

Session one: National Methods and Surveillance

**Antimicrobial resistance surveillance,
improving relevance and outputs**

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A statement of the obvious

“Good quality surveillance data on resistant micro-organisms are essential to underpin effective interventions to counter the problems of resistance and developing guidelines on prescribing antimicrobial drugs. Such data should be epidemiologically and clinically relevant.”

**Copenhagen Recommendations
European Union, 1998**

Functions of antimicrobial resistance surveillance

- **surveillance needed to monitor trends (continuous, sustainable, uniform, with minimum bias)**
- **surveillance needed to test effectiveness of interventions (conducted over the intervention, uniform, targeted relevant resistances and pathogens)**
- **surveillance should be multi faceted to allow for cross validation (results of surveillance should be widely available)**
- **data should be regularly disseminated to those who require it (electronic, paper media)**

**Path of Least Resistance, 1998, Department of Health;
Lewis 2002, JAC 49; 3-5**

Problems with surveillance in the late 1990s

- routine passive surveillance was biased by disease state, age, uneven methodologies in and outside labs. However, large data sets could be captured.
- sentinel focused surveillance using central laboratory overcomes some problems by use of standard within lab methods but not requesting bias and is costly
- multiple small short term studies funded by pharma in the UK and Ireland
- poor dissemination of data – public/private providers and funders

Livermore, MacGowan, Wale, 1998; BMJ 317, 614-5

Pitfalls with passive surveillance in the community

- **data skewed because patients who fail initial empirical therapy more likely to be tested**
- **age bias in LIMS towards the elderly and young**
- **location of patient (Admission Unit vs Primary Care)**
- **isolates from different disease states included in database disproportionately, i.e. acute sinusitis vs UTI, exacerbation COPD vs CAP**
- **Specimens may be sent for non-infective reasons**

(based on Livermore, MacGowan, Wale, 1998)

Assessment of Bias: Laboratory Database vs UTI

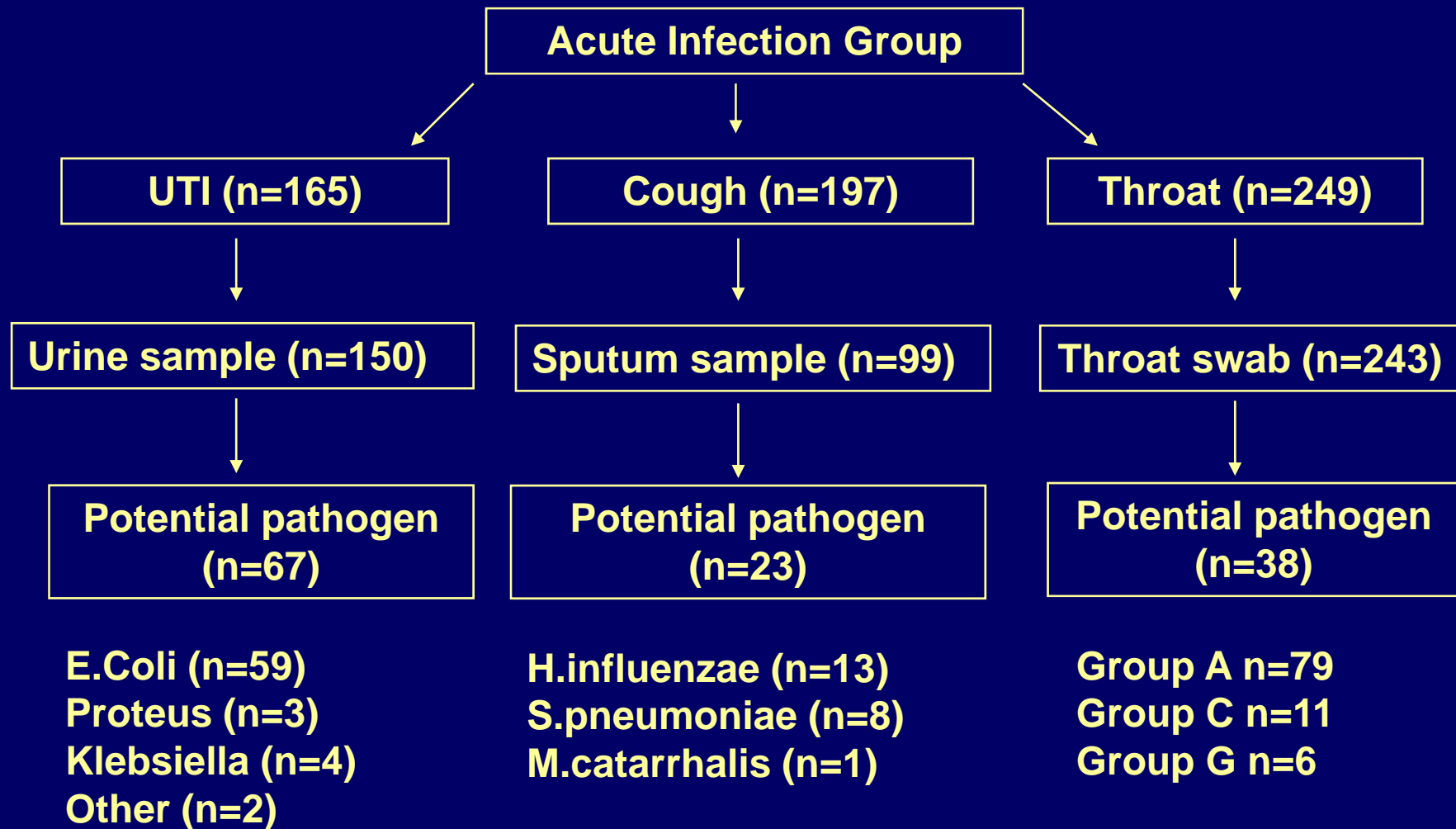
Symptoms in UTI Group, i.e. culture $>10^5$ pathogen

