The Real Threat of Antibiotic Resistance

Where does Antimicrobial Stewardship fit?
Penicillium mould effect on *Staphylococcus aureus* lawn culture

Sir Alexander Fleming
(1881-1955)

Ernst Boris Chain
(1906-1979)

Sir Howard Walter Florey
(1898-1968)
Antibiotics caused US deaths to decline by \( \sim 220 \) per 100,000 in 15 years.

All other medical technologies reduced deaths by \( \sim 20 \) per 100,000 over the next 45 years.


From IDSA Capitol Hill talk by Brad Spellberg May 11 2010.
www.idsociety.org/Content.aspx?id=4810
The introduction of a new antibiotic is soon followed by first reports of acquired resistance.

Note: Some of the dates are estimates only.

Source: Pray 2008.
Antibiotic resistance: The causes

• The **indiscriminate effects** of antibiotics

• The **indiscriminate use** of antibiotics

• The **global spread of resistance** facilitated by the rapid dynamics of gene transfer between bacteria, travel and trade and by poor sanitation and hygiene

• Alarming **decline in drug development**
The dwindling antibiotic pipeline...

No new drugs for Gram-negative bacterial infections
- ESBLs
- Typhoid fever
- Shigella
- Gonorrhoea-

Sulphonamides
Penicillins
Aminoglycosides
Macrolides
Glycopeptides
Tetracyclines
Quinolones
Lincosamides
Streptogramins
Trimetoprim
The pipeline of new agents is drying up
Total antibacterials approved for use by USA FDA

From IDSA Capitol Hill talk by Brad Spellberg May 11 2010.
www.idsociety.org/Content.aspx?id=4810
Percent MRSA of all isolates of *S. aureus* from blood in the EU 2008

Data from the European Antimicrobial Surveillance System, EARSS
Australia 24%
-Community 18%
-Hospital 34%

Percent MRSA of all isolates of *S. aureus* from blood in the EU 2008

Data from the European Antimicrobial Surveillance System, EARSS
Third-generation cephalosporin-resistant *Escherichia coli*, blood and CSF, 2008

- Green: <1%
- Light Green: 1–5%
- Yellow: 5–10%
- Orange: 10–25%
- Red: 25–50%
- Dark Red: >50%
- Gray: No data/low number
- Light Gray: Other countries

Country with:
- ↑ Significant increase (2005-2008)
- ↓ Significant decrease (2005-2008)

Source: European Antimicrobial Resistance Surveillance System (EARSS), 2008
Burden of multidrug-resistant (MDR) bacteria in the EU, Iceland and Norway

Human burden

Infections (6 most frequent MDR bacteria, 4 main types of infection)  approx. 400,000 / year
Attributable deaths  approx. 25,000 / year
Extra hospital days  approx. 2.5 million / year

Economic burden

Extra in-hospital costs  approx. € 900 million / year
Productivity losses  approx. € 600 million / year

So Limitation: these are underestimates

Consequences of resistance

• Some infections may become difficult or impossible to treat

• Many of modern medicine’s achievements are only possible with effective antimicrobials
  – Routine and complex surgery
  – Intensive care medicine
  – Neonatal care
  – Modern obstetrics
  – Organ transplantation
  – Cancer treatment
Consequences of resistance

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  – Modern obstetrics
  – Organ transplantation
  – Cancer treatment
Some parts of the world are already running out of effective antibiotics

Muhimbili hospital, Dar es Salaam Tanzania

The mortality rate from Gram-negative bloodstream infection in children (43.5%) was more than double that of malaria.

Blomberg et al. BMC Infect Dis. 2007
Case 1. Community acquired MRSA

32 yo schoolteacher from rural Qld town
Unwell with generalised aches and pain after gym workout
Painkillers, but 2 days later, found at home very unwell with severe breathlessness
Ambulance to local Emergency

Very hypoxic, severe chest pain, hypotension
?Pulmonary embolism, anticoagulated and transferred to city (PAH)
PAH ED, CXR showed bilateral lung consolidation
Diagnosed severe Community Acquired Pneumonia, Timentin and azithromycin, transferred to ICU and ventilated
Case 1. Community acquired MRSA

Day 2 Blood cultures showed Gram-positive cocci *Staph aureus*

Vancomycin added

Day 3 confirmed MRSA (non multi resistant)

8 week admission, recovered, multiple complications

May have had influenza A beforehand
Case 1. Community acquired MRSA

What was the impact of:
- delayed effective therapy?
- use of a less effective drug (vancomycin vs flucloxacillin)?

MRSA infection has a higher mortality than MSSA
Case 2. MRSA meningitis and cavernous sinus thrombosis after laceration of nose with concrete fragment.

