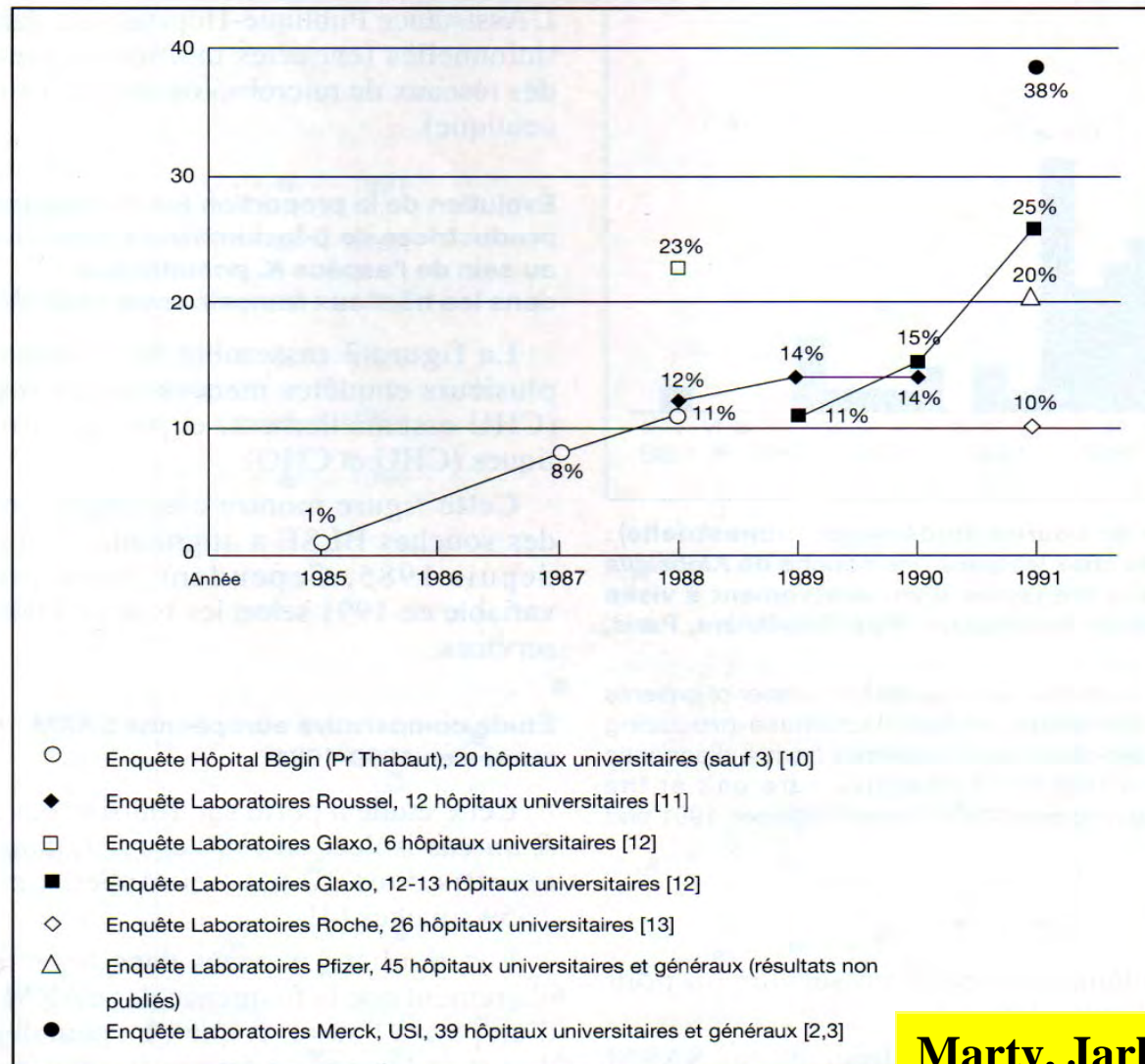


Entérobactéries productrices de BLSE en Europe et en France

**Vincent Jarlier
Bactériologie-Hygiène
Pitié-Salpêtrière, Paris**

ESBL : the 7 first years (1985-1991) in France

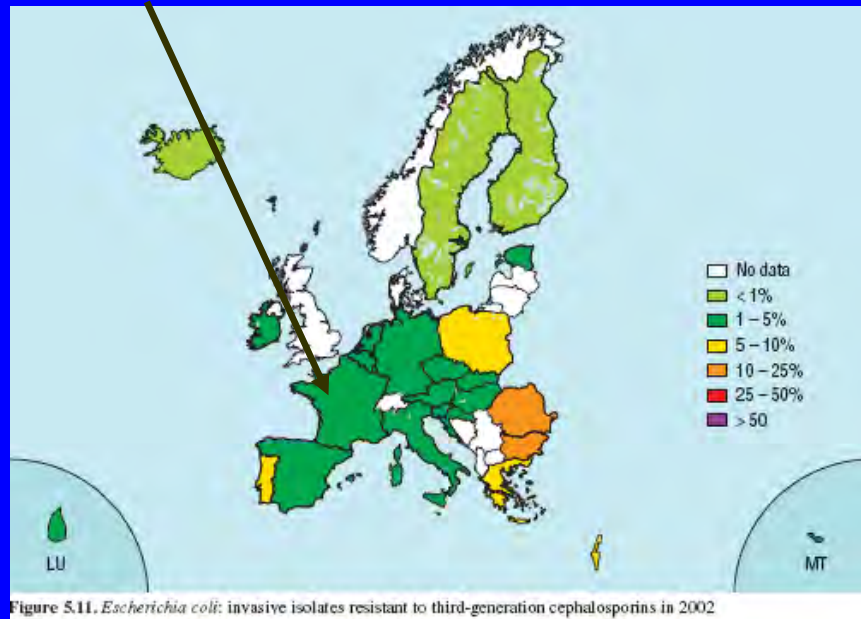


ESBL at European level

ESBL *E.coli*

EARSS : *E.coli* resistant to 3rd gen. cephalosporins (%) in bacteremias

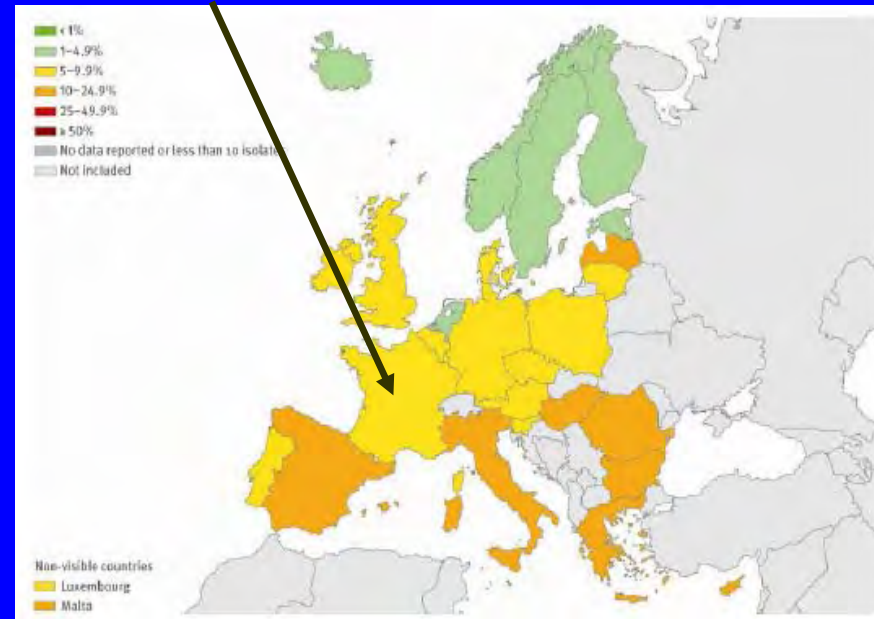
2%



2002

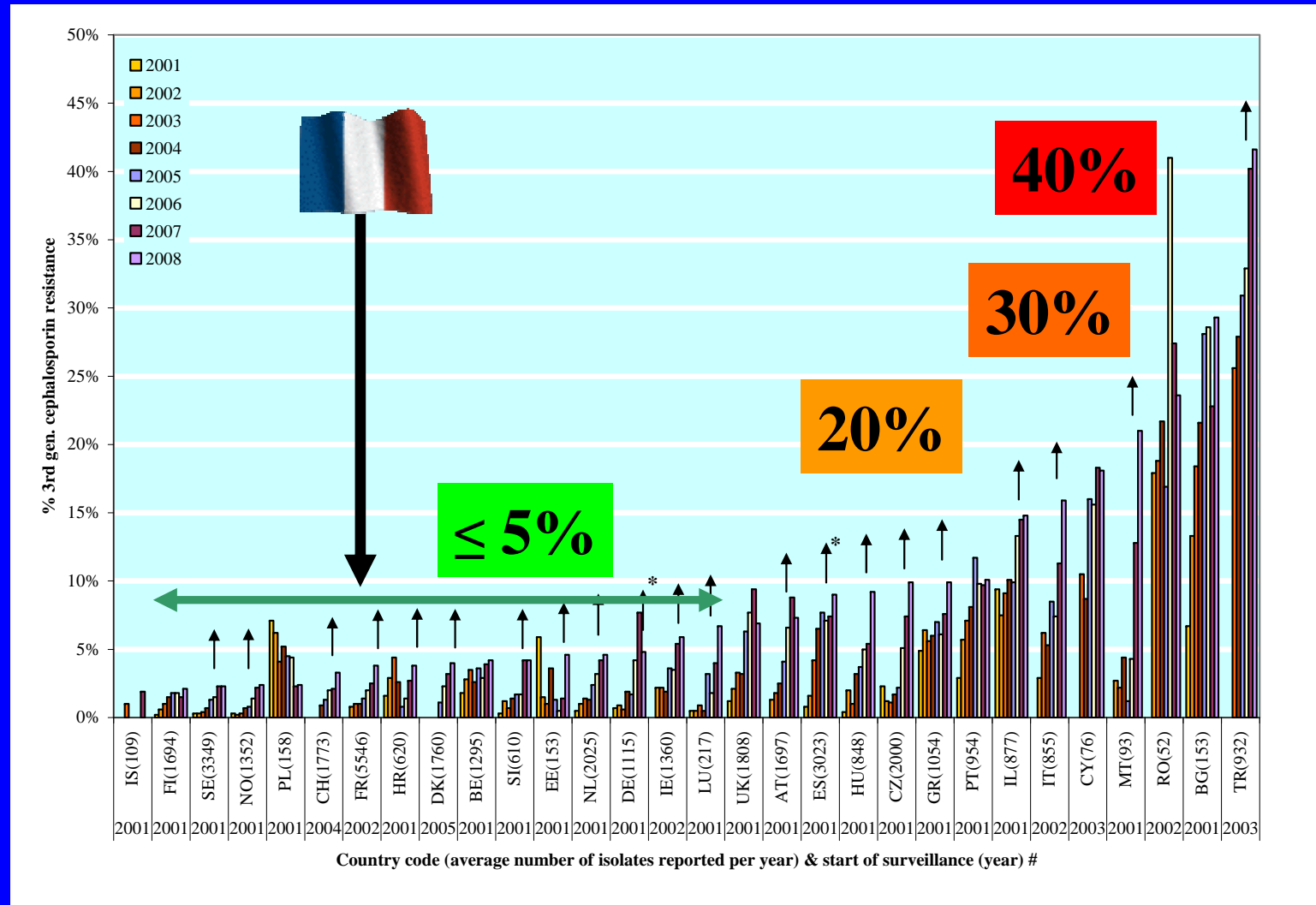
6.5%*

~5% ESBL

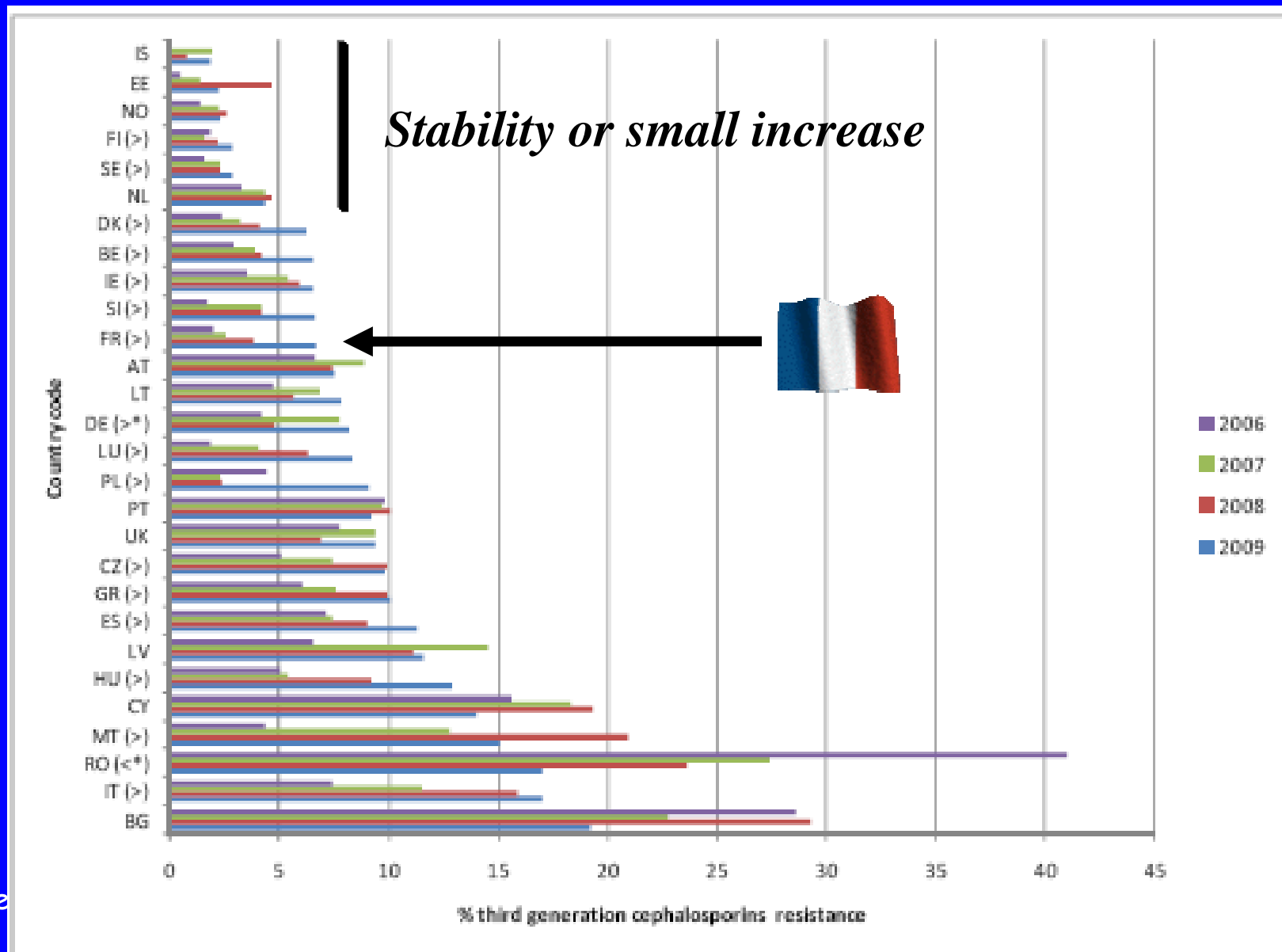


2009

% R 3rd gener. Cephalosporins in *E.coli* Bacteremias in Europe, EARSS 2001-08

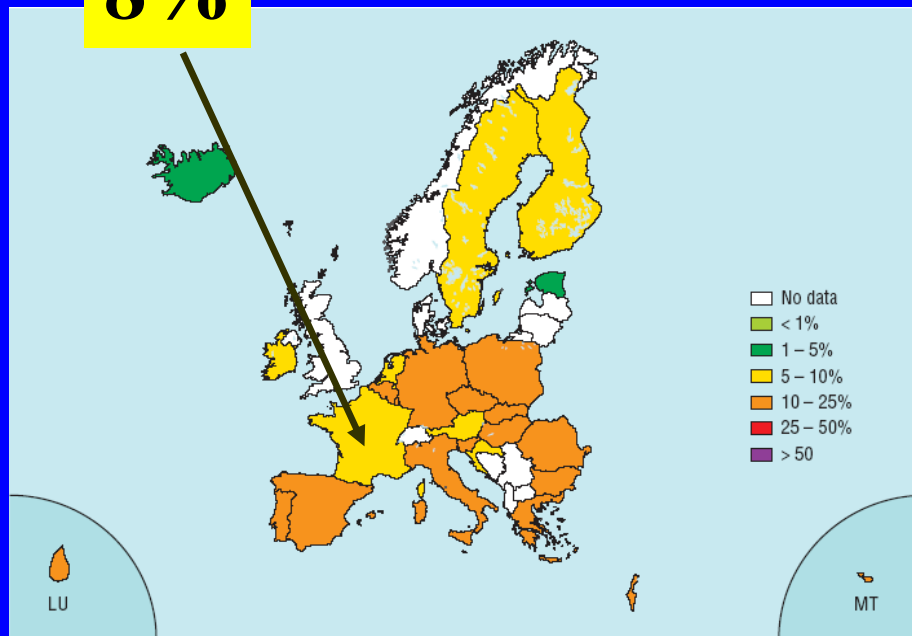


% R 3rd gener. Cephalosporins in *E.coli* Bacteremias in Europe, EARSS 2006-09



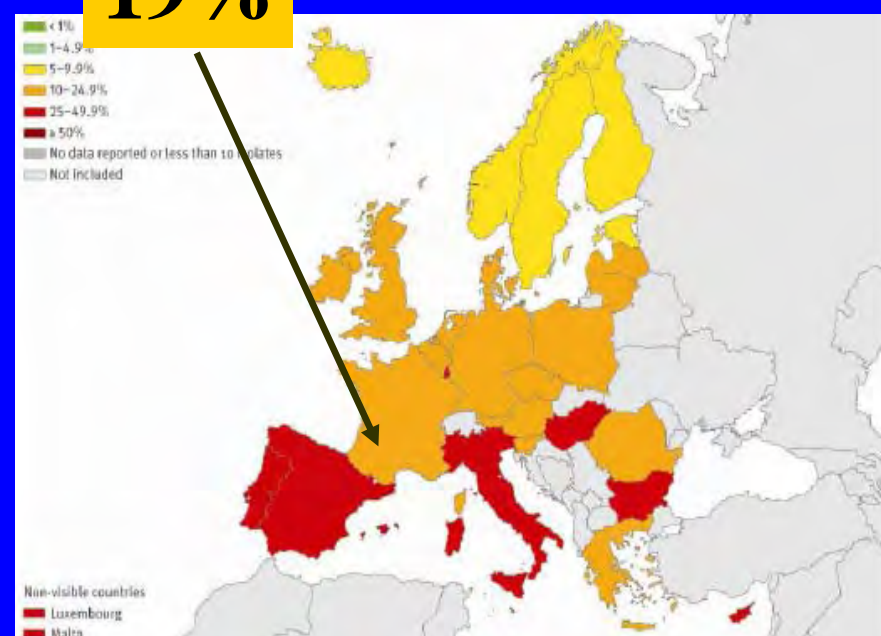
EARSS : *E.coli* resistant to fluoroquinolones (%) in bacteremias

8%



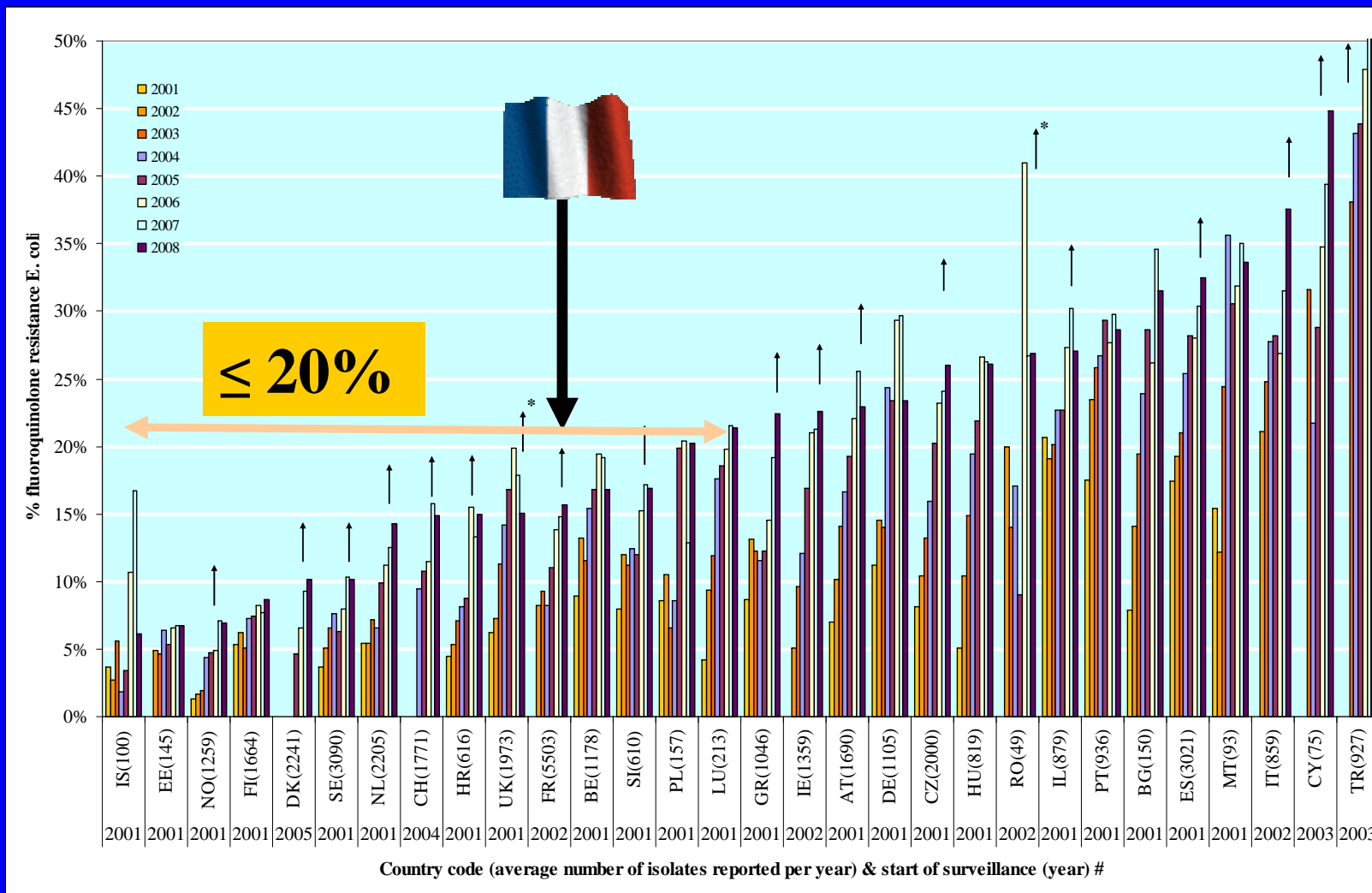
2002

19%

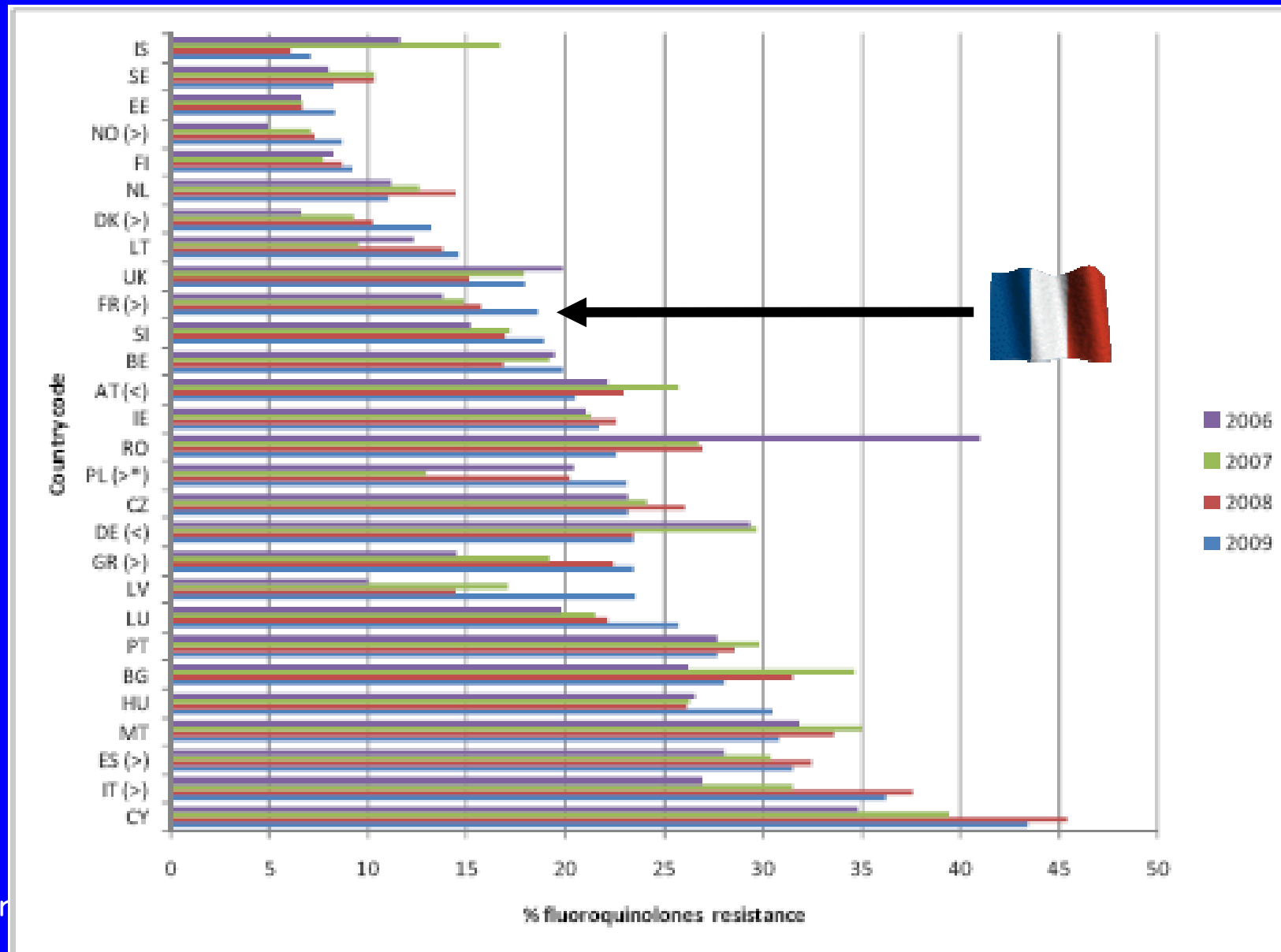


2009

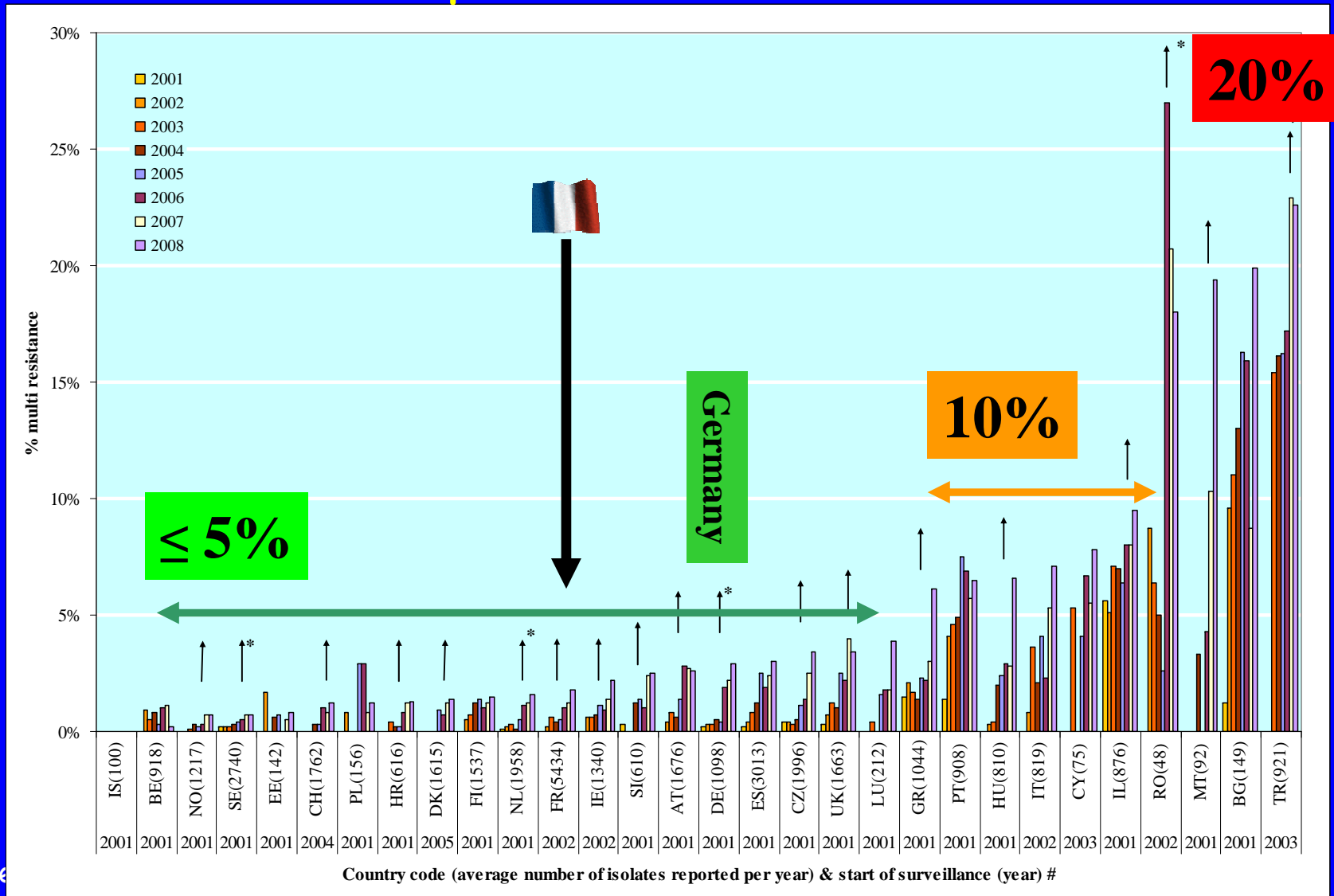
% R fluoroquinolones in *E.coli* Bacteremias in Europe, EARSS 2001-08



