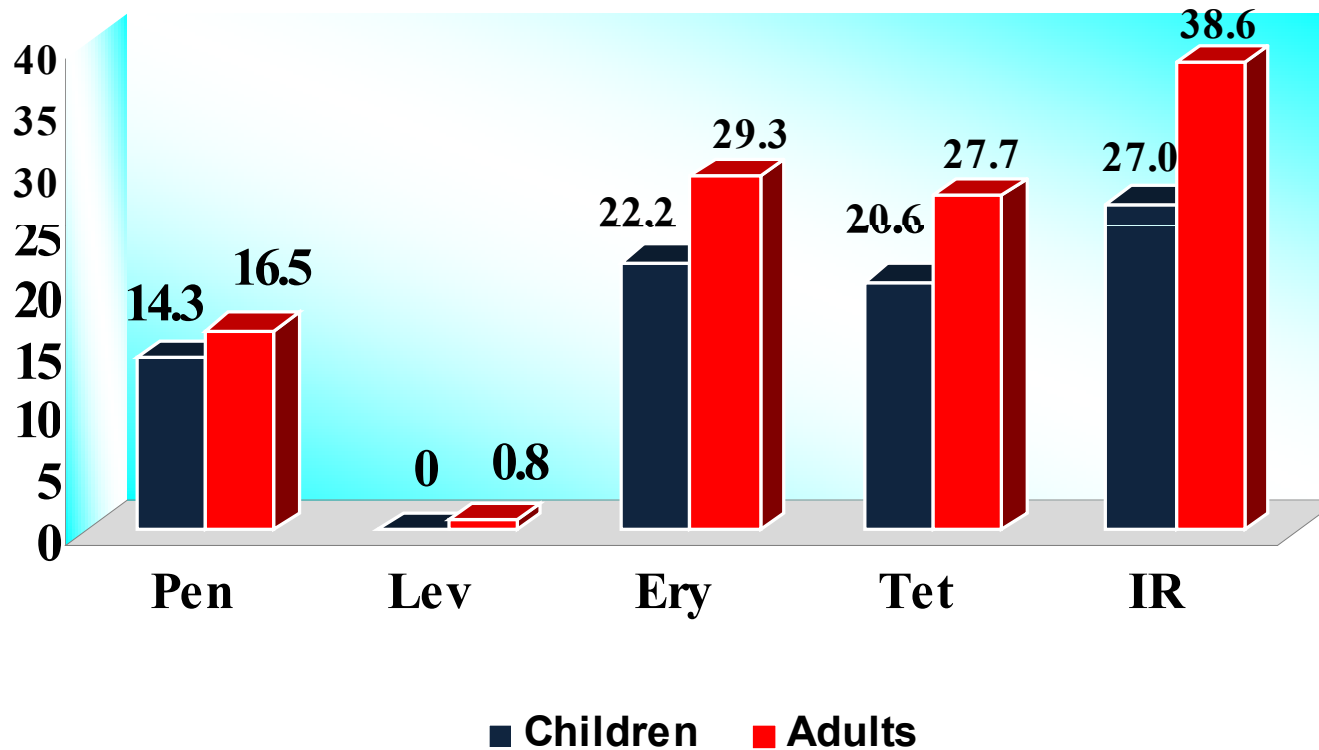


Evolution of mean age and % of children (≤ 5y)



## RESISTANCE and AGE

Resistance rates: Childrens versus Adults (SP2014)



## RESISTANCE and AGE



Non susceptibility rates (%)<sup>1</sup> for 4 indicator antibiotics in children (≤ 5 y) and adults

