North Carolina SPICE
Statewide Program for Infection Control & Epidemiology

North Carolina Clinical Antibiotic Stewardship Partners

STEWARDSHIP COLLABORATION WITH THE CLINICAL MICROBIOLOGY LAB

January 10, 2024

NC CLASP Hospital Stewardship
Year 2

INTRODUCTIONS

Please put your name, hospital, and location in the chat!

CONFLICT OF INTEREST DISCLOSURES

- The views and opinions expressed in this series are those of the speakers and do not reflect the official policy or position of any agency of the US or NC government or UNC.
- Our speakers have the following financial relationships with the manufacturer(s) and/or provider(s) of commercial services discussed in this activity:
  - Dr. Willis has performed contracted research with: Pfizer (pediatric nirmatrelvir-ritonavir and maternal RSV vaccine), Novavax (pediatric COVID-19 vaccine), and Merck (monoclonal antibody for RSV prevention)
- The speakers do not intend to discuss an unapproved/investigative use of a commercial product/device in this series, and all COI have been mitigated.
- These slides contain materials from a variety of colleagues, as well as the CDC, WHO, AHRQ, etc.

CME AND CE CREDIT

- CME & CE for participants
  - Attendance and active participation per learning session
  - Click the link in the chat during the session to document your attendance
  - Complete surveys as requested

NC CLASP: YEAR TWO

6 hour-long learning sessions

September 2023-May/July 2024

CE included: CME, RN, Pharmacist (ACPE)

Two in-person conferences

- **<u>Upcoming discussion topics include:</u>**
- Diagnostic stewardship/collaborating with the Clinical Microbiology lab
- Impacting empiric therapy decisions
- Handling antibiotic allergies
- Stewardship in skin/skin structure infections
- Stewardship in transitions of care to and from the Emergency Department
- May: in-person conference

Is there another topic you'd like to discuss in these sessions?

CLIN MICRO/DIAGNOSTIC STEWARDSHIP AND THE ANTIBIOTIC USE PROCESS

VITAL IMPORTANCE OF ANTIBIOTIC STEWARDSHIP – CLINICAL MICRO LAB COLLABORATION

- *"A hallmark of antimicrobial stewardship is helping clinicians obtain an accurate diagnosis"*[1]
- *Microbiologists can contribute to AS at several points in the antibiotic use process*[2]

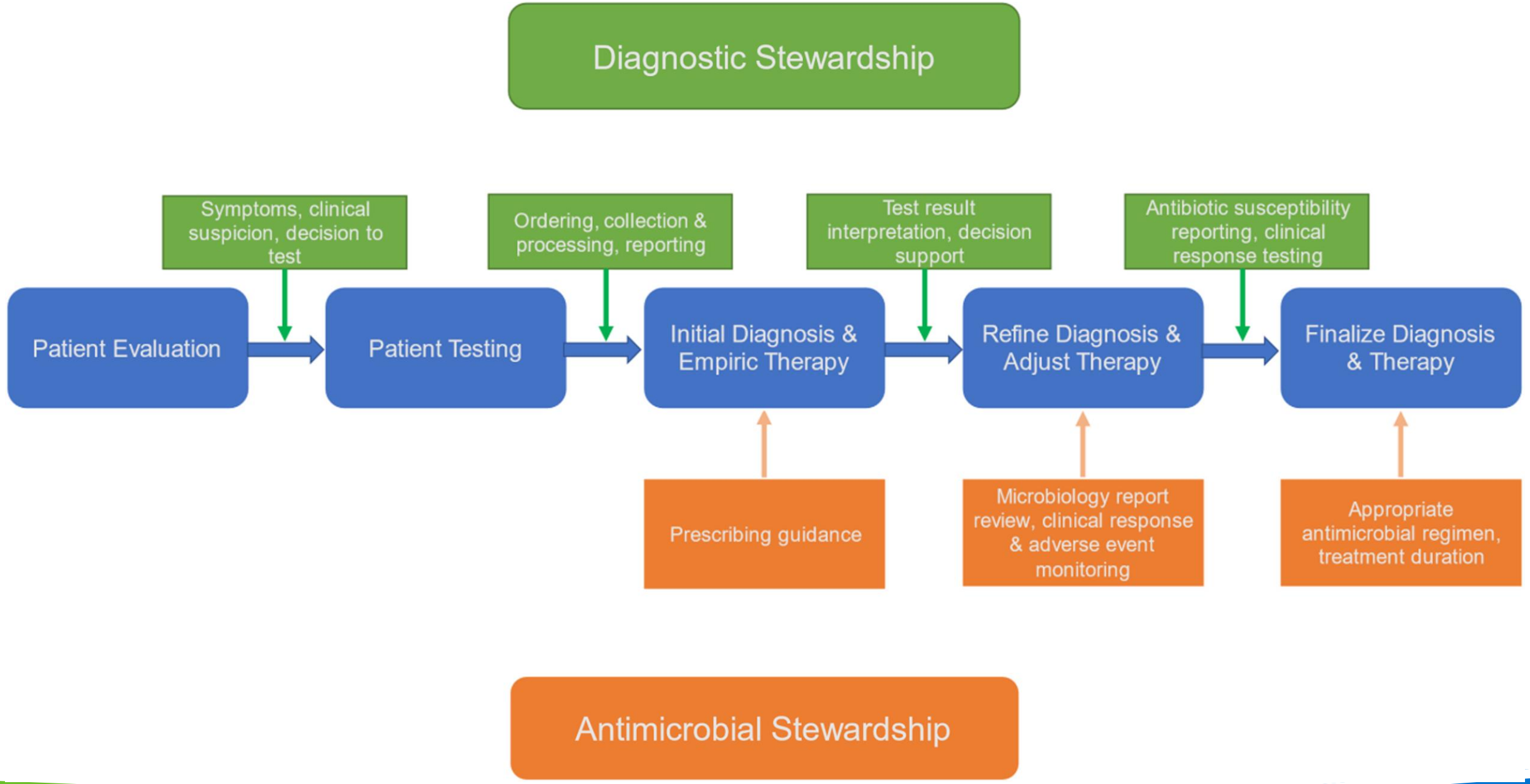
- Lots of variability here… we really need to share experiences UNMUTE and speak up!