Pain on urination	0.85
Increased frequency	0.87
Blood in urine	0.25
Increased urgency	0.65
Urination at night	0.56
Abdominal pain	0.56
Back pain	0.38
Smelly urine	0.44

Patient Group	n	%S	P	CI
Acute UTI	55	81	0.343	0.394 – 1.38
Laboratory data	5448	76		

Lovering & MacGowan, 2003

Problem with sentile surveillane in Primary Care



- **passive surveillance of antibiotic resistance in the community over estimates resistance**
- **surveillance of infected patients is difficult, costly, time consuming and will often fail to generate enough data**
- **passive surveillance may be preferred because it is affordable**
- **other sampling approaches are useful: postal**

BSAC antimicrobial resistance surveillance contribution:

Overcomes previous perceived problems:

- continuous since 1999
- based on uniform within laboratory methodology
- target at relevant resistances by use of a core testing set
- allow cross validation with other resistance data bases
- data is widely available

Does not overcome:

- bias related to passive surveillance in the community
- partly answers concerns about how representative sampling is (increase from 25 to 40 collecting labs)

The model

- **Working Party on Antimicrobial Resistance Surveillance co-ordinates the programme (co-ordinator Dr Rosy Reynolds)**
- **pharmaceutical partners provide funding to the BSAC for the surveillance programmes**
- **Quotient Bioresearch (respiratory), HPA (bloodstream) deliver the programme**
- **MRS Solutions host the website**
- **40 laboratories in the UK and Ireland provide 4-5,000 isolates per annum in the areas of bacteraemia and respiratory infection**

Sponsors

Abbott Laboratories	2000-2003
Astellas Pharma	2007-2011
AstraZeneca	2006-2008
Aventis Pharma	2000-2001
Bayer Schering Healthcare	2000-2004
Cerexa, Forest Laboratories	2008
Cubist Pharmaceuticals	2003
GeneSoft Pharmaceuticals	2003
GlaxoSmithKline	2000-2002
Johnson & Johnson Pharmaceutical R&D	2005-2011
Merck Sharp & Dohme	2001-2007
Novartis	2005-2010
Pfizer	2001-2011
Theravance	2005-2006
Wyeth	2001-2009