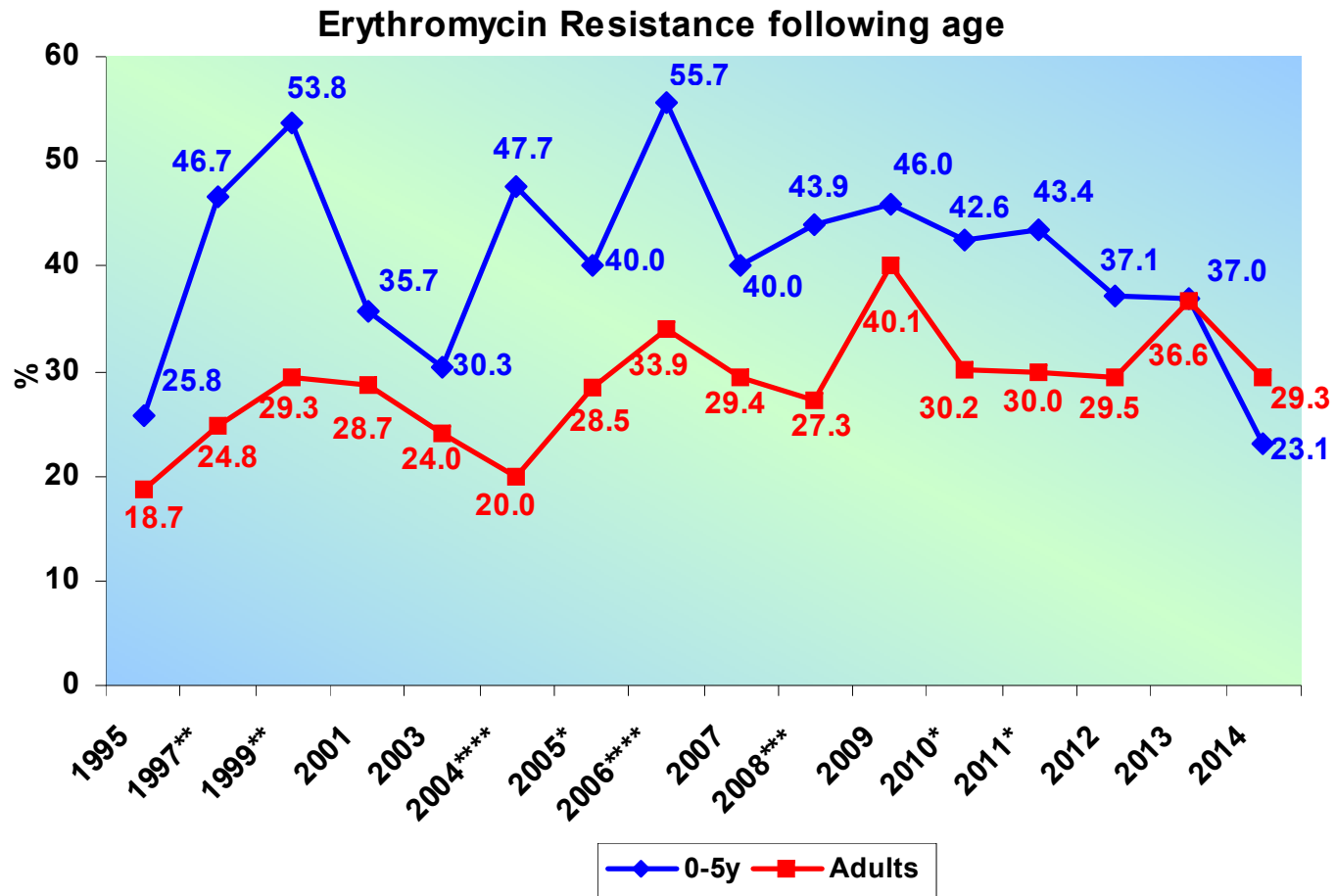
	PENICILLIN		LEVOFLOXACIN		ERYTHROMYCIN		TETRACYCLINE		NS-ISOLATES <sup>2</sup>	
	0-5y	Adults	0-5y	Adults	0-5y	Adults	0-5y	Adults	0-5y	Adults
1995	25.8**	7.5	0	0	25.8	18.7	29.0	26.2	41.9	32.7
1997	13.3	11.6	0	1.6	46.7**	24.8	33.3	28.7	53.3	34.9
1999	23.1	13.8	0.8	2.4	53.9**	29.3	34.6	24.4	61.5	43.9
2001	25.0	19.4	3.6	3.2	35.7	27.3	50.0	42.6	60.7	50.0
2003	11.7	15.6	1.9	3.7	29.1	24.3	46.6	38.3	55.3	47.6
2004	15.4	14.8	3.1	2.9	47.7****	20.0	40.0***	24.3	58.5***	35.1
2005	20.0	13.8	1.3	0.6	40.0*	28.5	35.0	28.5	50.0	40.6
2006	12.7	12.5	0	0.6	55.7****	33.9	44.3***	27.9	58.2****	37.6
2007	14.7	11.8	0	1.2	40.0	29.4	35.7	27.2	45.3	35.9
2008	15.2	11.4	0	0.8	43.9***	27.3	31.8	23.8	47.0*	32.4
2009	19.0**	8.7	0	0.9	46.0	40.1	36.5	30.2	49.2	43.1
2010	11.8	8.7	0	1.0	42.6*	30.2	33.8	29.9	47.1	36.8
2011	19.7***	7.8	0	1.4	43.4*	30.0	42.1	30.7	47.4	36.0
2012	25.7*	13.3	0	3.6	37.1	29.5	37.1	27.3	42.9	38.0
2013	15.2	18.3	0	1.6	37.0	36.6	30.4	32.2	39.1	43.2
2014	13.5	16.5	0	0.8	23.1	29.3	21.2	27.7	26.9	38.6