- *Diagnostic stewardship emerged from the desire to improve clinical care, with fewer false-positive test results and less overdiagnosis while identifying true-positive cases.*[3]

1. IDSA Antimicrobial Stewardship Core Curriculum
2. CDC Core Elements 2019
3. Clinical Microbiology Reviews 2017; 30: 381-407

BREAK OUT DISCUSSION

- Describe your relationship with the Clinical Micro Lab. Does a microbiologist participate on the Antibiotic Stewardship team?
- Briefly describe one point of collaboration your hospital has made with the Clinical Micro Lab to improve antibiotic use.
- What barriers to collaboration with Microbiology have you experienced?



Ku, et al. Infection Control & Hospital Epidemiology (2023)

STEPS IN DIAGNOSTIC TESTING

Pre-analytic

Ordering

Test only if clinical presentation is consistent with the infectious etiology (high pretest probability)

Test only when symptoms suggest urinary tract infection or, if asymptomatic, concordant with guidelines (eg, urologic surgery, pregnancy)

Pre-analytic

Sample Collection

Pay attention to sample collection and transport, to optimize yield and reduce contamination

Use aseptic technique—midstream clean catch after periurethral cleansing
Obtain catheter sample from collection port (not bag), prefer newly inserted catheter

Analytic

Processing

Recs/procedures to distinguish colonization from infection, Cascaded or reflexive testing

No reflex processing, process only if pyuria present (normal host)

Post-analytic

Reporting

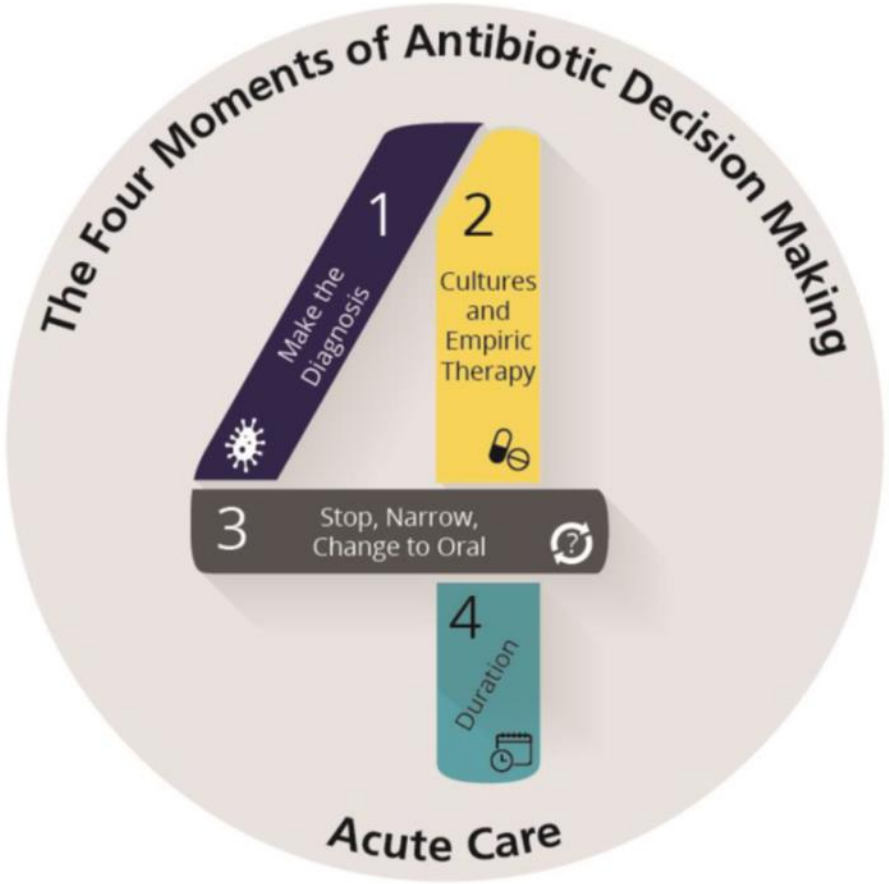
Report results in a format that guides appropriate practice.

