The Rise and Fall of MRSA in England

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November 2018

Why MRSA?

- It has not gone away

- Archetypical HCAI
- Explains the epidemiology of many HCAIS
- Explains why IPC fails/succeeds
- Supports the importance of IPC and antibiotic stewardship

The hospital epidemiology of SA known by 1940s-50s

- Surgical & neonatal infection (ex streptococci)
- Asymptomatic nasal, skin & faecal carriage
- Shed into air/environment
- Survives in dust & on clothes/fomites
- Direct & indirect transfer
- Self- and cross-infection of surgical wounds

SA designed hospitals and routine hygienic practice

- Surgical/dressing asepsis
- Plenum ventilation/air filtration/positive pressure, separation of beds/dressing rooms/ theatres/ITUs
- Sloping/cleanable surfaces, damp mopping
- Clean uniforms/laundry, cotton blankets
- Handwashing

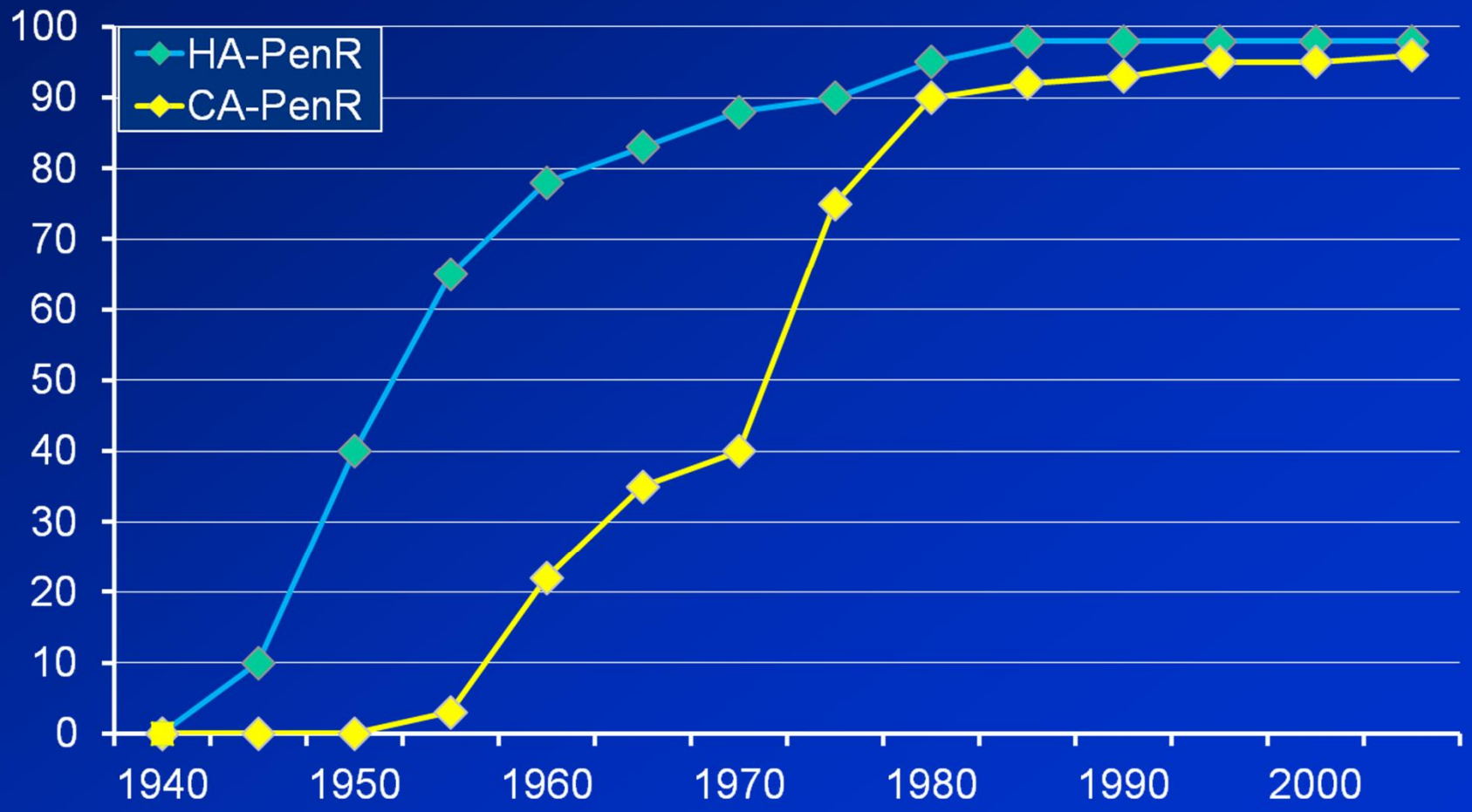
Helped by penicillin – but not for long

Penicillin resistance by production of penicillinase

- Appeared soon after penicillin introduced
- Eventually became almost universal
- First in hospitals, then community

North & Christie, 1946; Barber, 1947

Emergence of penicillinase-producing SA From McDonald LC, CID 2006



Extensive hospital outbreaks penicillin-resistant SA 1950s

- “The Hospital Staphylococcus”
- Often ‘phage type 80/81
- Epidemic & highly virulent
- Worldwide
- International concern, conferences

1959

MINISTRY OF HEALTH

CENTRAL HEALTH SERVICES COUNCIL

STANDING MEDICAL ADVISORY COMMITTEE

Staphylococcal Infections in Hospitals

Report of the Sub-Committee

LONDON
HER MAJESTY'S STATIONERY OFFICE
PRICE 2s. 6d. NET

The 1959 Report

- Infections continue to occur despite increased understanding of control
- Prudent antibiotic use not sufficient by itself
- *"The essence of the problem remains unchanged, namely, to prevent infection by the application of aseptic methods*"
  - including handwashing

Importance of organisation & management

- Extent of problem may be overlooked if no adequate system of recording
- The hospital ICC should review regularly
- Must involve senior staff & Hospital Management

Introduction of methicillin in early 1960s

- And other semi-synthetic penicillins resistant to staphylococcal penicillinase
  - methicillin, oxacillin, cloxacillin, flucloxacillin

Dramatic disappearance of the Hospital Staphylococcus

- Not due to change in control practice
- ? Related to methicillin
- Probably also loss of virulence

There then developed a magic sweetshop of antibiotic choice for SA

- Sulphonamides, trimethoprim, tetracyclines, chloramphenicol, macrolides, beta-lactams, co-amoxiclav, aminoglycosides, rifamycins, quinolones, fusidic acid, glycopeptides, streptogramins, [oxazolidinones, lipopeptides]

1970s: The Decade of complacency Shanson DC, JHI 1981;2:11-36

- No obvious outbreaks
- Plenty of antibiotics
- Lack of fear
- Sense of false security
- Carelessness
- Disregard of rules/good practice
- Hygiene no longer a priority

The vanquishing of SA allowed development of advanced medicine

- Intensive care
- Neonatal care
- Advanced surgery
- Transplantation

à Increasingly vulnerable patients

à Increasing antibiotic usage for GNBs

Antibiotic resistance was lurking

Early emergence of methicillin-resistance, initially rare

Cumulative

Year	Isolates tested	No. resistant	Contributing laboratories
1960	5440	3 (0.06%)	1
1960-1964	43867	213 (0.5%)	35

Parker MT, Jevons MP. Postgrad Med J 1964;40(Suppl):170–178.

Methicillin resistant SA

- Acquisition of *mecA,* which allows production of altered PBP
  - Resistance to all B-lactams
- Carried on staphylococcal cassette chromosome *mec* (SCC*mec*)
  - At least 5 types

Zetola N et al. CA-MRSA: an emerging threat. *Lancet Infect Dis* 2005; 5: 275–86.

Katayama Y et al., *AAC* 2000; 44: 1549–1555.

Hiramatsu K et al., *Trends in Microbiology* 2001; 9: 486-493.

The evolution of MRSA

- Major MRSA clones arise repeatedly by acquisition of *mecA* by successful epidemic MSSA strains
- Have appeared throughout the world in different geographical locations

  à then spread

Enright MC et al. PNAS USA 2002; 99: 7687–92.