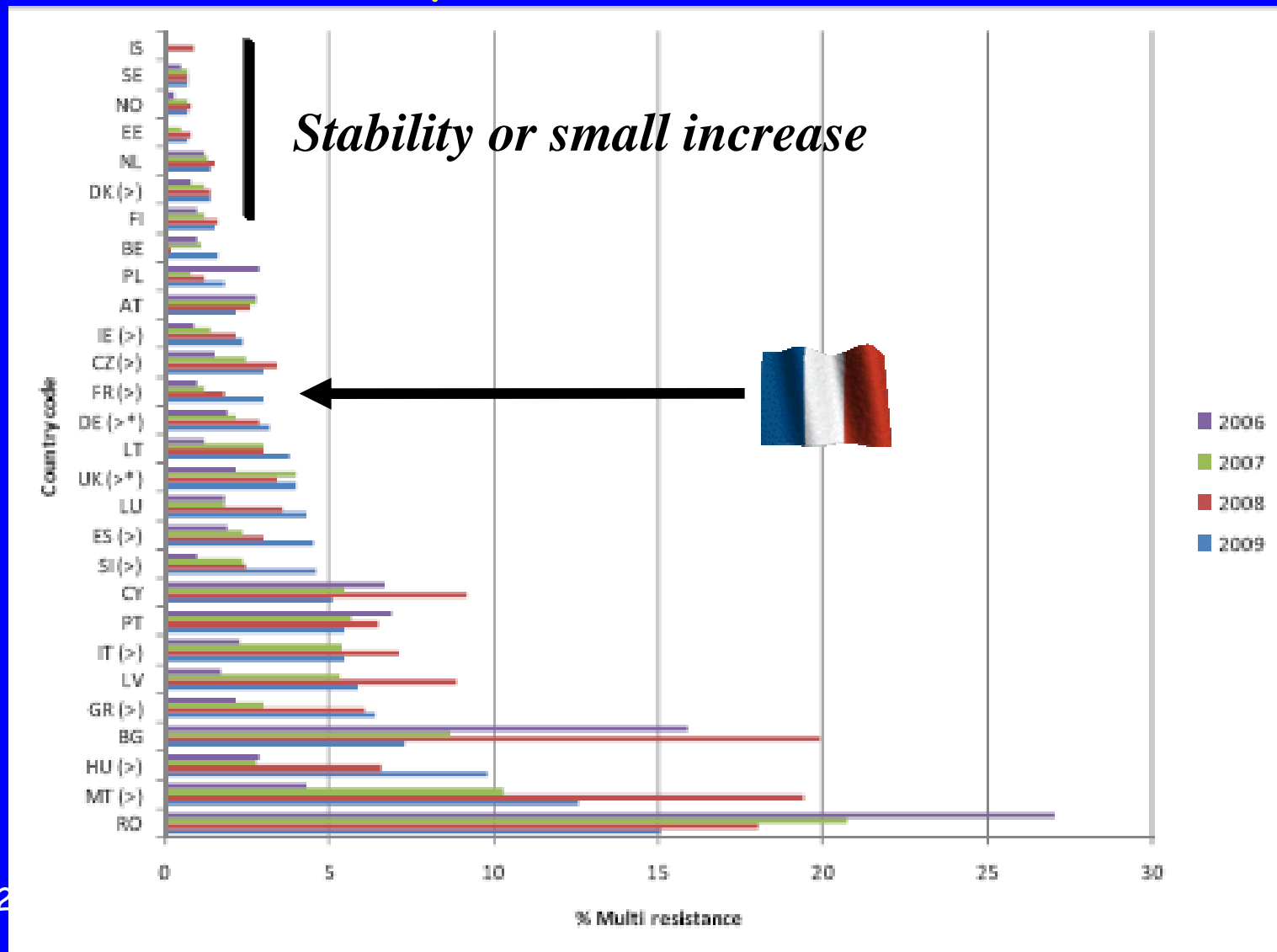
% R fluoroquinolones in *E.coli* Bacteremias in Europe, EARSS 2006-09



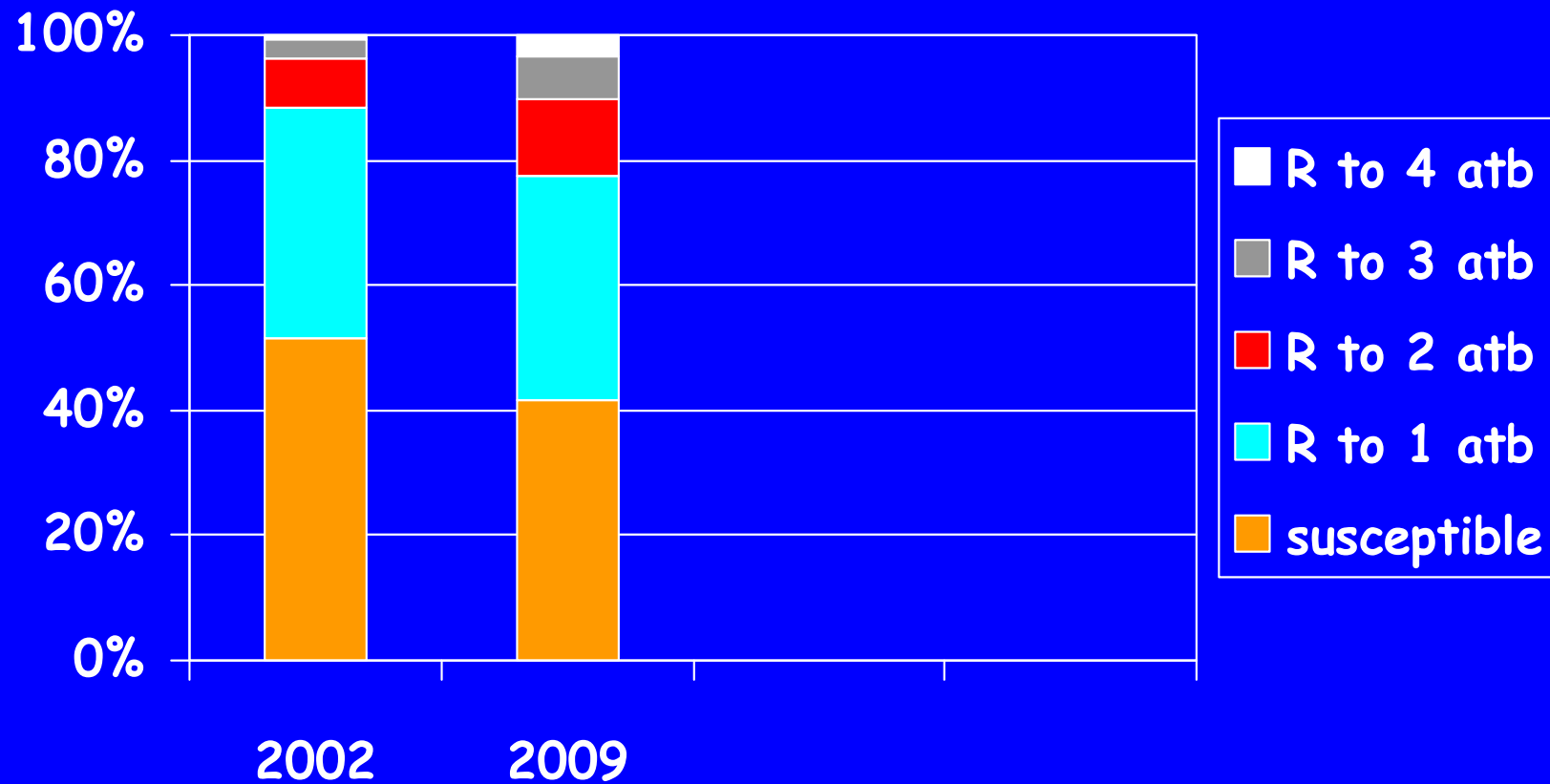
% R 3rd gener. Cephalosporins + FQ + aminoglycosides in *E.coli* Bacteremias in Europe, EARSS 2001-08



% R 3rd gener. Cephalosporins + FQ + aminoglycosides in *E.coli* Bacteremias in Europe, EARSS 2006-09



E.coli from bacteremias in Europe : evolution
of the proportions of resistance patterns
EARSS 2002 - 2009 (subset of 198
laboratories)

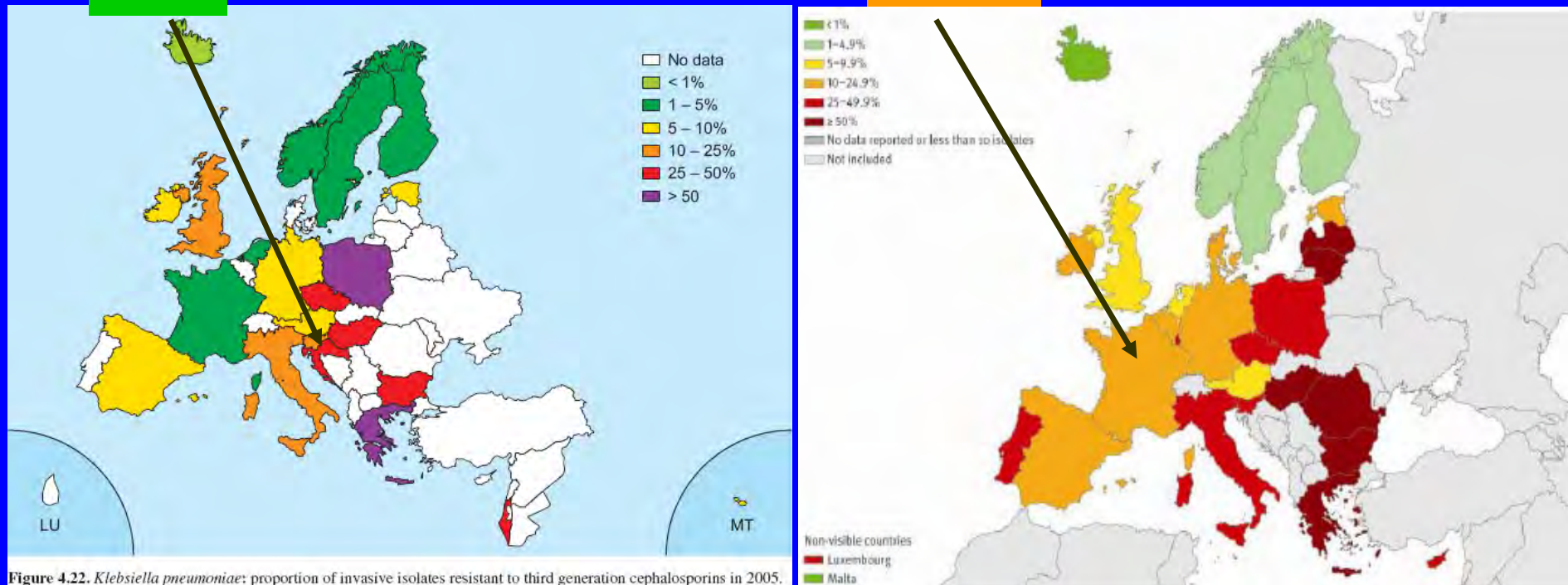


ESBL *K.pneumoniae*

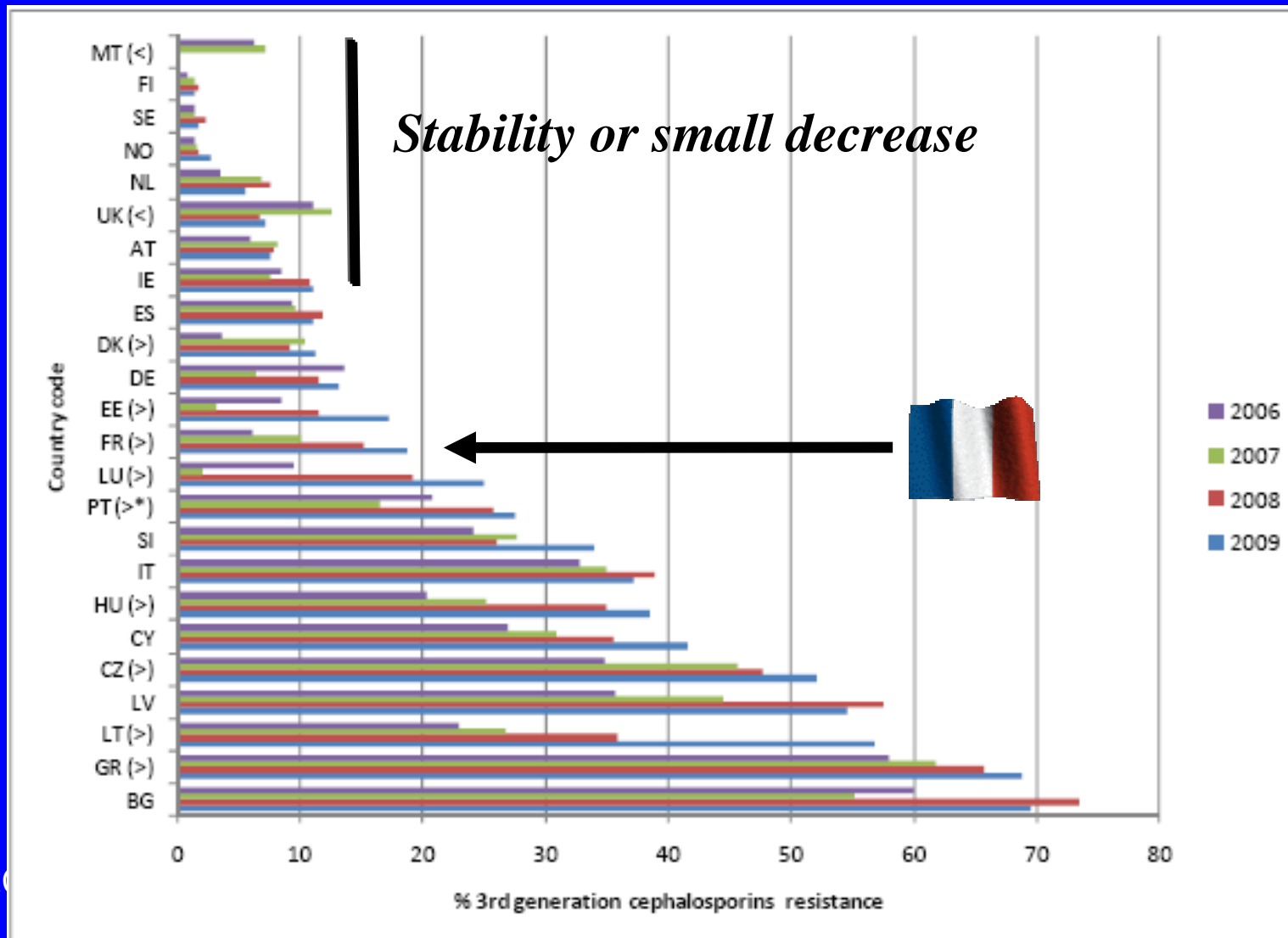
EARSS : *K.pneumoniae* resistant to 3rd generation cephalosporins in bacteremias

2%

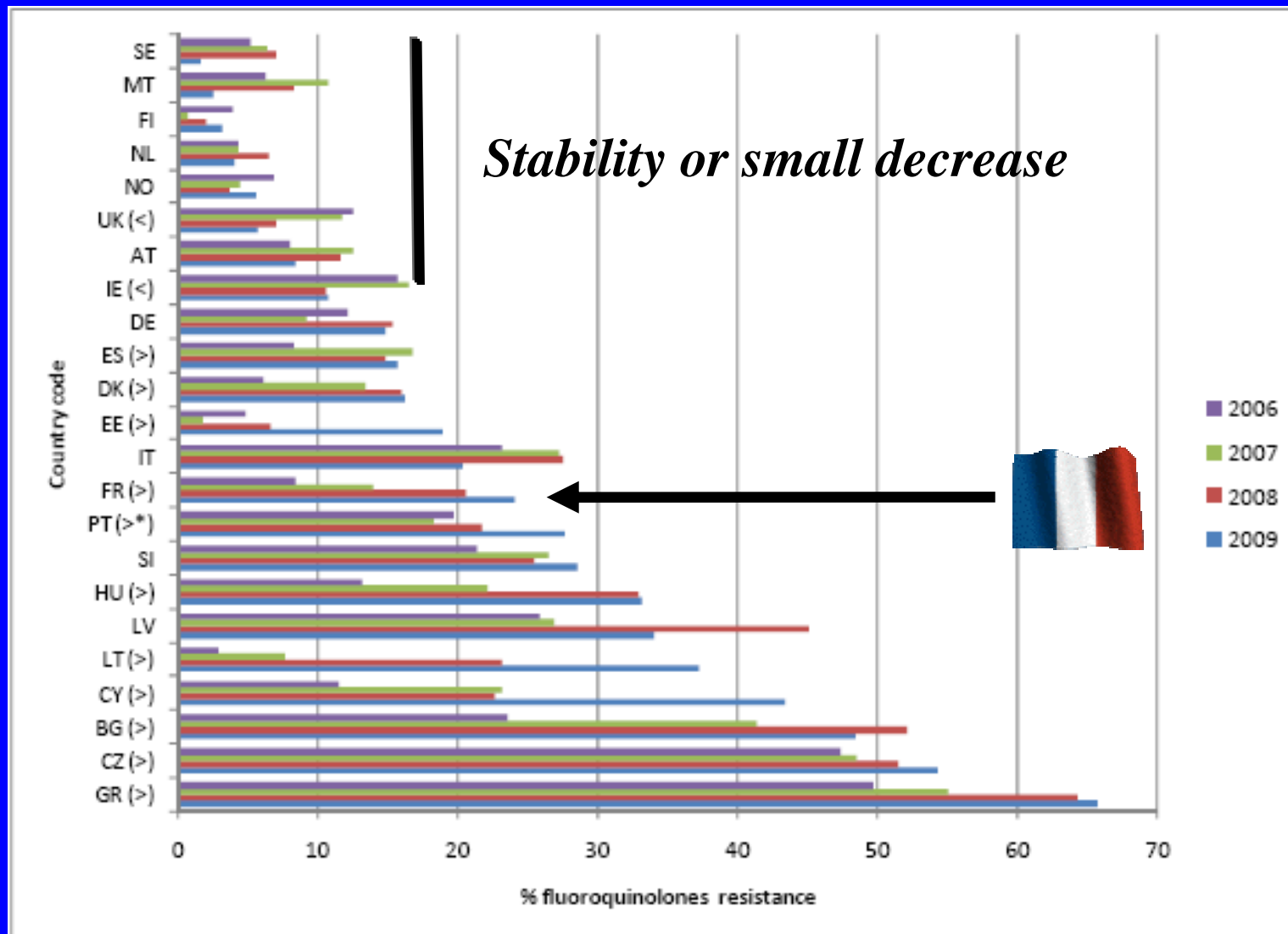
19%



% R 3rd gener. Cephalosporins in *K.pneumoniae* Bacteremias in Europe, EARSS 2006-09



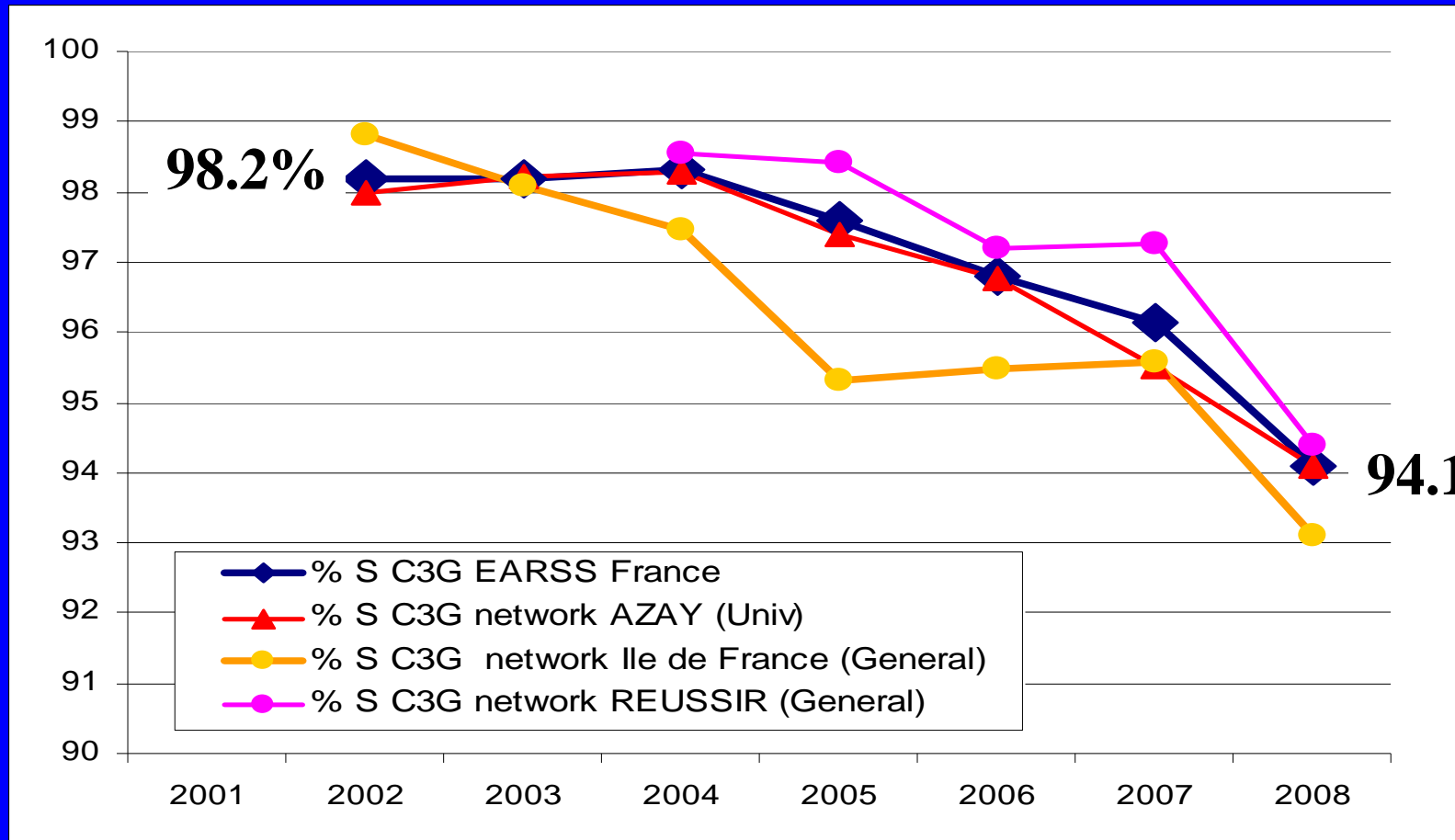
% R 3rd gener. Cephalosporins + FQ + aminoglycosides in *K.pneumoniae* Bacteremias in Europe, EARSS 2006-09



ESBL at national level

EARSS France (ONERBA - InVS)

E.coli: % R to 3rd gen. cephalosporins (mainly ESBL), EARSS France, 2001-2008

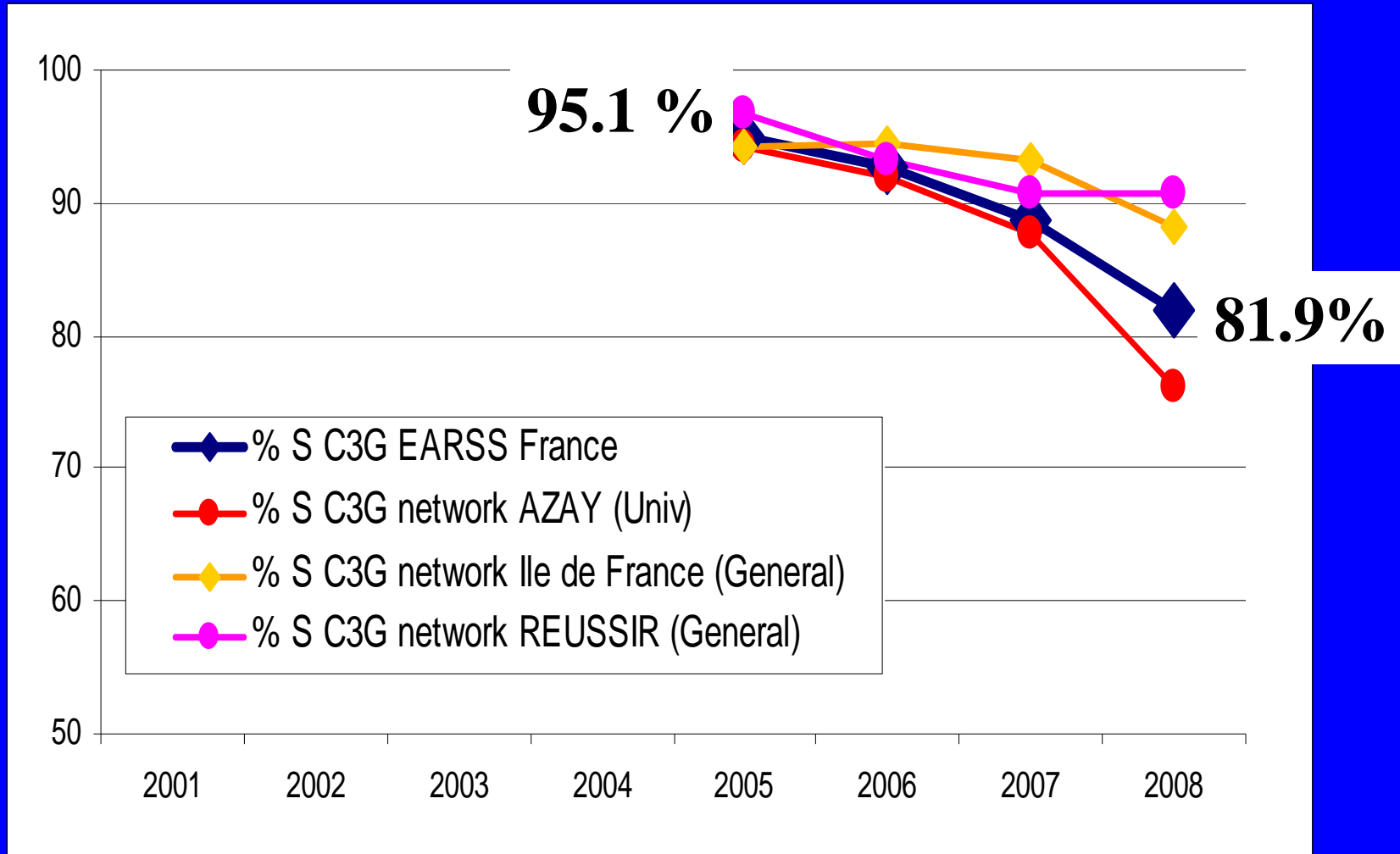


***National extrapolation :
~1,500 bacteremias /year***

K.pneumoniae : % R to 3rd gen. Cephalosp.
(mainly ESBL) and F.quinolones
EARSS France 2005-2008

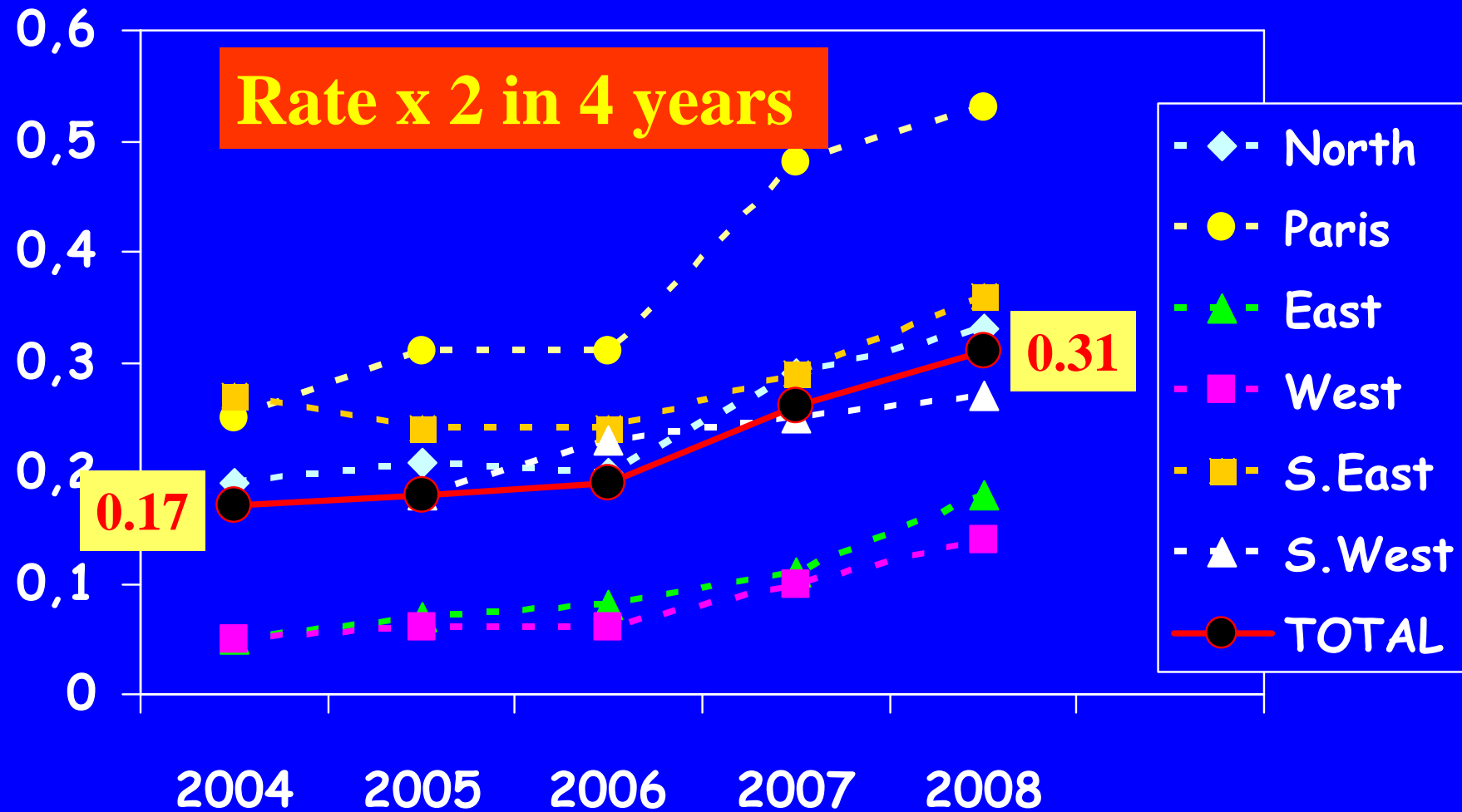
	2005	2006	2007	2008	2009
3rd gen Ceph	4	6	10	15	19
F.quinolones	7	9	14	21	24

