

Integrating Rapid Diagnostics and Antibiotic Stewardship

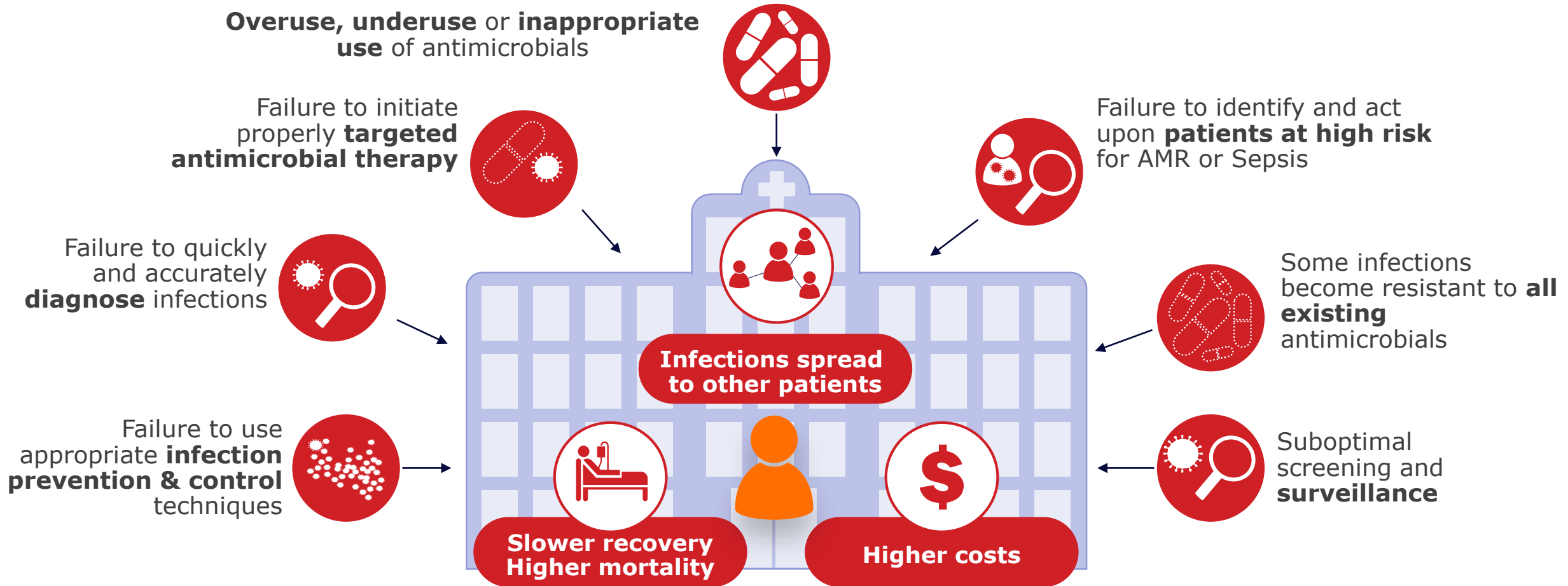
National Academies 10/14/2022

Diane Flayhart, BD



The Challenge of Antimicrobial Resistance (AMR)

Antimicrobial resistant infections in hospitals are exacerbated by insufficient or ineffective processes, tools, communication and coordination

