Objective

Develop actionable national strategies to address the challenge of antibiotic resistance in five low- and middle-income countries

– China
– India
– Kenya
– South Africa
– Vietnam
Specific Aims

• Develop the evidence base for policy action on antibiotic resistance
• Identify policy opportunities where research dissemination, advocacy, and information can have the greatest impact in slowing the development and spread of resistance.
Steps

• Create country profiles of baseline resistance and antibiotic use
• Assess the health and economic consequences of antibiotic resistance
• Develop mathematical models of specific approaches to delay emergence of antibiotic resistance
• Constitute GARP National Working Groups
Other objectives

• Create an IT platform for a global antibiotic resistance atlas
• International conference to compare policy approaches across the five target countries and to discuss the relevance of these approaches to other countries outside the initial partnership
Second Phase

- Dissemination of national strategies
- Policy communications
- Further research
Objectives for this meeting

• How serious a problem is antibiotic resistance in South Africa?
• What are the primary drivers of resistance?
• What policies could both help reduce the
  – Suboptimal use of antibiotics
  – Need for antibiotics
  – Emergence and spread of resistance
EXTENDING THE CURE

Policy responses to the growing threat of antibiotic resistance
The proportion of methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococcal infections is increasing (1987–2003).
The proportion of methicillin-resistant Staphylococcus aureus (MRSA) infections in the United States is high compared with other high-income countries (2004)
Growing resistance combined with an increasing number of Staphylococcus aureus infections has resulted in an increasing number of hospitalized patients who have MRSA infections.
The United States is among the most intensive users of antibiotics in the world
Fewer new antibiotics are being brought to market as more firms leave the anti-infectives business.

New antibacterial agents approved by FDA, 1983–2005
The Bug Wars

In the battle of bad bacteria vs. antibiotics, the drugs usually lose. Infectious diseases give us a stunning demonstration of evolution in action. The fittest bacteria—the ones that survive an antibiotic onslaught—transfer their resistance to new generations and across species. Their ability to fight back usually strengthens with each mutation, allowing them to thwart even the most intelligently designed drugs. Over the past 63 years, deadly bugs like Staphylococcus aureus, Enterococcus faecium, and Pseudomonas aeruginosa have evolved to withstand medicines like penicillin, tetracycline, and rifampicin. So scientists are now planning a flint attack—precisely targeted drug-delivery systems and bacteria-eating nanobots. But if history repeats itself, the bugs will ultimately win. —Patrick Di Gregorio
WAR against the MICROBES

How drug makers are fighting back against a global resurgence of infectious disease.
Health Care Consequences

Higher Cost of Care
- Higher prescription cost of newer antibiotics
- Rising insurance premiums

Lower Quality of Care
- Increased risk of morbidity and mortality
- Each year 63,000 deaths attributed to drug resistance in hospital infections by CDC
Difficulty in Measuring Burden of Resistance

• Resistance-related hospitalizations are not recorded
• Correlation between disease severity and colonization with resistant pathogen
• Not all antibiotic use is bad
Why is resistance increasing?

Factors internal to the health care system
- Overuse and inappropriate use (for instance, to treat viral infections)
- Sicker patients and longer hospital stays
- Inadequate infection control in hospital settings
- Insufficient treatment compliance
- Widespread use of broad spectrum agents

Factors external to the health care system
- Use in poultry and cattle feed as growth promoters
- Spread of drug resistance from other countries
What are the incentives to protect antibiotic effectiveness?

Those who use (or manufacture) antibiotics may not have sufficient incentives to consider the impact (cost) of this usage on the rest of society

– Incentives for patients
– Incentives for physicians
– Incentives for hospitals
– Incentives for pharmaceutical companies
– Government?
Incentives for Physicians

• Satisfying patient expectations
### TABLE 5

**Frequency of Antibiotic Prescribing by Factors Related to Patients’ Expectations of Antibiotics (N = 482)**

<table>
<thead>
<tr>
<th>Factor</th>
<th>No.* (%)</th>
<th>Antibiotic Prescribed No. (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient expects antibiotic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>290 (60)</td>
<td>213 (73)</td>
<td>2.6 (1.7-3.9) reference</td>
</tr>
<tr>
<td>No</td>
<td>150 (31)</td>
<td>78 (52)</td>
<td></td>
</tr>
<tr>
<td>No answer</td>
<td>42 (9)</td>
<td>28 (67)</td>
<td></td>
</tr>
<tr>
<td>Clinician believes patient expects an antibiotic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>298 (62)</td>
<td>236 (79)</td>
<td>4.7 (3.2-7.1) reference</td>
</tr>
<tr>
<td>No</td>
<td>182 (38)</td>
<td>81 (45)</td>
<td></td>
</tr>
<tr>
<td>No answer</td>
<td>2 (&lt;1)</td>
<td>2 (100)</td>
<td></td>
</tr>
<tr>
<td>Antibiotic helped similar illness in the past</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>284 (59)</td>
<td>212 (75)</td>
<td>4.5 (2.9-6.9) reference</td>
</tr>
<tr>
<td>No</td>
<td>170 (35)</td>
<td>88 (52)</td>
<td></td>
</tr>
<tr>
<td>Don’t know</td>
<td>19 (4)</td>
<td>12 (63)</td>
<td></td>
</tr>
<tr>
<td>No answer</td>
<td>9 (2)</td>
<td>5 (56)</td>
<td></td>
</tr>
</tbody>
</table>

