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Review Article

Toward smarter testing: Diagnostic stewardship in healthcare systems

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ABSTRACT

Diagnostic stewardship (DxS) is an emerging paradigm in healthcare that emphasizes the appropriate use of diagnostic tests to improve patient outcomes, reduce unnecessary treatments, and optimize resource utilization. This narrative review explores the principles, applications, and challenges of DxS across various clinical and global health settings. It highlights the critical role of DxS in combating antimicrobial resistance by reducing overdiagnoses/misdiagnoses and facilitating targeted therapy through evidence-based diagnostic practices. The review discusses the integration of DxS with antimicrobial stewardship programs and its potential to transform clinical decision-making by leveraging advancements such as rapid diagnostic tests and machine learning tools. In addition, it addresses barriers to implementation, including limited resources, clinician resistance, and systemic inefficiencies, particularly in low- and middle-income countries. The global health implications of DxS are explored, with an emphasis on equitable access to diagnostics and improved infectious disease surveillance. There is a need for a multidisciplinary approach to overcome the challenges in implementing DxS, including investments in infrastructure, education, and the development of evidence-based protocols. By fostering a culture of precision and accountability, DxS has the potential to transform healthcare delivery, improve patient safety, and advance global health equity. Analyzing current evidence and providing a roadmap for future research and policy initiatives, this review underscores the transformative potential of DxS in achieving sustainable, high-quality healthcare, and mitigating global health challenges.

Keywords: Antimicrobial resistance, Antimicrobial stewardship, Infection prevention and control, Diagnostic and therapeutic optimization

INTRODUCTION

The World Health Organization (WHO) defines diagnostic stewardship (DxS) in the Global Antimicrobial Resistance Surveillance System (GLASS) Manual (updated in 2017)[1] as –

"Coordinated guidance and interventions to improve appropriate use of microbiological diagnostics to guide therapeutic decisions. It should promote appropriate, timely diagnostic testing, including specimen collection, and pathogen identification and accurate, timely reporting of results to guide patient treatment."

According to the WHO DxS: A guide to implementation in antimicrobial resistance (AMR) surveillance sites (2016),[2] the main objectives of DxS are twofold –

- Delivery of safe, effective, and efficient patient care by timely microbiological data guided patient management; and
- Generation of accurate and representative AMR surveillance data to inform treatment guidelines and AMR control strategies.

As with antimicrobial stewardship (AMS), the goal is improved patient outcomes, guiding therapeutic options (particularly, appropriate use of antimicrobials), and detecting AMR patterns and outbreaks while promoting effective communication between the core patient care teams and microbiological teams. Indeed, the GLASS manual advocates an implicit symbiosis between AMS and DxS – allegorized by the fact that there is considerable overlap within the teams for antimicrobial and DxS and their overall goals.

In many institutions across the world, DxS has become an integral part of the AMS as well as the infection prevention and control activities. In 2022, Society for Healthcare Epidemiology of America (SHEA) put forth a position paper outlining the principles of DxS, while providing guidelines in developing institutional DxS programs.[3,4]

HISTORY OF DxS

The term DxS was first used in the Global Surveillance of Antibacterial Resistance in Humans – 2nd WHO Technical Consultation (2014),[5] and further expanded on in the WHO technical document in 2016.[2] However, the concept of DxS and its principles in the broader framework of healthcare optimization and quality improvement can be traced back to the 19th century.

1. Early laboratory medicine and test standardization (19th–20th Century):[6]
    - The regular use of laboratory medicine (tests such as urinalysis and blood smears) in the mid-19th century as an adjuvant to clinical decisions marked the beginning of systematic diagnostic testing in the context of patient care.
    - The rapid advances in biochemical and microbiological testing in the 20th century introduced more sophisticated diagnostic tests, such as cultures and enzyme assays, which have become integral to clinical care.
    - In the mid-20th century, accreditation bodies and quality control measures, such as proficiency testing programs, were introduced to ensure accuracy, reliability and harmonization among clinical laboratories.
2. Emergence of AMS (Late 20th Century):[7]
    - The rise of AMR and concurrent slowing of the development of newer antimicrobial classes in the early to mid-20th century highlighted the need for AMS.
    - Among other issues, early AMS programs emphasized the importance of diagnostics in identifying infections and tailoring treatments, laying the groundwork for DxS principles.
3. Formalization of DxS (late 2010s):[8]
    - The term "diagnostic stewardship" gained traction during the late 2010s as healthcare systems recognized the critical role of diagnostics in achieving high-value care.
    - Institutions began earnestly developing targeted interventions to optimize test utilization, such as reducing unnecessary imaging studies or refining microbiological testing practices.
4. Technological advances and digital health (2020s):[8]
    - The integration of artificial intelligence (AI) and machine learning (ML) into healthcare has revolutionized diagnostic capabilities, enabling real-time analysis and decision support.
    - Digital health tools, such as clinical decision support systems (CDSSs) and predictive algorithms and point-of-care testing (POCT), are being increasingly used by clinicians worldwide to optimize patient outcomes.

