ANTIBIOTIC RESISTANCE

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Conflicts – None

ANTIBIOTIC RESISTANCE

***The issue*: "Bad bugs, No drugs"**

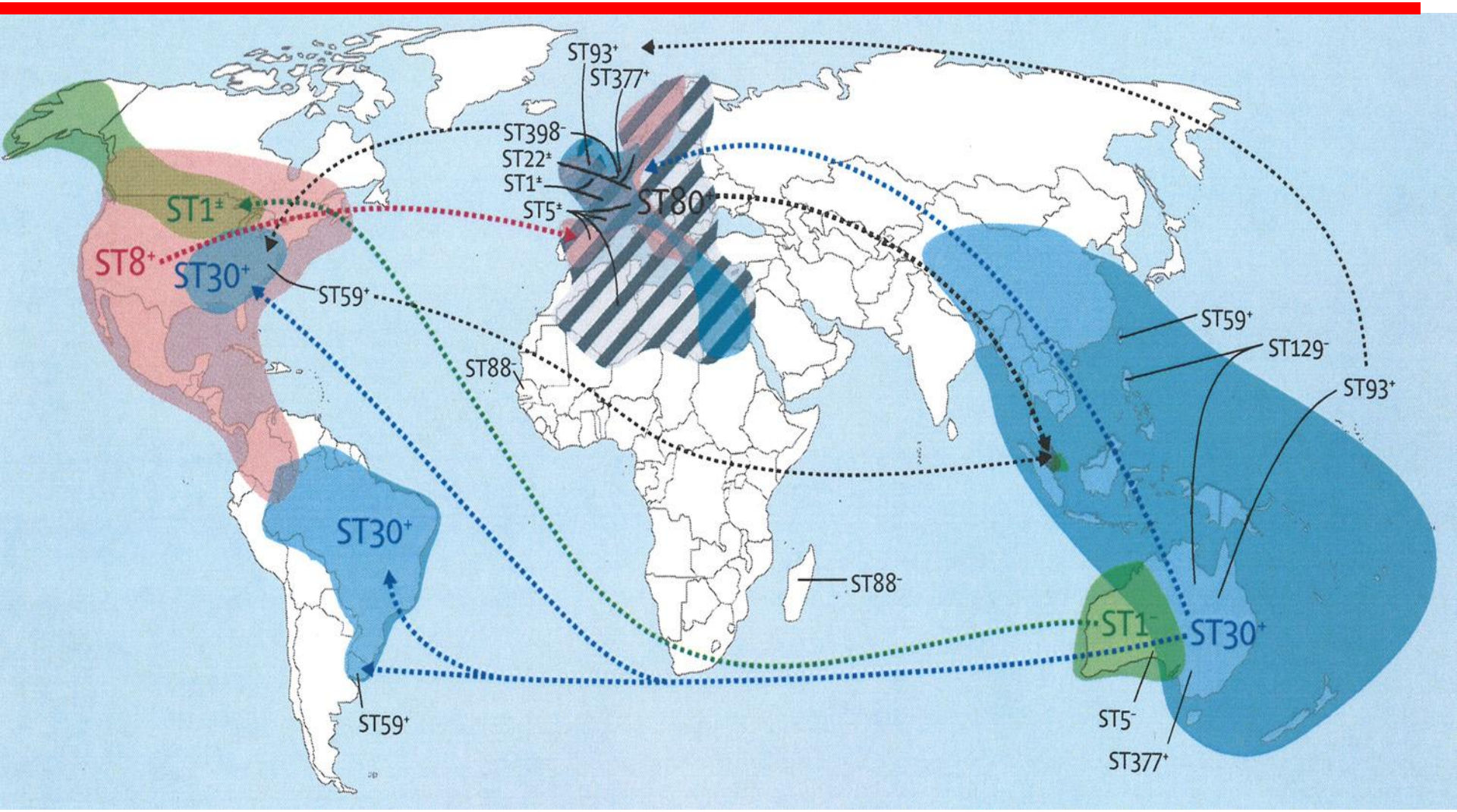