K.pneumoniae : % R to 3rd gen.
cephalosporins (mainly ESBL)
EARSS 2005-2008

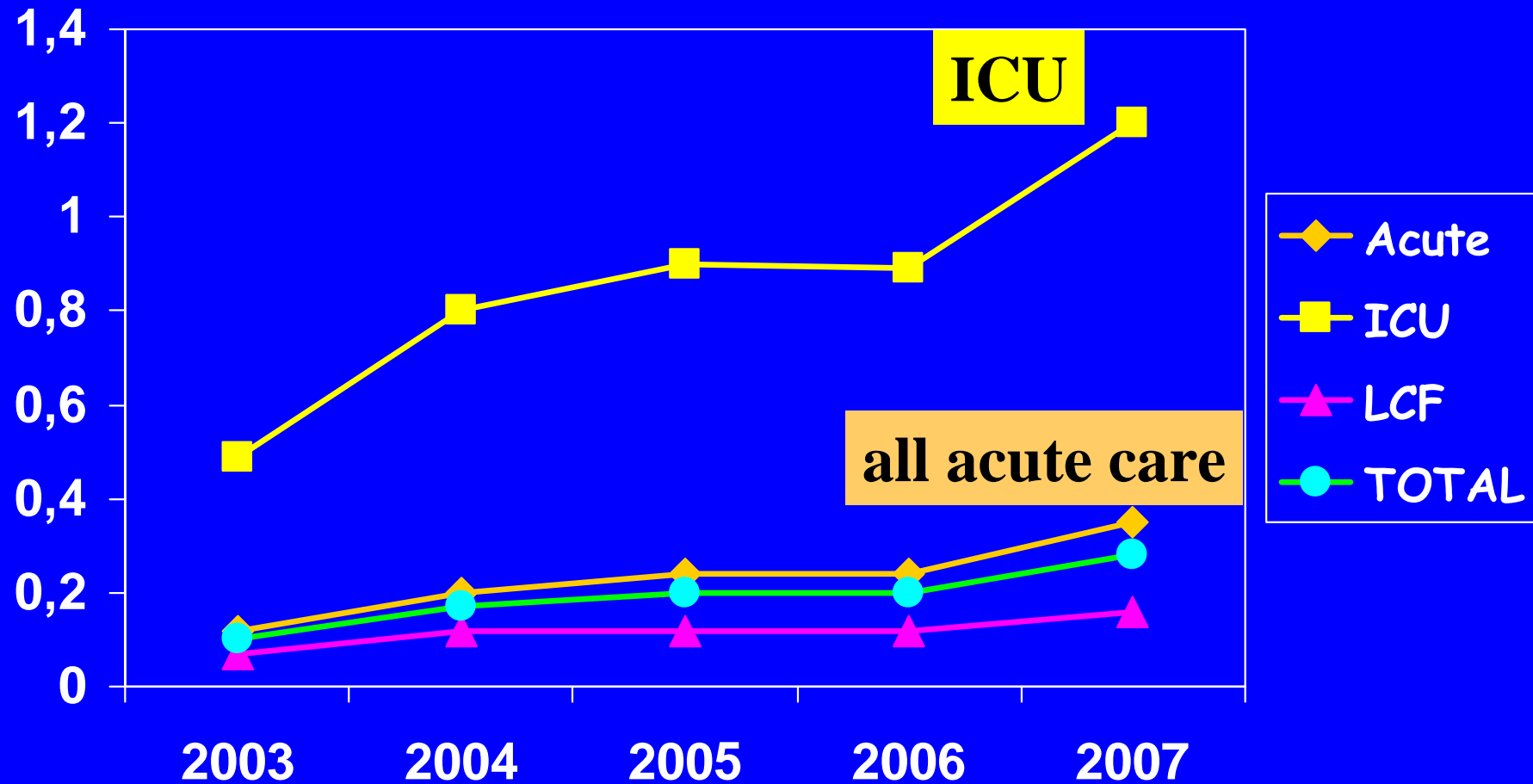


RAISIN (C-CLINs - InVS)

ESBL National survey (« RAISIN »)
Incidence rate / 1,000 DHs per area
2004-2008 (227 hospitals 3 months/year)



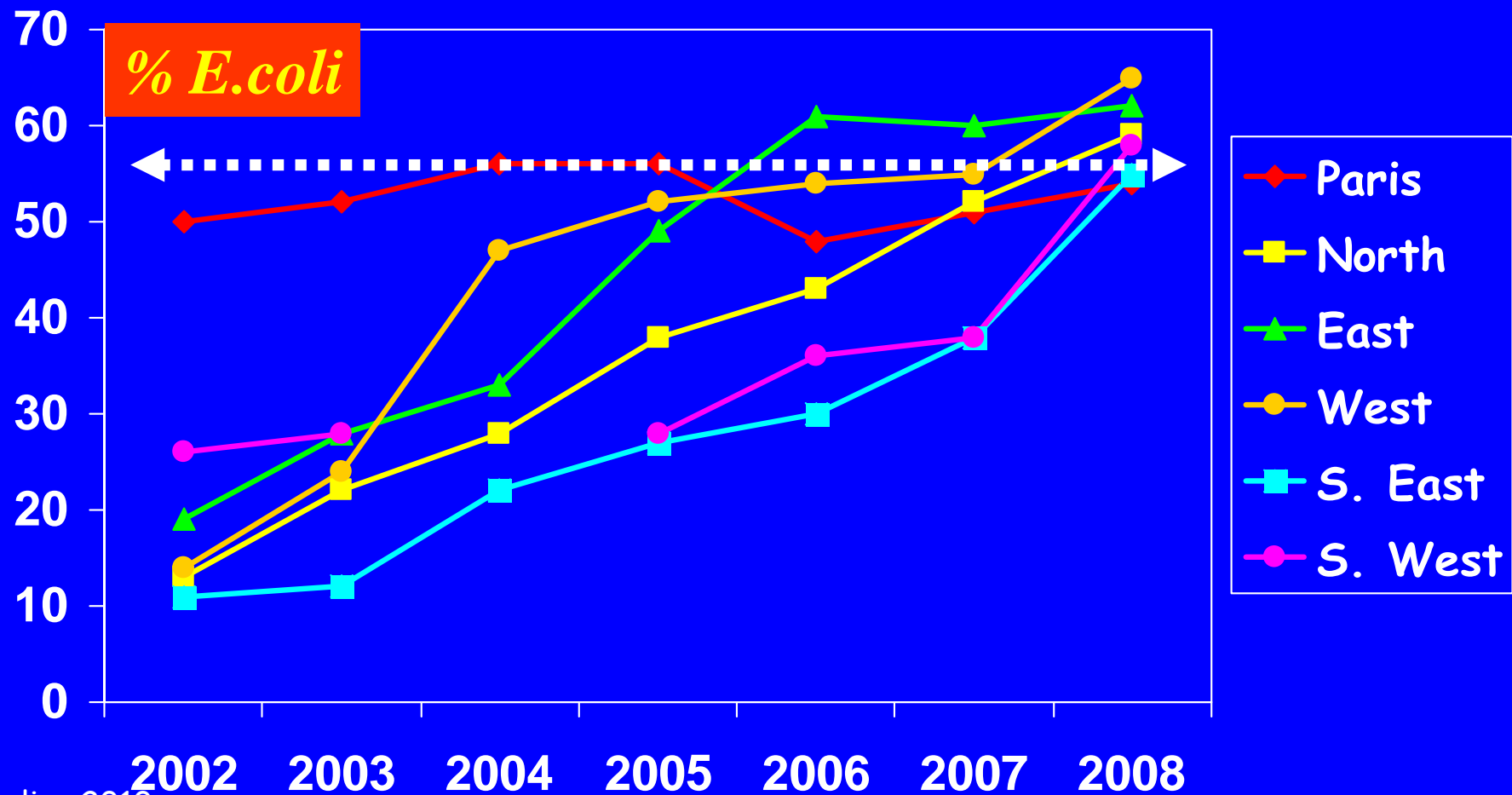
ESBL national survey (« RAISIN »)
Incidence rates / 1,000 DHs per activity
227 French hospitals (3 months/year)
2003-2007



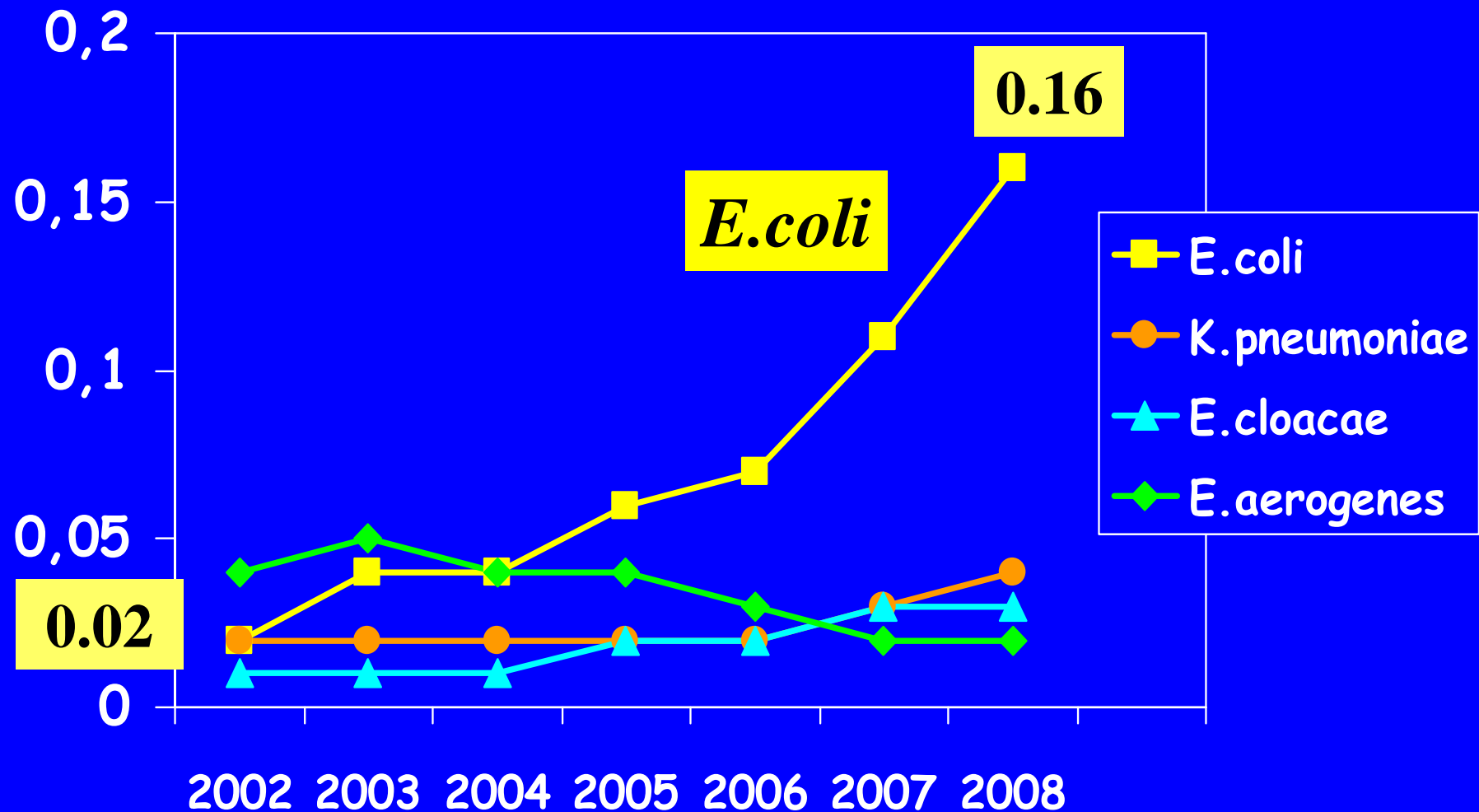
ESBL National survey (« RAISIN »)

Proportion of *E.coli* (%) among ESBL enterobacteria

per area 2002-2008 (3 months/year)



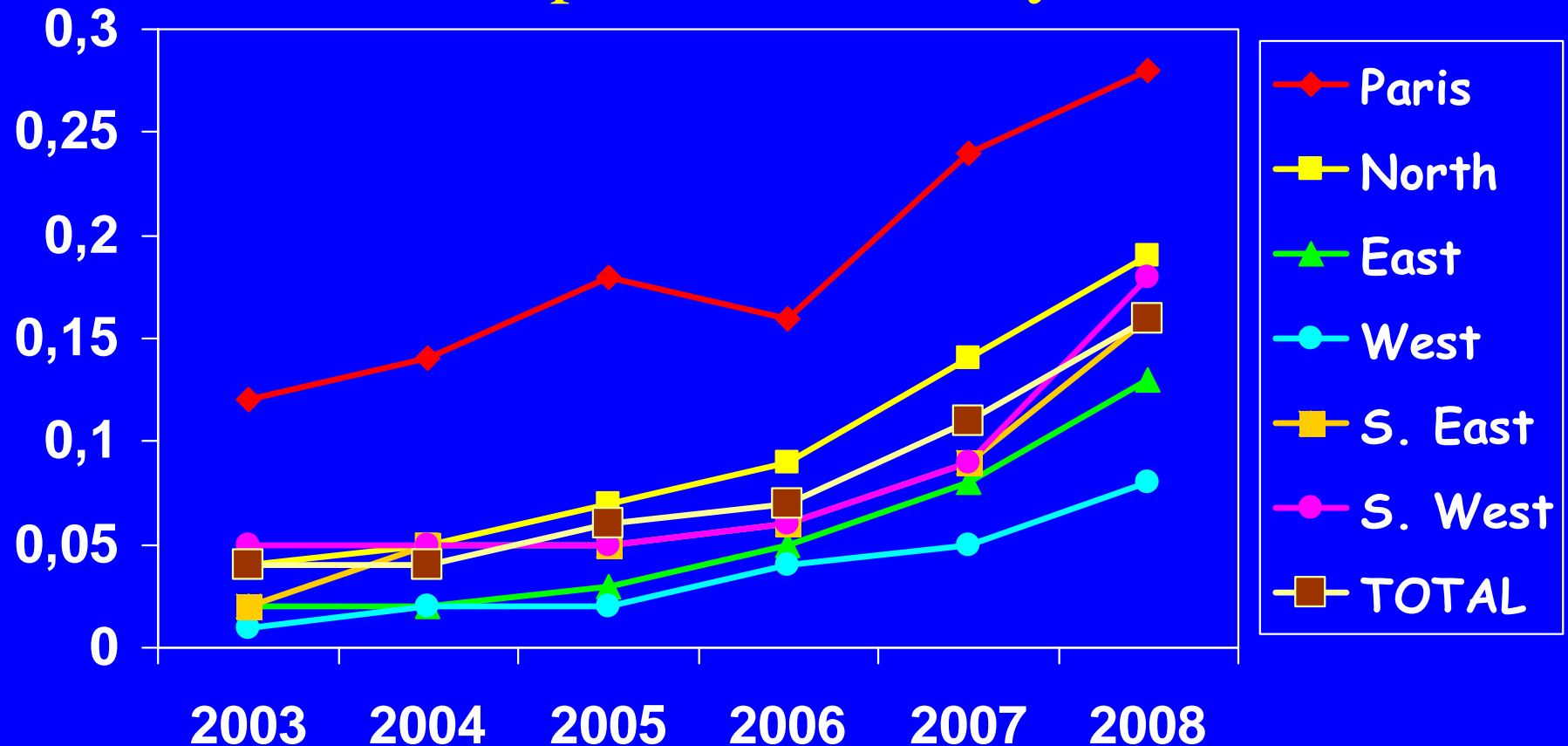
ESBL National survey (« RAISIN »)
Incidence rate / 1,000 DHs of ESBL per species
2002-2008 (3 months/year)



ESBL national survey (« RAISIN »)

Incidence rates of *E.coli*/ 1,000 DHs per area

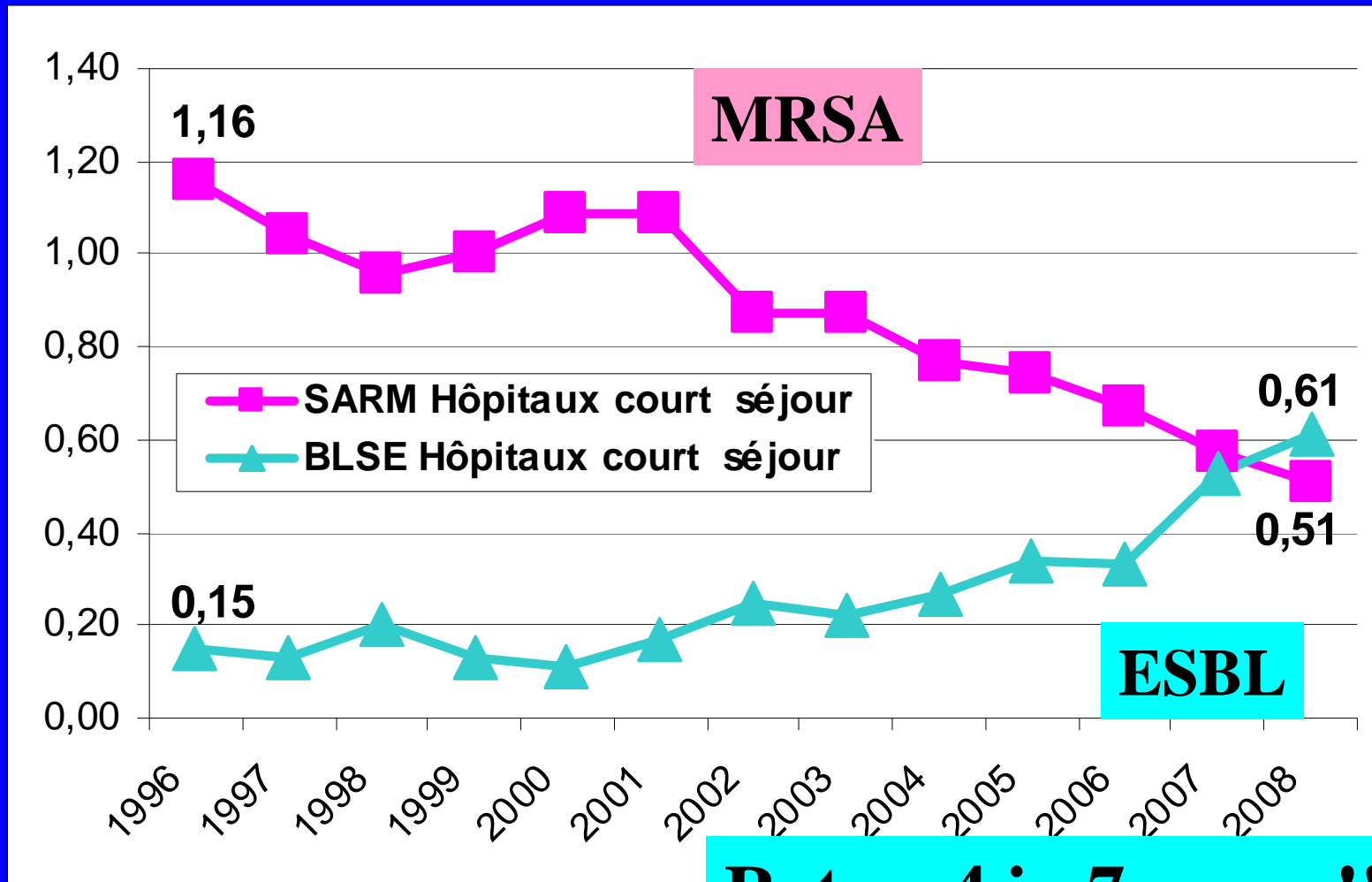
227 French hospitals 3 months/year 2003-2008



*National extrapolation :
~20,000 cases /year*

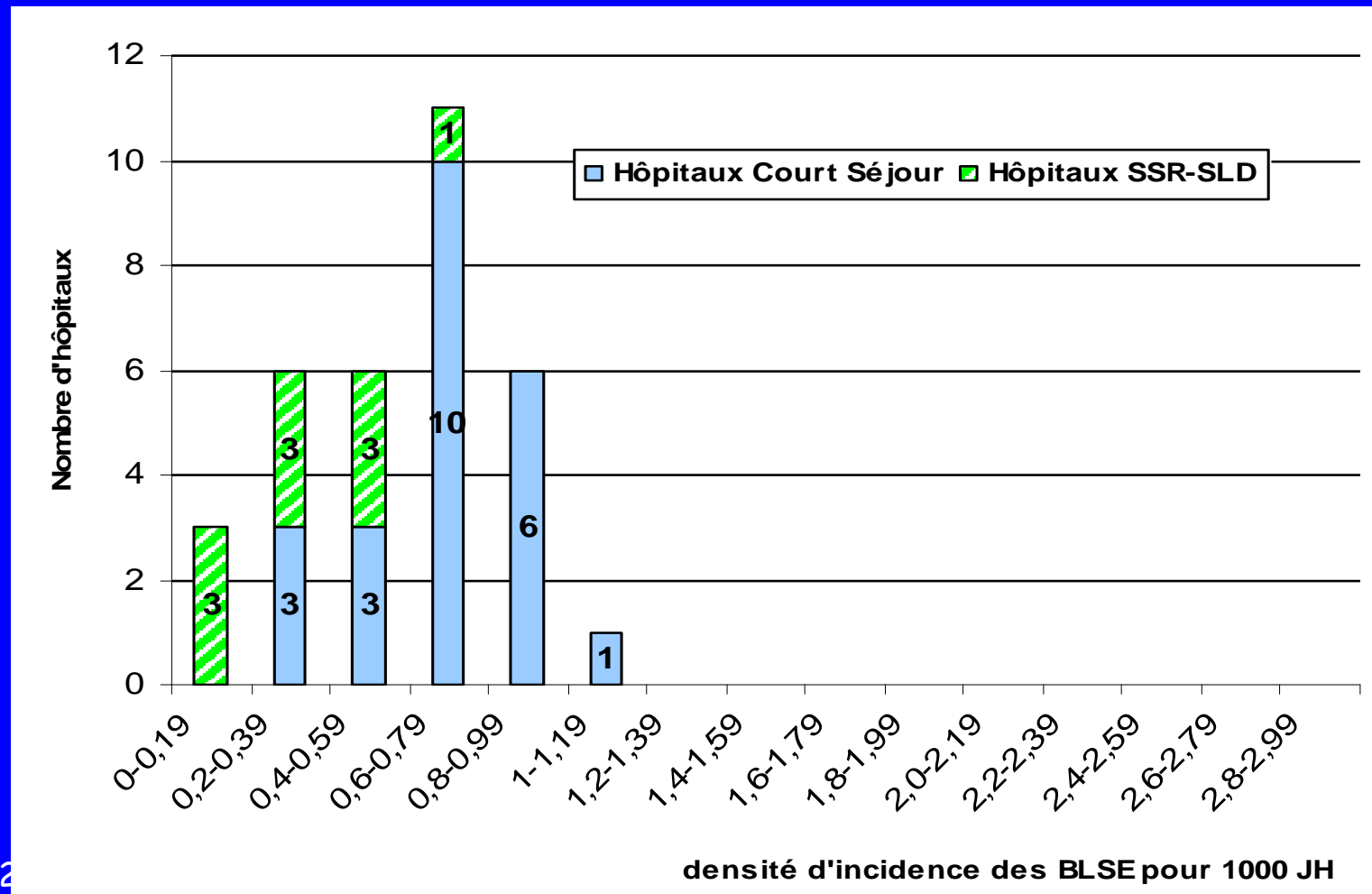
EBLSE at regional level
Assistance Publique -
Hôpitaux de Paris

MRSA and ESBL incidence/ 1,000 DHs Univ. hospitals of Paris area (n=39) 1996-2008



Rate x 4 in 7 years !!

Incidence (per 1,000 DHs) of EBLSE in the 33 hospitals of Assistance Publique - Hôpitaux de Paris, 2009



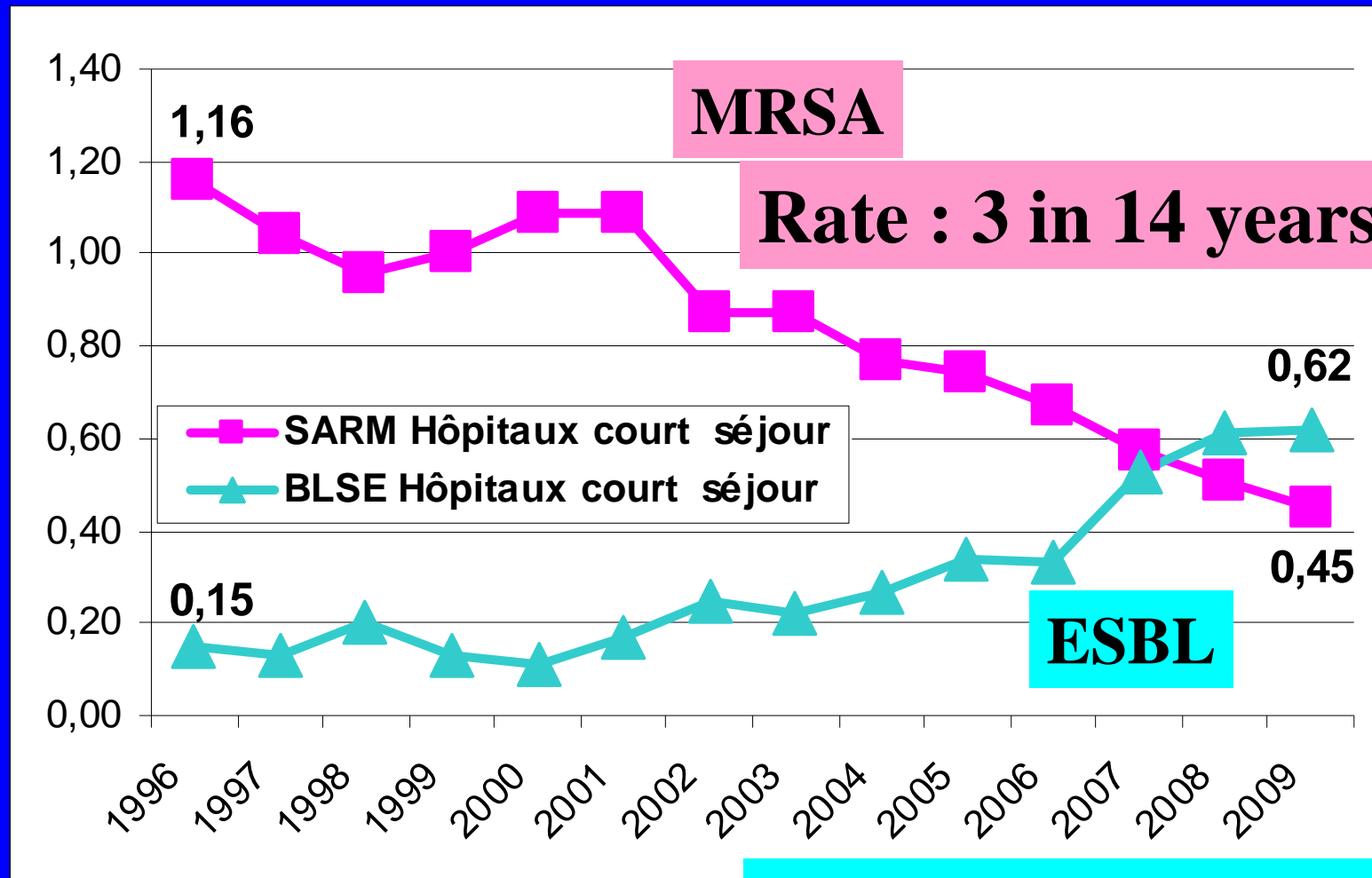
Types of wards where patients with EBLSE are hospitalized at the time of diagnosis, Paris area (Assistance Publique - Hôpitaux de Paris) 2009

Tous hôpitaux	955	100,0
Hôpitaux de Court séjour	825	86,4
dont : Urgences-service porte	54	6,5
Maternité	40	4,8
Pédiatrie	29	3,5
Médecine	231	28,0
Chirurgie	149	18,1
Total Soins Intensifs (SI) et Réanimation, dont	207	25,1
SI et Réa chirurgicale	83	10,1
SI et Réa médicale ou polyvalent	104	12,6
SI et Réa pédiatrique	20	2,4
Onco-hématologie	41	5,0
Services soins suite, réadaptation, longue durée	70	8,4
autre	3	0,3
Hôpitaux de SSR-SLD	130	13,6

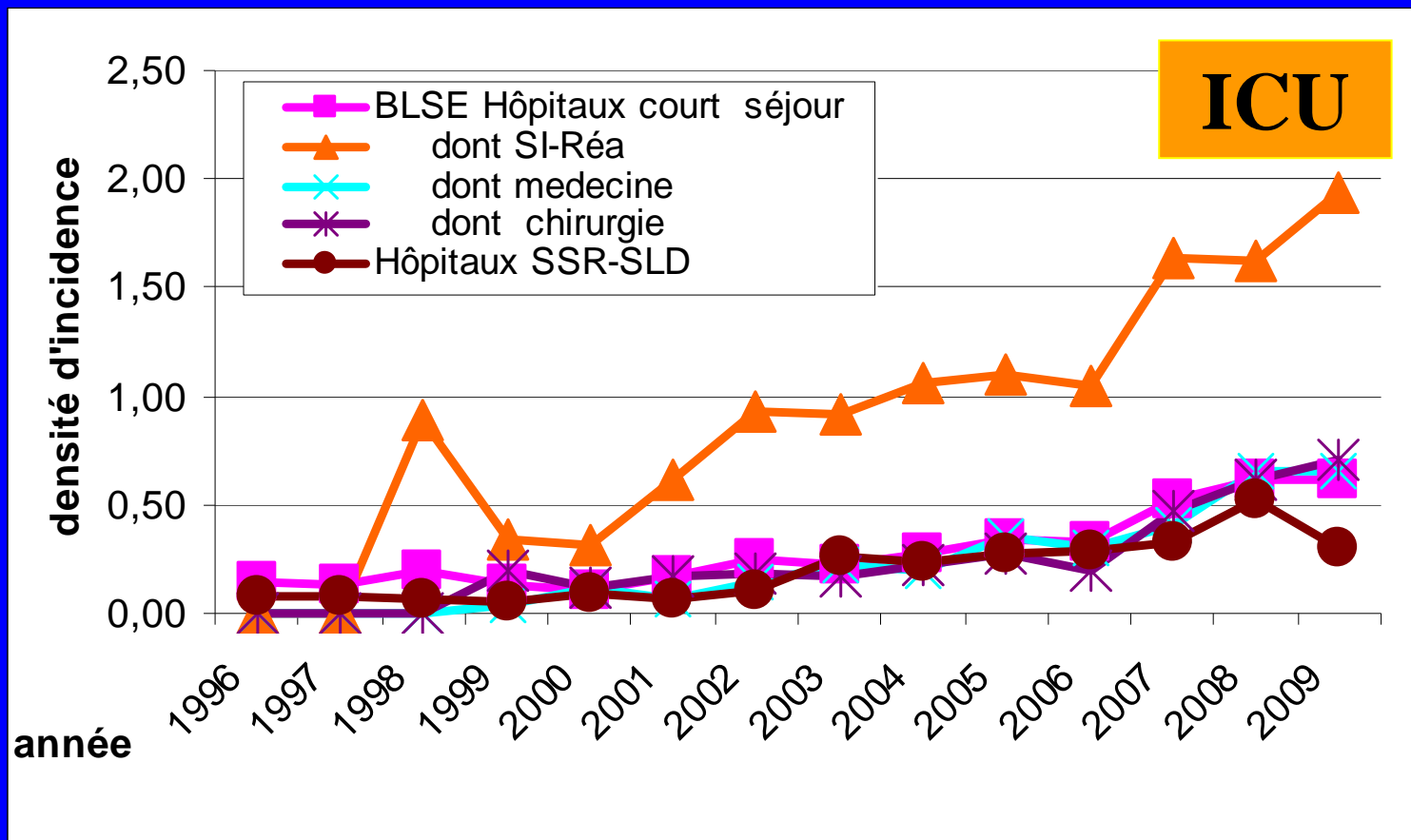
1st clinical sample from patient with EBLSE, Paris area (Assistance Publique - Hôpitaux de Paris) 2009