**NOTE:** Because some questions were unanswered, the numbers may not add up to 482.

*In outpatients with nonspecific upper respiratory infections, acute bronchitis, or acute sinusitis. OR denotes odds ratio; CI, confidence interval.
Incentives for Physicians

- Satisfying patient expectations
- Financial (reimbursement) incentives
  - Substitute for repeat visit
- Malpractice liability
Help protect our antibiotic lifeline.

Antibiotics fight bacteria, not viruses. Taking antibiotics for viral infections, like colds and flu, makes bacteria resistant to the medicine. Treat colds and flu with rest, liquids, and over-the-counter medicines. Get immunized and wash your hands often, especially after coughing and sneezing. Help stop antibiotic resistance. Together we can protect our antibiotic lifeline.

www.mi-marr.org

MARR
Michigan Antibiotic Resistance Research Center

Global Antibiotic Resistance Partnership

RESOURCES FOR THE FUTURE
Campaign to Prevent Antimicrobial Resistance

Centers for Disease Control and Prevention
National Center for Infectious Diseases
Division of Healthcare Quality Promotion

Clinicians hold the solution!

- Link to: Campaign to Prevent Antimicrobial Resistance Online
- Link to: Federal Action Plan to Combat Antimicrobial Resistance
Antibiotic resistance: What's that?

Bacteria are tiny, but firmly set on survival. They can develop four different ways to protect themselves against the deadly effect of antibiotics.

1. They change their vulnerable targets, so that antibiotics are unable to find points of attack.
2. They produce enzymes which make certain antibiotics ineffective.
3. They change their outer shell, so that antibiotics cannot penetrate the bug.
4. They simply pump already resistant antibiotics out.

If bacteria can react to the attack of antibiotics by these mechanisms, then they have become resistant to the antibiotic. Unfortunately, resistant bacteria multiply just as quickly as all other bacteria.

Resistant bacteria can be dangerous. Since certain antibiotics can no longer do them any harm, a simple infection can quickly turn into a threat that is difficult to treat. For this reason it is so important to prevent the emergence of resistance.

What can we do against resistance?

Patients can make three important contributions:
- Taking the antibiotics prescribed by the physician exactly as prescribed
- Not using antibiotics for colds or flu
- Not discontinuing antibiotics too early

Physicians can prevent the emergence of resistance:
- Prescribing a weak antibiotic, if possible
- Prescribing antibiotics after a bacterial infection has been confirmed
- Prescribing antibiotics that are specific for the pathogen

Bayer supports physicians and patients through:
- The LIBRA initiative, which promotes the responsible use of antibiotics and which supports the fight against resistance development
- Clinical trials and research to develop new antibiotics
- Promoting current data on resistance development – a global surveillance database: www.antimicrobialresistance.com
Hospital Incentives

- Antibiotics may be a substitute for infection control
Hospital Incentives

- Hospitals are “sources” for colonization with resistant pathogens
- Health facilities often “share” patients
- Positive external benefits of active surveillance and infection control
Who pays for hospital-acquired infections?

• Medicare/Medicaid bear greatest burden of additional cost
• 76% of 11,668 HAIs in 2004 billed to federal Medicare ($1 billion cost)
• Rest to Medicaid ($372 million cost)
• $20 billion burden on Medicare nationwide
Discovery of new classes of antibiotics

- Sulfonamides
- Oxazolidinones
- Penicillins
- Aminoglycosides
- Glycopeptides
- Macrolides
- Tetracyclines
- Chloramphenicol
- Streptogramins
- Quinolones
- Lincosamides
- Trimethoprim

Timeline:
- 1930s
- 1940s
- 1950s
- 1960s
- 1970s
- 1980s
- 1990s
- 2000s
Role for Government: Vaccinations

- Pneumococcal vaccinations
- Invest in R & D for a MRSA vaccine
Role for Government: Infection Control

- Require hospital reporting of infections and resistance
- Medicare reimbursement for HAIs
- Regional cooperation in infection control
Role for Government: Infection Control

- Invest in national surveillance
- Exercise regulatory oversight
Challenges in developing countries

• Rising incomes – greater access to antibiotics
Antibiotic Sales in India by Region

- **SOUTH**
- **WEST**
- **EAST**
- **NORTH**

**Annual Sales (10,000s of INR)**

- 2005
- 2006
- 2007
- 2008
- 2009

**Year**
Challenges in developing countries

• Rising incomes – greater access to antibiotics
• Yet many patients do not have access to effective antibiotics
• Counterfeit or expired antibiotics
• Second line drugs may be unaffordable to many low-income families
• Burden of infectious disease including pneumococcal disease
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