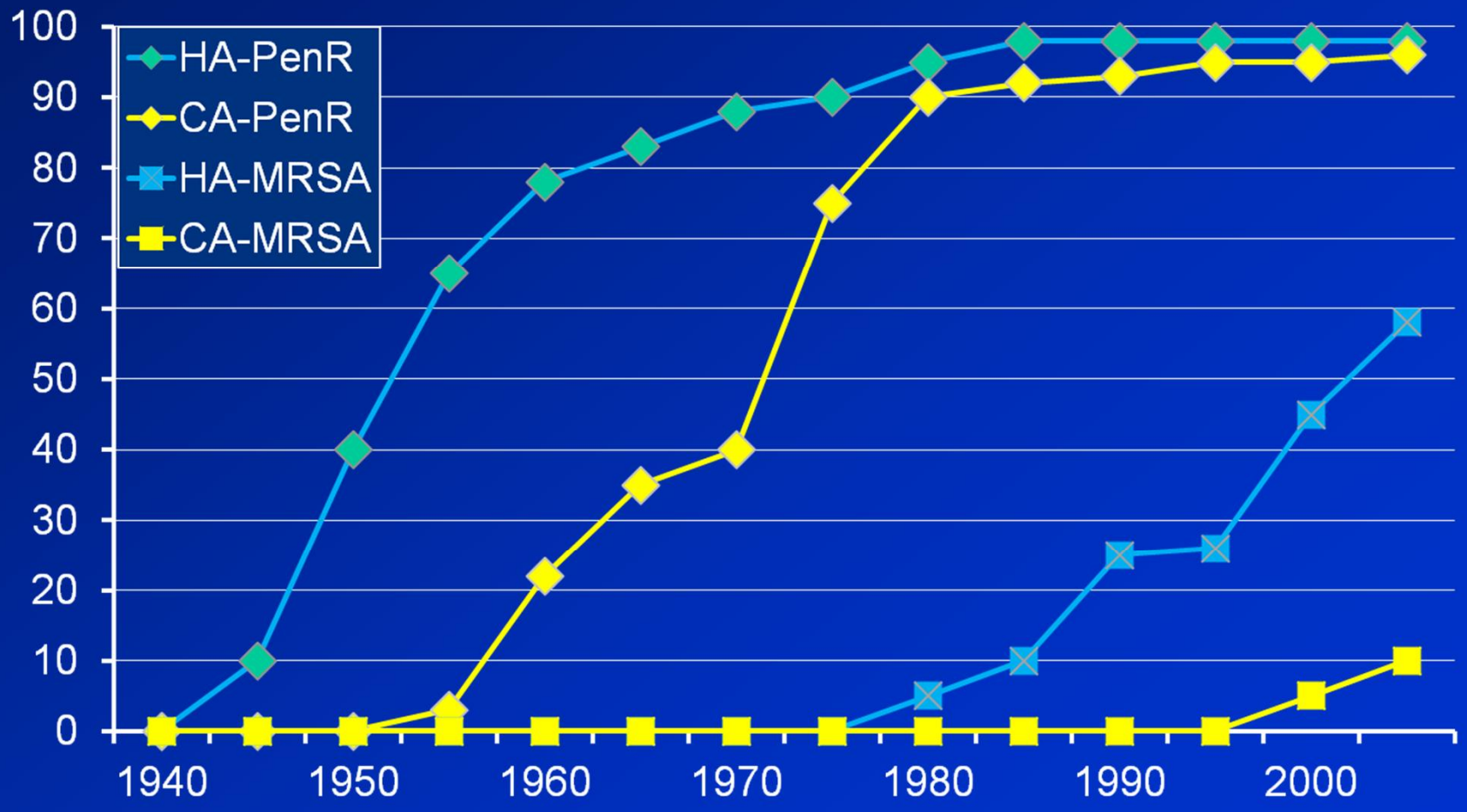
The evolution of MRSA

- Probably encouraged by antibiotic use
- Flucloxacillin etc
  - But also other antibiotics such as quinolones,
  - MRSA usually multi-resistant, especially quinolones

Holden TG et al. Genome Res 2013; 23:653–664

Emergence of resistant SA

From McDonald LC, CID 2006



Then a slow motion explosion of MRSA

- Rare in 1960s
- Sporadic in 1970s
- Epidemic in 1980s
- Endemic worldwide from 1990s
- Mainly hospital/ healthcare-associated

Emergence & spread of epidemic strains (EMRSA)

- Increase in UK in 1990s mainly due to :
- EMRSA-15 (ST22-IV)
- EMRSA-16 (ST36-II)

Johnson AP et al. JAC 2001;8:143–4.

EMRSA-15 & 16

- Both quinolone & macrolide resistant
- Distinct clonal types
- EMRSA-16 more successful
  - ?related to Hospital Staph 80/81

DeLeo FR et al. PNAS 2011;108:18091–6

Major outbreak of new MRSA phage-type, EMRSA-16 Cox R et al. JHI1995;29:87-106.

- 3 hospitals East Midlands 1991-1992
- 400 patients colonized/infected. 7 died
- Spread to all wards (ex paed/obs)
- Eventually controlled by isolation wards, screening, decolonization

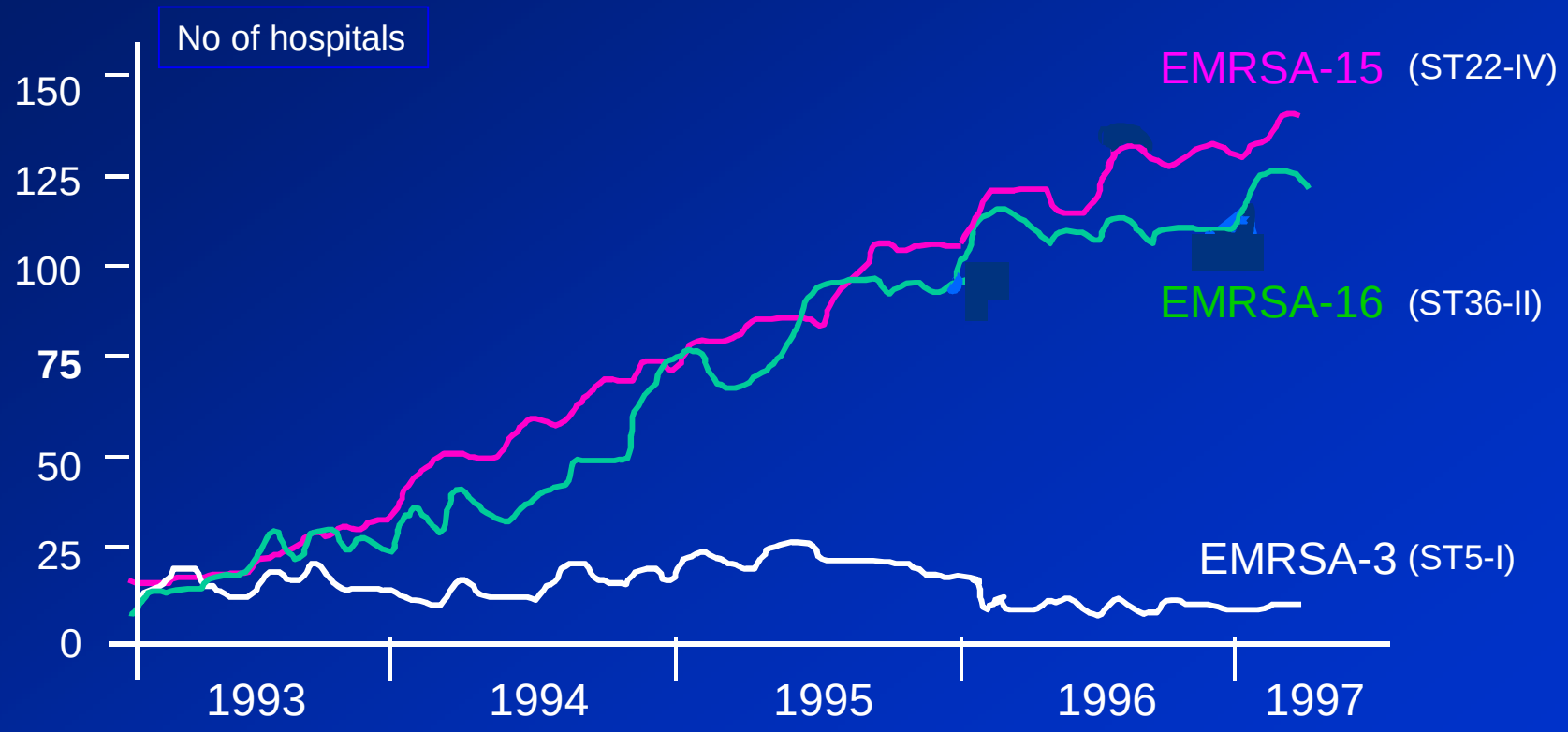
- Cost >£400,000 (£800,000 2018).

EMRSA-16 spread

- The EMRSA-16 had spread to 40 other UK hospitals by 1993, probably by patient transfer
- 443 outbreaks infection/colonization by 1995
  - Also appeared in Ireland, Scandinavia, SE Med, USA

Cox RA et al. JHI 1995;29:87-106;
Murchan S et al. J Clin Micro 2004;42:5154-60.

Epidemic MRSA in England & Wales: Number of hospitals affected



From CDR. Vol 7 No 22, 30 May 1997.

EMRSA-15 & EMRSA-16

- Caused 96% of all UK MRSA bacteraemias during 1999-2000
- (35% 15, 60% 16)

Johnson AP et al. JAC 2001; 48:143–144.

Epidemic MRSA (EMRSA)

- Epidemiology suggests that these EMRSA have special ability to survive & spread
- And that most of the MRSA epidemic was due to person-to-person transmission

MRSA Epidemiology & Control

- Understood by the mid 1990s
  - Actually similar to MSSA, known since late 1950s
- But now more antibiotic resistant and more transmissible
- Less virulent à more asymp colonisation à more silent spread

Mulligan ME et al, Am J Med 1993; 94: 313-328; Boyce JM et al. ICHE1994;15(2):105-15. Working Party JHI 1998;39:253-290.

Epidemiology of MRSA

- Hospital- and healthcare-associated
- Usually compromised patients
- Colonisation precedes infection
- Infection often associated with surgery & indwelling devices
- Antibiotic resistant
  - associated with antibiotic usage

Epidemiology of MRSA

- Brought into hospital by patient carriers
- Constant re-introductions (revolving door)
- And patient movement
  - Within & between hospitals
  - especially via ITU
- Organisms usually transferred via staff hands

Control of Hospital Infection

- Since we know the epidemiology of MRSA
- It should be possible to control it

By 2000s, MRSA IPC included:

- Policies, guidelines, education, training
- Standard hygienic practice
  - including hand washing, environmental cleaning,
  - IV catheter care etc
- Patient screening, decontamination, isolation
- Surgical prophylaxis
- Surveillance & feedback to clinical areas
- Prudent antimicrobial use

Working Party. JHI 1998;39:253-290; Arnold et al ICHE 2002;23:69-76.; Muto et al ICHE 2003;24:362-86; Coia et al JHI 2006;63(Suppl):S1-44.

