CLINICAL AND LABORATORY STANDARDS INSTITUTE®

5th Edition

M39

Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data

This guideline describes methods for recording and analyzing antimicrobial susceptibility test data, consisting of cumulative and ongoing summaries of susceptibility patterns of clinically significant microorganisms.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data

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Abstract

Susceptibility statistical data, consisting of the cumulative and ongoing summary of the antimicrobial susceptibility patterns of clinically important microorganisms, are important to the practice of medicine on several levels. If the methods used to create, record, and analyze the data are not reliable and consistent, many of the most important applications and benefits of the data will not be realized. Clinical and Laboratory Standards Institute document M39—*Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data* provides guidelines for medical laboratories and data analysis software providers for the routine generation and storage of susceptibility data and for the compilation of susceptibility statistics. This guideline also provides suggestions for medical laboratories, clinicians, and others involved in antimicrobial stewardship on effective use of their cumulative susceptibility statistics when empirical antimicrobial therapy is selected.

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Suggested Citation

Contents

Contents (Continued)

Contents (Continued)

Contents (Continued)

Foreword

Cumulative results from antimicrobial susceptibility tests performed on individual patients' microbial isolates can be useful when compiled and reported at regular intervals. For a cumulative report (eg, antibiogram) to be compared with reports from previous years or from other facilities, data need to be analyzed and presented in a clear and consistent manner.

The primary aim of M39 is to guide the preparation and use of antibiograms by clinicians for selecting the most appropriate antimicrobial agents for empirical therapy for initial infections when definitive antimicrobial susceptibility test results are not available. Various types of cumulative antimicrobial susceptibility test data reports are used to support antimicrobial stewardship and infection prevention efforts. In addition, cumulative antimicrobial susceptibility test data may be of value to researchers when antimicrobial resistance is assessed.

Since the last edition of this guideline, there have been many changes in public health and medical microbiology laboratories with the introduction of rapid diagnostic tools (eg, multiplex molecular panels) and advanced informatics. Furthermore, there has been an increased emphasis on antimicrobial stewardship and public health initiatives to help contend with the global health threat of antimicrobial resistant microorganisms. Therefore, many of the changes in this guideline reflect how the antibiogram and other types of cumulative antimicrobial susceptibility test data reports can support these needs.

Overview of Changes

This guideline replaces the previous edition of the approved guideline, M39-A4, published in 2014. Several changes were made in this edition, including:

- Adding definitions for "cumulative antimicrobial susceptibility test data report" and "antibiogram"
- Adding considerations for extracting data from different sources (eg, automated antimicrobial susceptibility testing instrument, LIS, electronic health record) for antibiogram preparation
- Combining results from rapid diagnostics and antimicrobial resistance marker testing with the antibiogram for empirical therapy selection
- Developing antibiograms for yeast and antifungal agents
- Developing antibiograms for multiple facilities, long-term care facilities, and veterinary practices
- Describing ways in which antimicrobial stewardship programs may use antibiogram data
- Adding considerations for preparing cumulative antimicrobial susceptibility test data for peer-reviewed publication
- Using statistical analysis techniques including the calculation of percentiles, interquartile ranges, minimal inhibitory concentration (MIC) required to inhibit the growth of 50% of the organisms (MIC_{50}), and MIC required to inhibit the growth of 90% of the organisms (MIC_{90})
- Adding general comment explaining the use of the "^" with intermediate breakpoints for applicable antimicrobial agents known to have the ability to concentrate in the urine
- Deleting recommendation to list percent intermediate in addition to percent susceptible for penicillin with viridans group streptococci

Part I. Introduction and Data Acquisition

Chapter ①

Introduction

Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data

Part I. Introduction and Data Acquisition

❶ Introduction

1.1   Scope

This guideline provides individuals involved with assessment of cumulative antimicrobial susceptibility test data with recommendations for the storage, analysis, and presentation of the data. The antimicrobial susceptibility test data from individual patient's isolates available for analysis are assumed to be final, accurate and in a usable format for health care providers. Recommendations cover the preparation of reports (eg, routine and enhanced antibiograms) to guide selection of empirical antimicrobial therapy. Reference to preparation of reports for other purposes is briefly discussed. This guideline is intended for use by individuals involved with:

- Analyzing and presenting cumulative antimicrobial susceptibility test data generated from testing microbial isolates from both humans and animals from single or multiple facilities (eg, clinical microbiologists, pharmacists, physicians, veterinarians, epidemiologists, infection prevention practitioners)

- Using antibiograms and other types of cumulative antimicrobial susceptibility test data to make clinical decisions, participate in antimicrobial stewardship programs, and/or participate in public health initiatives (eg, clinical microbiologists, infectious diseases specialists and other clinicians, infection prevention practitioners, pharmacists, epidemiologists, other health care personnel, and public health officials)

- Designing information systems for the storage and analysis of antimicrobial susceptibility test data (eg, LIS vendors, electronic health record [EHR] vendors, manufacturers of diagnostic products that include epidemiology analysis software, and manufacturers of epidemiology analysis or surveillance software)

This guideline does not include procedures for selecting isolates for antimicrobial susceptibility testing (AST), performing AST, interpreting AST results, nor confirming the accuracy of AST results.

1.2   Background

This guideline presents specific recommendations for collection, analysis, and presentation of cumulative antimicrobial susceptibility test data.

It is important to recognize that many of the specific recommendations presented for routine antibiogram development (eg, including only the first isolate of a given species from an individual patient during the analysis period) are made with the primary aim of guiding clinicians in the selection of empirical antimicrobial therapy for initial infections when definitive susceptibility results are not available. This report may not reveal some trends in emerging resistance, and thus cannot be used as a substitute for the careful analysis of all antimicrobial susceptibility test data derived from examining and/or analyzing all antimicrobial susceptibility test results obtained for individual patient management. For reports intended for purposes other than guiding empirical therapy (eg, identifying emergence of resistance, trending antimicrobial resistance for public health initiatives), alternative analyses may be more appropriate, and these are discussed briefly in this guideline, primarily in Subchapter 6.6.

Table 16. Antibiogram With Misleading Results for Ciprofloxacin and Levofloxacin

Organism	Number of Strains	%S									
		Ampicillin	Cefazolin (systemic[a])	Cefazolin (urine[b])	Ceftriaxone	Ciprofloxacin	Gentamicin	Imipenem	Levofloxacin[c]	Piperacillin-tazobactam	Trimethoprim-sulfamethoxazole
E. coli, all	3636	61	70	87	99	92	93	100	80	96	76

Abbreviation: %S, percent susceptible.
[a] Cefazolin (systemic), MIC ≤ 2 µg/mL susceptible for infections other than uncomplicated UTI.
[b] Cefazolin (urine), MIC ≤ 16 µg/mL susceptible when cefazolin 1 g is administered IV every 12 hours; also predicts susceptibility for the oral cefaclor, cefdinir, cefpodoxime, cefprozil, cefuroxime, cephalexin, and loracarbef when used for therapy of patients with 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.
[c] Tested on nonurine isolates only (N = 292). Therefore, results should not be compared with those of other antimicrobial agents listed, all of which were tested against both urine and nonurine isolates.

Table 17. Antibiogram With Data Contributing to Misleading Results for Ciprofloxacin and Levofloxacin

Organism	Number of Strains	%S									
		Ampicillin	Cefazolin (systemic[a])	Cefazolin (urine[b])	Ceftriaxone	Ciprofloxacin	Gentamicin	Imipenem	Levofloxacin	Piperacillin-tazobactam	Trimethoprim-sulfamethoxazole
E. coli, all	3636	61	70	87	99	92	93	100	—	96	76
E. coli, nonurine	292	44	64	—	96	80	87	100	80	93	62
E. coli, urine	3417	63	—	93	99	93	94	100	—	97	77

Abbreviation: %S, percent susceptible.
Symbol: —, not applicable.
[a] Cefazolin (systemic), MIC ≤ 2 µg/mL susceptible for infections other than uncomplicated UTI.
[b] Cefazolin (urine), MIC ≤ 16 µg/mL susceptible when 1 g of cefazolin is administered IV every 12 hours; also predicts 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.