<sup>1</sup>Significant difference are indicated by an asterisk. \*0.05>P>0.02; \*\*0.02>P>0.01; \*\*\*0.01>P>0.001; \*\*\*\*P<0.001

<sup>2</sup>Isolates showing resistance to whichever of the indicator antibiotics

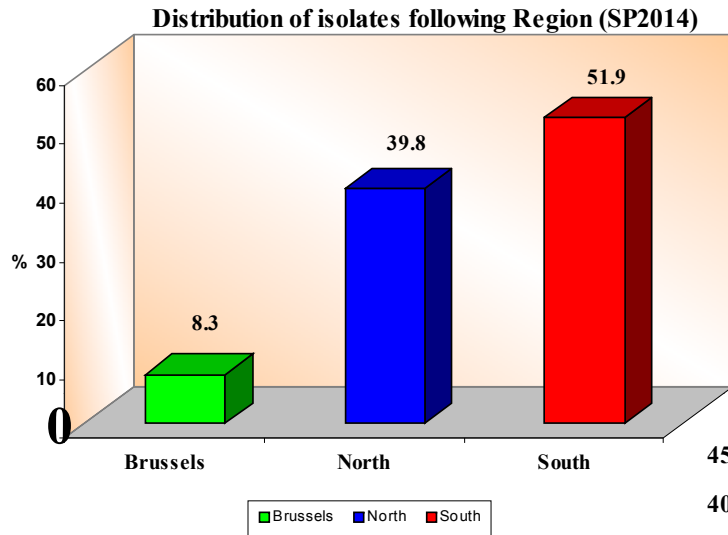