But MRSA infection rates increased inexorably

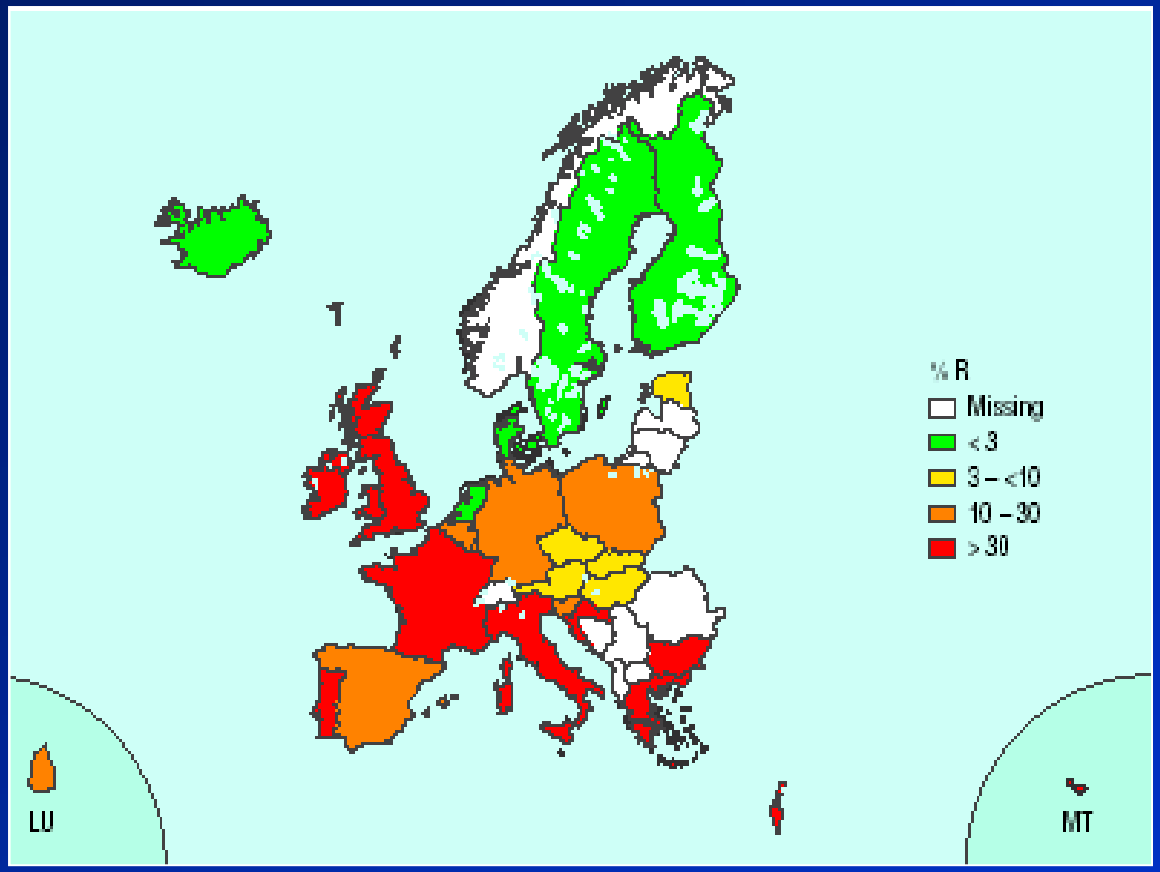
Rising MRSA infections in English hospitals (voluntary reporting)

Voluntary	1990	2003	1997-2005
MRSA Bacteraemias	68	~5800	
% SA Bacteraemias that were MRSA	2%	40%	
% of SSIs yielding MRSA			26% twice that of any other organism

NAO. Improving patient care by reducing the risk of hospital acquired infection. 2004. HPA. *Surveillance of Surgical Site Infection in England*. 2006. Johnston AP et al. JAC 2005; 56: 455–62.

By 2002: UK had the 2nd highest MRSA bacteraemia rate in Europe (27 countries)

Tiemersma EW et al. Emerg Infect Dis 2004;10:627-1634.



EARSS

Average 20%

UK ~45%,

Greece 55%

Netherlands,

Scandinavia <1%

Why did IPC fail?

Some did not believe in the importance of MRSA

- MRSA only counted because it has a marker
- Most are colonisations only
- MRSA = MSSA for pathogenicity, Rx, IPC
  - Indeed, less virulent (?less fit)
- Resources better used elsewhere

Lacey. MRSA - a suitable case for inactivity? JHI 1987;9:103-5. Rahman. Learning to live with MRSA. Postgr Med J 1988;74:385–386. Nair & Henderson. MRSA clinical importance remains unevaluated. BMJ 1994;308:57-8. Barrett et al. Trying to control MRSA causes more problems than it solves. JHI I998;39:85-93.

They should have done

MRSA and MSSA are equally pathogenic:

- Similar virulence in animal models
- Isolated in similar proportions from deep & superficial sites
- Bacteraemia mortality rates similar
- In animals & patients, MRSA mortality rates reduced by vancomycin

French GL et al. JHI 1990;15:117-l 25.

Indeed, MRSA infections are associated with worse outcomes

- Compared with MSSA, & controlled for risk, MRSA infections have increased:
  - mortality (x2), morbidity, prolonged hospital stay, increased healthcare costs & hospital resource utilization

Cosgrove SE et al. CID 2003;36:36:53–9. Engemann JJ et al. CID 2003;36:592-598. Stevens DL *et al*. CID 2002;34:1481-90. Li Z *et al*. Pharmacotherapy 2001;21(3):263-74.

Many thought the problem was primarily due to limited resources

- MRSA epidemiology & IPC unproven
- Isolation wards lost
- Increased bureaucracy, performance management & targets are counterproductive
- Staff are doing their best
- Improvements unlikely without more staff & resources

Dancer S, Simmons N. JHI 2006;62:261-3; Bair D. JHI 2006;64:336-8.

It is true there was a lack of evidence for MRSA IPC

- 2006 – 2014:
- Insufficient high-quality evidence to confirm effectiveness of:
  - Screening, isolation, decolonization, feedback, environmental cleaning

Loveday HP et al. JHI 2006;63(Suppl):S45–S70.
Kocke R et al. Euro Surveil 2014;24:19(29)

But much was probably true

For example: environmental contamination

- 1940s -1950s: environment regarded as very important for transmission
- 1970s -1980s: environment thought not to be usually contaminated and unimportant
- View persisted into 1990s

Weber DO et al. Arch Surg 1976;111:484–488.
Maki DG et al. NEJM 1982;307: 1562–1566.
Haley RW. Am J Med 1981;70:941–946.
McGowan JE. Rev Infect Dis 1981;3:760–769.

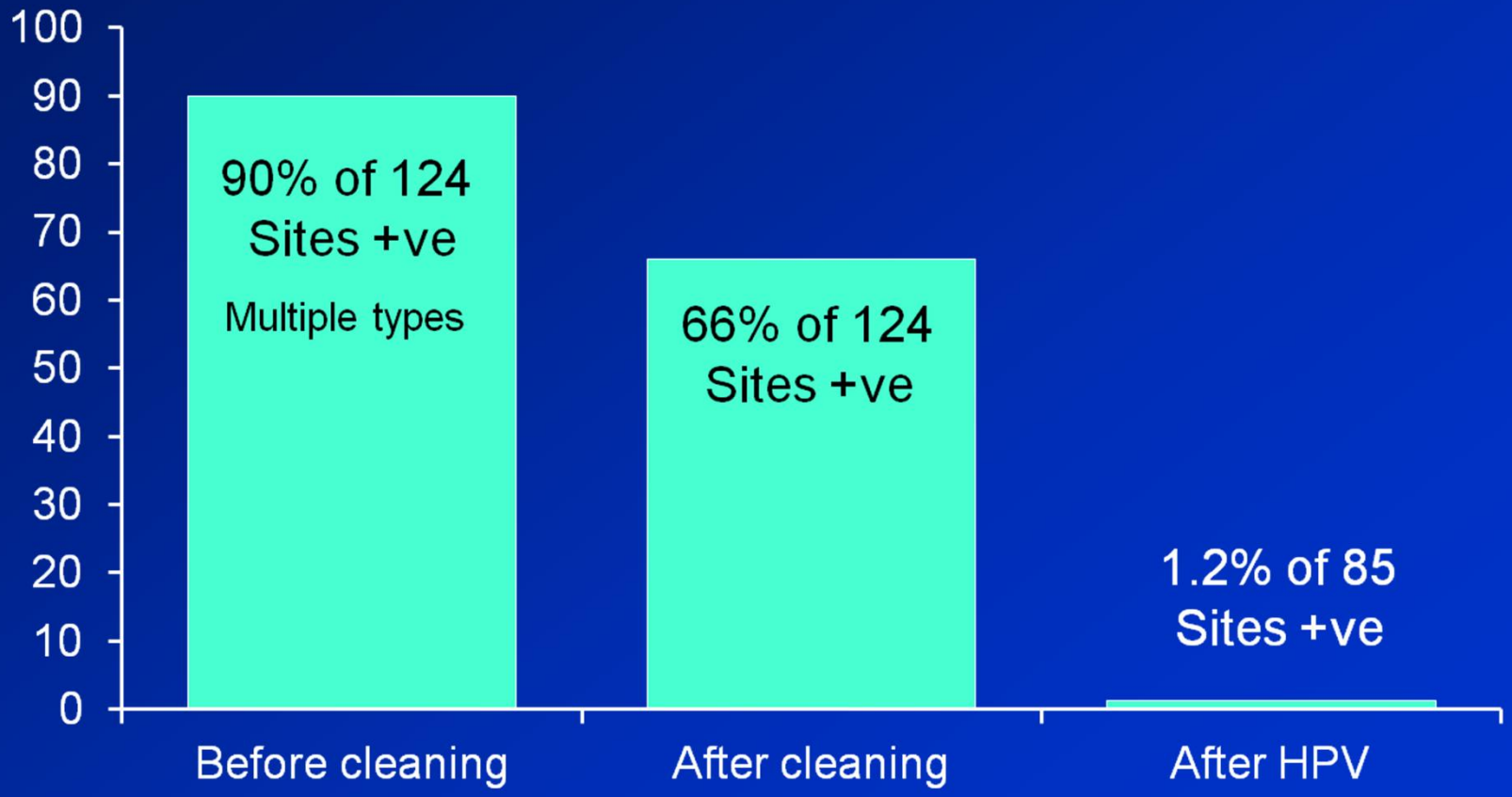
More recent studies show that MRSA & other nosocomial pathogens:

- Are shed by patients
- Contaminate hospital surfaces
- Survive for extended periods
- Persist despite cleaning/disinfection
- Contaminate hands of healthcare workers
- Contribute to patient-patient transmission

Otter JA, Yezli S, French GL. The role played by contaminated surfaces in the transmission of nosocomial pathogens ICHE 2011;32: 687-99.

MRSA contaminating isolation rooms

French GL et al, JHI 2004;57:31-7



The environment is important

- Admission to a room previously occupied by a patient with MRSA (and other nosocomial pathogens) increases acquisition risk for subsequent patients
- Improved cleaning and disinfection of room surfaces decreases the risk

Otter JA et al. ICHE 2011;32: 687-99.

Weber DJ et al. Cur Opin Infect Dis 2013;2:338-44.

Performance or Resources?

- *Either the guidelines have not been implemented or the conditions for their implementation are not present. Either way they have proved ineffective in practice.*

Cunningham JB. JHI 2006;64:296-7

The Guidelines were not being implemented

- Knowledge of MRSA epidemiology, IPC & treatment poor
- Hand decontamination compliance ~30%
- Staff often did not seem to understand or believe in hygienic practice
- They were deluded

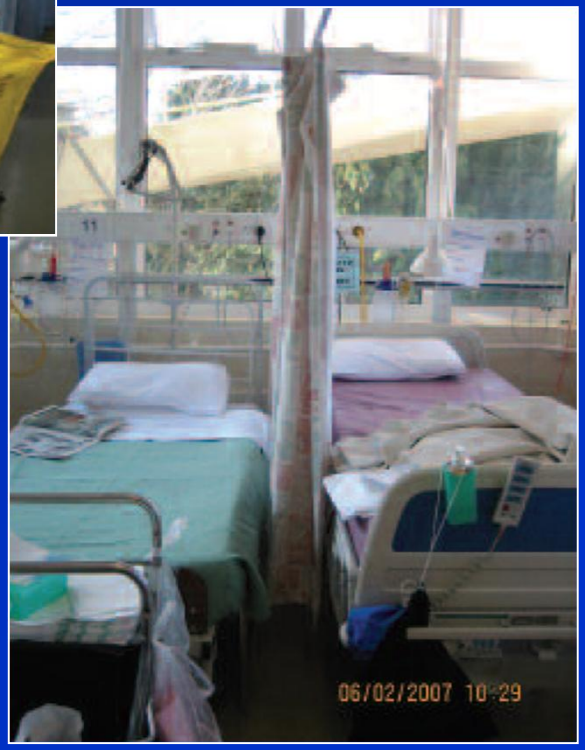
Seaton RA, Montazeri AH.JHI 2006;64:2979.

French GL. Dirty, deluded, and dangerous. BMJ 2012;345:8330.

The guidelines were not being implemented

- Little handwashing
- Dirty wards
- Little isolation
- Poor catheter care
- Little MRSA surgical prophylaxis
- No counting, feedback
- No ICC meetings
- Poor antibiotic control

Healthcare Commission. Investigations into outbreaks of *Clostridium difficile* at Stoke Mandeville 2006 and Maidstone and Tunbridge Wells 2007



Professionals vs Public

- Doctors played down the importance of MRSA
- Disputed the relationship between hospital cleanliness & infection
- Disputed the relationship between MRSA bacteraemias & IPC

In contrast, the public perceived MRSA as lethal ‘superbug’, indicating:

- Poor hygiene, Dirty hospitals

  = Medical, nursing, managerial, political failure
- A terrifying plague & national disgrace
  - 2880 articles on MRSA published in 12 UK news-papers between 1994 and 2005

Boyce T et al. JHI 2009;73:400-7.

Political action

- Taken up by patient action groups
- Debated in the Lords with personal stories

- Plowman et al had shown the high cost of HCAIs & the cost-effectiveness of control

- MRSA control became a political imperative

Plowman et al (1999). The socio-economic Burden of Hospital Acquired Infection. PHLS, London.

Mandatory Reporting 2001

- Minister of Health: Hospitals must report & publish their MRSA rates
- The measurement was MRSA bacteraemias
  - Bacteraemias = significant infection
  - Blood cultures taken in consistent way
  - Rates per 100,000 OBDs allows comparisons between different types and sizes of hospital

Individual hospital MRSA bacteraemia rates

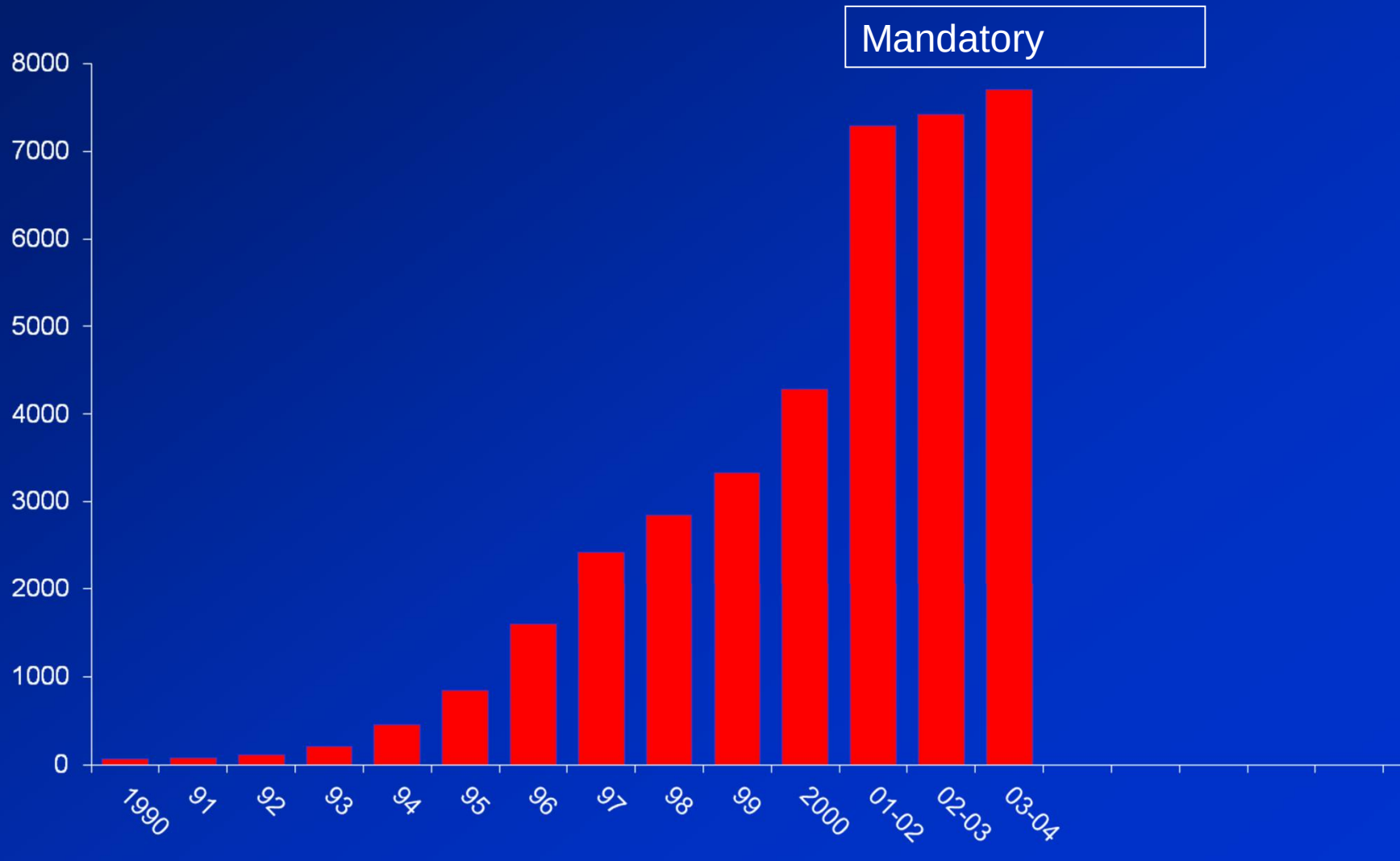
- Reported to the HPA
- Published on their website
- Available publicly

- All hospitals should match the best rates
  - à continuous reductions towards zero

Mandatory reporting began in October 2001

- Revealed >7000 MRSA bacteraemias annually
  - Much higher than with the voluntary scheme
- Numbers reached 7700 in 2003-4

MRSA Bacteraemias: Total Episodes, England 1990-2004



MRSA rates varied with risk

- Single specialty hospitals very low rates
- Smaller acute hospitals median rates
- Tertiary referral hospitals highest rates

- Rates were low in paediatric and obstetric units and high in ITUs

HPA 2004; Johnson et al 2005; Otter et al 2013

How much failure of IPC???