Illustrations courtesy W Munckhof

Int Med J 2008 p283
PAH Community Associated Non-Multi- MRSA New
GAM Chart from Jan 1999 to Dec 2010.

Data blue, Fitted GAM red, 95% CI brown, Control limit black.
Case 3. Extended Spectrum Beta-Lactamase producing (ESBL) E coli pyelonephritis

- 47 yo woman 5 days of **fevers and flank pain**
- Saw GP, gave Trimethoprim,
- **2 days later, no better, fevers and rigors.** Urine culture taken, sent to hospital

<table>
<thead>
<tr>
<th>E. coli (ESBL Producer)</th>
<th>&gt; 10^8/L</th>
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<tbody>
<tr>
<td>AMP</td>
<td>AUG</td>
</tr>
<tr>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>NA</td>
<td>CIP</td>
</tr>
<tr>
<td>R</td>
<td>R</td>
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</tbody>
</table>
Case 3. ESBL E coli pyelonephritis

- Empiric Ampicillin and Gentamicin IV
- Then IV Ertapenem for total 10 days
- No oral options, required inpatient care or HITH
- Holiday in South America in months prior to admission
- Effective therapy delayed, may have had serious consequences
Antibiotic susceptibility of UTI strains of E coli.
1995

<table>
<thead>
<tr>
<th>Drug</th>
<th>Hospital</th>
<th>Non hospital</th>
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<tbody>
<tr>
<td>Amoxycillin</td>
<td>47%</td>
<td>54%</td>
</tr>
<tr>
<td>Augmentin</td>
<td>90%</td>
<td>94%</td>
</tr>
<tr>
<td>Cephalothin</td>
<td>83%</td>
<td>90%</td>
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<tr>
<td>Ceftriaxone</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>81%</td>
<td>86%</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>99%</td>
<td>99%</td>
</tr>
</tbody>
</table>

Dr J Robson Sullivan and Nicolaides pathology
Antibiotic susceptibility of UTI strains of E coli. QE2, Redlands, Logan Hospitals Brisbane 2009

2935 isolates %suscept

- Amoxycillin 56%
- Augmentin 81%
- Cefazolin 90%
- Trimethoprim 87%
- Gentamicin 96%
- Norfloxacin 92%

- ESBL producers 1.4%

Dr Claire Heney. Pathology Queensland
Antibiotic susceptibility of UTI strains of E.coli.
QE2, Redlands, Logan Hospitals Brisbane 2009

2935 isolates %suscept

- Amoxycillin 56%
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- Cefazolin 90%
- Trimethoprim 87%
- Gentamicin 96%
- Norfloxacine 92%
- ESBL producers 1.4%

Dr Claire Heney. Pathology Queensland
## Susceptibility of *E. coli* - CHINA

<table>
<thead>
<tr>
<th></th>
<th>%S 2002</th>
<th>%S 2007</th>
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<tbody>
<tr>
<td>Amp/sulbactam</td>
<td>43%</td>
<td>19%</td>
</tr>
<tr>
<td>Amikacin</td>
<td>94%</td>
<td>89%</td>
</tr>
<tr>
<td><strong>Cefotaxime</strong></td>
<td><strong>82%</strong></td>
<td><strong>44%</strong></td>
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<tr>
<td>Ceftazidime</td>
<td>92%</td>
<td>74%</td>
</tr>
<tr>
<td><strong>Ciprofloxacin</strong></td>
<td><strong>57%</strong></td>
<td><strong>30%</strong></td>
</tr>
<tr>
<td>Ertapenem</td>
<td>100%</td>
<td>98%</td>
</tr>
<tr>
<td>Imipenem</td>
<td>100%</td>
<td>99%</td>
</tr>
<tr>
<td>Pip-tazo</td>
<td>96%</td>
<td>93%</td>
</tr>
</tbody>
</table>
ESBL E coli urosepsis

• Increasing in frequency
  – Often after travel to Asia, Africa, South America
• Now also seen in non travellers, typically elderly
• Most are gentamicin resistant.
• No oral options unless you import Fosfomycin, IV therapy needed
Consequences of resistance

• Some infections may become difficult or impossible to treat

• Many of modern medicine’s achievements are only possible with effective antimicrobials
  – Routine and complex surgery
  – Intensive care medicine
  – Neonatal care
  – Modern obstetrics
  – Organ transplantation
  – Cancer treatment
Case 4. ESBL *Klebsiella oxytoca* spinal abscess after trans rectal prostate biopsy

- 58 yo man, PSA test mildly elevated
- Trans-rectal biopsy (negative for malignancy)
- Prophylactic ciprofloxacin given as per guidelines
- 2 days later, fever, rigors, bedbound. “It's the flu”
- Put up with it for 3 days, back pain too much. Came to ED. Lumbar epidural abscess, incipient paraplegia, septic shock
- Blood cultures taken, flucloxacillin and gentamicin given.
Case 4. ESBL *Klebsiella oxytoca* spinal abscess after trans rectal prostate biopsy