NOTE: See Subchapter 3.5.1 for an explanation of why the number of isolates from two subsets of data, urine and nonurine isolates, in this example does not add up to the total number of strains for all *E. coli*.

5.7.2 Change in Drug Panel During the Analysis Period (eg, Antimicrobial Agent Is Removed or Added to the Routine Testing Panel)

The antimicrobial agents on a laboratory's routine testing panel may change during the analysis period because:

- Antimicrobial formulary changes occurred at the facility.
- The manufacturer changed drugs in available panels.
- The laboratory used an alternate panel to better reflect the formulary and/or serve clinician's needs.

When such changes occur, the data available can be analyzed and %S results highlighted with a footnote indicating testing has been performed for a limited number of isolates, as shown for cefepime in Table 18.

⑦ The Long-Term Care Facility Antibiogram

7.1 Antibiogram Preparation in Long-Term Care Facilities

Public health[13] and regulatory organizations recommend that all LTCFs develop an annual antibiogram to guide clinicians in selecting empirical antimicrobial therapy for initial infections. Currently, there are limited evidence-based reports in the literature that document the value of using a LTCF-specific antibiogram for empirical antimicrobial choice. The general recommendations in this guideline for antibiogram preparation should be applied to LTCF antibiograms (see Table 1). However, there are several challenges within LTCFs that may preclude the generation of these reports according to M39 guidelines, which include:

- Selective culturing practices (not culturing all patients with suspected infection)
  - It is recommended that LTCFs develop facility-specific algorithms to manage appropriate diagnostic testing (eg, culture and AST) for residents with suspected infection.[13]
- Outsourcing microbiology services and using multiple microbiology laboratories by the same LTCF
- Limited numbers of isolates (often < 30 isolates of the same species) (see Subchapters 3.4 and 4.2.2)
- Lack of understanding of the value of antibiogram data and/or how to apply information to patient care
- Lack of ownership for antibiogram preparation

7.2 Responsibility for Antibiogram Preparation in Long-Term Care Facilities

Similar to the approach used in acute care hospitals, a multidisciplinary group of LTCF staff and others providing service to the LTCF (eg, administrator, medical director, consultant pharmacist, infection preventionists, antimicrobial stewardship team member, laboratorian) should collectively develop a plan for antibiogram preparation. This plan should cover:

- Individual(s) responsible for preparing or overseeing antibiogram preparation
  - Laboratorians at the referral laboratory(ies) who will provide antimicrobial susceptibility test data and/or prepare the antibiogram should be identified.
- Guidelines that should be followed for antibiogram preparation (eg, those provided in this guideline)
- Organism/antimicrobial agent combinations to be analyzed
- Other details that should be included for data analysis and presentation (eg, time frame of antibiogram, data segregation, utility of infection-specific reports)
- Method for disseminating and educating staff about the antibiogram

7.3 Optimizing Culturing Practices in Long-Term Care Facilities

The reliability and accuracy of an antibiogram is highly dependent on the culturing practices within a facility, including attention to specimen quality issues. Selectively culturing patients with suspected infection will not provide an accurate representation of the susceptibility rates of organisms causing infection at the LTCF because:

- Data from only a subset of patients with infection are analyzed that often includes larger numbers of patients who fail empirical therapy. These patients tend to have more resistant organisms that leads to an overestimation of resistance.
- A minimum of 30 isolates of each species needed to get a reliable %S statistic is often not available.

Related CLSI Reference Materials[a]

M02 **Performance Standards for Antimicrobial Disk Susceptibility Tests. 13th ed., 2018.** This standard covers the current recommended methods for disk susceptibility testing and criteria for quality control testing.

M07 **Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically. 11th ed., 2018.** This standard covers reference methods for determining minimal inhibitory concentrations of aerobic bacteria by broth macrodilution, broth microdilution, and agar dilution.

