

# Fight Antimicrobial Resistance or Go Back to the Pre-Antimicrobial Era

*Mohan P. Joshi*, MBBS, MSc, MD

Principal Technical Advisor and Cluster Lead for Pharmaceutical Services, MSH/SIAPS

*Malaika Ludman*, MPH

Technical Advisor, MSH/SIAPS

Global Health Mini-University

March 2, 2015

Washington, DC



**USAID**  
FROM THE AMERICAN PEOPLE

**SIAPS**   
Systems for Improved Access  
to Pharmaceuticals and Services

# Outline of the presentation

- Articulate, with evidence and examples, the global threat of antimicrobial resistance (AMR) and its consequences
- Outline the World Health Organization's Global Action Plan to Combat AMR and the US government's National Strategy for the Containment of Antibiotic Resistant Bacteria
- Describe USAID support for coalition building, antimicrobial stewardship, and other health system strengthening interventions to contain AMR



# Antimicrobial resistance



- One of the biggest public health threats
- A major global health security risk
- Widespread in both the hospital and community
- Rapidly reducing the effectiveness of many first-line treatments
- Affects all infectious diseases including TB, malaria, HIV & AIDS



**USAID**  
FROM THE AMERICAN PEOPLE



# What is AMR?

- Resistance of a microorganism to an antimicrobial drug that was originally effective for treating infections caused by it
- Resistant microorganisms can withstand attack by antimicrobial drugs such as antibacterials, antifungals, antivirals, and antimalarials



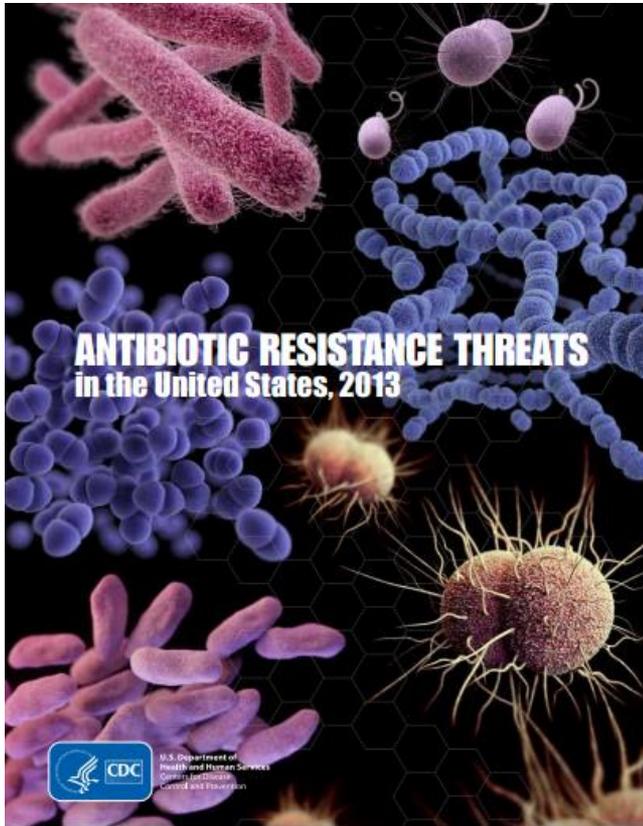
<http://jama.jamanetwork.com/article.aspx?articleid=1391920>



**USAID**  
FROM THE AMERICAN PEOPLE

**SIAPS**

# How does AMR affect individuals and health systems?



<http://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf>

- Increases morbidity and mortality
- Prolongs periods of infectiousness
- Increases direct costs (e.g., longer hospital stays, use of more expensive 2<sup>nd</sup> or 3<sup>rd</sup> line drugs)
- Increases indirect costs (e.g., prolonged absence from work)
- Causes psychological stress
- Creates financial hardships



**USAID**  
FROM THE AMERICAN PEOPLE

**SIAPS** 

# 700,000

**The current estimated  
number of deaths caused by  
AMR each year**



# 10 million

**The number of additional deaths  
caused by AMR every year by  
2050 if it is not contained**



**USAID**  
FROM THE AMERICAN PEOPLE



# \$100 trillion

**The cumulative costs that AMR  
is estimated to generate by 2050  
if it is not contained**



**USAID**  
FROM THE AMERICAN PEOPLE



# Burden of deaths from AMR: country examples

<b>UNITED STATES</b>	More than 2 million people are affected by drug-resistant infections every year, and more than 23,000 die as a direct result*
<b>THAILAND</b>	Antibiotic-resistant infections affect more than 140,000 people and claim more than 30,000 lives every year**
<b>CHINA</b>	About 80,000 people die every year from drug-resistant hospital-acquired infections**

\*Centers for Disease Control. 2013. *Antibiotic resistance threats in the United States*. Atlanta.