- Blood cultures: ESBL *Klebsiella oxytoca*

| AMP | AUG | KF | CFZ | TMP | SF | SXT | NIT | GEN | TOB | AK | CTX | CRO | CAZ | FEP | TIM | TAZ | NA | CIP | NDR | MER | TET | CHL | FOX | IPM | ESB | TGC |
|-----|-----|----|-----|-----|----|-----|-----|-----|-----|----|-----|-----|-----|-----|-----|-----|----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| R   | R   | R  | R   | R   | R  | R   | S   | R   | R   | S  | R   | R   | S   | R   | R   | R   | R   | R  | R   | S   | S  | S   |

- Changed to meropenem and then ertapenem. 6 weeks of therapy and recovered. 2 day delay in appropriate antimicrobials
- Frequently travelled to Papua New Guinea (probably acquired GI carriage there)
Asymptomatic bacteriuria and bacteraemia are common after transrectal prostatic biopsy, but infection is infrequent (sepsis, septic shock, urinary tract infection and prostatitis). However, prophylaxis has been shown to be of benefit; use:

ciprofloxacin 500 mg orally, as a single dose, 1 hour before the procedure.

- Advice to urologists: use a carbapenem for prophylaxis if patient has lived or travelled in Asia, Africa, South America in last 12 months
- Last line of defence?
- What happens when KPCs are brought home?
- When will it be too unsafe? Who is monitoring trends?
• Health care associated infection is difficult to manage, with multi-drug resistant organisms induced, amplified and spread in the hospital environment.

• It seems that developments in resistance in hospitals may antedate the same developments in the community.
Case 5. Nosocomial VRE

- 30 yo man, *motorcycle accident*. Multiple injuries to legs and pelvis
- Stabilized in regional hospital ICU
- Transferred for specialized orthopaedic and plastic surgical reconstruction
- Acquired MRSA, MRAB and VRE in regional ICU.
Case 5. Nosocomial VRE

- Polymicrobial osteomyelitis in femur and hip including VRE
- Treated with meropenem, and linezolid
- Osteomyelitis failed to respond, hindquarter amputation carried out

<table>
<thead>
<tr>
<th>Enterococcus faecium 1+</th>
<th>AMP</th>
<th>KF</th>
<th>CFZ</th>
<th>ERY</th>
<th>DA</th>
<th>GMS</th>
<th>VA</th>
<th>TEC</th>
<th>CHL</th>
<th>SCD</th>
<th>LZD</th>
<th>STS</th>
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<td>R</td>
<td>R</td>
<td>S</td>
<td>R</td>
<td>R</td>
</tr>
</tbody>
</table>
PAH VRE Monthly Burden
Spline Chart from Sep 2004 to Jan 2011.

Average Monthly Count

Sep04 Mar05 Sep05 Mar06 Sep06 Mar07 Sep07 Mar08 Sep08 Mar09 Sep09 Mar10 Sep10
Rate of patient-episodes of vancomycin-resistant Enterococcus faecium (VRE) bacteremia per 1000 separations at Austin Health over a 12-year period, with and without VRE sequence type (ST)203 included.


© 2010 by the Infectious Diseases Society of America
Resistance in the hospital

• Complex surgery on patients carrying multi-resistant organisms carries a high risk of untreatable infection complications.
• Transplantation a particular risk
• Newer antibiotics may not be as effective as older ones even when the organisms are susceptible
• In the end, no antimicrobial has yet proven immune to resistance development, given enough time
Evolution from the Bacterial Viewpoint
100 years = 1 second

Bacteria: January 1st
Fungi: June 18th
Mammals: December 24th
Humans: 23:56hr, Dec 31st
Antibiotic era: 23:59, last 0.5 second
Consequences of resistance. Where are we now?

• Resistance patterns are clearly changing.
• It is affecting small numbers of individuals, with the potential to be far greater as the years pass.
• Clinicians are coping, but last line antibiotics are being used on an every day basis for community acquired infection.
• Awareness of the problem will progressively drive prescribing patterns which will exert more pressure on evolution of resistance.
Antibiotic Resistance

Increased risk of failure of empiric therapy

Use of Antibiotics with a broader spectrum or combination therapy

The clinicians dilemma of empiric therapy.