***The magnitude*: Global crisis**

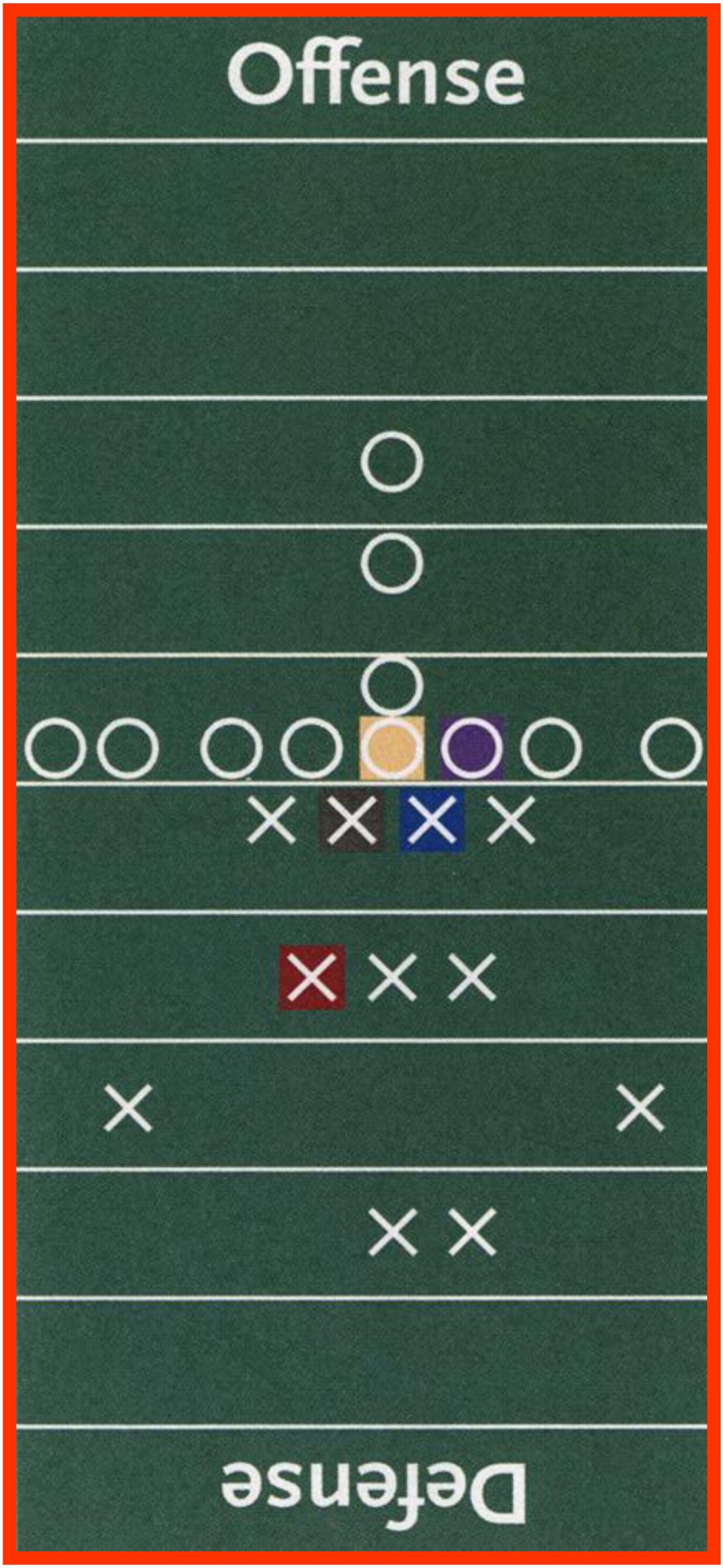
***Contributing factors*:**

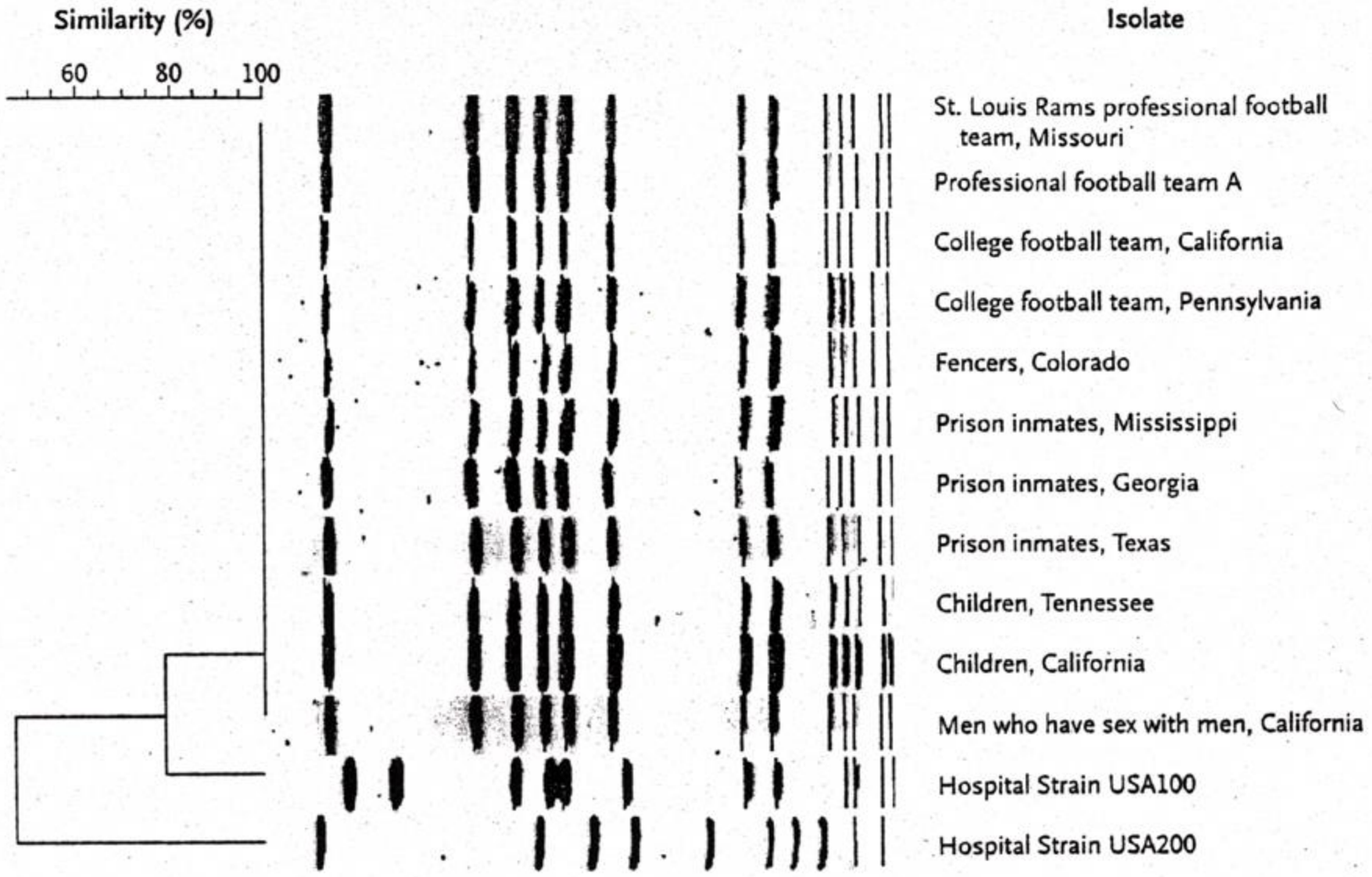
- **Antibiotic abuse – farm and patients**
- **Dry pipeline**
- **Paucity of data**