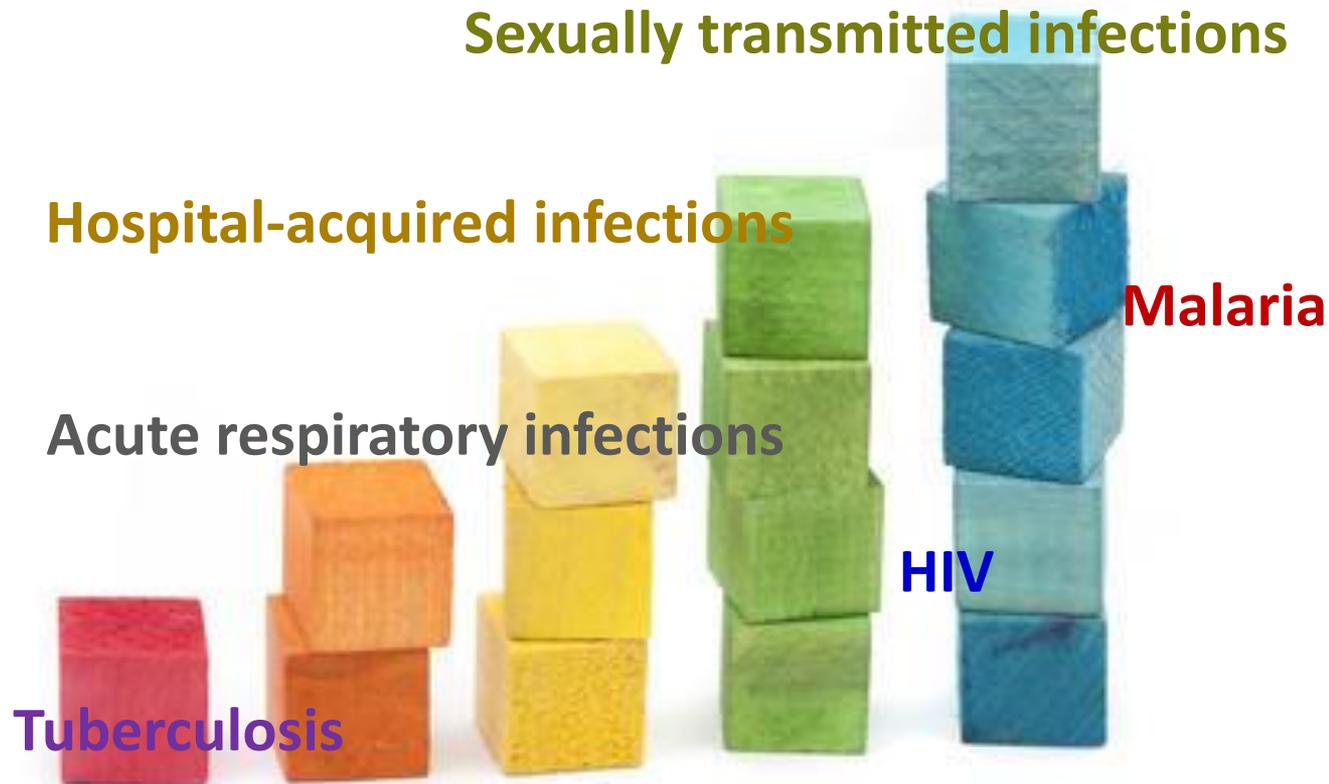
\*\* World Economic Forum. 2013. *Global risks 2013: Eighth edition*. Geneva.



**USAID**  
FROM THE AMERICAN PEOPLE



# Common infectious diseases are increasingly difficult to treat



**USAID**  
FROM THE AMERICAN PEOPLE



# Examples of multi-drug resistant (MDR) pathogens

- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Carbapenem-resistant Enterobacteriaceae (CRE)
- MDR *Neisseria gonorrhoeae*
- Extended spectrum  $\beta$ -lactamase-producing Enterobacteriaceae (ESBLs)
- MDR *Pseudomonas aeruginosa*
- Vancomycin-resistant *Staphylococcus aureus* (VRSA)
- Vancomycin-resistant *Enterococcus* (VRE)
- MDR *Acinetobacter*
- MDR and extensively drug-resistant (XDR) TB
- MDR *Plasmodium falciparum*



<http://blog.professionalsupplementcenter.com/the-rise-of-the-superbugs/>

## Tuberculosis

- The world had an estimated 480,000 new cases of multidrug-resistant TB in 2013, the majority of which were untreated\*

## Malaria

- Artemisinin-resistant malarial parasites have been identified in Cambodia, Myanmar, Thailand, and Vietnam\*\*

## HIV

- Recent studies in low- and middle-income countries have shown increases in transmitted HIV drug resistance\*\*\* among patients starting antiretroviral therapy\*\*

\*\*\*Transmitted HIV drug resistance occurs when previously uninfected individuals are infected with a drug resistant virus

\*WHO. 2014. *Global Tuberculosis Report*. WHO: Geneva.

\*\*WHO. 2014. *Antimicrobial Resistance: Global Report on Surveillance*. WHO: Geneva.

\*\*\*WHO. 2012. *HIV Drug Resistance Report*. WHO: Geneva



**USAID**  
FROM THE AMERICAN PEOPLE



# Comparative data on death rates: drug-sensitive versus drug-resistant bacteria

<b>Bacteria</b>	<b>Death rate from <i>sensitive</i> strain</b>	<b>Death rate from <i>resistant</i> strain</b>
<i>E. coli</i>	17.0%	<b>32.0%</b>
<i>A. baumannii</i>	5.4%	<b>16.4%</b>
<i>K. pneumoniae</i>	18.9%	<b>42.9% (CRKP)</b>
<i>K. pneumoniae</i>	12.5%	<b>43.8% (CRKP)</b>
<i>K. pneumoniae</i>	12.0%	<b>38.0%</b>
<i>S. aureus</i>	27.0%	<b>36.4% (MRSA)</b>
<i>S. aureus</i>	11.5%	<b>23.6% (MRSA)</b>

CRKP = Carbapenem-resistant *Klebsiella pneumoniae*

MRSA = Methicillin-resistant *Staphylococcus aureus*



**USAID**  
FROM THE AMERICAN PEOPLE



# Key contributors to AMR development or spread

*Inappropriate medicine use by providers and patients*



*Inadequate infection control or prevention practices*

*Weak regulation, including poor quality medicines*



<http://www.state.gov/e/oes/intlhealthbiodefense/falsified/>



*Inappropriate antibiotic use in animals*

<https://www.avma.org/KB/Resources/Reference/Pages/Antimicrobial-Use-and-Antimicrobial-Resistance.aspx>



