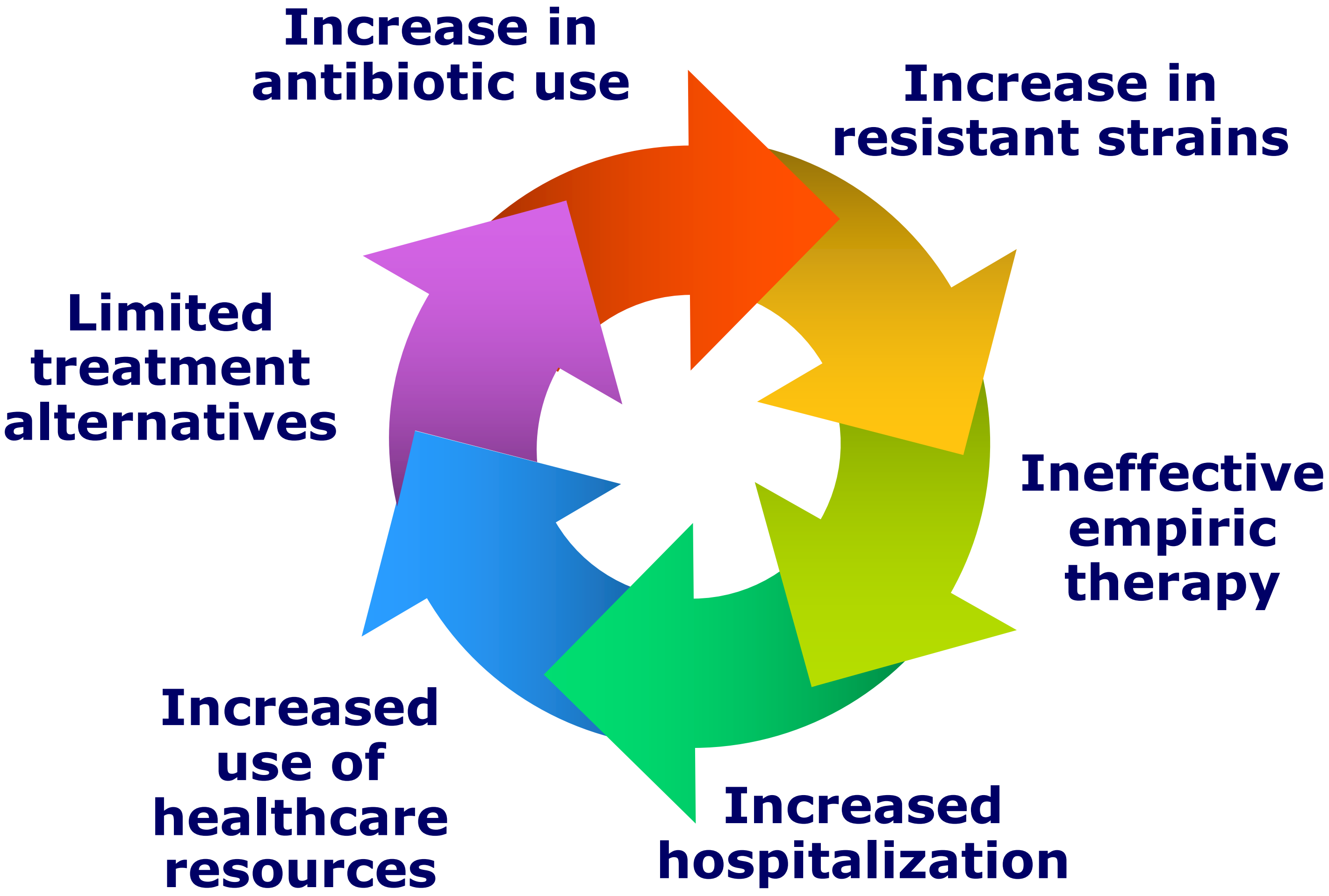
Integrated Activity and Tools for Antimicrobial Stewardship, Infection Prevention & diagnostic Stewardship

One Health Approach to AMR

The Next Pandemic is <u>Here</u>

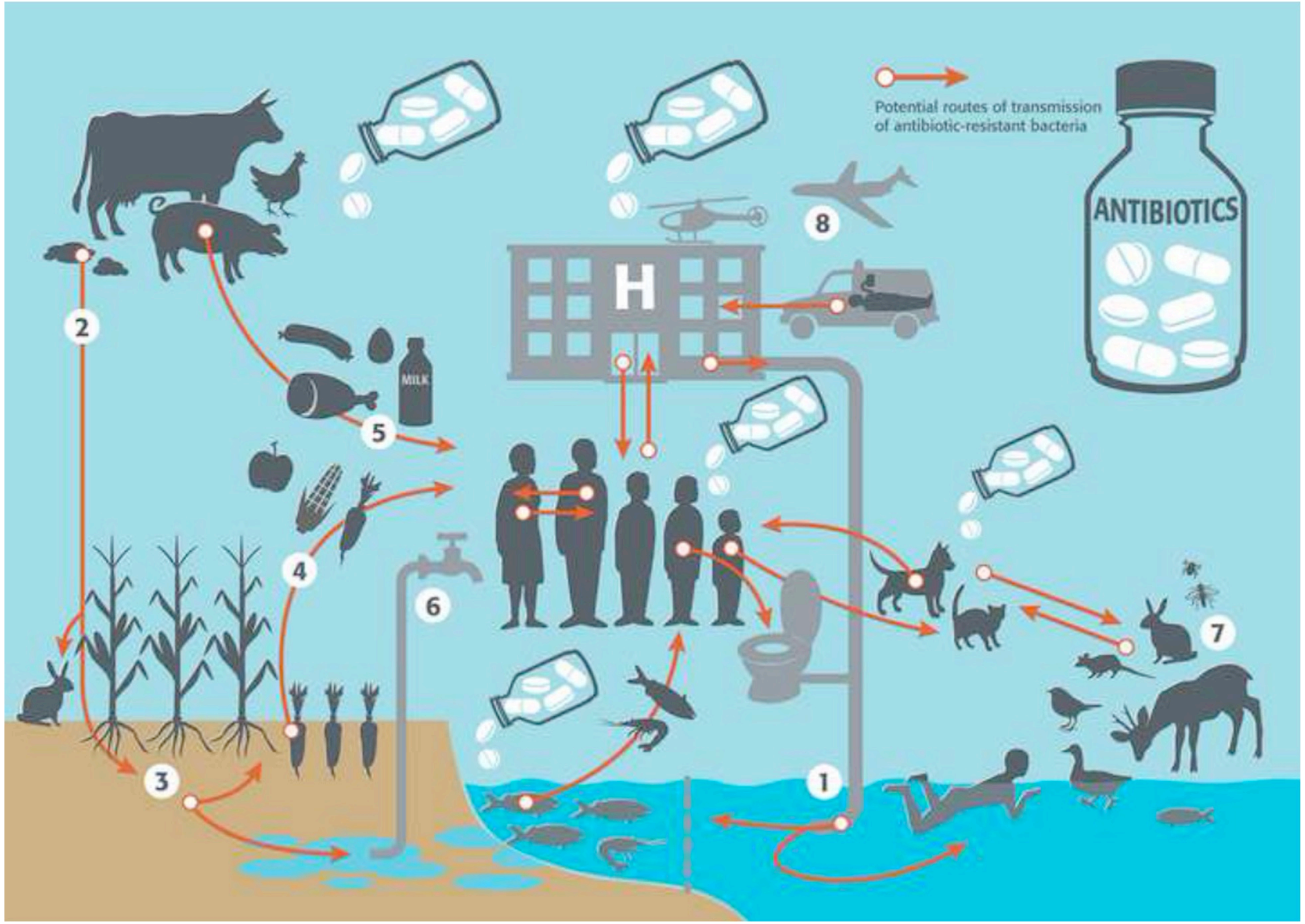


A global problem needs a global solution.