***Solution*: Coordinated plan**

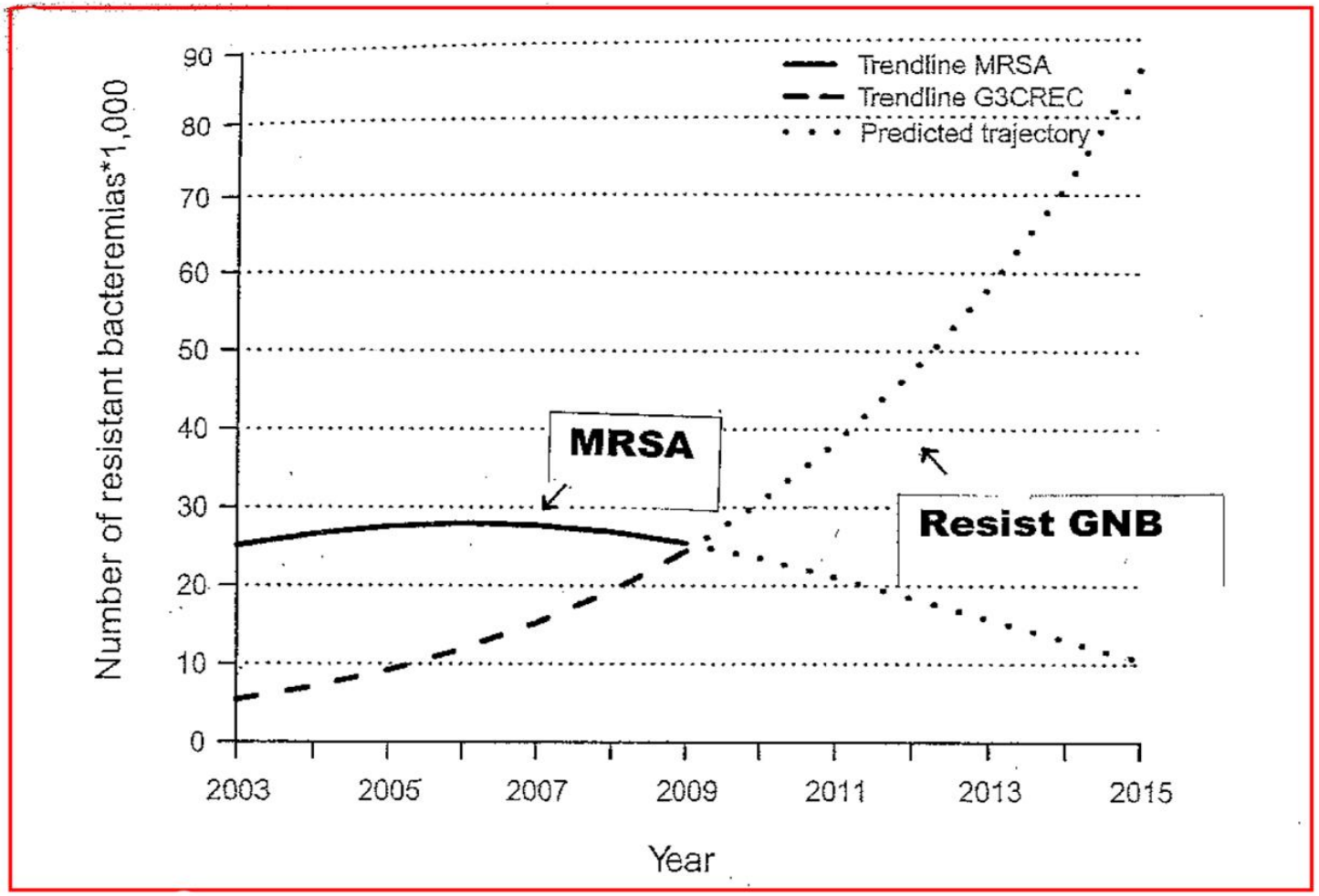
MRSA: USA 300 STRAIN



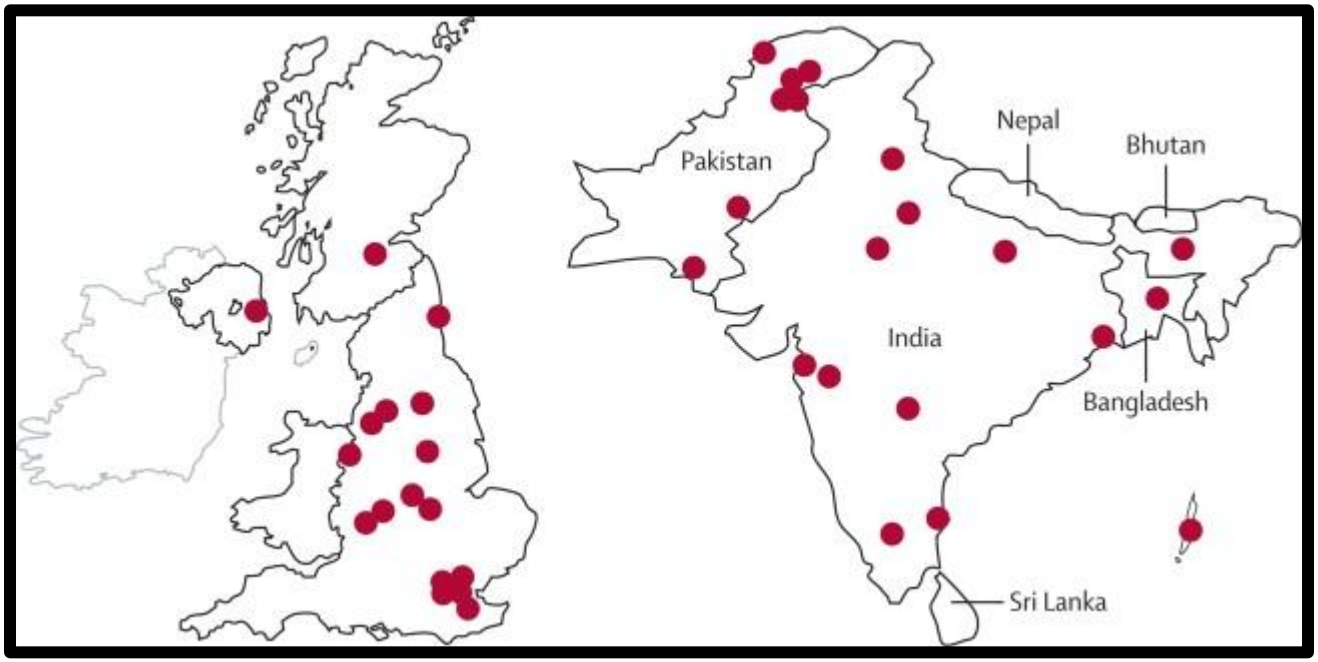

Offense
Defense


Similarity (%)
60
80
100
Isolate
St. Louis Rams professional football team, Missouri
Professional football team A
College football team, California
College football team, Pennsylvania
Fencers, Colorado
Prison inmates, Mississippi
Prison inmates, Georgia
Prison inmates, Texas
Children, Tennessee
Children, California
Men who have sex with men, California
Hospital Strain USA100
Hospital Strain USA200