- Rule of thumb 1 in 10:

  8,000 MRSA bacteraemias pa

  = 80,000 serious MRSA infections

  = 800,000 colonisations

  = 8,000,000 failures of IPC pa

  = 19,000 failures per day

  = 800 per hour

Action

- Hospitals encouraged reduce MRSA rates
- Publication of new (old) IPC policies and guidelines

Publications 2000-2003

National Audit Office (NAO) (2000). *The Management and Control of Hospital Acquired Infection in Acute NHS Trusts.*

NHS Controls Assurance Standards: *Infection Control. 2000-2003.*

Health Services Circular 200/002. *Action for the NHS for the Management and Control of Infection in Hospitals in England*

EPIC (2001). *Guidelines for preventing hospital-acquired infections.*

CMO Report: Getting ahead of the curve (2003). *A strategy for combating infectious diseases.*

NICE (2003). *Infection control: prevention of Healthcare-Associated Infections in* primary and community *care.*

CMO Report: Winning Ways (2003). *Working together to reduce Healthcare Associated Infections in England*

MRSA Guidelines

Guidelines for the control of MRSA. JHI 1986;7:193-201.

Guidelines for the control of epidemic MRSA. JHI 1990;16:351-77.

Revised MRSA guidelines for hospitals. JHI 1998;39:253-290.

Guidelines for the control and prevention of MRSA in healthcare facilities. JHI 2006;63S:S1-S44

Guidelines for the prophylaxis and treatment of MRSA infections in the UK. JAC 2006;57:589–608

Lack of progress

Implementation has been patchy. Progress is dependent on changing staff behaviour, but change constrained by limited progress in mandatory surveillance

National Audit Office (2004). Improving patient care by reducing the risk of hospital acquired infection: A progress report

Chief Medical Officer 2005

- The time for exhortation is over

Care bundles published for:

- Contact precautions
  - Improved hand hygiene with bedside alcohol gel
- Isolation and decolonisation of carriers
- Management of intravascular lines
- Changes in antibiotic prescribing
- Environmental cleaning
- MRSA admission screening

Saving Lives (2005): A delivery programme to reduce HCAI, including MRSA

AND AUDITED

- Bacteraemia reporting
- Hand decontamination
- IV catheter care
- Environmental cleanliness
- Antibiotic prescribing
- Surgical check lists
- Admission screening

Targets set in 2004

- Reduce MRSA bacteraemias by 50% by 2008
- Trusts that failed to show continuing monthly reduction in rates inspected by special Teams
  - Issued improvement plans that had to be implemented by Trust Senior Management

The Health Act 2006

- For the first time a legal requirement for Hospitals to comply with a Code of Practice for IPC
- Required IPC to be embedded into everyday practice & applied consistently by everyone
- Establishment of DIPC,who sat on Board

Healthcare Commission set up to audit compliance

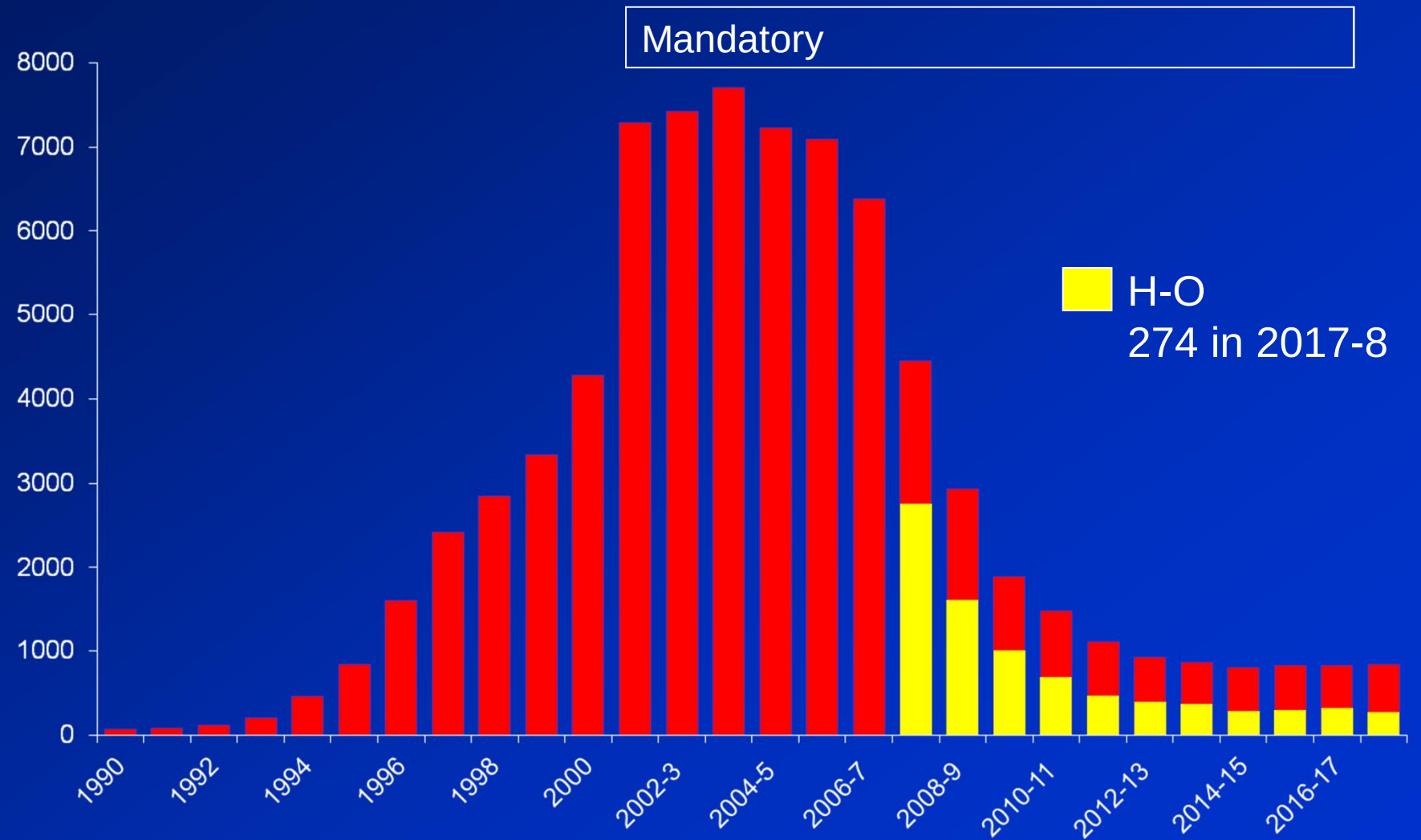
- Failure to comply à legally binding improvement notices
- Hospital management might be replaced
- à Concentrated minds

Change in culture

- Training
- Hand decontamination (bedside/ward)
- Clean wards
- Strict catheter care
- Feedback of Audits (ward charts)
- Expanded ICC
- Feedback to Board
- Internal performance management

There was a fall in MRSA bacteraemias

MRSA Bacteraemia Total Episodes, England 1990-2018



Fall in MRSA bacteraemias in 150 English Hospital Trusts 2003 - 2018

Mean	2003-4	2008-9	2012-3	2017-8	% Fall since 2004
Total	7700	2935	924	846	89%
Mean HO*	47.2	19.6 10.7	6.6 2.7	5.7 1.8	88% 96%
Mean rate** HO*	16.9	7.8 4.3	2.6 1.2	2.4 0.8	86% 95%