Associate sponsors

Basilea	2003-2004
Cerexa	2009
Theravance	2007

BSAC resistance surveillance: examples of outputs

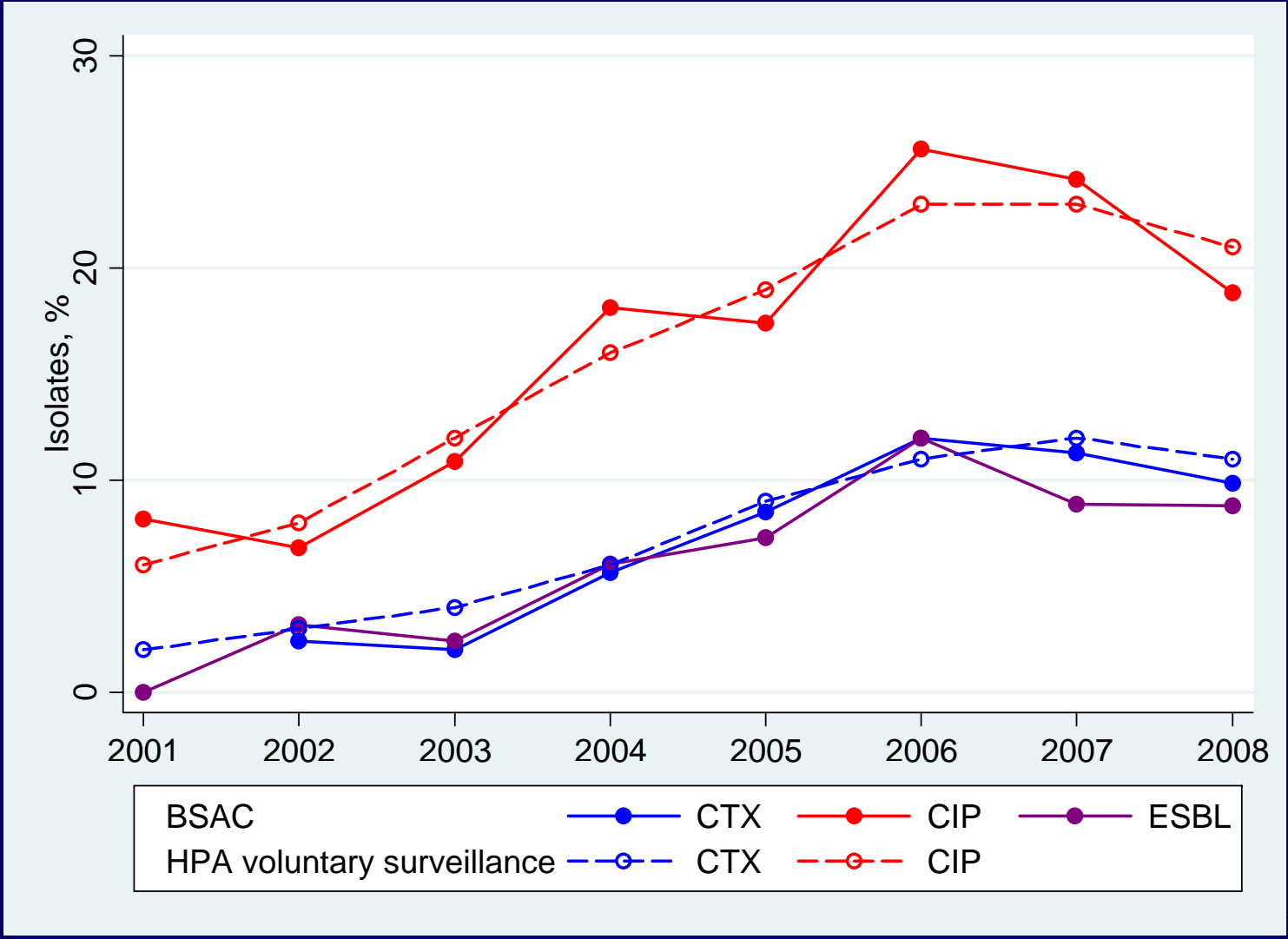
- decline in penicillin non susceptible *S.pneumoniae*
- rise and fall of ESBL producing *E.coli* and *Klebsiella spp*
- the fall of MRSA blood stream infection in England
- the illusion of vancomycin MIC creep in MRSA