	N	%
Tous prélèvements	955	100,0
dont : Hémocultures	90	9,4
Séreuses, pus profonds	82	8,6
Prélèvements respiratoires protégés	57	6,0
Prélèvements respiratoires non protégés	42	4,4
Dispositifs intravasculaires	18	1,9
Urines	560	58,6
Autres	106	11,1

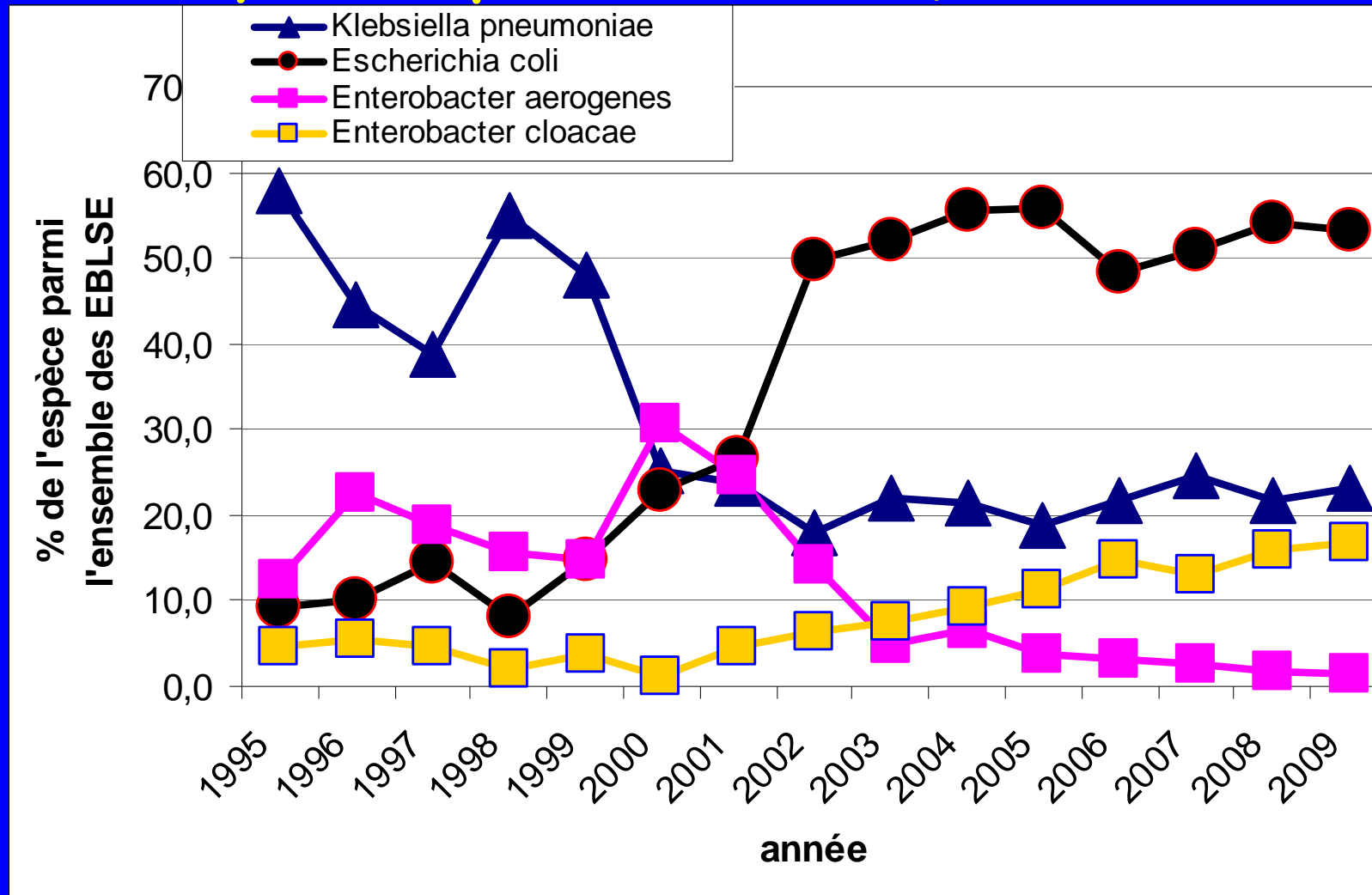
Incidence (per 1,000 DHs) of MRSA and EBLSE in acute care hospitals, Paris area (Assistance Publique - Hôpitaux de Paris) 1996-2009



Incidence (per 1,000 DHs) of EBLSE in different hospital activities, Paris area (Assistance Publique - Hôpitaux de Paris) 1996-2009



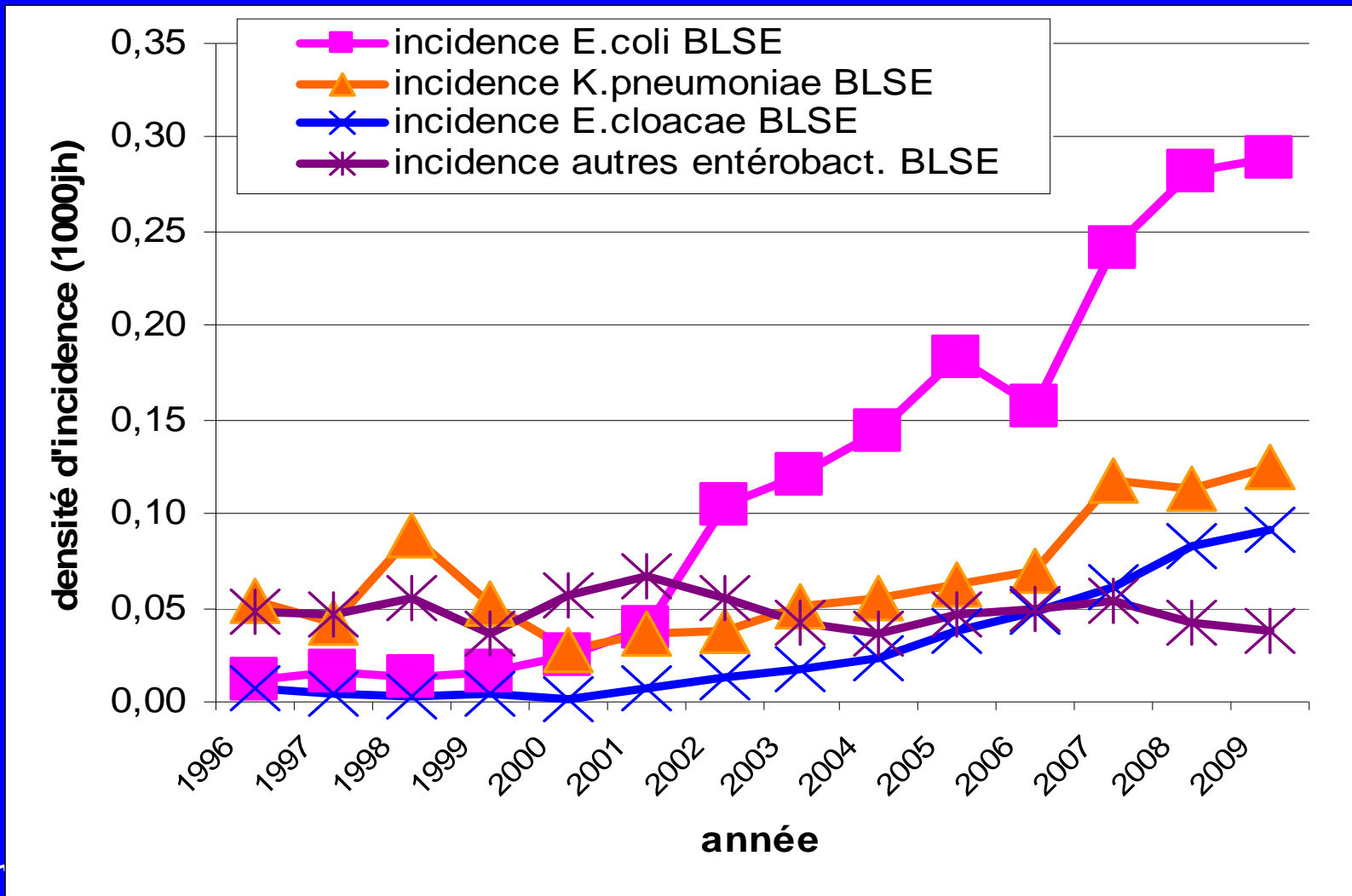
Proportion of main species (%) among ESBL enterobacteria, Paris area (Assistance Publique - Hôpitaux de Paris) 1995-2009



Proportion of species (%) among ESBL enterobacteria, Paris area (Assistance Publique - Hôpitaux de Paris) 2009

Espèces	N	%
<i>Escherichia coli</i>	507	53,1
<i>Klebsiella pneumoniae</i>	220	23,0
<i>Enterobacter cloacae</i>	161	16,9
<i>Enterobacter aerogenes</i>	14	1,5
<i>Citrobacter freundii</i>	12	1,3
<i>Klebsiella oxytoca</i>	12	1,3
<i>Proteus mirabilis</i>	12	1,3
<i>Citrobacter koseri</i>	5	0,5
<i>Providencia spp.</i>	0	0,0
<i>Serratia marcescens</i>	2	0,2
<i>Morganella morganii</i>	1	0,1
Autres	9	0,8
Total	955	100

Incidence (per 1,000 DHs) of *E.coli*, *K.pneumoniae*, *E.cloacae* BLSE, Paris area (Assistance Publique - Hôpitaux de Paris) 1996-2009



Suite sur autre diaporama

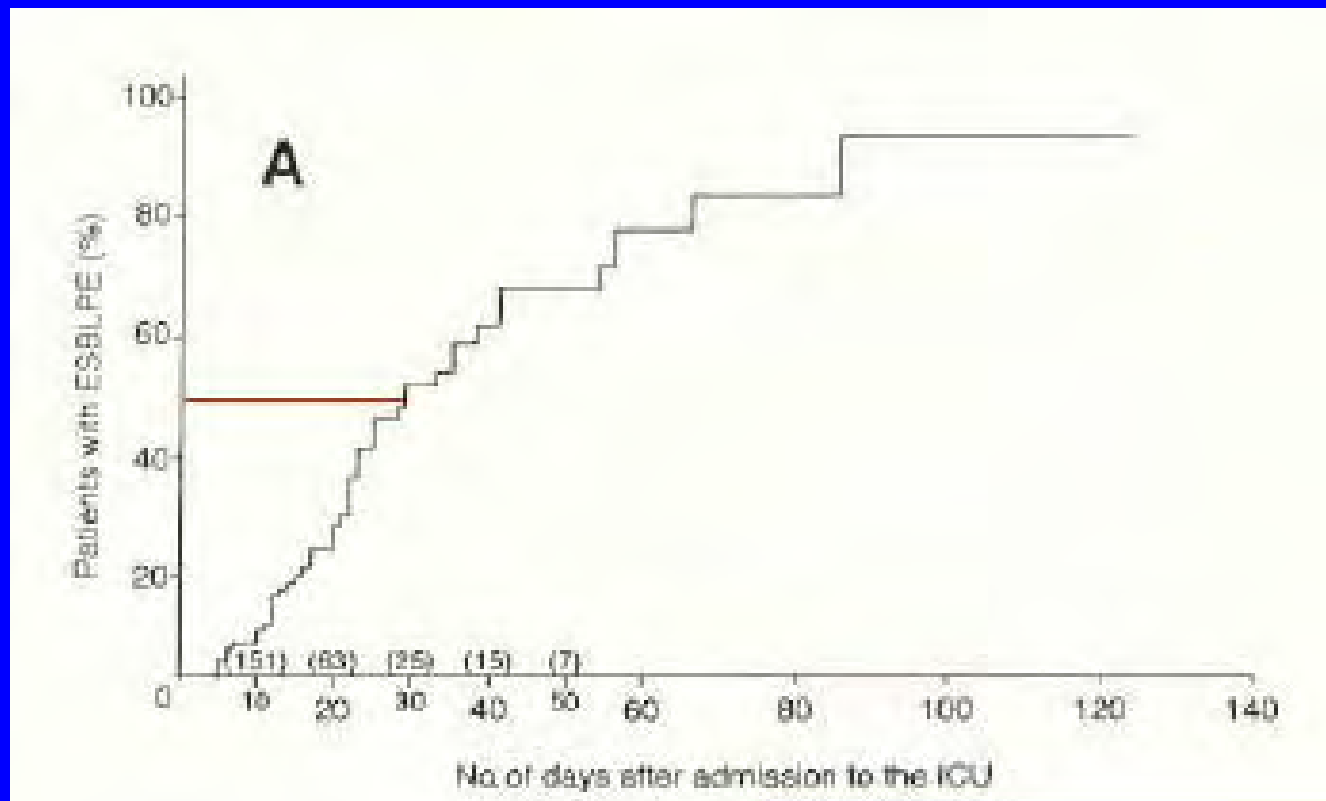
BLSE evolution : some tracks for analysis

ESBL in hospital
during the 1990s :

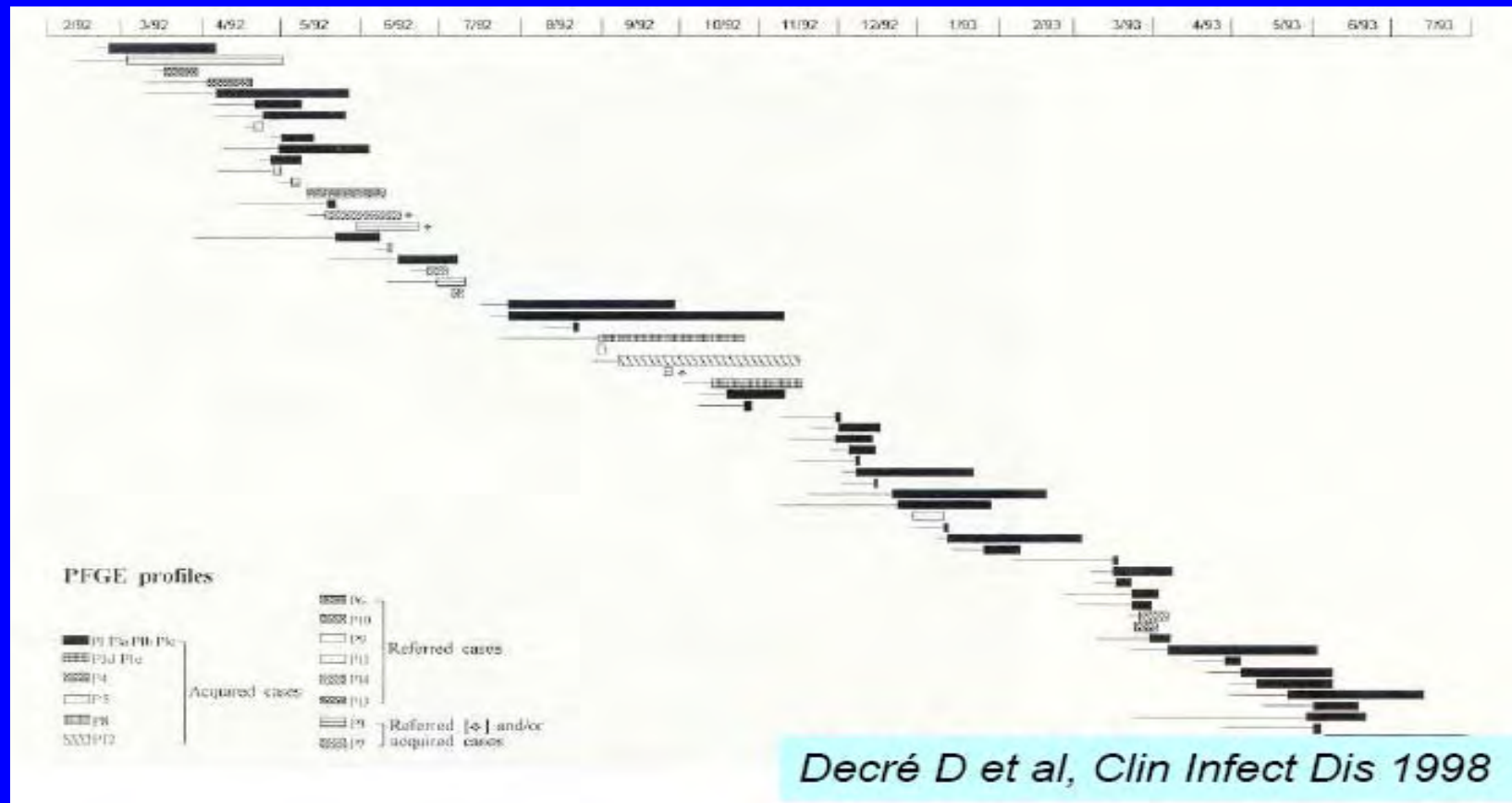
- cross-transmission
- antibiotic pressure

EBLSE and cross- transmission

Acquisition of ESBL over time in ICU (France)



Cross transmission of ESBL (5 french ICU)

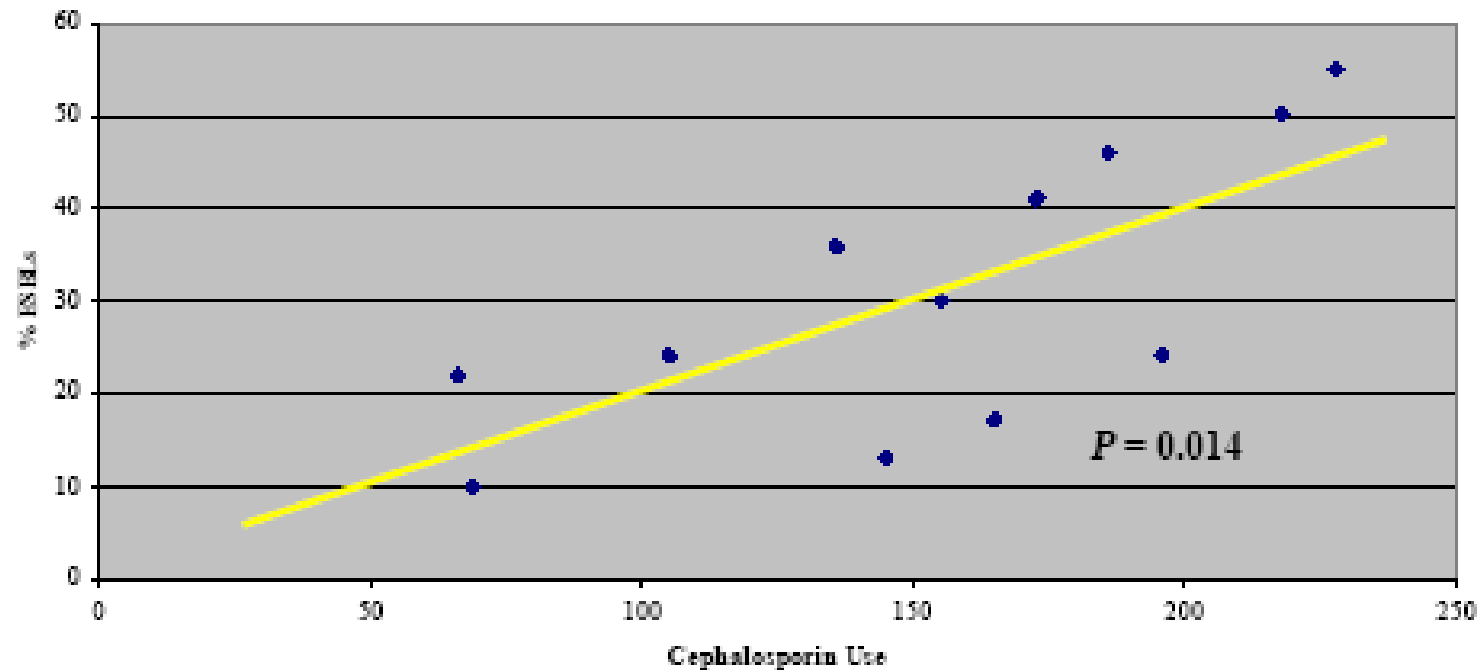


EBLSE and antibiotic pressure

ESBL rates end antibiotic consumption

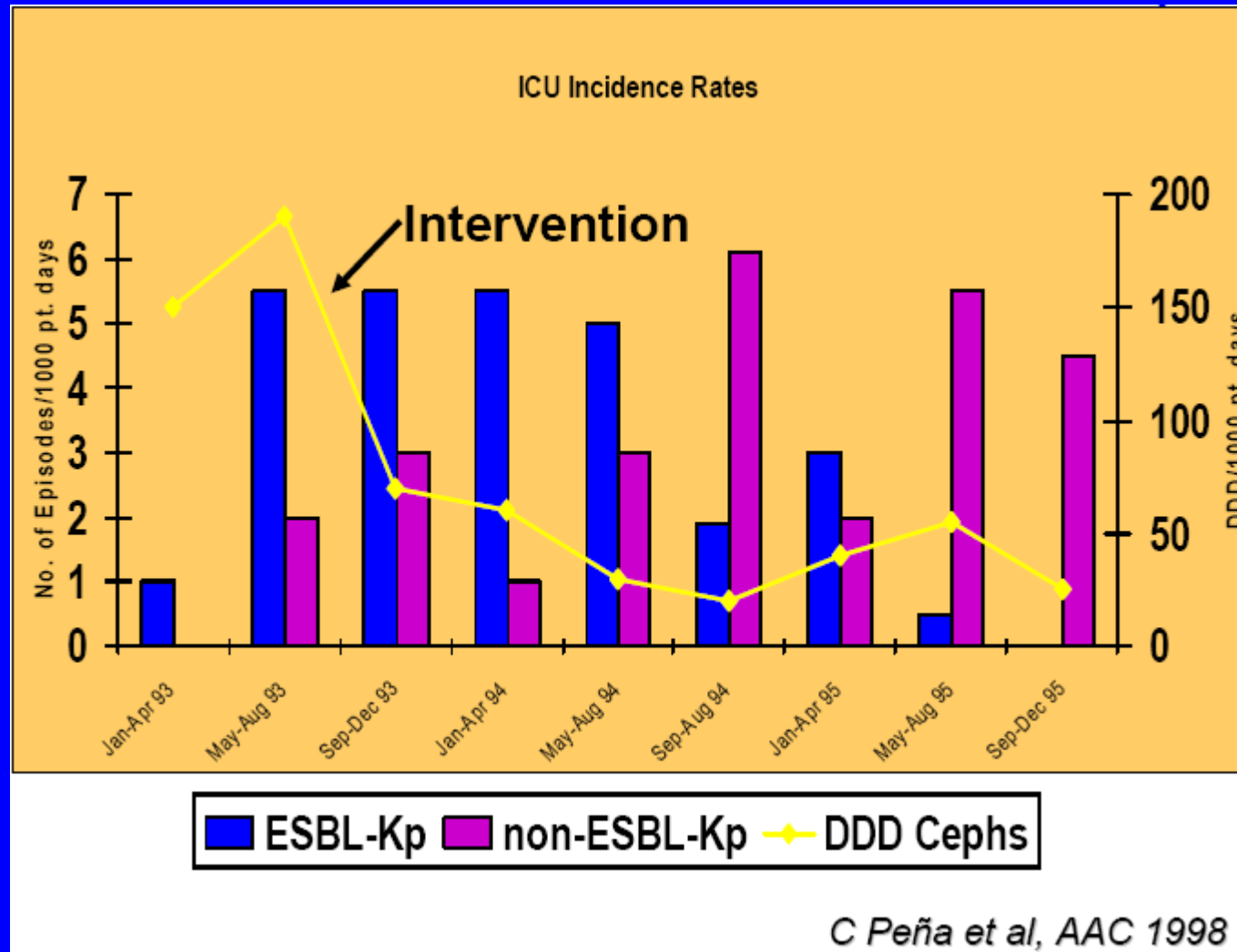
ESBLs in 12 Brooklyn Hospitals

Cephalosporin Use (DDD/1,000 days) vs % ESBLs in *Klebsiella*



JM Quale et al, CID, 2002

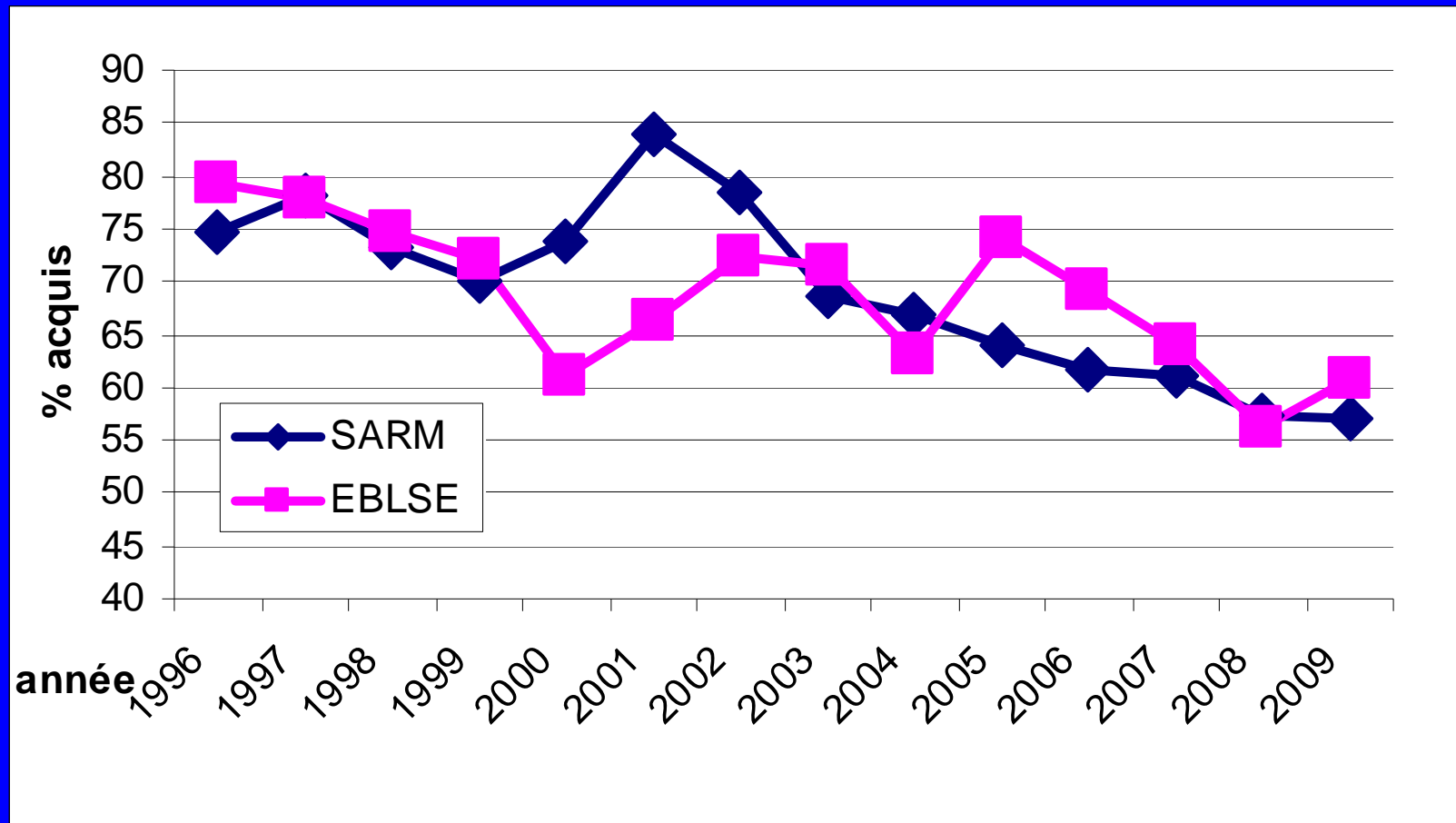
Impact of antibiotic restriction on ESBL rates



ESBL in hospital in recent years :

- Importation vs. acquisition ?
 - Community vs. hospital ?
 - animals and Environment ?