TRENDS IN ESTIMATED NOSOCOMIAL BACTEREMIA IN EUROPE



Distribution of NDM-1 producing Enterobacteriaceae strains in Bangladesh, India, Pakistan and the UK



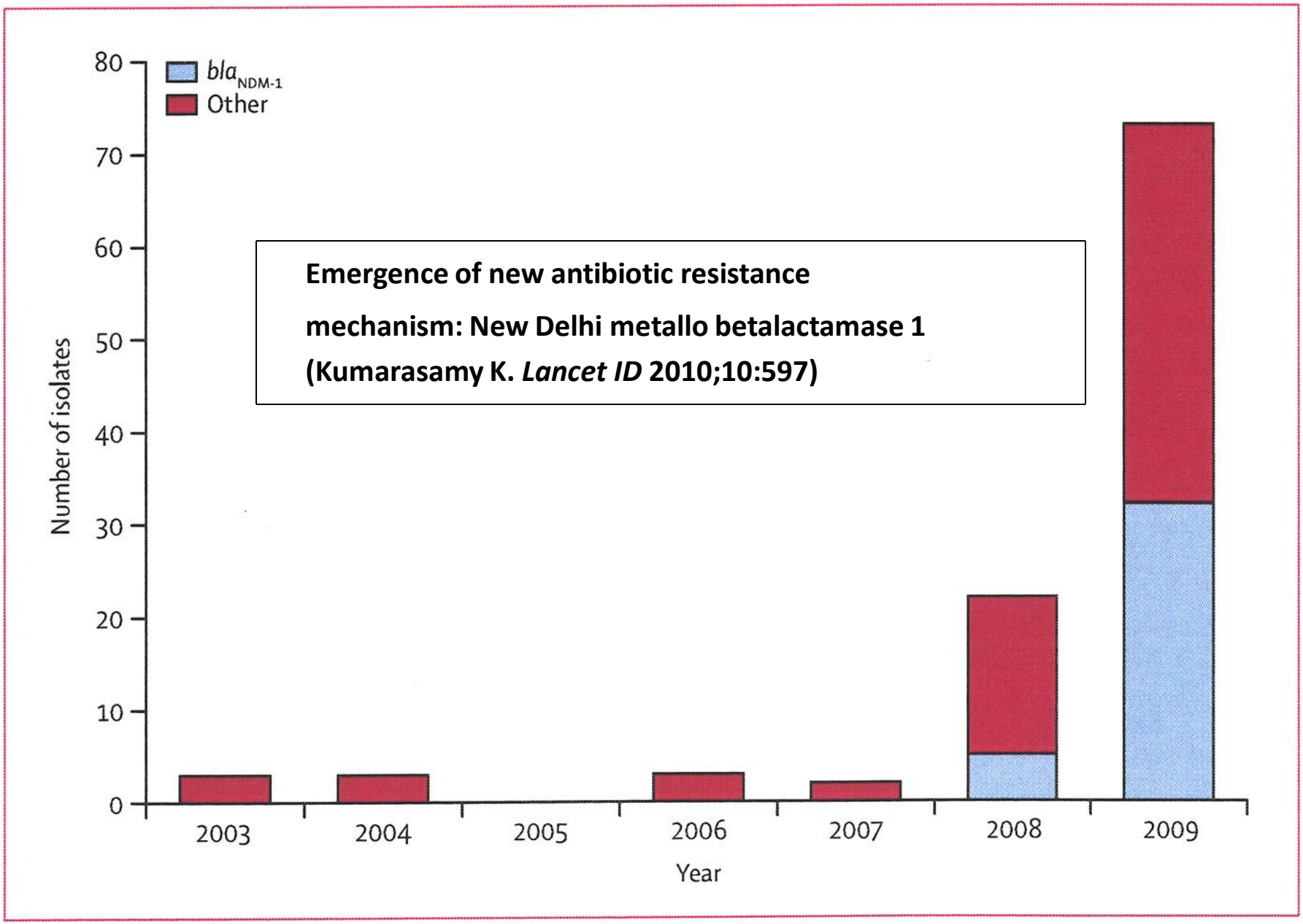


Figure 1: Numbers of carbapenemase-producing Enterobacteriaceae referred from UK laboratories to the UK Health Protection Agency's national reference laboratory from 2003 to 2009

EPIDEMIOLOGY OF NDM-1 POSITIVE ENTEROBACTERACEAE (Kamarasamy. Lancet 2010;10:59)

Method: Enterobacteraceae isolates in Reference Labs (UK and India) → carbapenem resistance → Hodge test, etc. → PCR for bla NDM-1 gene