From Nordberg, Monnet and Cars. STRAMA
The Empiric Antibiotic Balance
adapted from Kollek MH Crit Care Med 2005; 33:1845

APPROPRIATE INITIAL ANTIMICROBIAL TREATMENT

AVOID UNNECESSARY ANTIMICROBIAL USE
The Empiric Antibiotic Balance
adapted from Kollek MH Crit Care Med 2005; 33:1845

Overuse of Broad spectrum agents

Induction or Amplification of resistance
The Empiric Antibiotic Balance
adapted from Kollek MH Crit Care Med 2005; 33:1845

Increased Mortality and Morbidity

Inadequate Antibiotic Therapy
Consequences of resistance

• What can we expect?
  – Until now we have kept ahead by producing new antibacterials. The supply has all but dried up.
  – Resistance has become a far greater problem in other countries and provides an example to us of what is likely to happen in Australia.
  – Australia cannot live in isolation from these developments
    • Air travel
    • Globalisation of food production
  – Australia should expect a steady increase in resistance in its common bacterial pathogens.
  – We need to plan for 10 years, 20 years and 50yrs from now.
WHO Global Strategy for Containment of Antimicrobial Resistance

FIFTY-EIGHTH WORLD HEALTH ASSEMBLY

W HA58.27

Agenda item 13.10
25 May 2008

Improving the containment of antimicrobial resistance

The Fifty-eighth World Health Assembly,

Having considered the report on rational use of medicines by physicians and patients;

Acknowledging that the containment of antimicrobial resistance is a prerequisite for attaining several of the internationally agreed health-related goals contained in the United Nations Millennium Declaration;

Recalling the recommendations of the Second International Conference on Improving Use of Medicines (Chiang Mai, Thailand, 2004);

Recalling also the findings of relevant WHO reports, including “Priority medicines for Europe and the world” and the Copenhagen Declaration from the European Union conference on “The Microbial Threat” (Copenhagen, 1998);

Aware that the spread of antimicrobial resistance recognizes no national boundaries and has reached proportions that require urgent action at national, regional and global levels, especially in view of the decreasing development of new antimicrobial agents;

Recalling previous resolutions W HA55.27 and W HA57.12 on the rational use of drugs, W HA51.17 on antimicrobial resistance, and W HA54.14 on global health security;

Recognizing the efforts of WHO in collaboration with governments, universities, the private sector and non-governmental organizations to combat antimicrobial resistance, thereby contributing to prevention of the spread of infectious diseases;

Noting that, despite some progress, the strategy for containment of antimicrobial resistance has not been widely implemented;

Welcoming the many ongoing efforts to contain antimicrobial resistance and to promote rational use of antimicrobial agents by physicians and consumers in order to improve global health security;

1 Decision W HA55/50, 2001;

Re-emphasizing the need for a coherent, comprehensive and integrated national approach to promoting the containment of antimicrobial resistance;

Convinced that it is time for governments, the health professions, civil society, the private sector and the international community to reaffirm their commitment to ensuring that sufficient investment is made to contain antimicrobial resistance,

1. URGES Member States:

(1) to ensure the development of a coherent, comprehensive and integrated national approach to implementing the strategy for containment of antimicrobial resistance taking account, where appropriate, of financial and other incentives that might have a harmful impact on policies for prescribing and dispensing;

(2) to enhance rational use of antimicrobial agents, including through development and enforcement of national standard practice guidelines for common infections, in public and private health sectors;

(3) to strengthen, as appropriate, their legislation on availability of medicines in general and of antimicrobial agents in particular;

(4) to mobilize human and financial resources in order to minimize the development and spread of antimicrobial resistance, in particular by the promotion of the rational use of antimicrobial agents by providers and consumers;

(5) to monitor effectively and to control nosocomial infections;

(6) to monitor regularly the use of antimicrobial agents and the level of antimicrobial resistance in all relevant sectors;

(7) to share actively knowledge and experience on best practices in promoting the rational use of antimicrobial agents;
Box 1. The World Health Organization’s policy package to combat antimicrobial resistance

- Commit to a comprehensive, financed national plan with accountability and civil society engagement
- Strengthen surveillance and laboratory capacity
- Ensure uninterrupted access to essential medicines of assured quality
- Regulate and promote rational use of medicines, including in animal husbandry, and ensure proper patient care
- Enhance infection prevention and control
- Foster innovations and research and development for new tools
WHO World Health Day 2011

COMBAT DRUG RESISTANCE

No action today, no cure tomorrow

7 April 2011 World Health Day
Welcome

Recently, the World Health Organization (WHO) identified antimicrobial resistance as one of three greatest threats to human health, jeopardising patient safety and public health. Whilst research into and the development of new, effective antibiotics is decreasing, we are all aware of rapidly increasing rates of multi-resistant bacteria that cannot be treated with currently available antibiotics.

The problem of antibiotic resistance worldwide, including Australia, is one of the foremost issues that we face in the coming decades. We strongly believe that there is an urgent requirement for a debate within Australia on how to comprehensively address the problems of antimicrobial resistance, with the goal to implement a coordinated national approach.