One World

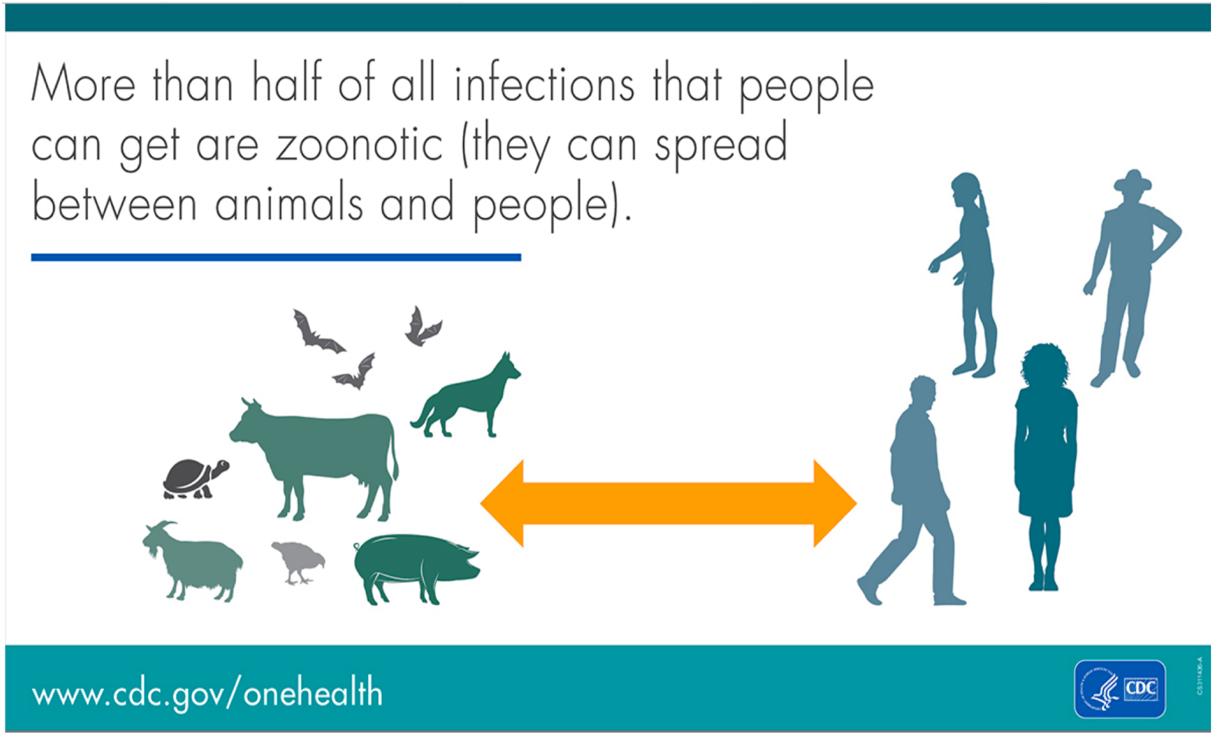
One Health

The State of the World



Animal Health

- Two-thirds of emerging infectious diseases and pathogens result from zoonoses
    - The majority originate in wild-life
- More people are living in contact with wild and domestic animals, both livestock and pets
- Diseases in food animals threatens supplies, livelihoods, and economies