M11 **Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria. 9th ed., 2018.** This standard provides reference methods for determining minimal inhibitory concentrations of anaerobic bacteria by agar dilution and broth microdilution.

M23 **Development of *In Vitro* Susceptibility Testing Criteria and Quality Control Parameters. 5th ed., 2018.** This guideline discusses the necessary and recommended data for selecting appropriate breakpoints and quality control ranges for antimicrobial agents.

M27 **Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts. 4th ed., 2017.** This standard covers antifungal agent selection and preparation, test procedure implementation and interpretation, and quality control requirements for susceptibility testing of yeasts that cause invasive fungal infections.

M29 **Protection of Laboratory Workers From Occupationally Acquired Infections. 4th ed., 2014.** Based on US regulations, this document provides guidance on the risk of transmission of infectious agents by aerosols, droplets, blood, and body substances in a laboratory setting; specific precautions for preventing the laboratory transmission of microbial infection from laboratory instruments and materials; and recommendations for the management of exposure to infectious agents.

M38 **Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi. 3rd ed., 2017.** This standard includes antifungal agent selection, preparation of antifungal stock solutions and dilutions for testing, test procedure implementation and interpretation, and quality control requirements for susceptibility testing of filamentous fungi (moulds) that cause invasive and cutaneous fungal infections.

M44 **Method for Antifungal Disk Diffusion Susceptibility Testing of Yeasts. 3rd ed., 2018.** This guideline provides an established methodology for disk diffusion testing of *Candida* spp., along with recommendations for results interpretation and quality control testing.

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[a] CLSI documents are continually reviewed and revised through the CLSI consensus process; therefore, readers should refer to the most current editions.

Related CLSI Reference Materials (Continued)

M45 **Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria. 3rd ed., 2016.** This guideline informs clinical, public health, and research laboratories on susceptibility testing of infrequently isolated or fastidious bacteria that are not included in CLSI documents M02, M07, or M100. Antimicrobial agent selection, test interpretation, and quality control are addressed.

M59 **Epidemiological Cutoff Values for Antifungal Susceptibility Testing. 3rd ed., 2020.** This document provides epidemiological cutoff values developed according to the criteria in the Clinical and Laboratory Standards Institute (CLSI) guideline M57 and generated according to the reference broth dilution methods described in the CLSI standards M27 and M38.

M60 **Performance Standards for Antifungal Susceptibility Testing of Yeasts. 2nd ed., 2020.** This document provides updated minimal inhibitory concentration, zone diameter, and quality control tables for the Clinical and Laboratory Standards Institute antifungal susceptibility testing documents M27 and M44.

M100 **Performance Standards for Antimicrobial Susceptibility Testing. 31st ed., 2021.** This document includes updated tables for the Clinical and Laboratory Standards Institute antimicrobial susceptibility testing standards M02, M07, and M11.

VET01 **Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals. 5th ed., 2018.** This standard covers the current recommended methods for disk diffusion susceptibility testing and the reference methods for determining minimal inhibitory concentrations of aerobic bacteria by broth macrodilution, broth microdilution, and agar dilution for veterinary use.

VET01S **Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals. 5th ed., 2020.** This document includes updated tables for the Clinical and Laboratory Standards Institute veterinary antimicrobial susceptibility testing standard VET01.

VET03 **Methods for Antimicrobial Broth Dilution and Disk Diffusion Susceptibility Testing of Bacteria Isolated From Aquatic Animals. 2nd ed., 2020.** This guideline provides the most up-to-date techniques for the determination of minimal inhibitory concentrations and zones of inhibition of aquatic bacteria and criteria for data interpretation and quality control testing.

VET04 **Performance Standards for Antimicrobial Susceptibility Testing of Bacteria Isolated From Aquatic Animals. 3rd ed., 2020.** This document includes updated tables for the Clinical and Laboratory Standards Institute veterinary antimicrobial susceptibility testing guideline VET03.

Sample