In 1999 Australia developed a blueprint for tackling antibiotic resistance for human and non-human use of antibiotics, the Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR) report(1), and established committees for its implementation. This effort has now dissipated and the committees disbanded. The WHO has endorsed similar policies in a report in 2001(2).

The problem of resistance as a public health threat has increased significantly over the last decade and local solutions are needed more than ever. With this in mind, the Australasian Society for Infectious Diseases and the Australian Society for Antimicrobials are conjointly convening a “Summit on Antimicrobial Resistance” at the Law School at the University of Sydney on Monday and Tuesday, 7th and 8th February 2011.

We realise that the success of such a forum requires a co-operative effort by an interdisciplinary group from the scientific, medical, veterinary, public health and health policy communities. We therefore invite and hope to bring together as participants key stakeholder groups including professional bodies (medical and surgical colleges, special societies and veterinary societies), the universities, state and federal departments of health, national bodies such as the NPS Australian Commission on Safety and Quality in Healthcare and consumer organisations. We intend to discuss health-care and community-associated drug resistance, infection control strategies, the role of national surveillance, antibiotic stewardship, antibiotic use in food production, and research needs. With a broad representation, we aim to achieve a dialogue for national control strategies and to formulate an agenda for minimising antimicrobial resistance in the future.
1 An agenda for addressing antimicrobial resistance

**SURVEILLANCE**
- Resistance surveillance
  - Human isolates (hospital, community)
  - Animal isolates
- Usage surveillance
  - Human (hospital, community)
  - Animal health
  - Health care-associated infection
- Disease burden
- Disease outcome

**INTERVENTION**
- Regulation
  - Registration
  - Reimbursement
  - Animal use
  - Access to new drugs
- Infection prevention
  - Infection control
  - Immunisation
  - Health care epidemiology
- Education
  - Stewardship programs
  - Prescribers
  - Consumers
  - Clinical practice guidelines

**Antimicrobial resistance management body**

**RESEARCH**
- Basic science
- Epidemiology
- Social drivers
Strategies to address the rising problem of resistance

- Prevent Infections
  - Infection control
  - Immunisation
- Prolong effectiveness of existing antibiotics
  - early and accurate diagnosis
  - antimicrobial stewardship
- Develop New Therapies
- Minimise antimicrobial use in agriculture and veterinary medicine
National comprehensive antimicrobial resistance management plan

- **Surveillance**
  - Infections and resistance
  - Antibiotic use
  - Human, animal, agricultural

- **Prevention**
  - Immunisation
  - Infection control

- **Stewardship**
  - Treatment guidelines
  - Prescriber education
  - Audit and feedback

- **Regulation and licensing**
  - Human, animal, agricultural

- **Research**
  - Applied (stewardship)
  - new agents
  - Prevention
National comprehensive antimicrobial resistance management plan

• Surveillance
  – Infections and resistance
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• Regulation and licensing
  – Human, animal, agricultural

• Research
  – Applied (stewardship)
  – new agents
  – Prevention
What are other countries doing?

• Examples:
  – SWEDEN: STRAMA
  – SCOTLAND:
  – USA: CDC
Strama
Welcome to Strama - the Swedish strategic programme against antibiotic resistance.

SWEDRES 2010

Download Swedres as pdf here

The majority of Swedish population is willing to abstain from antibiotics
The results from an interview study called the Health Barometer 2010 shows that 78% of the Swedish population is willing to abstain from antibiotics even if they risk a few additional days of morbidity. The proportion willing to abstain from antibiotics varies between counties, from 84% in Uppsala to 73% in Göteborg.

Click here to read the report (In Swedish)
Click here for link to the home page
Among the domestic MRSA cases 2006-2010, the incidence was highest in the age group 80 years and older, Figure 4.3. In this age group there has been a decreasing trend since 2006, but in 2010 the incidence increased again. In the age group 0-5 years the incidence was generally 11-14, except for 2009 when it was 17. In all other age groups the incidence of domestic MRSA has remained at a low and stable level around 5.

![Graph showing incidence of domestic MRSA cases in Sweden 2006-2010.](image)

**FIGURE 4.3**. Age group adjusted incidence of notified domestic MRSA cases in Sweden 2006-2010.

In 2010, 45% of the domestic cases were identified through contact tracing, 10% in argued screening, and 47% during investigations of clinical symptoms, Figure 4.4. For imported cases the corresponding figures were 9%, 56% and 34%, respectively. Invasive MRSA infections was reported in 15 cases 2010. 13 of those were newly notified cases 2010 and two occurred in patients previously known to carry MRSA.