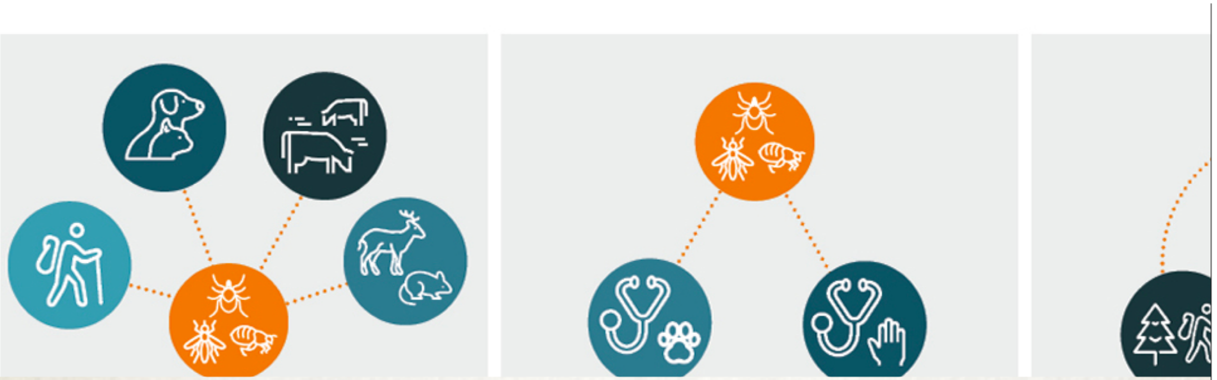


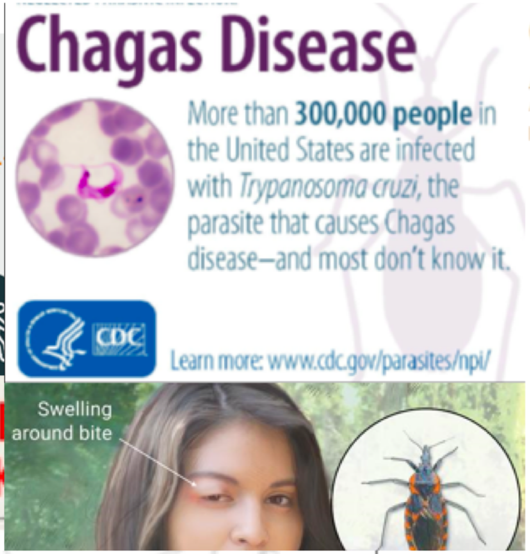
Environmental Health

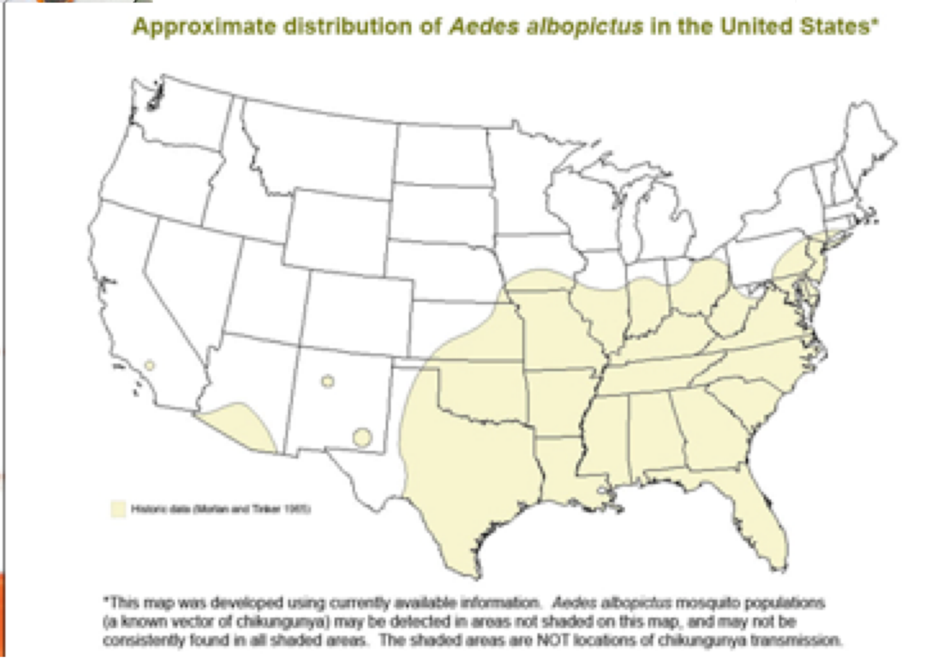
- Higher temperatures are associated with higher MIC levels in common pathogens including *E coli, K pneumoniae, S aureus*
  - Bacteria like *Salmonella* and cholera survive better in warmer temperatures as well
- Migrants and refugees not only exist due to conflict and war, but also due to climate crises
  - In 2022, weather-related events displaced 32.6 million people, a record high
- Industrial agriculture relies heavily on widespread antimicrobial use for livestock farms
- Small doses of antibiotics from urine, feces, manure, and pharmaceutical waste are being released into the environment through rivers, lakes, and soil

Climate Change & Vector-Borne Diseases

VECTOR-BORNE DISEASES ARE A ONE HEALTH ISSUE.







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What antibiotic use contributes to the development of antimicrobial resistance?

ⓘ Start presenting to display the poll results on this slide.

To summarize…

- The pipeline of new antimicrobials is **dry**
    - There is a **lack of access** to quality antimicrobials globally
    - Shortages are affecting countries at **all levels**
- The world (and its’ microbiome) is changing **rapidly**
    - Global warming
    - War, conflict, natural disasters
    - Human and animal migration
- The **cost** of AMR to national economies and health systems is significant

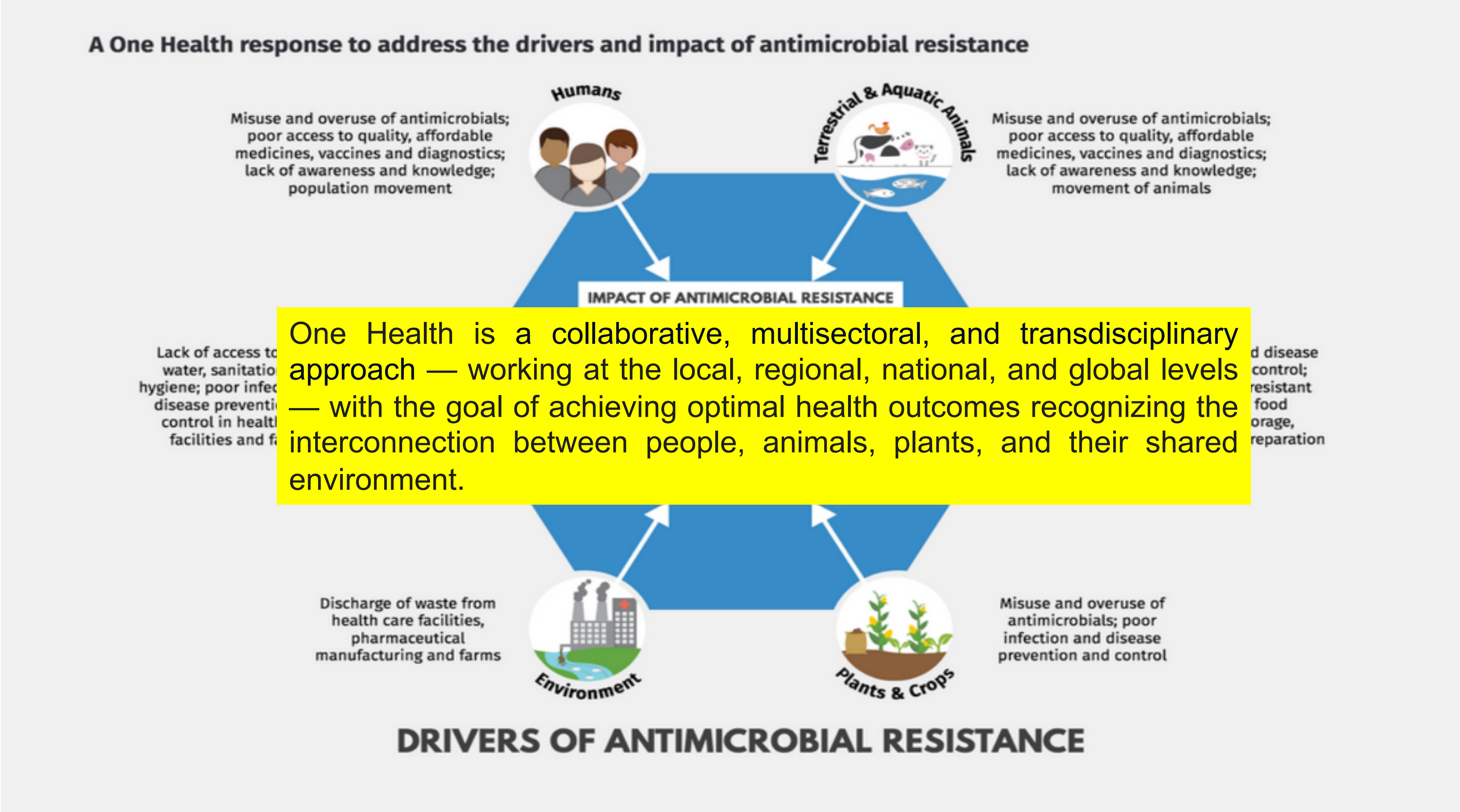
Trouble is coming…

We Need a Coordinated Plan

- Multisectoral **One Health approach**
  - Started sometime around September 2016 (UN General Assembly)