## RESISTANCE and AGE

✓ NS-rates mostly CHILD > ADULT; except FQ

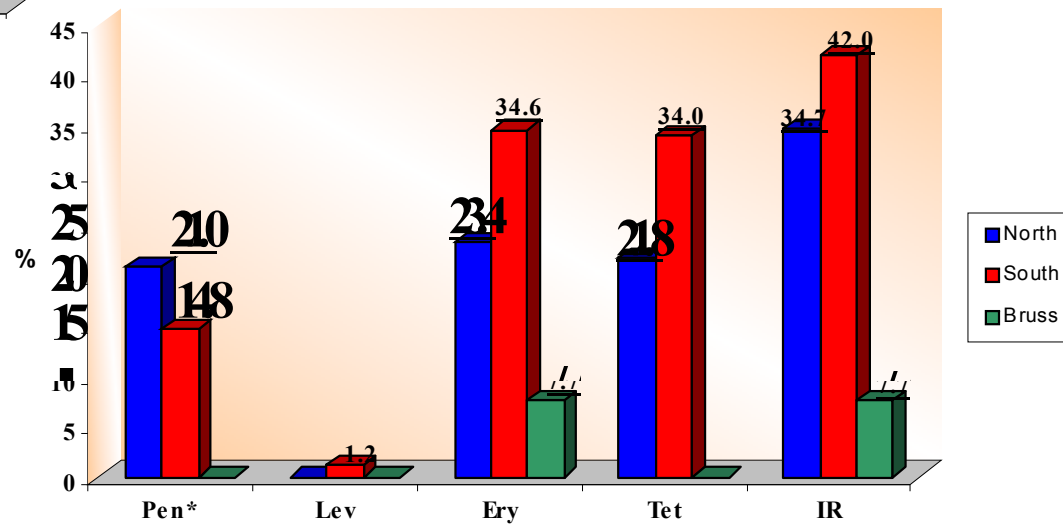




# RESISTANCE and REGION



**Resistance rates by region (SP2014)**

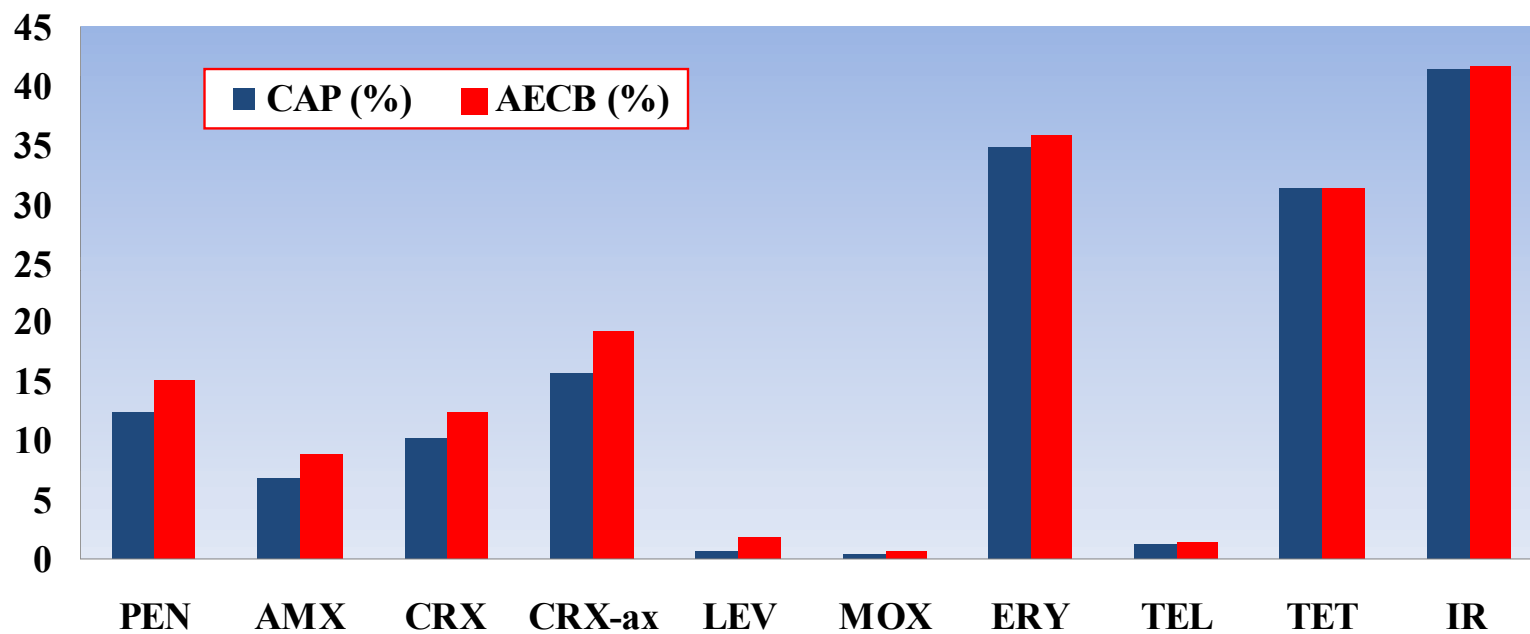


## RESISTANCE and REGION



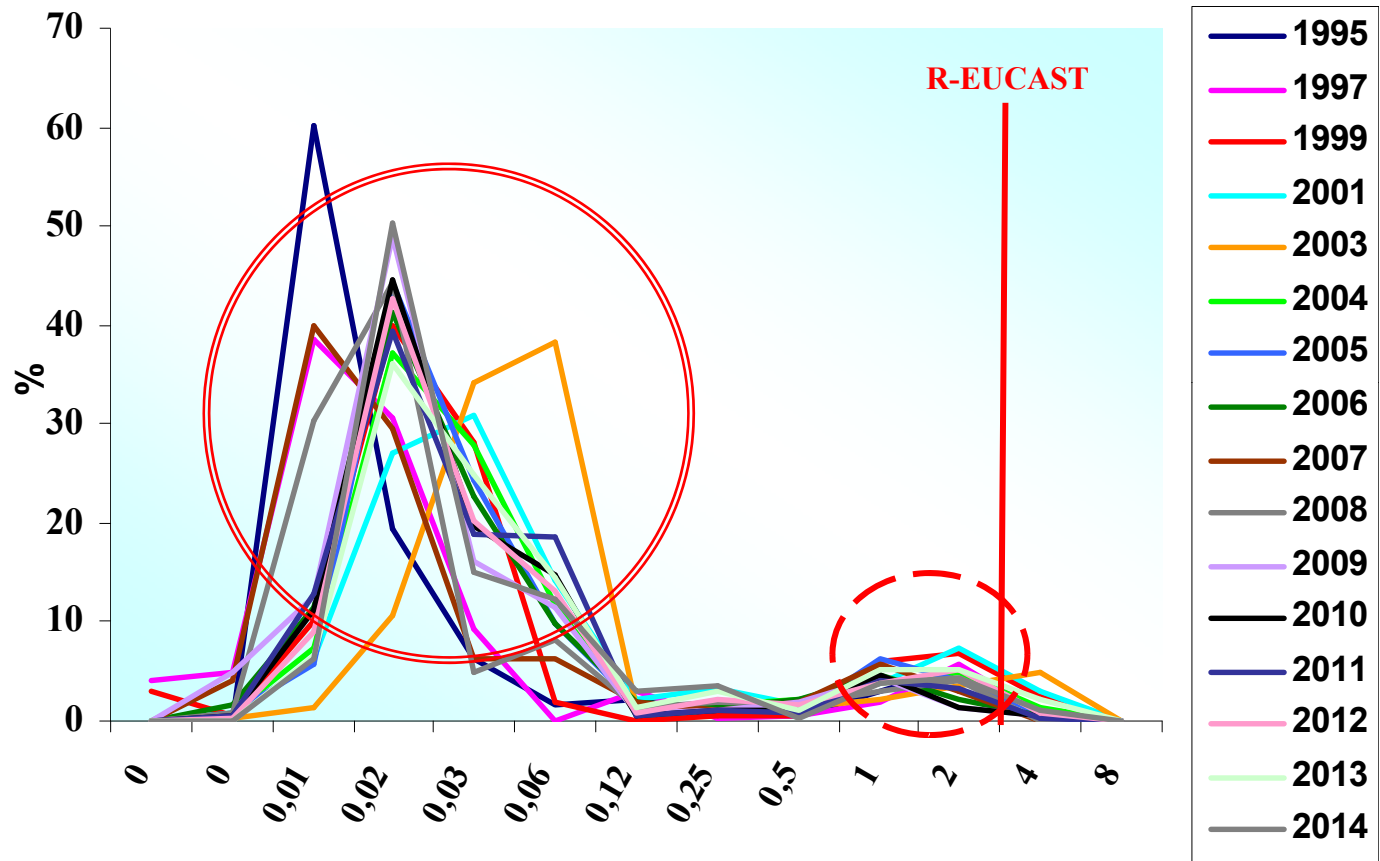
	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
<b>PEN</b>	S	S	S***	S**	S	S	S	S	S****	S	S	N
<b>LEV</b>	S*	S	N	N	S	N	N	N	S	N*	S	S
<b>ERY</b>	S*	S***	S***	S	S	S	S**	S****	S****	S***	S***	S***
<b>TET</b>	S	S	S	S	S	S	S***	S***	S*	S	S	S****
<b>IR</b>	S*	S***	S****	S	S	S	S**	S****	S***	S*	S*	S***