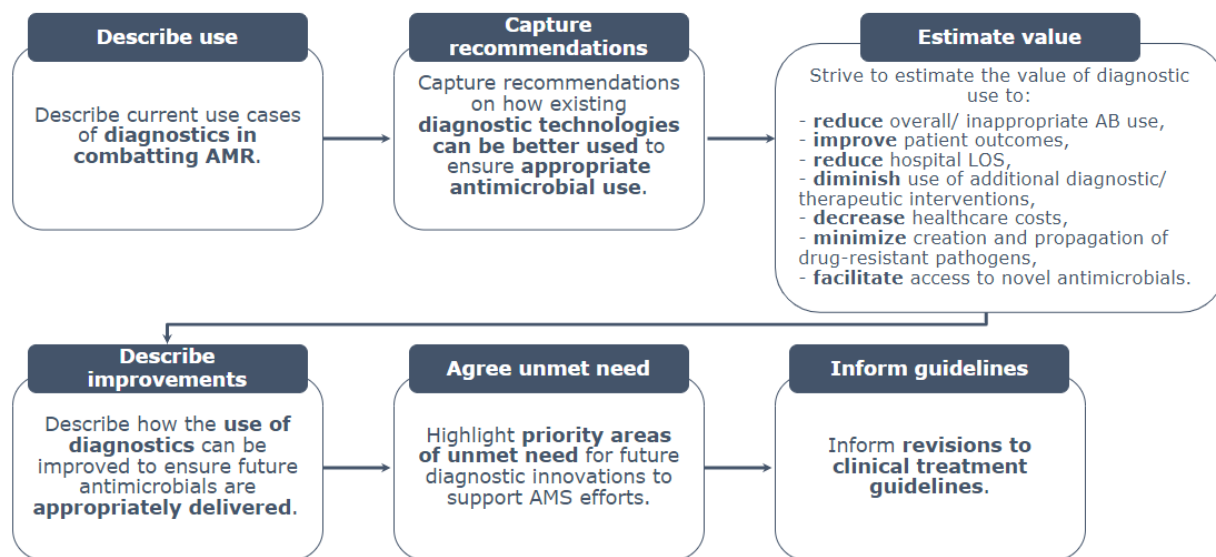


Questions to be considered:

- How effectively do current diagnostics inform antibiotic stewardship?
- Do we have enough data to understand how drug-resistant infections impact patient populations?
- Are new metrics needed to drive dx use and Antibiotic Stewardship efforts?
- Do we need more advocates to drive awareness for the need for Diagnostic and Antibiotic Stewardship?

Collaborating to better understand the use of diagnostics to inform therapy decisions

A Multinational Survey on Antimicrobial Stewardship Program Practice and Rapid Diagnostic Utilization



Study geographies:

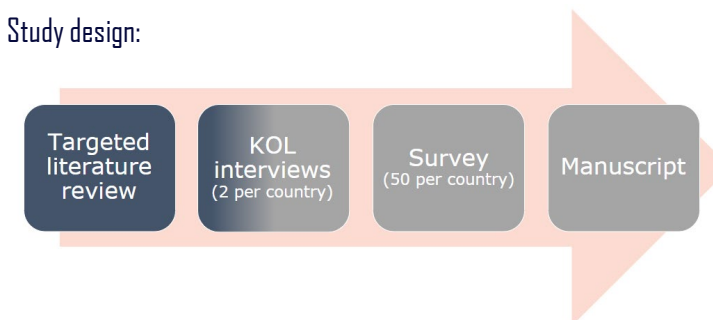
- **US**
- **Germany**
- **Italy**



- **China**
- **India**
- **Brazil**



Study design:



Study partners:



Publication expected early Spring 2023

Key questions for Targeted Literature Review

Theme 1: Current state of diagnostics

What is the current state of diagnostic use in driving AMS programs?

Theme 2: Impact of diagnostics

Estimate the impact of appropriate and optimal diagnostic testing on AMS programs and driving compliance to practice guidelines.

Theme 3: Diagnostics and product use

What impact does diagnostic testing have upon the uptake and use of novel and recently approved antimicrobials?

Theme 4: Barriers to using diagnostics

What are the key drivers and barriers to broader use of existing diagnostic technologies in making empiric and definitive treatment decisions?



>300 publications reviewed, both international and regional publications from the six countries

Selected key findings from Targeted Literature Review

Theme 1: Current state of diagnostics

- Guidelines on ASPs from large international bodies (including IDSA, SHEA, PAHO, DGI, EU Commission) **recommend the use of rapid/ POC diagnostics in combination with traditional methods.**
- For individual clinical practice areas, recommendations for rapid diagnostic use are **more sparse**: sporadic recommendation for PCR, sequencing, and POC tests; **majority of guidelines recommended traditional methods.**
- There is an emphasis in the guidelines of **suitable antimicrobial prescribing based on microbiological test results and results of AST.**
- Clinician views on **choices and drivers behind decision making were not captured** across the identified publications in the TLR.