*Hospital onset; **Per 100,000 OBDs

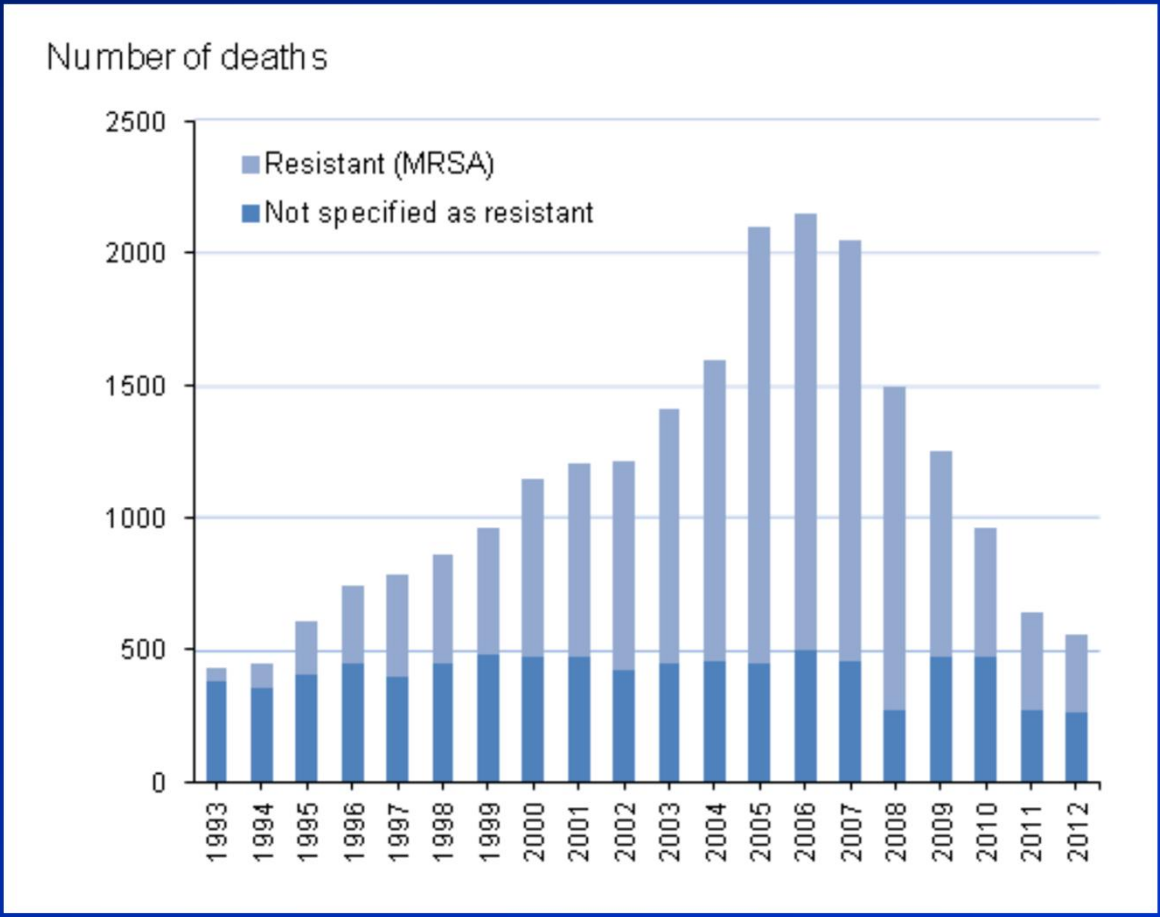
Reasons for success

- After the introduction of the national programme, there was:
  - A change in hospital culture
  - Improvement in IPC compliance
  - Improvement in antibiotic prescribing
  - Good medical practice

- Enforced by performance management

Was it true?

Parallel fall in MRSA mentioned on death certificates in England



EARSS: European MRSA bacteraemia rates 2002-15

- 2002: average = 20%
  - UK 45%, 26th/27 countries
- 2015: average = 17%,
  - UK 11%, 13th/30

EARSS: Rising & falling MRSA rates

- By 2012:

  Significant increases in 4 countries

  – Norway, Poland, Portugal, Romania

  Significant decreases in 7 countries

  – Belgium, Croatia, France, Germany, Hungary, Ireland, UK

- 2015: MRSA rates ranged 0 - 57%

  – 8/30 countries had rates of >25%

EARSS-Net, 2016

EARSS 2016

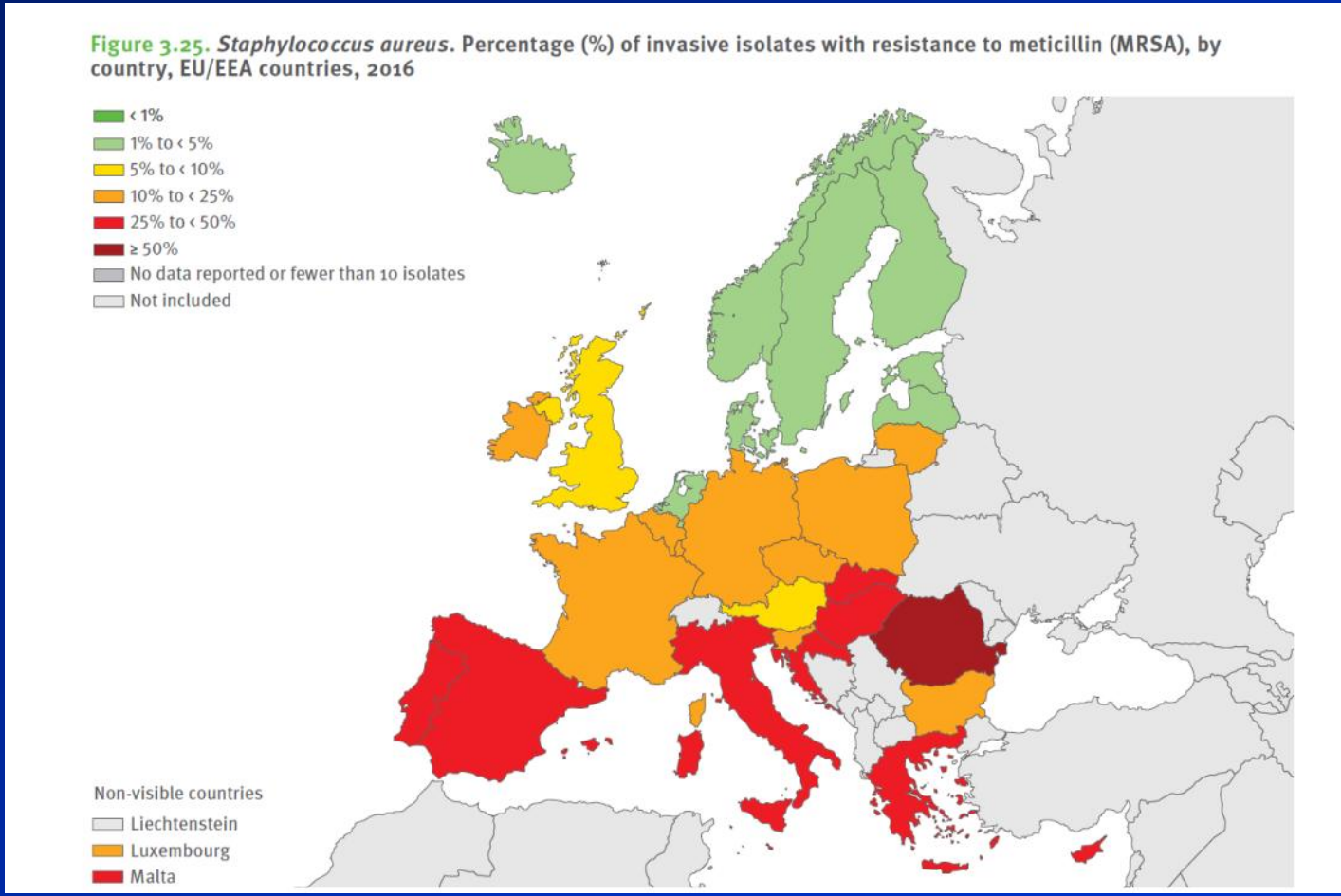


Figure 3.25. *Staphylococcus aureus*. Percentage (%) of invasive isolates with resistance to meticillin (MRSA), by country, EU/EEA countries, 2016
< 1%
1% to < 5%
5% to < 10%
10% to < 25%
25% to < 50%
≥ 50%
No data reported or fewer than 10 isolates
Not included
Non-visible countries
Liechtenstein
Luxembourg
Malta