![Graph showing reasons for detection of domestic MRSA cases in Sweden 2006-2010.](image)

**FIGURE 4.4**. The reasons for detection of domestic MRSA cases in Sweden 2006-2010. It refers to the number of reported cases each year.

Epidemiological classification of the acquisition of MRSA was based on information in the clinical notifications and from subsequent investigations by the CMOs, Figures 4.5.a and b.

Community-acquired infections dominated among domestic cases 2010 and comprised 67% (n=434) of all domestic cases. There has been a continuous increase in the proportion of community acquired cases since 2007, and in Sweden today MRSA is acquired primarily in the community. Among the imported cases the proportion of community acquired infections was 16% (n=213). Community acquisition was reported in 75% of the cases for which it was uncertain whether MRSA was acquired domestically or imported (n=288, not presented graphically).

Hospital-acquired MRSA was comparatively more common in imported cases, 40% (n=237), than among domestic cases, 9% (n=64). The number of domestic cases with hospital acquired MRSA decreased from 88 to 54 compared with 2009 and the number of domestic hospital acquired cases has been halved as compared with 2006 and 2007, when 115 and 117 cases were reported, respectively.

The number and the proportion of domestic cases with MRSA acquired in healthcare/ care outside the hospital increased to 102 (17%) in 2010 compared with 88 (12%) in 2009.

During 2010 only minor outbreaks in different counties were reported from the Swedish healthcare system and from long-term care facilities.
National comprehensive antimicrobial resistance management plan: STRAMA

- **Surveillance**
  - Infections and resistance
  - Antibiotic use
  - Human, animal, agricultural

- **Prevention**
  - Immunisation
  - Infection control

- **Stewardship**
  - Treatment guidelines
  - Prescriber education
  - Audit and feedback

- **Regulation and licensing**
  - Human, animal, agriculture
  - Research
  - Applied (stewardship)
  - New agents
  - Prevention
THE SCOTTISH MANAGEMENT OF ANTIMICROBIAL RESISTANCE ACTION PLAN [ScotMARAP] 2008

HEALTHCARE ASSOCIATED INFECTION TASK FORCE
The Scottish Antimicrobial Prescribing Group (SAPG) is a national clinical forum that has been convened by the Scottish Medicines Consortium (SMC) as an action from The Scottish Management of Antimicrobial Resistance Action Plan 2008. The group is supported by the Scottish Government Health Directorate (SGHD) and Healthcare Associated Infection (HAI) Task Force and was launched in March 2008.

SAPG is planning to undertake important pieces of work related to antibiotic consumption and prescribing, resistance surveillance, organisational accountability for antimicrobial stewardship, antimicrobial prescribing education for healthcare professionals and infection management.

SAPG Publications

- Scottish Antimicrobial Prescribing Group (SAPG) - Report on Antimicrobial Use and Resistance in Humans in 2009
- Scottish Antimicrobial Prescribing Group (SAPG) - Primary Care Prescribing Indicators - Annual Report 2009-10.
Table 3
National antimicrobial prescribing indicators introduced by the Scottish Government in 2009.

- **Hospital-based empirical prescribing**: antibiotic prescriptions are compliant with the local antimicrobial policy and the rationale for treatment is recorded in the clinical case note in $\geq 95\%$ of sampled cases.
- **Surgical antibiotic prophylaxis**: duration of surgical antibiotic prophylaxis is $< 24\,h$ and compliant with local antimicrobial prescribing policy in $\geq 95\%$ of sampled cases.
- **Primary care empirical prescribing**: seasonal variation in quinolone use (winter months versus summer months) is $\leq 5\%$, calculated from PRISMS data held by NHS boards.

PRISMS, Prescribing Information System for Scotland.
Join IDSA in recognizing World Health Day on April 7, 2011

Without immediate and sustained action to address antibiotic resistance, we face a future in which people die of common infections and many of the medical advances we take for granted today are impossible. On World Health Day 2011, which focuses on raising global awareness about antibiotic resistance, IDSA is rolling out a comprehensive, multifaceted plan to address this crisis.

**Antibiotic Resistance Affects All of Us**

- **World Health Day Press Conference at the National Press Club**
  - View the live webcast
  - Read the press release

- **Congressional Briefing for Policymakers**

- **IDSA’s New Policy Paper:** "Combating Antimicrobial Resistance: Policy Recommendations to Save Lives" (PDF) (HTML) (One-page summary PDF)

**How Antibiotic Resistance Affects Us**

Ricky Lannetti was killed on December 6, 2003. His killer, MRSA, is still on the loose. Ricky’s mother, Theresa Drew, will be speaking at IDSA’s World Health Day events.