Theme 2: Impact of diagnostics

- Diagnostic tests lead to **antibiotic de-escalation and treatment change, reduced treatment duration, and cost savings.**

Theme 3: Diagnostics and product use

- Diagnostics **enable appropriate use of drugs when they are introduced**, especially novel narrow-spectrum agents.
- Individual hospitals are able to make individual antimicrobial choices, but **minimal data were gathered for examples of how surveillance and diagnostics have impacted formulary access policy.**

Theme 4: Barriers to using diagnostics

- Barriers to broader use of diagnostics were similar across countries/ income levels; the decision to utilize diagnostic technologies are impacted by **education, technology infrastructure, human resources, quality control, evidence, and economics.**

KOL interviews included 20 questions in four categories; next step: survey

Technology for infectious disease management

★ Experience with diagnostics

Q1: When managing patients with a potential infection requiring antibiotics, what is your experience with the use of diagnostics tests, including rapid tests, personally and at your hospital?

1. Rapid diagnostics are considered an 'add-on' test¹.



"There is a standard range of tests, with additional specific tests used for patients with a particular presentation."

2. Experts from multiple specialties are involved in determining the appropriate diagnostic test.



Clinicians, microbiologists, pharmacists and ID specialists are involved.

3. Infectious disease specialists provide consultancy services to other disciplines.



"Hospital policy dictates that patients with a positive test result is reviewed by the ID team."

4. In two MICs, KOLs described a great heterogeneity of diagnostic test availability.



Access to diagnostics (including rapid diagnostics) in rural settings was said to be significantly more challenging than in urban areas.

This is due to sparse resources, high cost, and low demand.

Challenges of diagnostic test uptake

★ Challenges for diagnostic use

Q10: What are the primary challenges to more extensive use of diagnostics (including rapid diagnostics) to guide clinical treatment decisions and to inform antimicrobial stewardship programs?

1. Cost was the most commonly cited challenge.



- This includes the upfront cost to acquire equipment and the cost per test.



"Cost is the primary concern."

"The main challenge is cost and reimbursement."

2. KOLs discussed the lack of awareness of AMR and rapid diagnostic tests available.



"We need to be creating awareness and developing training modules to train absolutely anybody."

"Many clinicians do not want to change their old patterns and want to keep doing things as is."

3. It was noted that there is a lack of clinical and economic studies.



- Clinical and economic studies were important sources when incorporating new, rapid diagnostics (slide 31).

4. The over/ under sensitivity of rapid diagnostics leading to incorrect results.



"The current concern lies in [the diagnostics] accuracy and sensitivity, and how valuable they are to our clinical work."

5. Additional challenges varied by country.



- Cultural and process barriers.
- Potential for overuse.
- Lack of an automated electronic system for results.
- Availability of rapid diagnostics at smaller institutes.
- The need for a specialist to interpret results.
- Logistics and personal resources.
- Consultation by ID team.

Role of diagnostic testing in AMS

Diagnostics and treatment decision-making

Q8: What influences your empirical therapy choices and at what timepoint do you reassess empirical therapy for more narrow or broader coverage? Are there any barriers in place to question narrow-spectrum agents being used earlier in the treatment pathway? (2/2)

4. There is a reluctance by clinicians to de-escalate, particularly if the patient is improving.



Approximately 33% of patients are de-escalated. Up to 80% of patients treated by ID clinicians are de-escalated. This reduces to 10% for non-ID doctors.



"Never change the winning team."

"De-escalation is a difficult duty to promote: you don't change a team that wins."

5. AMR efforts are crucial for successful de-escalation efforts.



An AMR initiative involving weekly ward visits by ID clinicians with the goal of educating antimicrobial prescribers on how to use diagnostics and interpret their results was described as very successful.

ID consultations encourage clinicians to de-escalate and provide advice on how to do so.



"The most important role of antimicrobial stewardship is to give the correct antibiotics to the correct patient and avoid the use of antibiotics with a large spectrum of action."