Penicillin non-susceptible *S.pneumoniae*

- Great Britain data

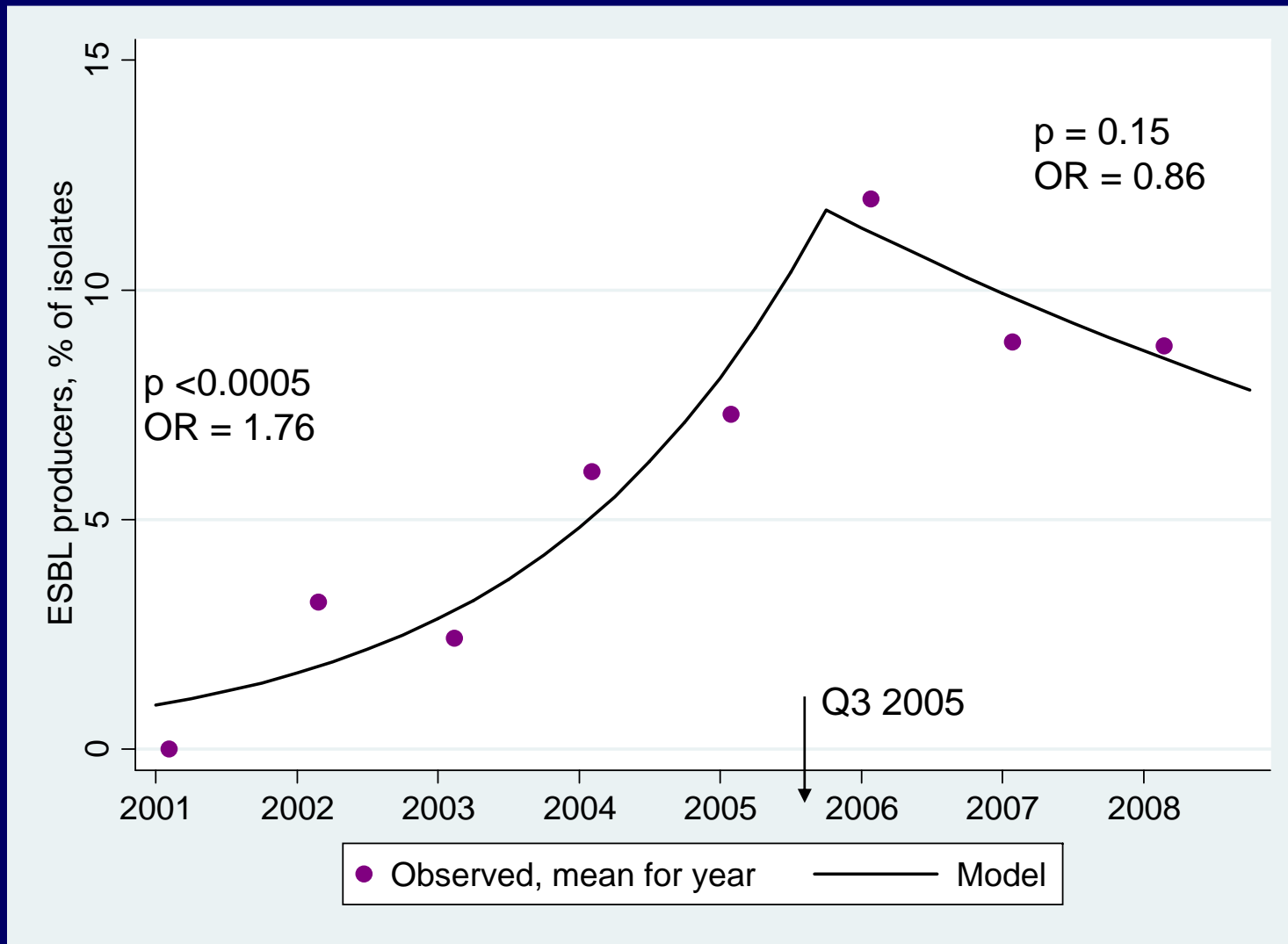
Year	Respiratory programme	Bacteraemia programme
1999-00	7.2%	
2000-01	7.2%	6.8%
2001-02	4.4%	7.1%
2002-03	6.1%	8.0%
2003-04	5.7%	3.0%
2004-05	5.3%	2.0%
2005-06	4.3%	4.2%
2006-07	4.9%	4.3%
2007-08	4.7%	2.2%
2008-09	5.3%	3.7%