Read Ricky’s story, and the stories of other patients and families affected by antibiotic-resistant infections.
Table 1. Summary of Legislative Recommendations for Congress

<table>
<thead>
<tr>
<th>Legislative Recommendations</th>
<th>Section(s)</th>
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<tbody>
<tr>
<td>The Generating Antibiotic Incentives Now (GAIN) Act (H.R. 6331 in the 111th Congress) should be further strengthened, with additional incentives to stimulate antibiotic and related diagnostics R&amp;D as well as safeguards to ensure approved antibiotics are used appropriately, and quickly enacted in the 112th Congress.</td>
<td>I.1, VII.2</td>
</tr>
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<td>Congressional leaders should discuss incentives with representatives of the European Commission, as the European Union has set a December 2011 deadline for evaluating and developing an action plan of concrete incentives to spur antibiotic R&amp;D.</td>
<td>I.1</td>
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<tr>
<td>Public-private partnerships (PPPs) and the Assistant Secretary for Preparedness and Response’s (ASPR) proposed independent strategic investment firm should be established and funded and existing government-supported collaborations (e.g., ASPR’s Biomedical Advanced Development and Research Authority (BARDA)) should be further strengthened to supplement traditional industry R&amp;D for critically needed antimicrobial drugs.</td>
<td>I.2</td>
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<tr>
<td>An “Antibiotic Innovation and Conservation (AIC) Fee” should be established, 75% of which should be used to fund new antibiotic development and 25% of which should be used to fund antimicrobial stewardship.</td>
<td>I.2, V.6</td>
</tr>
<tr>
<td>Value-based reimbursement strategies that encourage antibiotic and related diagnostics development must be pursued.</td>
<td>I.3</td>
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<td>An expert panel should be created to identify priority pathogens, infections, and the purpose of targeting incentives, possibly as part of the Public Health Antimicrobial Advisory Board (PHAAB) contained in the Strategies to Address Antimicrobial Resistance (STAAR) Act (H.R. 2400 in the 111th Congress).</td>
<td>I.4, III.1</td>
</tr>
<tr>
<td>Congressional leaders should discuss with the Food and Drug Administration (FDA) the need for additional statutory authority to allow for conditional approvals, post-approval approaches or other novel approaches that will lead to approval and appropriate use of antibiotics that treat urgent unmet medical needs.</td>
<td>II.4, V.8</td>
</tr>
<tr>
<td>The STAAR Act should be quickly enacted to establish within the US Department of Health and Human Services (HHS) an Antimicrobial Resistance Office (ARO) and a PHAAB, and to strengthen surveillance, data collection, research, and prevention and control efforts, including development of a network of sentinel surveillance and research sites (i.e., the Antimicrobial Resistance Surveillance and Research Network (ARSRN)) and creation of an Antimicrobial Resistance Strategic Research Plan.</td>
<td>III, IV.1 &amp; 2, V.1, VI.1</td>
</tr>
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<td>The STAAR Act should be further strengthened to permit collection of local level antibiotic use data in humans and animals (species-specific).</td>
<td>IV.3</td>
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<tr>
<td>Congressional leaders, including sponsors of the STAAR Act and GAIN Act, should consider novel and innovative ways to strengthen antimicrobial resistance prevention and control efforts including through: 1) the establishment and support of antimicrobial stewardship programs in all health care settings (e.g., hospitals, long-term care facilities, long-term acute care facilities, ambulatory surgical centers, dialysis centers, outpatient clinics, private practices), which should be required as a condition of participation in the federal Medicare and Medicaid programs or through another regulatory mechanism; 2) strengthened public health and research efforts; and 3) creation of the AIC Fee.</td>
<td>V</td>
</tr>
<tr>
<td>Opportunities to support career development are necessary to reverse the “brain drain” that has occurred in antibiotic and microbiology research in both academia and industry. Incentives to address this problem should be included in legislation.</td>
<td>VI.7</td>
</tr>
<tr>
<td>A clinical specimen repository should be established by the National Institute of Allergy and Infectious Diseases and FDA to support R&amp;D of novel molecular diagnostic tests as part of the GAIN Act or other legislation.</td>
<td>VII.3</td>
</tr>
<tr>
<td>The Preservation of Antibiotics for Medical Treatment Act (PAMTA) (H.R. 1540/S. 619 in the 111th Congress) should be enacted and other measures (including FDA regulations) adopted to end the use of antibiotics for growth promotion, feed efficiency, and routine disease prevention purposes in animal agriculture.</td>
<td>VIII.1</td>
</tr>
</tbody>
</table>
Interagency Task Force on Antimicrobial Resistance

Background
The Interagency Task Force on Antimicrobial Resistance was initiated in 1999 following a congressional hearing on the topic "Antimicrobial Resistance: Solutions to a Growing Public Health Problem." The Task Force brings together multiple federal agencies to address the complex issue of antimicrobial resistance.