Guidelines

★ National and international guidelines

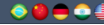
Q16: Are you aware of international and national guidelines for individual clinical practice areas and guidelines for antimicrobial stewardship programs (ASPs) that contain recommendations on diagnostic testing use, including rapid diagnostics? Please provide brief details of these guidelines.

1. KOLs perceived a lack of national guidelines.



"[There are] some suggestions but not real guidelines with strict recommendations."

2. Certain international guidelines were frequently mentioned.



- Infectious Disease Society of America.
- Surviving Sepsis.
- World Health Organization.

3. Technology is being used in the distribution of guidelines.



- One KOL spoke about an app which contained the up-to-date hospital guidelines.

4. Clinicians from MICs described adaptations to international guidelines.



- Clinicians consult international guidelines and make adaptations.
- National guidelines refer to international guidelines and make adaptations.

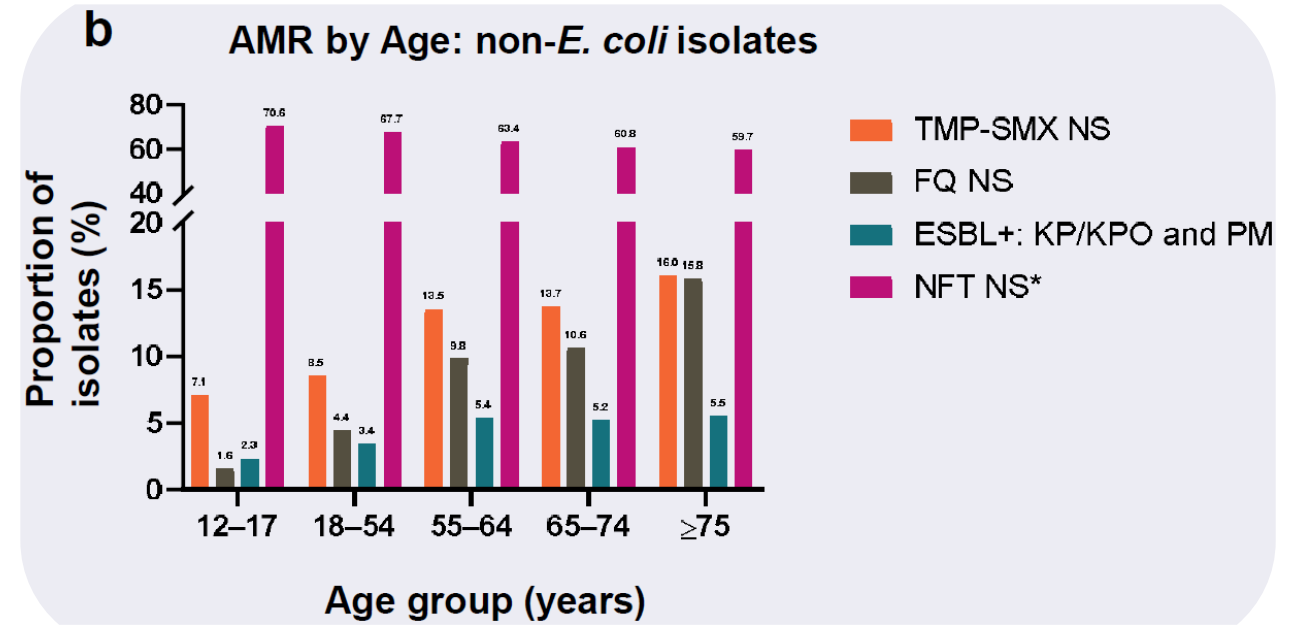
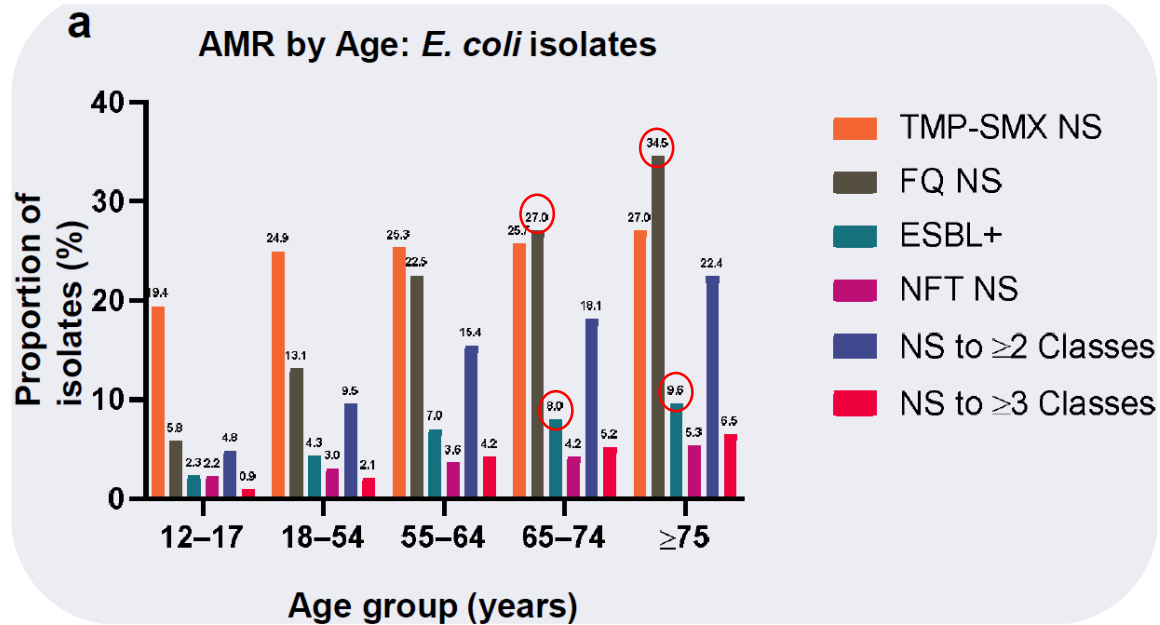
Country	National	International	Independent ¹
Brazil	✓/x ²	✓	✓
China	✓	✓	✓
India	x	✓	-
Italy	✓/x ²	✓	-
Germany	✓	✓	-
US	-	-	✓