E.coli % non-susceptibility and ESBLs

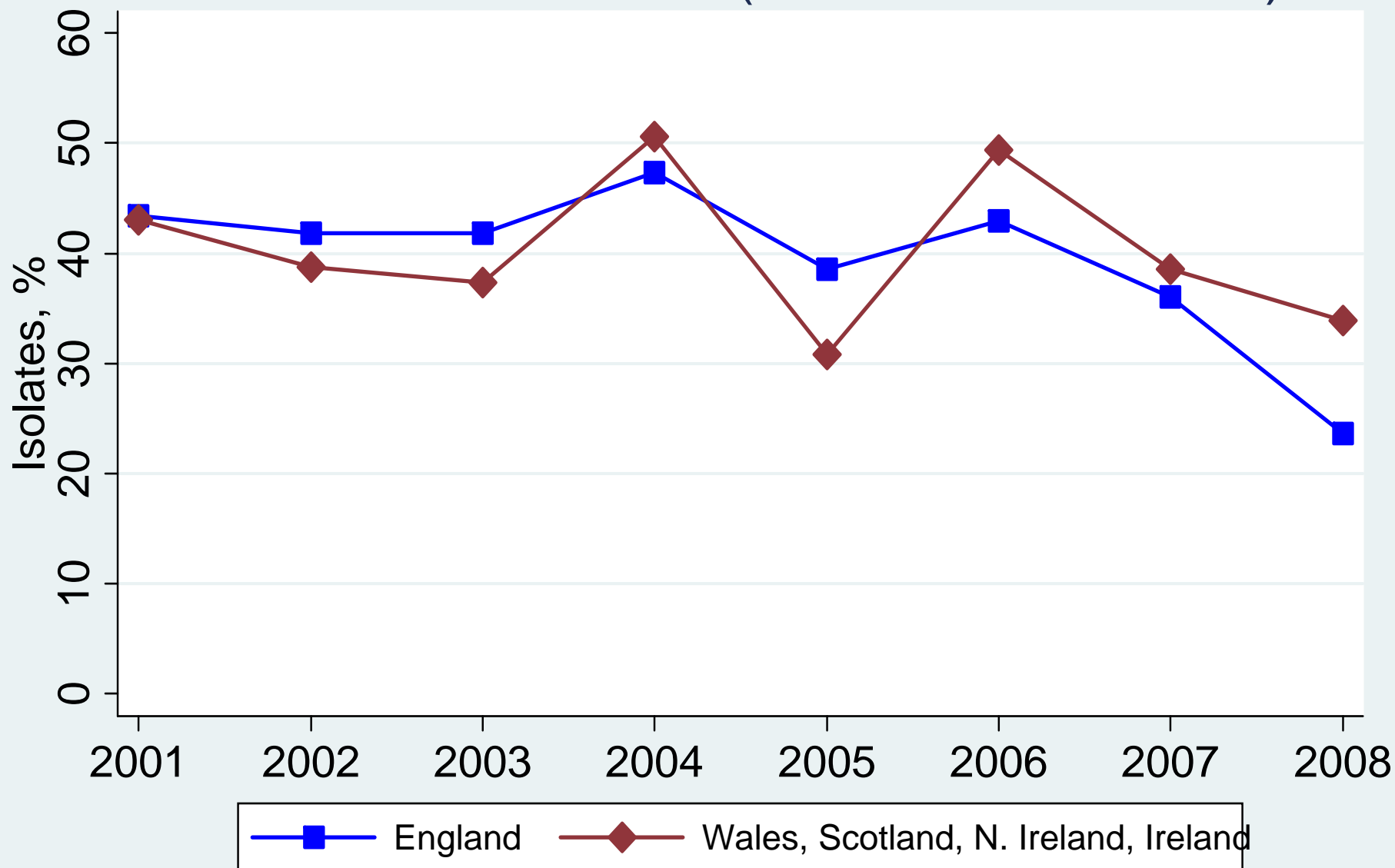


BSAC Bacteraemia 2001-2008; HPA voluntary