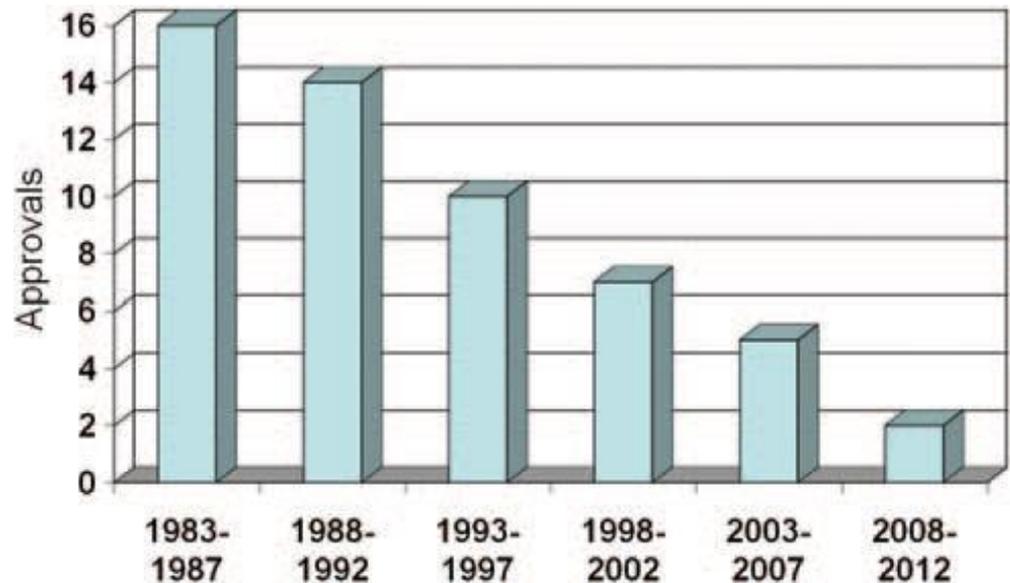
**USAID**  
FROM THE AMERICAN PEOPLE



# Adding to the urgency: a dwindling antimicrobial pipeline

- The pipeline for new antimicrobials is drying up
- We have fewer options to treat resistant pathogens
- **Preserving the effectiveness of existing antimicrobials is more urgent than ever**

**New systemic antibacterial agents approved by FDA per five-year period**



Boucher et al. 2013. *10 × '20 Progress—Development of New Drugs Active Against Gram-Negative Bacilli: An Update From the Infectious Diseases Society of America*. Clin Infect Dis. doi: 10.1093/cid/cit152



**USAID**  
FROM THE AMERICAN PEOPLE



# The World Health Organization's efforts to fight AMR

2001

- WHO Global Strategy for Containment of AMR

2005

- WHA resolution 58.27: Improving the containment of antimicrobial resistance

2007

- WHA resolution 60.16: Progress in the rational use of medicines

2011

- World Health Day on AMR, with 6-point policy package

2012

- The Evolving Threat of AMR: Options for Action

2014

- AMR: Global Report on Surveillance ; WHA resolution 67.25: Antimicrobial resistance ; and Draft Global Action Plan to Combat AMR



**USAID**  
FROM THE AMERICAN PEOPLE

**SIAPS** 

# WHO's Global Action Plan to Combat AMR

- Will be submitted to the 68<sup>th</sup> World Health Assembly in May 2015. Draft available at [http://apps.who.int/gb/ebwha/pdf\\_files/EB136/B136\\_20-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/EB136/B136_20-en.pdf)
- Includes five strategic objectives
  1. Improve awareness and understanding of AMR
  2. Strengthen knowledge through surveillance research
  3. Reduce the incidence of infection
  4. Optimize the use of antimicrobial agents
  5. Develop the economic case for sustainable investment that accounts for the needs of all countries and increase investment in new medicines, diagnostic tools, vaccines, and other interventions

**USAID, ReAct, and other organizations are supporting the development and implementation of the WHO Global Action Plan on AMR**

USAID = U.S. Agency for International Development;  
ReAct -- Action on Antibiotic Resistance

WHO. *Drug resistance*. [http://www.who.int/drugresistance/global\\_action\\_plan/en/](http://www.who.int/drugresistance/global_action_plan/en/)