## RESISTANCE RATES (%) in CAP and AECB isolates\*



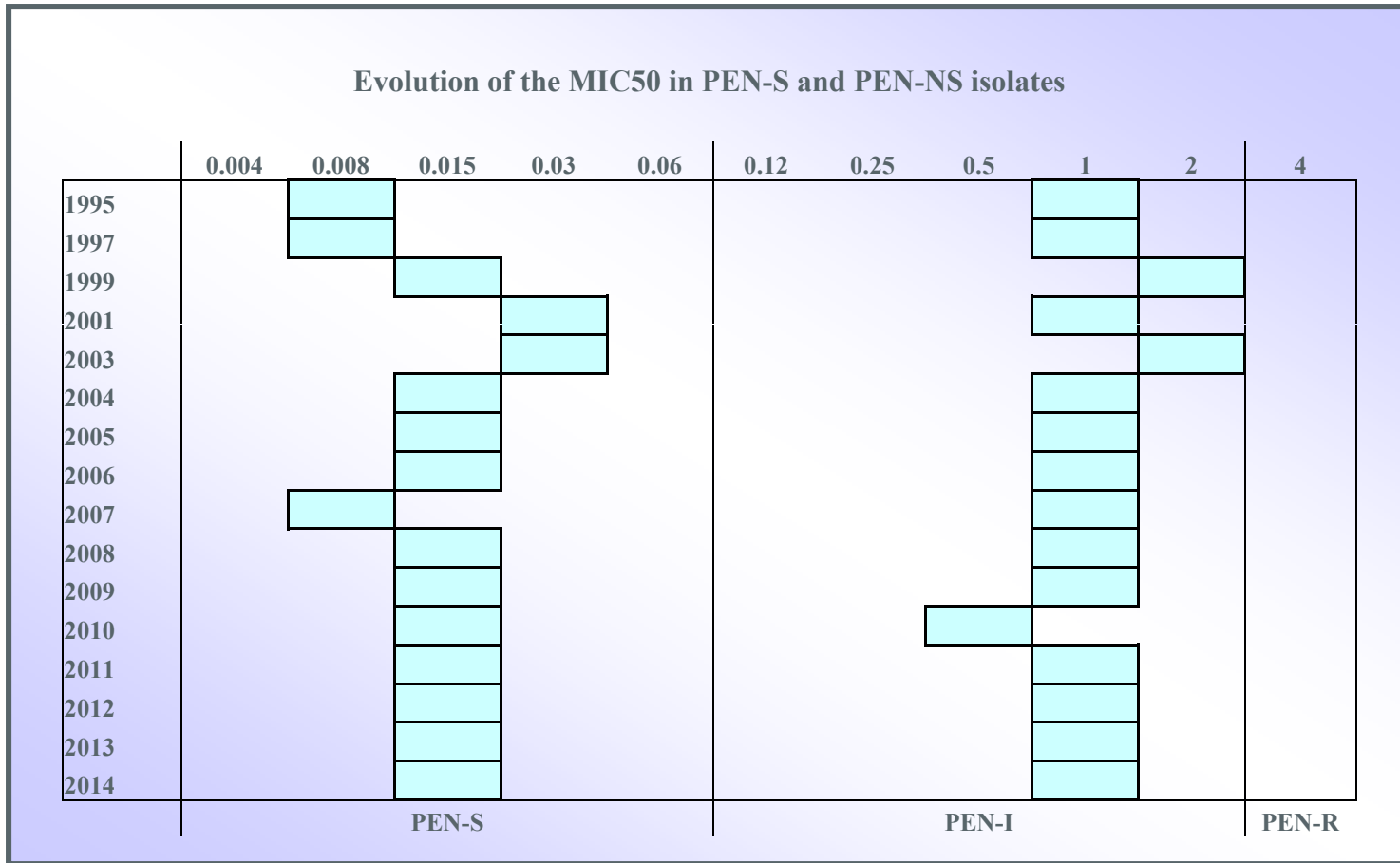
\*Period 2006-2014; compiled data