% of "acquired in hospital" among MRSA and EBLSE cases, Paris area (Assistance Publique - Hôpitaux de Paris) 1996-2009



Time (days) between admission and
E.coli
bacteremia diagnosis
EARSS 2005-07 (distribution in %)

	<i>E. coli</i> 19.692		
	IR CTX	R ampi	S ampi
1-2 days	47	61	66
3-7 days	12	10	11
2-3 weeks	18	16	15
> 3 weeks	23	13	8

Time (days) between admission and *E.coli*
or *S.aureus* bacteremia diagnosis
EARSS 2005-07 (distribution in %)

	<i>E. coli</i> (n=19.692)			<i>S. aureus</i> (n=12.980)	
	IR CTX	R ampi	S ampi	SARM	SASM
1-2 days	47	61	66	34	44
3-7 days	12	10	11	15	20
2-3 weeks	18	16	15	22	23
> 3 weeks	23	13	8	29	13

**Ward where *E.coli*
bacteremias are diagnosed
EARSS-France 2005-07 (distribution in %)**

	<i>E. coli</i> 19.692		
	IR CTX	R ampi	S ampi
emergency	19	29	34
pediatrics	<1	2	2
obstetrics	<1	2	2
medicine	28	29	30
surgery	16	12	11
hemato K	9	5	4
ICU	17	13	8

**Ward where *E. coli* or *S. aureus*
bacteremias are diagnosed
EARSS-France 2005-07 (distribution in %)**

	<i>E. coli</i> (n=19.692)			<i>S. aureus</i> (N=12.980)	
	IR CTX	R ampi	S ampi	SARM	SASM
Emerg.	19	29	34	13	15
Pediatrics	<1	2	2	<1	3
Obstetrics	<1	2	2	<1	1
Medicine	28	29	30	37	35
Surgery	16	12	11	18	18
Hemato-K	9	5	4	3	5
ICU	17	13	8	20	18

**Ward where *E.coli*
bacteremias are diagnosed
EARSS-France 2002-08 (distribution in %)**

	2002	2003	2004	2005	2006	2007	2008
Emergency	2,1	1,3	1,2	1,4	2	2,6	3,6
Obstetrics	0	0	0,8	0,9	0	1,4	3,5
Pediatrics	0	0	2,1	0	0	2,7	5,8
Medicine	1,3	1,7	1,7	2,3	2,6	3,4	6,2
Surgery	1,6	1,3	2,1	3	3,5	4,1	7
ICU	2,7	3,6	2,7	3,7	7,1	7,3	9,9
TOTAL	1,7	1,8	1,7	2,4	3,1	3,9	5,9

Time (days) between admission and *E.coli*
bacteremia diagnosis
EARSS 2002-08 (distribution in %)

	2002	2003	2004	2005	2006	2007	2008
0-1 days	1,3	1,5	1,1	1,7	2,6	2,7	4
2-7 days	2,2	2,1	1,2	2,8	3,1	4,4	8,2
2 nd weeks	1	2,2	2,8	4,6	3,3	5,7	8,6
3rd-4th weeks	1,7	4,3	5	6,1	5,2	6,9	10,9
> 1 month	4,6	2,7	3,5	5,1	8,1	5,9	14,2
TOTAL	1,7	1,8	1,7	2,4	3,1	3,9	5,9

Ward where *K.pneumoniae* bacteremias (n=1.741) are diagnosed and time (days) between admission and bacteremia diagnosis
 EARSS-France 2005-07 (in %)

	IR CTX	S CTX
emergency	8	18
pediatrics	<1	3
obstetrics	<1	1
medicine	27	33
surgery	18	18
hemato K	6	7
ICU	30	13

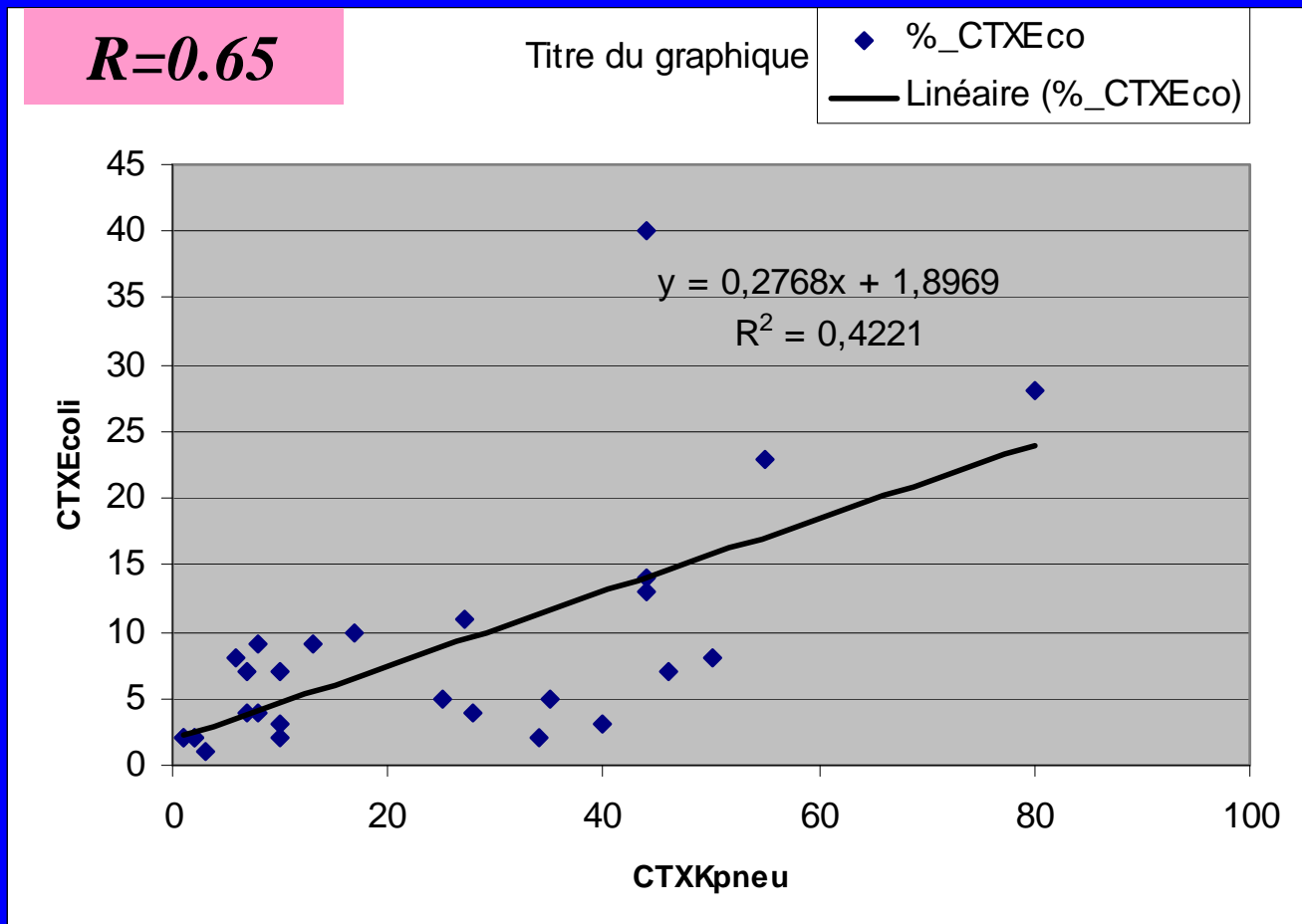
	IR CTX	S CTX
1-2 days	27	46
3-7 days	12	20
2-3 weeks	26	19
> 3 weeks	35	15

Ward where bacteremias are diagnosed and time (days) between admission and bacteremia diagnosis : *E.coli* vs. *K.pneumoniae* BLSE EARSS-France 2005-07 (in %)

	K.pn	E.coli
emergency	8	19
pediatrics	<1	<1
obstetrics	<1	<1
medicine	27	28
surgery	18	16
hemato K	6	9
ICU	30	17

	K.pn	E.coli
1-2 days	27	47
3-7 days	12	12
2-3 weeks	26	18
> 3 weeks	35	23

Relation 3rd Gen Cephalosporin-Resistance E.coli vs. K.pneumoniae EARSS 2007



Bactériémies E.coli BLSE Pitié-Salpêtrière 2001-06 (n=16)

Jours hôpital avant hémoculture :
moyenne 23, médiane 10, extrêmes 0-99

Réanimation >5 jours moment hémoc	9
ATCD hospitalisation	7
Procédures invasives	13*
Site primaire = urines	8
ATCD antibiothérapie	11**
Acquisition « nosocomiale »	11
Acquisition « liée aux soins »	4
Acquisition « communautaire »	1

V.Tarlier 2010

* 11 Sonde urinaire, 12 DIV, 6 ventilation ** 6 C3G, 8 FQ

Drieux 2009 ICHE

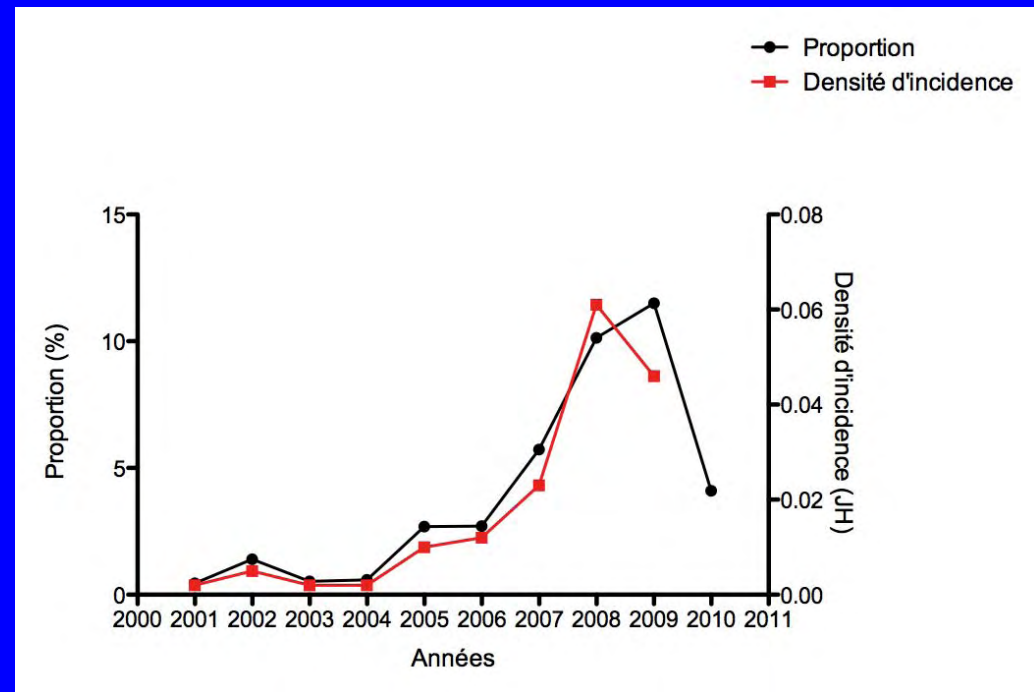
Bactériémies E.coli BLSE

Pitié-Salpêtrière 2001-06 (n=16)

	N	2001	2002	2003	2004	2005	2006 *
CTX-M15	8		2	1		2	3
CTX-M1	3				1	1	1
CTX-M9	2	1				1	
CTX-M14	1					1	
TEM-52	2		1				1

Bactériémies à *E.coli* BLSE isolés Hôpital Pitié-Salpêtrière 2001-2010

- ◆ N = 58
- ◆ Densité d'incidence 0,06 pour 1,000 JHs en 2009
- ◆ Proportion des *E.coli* BLSE 10% en 2009
- ◆ Tendence à la diminution durant en 2010 ????



Proportion des *E.coli* BLSE par rapport aux *E.coli* isolés d'hémocultures et densité d'incidence pour 1000 JH

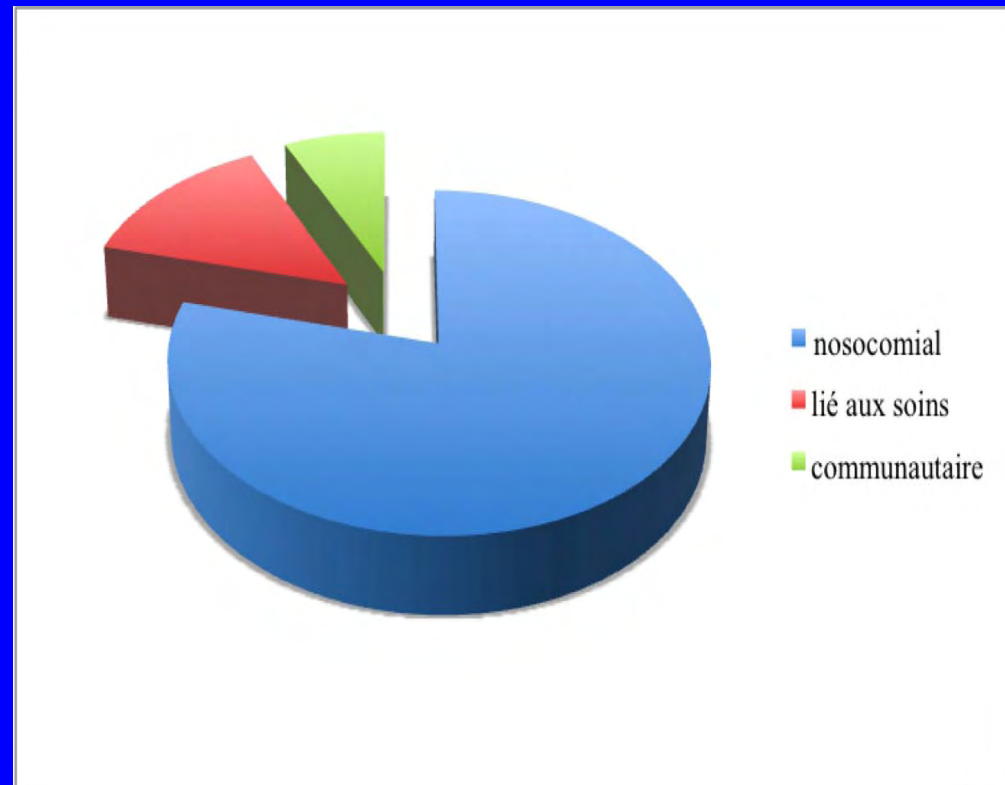
Bactériémies à *E.coli* BLSE

Pitié-Salpêtrière 2006-2009 : Origine des cas (critères de Friedman*)

- 46 cas considérés comme nosocomiaux : **79 %**
- 8 cas associées aux soins : **14 %**
- 4 cas considérés comme communautaires : **7 %**

* Délai entre la date d'admission à l'hôpital et la date de la 1ère hémoculture < 48h, n=13

* Pas d'antécédent d'hospitalisation dans les 3 mois, n=24



Bactériémies à *E.coli* BLSE

Pitié-Salpêtrière 2006-2009 : Types de BLSE

52 CTX-M

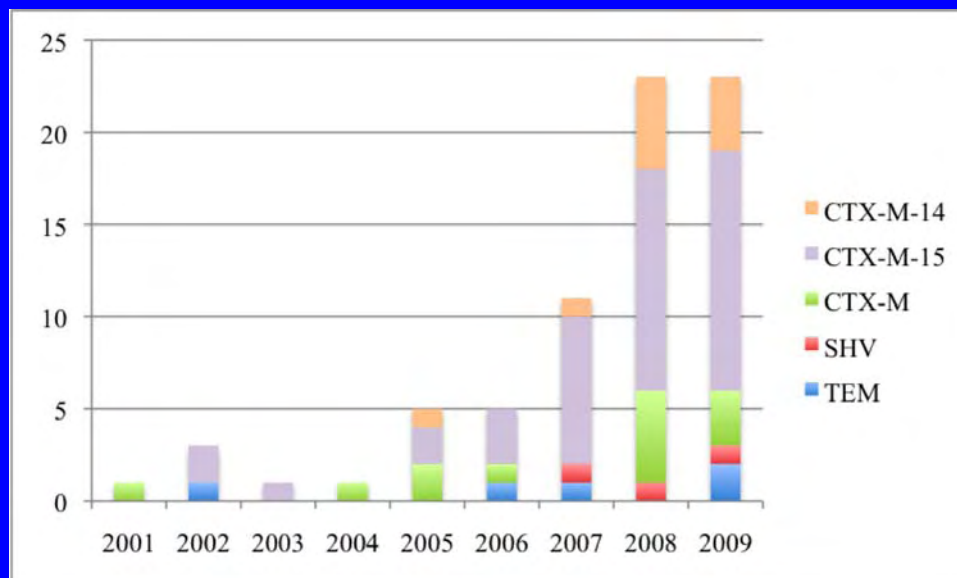
- 34 CTX-M-15
- 10 CTX-M-14
- 4 CTX-M-1
- 2 CTX-M-27
- 1 CTX-M-2

3 SHV

- 3 SHV-12

3 TEM

- 2 TEM-52
- 1 TEM-29



Bactériémies à *E.coli* BLSE

Pitié-Salpêtrière 2006-2009 : Gènes de résistance associés et co-résistances

◆ Corésistances :

aminosides 45%, sulfamides 79%, fluoroquinolones 79%

◆ Gènes de résistance aux aminosides et aux quinolones

- *aac(3)-II* (R à KGTN) : n=19 (33%)

- *aac(6')-Ib-cr* (R à KTNA + CIP NOR) : n =22 (40%)

- *qnrB* : résistance aux quinolones : n = 1

◆ CTX-M-15

91% CTX-M-15 : TEM-1 et/ou OXA-1

30% CTX-M-15 : TEM1, OXA-1 et AAC(6')-Ib-cr

Bactériémies à *E.coli* BLSE

Pitié-Salpêtrière 2006-2009 : Comparaison bactériémies *E.coli* non BLSE de 2006 à 2009

	AMX S	AMX I/R CTX S	BLSE	P	p CTX S vs. BLSE
N	224	328	58		
Age	61+/-18	59+/-18	57+/-15	0,22	
Sexe ratio	1,15	1,34	1,71	0,36	
Urgences	26 %	22 %	12 %	0,08	0,03
Réanimation	23 %	25%	46%	0,001	
Délai admission- hémoculture	10,3 +/-17j (médiane = 5j)	14 +/-29j (médiane = 7j)	20,1 +/-23,6 (médiane = 15,5j)	0,06	0,03
Durée séjour	32+/-34,5j	35+/-45j	47+/-41j	0,04	
Durée séjour après hémoc	23 j+/-32j (médiane = 10j)	24+/-43j (médiane = 11j)	28+/- 26j (médiane = 22j)		

Drieux 2010 soumis

Bactériémies à *E.coli* BLSE

Pitié-Salpêtrière 2006-2009 : Comparaison cas de bactériémies *E.coli* BLSE 2001-2006 vs 2006-2009

	2001-2006	2006-2009	p
Nombre de patients	16	58	
Age (ans)	51,1+/-11,1	57,3+/-15,4	
Antécédent d'hospitalisation	7 (44%)	39 (67%)	0,09
Délai admission-hémoculture (j)	17,9+/-21,3	16,9+/-16,2	0,8
Antécédent traitement antibiotique	11 (68%)	38 (65%)	
ATCD Fluoroquinolones	8 (50%)	13 (22%)	
Dispositif invasif	13 (81%)	45 (78%)	
Origine du cas : nosocomiale	14 (88%)	46 (79%)	
Mortalité à 30 jours	3 (19%)	8 (14%)	
Décès imputable à <i>E.coli</i> BLSE	3 (19%)	4 (7%)	0,4
BLSE type CTX-M-15	8 (50%)	34 (59%)	
Groupe phylogénique souches « extra-intestinales » »	10 (62%)	39 (67%)	

MDRO carriage rates at discharge of ICUs Pitié-Salpêtrière, Paris, 2008

		No samples	positive	No patients	positive
MICU	MRSA	1097	23 (2 %)	422	10 (<u>2 %</u>)
	ESBL all	1104	114 (10 %)	421	40 (<u>10 %</u>)
	id <i>E.coli</i>		75 (7 %)		28 (6 %)
SICU	MRSA	873	15 (2 %)	362	7 (<u>2 %</u>)
	ESBL all	783	124 (15 %)	340	39 (<u>11 %</u>)
	id <i>E.coli</i>		62 (7 %)		20 (6 %)

MDRO active surveillance (systematic screening) in ICUs at Pitié-Salpêtrière, Paris 2008

		ICU positive patients			
		No	admission	days / entry*	latter
MICU	MRSA	10	9/10	3	1/10
	ESBL <i>E.coli</i>	28	21/28	6	7/28
	Other <i>ESBL</i>	12	5/12	18	7/12
SICU	MRSA	7	6/7	15	1/7
	ESBL <i>E.coli</i>	19	14/19	12	5/19
	Other <i>ESBL</i>	20	9/20	22	11/20

MDRO baseline study in Chinese ICUs 2008-2009

MDRO carriage study in 8 teaching hospitals in RP China 2008-09

Hospital	No patients
Zhongshan Hospital Shanghai	140
Sino Japan Friendship Hospital	135
Guandong South Hospital	103
Shanghai Ruijin Hospital	95
Beijing People Hospital	79
Peking Union Hospital	73
Hunan Xiangya Hospital	69
Affiliated Hosp. of Peking Univ. 1st	22
Total	716

VJarlier 2010

**Robert,
Ma,
Jarlier
2010
en soumission**

Global MDRO carriage rates (%) at ICU discharge (MDRO China study)

	Global	Median	Range 8 hospitals
Any MDRO	52	44	28-71
MRSA	8	9	0-15
ESBL	42	34	19-68
A.baumannii	6	5	0-23

**MDRO carriage and "before ICU" features
(MDRO China study) : Length of stay in hospital
before ICU admission (days)**

	Mean	Median
No MDRO	12	6
MRSA	25	10
ESBL	28	8
Any MDRO	27	7

Length of stay before ICU = risk factor for MDRO in ICU

MDRO carriage and "ICU" features (MDRO China study)

1. stay in ICU : all patients

	% entry	% discharge	X
MRSA	3	8	2.7
ESBL	27	42	1.6
A.baumannii	1	6	6
Any MDRO	30	52	1.7

stay IN ICU = risk factor for MDRO acquisition

MDRO carriage and "ICU" features (MDRO China study)

2. stay in ICU : patients free of MDRO at ICU entry

	entry	% discharge
MRSA	0	5
ESBL	0	20
A.baumannii	0	6
Any MDRO	0	28

stay IN ICU = risk factor for MDRO acquisition

**MDRO carriage (%) and "ICU" features
(MDRO China study)
3. Antibiotic in ICU**

Yes/No antibiotics : non applicable since 98% Yes

	Prophylaxis (mean <u>3</u> days)	Treatment (mean <u>11</u> days)
MRSA	3	14
ESBL	35	49
A.baumannii	1	12
Any MDRO	40	65

Length antibiotherapy in ICU = risk factor for MDRO

MDRO carriage and "ICU" features (MDRO China study)

4. Antibiotic in ICU

Time of antibiotic start

	Prophylaxis (mean <u>3</u> days)	Treatment (mean <u>11</u> days)
Day 0	92	<u>93</u>
Day 1	8	<u>5</u>
Day 2	0	<u>1</u>
>day 2	0	<u>1</u>

Antibiotherapy in ICU = starts very early

MDRO carriers (%) and "post ICU" outcome (MDRO China study)

	Still in ICU at day 28	Another ward	Discharge
MRSA	14	51	16
ESBL	9	69	14
A.baumannii	13	14	18
Any MDRO	9	53	15

**Transfers after ICU =
risk factor for MDRO dissemination in hospital**

E.coli BLSE au CHU de Reims

- 159 malades avec E.coli BLSE en 12 mois (11/2006-10/2007)
- 1.7 % des E.coli
- Incidence 0.11 pour 1000 JH
- Médiane âge 74 ans
- 93% commorbidités :
18 % grabataires, 21% cancer, 33% diabétiques
- 16% traitement immunosuppresseur dans l'année précédente

E.coli BLSE au CHU de Reims

- 47% intervention chirurgicale dans l'année précédente
- 8% soins intensifs dans l'année précédente
- 37% soins à domicile avant hospitalisation
- Mode admission :
domicile 83%, transfert 13%, maison retraite 4%
- Nombre moyen de services avant Dg : 1,6
- Délai moyen hospitalisation avant Dg : 83 jours
- Délai hospitalisation avant Dg > 2 jours : 72%

E.coli BLSE au CHU de Reims

- 79% dispositif invasif :
DIV 62%, sonde urinaire 33%
- 79% antibiothérapie année précédente :
53% pénic, 36% céphalo 41% fluoroquin
- 3 hémocultures, 3 pus profonds, 54 ECBU
- Sensibilité aux antibiotiques :
40% tobramycine, 70% gentamicine,
18% nal, 43% ciproflo, 22% cotrimoxazole

E.coli BLSE au CHU de Reims

Service au moment du Dg

- réanimation 5%
- chirurgie 21%,
- médecine 42%
- SSR 25%
- SLD 4%
- pédiatrie 3%

E.coli BLSE au CHU de Reims

Principaux clones épidémiques

(BLSE, antibiotype, RAPD, pulsotype)

- CTX-M-9 = 31 cas
 - CTX-M-27 = 29 cas
 - CTX-M-15 a = 5 cas
 - CTX-M-15 b = 5 cas
 - CTX-M-15 c = 2 cas
 - CTX-M-15 d = 2 cas
 - CTX-M-61 a = 3 cas
 - CTX-M-61 b = 3 cas
 - CTX-M-14 = 2 cas
 - CTX-M-2 = 2 cas
- Total : 84 / 159

E.coli ESBL vs. non ESBL case-control study
2008-09, 8 AP-HP hospitals, 152/152 patients
Multivariate analysis

	OR (95 % CIs)	P
Birth out of Europe	2.4 (1.3 – 4.5)	0.01
Chronic infection	2.4 (1.0 – 5.8)	0.04
Previous hosp. < 6 months	2.0 (1.1 – 3.6)	0.03
ATB before hosp (<6 months)	2.0 (1.0 – 3.8)	0.04
ICU	2.3 (1.1 – 5.0)	0.03
ATB current hosp	2.0 (1.0 – 3.8)	0.04

E.coli ESBL vs. no + samples
 case-control study
 2008-09, 8 AP-HP hospitals, 152/152 patients
 Multivariate analysis

	OR (95 % CIs)	P
Birth out of Europe	2.6 (1.3 – 5.4)	0.01
Chronic infection	9.7 (2.5 – 38.1)	0.001
Female	2.1 (1.1 – 4.0)	0.003
Dependent before hosp	4.8 (1.7 – 13.3)	0.003
≥ invasive device in hosp	3.6 (1.5 – 8.6)	0.005
ATB current hosp	3.1 (1.5 – 6.5)	0.003

E.coli ESBL vs. control (≤ 2 days)
 case-control study
 2008-09, 8 AP-HP hospitals, 66/66 patients
 Multivariate analysis

	OR (95 % CIs)	P
Vs. non ESBL		
Previous hosp. < 6 months	4.1 (1.5 – 11.1)	0.006
ATB before hosp (<1 months)	3.2 (1.1 – 9.0)	0.03
Vs. no + sample		
Collective housing	17.1 (1.9 – 152)	0.01
Invasive device before hosp	3.6 (1.5 – 8.9)	0.006

Suite sur autre diaporama

ESBL enterobacteria
in wastewater system :
a new concern for the
future

ESBL in hospital wastewater (1) Brazil

Detection of extended-spectrum β -lactamase-producing *Klebsiella pneumoniae* in effluents and sludge of a hospital sewage treatment plant

T. Prado¹, W.C. Pereira¹, D.M. Silva¹, L.M. Seki², A.P.D'A. Carvalho² and M.D. Asensi²

1 Department of Sanitation and Environmental Health – Public Health National School, Oswaldo Cruz Foundation – Rio de Janeiro (RJ), Brazil

2 Department of Bacteriology – Oswaldo Cruz Institute, Oswaldo Cruz Foundation – Rio de Janeiro (RJ), Brazil

Letters in Applied Microbiology 2008

ESBL producing *Klebsiella pneumoniae* in hospital wastewater in Rio de Janeiro, Brazil

- Hospital of metropolitan area of Rio de Janeiro, Brazil
- Surgery, dialysis, medicine, rehabilitation, laboratories, laundry
- 2,000 patients per month, 800 employees
- Analyzing wastewater before and after treatment plant

Total coliforms :

influent (before treatment plant) 10^6 /ml

Effluent (after) 10^5 /ml, filtered effluent 10^3 /ml

ESBL *K.pneumoniae* :

Table 2 Frequency (%) of extended-spectrum β -lactamase (ESBL)-producing *Klebsiella pneumoniae* isolates from the different stages of the hospital sewage treatment plant

Site (n = number of bacterial isolates)	ESBL-positive isolates n (%)	ESBL-negative isolates n (%)
Influent (n = 15)	8 (53.3)	7 (46.7)
Sludge (n = 6)	3 (50.0)	3 (50)
UASB effluent (n = 16)	7 (43.7)	9 (56.3)
Filtered effluent (n = 6)	2 (33.3)	4 (66.7)
Total (n = 43)	20 (46.5)	23 (53.5)

ESBL in hospital wastewater (2) Portugal

**Leakage into Portuguese aquatic environments
of extended-spectrum- β -lactamase-producing
Enterobacteriaceae**

Elisabete Machado^{1,2}, Teresa M. Coque³⁻⁵,
Rafael Cantón³⁻⁵, João Carlos Sousa², Diana Silva¹,
Mayra Ramos¹, Joana Rocha¹, Helena Ferreira¹ and
Luísa Peixe^{1*}

J Antimicrob Chemother 2009

ESBL producing *Enterobacteria* in hospital wastewater in Portugal

- **8 samples :**
 - Raw wastewater downstream of 4 hospitals located in Porto area (n=5)
 - Sousa river, north of Portugal (n=1)
 - Porto marine coastal water (n=2)
- **16 ESBL enterobacteria :**
 - 11 *Klebsiella pneumoniae*
 - 4 *Escherichia coli*
 - 1 *Enterobacter aerogenes*

ESBL producing *Enterobacteria* in hospital wastewater in Portugal

- **Hospital wastewater :**
 - *E.coli* TEM 52
 - *K.pneumoniae* TEM-116
 - *K.pneumoniae* TEM-10 + SHV-27 + VIM-2
 - *K.pneumoniae* SHV-12
- **Sousa river :**
 - *E.coli* TEM-52
 - *E.aerogenes* TEM-24
- **Marine coastal water :**
 - *E.coli* CTX-M-14

ESBL in community wastewater in Spain

Extended-spectrum β -lactamase-producing Enterobacteriaceae in different environments (humans, food, animal farms and sewage)

Raúl Jesús Mesa^{1,2}, Vanessa Blanc², Anicet R. Blanch³, Pilar Cortés², Juan José González⁴, Susana Lavilla⁴, Elisenda Miró¹, Maite Muniesa³, Montserrat Saco⁵, M^aTeresa Tórtola^{2,4}, Beatriz Mirelis^{1,2}, Pere Coll^{1,2}, Montserrat Llagostera^{2,6}, Guillem Prats^{2,4} and Ferran Navarro^{1,2*}

J Antimicrob Chemother 2006

ESBL producing *Enterobacteria* in wastewater in Spain

- Raw urban sewage at 2 treatment plants :
 - a. Urban area 1,400,000 inh.
 - b. Population 400,000 inh.
- 5 samples
- **32 ESBL *Escherichia coli* clones**

ESBL in drinking water in Nepal

Serotyping, PCR, phage-typing and antibiotic sensitivity testing of *Salmonella* serovars isolated from urban drinking water supply systems of Nepal

D.R. Bhatta^{1,2}, A. Bangtrakulnonth³, P. Tishyadhigama³, S.D. Saroj⁴, J.R. Bandekar⁴, R.S. Hendriksen⁵ and B.P. Kapadnis¹

Letters in Applied Microbiology 2007

ESBL and drinking water in Nepal

- 300 samples of urban water supply system in Kathmandu (200), Pokhara (50), Biratnagar (50)
- 41 samples (14 %) positive for *Salmonella enterica* (all positive for *E.coli* used as a marker of fecal contamination)
 - 16 *Salmonella* Typhi
 - 7 *Salmonella* Paratyphi A
 - 16 *Salmonella* Typhimurium

ESBL and drinking water in Nepal

- All strains were susceptible to fluoroquinolones
- 3 *Salmonella* Enteritidis and 4 *Salmonella* Typhimurium carried the gene encoding SHV-12

ESBL and drinking water in Nepal

Authors Remarks

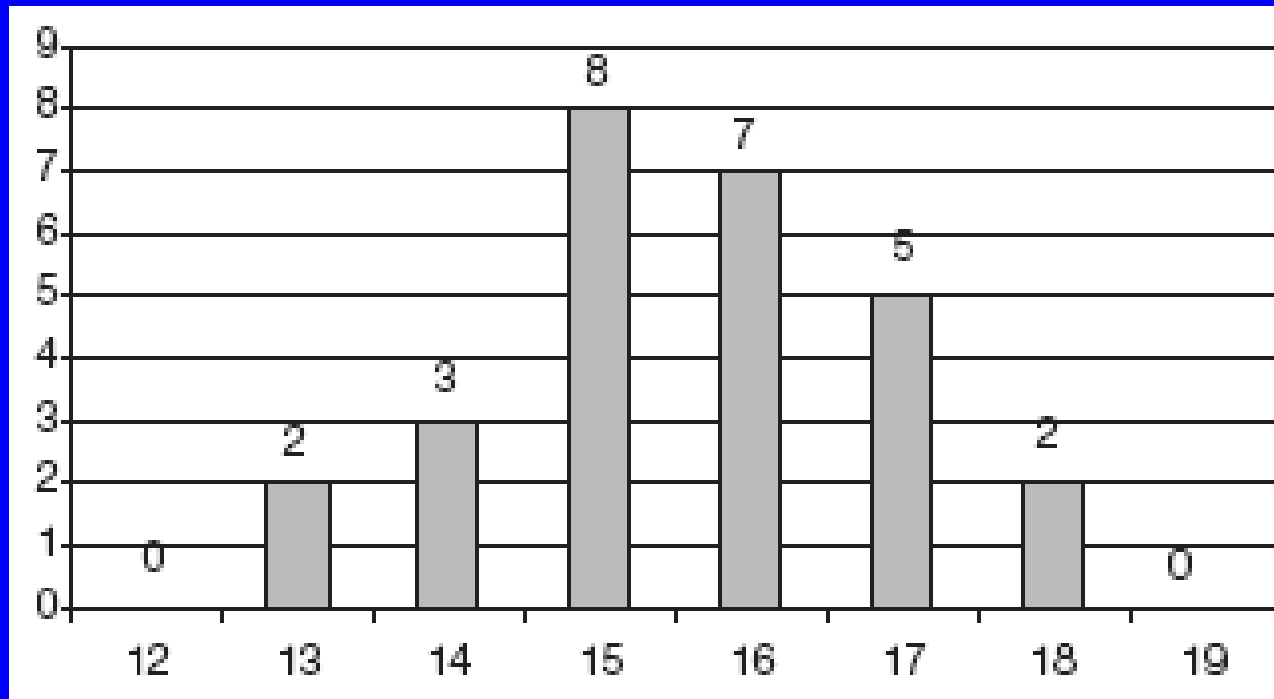
- Infrequent chlorination of drinking water
- Distribution pipelines are old , no regular maintenance
- Wastewater and drinking water pipelines are

Suite sur autre diaporama

ESBI *E.coli*:
outbreaks of single
strains ?