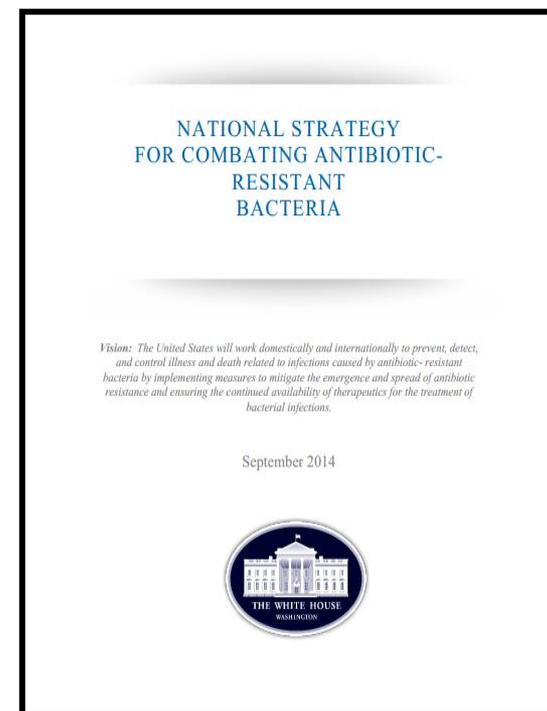


**USAID**  
FROM THE AMERICAN PEOPLE



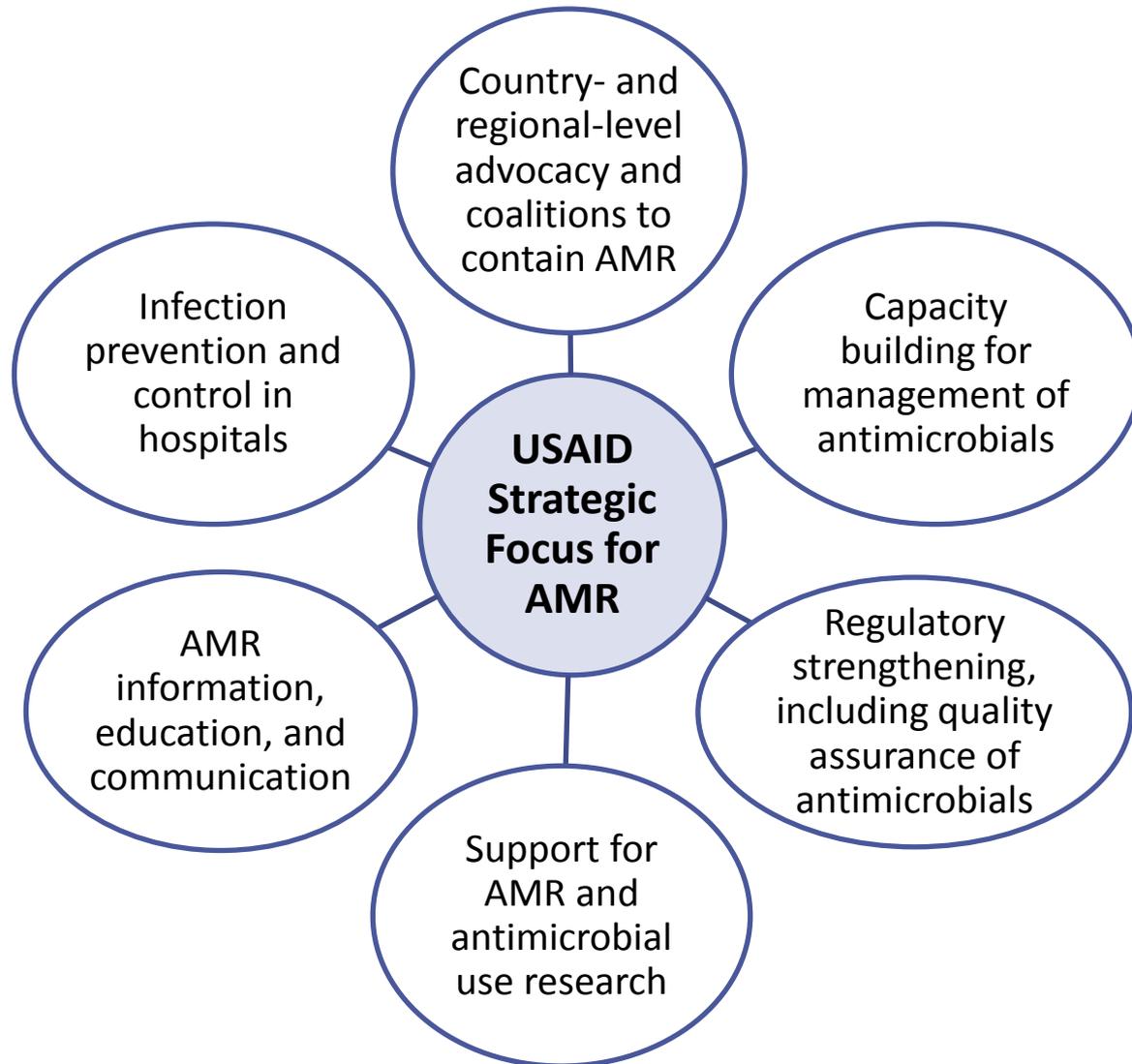
# U.S. National Strategy for Combating Antibiotic-Resistant Bacteria

- Sep. 2014 **Executive Order** from President Obama on combating antibiotic resistance  
<http://www.whitehouse.gov/the-press-office/2014/09/18/executive-order-combating-antibiotic-resistant-bacteria>
- Release of **National Strategy** for Combating Antibiotic-Resistant Bacteria (CARB), 2015-2020  
[http://www.whitehouse.gov/sites/default/files/docs/carb\\_national\\_strategy.pdf](http://www.whitehouse.gov/sites/default/files/docs/carb_national_strategy.pdf)
- One objective of the strategy is to improve international collaboration for CARB
- The Executive Order directs the Secretaries of HHS and State to **support the WHO Global Action Plan on AMR**
- The Executive Order complements the **Global Health Security Agenda**, which also addresses the threat of AMR



HHS = Health and Human Services

# USAID investments to combat AMR



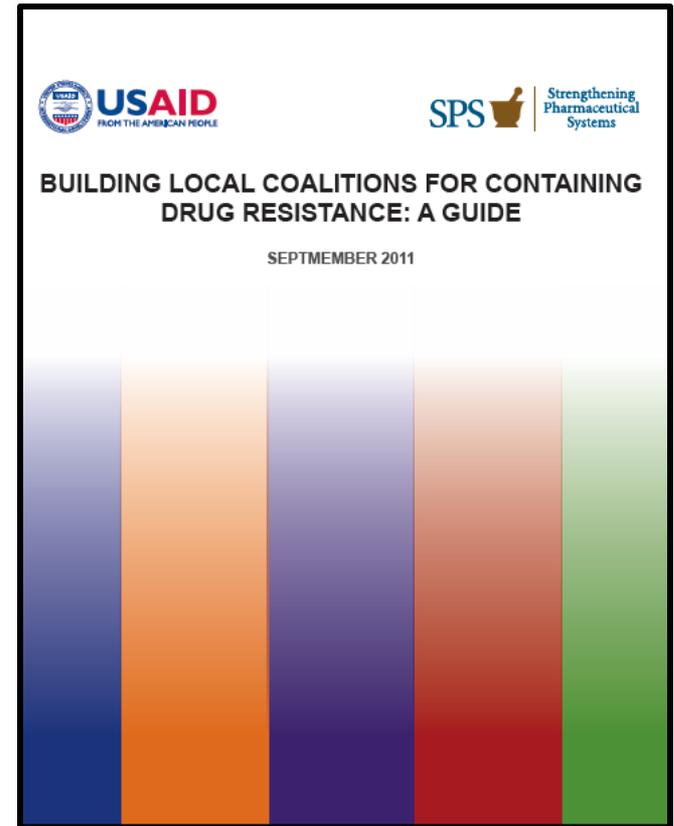
**USAID**  
FROM THE AMERICAN PEOPLE



# Example of USAID investment: advocacy and coalition building (1)

The USAID/SIAPS Program and its predecessors have helped build capacity to generate coalitions for advocacy and interventions to fight AMR at

- **country level** in **Zambia, Ethiopia, and Namibia**
- **regional level** in **Africa** through EPN, a faith-based regional network



Available for download at  
[http://projects.msh.org/projects/sps/SPS-Documents/upload/AMR-guide-English\\_FINAL.pdf](http://projects.msh.org/projects/sps/SPS-Documents/upload/AMR-guide-English_FINAL.pdf)