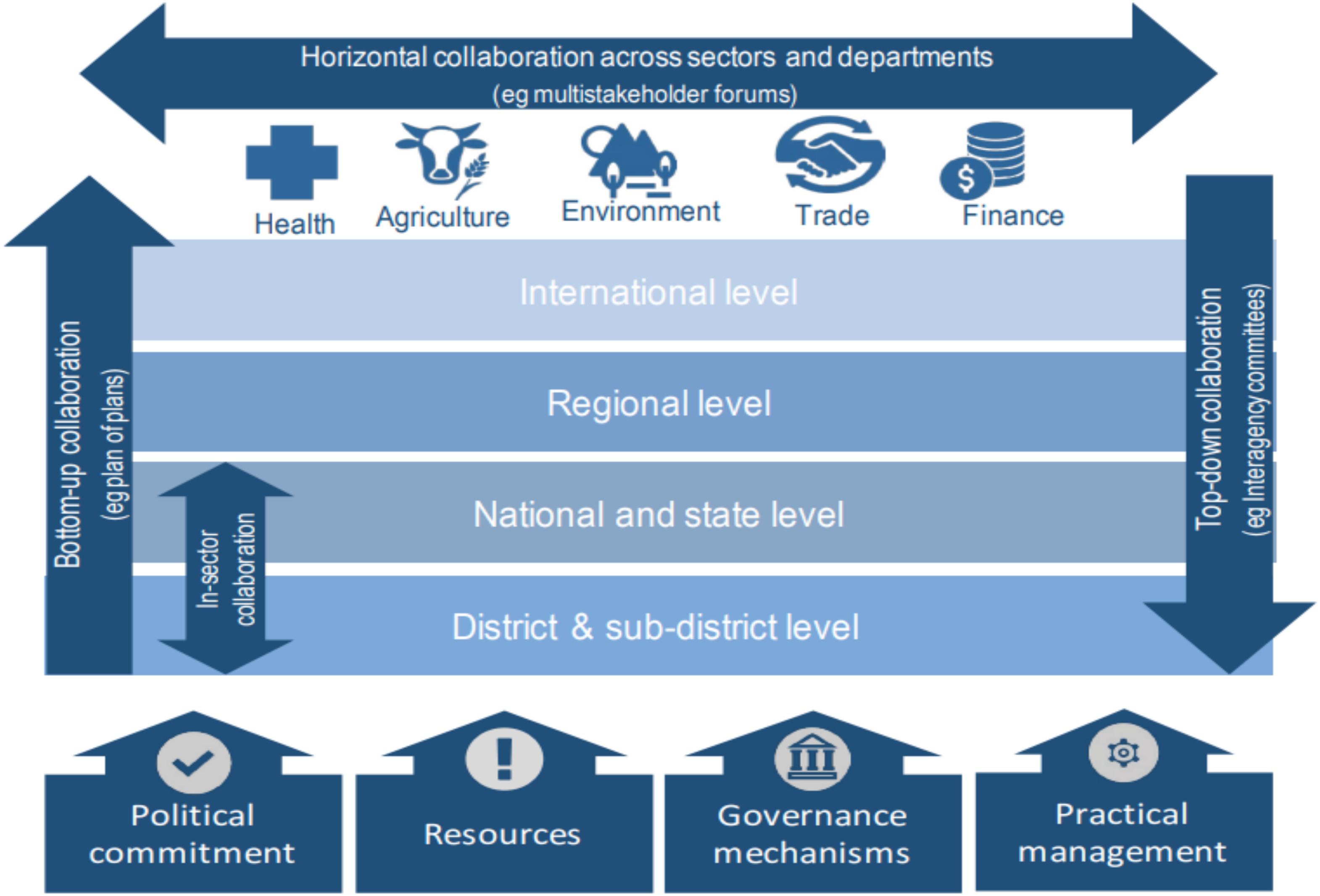
- World Antimicrobial Awareness Week
  - Nov 18 - Nov 24, since 2015

- *GL*obal *A*MR and Use *S*urveillance *S*ystem (GLASS)
  - https://www.who.int/initiatives/glass



One Health is a collaborative, multisectoral, and transdisciplinary approach — working at the local, regional, national, and global levels — with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment.

Figure 1: Multisectoral collaboration can be both horizontal across sectors as well as vertical across levels, and is enhanced by four groups of tools and tactics



Food and Agriculture Organization of the United Nations

OIE WORLD ORGANISATION FOR ANIMAL HEALTH

World Health Organization

Global Action Plan on Antimicrobial Resistance

Global Action Plan: 5 Objectives

1. Improve awareness and understanding of AMR

- Risk communication
- Education

2. Strengthen knowledge through surveillance and research

- National AMR surveillance
- Laboratory capacities
- Research and development

3. Reduce the incidence of infection

- IPC, WASH, HAI
- Community level prevention
- Animal health: prevention and control

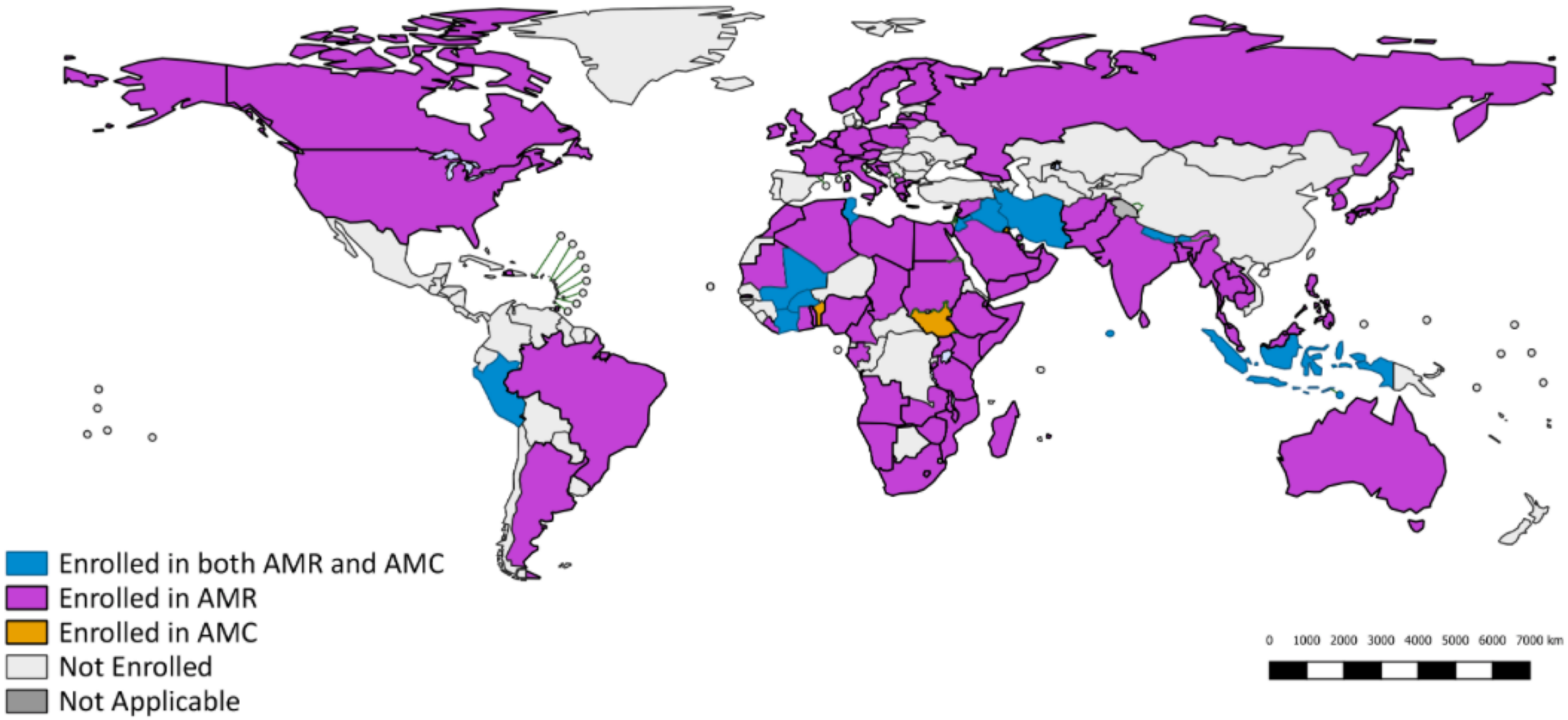
4. Optimize the use of antimicrobial medicines