Epidémie *E. coli* BLSE Hôpital Trousseau

- Epidémie de 27 cas en 6 semaines
- Taux d'attaque 46 %
- 2 infections dont 1 méningite
- TEM-52



Diffusion épidémique E.coli
BLSE
en réanimation
à Baltimore

Harris AJIC 2007

E.coli BLSE en réanimation (Baltimore USA)

- Réa chirurgicale 19 lits, Réa médicale 10 lits**
- 2001-2004**
- 1806 admissions**
- Contexte de programme VRE**
- Prélèvement rectal admission puis hebdomadaire**
- 90 % malades inclus**
- 97 malades E.coli +**
- 74 à JO**
- 23 > JO (« acquis »)**

Harris AJIC 2007

E.coli BLSE en réanimation (Baltimore USA)

- **23 « acquis » :**
 - **3 (13%) même pulsotype**
et séjour « recouvrant » autre cas
 - **9 (39 %) même pulsotype**
- **Sur total 97 malades : 41 pulsotypes**
- **61/97 en 9 pulsotypes :**
15, 12, 9, 7, 5, 3, 3, 3 cas
- **n.b. 27 acquisition K.pneumoniae BLSE**

Harris AJIC 2007

Epidémies de *E. coli* BLSE

- **Cukier, Pathol Biol. 1999 :**
 - 1994, épidémie, SSR-SLD, AP-HP (G. Clémenceau)
 - 11 infections urinaires et 6 portages digestifs en 6 mois: même ribotype
 - Efficacité des mesures de signalisation, d'isolement technique et géographique
- **Paterson, CID 2001 :**
 - 1998, épidémie, transplantation hépatique, Pittsburgh
 - 6 cas dont 2 bactériémies, transmission croisée (PFGE)
 - Mains du personnel : prélèvements négatifs pour Ec BLSE
 - Efficacité des mesures d'isolement contact et de renforcement de l'hygiène des mains
- **Fang, JCM 2004**
 - 1999-2002, épidémie, 2 hôpitaux de Stockholm
 - 18 cas, 2 clones (PFGE) (10 et 5 patients), CTX-M-1 ± OXA ± TEM
- **Rodríguez-Baño, CID 2006 :**
 - 2001-2002, étude systématique, 1 centre « tertiary care » + 1 centre de soin de suite (transferts fréquents)
 - 47 cas en 16 mois dont 26 souches en 4 clones (REP-PCR, PFGE): 11, 11, 2, 2 cas : SHV-12 ± TEM ± CTX-M
 - Extension de l'épidémie entre les centres par transfert de patients
- **Pai H, Infect Control Hosp Epidemiol 2006 :**
 - 2003, épidémie, CHU, Corée
 - 29 cas en 10 mois, 18 souches identiques (ribotype) dont CTX-M-15+OXA-30+TEM-1
 - services différents, mais personnel partagé
- **Mendonça, AAC. 2007 :**
 - 2004-2006, étude systématique, Portugal, 3 régions, 9 hôpitaux:
 - 119 *E. coli* BLSE CTX-M (109 CTX-M-15, 9 CTX-M-14, 1 CTX-M-32),
 - 5 clones (PFGE) dont 76% 1 clone (OXA-30+TEM-1)
 - Transmission croisée de ce clone entre services et de l'hôpital vers l'extérieur

Enterobacteriaceae (Pseudomonas aeruginosa) in feces : % of carriers (load in log per gr dry weight)

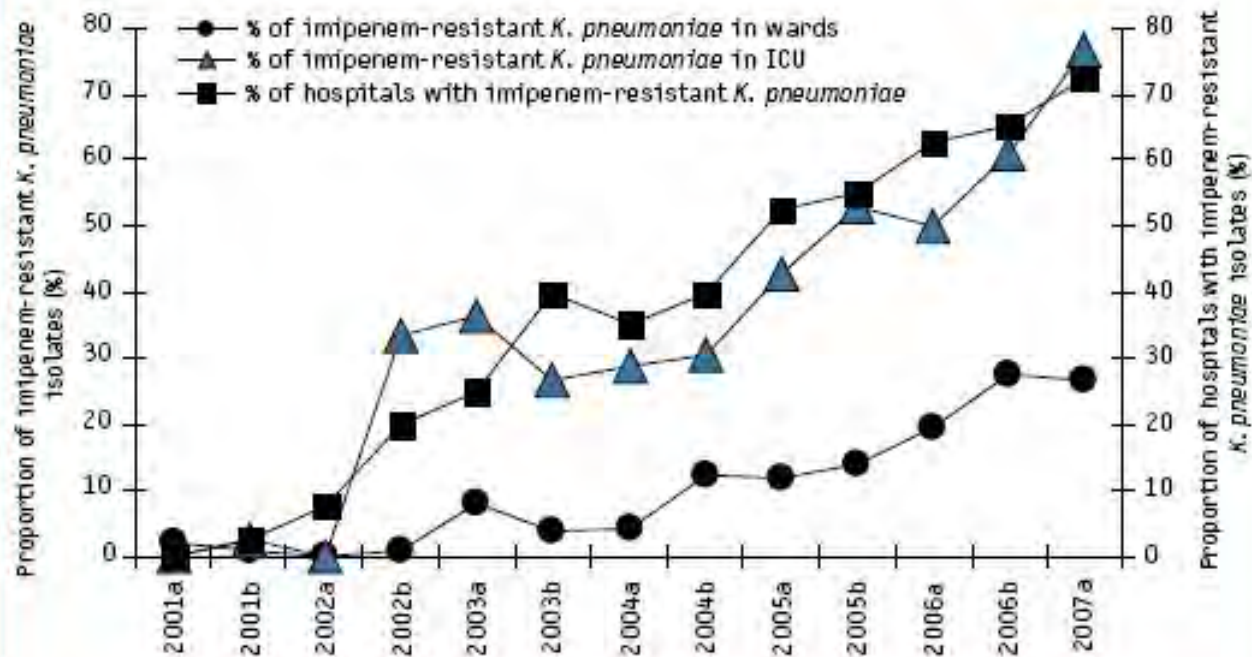
	Western diet (n = 62)	Vegetarian (13 strict, 14 partly)
<i>Escherichia coli</i>	94 % (9)	86-92 % (8)
<i>Klebsiella pneumoniae</i>	15 % (7)	43-46 % (8)
<i>Enterobacter cloacae</i>	13 % (7)	29-46 % (7)
<i>Enterobacter aerogenes</i>	2 % (7)	8-0 % (7)
<i>Pseudomonas aeruginosa</i>	5 % (5)	23-0 % (5)

**Tomorrow
(actually today) :
ESBL and
Carbapenemases :
break « the infernal
circle »**

K.pneumoniae IMP-R en GRECE

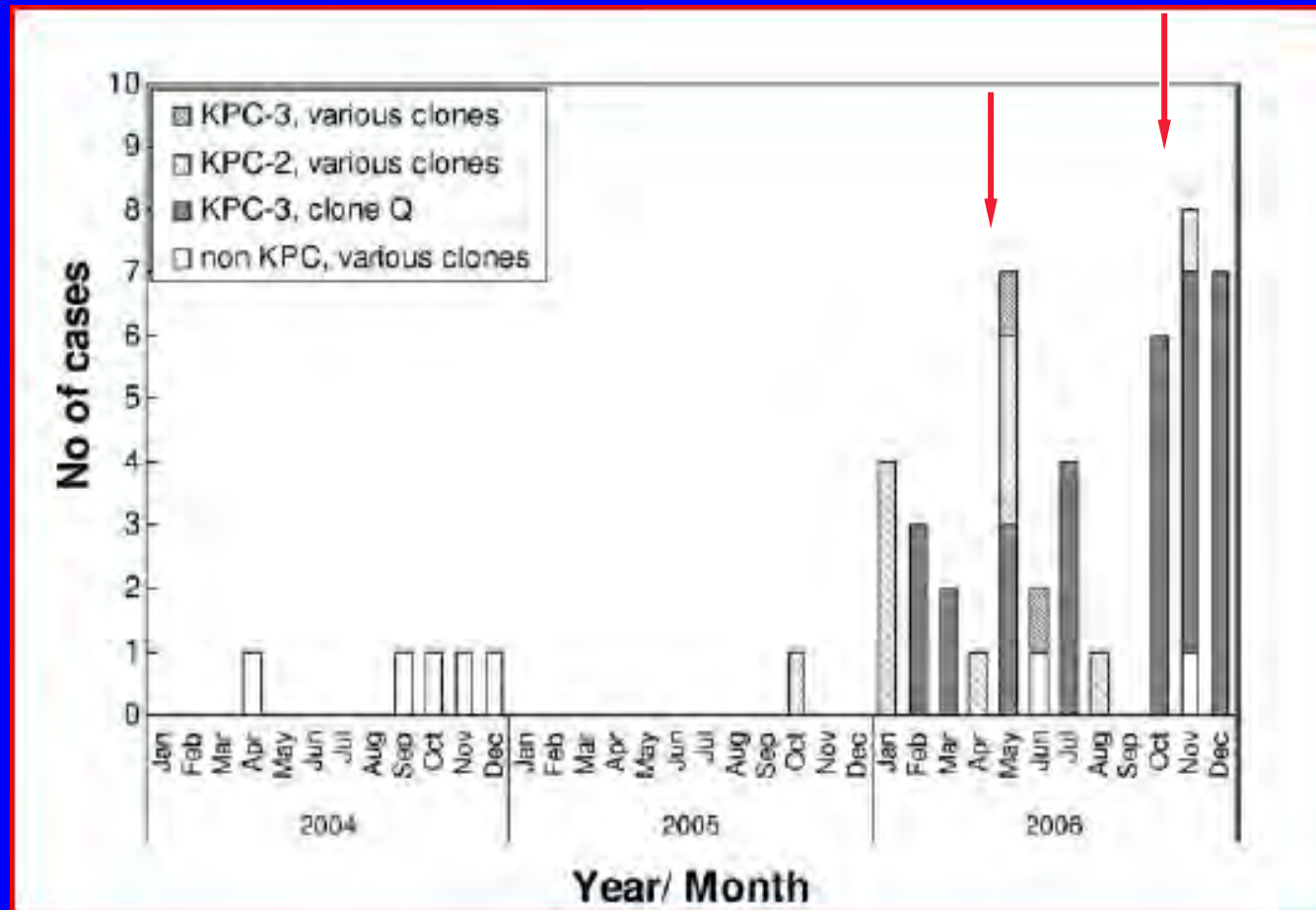
FIGURE 2

Trends in proportion of imipenem-resistant *Klebsiella pneumoniae* isolates in hospitals in Greece, 2000-2006



Data from the Greek System for the Surveillance of Antimicrobial Resistance (<http://www.mednet.gr/whonet>)

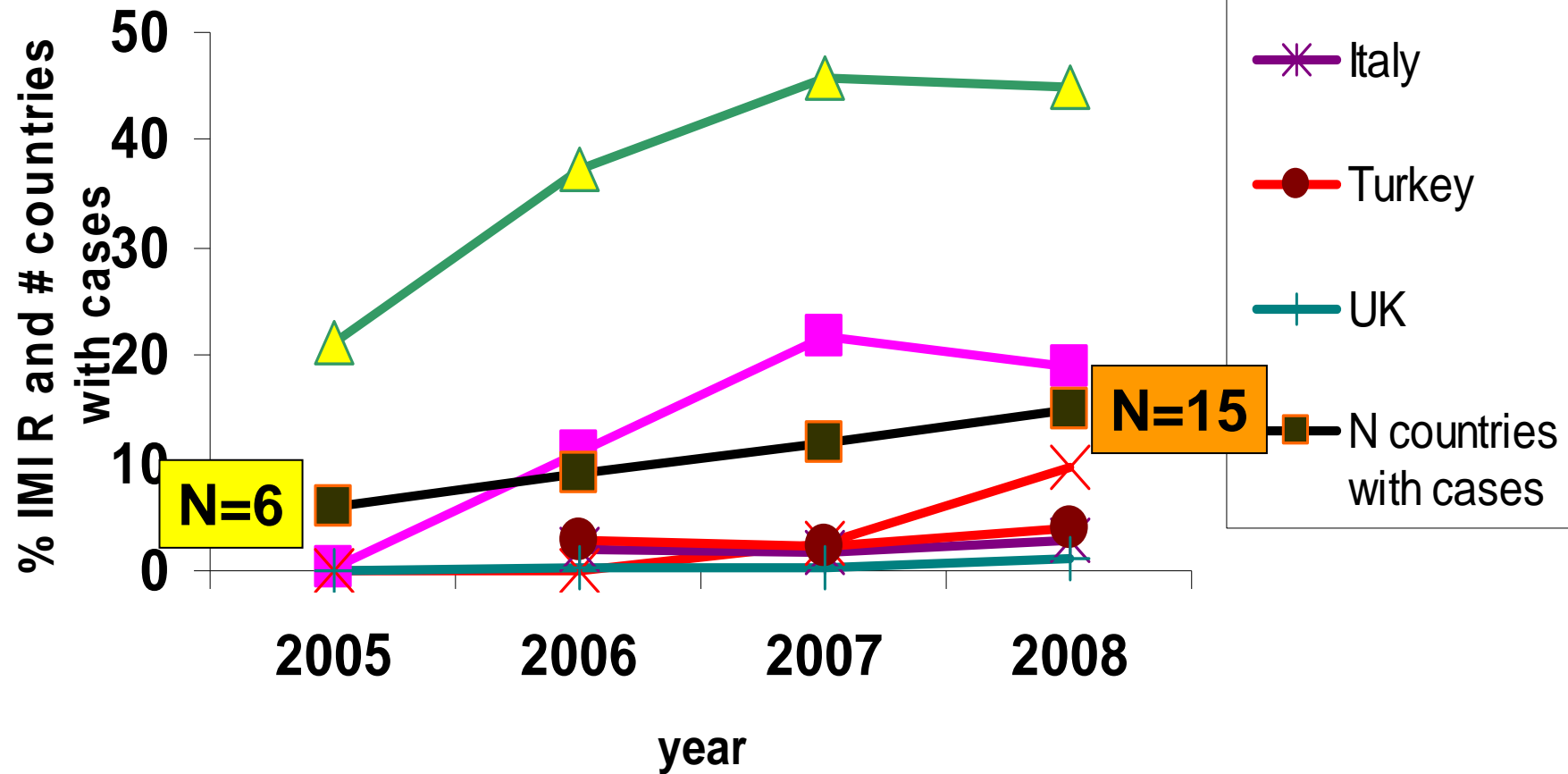
K.pneumoniae IMP-R en ISRAEL (Tel Aviv)



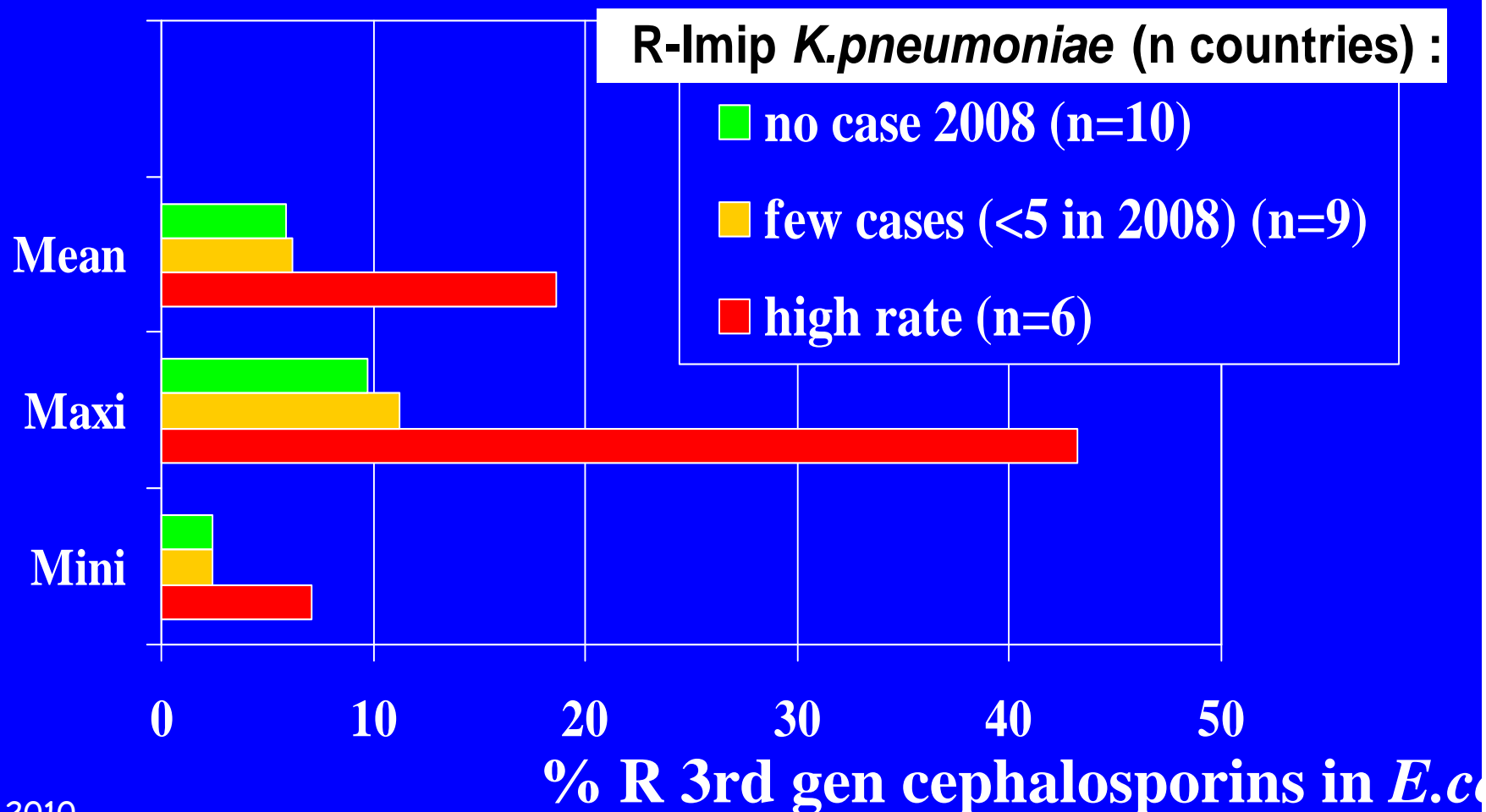
Epidémie de souches *K. pneumoniae* résistantes aux carbapénèmes possédant KPC-2 et KPC-3 dans un hôpital à Tel Aviv de 2004 à 2006.

12 clones différents et un clone majeur Q avec des **profils de sensibilité différents**

% R Imipenem in *K.pneumoniae* Bacteremias, EARSS 2005-08

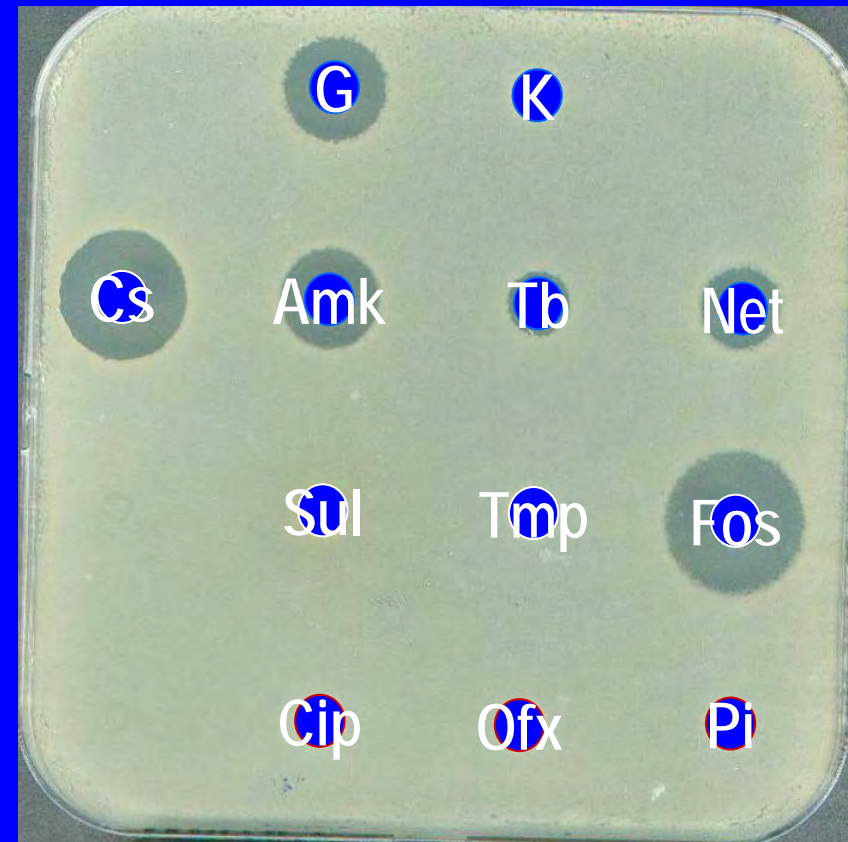
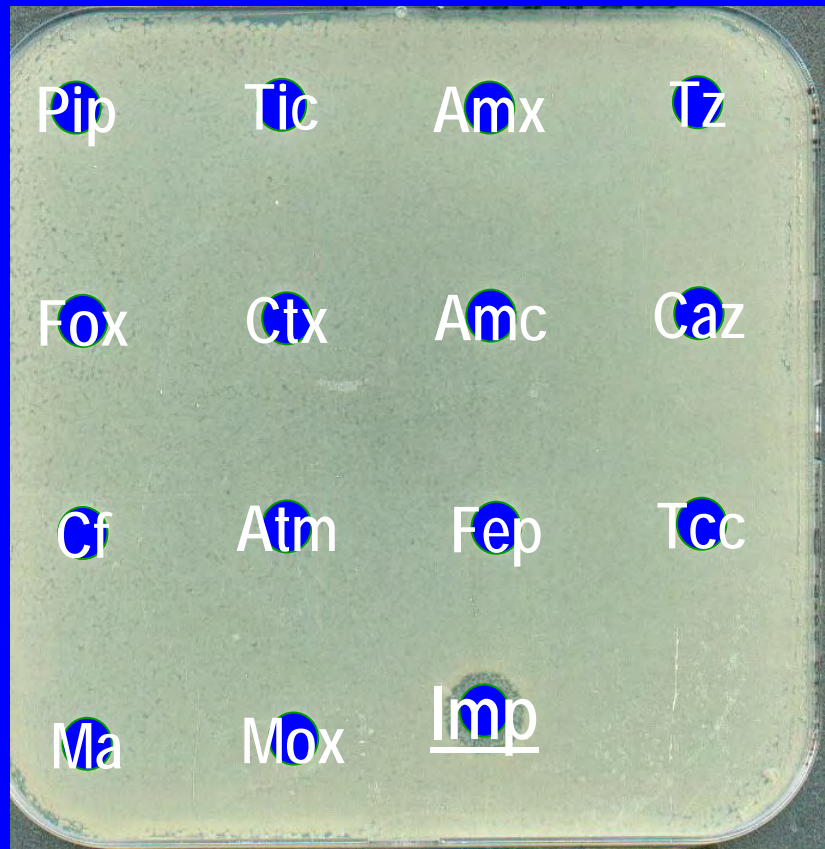


**% of strains R to 3rd cephalosporins in *E.coli*
according to the rates of Imip-R strains in
K.pneumoniae
 Bacteremias, EARSS 2008**



Paul Brousse hospital (Paris) 2004

Klebsiella pneumoniae VIM-1 + SHV-5
(index case : transfer from Athens)



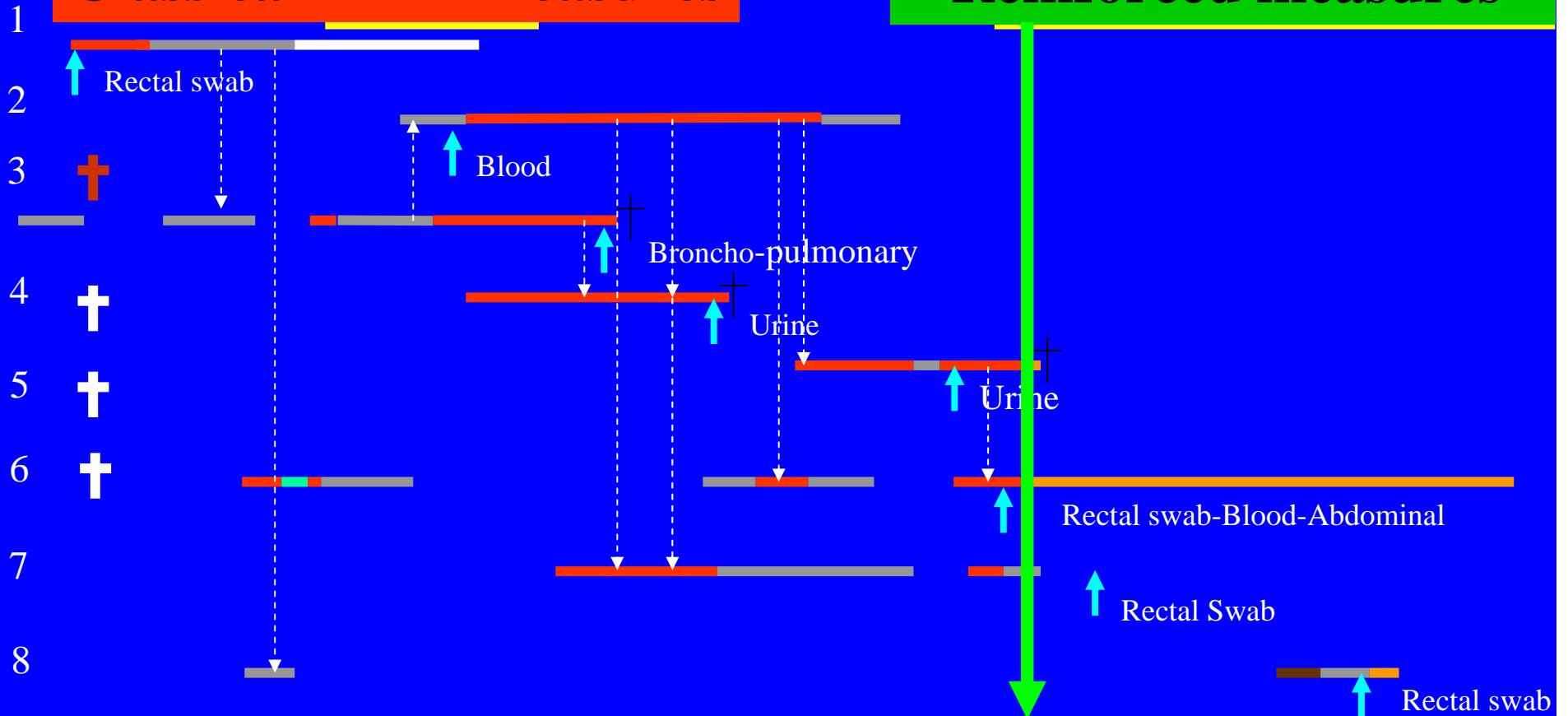
MIC : imipenem 32 mg/l ; gentamicin 8 mg/l