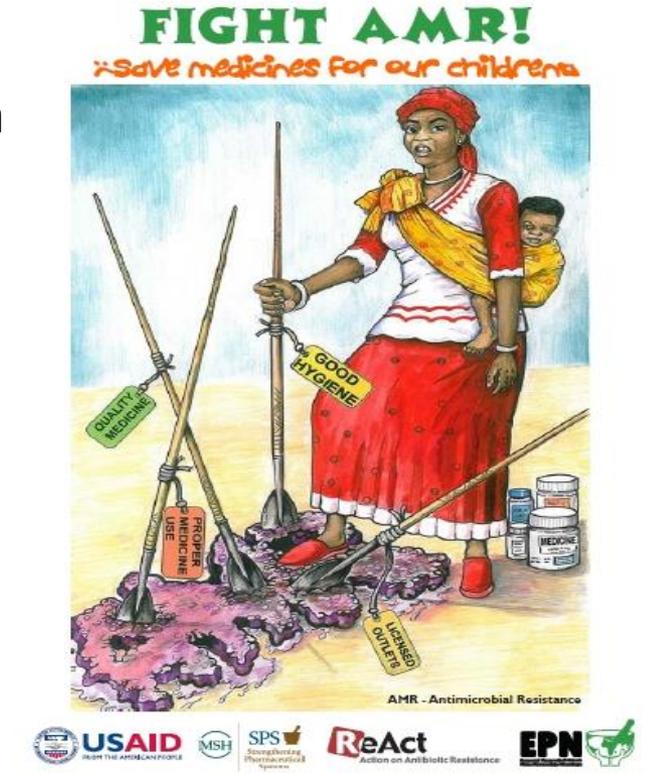
# Example of USAID investment: advocacy and coalition building (2)

<p><b>Zambia</b></p>	<ul style="list-style-type: none"> <li>• Mobilized key stakeholders against AMR through call-to-action meeting</li> <li>• Revised national standard treatment guidelines</li> <li>• Improved medicine quality assurance system</li> <li>• Used TV programs on AMR to educate the public</li> <li>• Incorporated AMR and rational medicine use (RMU) topics into University of Zambia medical curriculum</li> </ul>
<p><b>Ethiopia</b></p>	<ul style="list-style-type: none"> <li>• Mobilized key stakeholders against AMR through call-to-action meeting</li> <li>• Conducted national baseline study on AMR and developed action plan</li> <li>• Revised Medicines Formulary (2013) and Standard Treatment Guidelines (2014)</li> <li>• Trained journalists, which led to hundreds of radio, TV, and newspaper spots on AMR and RMU topics</li> </ul>
<p><b>Namibia</b></p>	<ul style="list-style-type: none"> <li>• Mobilized key stakeholders against AMR through call-to-action meeting</li> <li>• Collaborated with Namibians Against Antimicrobial Resistance and Pharmaceutical Society of Namibia</li> <li>• Helped University of Namibia School of Pharmacy integrate AMR and RMU topics into pre-service pharmacy curriculum</li> <li>• Helped implement HIV drug resistance early warning indicators</li> </ul>

# Example of USAID investment: advocacy and coalition building (3)

EPN's key accomplishments:

- Developed and distributed AMR call-to-action document in five languages
- Organized *Fight AMR! Save Medicines for our Children* campaign
- Produced educational materials on AMR topics
- Conducted regional meetings and training-of-trainers workshops on AMR
- Included AMR as a priority in its 2016-2020 strategic plan



Joshi et al. 2011. *Capacity building for country- and regional-level advocacy and interventions to contain antimicrobial resistance in Africa* [PPT]. Presented at ICIUM 2011.

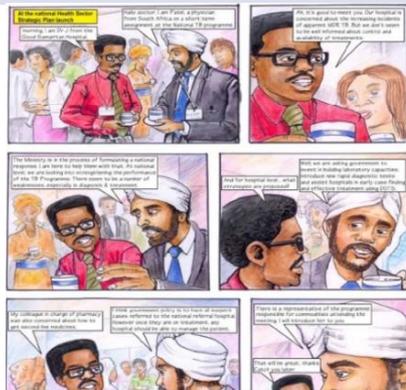
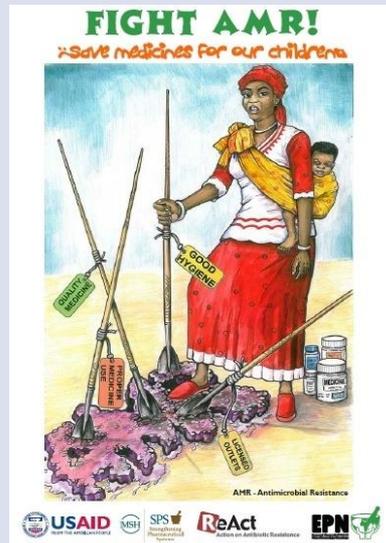
Joshi and Kusemererwa. 2011. *How to build local coalitions for containing drug resistance: country level and regional experiences* [PPT]. Presented at 1<sup>st</sup> Global Forum for Bacterial Infections.



**USAID**  
FROM THE AMERICAN PEOPLE

**SIAPS** 

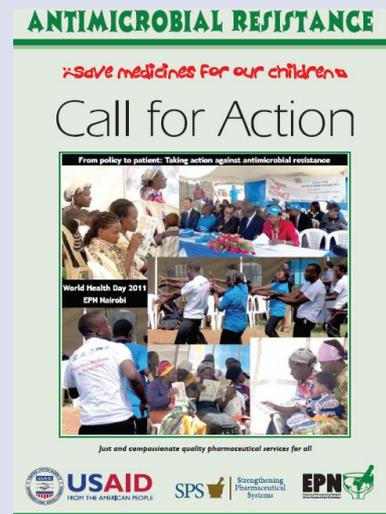
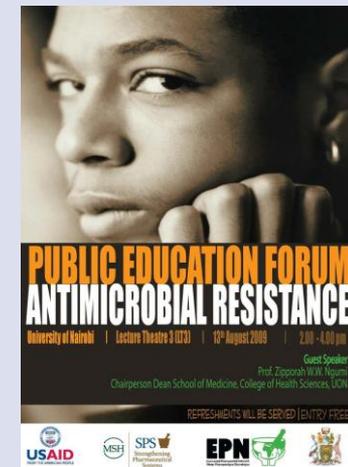
# Example of USAID investment: advocacy and coalition building (4)