# MIC Distributions of PEN G

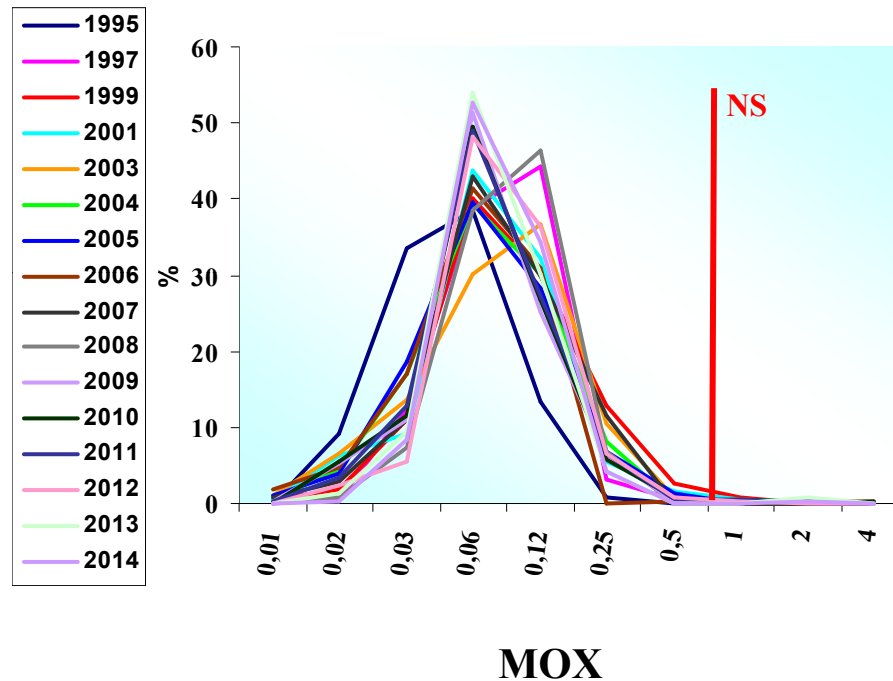
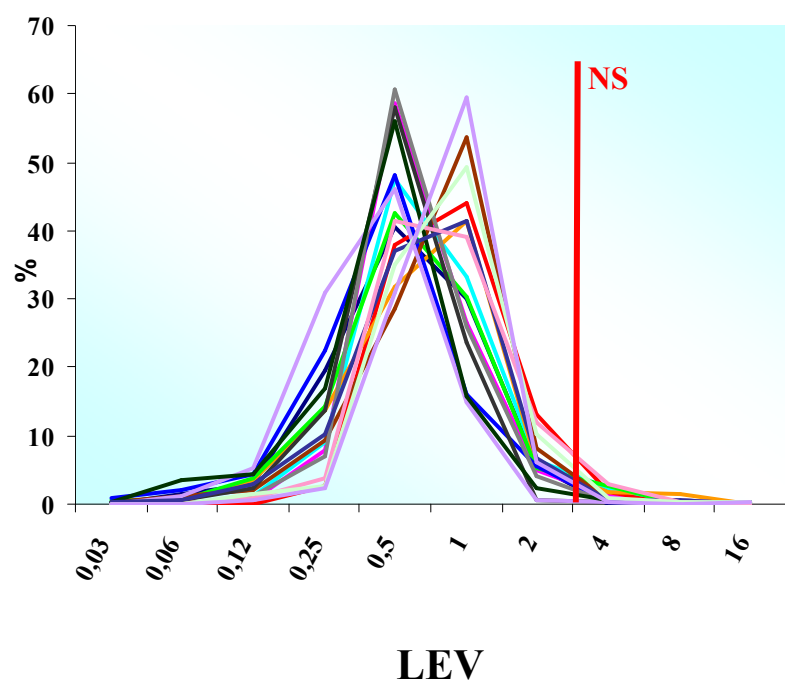