Results: UK-37, India-70

Sensitivity	107
Pip-tazo	0
Meropenem	3%
Cephalosporins	0
Amikacin	0
Ciprofloxacin	8%
Tigecycline	67%
Colistin	100%

TRACKING A HOSPITAL OUTBREAK OF CARBAPENEM – RESISTANT KLEBSIELLA PNEUMONIAE

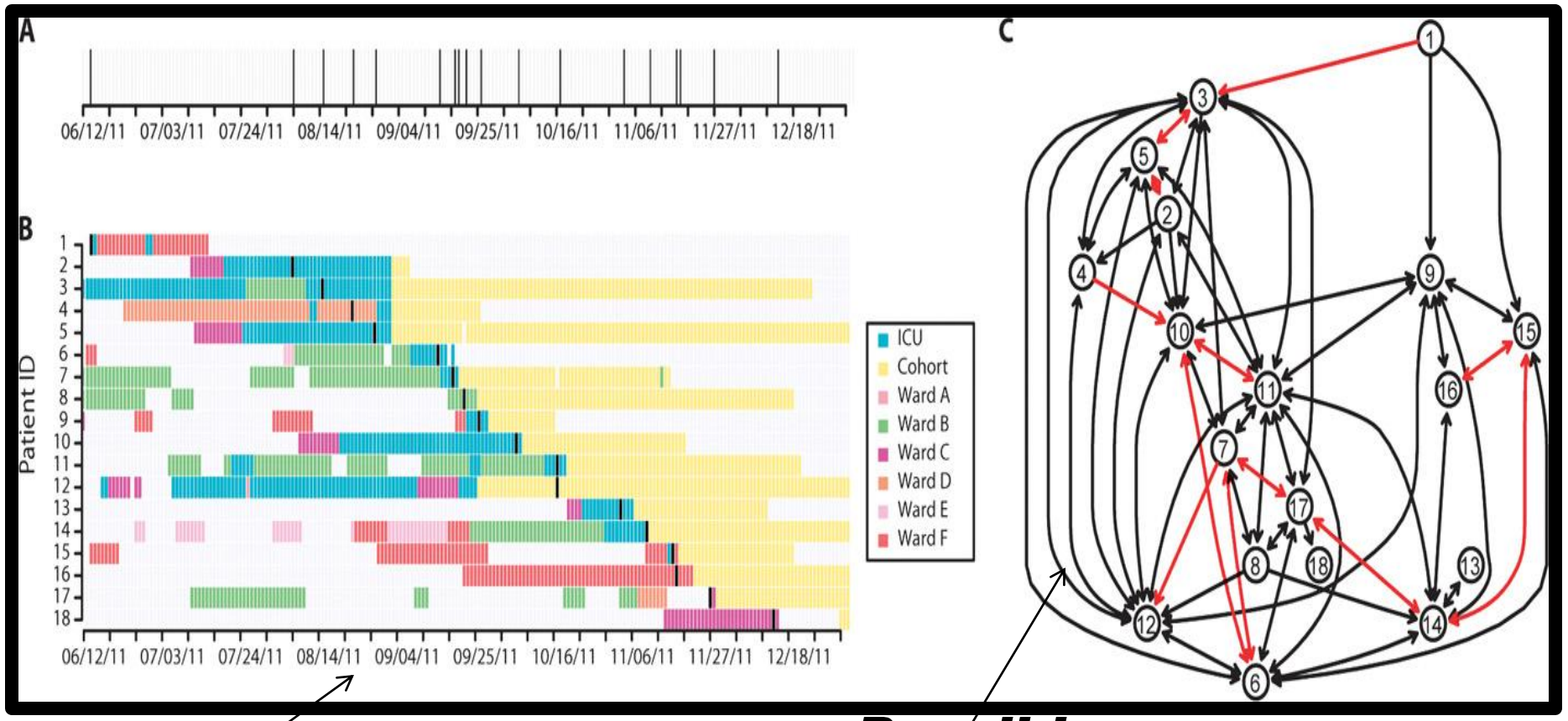
(Snitkin ES, et al. Sci Transl Med 2012;4:148ra116)

***Issue*: Epidemiology of outbreak of KPC K. pneumoniae**

***Methods*:**

- ***Patient #1*: Transferred from NYC ICU with KPC 6/13 → 7/13/11 (enhanced precautions)**
- ***Patient #2*: Tracheal aspirate 8/5/11 – positive – but never on same ward**
- ***Patients #3-18* with 6 attributable deaths (7/13/11 – 1/1/12)**

Patient location and time line to first positive culture (black line) ICU=blue (Snitkin ES, et al. Sci Transl Med 2012;4:128ra116)



Timeline and location

Possible transmission links

SURROGATE FOR SERIOUS INFECTIONS CAUSED BY MULTIPLY-RESISTANT GNB: COLISTIN COURSES: JHH*

Year	Pts.	Courses
2002	6	6
2003	7	8
2004	6	6
2005	4	4
2006	20	22
2007	40	47
2008	43	64
2009	68	96
2014	1156	1632