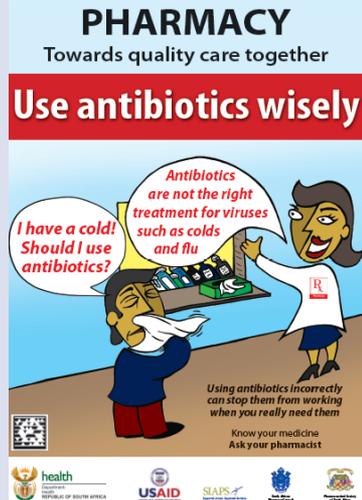
Comic book on AMR by EPN



AMR Call-to-Action Meeting, Namibia, 2013



Journalist training, Ethiopia, 2012



# Example of USAID investment: antimicrobial stewardship in Jordan

- **Problem:** Inappropriate use of antibiotic prophylaxis during cesarean section\*
- **Intervention at a glance:\*\***
  - Conducted medicine use evaluation at three public hospitals
  - Collaborated with multidisciplinary groups
  - Developed hospital-specific protocol and procedures
  - Implemented protocol using continuous quality improvement approach
  - Measured results through indicators



[http://www.fotosearch.com/ARP124/lc03\\_birth\\_c/](http://www.fotosearch.com/ARP124/lc03_birth_c/)

\*Jordan Food and Drug Administration. Rational antibiotic use in Jordan: auditing antibiotic use targeting surgical prophylaxis at Jordanian hospitals. JFDA, Rational Drug Use Department, May 2009.

\*\*Gammouh S and Joshi M. 2013. *Improving Antibiotic Prophylaxis in Cesarean Section in Jordanian Hospitals: SIAPS Technical Report*. Submitted to USAID by SIAPS/MSH, Arlington, VA.

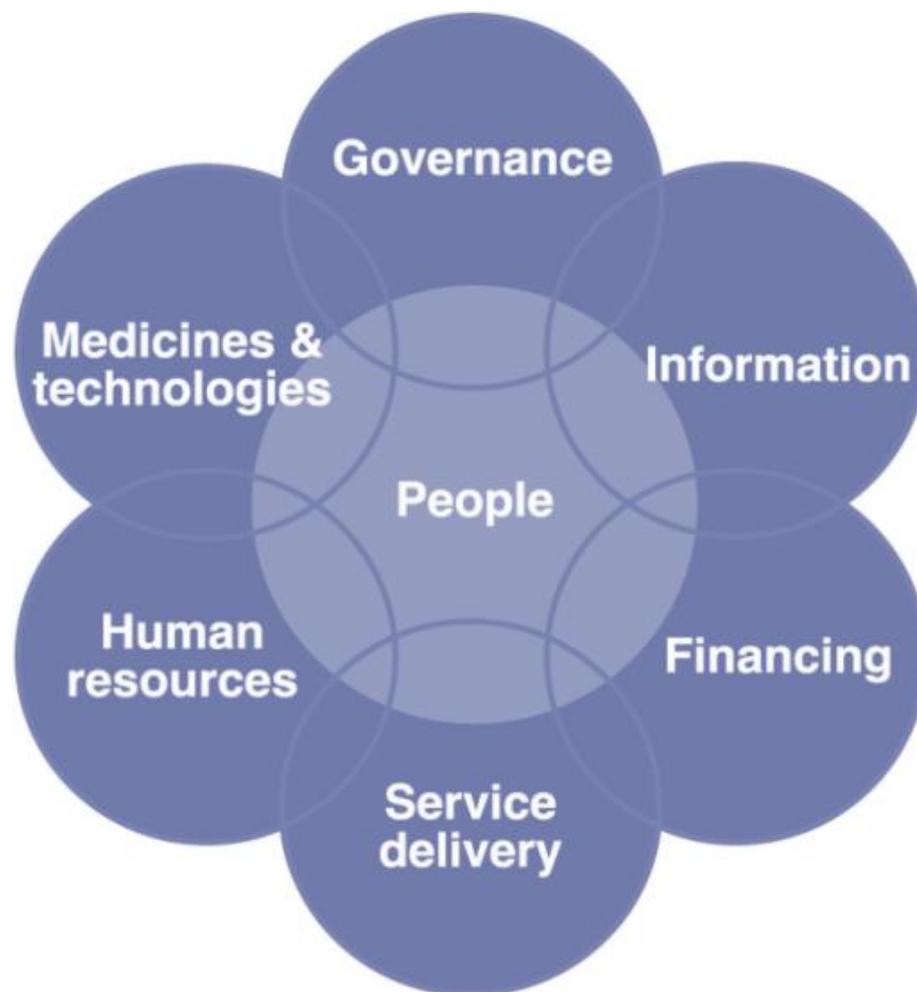


**USAID**  
FROM THE AMERICAN PEOPLE

**SIAPS** 

# Addressing health systems strengthening building blocks (1)

USAID/SIAPS focused on the six health systems strengthening building blocks to bring about positive and sustainable changes in antibiotic prophylaxis practices for cesarean section



[http://openi.nlm.nih.gov/detailedresult.php?img=3026705\\_pmed.1000397.g001&req=4](http://openi.nlm.nih.gov/detailedresult.php?img=3026705_pmed.1000397.g001&req=4)  
Image Credit: Fusión Creativa.



**USAID**  
FROM THE AMERICAN PEOPLE

**SIAPS** 

# Addressing health systems strengthening building blocks (2)

Building block	Achievements
<b>Service delivery</b>	<ul style="list-style-type: none"><li>• Developed evidence-based standard protocol and procedures: <i>right drug, right dose, right time, right duration</i></li><li>• Promoted pharmaceutical care</li><li>• Tracked surgical site infections</li></ul>
<b>Human resources</b>	<ul style="list-style-type: none"><li>• Oriented stakeholders on international evidence</li><li>• Trained staff to increase capacity</li><li>• Developed skills in continuous quality improvement process</li></ul>
<b>Information</b>	<ul style="list-style-type: none"><li>• Agreed on indicators to track progress</li><li>• Developed worksheet, cesarean section log, and Excel monitoring tool for data capture</li><li>• Collected monthly reports from infection control committee (ICC) via drug and therapeutics committee (DTC)</li></ul>

# Addressing health systems strengthening building blocks (3)

Building block	Achievements
<b>Medical products</b>	<ul style="list-style-type: none"><li>• Ensured availability of the preferred antibiotic (cefazolin) in hospitals, which was not available at program start</li></ul>
<b>Finance</b>	<ul style="list-style-type: none"><li>• Selected evidence-based, cost-effective antibiotic prophylaxis</li><li>• Analyzed and tracked financial costs</li></ul>
<b>Leadership/ governance</b>	<ul style="list-style-type: none"><li>• Mandated protocol and transparently tracked compliance</li><li>• Promoted interdisciplinary effort and coordination</li><li>• Defined roles of stakeholders through procedures</li><li>• Activated and engaged DTC and ICC</li><li>• Supported the hospital accreditation process</li></ul>