✓ yes; x no; - not specified.

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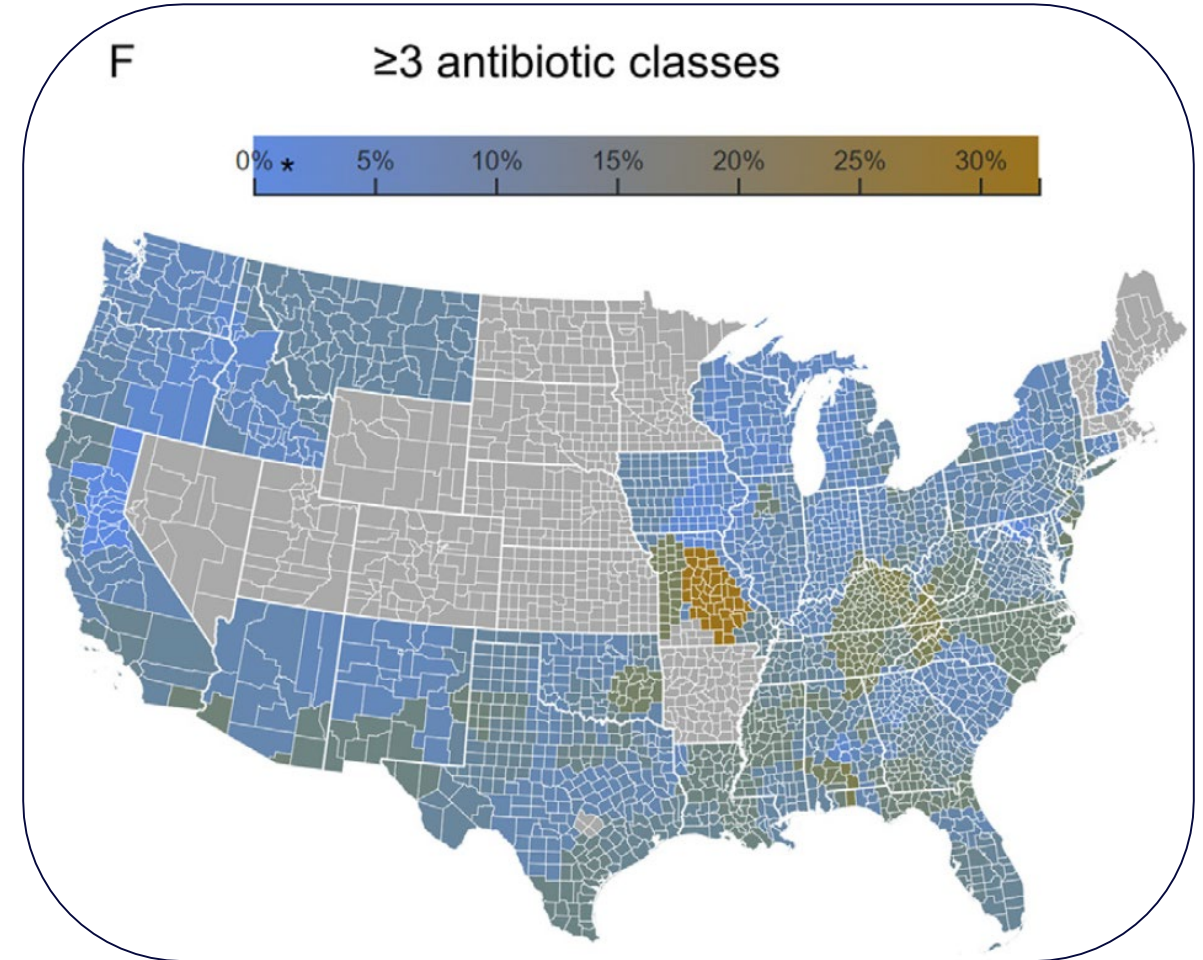