Text interpreting result, eg, "multiple organisms indicating likely contamination;" "no pyuria, culture not performed." Selective reporting of antibiotic susceptibilities—display preferred antibiotics only.

Urine examples

THE INFECTION TREATMENT PROCESS

Moment 1: Decision support/ nudges to help guide optimal diagnostics



Moment 2: Appropriate sample collection, sample rejection protocols

Moment 4: Report susceptibility on oral options, etc for next level of care

Moment 3: Guidance embedded in how results are reported. Cascaded susceptibility reporting

AHRQ Pub No 17 (20)-0028-EF, Nov 2019

Infection Control & Hospital Epidemiology (2023), 44, 1901–1908

4 MOMENTS EXAMPLE: SEPSIS

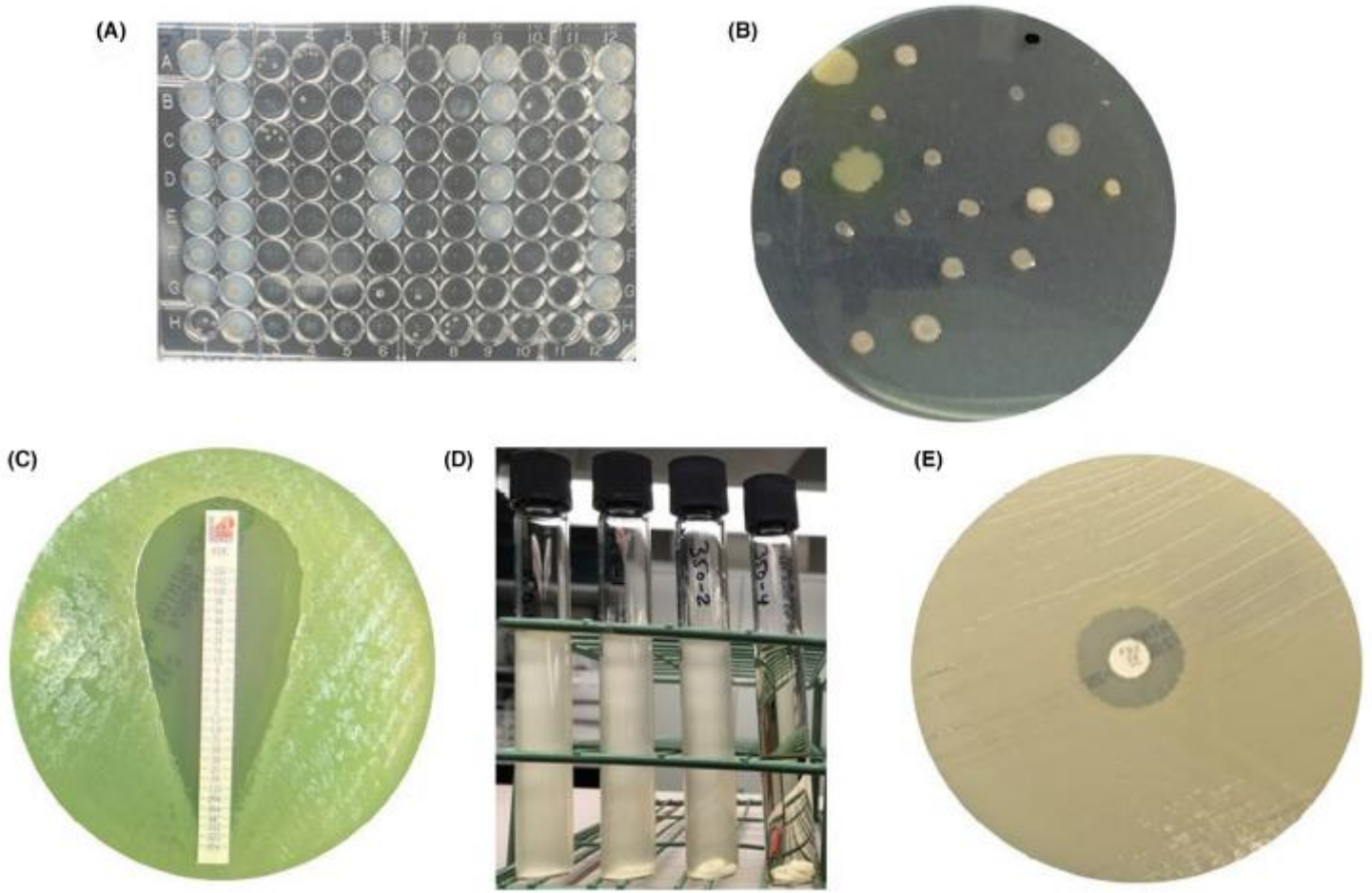
Moment	Diagnostic Stewardship Role
1. Make the diagnosis	Ensure sepsis protocol calls for two large-volume blood cultures *before* antibiotics are given
2. Cultures and Empiric Therapy	-Ensure that appropriate blood culture volumes are being obtained. -Blood drawn by phlebotomists have lower contamination rates
3. Stop, Narrow, Change to Oral	-Design protocols for targeting therapy in response to rapid results. If the rapid identification finds MSSA, providers can stop vancomycin and cefepime and start cefazolin. -Cascade susceptibility reports. If *E. coli* is susceptible to ceftriaxone, the lab can withhold reporting of carbapenems and advanced cephalosporins.
4. Duration	-Managed by traditional antibiotic stewardship