bacteraemia surveillance 2008

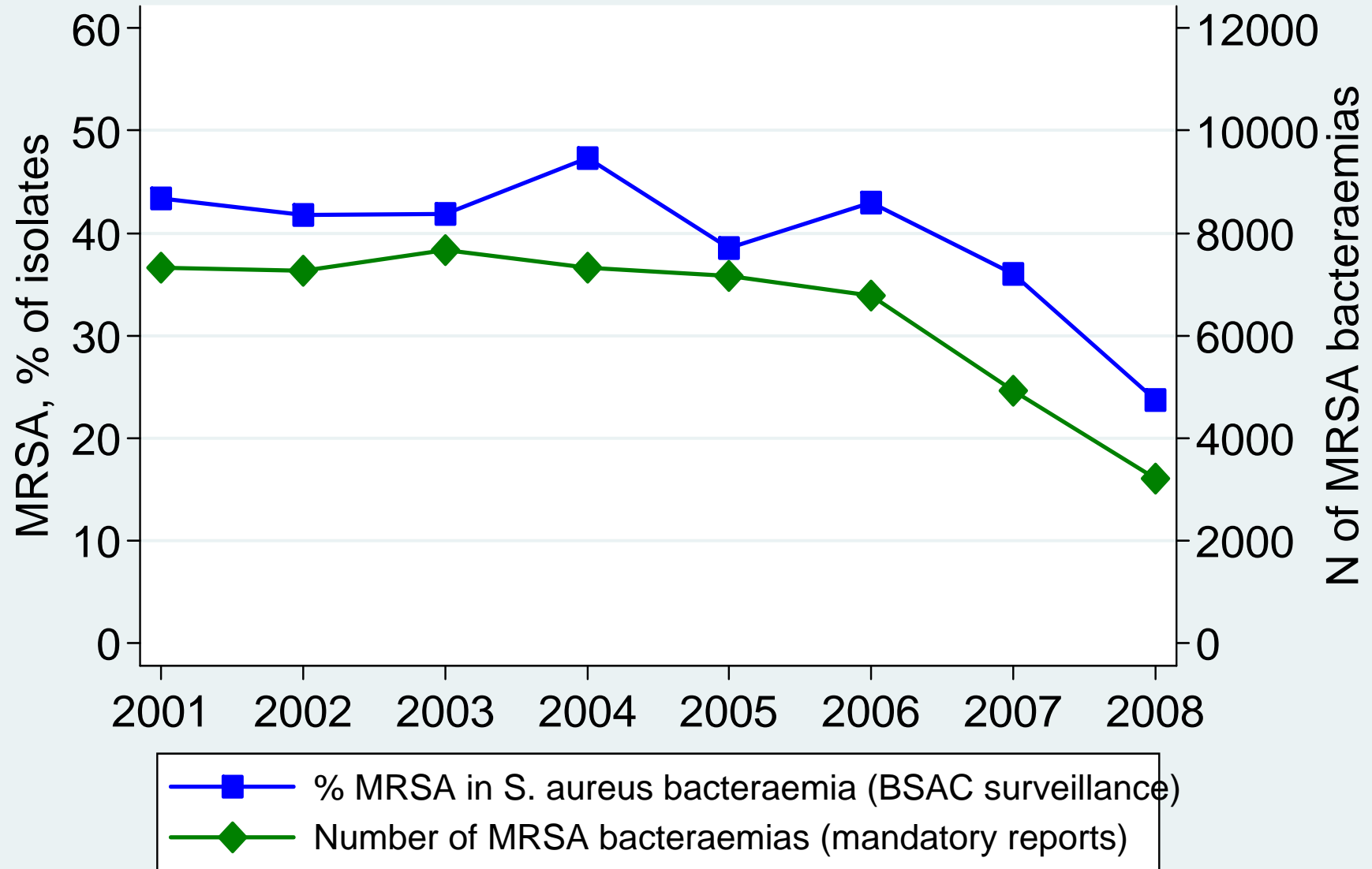
E.coli - ESBL prevalence segmented logistic regression