Members
Currently, ten federal agencies participate as members of the Task Force.

Co-chairs:
- Centers for Disease Control and Prevention (CDC)
- Food and Drug Administration (FDA)
- National Institutes of Health (NIH)

Other Members:
- Agency for Healthcare Research and Quality (AHRQ)
- Centers for Medicare and Medicaid Services (CMS)
- Health Resources and Services Administration (HRSA)
- Department of Agriculture (USDA)
- Department of Defense (DoD)
- Department of Veterans Affairs (VA)
- Environmental Protection Agency (EPA)

Public Health Action Plan
In 2001, the Interagency Task Force on Antimicrobial Resistance developed A Public Health Action Plan to Combat Antimicrobial Resistance Part 1: Domestic Issues [PDF - 261 KB] as a blueprint for specific, coordinated federal actions to address the emerging threat of antimicrobial resistance. Progress on implementation of the Action Plan is reported on a yearly basis in Annual Reports.

In December 2007, the Interagency Task Force held a consultants meeting to obtain suggestions and recommendations for revising and updating the Action Plan. The revised Action Plan focuses on federal activities that are critical in the next three to five years. The Federal Register Notice of March 16, 2011 [PDF - 544 KB] is a request for review of and comment on the revised Action Plan which is entitled draft document A Public Health Action Plan to Combat Antimicrobial Resistance [PDF - 544 KB].
A PUBLIC HEALTH ACTION PLAN TO COMBAT ANTIMICROBIAL RESISTANCE

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National comprehensive antimicrobial resistance management plan: CDC

- **Surveillance**
  - Infections and resistance
  - Antibiotic use
  - Human, animal, agricultural

- **Prevention**
  - Immunisation
  - Infection control

- **Stewardship**
  - Treatment guidelines
  - Prescriber education
  - Audit and feedback

- **Regulation and licensing**
  - Human, animal, agricultural

- **Research**
  - Applied (stewardship)
  - new agents
  - Prevention
National comprehensive antimicrobial resistance management plan: Australia

• Surveillance
  – Infections and resistance
  – Antibiotic use
  – Human, animal, agricultural

• Prevention
  – Immunisation
  – Infection control

• Stewardship
  – Treatment guidelines
  – Prescriber education
  – Audit and feedback

• Regulation and licensing
  – Human, animal, agricultural

• Research
  – Applied (stewardship)
  – new agents
  – Prevention

A patchwork with many of the elements, but essentially incomplete
National comprehensive antimicrobial resistance management plan: Australia

- **Surveillance**
  - Infections and resistance
  - Antibiotic use
  - Human, animal, agricultural

- **Prevention**
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- **Stewardship**
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- **Research**
  - Applied (stewardship)
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  - Prevention

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**National:**

**Leadership**

**Coordination**

**Planning**
“Colloquium” July 13 Sydney

• Chaired by Commonwealth CHO
• Reps:
  – ACSQHC
  – NHMRC
  – NPS
  – PBS
  – ASID
  – ASA
“Colloquium” July 13 Sydney

• Actions agreed:
  – Produce a well researched report on internal and external threats of AMR
  – Gap analysis to:
    • Identify current national activity
    • Define how current activity links to national goals
    • Define elements for a national strategy with priorities for action
“Colloquium” July 13 Sydney

– Recognised importance of whole of system approach:
  • Human, veterinary and agricultural
  • Vaccines, infection control

– Articulate the process required to advance actions and provide prioritised options clearly linked to aims and goals

– Produced for health ministers mid 2012

– Co-badged by NHMRC and ACQSHC
Strategies to address the rising problem of resistance

– Prevent Infections
  • Infection control
  • Immunisation

– Prolong effectiveness of existing antibiotics
  • early and accurate diagnosis
  • antimicrobial stewardship

– Develop New Therapies

– Minimise antimicrobial use in agriculture and veterinary medicine
Antimicrobial Stewardship:

- Apart from targeted reductions (e.g., 3rd gen cephalosporins and ESBL infections), a general lowering of antimicrobial use has a general impact on resistance induction.
- Comprehensive AMS programs consistently demonstrate a decrease in antimicrobial use (22-36% reduction in Dellit review CID 2007;44:159)
  - Stopping unnecessary antimicrobials
  - Switching from IV to oral
  - De-escalation from broad to narrow spectrum agents
Antimicrobial Stewardship:

• Improving the prescribing of our currently available agents is something we can do now to help slow the tide of resistance
  – More accurate prescribing
  – Minimal necessary usage
  – More precise diagnosis

• “As antimicrobial resistance increases and new drug development declines, it is critical that antimicrobials are used wisely and judiciously” Antimicrobial Stewardship in Australian Hospitals ACSQHC 2011