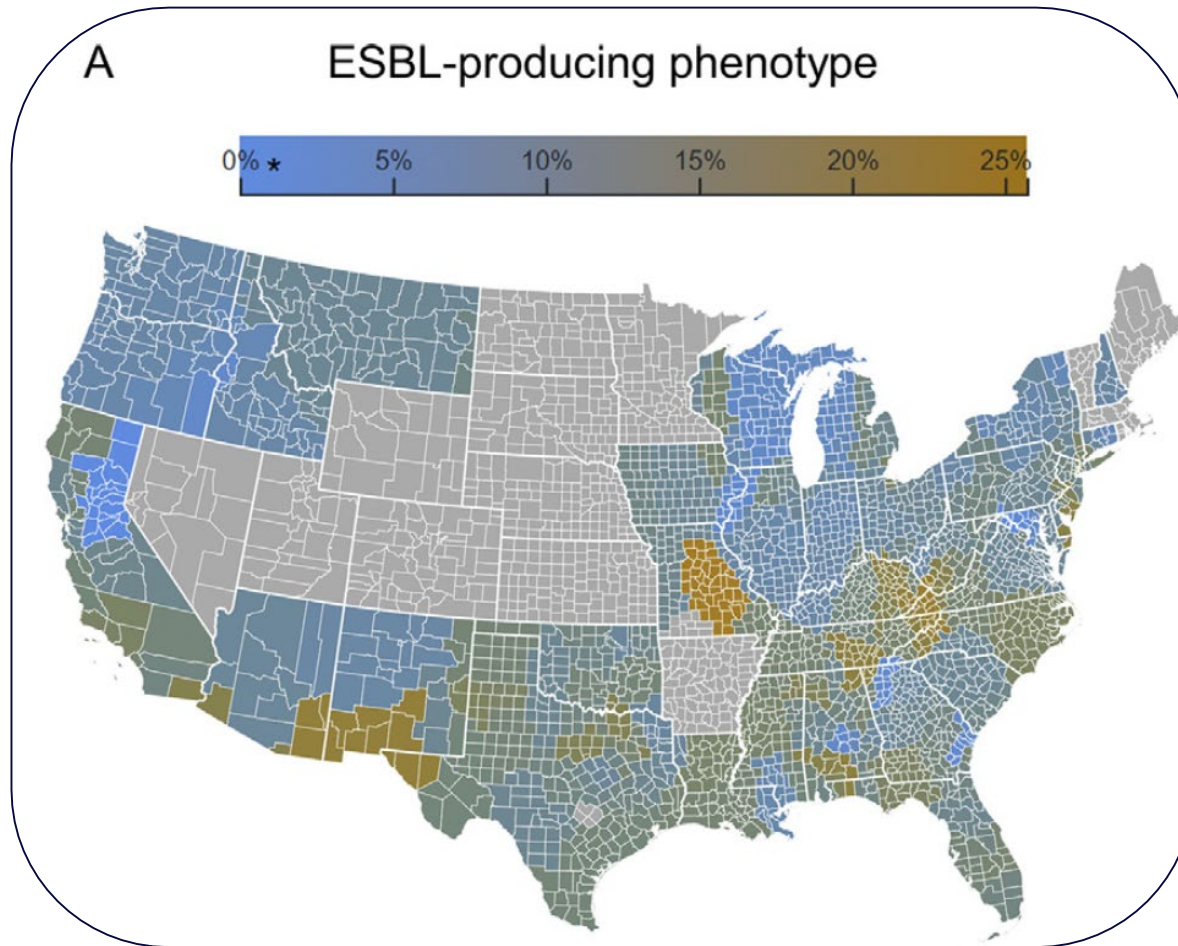
Prevalence of AMR Among Enterobacteriales Outpatient Isolates From US Females Increases With Age