- Access to qualified antimicrobial medicines, regulation, AMS
- Use in veterinary and agriculture

5. Ensure sustainable investment in countering antimicrobial resistance

- Measuring the burden of AMR
- Assessing investment needs
- Establishing procedures for participation

GLASS Enrolment Map Jan 2021



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data source: World Health Organization
Map production: Information Evidence and Research (IER)
World Health Organization
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World Health Organization

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What is One Health?

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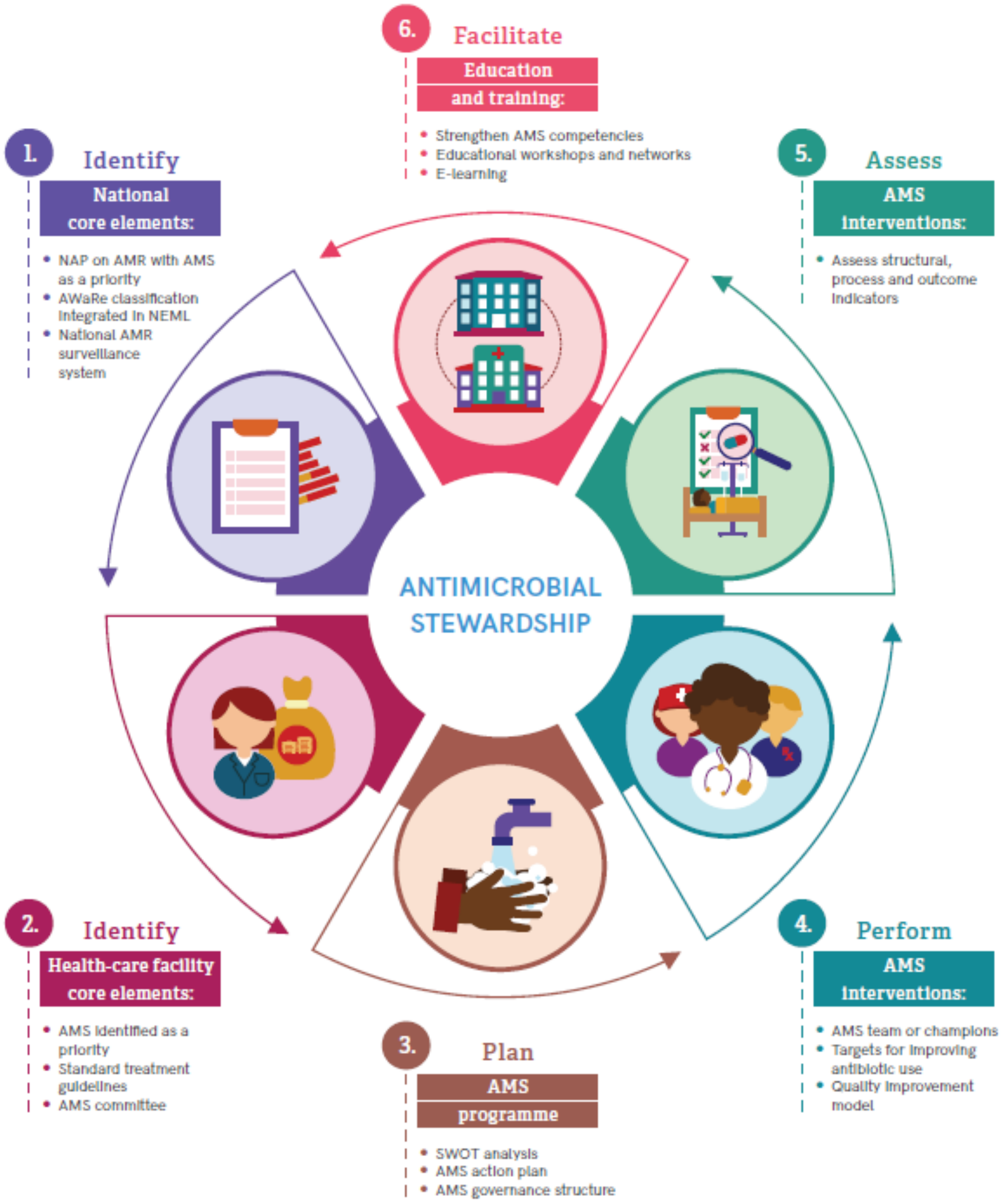
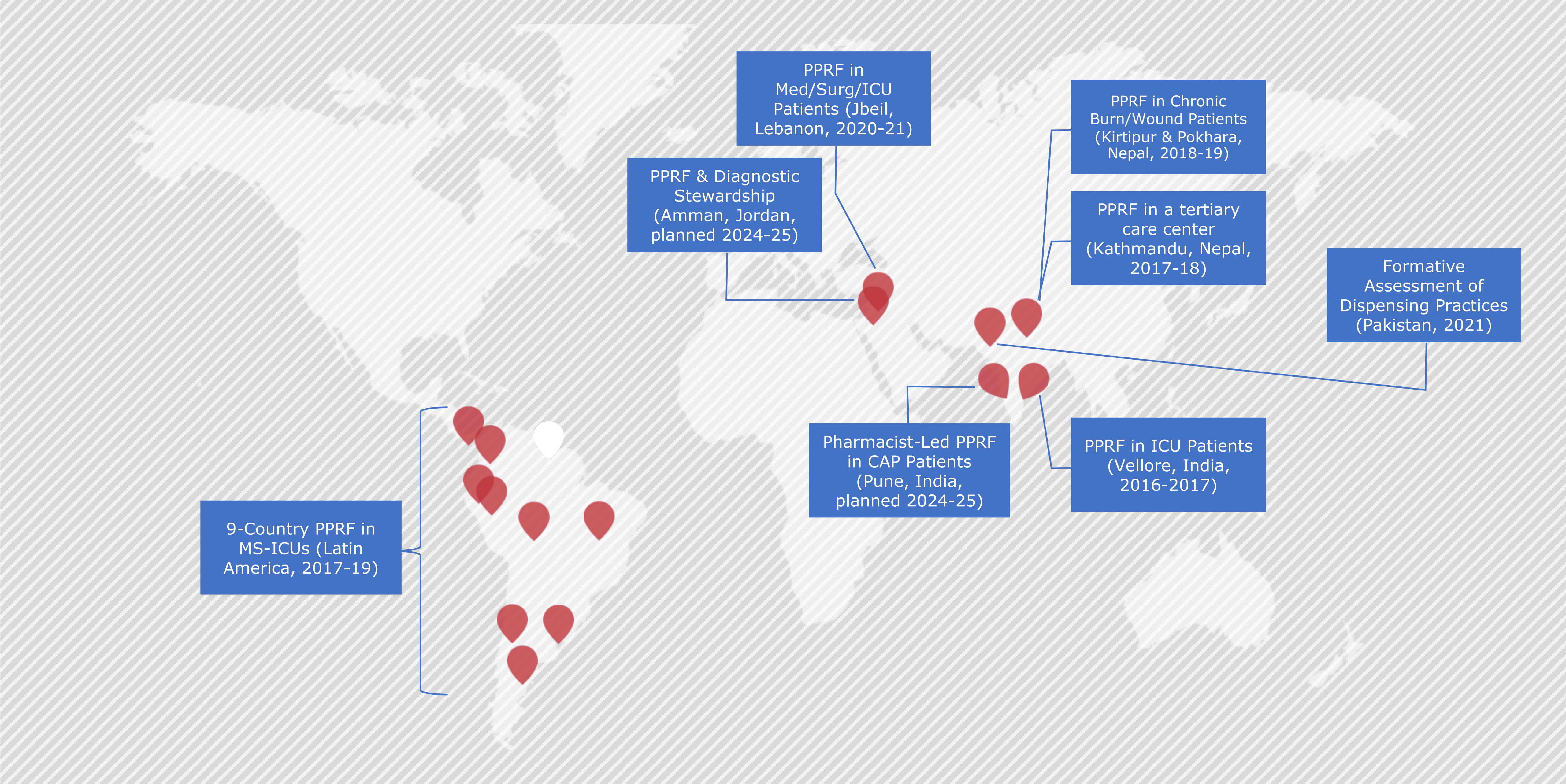
What is stewardship?