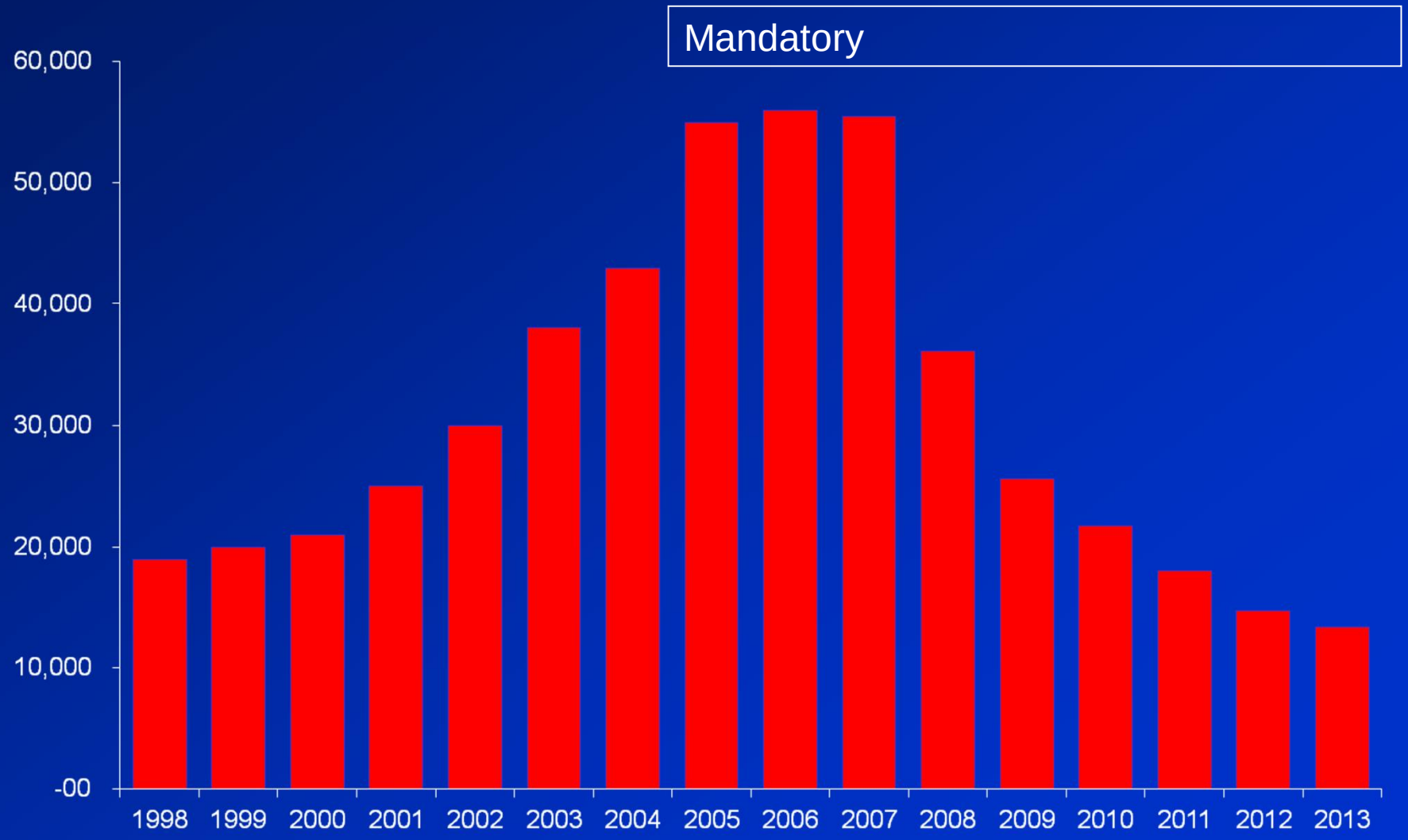
MRSA has revolving door epidemiology

- As MRSA rates fall, the number of patients admitted with MRSA carriage should also fall
  - STH 2008-9: 2% admissions were carriers
  - Compared with 7% in 2006-7 and 9% at another London hospital in 2004
- Thus the burden of MRSA had fallen also

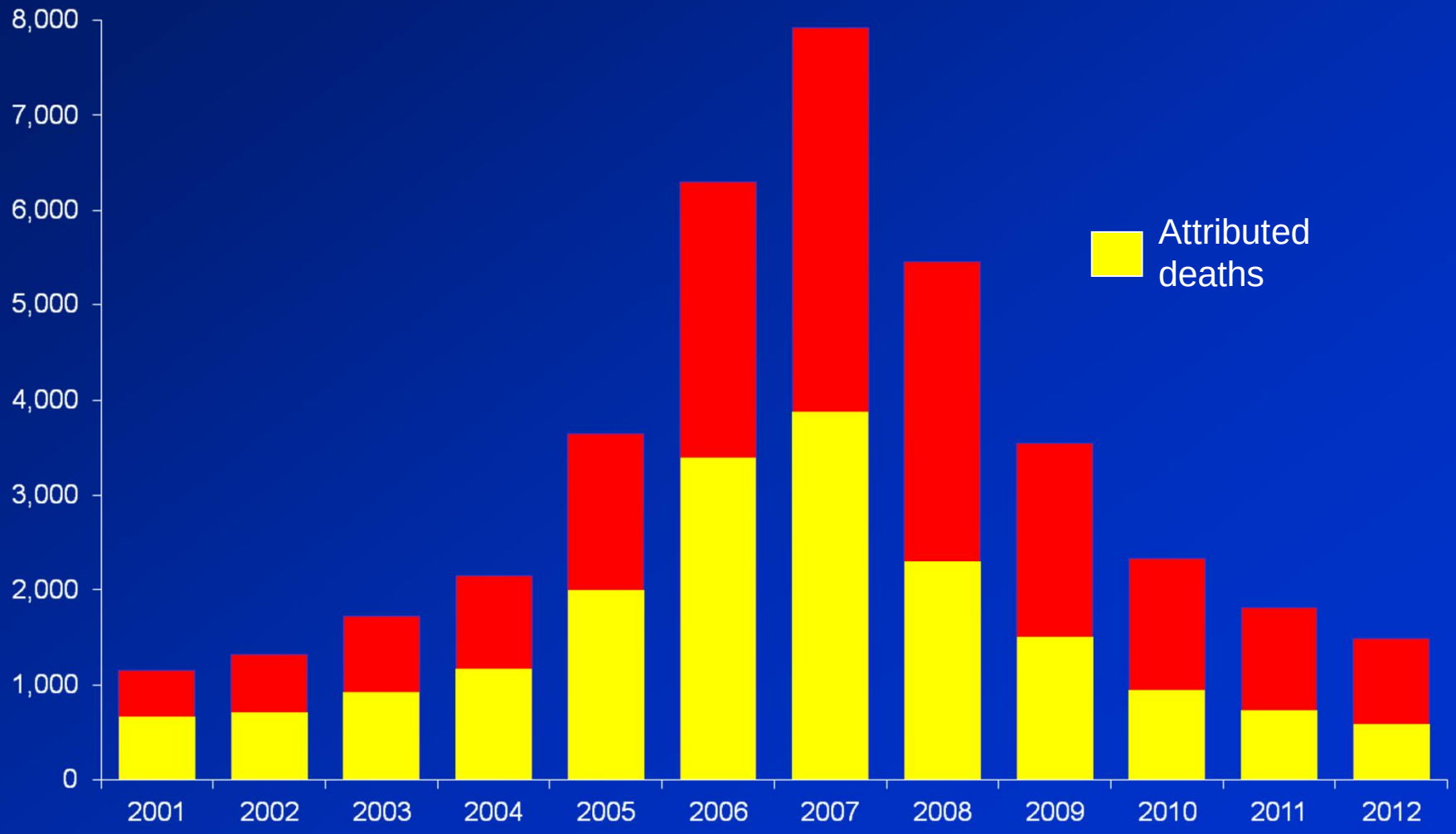
Jeyaratnam et al, 2008; Gopal Rao et al, 2007

Similar performance-managed interventions for Cdiff were followed by fall in Cdiff rates in England

Clostridium difficile surveillance England PHE 2018



Clostridium difficile mentioned on death certificates, England ONS 2012



Supported by evidence from Cleanyourhands campaign

- 87 acute trusts 2004-8
- Procurement soap & alcohol hand rub tripled
- MRSA bacteraemia rates & CDIs fell
- MSSA bacteraemia rates did not fall

Stone SP et al. BMJ 2012;344:e3005.

Cleanyourhands campaign

- Increased soap associated with reduced CDI
- Increased alcohol hand rub associated with reduced MRSA in last 4Qs
- Publication Health Act 2006 strongly associated with reduced MRSA & CDIs
- Reduced MRSA & CDIs for at least 2Qs after each Improvement Team visit

Stone SP et al. BMJ 2012;344:e3005,

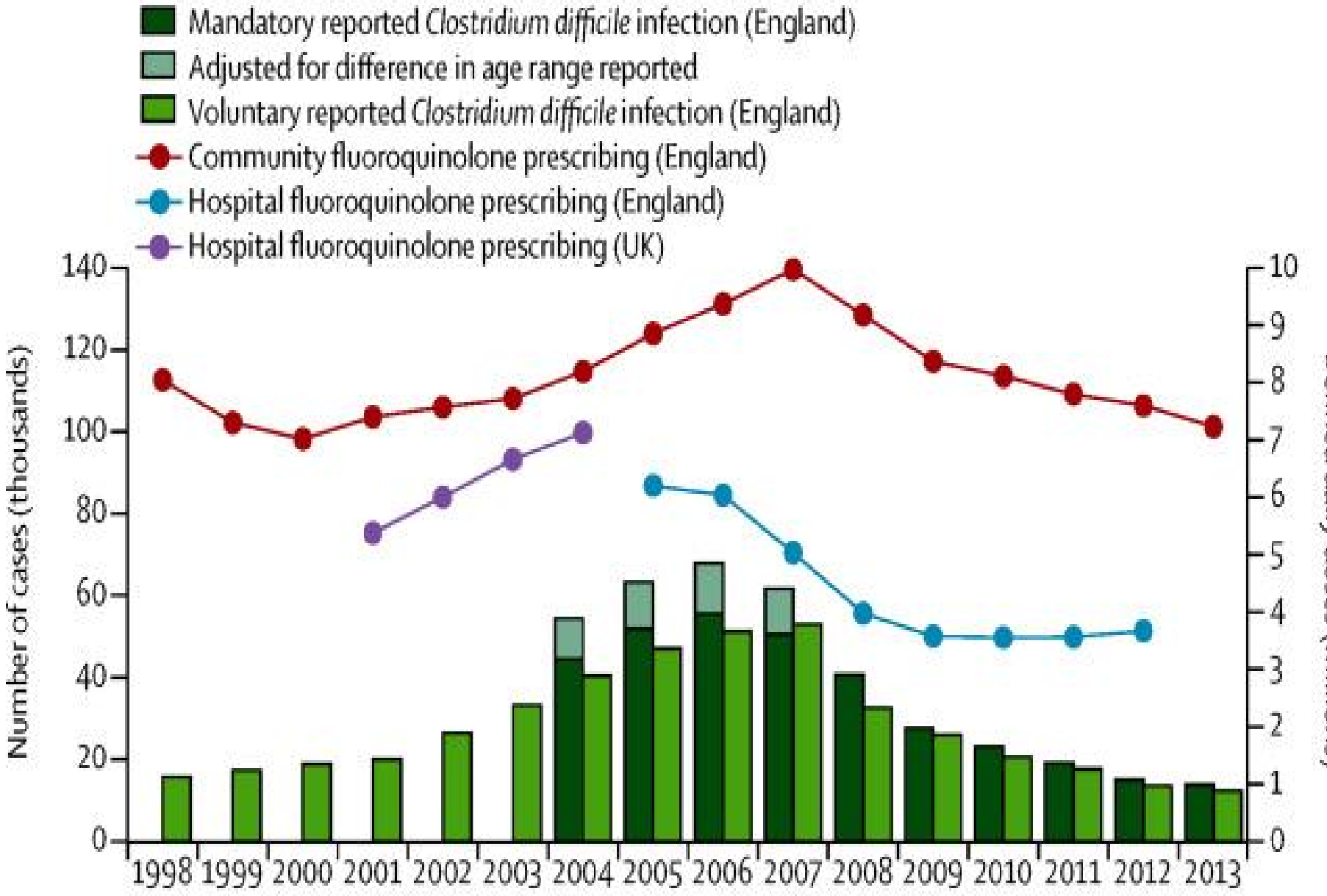
But did IPC really have any effect at all?