KP/KPO, *K. pneumoniae/oxytoca*; PM, *P. mirabilis*; Non-*E. coli* Enterobacteriales isolates included *K. pneumoniae*, *K. oxytoca*, *E. cloacae*, *E. aerogenes*, *P. mirabilis*, *M. morganii*, *C. freundii*, and *S. marcescens*

Kaye KS, Gupta V, Mulgirigama A, et al. 1699. Open Forum Infectious Diseases, Volume 7, Issue Supplement_1, October 2020, Page S832. <https://doi.org/10.1093/ofid/ofaa439.1877>

Geographic Distribution of Urine Enterobacteriales Resistance in Ambulatory Settings



Aronin SI, Gupta V, Dunne MW, et al. *Int J Infect Dis.* 2022;119:142-145. doi:10.1016/j.ijid.2022.03.052

Health equity is at the core and forefront of our CDC AR prevention efforts.

Some links between disparities/inequities and AR or antibiotic use

- Community-associated ESBL-Enterobacterales – Higher incidence rates in areas with lower median incomes, lower high school education rates, higher percentages of persons without health insurance, and those with limited English proficiency.
- Community-associated *C. difficile* infections – Higher incidence rates in communities with low-incomes, foreign-born populations, non-English speaking households, and crowding in the home.
- Candidemia and MRSA – Higher rates in Black individuals, possibly reflecting differences in medical conditions, healthcare access, socioeconomic status, and access to housing.
- Antibiotic prescribing and/or inappropriate prescriptions – Higher volumes/rates in rural areas, non-Hispanic White individuals, pediatric populations, and older persons with viral respiratory diseases.
- Antibiotic prescribing or diagnosis with bacterial pathogen – Lower volumes in Black individuals.

Slide from Dawn Siewert, Antimicrobial Resistance Coordination and Strategy Unit, National Center for Emerging and Zoonotic Infectious Diseases, U.S. Centers for Disease Control and Prevention; presented at World AMR Congress September 2022

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Measuring antibiotic use (AU) at a hospital level as a AS metric