The right *Antibiotic*
for the right *Patient*
at the right *Time*
with the right *Dose*
and the right *Route*,
causing the *least* harm to the patient
and *future* patients.




PPRF in Med/Surg/ICU Patients (Jbeil, Lebanon, 2020-21)
PPRF & Diagnostic Stewardship (Amman, Jordan, planned 2024-25)
PPRF in Chronic Burn/Wound Patients (Kirtipur & Pokhara, Nepal, 2018-19)
PPRF in a tertiary care center (Kathmandu, Nepal, 2017-18)
Formative Assessment of Dispensing Practices (Pakistan, 2021)
Pharmacist-Led PPRF in CAP Patients (Pune, India, planned 2024-25)
PPRF in ICU Patients (Vellore, India, 2016-2017)
9-Country PPRF in MS-ICUs (Latin America, 2017-19)

Multicenter Study > Infect Control Hosp Epidemiol. 2022 Feb;43(2):181-190.
doi: 10.1017/ice.2021.80. Epub 2021 Apr 8.

Antimicrobial stewardship programs in adult intensive care units in Latin America:

> Antibiotics (Basel). 2020 Aug 29;9(9):556. doi: 10.3390/antibiotics9090556.

Feasibility Study of the World Health Organization Health Care Facility-Based Antimicrobial Stewardship Toolkit for Low- and Middle-Income Countries

Gina Maki [1], Ingrid Smith [2], Sarah Paulin [2], Linda Kaljee [3], Watipaso Kasambara [4], Jessie Mlotha [4], Pem Chuki [5], Priscilla Rupali [6], Dipendra R Singh [7], Deepak C Bajracharya [8], Lisa Barrow [9], Eliaser Johnson [9], Tyler Prentiss [3], Marcus Zervos [1] [10]

Affiliations + expand

PMID: 32872440 PMCID: PMC7558985 DOI: 10.3390/antibiotics9090556

Free PMC article

Abstract

Antimicrobial stewardship (AMS) has emerged as a systematic approach to optimize antimicrobial use and reduce antimicrobial resistance. To support the implementation of AMS programs, the World Health Organization developed a draft toolkit for health care facility AMS programs in low- and middle-income countries. A feasibility study was conducted in Bhutan, the Federated States of

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Infection Control & Hospital Epidemiology (2019), 40, 512–519
doi:10.1017/ice.2019.29

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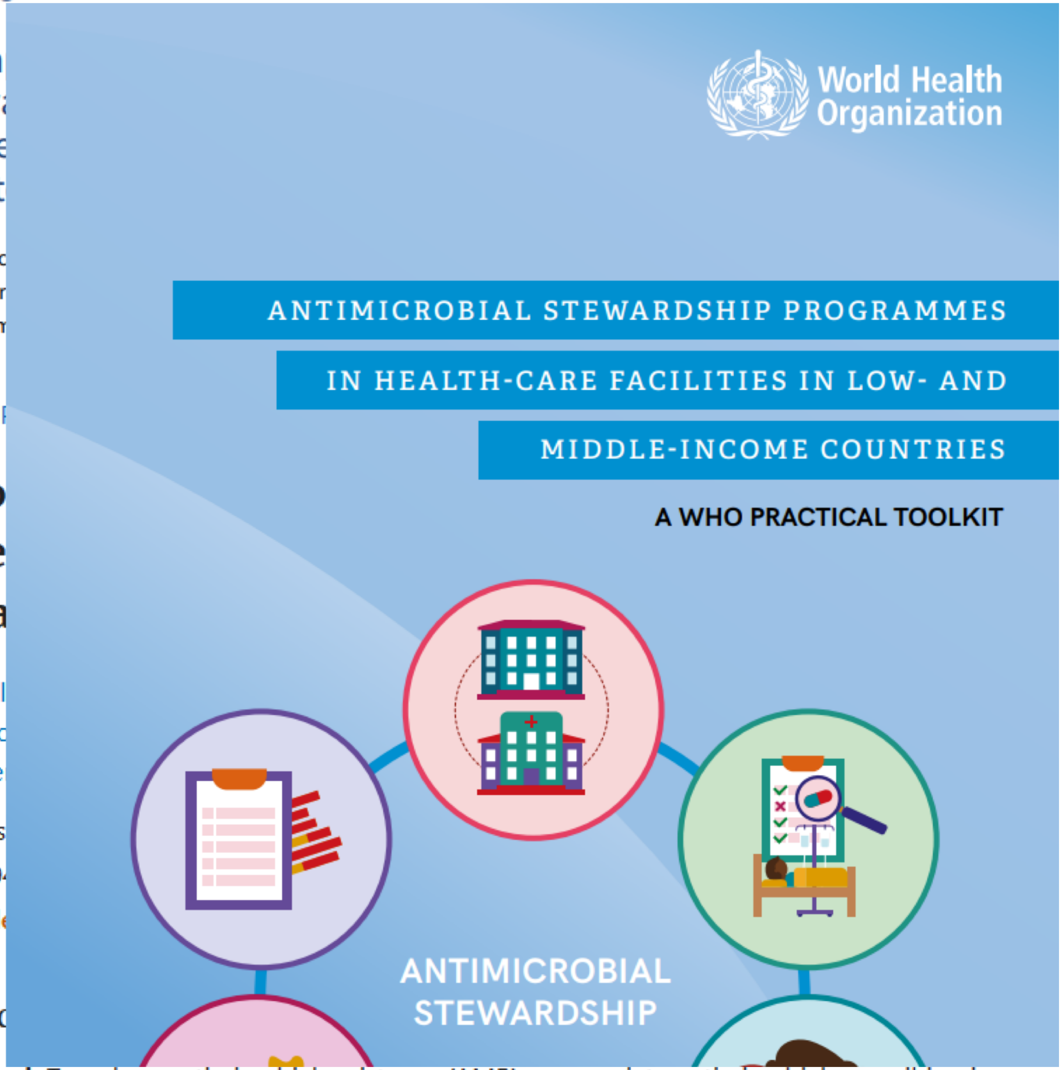

Abstrac

Background: To reduce antimicrobial resistance (AMR), appropriate antimicrobial prescribing is critical. In conjunction with Infection Prevention & Control (IPC) programs, Antimicrobial Stewardship Programs (ASP) have been shown to improve prescribing practices and patient outcomes. Low- and middle-income countries (LMIC) face challenges related to inadequate ASP policies and guidelines at both the national and healthcare facility (HCF) levels.