Paul Brousse hospital 2004

December January February March April May June July August

Classical MDR measures

Reinforced measures

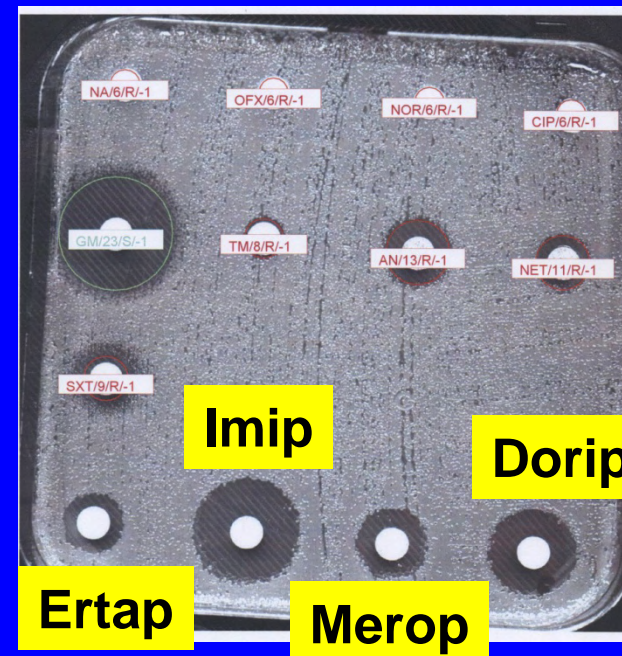


— ICU
— 4th floor
— 3rd floor
 VJarlier 2010
— Medecine unit

↑ First isolation of KP
+ No link + link

No new case since 2005

Kassis Chikhani 2009 submitted

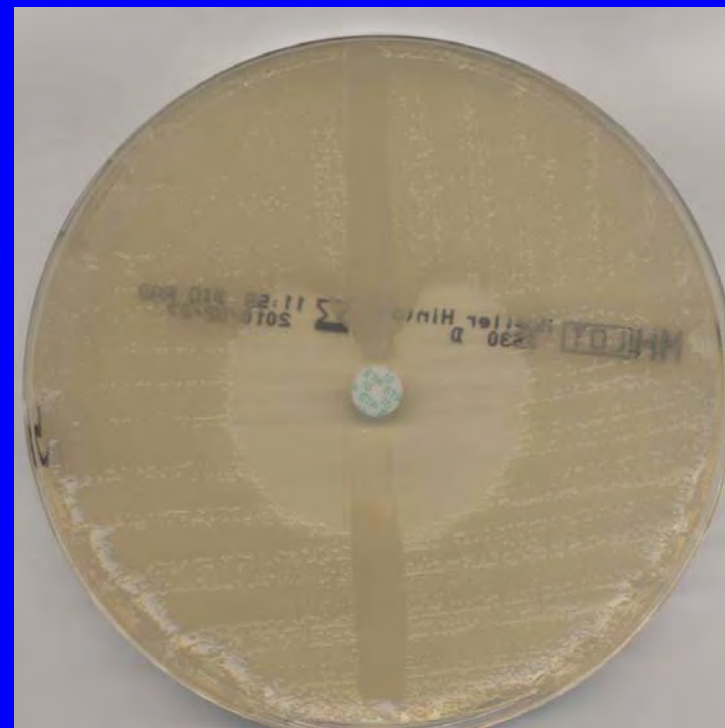


K.pneumoniae

KPC-2

P.Brousse 2009

**Courtesy :
N. Kassis-Chikhani**



Epidémie *K.pneumoniae* KPC-2 Bicêtre, Paul Brousse, Poissy Septembre-novembre 2009

- Cas initial suspecté : transfert hôpital de Grèce
- 7 cas secondaires en relation très probable avec endoscopie digestive
- 5 cas secondaires très probablement par transmission croisée

Application des mesures renforcées

« AP-HP 2008 » « émergence »

→ Pas de nouveau cas depuis novembre

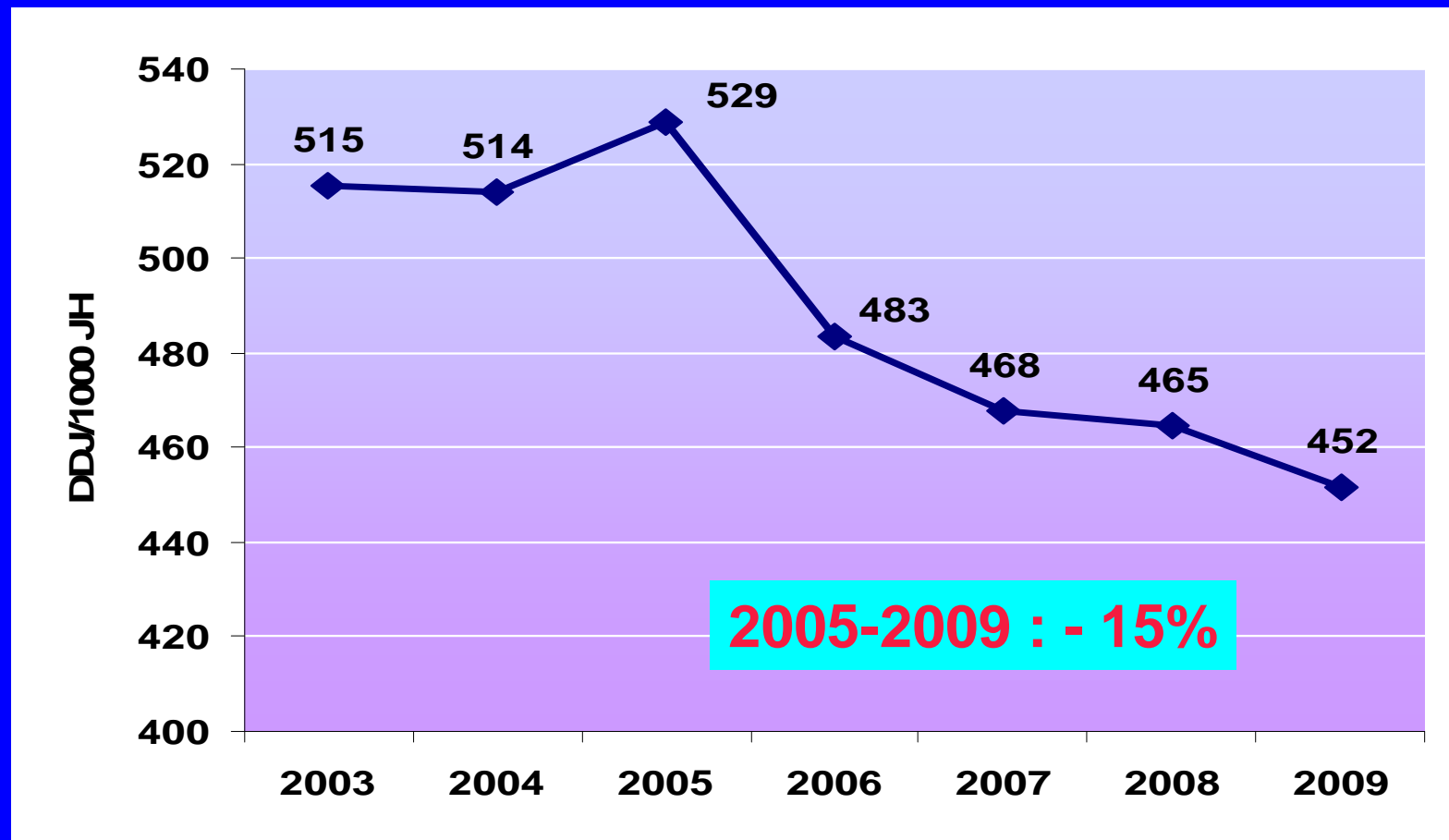
4 épidémies d'entérobactéries résistantes à l'imipénème à l'AP-HP 2004-2009

- 2004 Paul Brousse (Kassis-Chikhani JAC 2006)
 - *K. pneumoniae* VIM-1
 - 8 cas
 - patient source transféré d'un hôpital d'Athènes
- 2007 Saint Antoine
 - *K. pneumoniae* 4 cas
- 2008 Ambroise Paré
 - *K. pneumoniae* KPC2
 - 2 cas
 - patient source transféré d'un hôpital d'Athènes
- 2009 Bicêtre, P.Brousse, Poissy
 - *K. pneumoniae* KPC2
 - 13 cas (endoscope et transmission croisée classique)
 - Probable patient source transféré d'un hôpital de Grèce

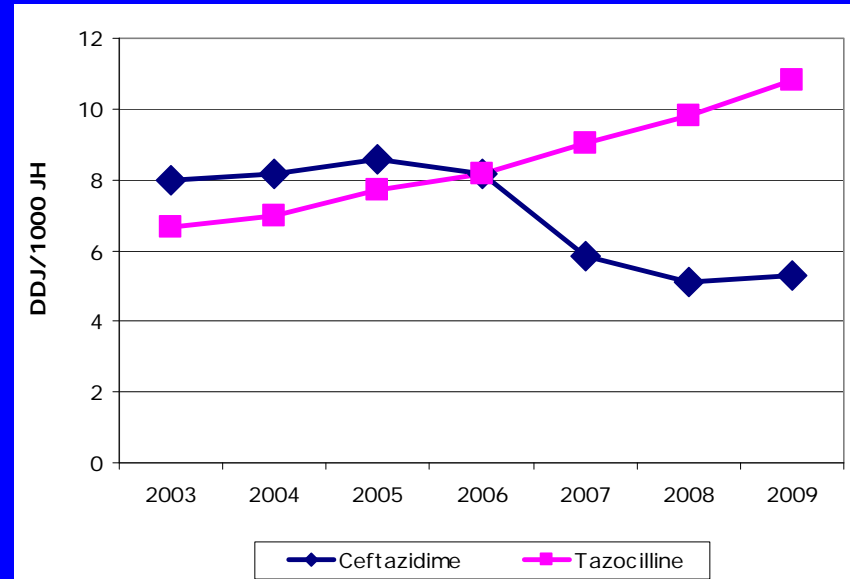
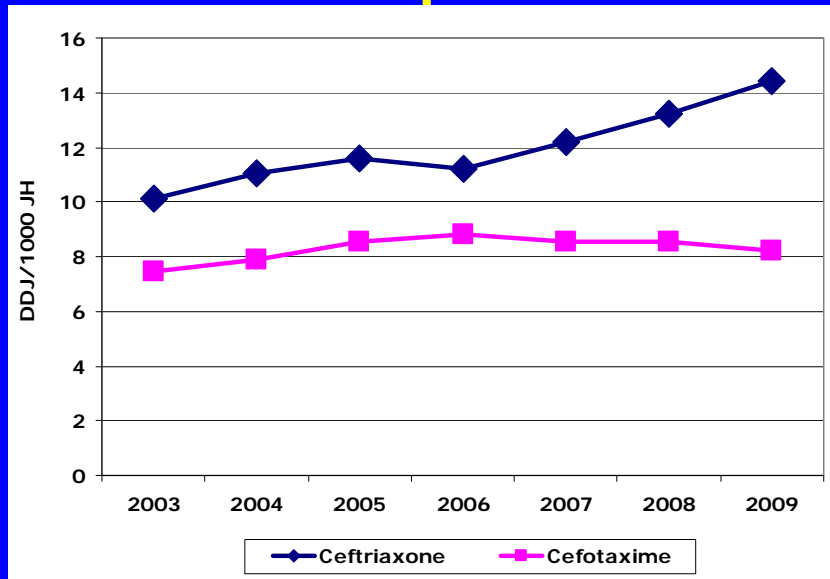
Evolution de la consommation des antibiotiques à l'AP-HP 2003-09

Source : AGEPS-Direction des finances

Analyse : EOH/DPM



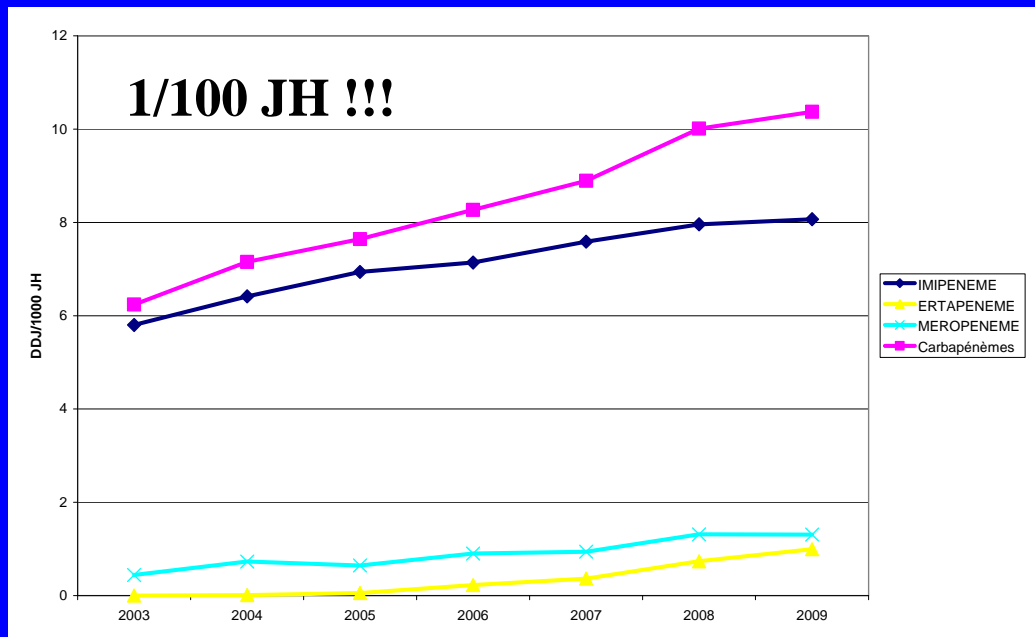
Consommation des Blactamines à large spectre à l'AP-HP 2003-09



**Cefotaxime
Ceftriaxone**

**Ratio
2 - 1 - 1**

PIP-TAZ



Carbapénèmes

The control programs

MDR program

National

1999

VJarlier 2010



**Maîtrise de
la diffusion
des bactéries
multirésistantes
aux antibiotiques**

1999

**Recommandations pour
les établissements de santé**



MINISTÈRE DE L'EMPLOI
ET DE LA SOLIDARITÉ

Alcool based hand rub solution campaigns

2001-02

VJarlier 2010



**Le lavage des mains
C'est bien! Mais...**

*...vous lavez-vous
toujours les mains
avant et après
chaque contact?*

**La Friction Hydro-Alcoolique
des mains c'est simple !**

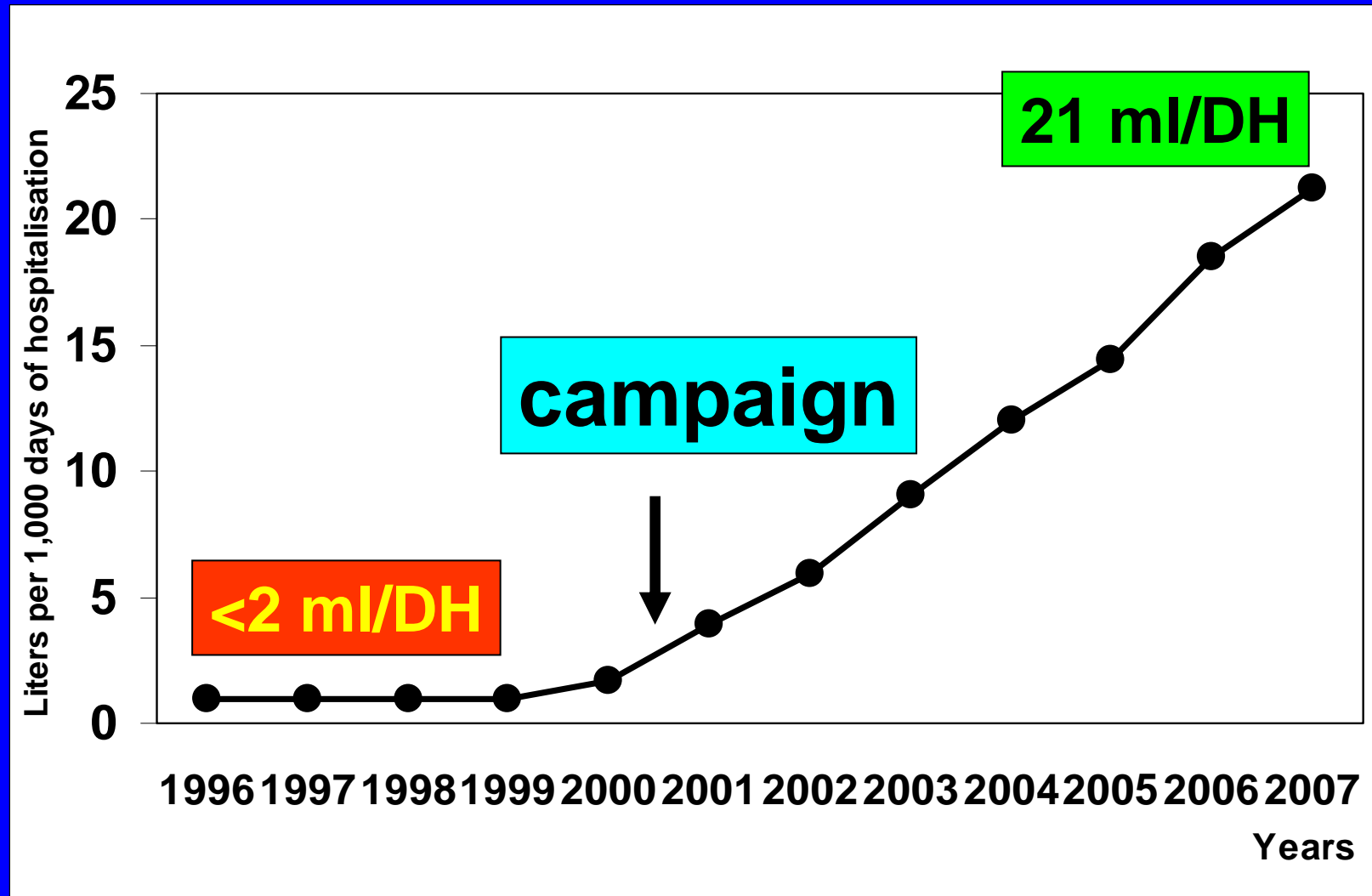
C'est pratique, on peut l'utiliser partout.

La Friction Hydro-Alcoolique
Le contrôle des germes à partir de mains.

ASSISTANCE
PUBLIQUE HÔPITAUX
DE PARIS

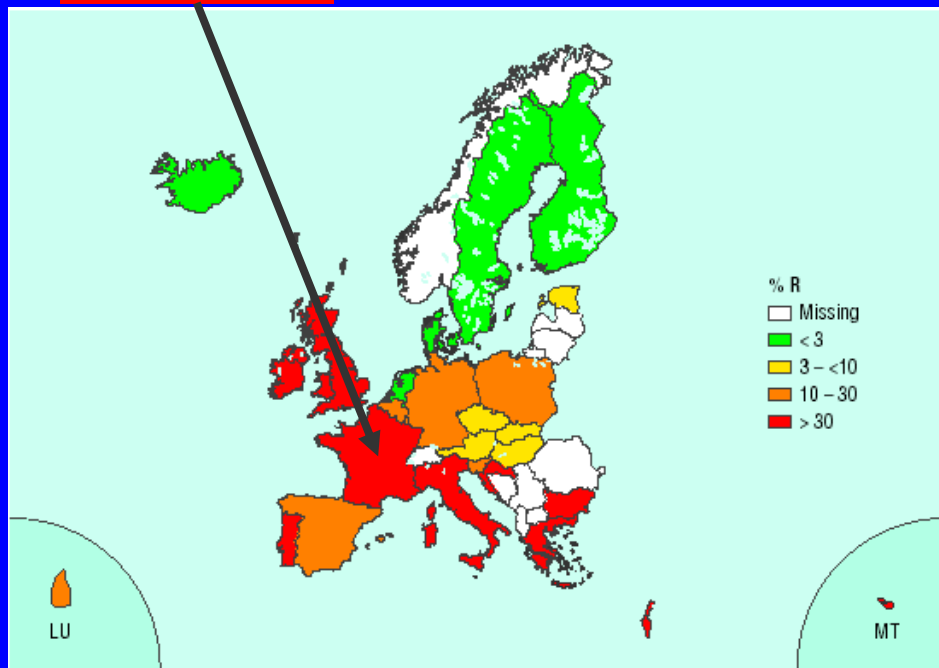
Donc la lutte contre les infections nosocomiales. L'AP-HP a financé.

Alcool based hand rub solutions Paris area hospitals (AP-HP)



MRSA in Europe (% in *S.aureus*) EARSS 2001-2009

33.2%

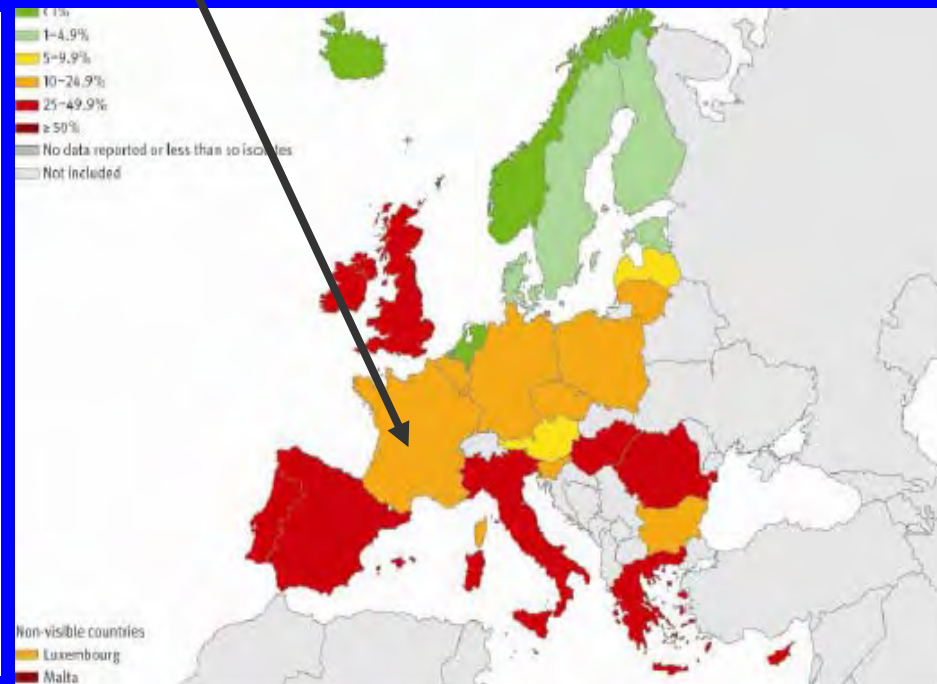


2001

VJarlier 2010

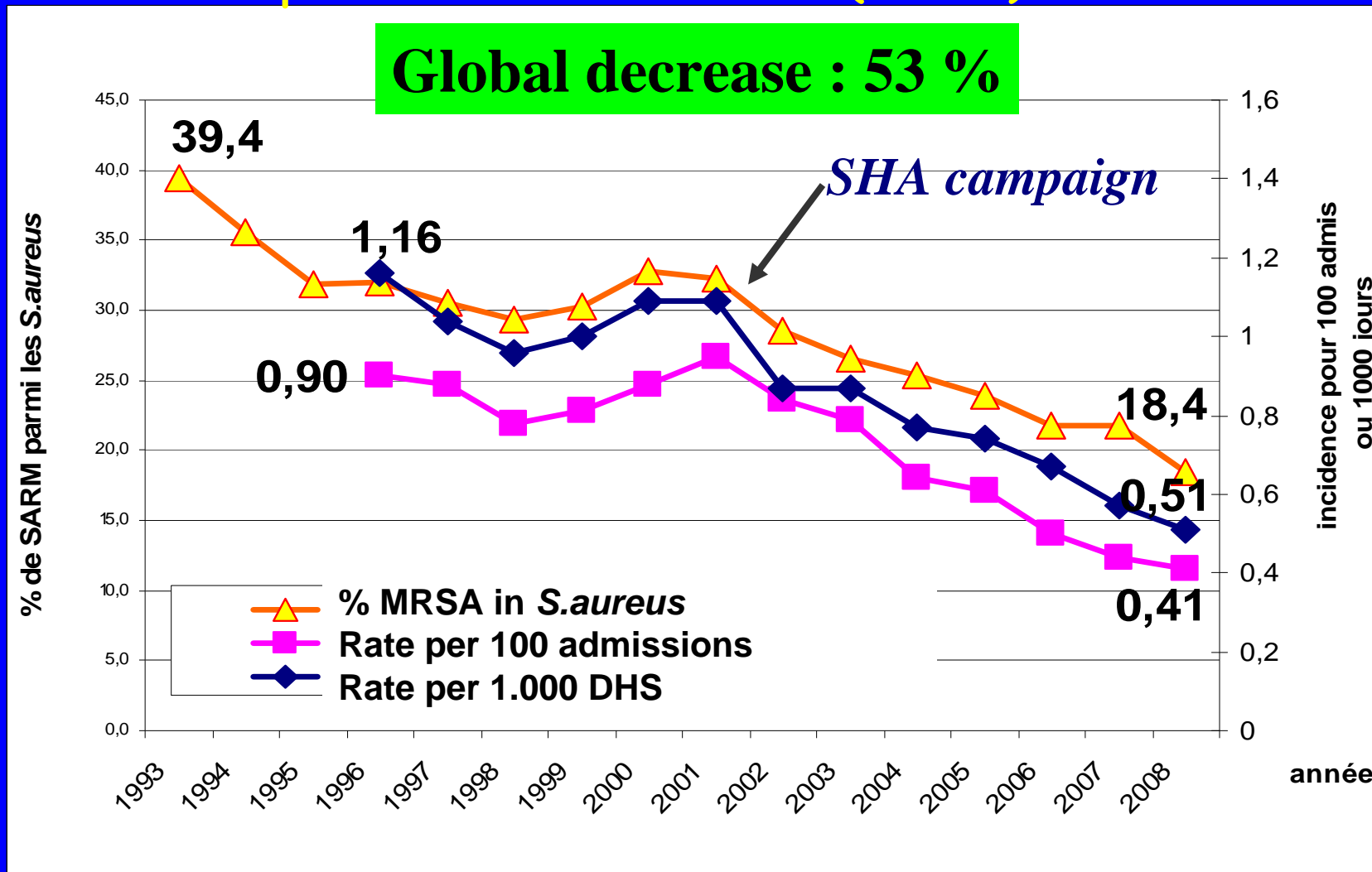
24% in 2008

23%



2009

% MRSA in *S.aureus* and MRSA incidence in acute care Univ. hospitals of Paris area (n=39) 1993-2007