CONVENTIONAL SUSCEPTIBILITY METHODS

A. Broth micro dilution
B. Antibiotic impregnated agar
C. Antibiotic-impregnated gradient strip
D. Broth disk elution
E. Disk diffusion

All require ***bacterial growth*** in broth or on agar.

Time to result: 36-48 hrs



BACTERIAL PATHOGEN PROCESSING METHODS

PHENOTYPIC METHODS

Require bacterial growth for result: 36-48hrs

* Can provide both pathogen identification and susceptibility

- Broth microdilution*
- Disk Diffusion
- Gradient strip
- Chromogenic media*
- Automated dilution* devices (18-24hr)

MOLECULAR METHODS

Require pure sample
Result in 4-6 hrs
Identifies pathogen and some resistance by gene sequences

- QPCR
- Multiplex PCR

MASS SPECTROMETRY

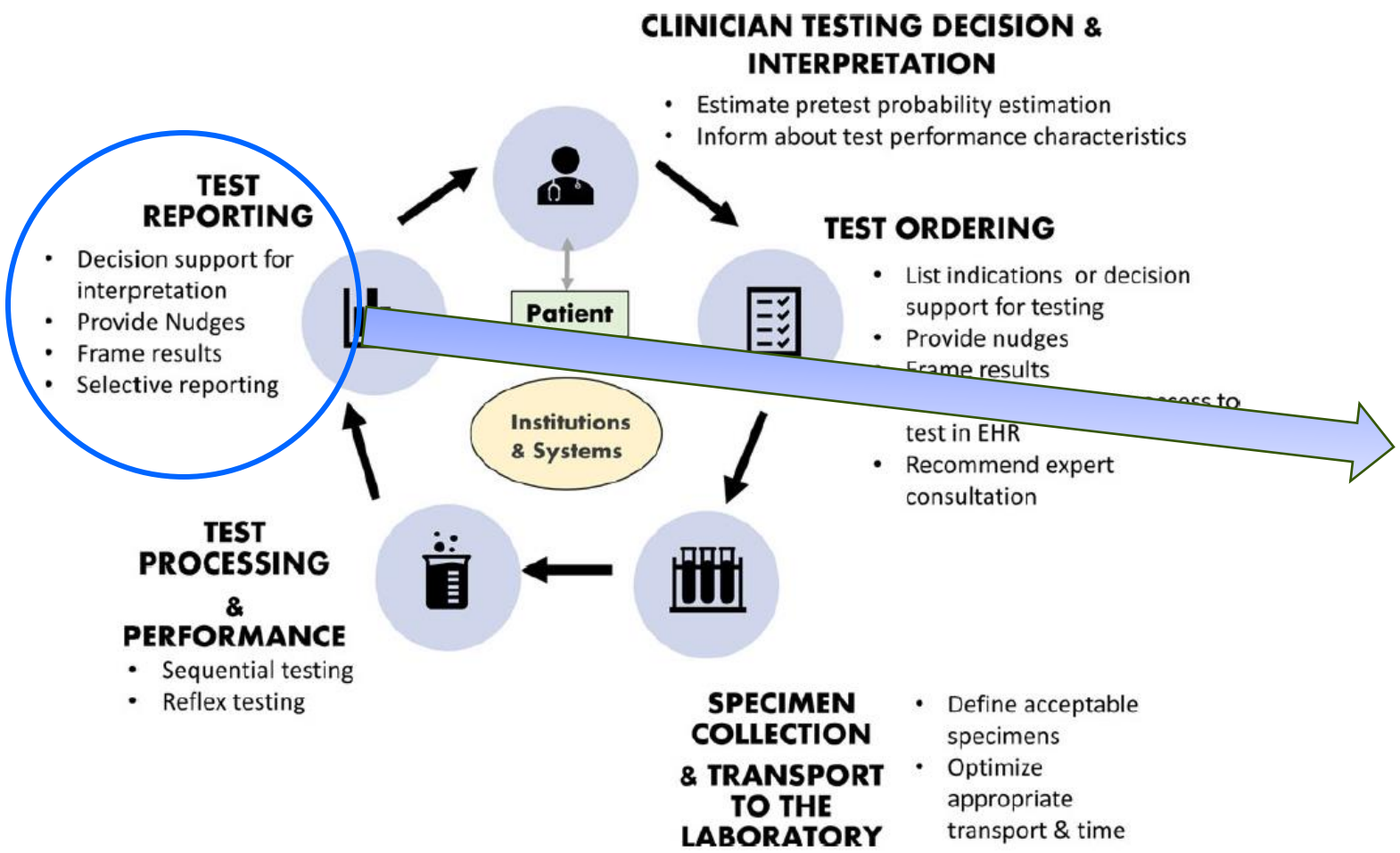
Primary application is pathogen identification
Very accurate
Result in several hours