Bimodal Distribution

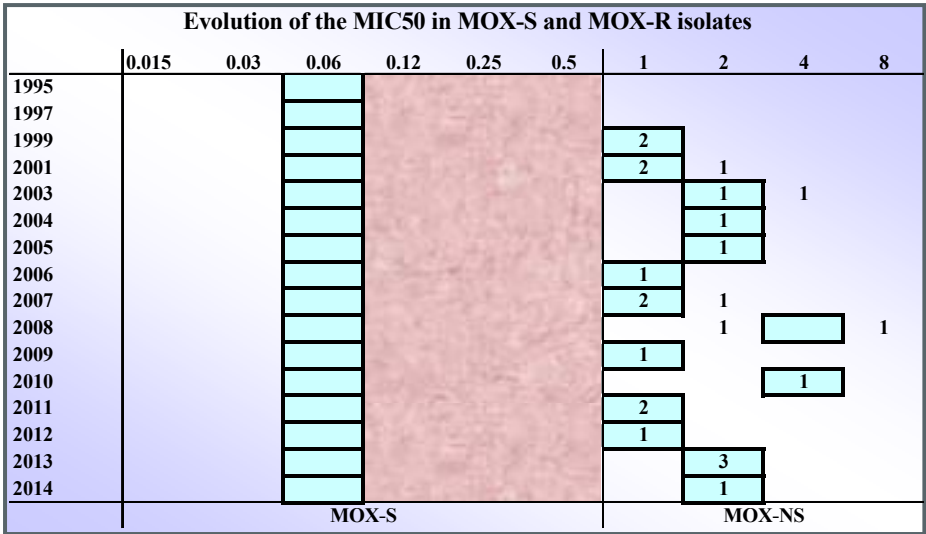
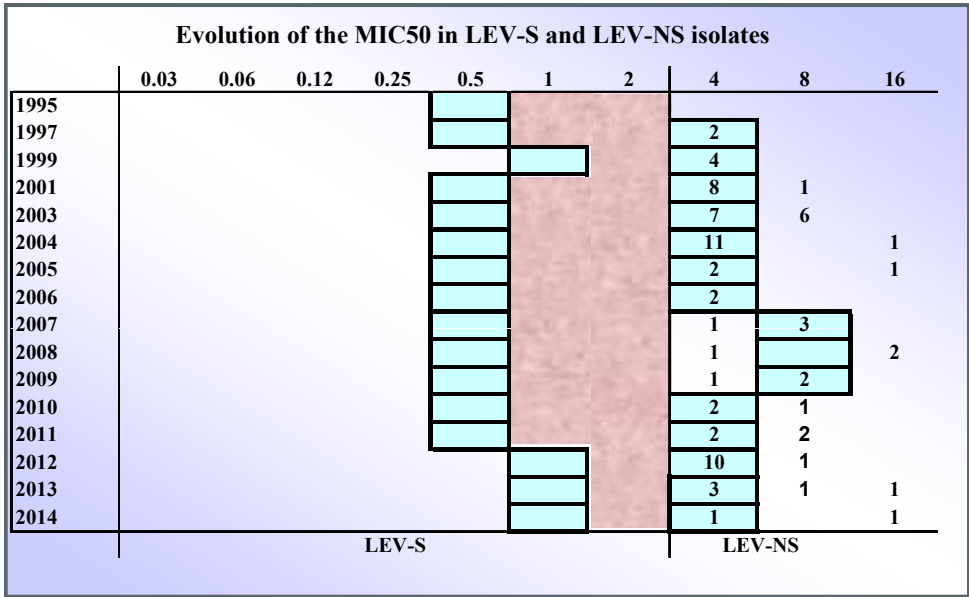
# MIC Distributions of PEN G



# MIC Distributions of FQ



# MIC Distributions of FQ



## Cross-Resistance



Degree of activity (%) of the indicated antimicrobials on *S. pneumoniae* isolates non-susceptible (NS) to the various compounds (1995-2014)

%Susceptible	PEN-NS	AMX-NS	CRX-NS	LEV-NS	MOX-NS	ERY-NS	TEL-NS	TET-NS
PEN	-	0	0.3	65.8	58.3	69.1	45.8	71.2
AMX	46.7	-	36.5	79.7	62.5	82.2	64.9	84.0
CRX	17.7	0.5	-	68.4	58.3	72.7	49.4	74.9
LEV	96.5	95.9	95.9	-	0	98.0	92.8	98.0
MOX	98.6	97.7	98.2	69.6	-	99.5	96.4	99.4
ERY	32.7	22.7	23.2	55.7	62.5	-	0	19.8
TEL	93.0	90.4	92.1	90.8	84.2	94.6	-	94.7
TET	34.2	30.9	30.5	57.0	58.3	21.1	8.4	-
	Degree exceeding 90%							
	Degree exceeding 95%							



## Conclusions



- ✓ **Decreasing Rates of Non Susceptibility (NS) in period 2001-2010**
- ✓ **Significant increase of PEN-, AMX-, CRX-NS since 2011.**
  - ❖ **PEN-NS isolates: 40 - 57% of isolates comprised in PCV13**
  - ❖ **Especially in adults ( $\geq 80\%$ )**
  - ❖ **Decrease RR in 2014**
- ✓ **In general Rate of NS: Children > Adults (not always significant)**
- ✓ **Regional Differences can be found**
- ✓ **Rate of NS AECB > CAP (not significant)**
- ✓ **Cross-Resistance: important %S to MOX, LEV, TEL**