% MRSA over time (BSAC surveillance)

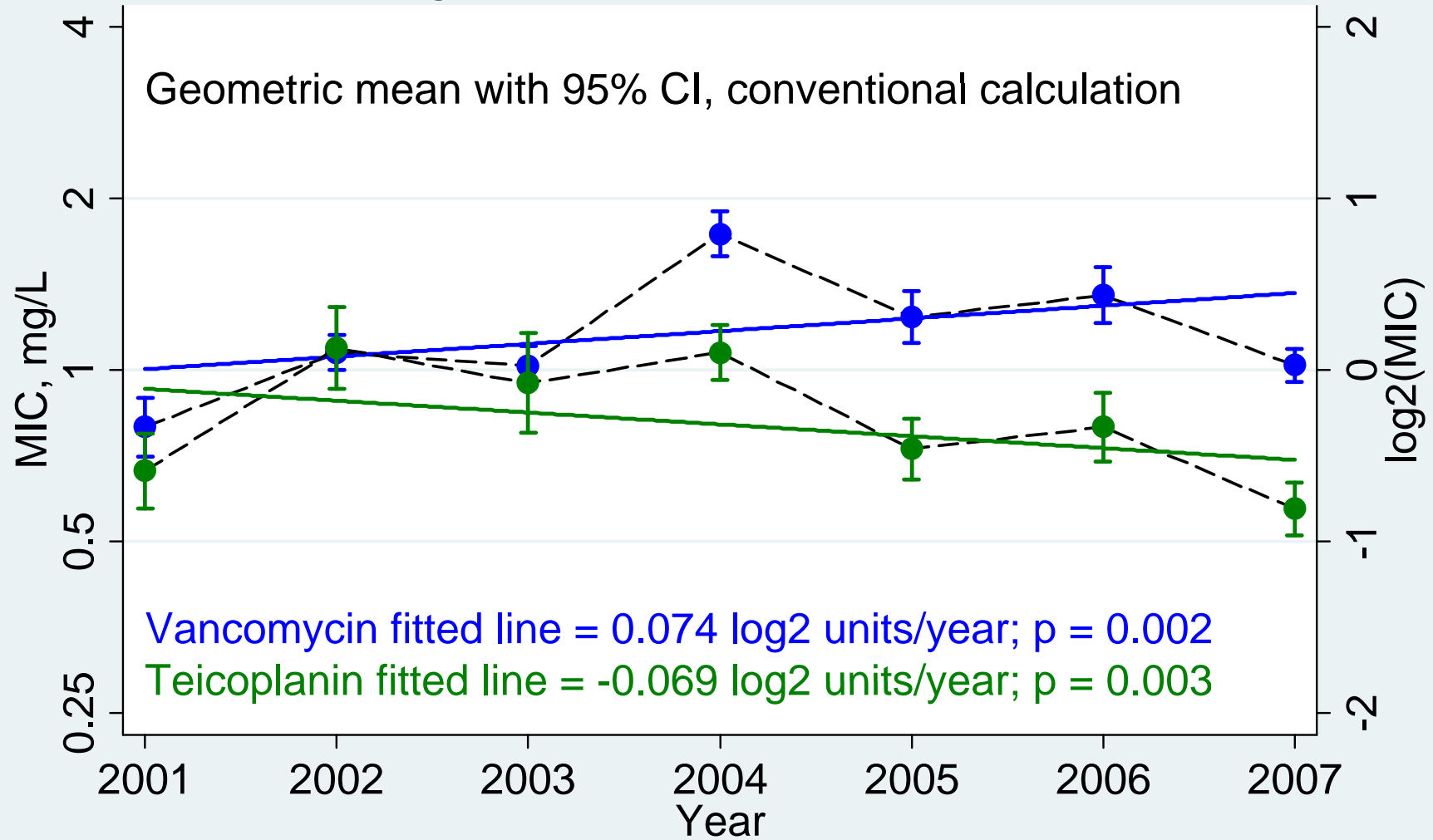


MRSA bacteraemia in England

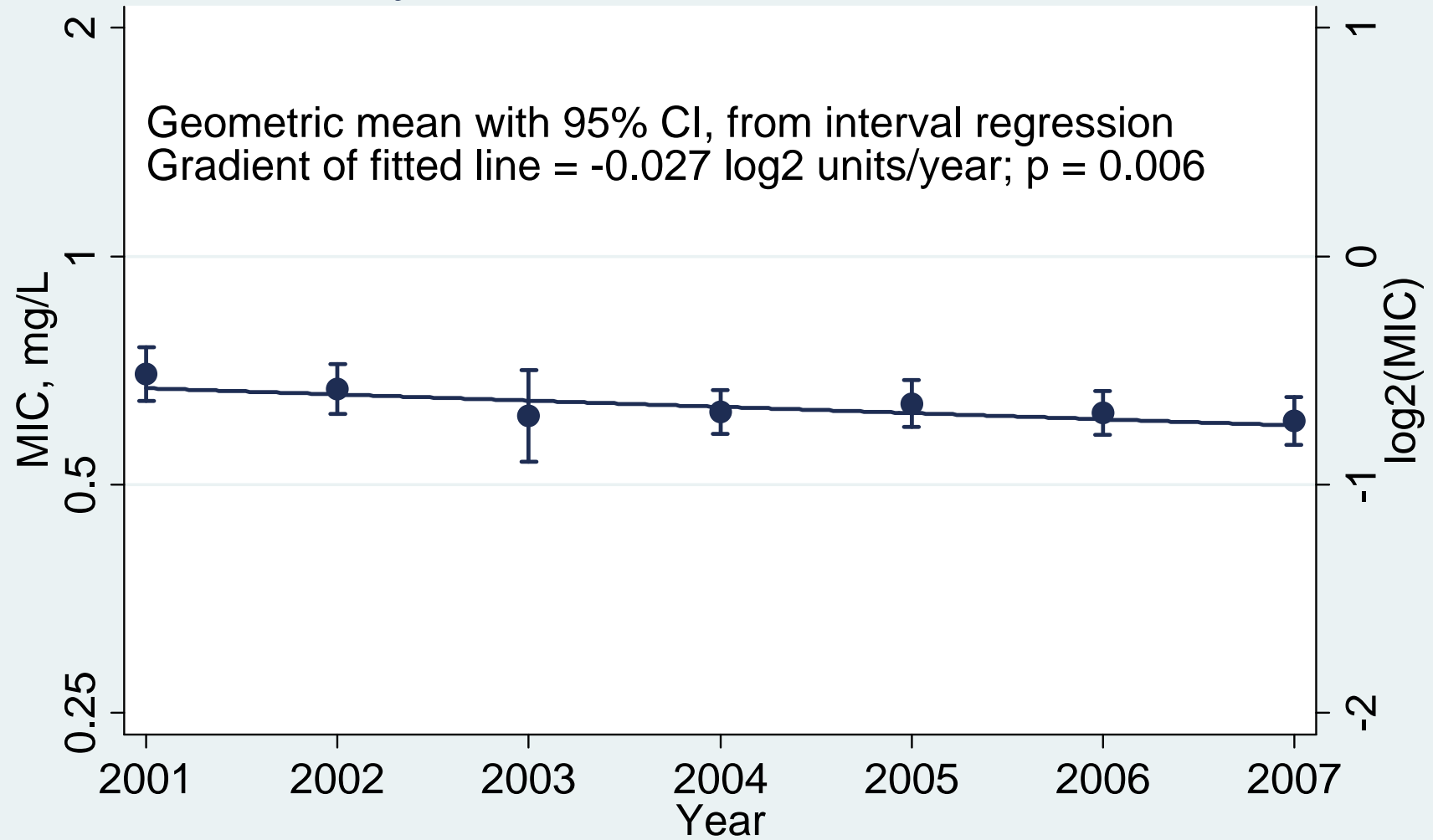


Vancomycin MIC creep

Original MICs for 271 MRSA



Vancomycin MICs for 271 MRSA - re-test

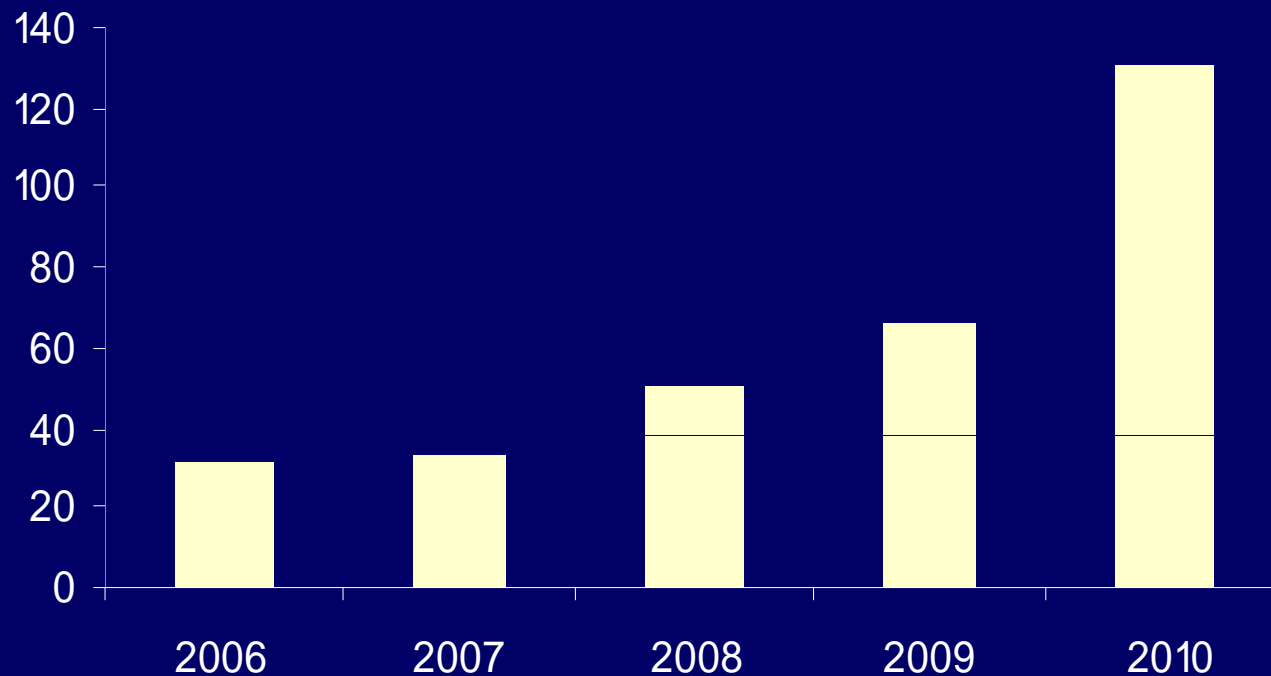


Dissemination of data

Publications in JAC: 13 papers

**Abstracts/Posters/Presentations – FIS, ECCMID
and ICAAC 2001-present: 57**

Average number of daily visits to website



Improving the relevance of surveillance outputs

Unresolved issues

- overcoming bias in the community surveillance
- performing sentinel surveillance in areas where little pharmaceutical interest (UTI, *H.pylori*, cSSTI)
- moving to ISO-20776-1 standard for susceptibility testing

Progress since 1999

- sustainable model established for surveillance in blood stream infection, CAP and HAP
- clinical relevance improved by use of EUCAST clinical breakpoints
- epidemiological/clinical relevance protected by testing “core set” of antimicrobials, and increase in collecting centres
- value to infection practitioners is enhanced by freely available data (e-forms supported by paper)
- BSAC model provides an illustration of how professional societies and industry can work together to enhance national surveillance

Thanks to

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Members of the Working Party

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BSAC HQ Staff

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Website

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Present & Former Sponsors