- MALDI-TOF MS

(matrix-assisted laser desorption/ionization time-of-flight mass spectrometry)

Gagic, et al. Antibiotics 2022;11:427
Pharmacotherapy 2023;43:264

Complex cycle: Opportunity for AS involvement



As diagnostic results return, the number of "decision points" increases.

This can be confusing OR can serve as an opportunity for antimicrobial stewardship involvement.

CHALLENGES AT THE DIAGNOSTIC/ANTIMICROBIAL STEWARDSHIP INTERFACE

- Cost/benefit of rapid diagnostics
- Implementing communication channels for rapid result reporting
  - Multiple studies demonstrate the value of channeling results through stewardship personnel
- Helping clinicians distinguish colonization from infection, contamination from pathogenicity
- Incorporating trends in molecular susceptibility results into local antibiogram
- Incorporating local susceptibility trends into treatment guidelines
- Changing MICs and the lag time to uptake/approval in automated systems

DIAGNOSTIC STEWARDSHIP: DANGERS AND CAVEATS

- To prevent disruptions, first conduct a careful analysis to identify any system processes that could be affected by a change in procedure or reporting
- Highly sensitive molecular diagnostics can detect minute amounts of microbial target may identify colonized rather than clinically infected patients[3]
- Diagnostic Stewardship can be viewed as a threat to clinician autonomy
  - Be careful not to apply rigidly so as to impede patient-specific, nuanced care
  - Maintain open, transparent discussion
  - Transparent guidance wins over rigid algorithms or guidelines

1. Ku, et al. Infect Control Hosp Epidemiol 2023
2. Morgan, et al. JAMA 2017;318:607
3. Madden GR, et al. Infect Control Hosp Epidemiol 2018;39:214–218.

- Questions?
- Comments?
- Discussion?

THE CUMULATIVE ANTIMICROBIAL SUSCEPTIBILITY REPORT OR "ANTIBIOGRAM"

Memorial Medical Center
1 January - 31 December 2020 Antibiogram[a]
Percent Susceptible

Organism	Number of Strains	Amikacin	Ampicillin	Cefazolin (systemic[b])	Cefazolin (urine[c])	Cefepime	Ceftriaxone	Ceftazidime	Ciprofloxacin	Ertapenem	Gentamicin	Meropenem	Piperacillin-tazobactam	Trimethoprim-sulfamethoxazole	Tobramycin
Acinetobacter baumannii	32	60	R	R	R	33	34	42	41	R	57	60	46	48	59
Citrobacter freundii	49	100	R	R	R	81	72	67	90	98	96	99	83	67	97
Enterobacter cloacae	76	99	R	R	R	78	61	62	92	89	90	99	77	84	90
Escherichia coli	1433	99	35	68	87	92	93	90	72	99	91	99	94	73	92
Klebsiella (formerly *Enterobacter*) *aerogenes*	31	100	R	R	R	81	68	60	92	99	91	99	74	95	91
Klebsiella pneumoniae	543	99	R	72	89	93	91	87	84	99	94	95	86	81	94
Morganella morganii	44	100	R	R	R	94	85	81	89	98	100	99	96	75	100
Proteus mirabilis	88	100	87	80	92	99	99	92	79	100	90	100	70	73	93
Pseudomonas aeruginosa	397	97	R	R	R	88	R	86	75	R	80	80	85	R	83
Salmonella spp.	32	-	88	-	-	98	97	97	90	100	-	100	91	86	-
Serratia marcescens	50	100	R	R	R	95	87	80	95	99	94	99	94	91	89
Shigella spp.	33	-	64	-	-	98	98	96	90	100	-	100	91	69	-
Stenotrophomonas maltophilia	72	R	R	R	R	-	R	63	6	R	R	R	-	98	R

Abbreviation: R, intrinsic resistance.
Symbol: -, drug not tested or drug not indicated.
[a] The percent susceptible for each organism/antimicrobial agent combination was generated by including the first isolate of that organism encountered in a given patient.
[b] Cefazolin (systemic) refers to application of susceptibility breakpoint minimal inhibitory concentration (MIC) ≤ 2 µg/mL and applies to the treatment of patients with infections other than uncomplicated urinary tract infections (UTIs).
[c] Cefazolin (urine) refers to application of urinary susceptibility breakpoint MIC ≤ 16 µg/mL (using a cefazolin dosage regimen of 1 g intravenously [IV] every 12 hours) and can be used to predict susceptibility for oral cefaclor, cefdinir, cefpodoxime, cefprozil, cefuroxime, cephalexin, and loracarbef when used for therapy of uncomplicated UTIs due to *E. coli*, *K. pneumoniae*, and *P. mirabilis*. Cefazolin as a surrogate may overcall resistance to cefdinir, cefpodoxime, and cefuroxime. If cefazolin tests resistant, these drugs should be tested individually if needed for therapy.