- Abx use en mass during cold/flu season is correlated with more Hospital Onset resistant infections for specific abx during same time <https://doi.org/10.1093/ofid/ofac039>
- Abx use increases during cold/flu season (ie viral season) and presents opportunities for ASPs
 - <https://www.cambridge.org/core/journals/antimicrobial-stewardship-and-healthcare-epidemiology/article/multicenter-analysis-of-inpatient-antibiotic-use-during-the-20152019-influenza-seasons-in-the-united-states-untapped-opportunities-for-antimicrobial-stewardship/8A27534142B1570684D1B9D5CE3ABD44>
- Better risk adjustment for observed over expected abx use can be achieved via electronic health record data and may help inform ASPs on more appropriate antimicrobial use
 - <https://doi.org/10.1093/cid/ciy354>
 - <https://doi.org/10.1093/cid/ciy359>
- An increase in 100 DOT of high-risk CDI abx correlates with 12% increase of hospital associated C. diff
 - <https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/abs/hospitallevel-highrisk-antibiotic-use-in-relation-to-hospitalassociated-clostridioides-difficile-infections-retrospective-analysis-of-20162017-data-from-us-hospitals/7447205676EF00E16E8EE02136F47C28>

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Adding voices to improve Diagnostic and Antibiotic Stewardship

Current/new
rapid sepsis dx



ENDSEPSIS
The Legacy of Rory Staunton



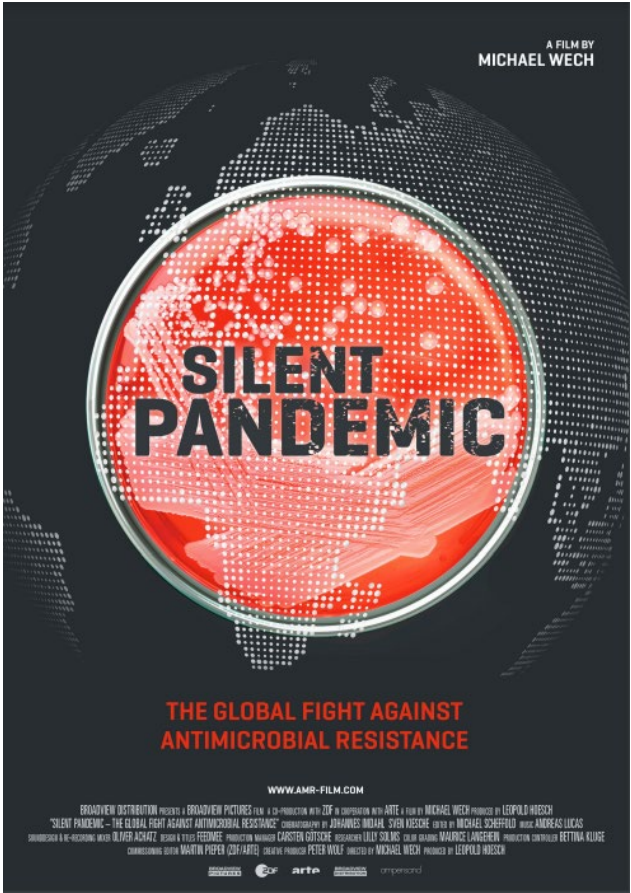
Current/new
testing for rapid dx

Cancer & AMR Consortium
Demonstrating the link between AMR and Cancer
to accelerate advocacy, policy, and innovation



OTC testing for
Flu/RSV/COVID

Educating outside of the
AMR bubble



[Video](#)

In conclusion,

- We need to act now to improve infection prevention and stewardship by using the **tools available today** and build momentum for new innovations and solutions for the long term.
- **Improved utilization of diagnostics is a critical** to improved antibiotic utilization. However, lab strengthening is needed, globally, with needs and challenges spanning from implementation to innovation.

Policies should:

Ensure access to accurate diagnosis and treatment of patients

- Promote value based, automated diagnostic technology** to minimize human error and enhance lab workflow through integrated solutions and to decrease inappropriate prescription
- Implement diagnostic test protocols** to identify and confirm the type of infection, enabling physicians to tailor treatment and potentially decrease reliance on broad-spectrum antibiotics. Rapid antimicrobial susceptibility tests (AST) should be available to enable appropriate use.
- Promote development of Sepsis detection programs** based on international best practices to reduce time to actionable result for better patient safety
- Incentivize innovation in diagnostics** to improve speed and accuracy and move testing & promote innovation and use of Point of Care tests to enable faster response