Table 3. Key findings for Implementation of AMS in LMIC.

Implementation Category	Key Findings
AMS implementation facilitators	• Strong national and health care facility leadership. • Clinical staff engagement in AMS committees.
AMS implementation barriers	• Inadequate human and financial resources. • Limited supplies of antibiotics, particularly in remote regions. • Lack of enforcement of regulations for prescription-only sales of antibiotics. • AMS competencies among health care workers and limited training and education in AMR, AMS, and IPC.
Recommendations to strengthen health care facility-based AMS	• Dedicated financial resources and AMS leaders and champions. • Use of stepwise approaches for AMS implementation based on country and health care facility contexts. • Mechanisms for reporting and feedback. • Implementation of interdisciplinary AMS training workshops and AMS curricula.

AMR—antimicrobial resistance; AMS—antimicrobial stewardship; IPC—infection prevention and control.

Antibiotics. 2020 Aug 29;9(9):556.

Journal of Antimicrobial Chemotherapy (2005) **55**, 127–130
doi:10.1093/jac/dkh508
Advance Access publication 1 December 2004

JAC

Epidemiology of antimicrobial resistance in enterococci of animal origin

Ellie Hershberger[1,2], Simona F. Oprea[1,2], Susan M. Donabedian[1,2], Mary Perri[1,2], Pamela Bozigar[1,2], Paul Bartlett[3] and Marcus J. Zervos[1,2,4]*

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Received 8 June 2004; returned 15 July 2004; revised 20 October 2004; accepted 23 October 2004

Objective: **We evaluated the epidemiology of antimicrobial resistance in enterococci from animal farms and the potential relation of resistance to antimicrobial use.**

Methods: **Enterococci from faecal samples from 18 beef cattle, 18 dairy cattle, 18 swine, 13 chicken, and eight turkey farms were prospectively evaluated over a 6 year period from 1998 to 2003.**

Results: **We evaluated 1256 isolates of *Enterococcus faecium* and 656 isolates of *Enterococcus faeca-***

- Enterococci from fecal samples from 18 beef cattle, 18 dairy cattle, 18 swine, 13 chicken, and eight turkey farms were prospectively evaluated over a 6-year period from 1998 to 2003.
- We evaluated 1256 isolates of E*nterococcus faecium* and 656 isolates of *Enterococcus faecalis*.
- For *E. faecalis*, gentamicin resistance was more frequently detected on dairy and swine farms using gentamicin ($P<0.0001$ and $P=0.0052$, respectively) and ciprofloxacin resistance was more common on beef farms using enrofloxacin ($P<0.0001$) compared with farms not using these antimicrobials.

Molecular Characterization of Gentamicin-Resistant *Enterococci* in the United States: Evidence of Spread from Animals to Humans through Food

S. M. Donabedian,[1,2] L. A. Thal,[1,2] E. Hershberger,[1,2] M. B. Perri,[1,2] J. W. Chow,[1,3,4] P. Bartlett,[5] R. Jones,[6] K. Joyce,[7] S. Rossiter,[7] K. Gay,[7] J. Johnson,[8] C. Mackinson,[8] E. Debess,[9] J. Madden,[10] F. Angulo,[7] and M. J. Zervos[1,2,4]*

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Received 3 July 2002/Returned for modification 3 September 2002/Accepted 21 November 2002

We evaluated the molecular mechanism for resistance of 360 enterococci for which the gentamicin MICs were ≥128 μg/ml. The *aac(6′)-Ie–aph(2″)-Ia*, *aph(2″)-Ic*, and *aph(2″)-Id* genes were identified by PCR in isolates from animals, food, and humans. The *aph(2″)-Ib* gene was not identified in any of the isolates. Two *Enterococcus faecalis* isolates (MICs > 1,024 μg/ml) from animals failed to generate a PCR product for any of the genes

- Data indicate much diversity among gentamicin-resistant enterococci
- The data also suggest similarities in gentamicin resistance among enterococci isolated from humans, retail food, and farm animals from geographically diverse areas and provide evidence of the spread of gentamicin-resistant enterococci from animals to humans through the food supply.

JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 2010, p. 4156–4160 Vol. 48, No. 11
0095-1137/10/$12.00 doi:10.1128/JCM.02346-09
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Characterization of Vancomycin-Resistant *Enterococcus faecium* Isolated from Swine in Three Michigan Counties▽‖

Susan M. Donabedian,[1] Mary Beth Perri,[1] Nodira Abdujamilova,[2] Mary Joy Gordoncillo,[2] Amir Naqvi,[2] Katherine C. Reyes,[1] Marcus J. Zervos,[1,3]* and Paul Bartlett[2]

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Received 30 November 2009/Returned for modification 20 April 2010/Accepted 13 August 2010

Vancomycin-resistant enterococci are a major cause of nosocomial infections but are rarely found in humans in the community and have not been identified in food animals in the United States. We evaluated a total of 360 fecal specimens from humans and their animals being raised for exhibit at three county fairs in Michigan. Fecal samples from 158 humans, 55 swine, 50 cattle, 25 horses, 57 sheep, 14 goats, and 1 llama were obtained and plated onto Enterococcosel agar containing 16 μg/ml of vancomycin. Vancomycin-resistant *Enterococcus faecium* (VREF) was isolated from six pigs but not from humans or any animal other than pigs. All six VREF isolates had a MIC to vancomycin of ≥256 μg/ml and contained the *vanA* gene. Pulsed-field gel electrophoresis (PFGE) patterns of the six VREF isolates were ≥80% similar. Multilocus sequence typing (MLST) revealed sequence type 5 (ST5) (n = 2), ST6 (n = 3), and ST185 (n = 1), which are *E. faecium* sequence types belonging to clonal complex 5 (CC5). These findings show the dissemination of VREF strains among pigs in three Michigan counties. This is the first report of VRE found in food animals in the United States.

Enterococci are a major cause of morbidity and mortality in hospitalized patients in the United States. In a 2006-2007 report to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, *Enterococcus* species were the second most common pathogen in U.S. hospitals (29).

animals, the environment, and humans without hospital exposure in the community (10, 42, 48, 52).