J Clin Micro 2022;60:1

KEY COMPONENTS OF ANTIBIOGRAMS

- Prepare regularly – at least annually
- Remove duplicates
- Report only species with >30 isolates per time period
- Include only routinely tested antibiotics, but DO include those selectively reported
- Report % susceptible, NOT % intermediate or % susceptible dose-dependent

Simner, et al. J Clin Micro 2022:60:1
CLSI document M-39, 5th edition, 2022

ANTIBIOGRAM PREPARATION, DISSEMINATION

Data sources

- Automated or semiautomated AST instrument
- Laboratory information system (LIS)
- Hospital electronic health record (EHR)
- Third-party clinical decision support system (CDSS)
- If your hospital participates in NHSN AR module, NHSN can prepare an antibiogram for you
  - Does anyone have experience with this?

- **An important space for AS/Clin Micro collaboration**
- AS team can facilitate trend-interpretation and dissemination of antibiogram data
- Make it easy to find
- Use to inform empiric treatment decision and local treatment guidelines

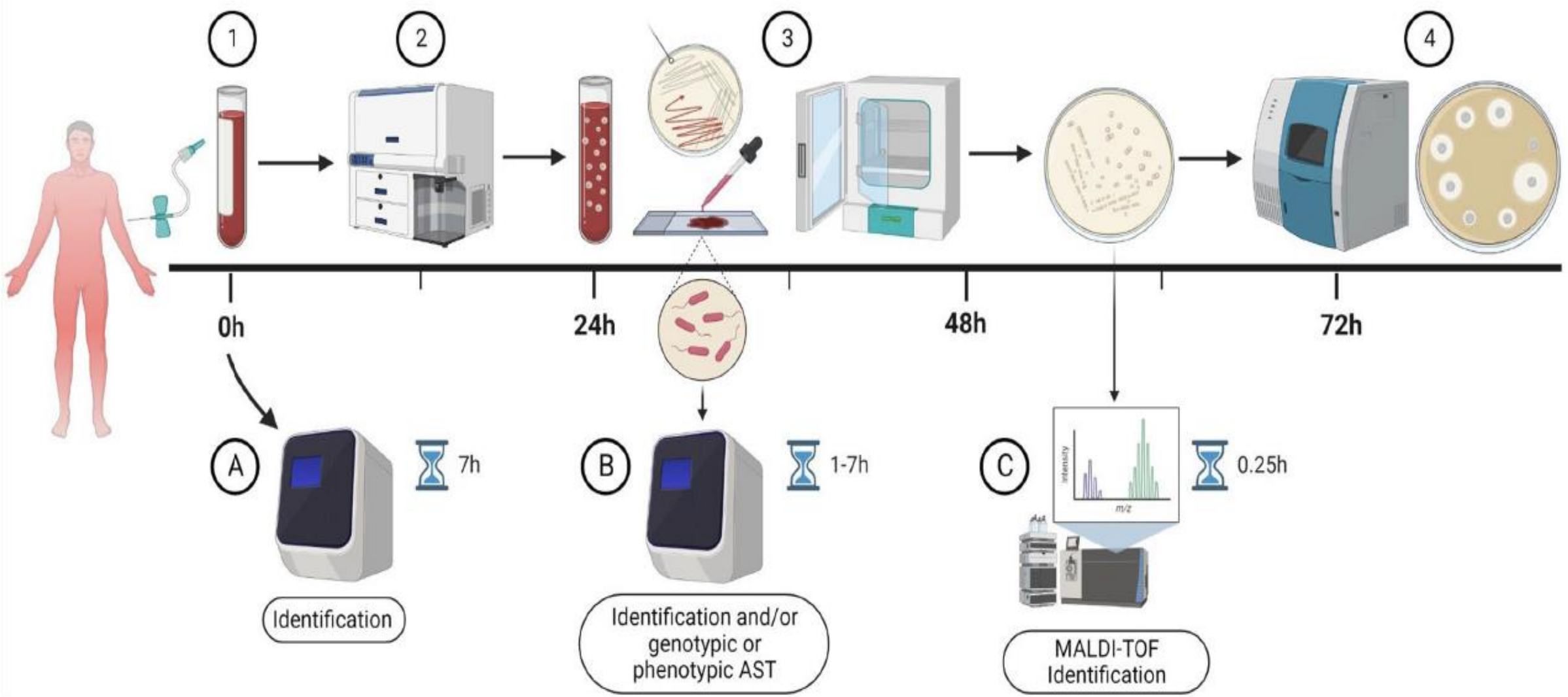
- Questions?
- Comments?
- Discussion?