Antibiotic consumption in Europe - Community - ESAC 2002

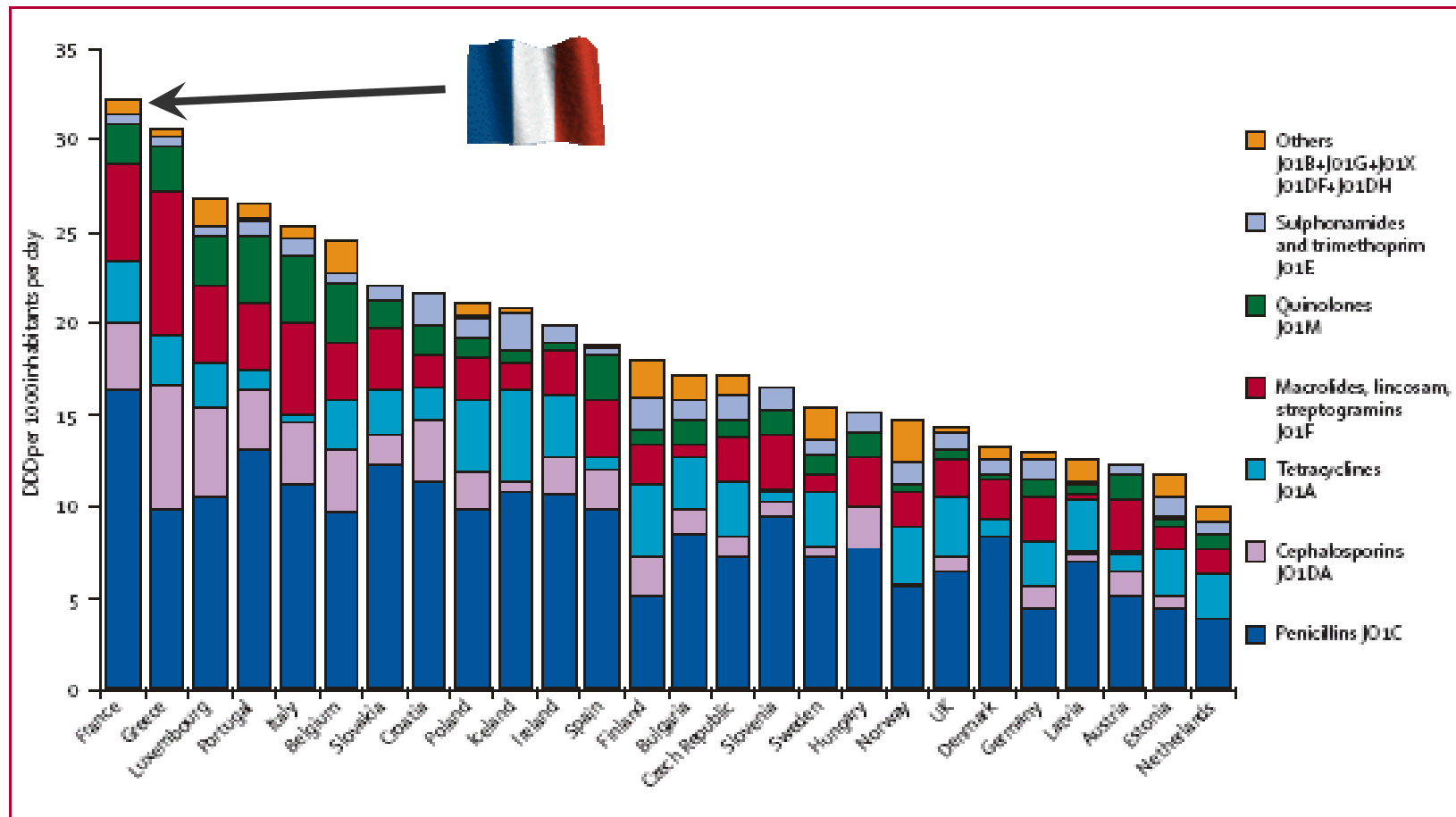
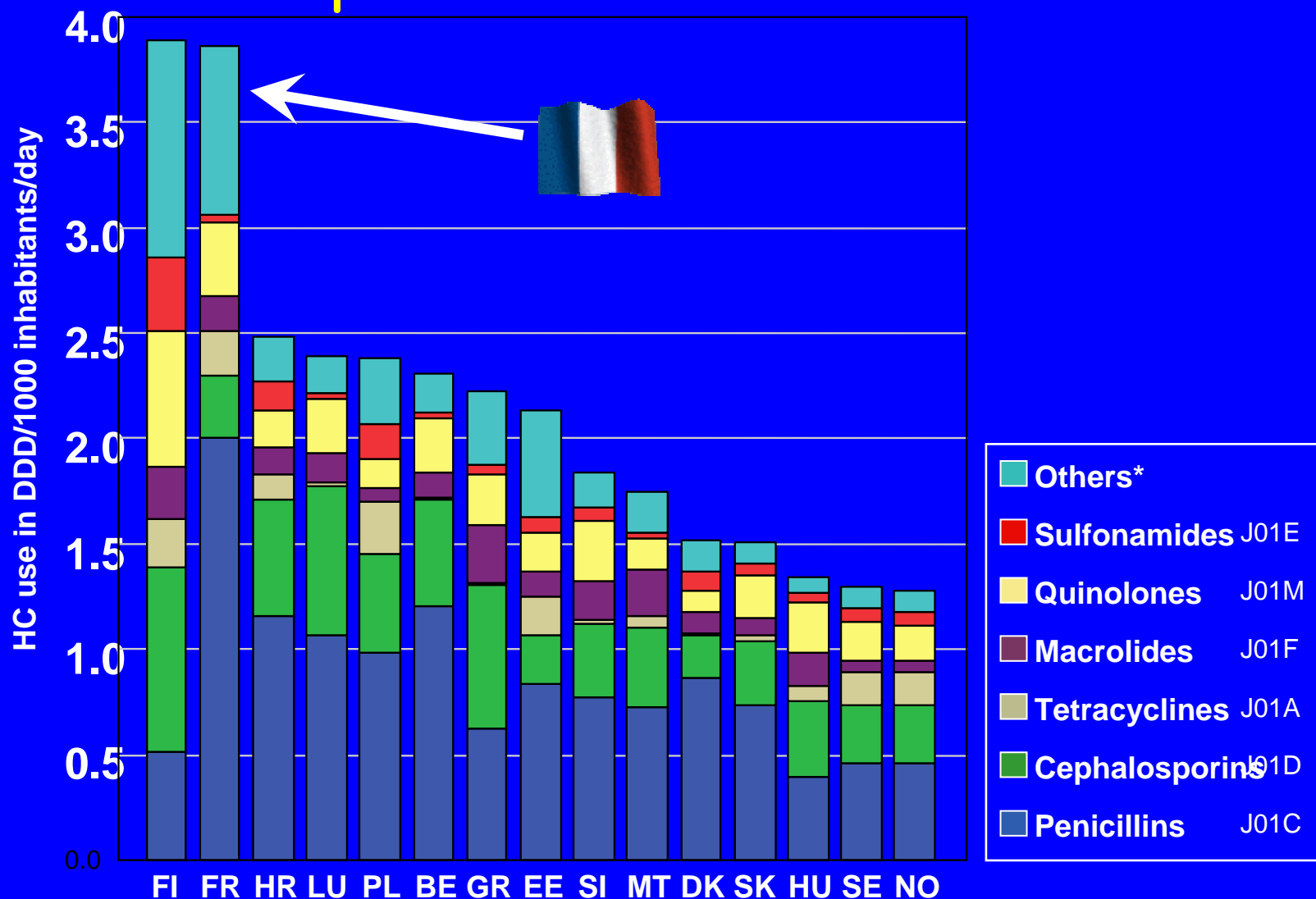


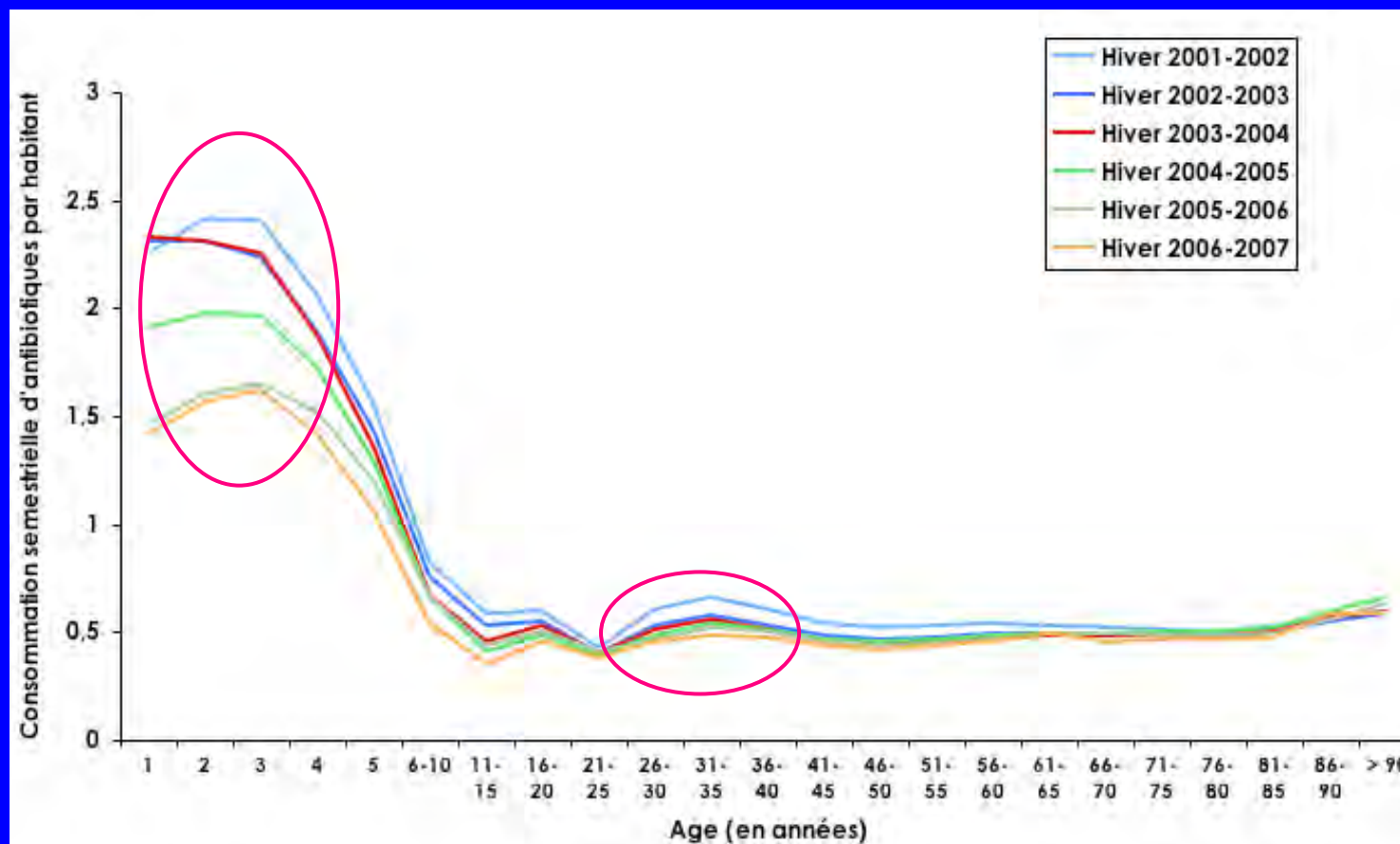
Figure 1: Total outpatient antibiotic use in 26 European countries in 2002

Antibiotic consumption in Europe - Hospital - ESAC 2002



Evolution de la consommation antibiotique par tranche d'âge (périodes octobre - mars)

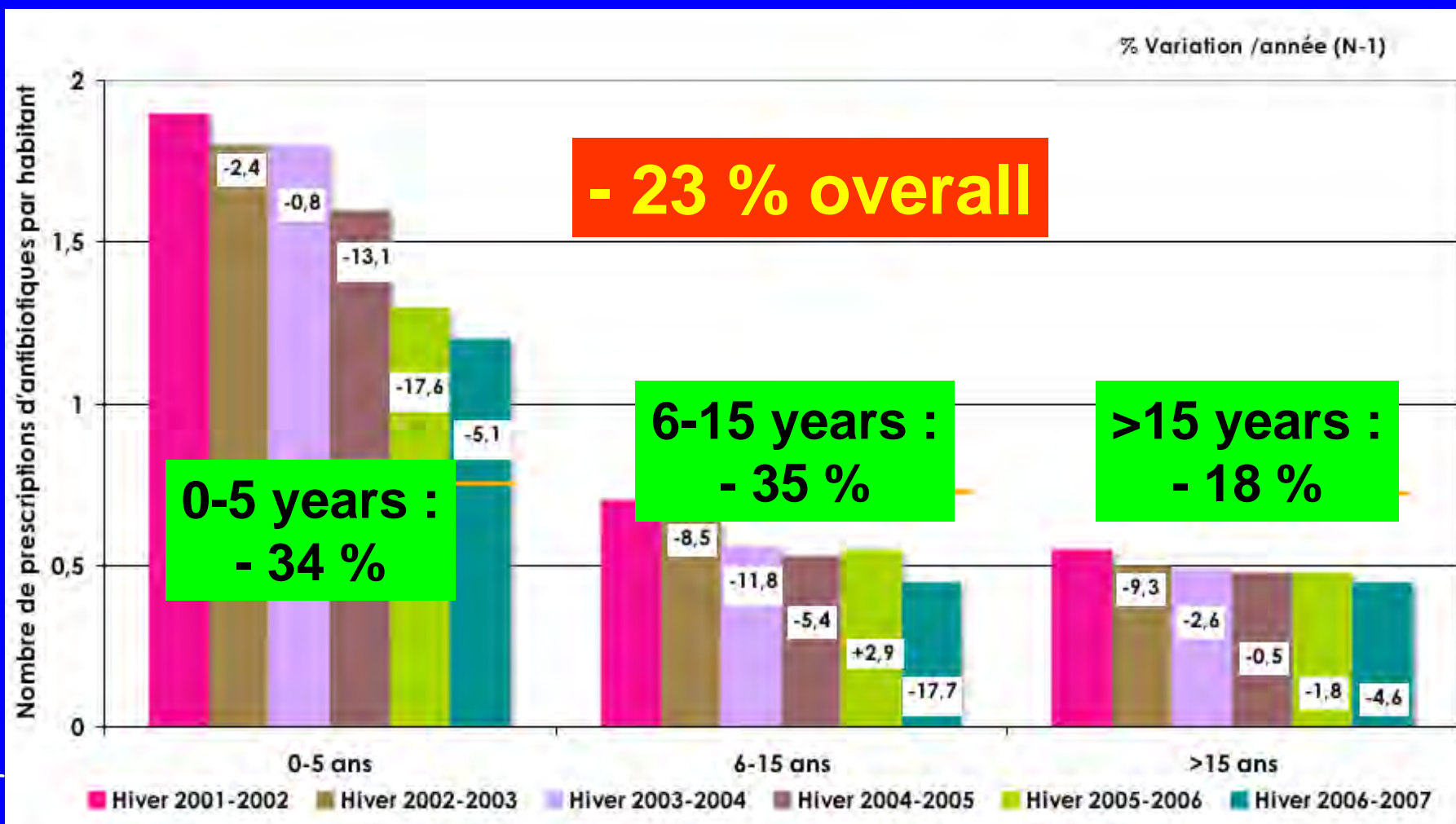
Prescriptions d'antibiotiques en fonction de l'âge sur les périodes octobre – mars



Jeunes actifs (26/35 ans) : baisse continue de la consommation d'antibiotiques (-5,7 % de 2002 à 2007)

Antibiotic consumption during winter months per classes of age France 2001-2006

*Courtesy
 D. Guillemot*



Antibiotic policy
campaign
in hospitals
of Paris area
(AP-HP)
2006-08

VJarlier 2010

LES ANTIBIOTIQUES
C'EST PAS AUTOMATIQUE



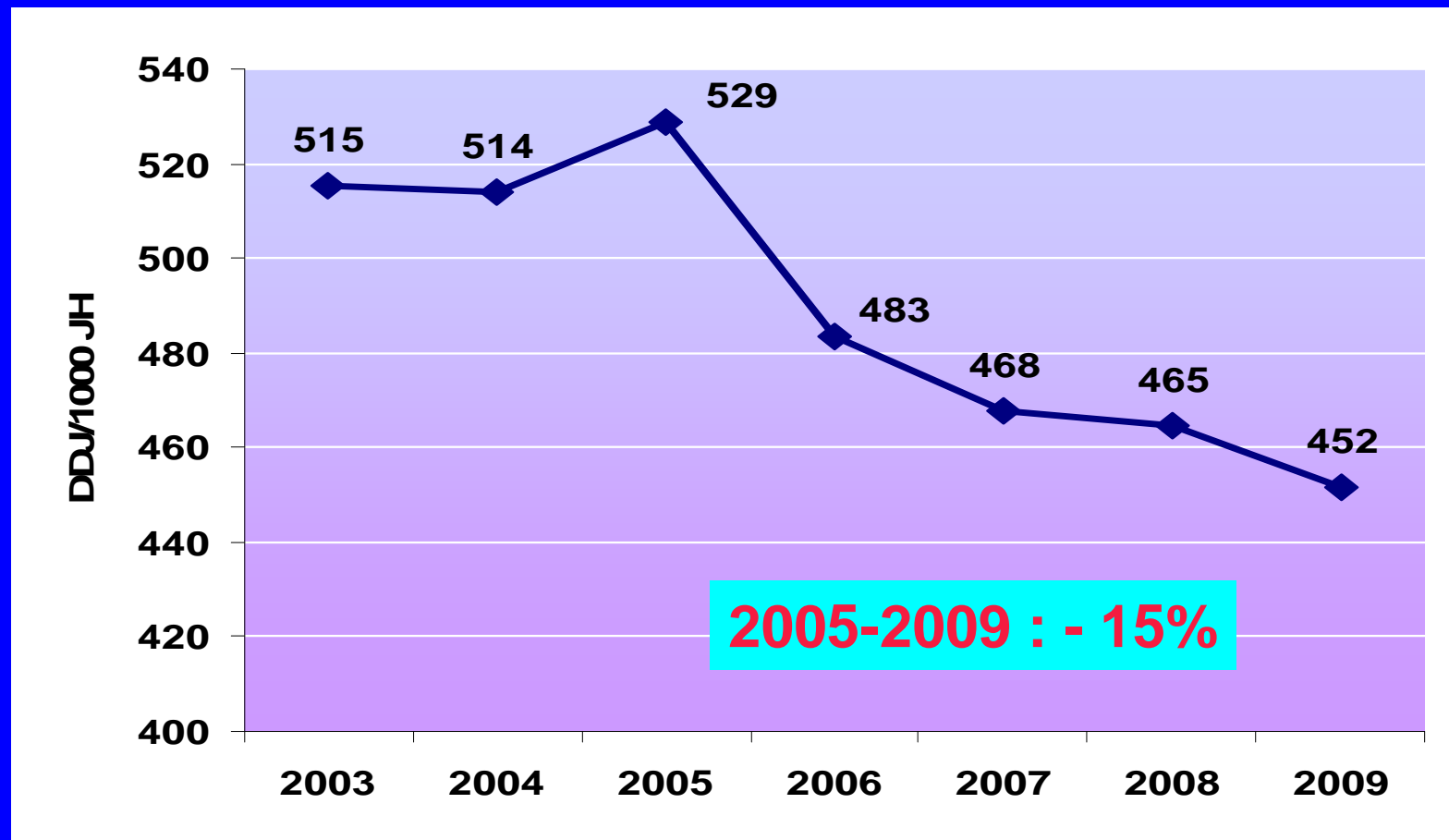
**Mieux utiliser les antibiotiques
pour préserver leur efficacité.**

ASSISTANCE
PUBLIQUE  HÔPITAUX
DE PARIS

Evolution de la consommation des antibiotiques à l'AP-HP 2003-09

Source : AGEPS-Direction des finances

Analyse : EOH/DPM



ESBLs and carbapenemases : the infernal circle

Increase Carb^{ases} strains

*Prevent X
transmission*

*Act on ESBL
incidence*

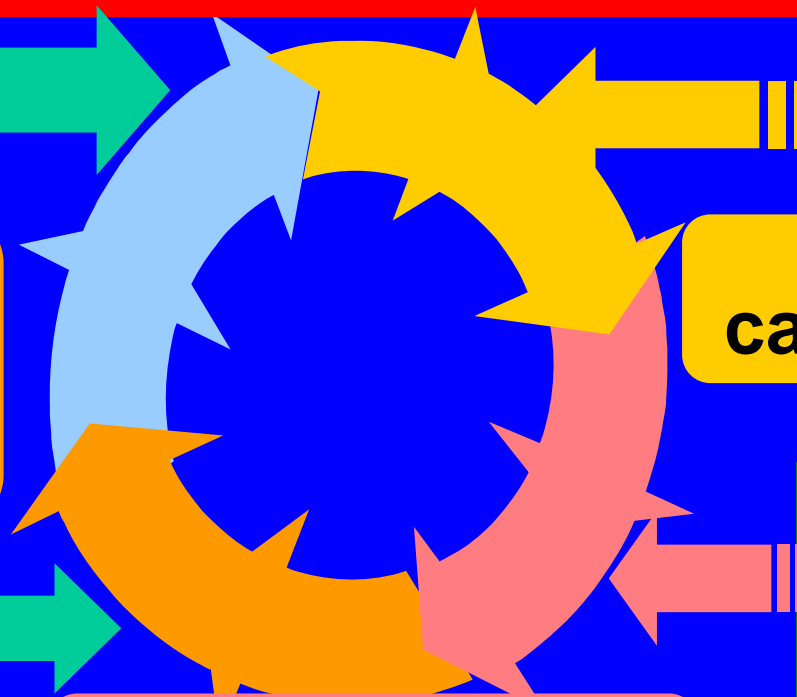
**Cross
transmission
of Carb^{ases}
strains**

**Increase
carbapenem use**

*Act on
colo-
nization*

*Act on
carbapenem
use
(alternative
ATBs.....)*

**Pressure on
Carb^{ases}
strains**



Environment, water supply, food chain

ATB policy + prevent X transm. (school, family, elderly homes..) *Wastewater treatment* *Farming, Food & water*

ESBL spread in community (x trans + ATB)

Identify carriers at discharge Admission *Identify risk factors for carriage at entry*

X transmission in HCFs

Patients entering HCFs with ESBL (low con^{tration})

Prevent X transmission

Decrease antibiotic pressure

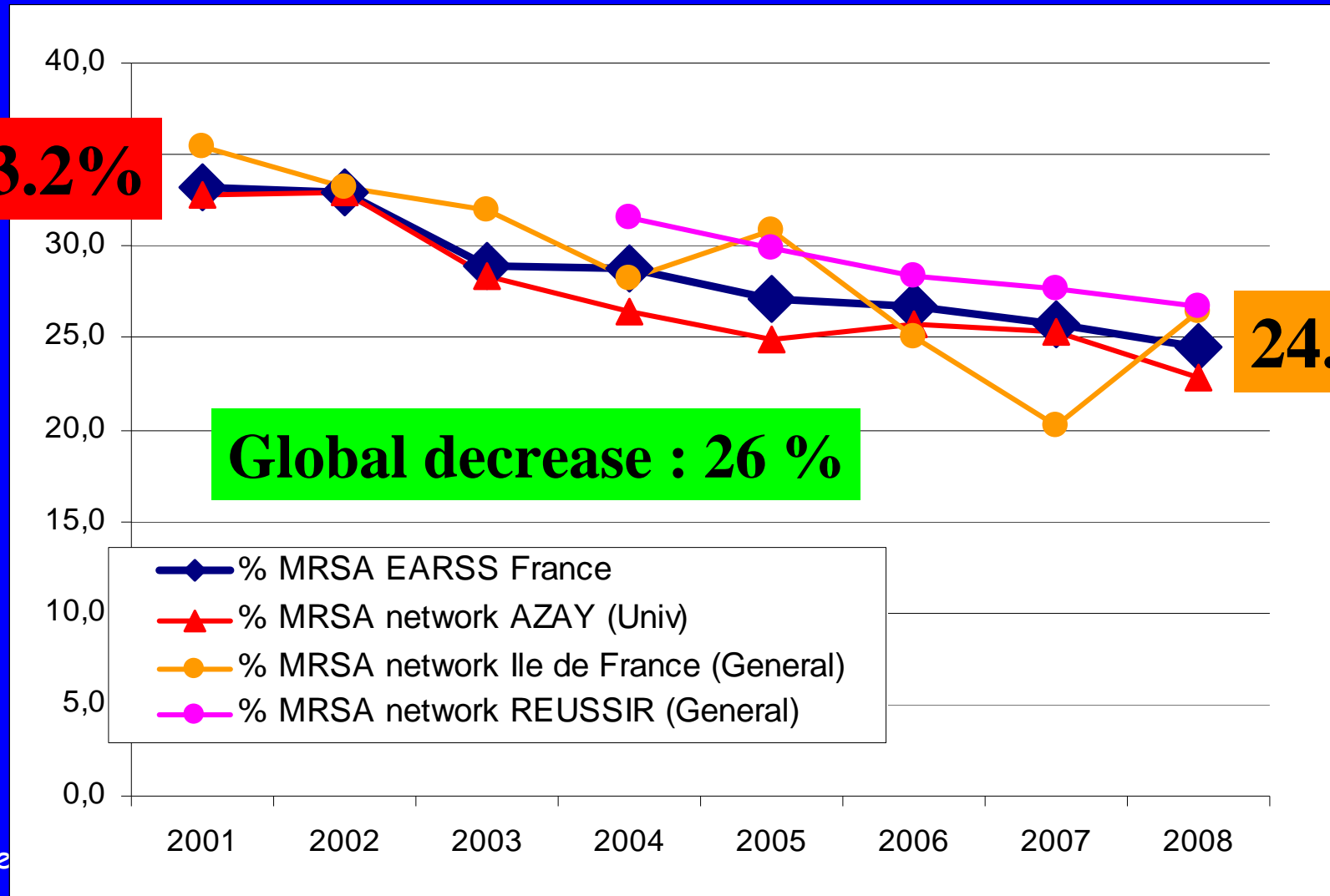
Colonization (high con^{tration})

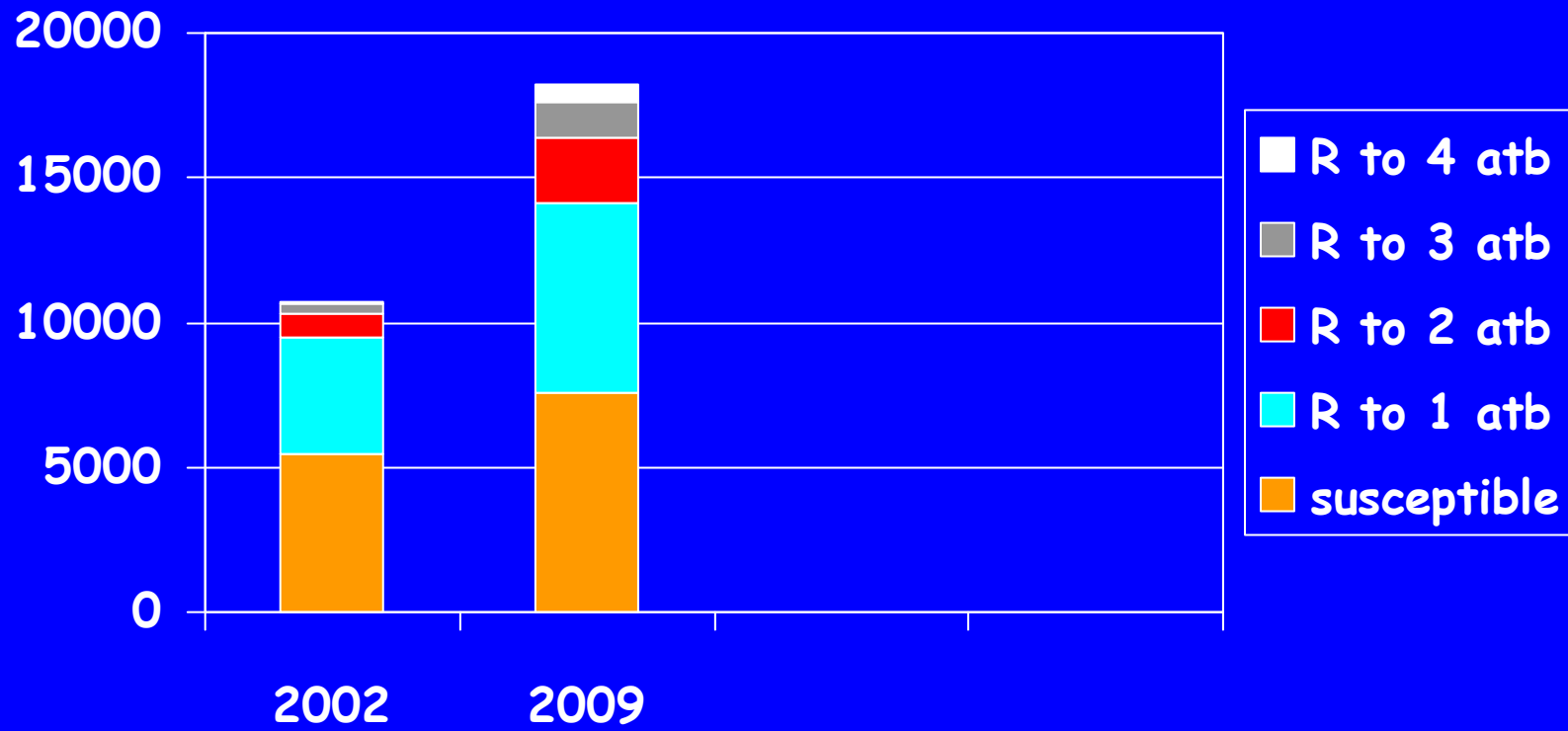
Discharge

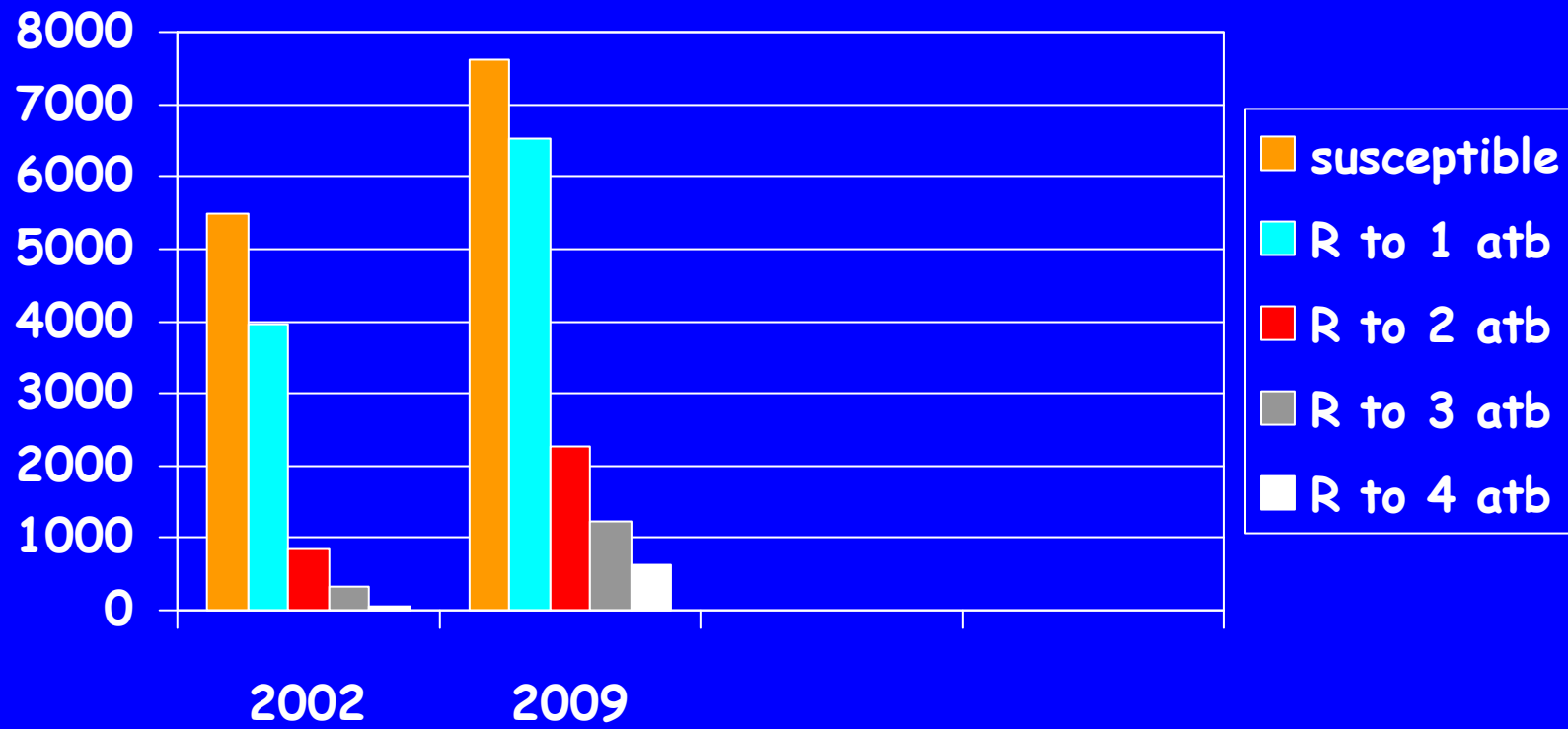
ATB

Fin sur autre diaporama

**% MRSA in *S. aureus* from bacteremias in
the 3 French networks participating in EARSS
(21 Univ Hosp, 9 GH Paris area, 30 GH all country)
2001-2008**







MDR program
Interregional
North of France
(CCLIN Paris-Nord)

1998

**Fiches de
recommandations**

**Maîtrise
de la diffusion
des bactéries
multirésistantes
aux antibiotiques**