In Europe, the glycopeptide avoparcin was used for growth promotion on farms for many years. When it was found that VRE could commonly be isolated from food animals, retail

- Evaluated a total of 360 fecal specimens from humans and their animals being raised for exhibit at three county fairs in Michigan
- Vancomycin-resistant *Enterococcus faecium* (VREF) was isolated from six pigs but not from humans or any animal other than pigs
- This is the first report of VRE found in food animals in the United States.

Additional Examples of HFH-GHI Work

- All patients hospitalized with MDR bacterial infections over a 12-month period were retrospectively evaluated.
  - MDR bacteria included those with extended spectrum beta lactamase (ESBL), carbapenem (CRE) or colistin resistance
- Water surveillance was performed to identify a potential source of environmental exposure
- The majority of infections in both groups were community acquired.
- Study demonstrated gram negative bacteria in the drinking water in various locations throughout Kathmandu. This is a possible source of community acquired MDR bacterial infection.
  - Collection and culturing of vials from various points of drinking water to assess for resistant organisms

Maki, G. et al. International Journal of Infectious Diseases, Volume 79, 44 - 45

Additional Examples of HFH-GHI Work

- Investigating fresh river water contribution to the transmission of hospital-associated VRE clonal lineages
  - Isolates from hospital-acquired infections, chronic ulcers, but also fresh water sources in downstream area from the hospital and a local wastewater treatment plant
  - Performed whole genome sequencing
  - Phylogenetic analysis revealed homogeneity between infection isolates and environmental isolates supporting the hypothesis that environment may act as a reservoir or means of dissemination

10:15 MI-08

Contribution of fresh river water to the dissemination of hospital-associated Enterococcus faecium CC17 strains in Córdoba

Blasko, E.G.; González, M.J.; Bardossy, A.C.; Sosa, E.J.; Prentiss, T.; Suleyman, G.; Jagjeet, K.; Maki, G.; Ruiz, S.E.; Grupo de Estudio de colonización por VRE de CBA; Fernández Do Porto, D.; Bocco, J.L.: Saka, H.A.; Amé, V.; Zervos, M.; Sola, C.

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What are some of the ways antimicrobial resistance can be reduced at the human-animal interface?

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Five Steps To Addressing Global Burden of AMR

Infection prevention and control

Five Steps To Addressing Global Burden of AMR

- Infection prevention and control
- Immunizations and vaccine equity

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- Infection prevention and control
- Immunizations and vaccine equity
- Reduce exposures to antibiotics unrelated to treating human disease

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- Infection prevention and control
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- Minimizing use of antibiotics when they are not necessary to improve human health

Five Steps To Addressing Global Burden of AMR

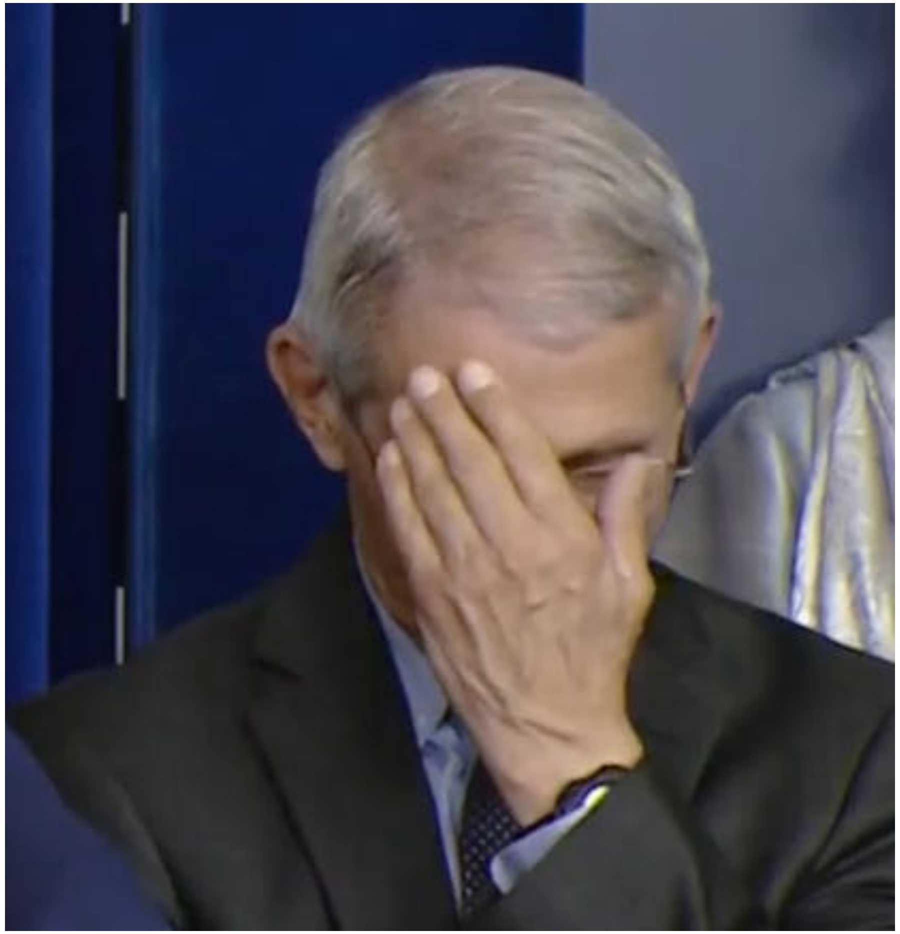
- Infection prevention and control
- Immunizations and vaccine equity
- Reduce exposures to antibiotics unrelated to treating human disease
- Minimizing use of antibiotics when they are not necessary to improve human health
- Maintain investment in the development pipeline for new antibiotics, and increase access to second-line antibiotics in locations without access

Getting Creative

- Thinking outside the box – aka outside of antibiotics
  - **Bacteriophage and phage-derived enzyme therapy:** Phages are viruses that infect bacteria, to treat bacterial infections. Phages are highly specific to certain bacteria, so they can target bacteria without harming human cells or the surrounding microbiota. Phage therapy is being increasingly used to treat infections that are resistant to antibiotics or persist.
  - **Monoclonal antibody infusions:** target conserved pathways, activate the immune system, and neutralize bacterial toxins and virulence factors. They can also inhibit biofilm formation
  - **Immunomodulators:** used to treat bacterial infections by enhancing the immune system's response to pathogens. E.g., Interferons and Interleukins
  - **Microbiome-modulating agents:** include probiotics, prebiotics, synbiotics, fecal microbiota transplantation (FMT), bacteriophages (phage therapy), dietary interventions, and certain antimicrobial peptides (bacteriocins), all aimed at promoting beneficial bacteria while suppressing pathogenic ones, thereby restoring a healthy microbiome balance and combating infection

Dr Fauci...

Winning does not mean stamping out every disease but rather getting out ahead of the next one.



HENRY FORD HEALTH

Misuse of **ANTIBIOTICS** puts us all at risk.

Taking antibiotics when you don't need them speeds up antibiotic resistance. Antibiotic resistant infections are more complex and harder to treat. They can affect anyone, of any age, in any country.

Always seek the advice of a healthcare professional before taking antibiotics.

HANDLE ANTIBIOTICS WITH CARE

World Health Organization