PRACTICAL STEPS TO FACILITATE INVOLVEMENT WITH CLIN MICRO

BECOME A CLINICAL MICROBIOLOGY LEARNER

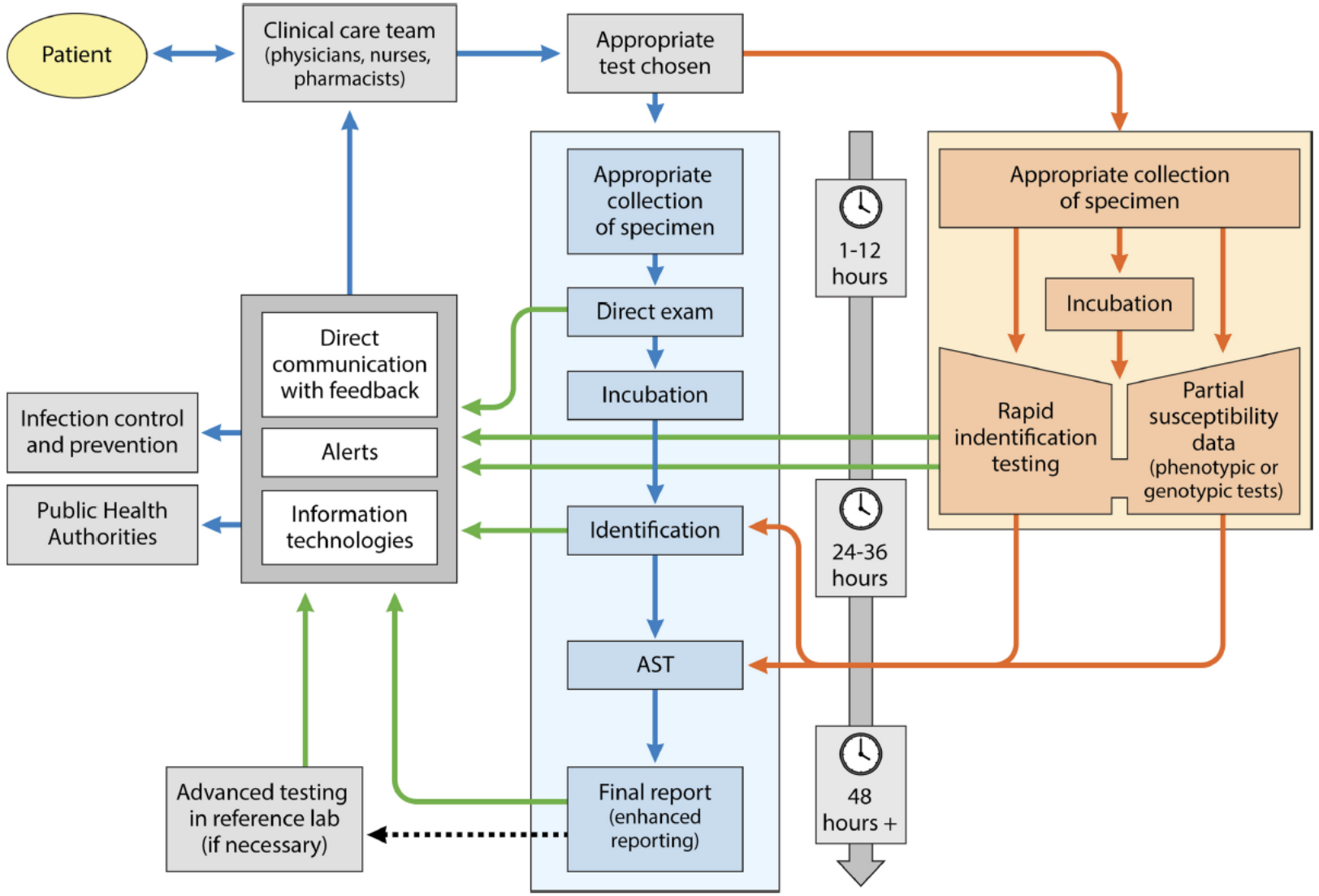
- Learn the types of procedures they perform
  - Pathogen identification
  - Pathogen susceptibility
- Plan onsite visit(s) if possible
  - Study processes
  - Build relationships
- Map out their processes

Blood Culture Process



Wenzler, et al, Pharmacotherapy 2023;43:264.