COLISTIN

***FDA approval*: 1961**

***Recommendation dose (PI)*: 2.5-5.0 mg/kg/d in 2-4 doses (max – 350 mg/d)**

***Correct dose* (Nation AAC 2011;55:3284)**

Target serum level 3.4 ug/mL

Maximum dose: 475 mg/d

***Toxicity renal*: 6-55%**

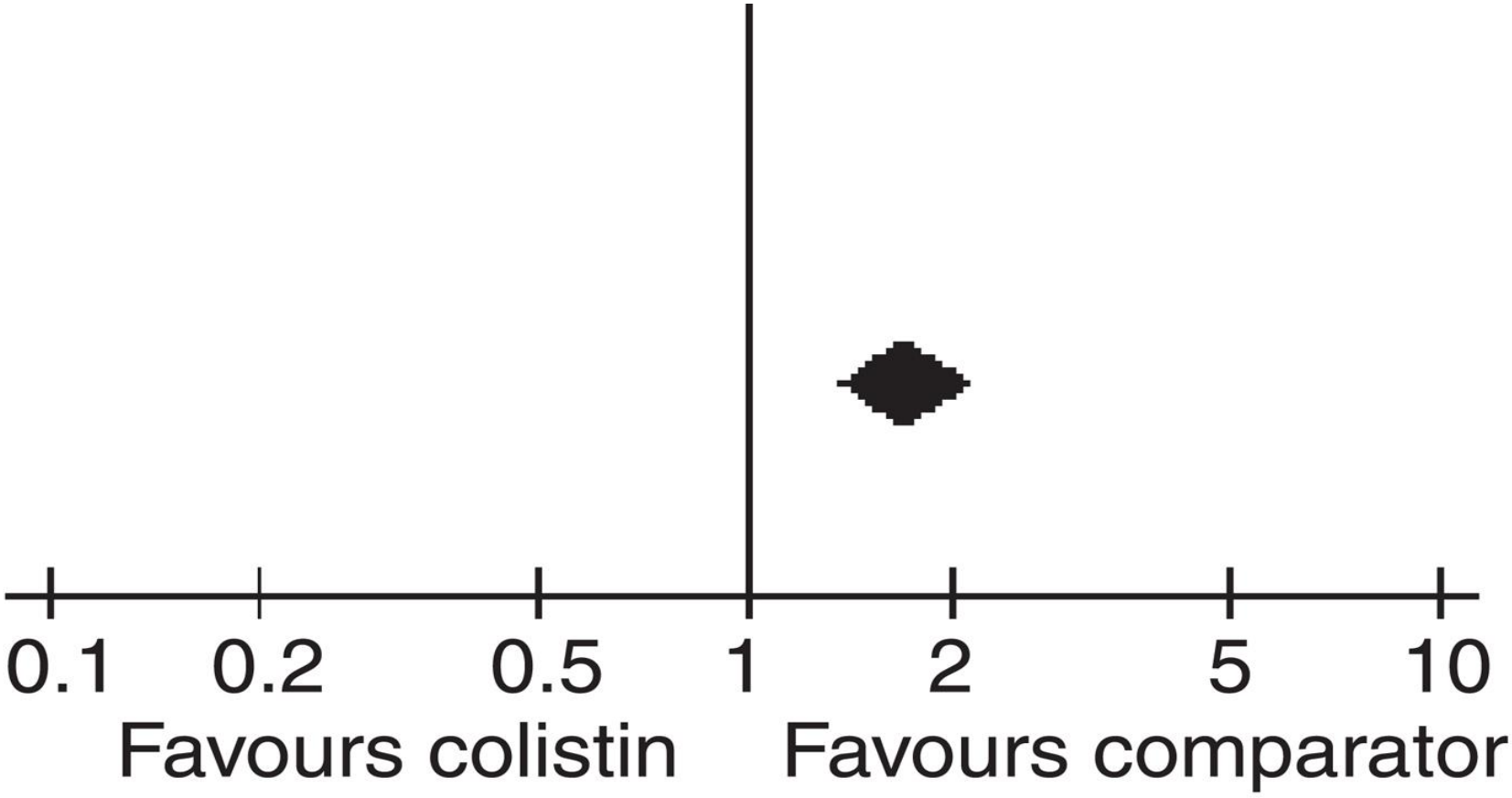
***Combine*: Rif, Mero, Mino, Carb**

***Efficacy*: Maybe**

Meta-analysis of "Comparative" Trials with Colistin

(Eur J Clin Micro & ID 2011;18:18)

Mortality



COST OF ANTIBIOTIC RESISTANCE

***Cook County Hospital*: Review 1,392 charts**

- ***Average cost: $23,700***
- ***LOS increase: 9.5 days***
- ***Mortality: 6.5%***

Extrapolated for US hospitals

- ***Total cost: $23 billion/yr***
- ***Hospital days: ↑ 17,000,000 hospital days***

NO ANTIBACTERIALS – WHY?

Duration of use:

- ***Antibiotics: 1-2 weeks***
- ***Chronic disease: yrs (Lipitor)***

Alternative markets: ***(London School of Economics – 2010)***

- ***Neuromuscular drug: +$1.5 billion/yr***
- ***New antibiotic: -$50 million/yr***

Market Forces: ***IDSA***

- ***Only Drugs (except narcotics) that loose potency with more use***
- ***Pricing: Antibiotics: $150/day***
- ***Advocacy: Best for chronic disease***

HUMBLING US DATA

- ***80% of antibiotic use in US is for agriculture (growth promotion and infection prevention)***
- ***Risk of MRSA bacteremia is 49 x more likely in a US hospital compared to The Netherlands***
- ***US accounts for 4.6% of the global population and 46% of the global antibiotic market***
- ***The EU has country-specific data for antibiotic use and resistance for 26 countries x 15 yrs. US has no clue.***