# Combined results for three participating hospitals in Jordan

Indicator	2010 (baseline)	2012
Correct antibiotic use (cefazolin)	0%	86%*
Correct timing of first dose	0%	92%*
Correct number of doses	0%	88%*
Result area	Achievement	
Average cost for antibiotic prophylaxis per case	79% decrease in 2012 compared to baseline	
Cesarean section surgical site infection rate	1.59 % (within international rate benchmark**)	

\* in log-captured cases (log capture rate = 81%)

\*\* Ghuman M et al. Post-caesarean section surgical site infection: rate and risk factors. The New Zealand Medical Journal 2011; 124

# Institutionalization, sustainability, and impact of antimicrobial stewardship program

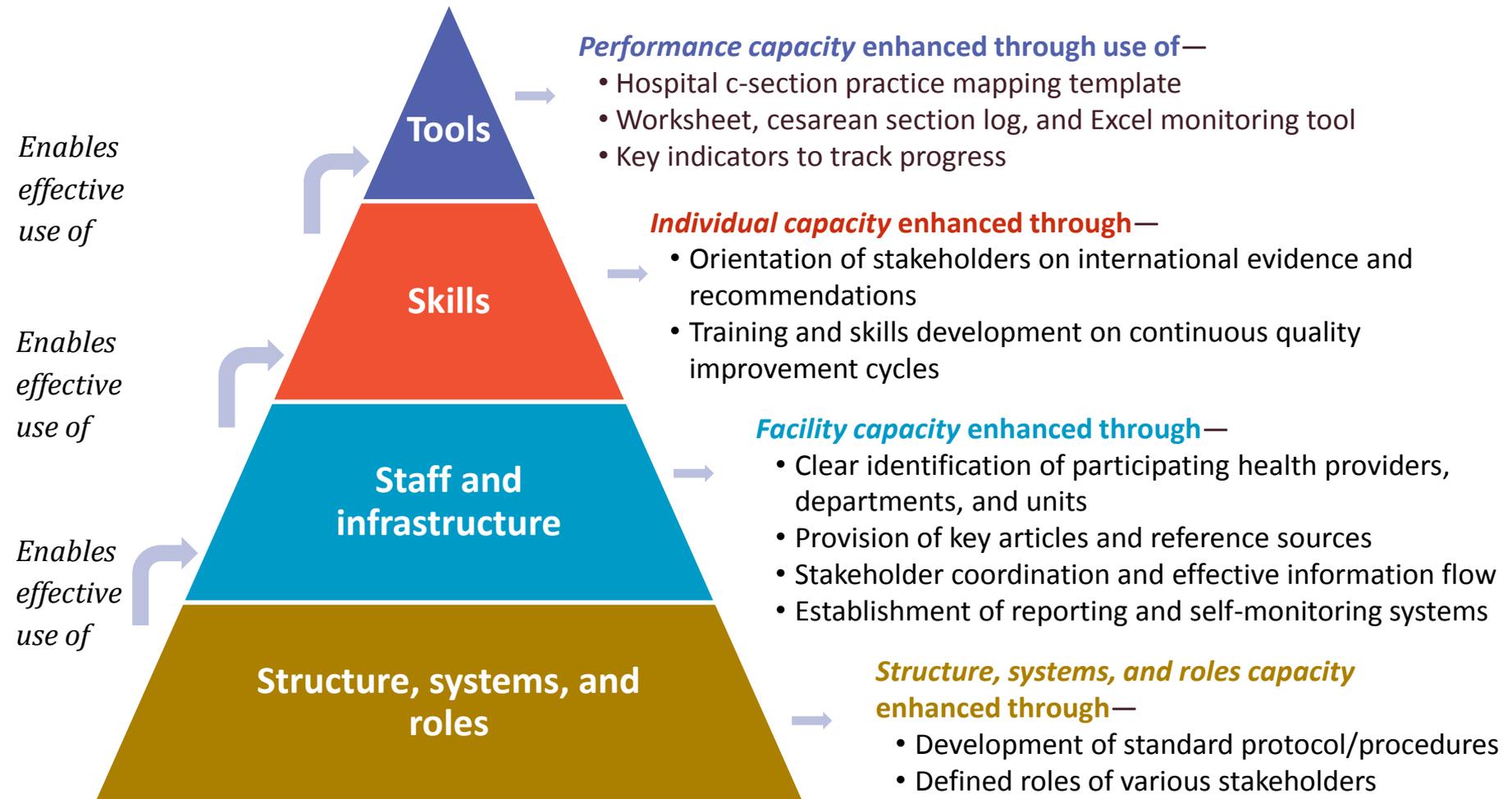
- **Institutionalization and sustainability:** mandate of a ‘unified’ protocol for all Ministry of Health OB-GYN hospitals
- **Spillover effect:**
  - Self-initiation of similar c-section antibiotic prophylaxis programs by other hospitals
  - Expansion of the approach to another procedure (hernia)
- **Support for accreditation:** contributed to HCAC’s NQS goal of “appropriate use of prophylactic antibiotic during surgery”
- **Contribution to maternal and child health goals:** national, USAID, and other global initiative goals

HCAC = Health Care Accreditation Council

NQS = National Quality and Safety



# Capacity building in Jordan hospitals for cesarean section antibiotic prophylaxis



Adapted from: Potter C, Brough R. Systemic capacity Building: A Hierarchy of needs. Health Policy and Planning 2004; 19(5): 336-345

# Conclusion (1)

- We lived in a pre-antimicrobial era 75 years ago...
- Then came the miracle medicines—antimicrobials—which have saved countless lives...
- But now we are in danger of losing all the antimicrobials we have and entering an era of pan-resistant infections (*XDR-TB being a particularly instructive example*)

We all need to  
**ACT NOW !**  
**ACT SERIOUSLY !**  
and  
**maintain the**  
**momentum as we**  
**move forward**