BUILD MAPS THAT INCLUDE COMMUNICATION & INPUT BY THE STEWARDSHIP TEAM



IDENTIFY AND DISCUSS COMMON GOALS

Diagnostic Stewardship Goals[1]
Improve patient care and outcomes
Avoid patient harm
Optimize antimicrobial use
Improve efficiency of care
Improve institutional costs and metrics

- Most successful microlab - AS "interventions" promote more fluid communication with clinicians[2]

- Participation in AS can keep clinical microbiologists closer to patient care and make better use of their expertise
- Get their opinion on tests that may be misused
- Help with appropriate implementation of new diagnostics

1. Fabre, et al. Infect Control Hosp Epidemiol. 2023
2. Morency-Potvin, et al. Clin Micro Rev 2017, JAMA 2017;318:607

SOME IMPORTANT CLSI GUIDANCE DOCUMENTS

Number / availability	Title	Content
M-100 FREE	Performance Standards for Antimicrobial Susceptibility Testing Updated 1-2 x per year	What antimicrobials to test for common bacteria Breakpoints by pathogen or group (Upper limits of susceptibility, lower limits of resistance) Testing methodologies Resistance tests Don't miss Appendix B: the "Intrinsic Resistance" chart
CLSI M-27 M44S-ED3:2022 FREE	Performance Standards for Antifungal Susceptibility Testing of Yeasts, 3rd Edition	Similar to M-100
M-39 paid*	Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data, 5th Edition 2022	Guidance document on antibiogram preparation and use. Extensive 2022 update includes recommendations on extracting data from various sources, combining results from rapid diagnostics and resistance markers with the antibiogram, and more.

- Questions?
- Comments?
- Discussion?

- See supplementary info in slides posted online.

THE NORTH CAROLINA CLINICAL ANTIBIOTIC STEWARDSHIP PARTNERS (NC CLASP)

- All the information from today's session will be on our website https://spice.unc.edu/ncclasp/

RESOURCES

- Morency-Potvin P, Schwartz DN, Weinstein RA. Antimicrobial Stewardship: How the Microbiology Laboratory Can Right the Ship. Clinical Microbiology Reviews 2017; 30: 381-407. https://doi.org/10.1128/CMR.00066-16.
- Fabre V, Davis A, Diekema DJ, Granwehr B, Hayden MK, Lowe CF, Pfeiffer CD, Sick-Samuels AC, Sullivan KV, Van Schooneveld TC, Morgan DJ. Principles of diagnostic stewardship: A practical guide from the Society for Healthcare Epidemiology of America Diagnostic Stewardship Task Force. Infect Control Hosp Epidemiol. 2023 Feb;44(2):178 -185. doi: 10.1017/ice.2023.5. PMID: 36786646.
- Ku TSN, Al Mohajer M, Newton JA, Wilson MH, Monsees E, Hayden MK, Messacar K, Kisgen JJ, Diekema DJ, Morgan DJ, Sifri CD, Vaughn VM. Improving antimicrobial use through better diagnosis: The relationship between diagnostic stewardship and antimicrobial stewardship. Infect Control Hosp Epidemiol. 2023 Sep 4:1-8. doi: 10.1017/ice.2023.156. Epub ahead of print. PMID: 37665212
- Wenzler, et al. Antimicrobial susceptibility testing: An updated primer for clinicians in the era of antimicrobial resistance: Insights from the Society of Infectious Diseases Pharmacists. *Pharmacotherapy.* 2023;43:264–278. DOI: 10.1002/phar.2781
- Morgan DJ, Malani P, Diekema DJ. D*iagnostic Stewardship—Leveraging the Laboratory to Improve Antimicrobial Use*. JAMA. 2017;318(7):607-8.
- https://www.cdc.gov/antibiotic-use/pdfs/Selective-Reporting-508.pdf
- CLSI free documents: Free Resources From CLSI

IF NOT FAMILIAR, LEARN PRINCIPLES OF DIAGNOSTIC TESTING

An awareness and understanding of pretest probability of infection is essential for designing diagnostic stewardship interventions that improve the usefulness of tests.

Many diagnostic stewardship interventions function by increasing test use in high-value settings with higher probability of disease (eg, blood cultures for patients with meningitis). They also discourage or block testing in low value settings where there is a low probability of disease and greater potential for false-positives results, which may result in patient harm (eg, blood cultures for cystitis).

- Prevalence: the proportion of a population that has a specific disease in a given time period. Contrast with incidence.
- Sensitivity: the ability of a test to correctly identify those with the disease.
- Specificity: the ability of a test to correctly identify those without the disease.
- Positive predictive value: the probability that a person with a positive test truly has the disease; influenced by prevalence.
- Negative predictive value: the probability that a person with a negative test truly does not have the disease; influenced by prevalence.
- Posttest probability: estimated probability of a person having the disease after a diagnostic result is known.
- Pretest probability: estimated probability of a person having the disease before a diagnostic is performed.

Tutorial with “playground” to help learn these.
www.testingwisely.com

Fabre, et al. Infect Control Hosp Epidemiol. 2023 Feb;44(2):178 -185
Curren et al. Clinical Infectious Diseases 2022;74:723–8