TWITTER AND ANTIBIOTICS

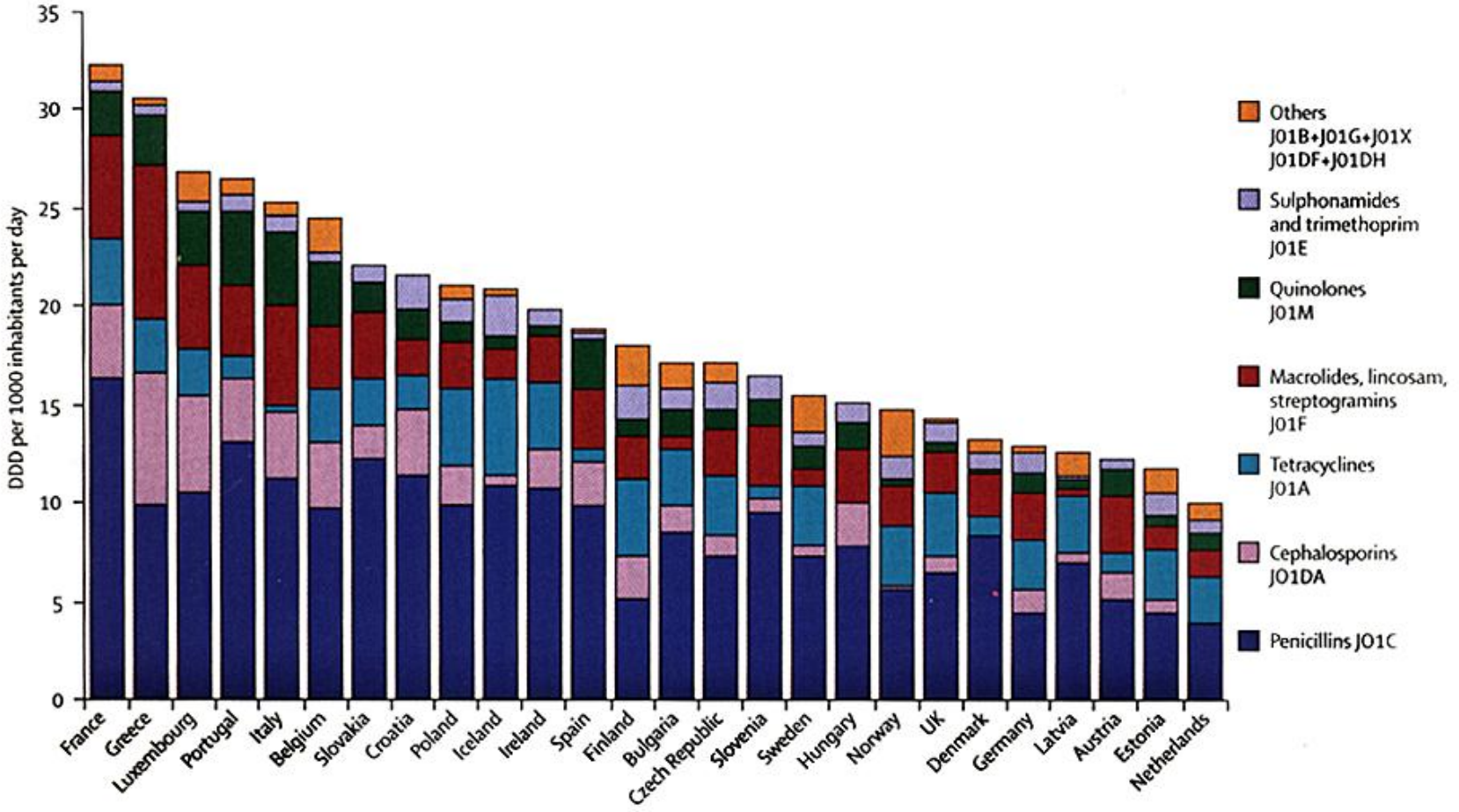
(Scanfeld D. Am J Inf Control 2010;38:182)

***Method**: Review 1000 Twitter updates that mention antibiotics*

***Results**: Abx + flu (345) or cold (302)*

Statement	Followers
"Finally over my cold thank you Z pack"	850,375
"Starting to feel better from flu. One antibiotic to go"	172,571
"Need antibiotic. If you have any left over, I will pay u"	6,216

Per Capita Antibiotic Use in 26 European Countries in 2002



DDD=defined daily dose.
ESAC. Available at: http://www.esac.ua.ac.be/main.aspx?c=*ESAC2&n=24345. Accessed September 18, 2006.

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Significant Reduction of Antibiotic Use in the Community after a Nationwide Campaign in France, 2002–2007

Elifsu Sabuncu[1,2], Julie David[1,2], Claire Bernède-Bauduin[1,2], Sophie Pépin[3], Michel Leroy[4], Pierre-Yves Boëlle[5,6], Laurence Watier[7,8], Didier Guillemot[1,2,9,10]*

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Abstract

Background: Overuse of antibiotics is the main force driving the emergence and dissemination of bacterial resistance in the community. France consumes more antibiotics and has the highest rate of beta-lactam resistance in *Streptococcus pneumoniae* than any other European country. In 2001, the government initiated "Keep Antibiotics Working"; the program's main component was a campaign entitled "Les antibiotiques c'est pas automatique" ("Antibiotics are not automatic") launched in 2002. We report the evaluation of this campaign by analyzing the evolution of outpatient antibiotic use in France 2000–2007, according to therapeutic class and geographic and age-group patterns.

Methods and Findings: This evaluation is based on 2000–2007 data, including 453,407,458 individual reimbursement data records and incidence of flu-like syndromes (FLSs). Data were obtained from the computerized French National Health Insurance database and provided by the French Sentinel Network. As compared to the preintervention period (2000–2002), the total number of antibiotic prescriptions per 100 inhabitants, adjusted for FLS frequency during the winter season, changed by −26.5% (95% confidence interval [CI] −33.5% to −19.6%) over 5 years. The decline occurred in all 22 regions of France and affected all antibiotic therapeutic classes except quinolones. The greatest decrease, −35.8% (95% CI −48.3% to −23.2%), was observed among young children aged 6–15 years. A significant change of −45% in the relationship between the incidence of flu-like syndromes and antibiotic prescriptions was observed.

Conclusions: The French national campaign was associated with a marked reduction of unnecessary antibiotic prescriptions, particularly in children. This study provides a useful method for assessing public-health strategies designed to reduce antibiotic use.

Please see later in the article for the Editors' Summary.