- It took a long time to get MRSA under control
- All epidemics eventually go away
- Epidemic strains appear and disappear
  - disappearance of The Hospital staphylococcus; the decline of MRSA-16 (began before national interventions) & then -15; decline of USA-300 CA-MRSA

- Ellington MJ et al. JAC 2010;65:446–8. Wylie D et al. JAC 2011; 66: 2685–88; BMJ Open 2011;1:e000160. Benning A et al. BMJ 2011; 342: d199. Planet PJ. JID 2017;215(S1):S71-7

Was reduction in quinolone use more important than IPC for control of Cdiff?

Dingle KE et al. Effects of control interventions on Clostridium difficile infection in England: an observational study. LID Dis 2017; 17: 411–21.


Mandatory reported Clostridium difficile infection (England)
Adjusted for difference in age range reported
Voluntary reported Clostridium difficile infection (England)
Community fluoroquinolone prescribing (England)
Hospital fluoroquinolone prescribing (England)
Hospital fluoroquinolone prescribing (UK)
Number of cases (thousands)
Defined daily doses (millions)
0
20
40
60
80
100
120
140
0
1
2
3
4
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6
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1998
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Was reduction in quinolone use more important than IPC for control of Cdiff?

Oxford & Leeds: Significant declines in transmission caused by quin-RES isolates ($p<0{\cdot}0001$) vs no change in transmission of quin-SENS isolates ($p>0{\cdot}2$)

But has been debated

Donskey CJ. Comment. LID2017 17:353-4.

van Kleef E et al. Can we stop washing our hands? LID 2017;17:478.

Authors' reply. LID 2017;17:478-9.

Did IPC really have any effect?

- EMRSA-16 derived from 80/81 but less virulent and quinolone resistant
- Pandemic of EMRSA-16 triggered by introduction of quinolones
- Decline of MRSA began before improvement in IPC and associated with decline in quinolone use

Holden MTG et al. Genome Res 2013;23:653-64

Decline of MRSA-16 in BSAC bacteraemia isolates

	% EMRSA-15	% EMRSA-16
1999-2000	60	35
2001	76	21
2003	74	21
2005	82	14
2007	85	9

Ellington MJ et al. JAC 2010;65:446–448.

The evidence surely is that IPC *plus* antibiotic control is effective

- Both are essential
- They are a package

Conclusions

- SA is a virulent organism
- Less virulent strains still cause severe infection in hospital patients
- MRSA have worse outcomes than MSSA
- Epidemic strains come and go
- EMRSA spread rapidly and widely without proper IPC & antibiotic stewardship

Conclusions

- The prolonged epidemic in England due to:
  (1) Epidemic strains
  (2) Overuse of quinolones & other Abs
  (3) Catastrophic failure IPC & good practice
  Due to complacency, ignorance, carelessness, self-delusion

Conclusions

- Exhortation, education failed
- Surveillance & publication of data, legislation & performance management succeeded
- Dramatic fall in MRSA
- There has been a change in culture, which must be maintained

Conclusions

- MRSA has not gone away
- Epidemic, more resistant & more vicious strains may appear at any time
- We must keep our guard up
- Good IPC & antibiotic stewardship are essential for prevention & control of present & future hospital epidemics
- This is simply good medical practice

Thanks

- Aathithan S, Abdulla Y. Adams N, Ajoku U, Anthony RM, Armstrong J, Ayliffe GA, Bagg LR, Barbut F, Barker RD., Barrett SP, Bassetti M, Bateman NT, Bathgate T, Batra R, Beattie H, Bisnauthsing KN, Bouza E, Boyce JM, Branson M, Breathnach A, Brown DF, Brown E, Brown NM, Brown TJ. Bruggraber SF. Buckles A, Cameron J, Carroll KC, Casewell MW, Carlson JR,Chadwick C, Chaibi EB. Chan CH, Chan CL, Chan CY, Chan HS, Chan KY, Chan RS, Chang AMZ, Cheung SW, Cheng AF, Chinn S, Chung SCS, Chanal-Claris C, Charlton JRH, Chartier Y, Chahal B, Chastre J, Chaudry AN, Cheng AFB, Chow KL, Mark KK, Christiansen B, Chrystie IL, Cleverley J, Cliff PR, Cobb R, Connor AM, Cookson B, Cooper BS, Corbett K, Cornaglia G, Cox RA, Daly S, Davies DP, Dawson S, de Angelis D, de Ruiter A, Dickens A, Dieringer T, Dilworth P, Donnan S. Dowling RH, Drobniewski FA, Dryden M, Duckworth GJ, Duthie R, Cockram CS, Dybowski R, Edgeworth JD, El Bakri F, Esposito S, Exner M, Farrington M, Molyneaux E, Evans-Jones JC, Fenelon L, Finch RG, Fok TF, Fry C, Fung K, Gallagher C, Galloway A, Gardner MB, Gascoigne AD, Gaya H, Gebel, Gemein S, Georgeu C, Giamarellou H, Goldenberg SD, Golder M, Goossens H, Goroncy-Bermes P, Go SH, Gottlieb A, Gould D, Graham EM, Gransden WR, Griffiths-Jones A, Gumban M, Gutteridge CS, Gyssens IC, Hall A, Halligan E, Hartemann P, Hateley P, Havill NL, Hawkey PM, Heathcock R, Hemsley C, Herdman MT, Heudorf U, Hill M, Hodson M, Hoffman PN, Holdsworth GMC, Homi J, Hosein IK, Humphreys H, Hung SCS, Lam A, Hunter PA, Hutchinson D, Hui YW, Humphries MJ, Hylemon PB, Ip PLS, Isalska B, Issack MI, Jain BK, Jeanes A, Jeannon JP, Jenkins SG, Jenner E, Johnson A, Jones RN, Joshi A, Kaiser AM, Kam KM, Keane CT, Khan H, King A, King JD, Ramachander N, King L, Klein JL, Knight S, Knox A, Kramer A, Kuijper EJ, Kuloglu F, Kypraios T, Labia R, Lacey S, Lee JCK, Leong NG, Leung DTY, Leung KT, Lewis D, Li PKT, Chung WWM, Ling Ling J, Ling TKW, Littlewood J, Liu D, Livermore DM, Low DE, Lowry MF, Lyon DJ, MacLennan AH, Macrae MB, Maillard JY, Mak KH, Marples R, Masterton RG, May J, McCulloch J, McGeer A, McHugh TD, Melzer M, Milburn H, Miller CE, Milner M, Mistry R, Morgan M, Murphey GM, Murray HGS, Mutlu B, Nadler H, Nathwani D, Ng E, Nixon I, O'Sullivan DGM, Oakley R, O'Farrell N, Oltmanns P, O'Mahony G, O'Neill PD, Oo KT, LI EK, Orezzi C, O'Shea S, Otter JA, Pallett A, Pang JA, Pang L, Pantelidis P, Parks MJ, Passaretti CL, Patel A, Patrick WDG, Perl TM, Peters BS, Phillips I, Phillips J, Phillips K, Piddock LJ, Pierce KE, Pitt T, Plant JC, Poon D, Poston S. Postulka A, Powell JJ, Power EGM, Abdulla YH, Price NM, Price T, Qureshi SA, Rajan MS, Rao G, Rayner D, Rees PJ, Revathi G, Roberts RB, Robotham JV, Rogers MS, Roncoroni AJ, Ross T, Rotter M, Roxburgh J, Russell-Jones D, Salkeld JA, Schelenz S, Schiff R, Schwieger M, Scott G, Scotton W, Shannon KP, Shanson DC, Shaw PC, Shelton D, Simmons NA, Simo R, Simon MTP, Simpson E, Sirot D, Slack R, Smith AW, Smith S, Snashall D, Snur I, Sonntag HG, South JR Spencer R, Stanford MR, Stanwell-Smith R, Stapleton PD, Starke I, Stone S, Storring RA,Street M, Struelens MJ, Sung JY, Sung RYT, Swaminathan R, Tacconelli E, Talsania H, Tam JS, Tambic A, Tabic T, Tansel O. Taylor DJ, Teale CJ, Teare L, Tebbs E, Teoh R, Thomas LA, Thompson RP, Tinsley H, Tong CY, Tosas O, Tse KK, Tseng RYM, Tucker D, Unal S, Vallence-Owen J, van Hasselt CA,Veysey MJ, Volpé H, Voss A. Wade P, Walsh M. Wangh LJ. Warley A. Warren RE, Wass JA. Watling D. Watson J, Webster M, Whitty CJ, Wilcox M. Willems CD, Willey BM, Williams D, Williams L. Wilson J. Witte W, Woo ML, Woo THS, Woodford N. Worby CJ, Wynn RM, Wu PJ, Wulf MW, Wyncoll D, Wynn RM, Xiang X, Yee J, Yezli S, Zhang LC, Zhou QM