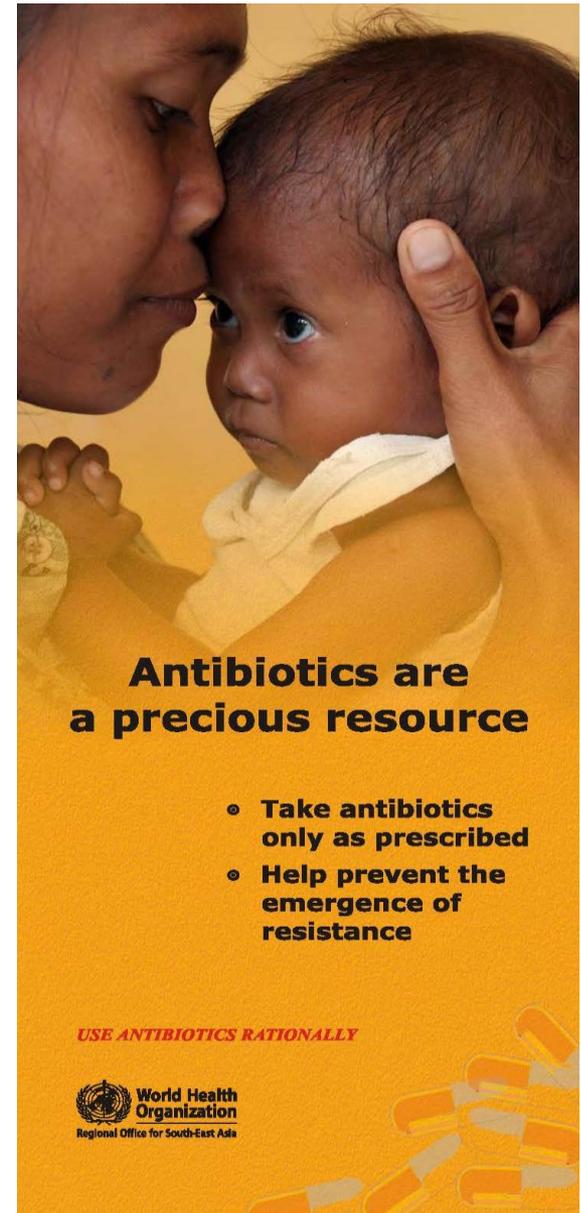
**USAID**  
FROM THE AMERICAN PEOPLE

**SIAPS** 

The SIAPS logo consists of the word "SIAPS" in a bold, green, sans-serif font, followed by a stylized blue figure of a person with arms raised in a celebratory or active pose.

## Conclusion (2)

- Individuals, countries, and international bodies all share responsibility in fighting the common threat of AMR
- *Our efforts should be two-pronged:*
  1. Preserve the effectiveness of existing antimicrobials and contain AMR
  2. Foster innovative ways of developing new antimicrobials, vaccines, and rapid diagnostics



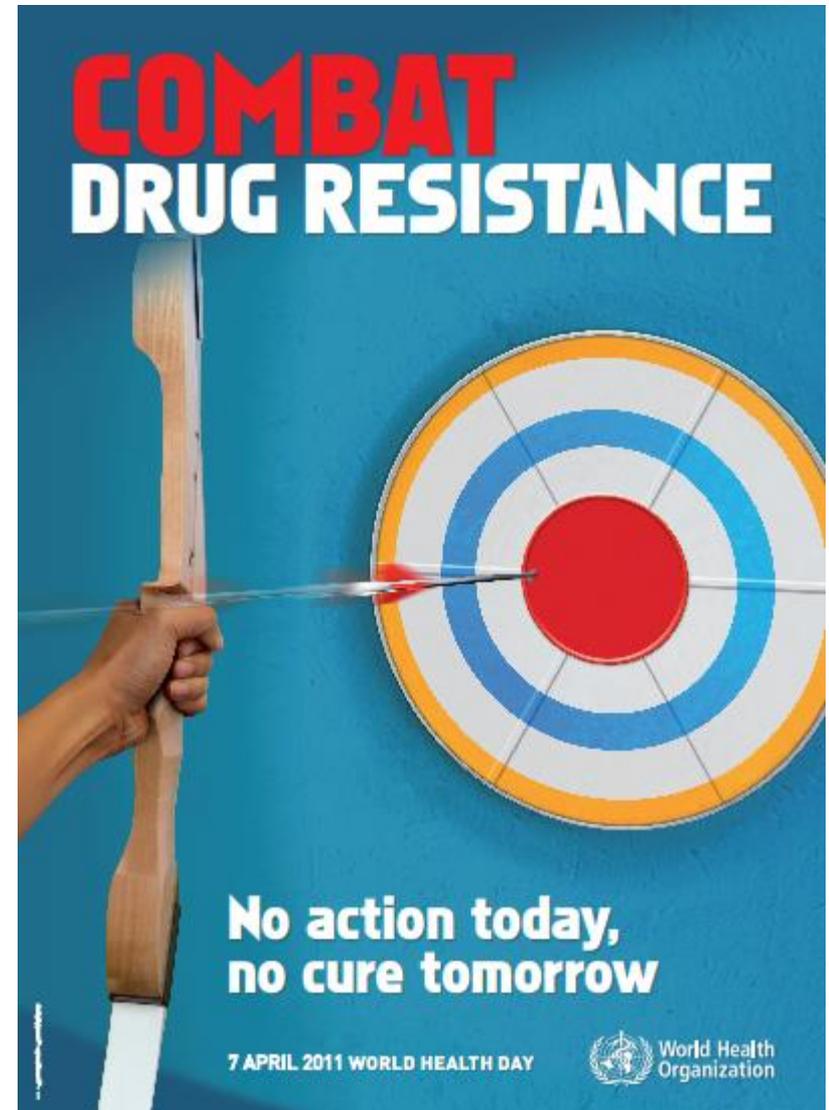
**USAID**  
FROM THE AMERICAN PEOPLE

**SIAPS**

# AMR resource flash drive

Contains a comprehensive set of AMR resources including:

- WHO publications
- USAID-supported tools, guidance documents, flyers, presentations, and reports
- Other U.S. government-supported publications
- Journal articles
- Other AMR-related materials



**USAID**  
FROM THE AMERICAN PEOPLE

**SIAPS** 