REDUCTION IN ANTIBIOTIC USE IN FRANCE

(Sabuncu E. PLoS Med 2009;6:e1000084)

Issue: France consumes most antibiotics and has most penicillin resistant S. pneumoniae

Method: National campaign including detailing

Data: reimbursement data especially for ILI

Results: 26% decline in Abx prescriptions and reduced S. pneumoniae resistance

Global antibiotics market 2011: France has greatest decrease in Abx use (21% decrease)

DOES ANTIBIOTIC USE CORRELATE WITH RESISTANCE

Pathogen	Country	Abx use (DDD/1000	Rate
Klebsiella*	Greece	38	38%
	The Netherlands	11	0.2%
MRSA**	Greece	38	58%
	The Netherlands	11	1.6%

*Bacteremic Klebsiella-carbapenemase positive

**MRSA as % of S. aureus isolates

Europe launches 12 point plan to tackle resistance to antibiotics as 25 000 die from resistant bacteria

Rory Watson BRUSSELS

The European Commission presented its first action plan to tackle antimicrobial resistance to drugs on 17 November, as new research that was based on Europe-wide surveillance data confirmed that *Klebsiella pneumoniae* that is resistant to carbapenems is on the rise.

CDC

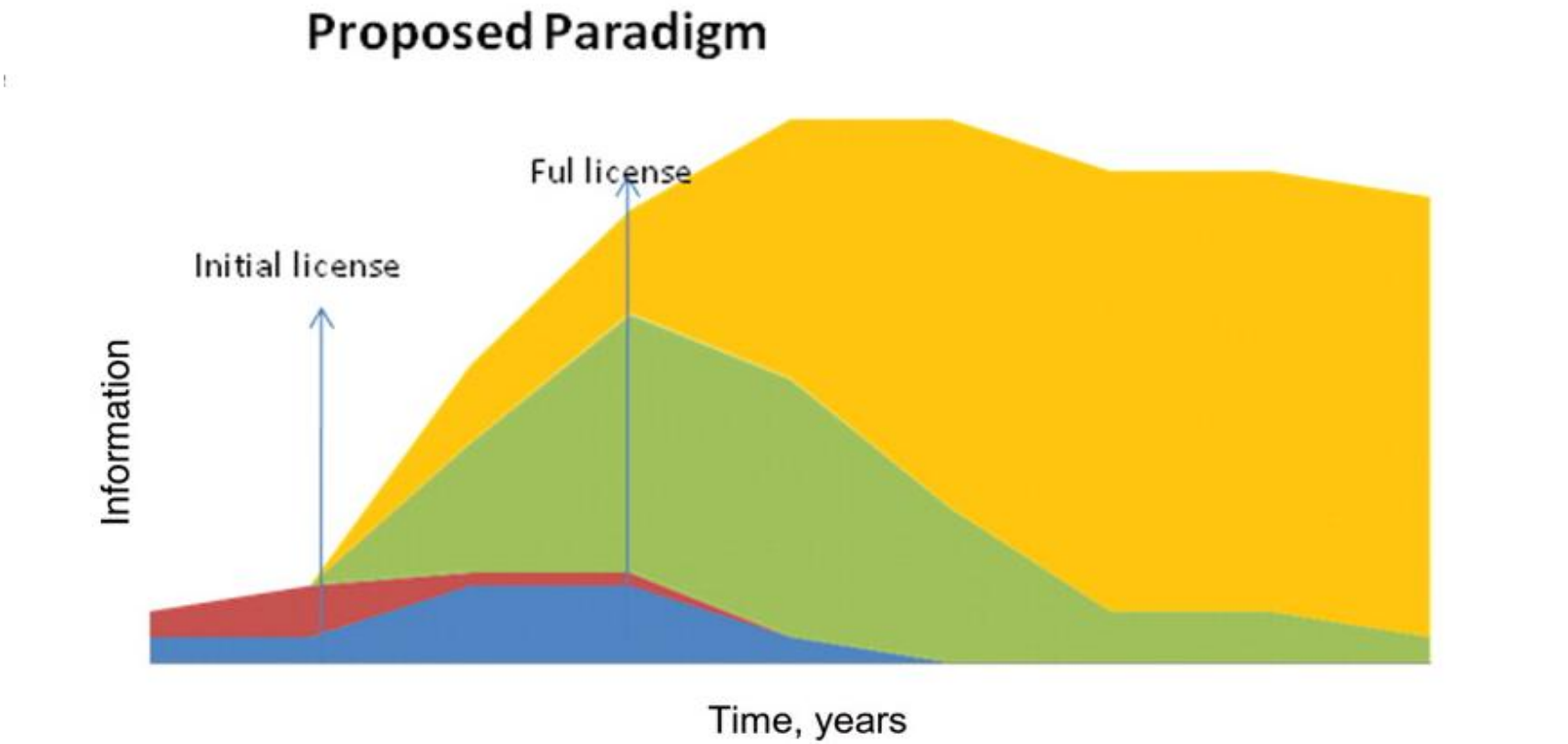
Several European countries say that between 15% and 50% of *K pneumoniae* are resistant to carbapenems

PROPOSED DRUG DEVELOPMENT MODEL (LPAD)

(Alemayehu D. CID 2012;15:562)

Red: PK/PD; Blue: Intervention;

Green: observational; Yellow: "real world"



RESISTANCE: NEW THREATS

GNB – Carbabenems, etc

MRSA – Vancomycin

N. Gonorrhoeae – Cefixime, FQ

Influenza – Oseltamivir

M. Tuberculosis – Rif, INH

Malaria – Artemisinin

Cholera – ESBL, FQ

ANTIBIOTIC RESISTANCE: PLAYERS

- ***Pharma***
- ***Diagnostics***
- ***IDSA (ACP, AMA)***
- ***SHEA***
- ***Payors***
- ***Press***
- ***FDA***
- ***CMS***
- ***HCR***
- ***CDC***
- ***NIAID***
- ***Congress***

Thanks to:

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≈

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Vance Fowler – Duke

≈

Bob Guidos – IDSA

≈

Otto Cars – Sweden

≈

Jan Klutmans – The Netherlands