RATIONALE FOR DxS

Diagnostic testing (microbiological, biochemical, biomarkers, etc.) is critical to the delivery of appropriate healthcare–guiding treatment decisions, prognostic evaluations, and disease prevention strategies. However, inappropriate utilization of diagnostic modalities – whether overuse or underuse – can lead to significant issues. Accordingly, the rationale for DxS is as follows:[2-4]

- Overtesting: This can lead to overdiagnosis/misdiagnosis (false positives/false negatives), unnecessary treatments, and increased healthcare costs. For example, overuse/misinterpretation of non-specific tests like procalcitonin, C-reactive protein, and even differential leukocyte counts can lead to misdiagnosis of infection, leading to unnecessary use of antimicrobials.
- Underutilization: Delays diagnoses, resulting in missed opportunities for timely and effective treatment. For example, misdiagnoses in the absence of blood/urine cultures may lead to faulty empirical treatments. A culture of sending cultures among caregivers can improve patient care outcomes by increasing culture-sensitivity-directed definitive treatments.[7]
- Resource wastage: Redundant or low-value testing can lead to misinterpretations and increase healthcare costs for both the provider and the patient. For example, unnecessary radiological testing.
- Patient safety: Inappropriate testing, such as unnecessary radiation exposure or invasive procedures, can adversely affect patient safety. Conversely, not using tests appropriate for the patient can lead to inappropriate use of antimicrobials, whose adverse effects can sometimes cause serious patient harm.

- Improving infection prevention efforts: Accurate diagnostics aid in identifying pathogens, enabling timely isolation and infection control measures, which, in turn, helps prevent nosocomial infections.

Diagnostic errors due to the aforementioned issues are a significant contributor to patient harm, with studies estimating that they impact approximately 10% of patients annually in high-income countries.[9] These errors often stem from issues in the diagnostic process, including test selection, sample handling, result interpretation, and communication of findings.[3] DxS aims to mitigate these risks by fostering a systematic approach to test utilization. It bridges these gaps by promoting practices that align diagnostic testing with clinical needs and evidence-based guidelines. In healthcare systems increasingly focused on value-based care, DxS contributes to safer, more efficient, and cost-effective care delivery through informed test utilization and streamlined processes.[2,3]

OBJECTIVES OF DxS

1. Accuracy: Enhance diagnostic precision using validated tests and reducing errors[2,3]
2. Appropriateness: Ensure tests are clinically justified and evidence-based[2,3]
3. Timeliness: Facilitate timely diagnoses to improve patient outcomes[2,3]
4. Efficiency: Optimize the use of diagnostic resources to reduce healthcare costs.[2,3]

CORE PRINCIPLES OF DxS

1. Integration with AMS:[2,3,8]
    - DxS should complement AMS programs to ensure appropriate antimicrobial use
    - DxS programs work alongside AMS to implement evidence-based guidelines for both testing and treatment
    - Healthcare institutions are encouraged to develop diagnostic pathways, institute guidelines and protocols for the implementation of diagnostic care bundles, and form either individual DxS teams or those integrated with AMS teams.
2. Right test, right patient, right time:[3]
    - Ensuring that the most appropriate test guided by evidence-based practices is ordered for the right patient at the optimal time with prompt turn-around time.
    - Timely utilization of diagnostic tests, with accurate interpretation of results and initiation of effective treatments, should improve clinical outcomes and reduce morbidity and mortality.
    - Educating clinicians to avoid unnecessary duplication of tests while ensuring critical diagnostic tests are not overlooked.
    - For example, using rapid polymerase chain reaction (PCR) or POCT tests for detecting respiratory pathogens in patients with suspected pneumonia can speed up the selection of appropriate antimicrobial therapy.
3. Appropriate test selection:[8]
    - To avoid unnecessary testing (e.g., routine or screening tests) and to ensure essential tests are not missed, diagnostic tests should be ordered based on clinical indications, directed by evidence-based guidelines, and aligned with the patient's clinical presentation.
    - Educating clinician to understand the diagnostic tests – their need, rationale, sensitivity, specificity, results, and interpretation.
    - For example, avoiding unnecessary urine cultures for asymptomatic patients and ensuring that respiratory pathogen panels are only used for suspected pneumonia cases.
4. Reducing overuse and underuse of diagnostic tests:[2,3]
    - DxS aims to minimize both overuse and underuse of diagnostic tests to prevent overdiagnosis and missed diagnoses.
    - It is imperative to balance the need for comprehensive testing with the risk of overtesting, which may lead to unnecessary treatments, patient anxiety, and increased healthcare costs.
    - Institutions are encouraged to establish guidelines and decision-support tools that guide clinicians in ordering tests when clinically appropriate.
    - For example, using clinical algorithms that limit unnecessary imaging in patients with low risk of certain diseases.
5. Pre-analytical phase optimization:[2,3]
    - Ensure proper training for healthcare providers on correct sample collection techniques, including the correct timing, volume, and use of appropriate containers and equipment
    - Addressing factors such as proper patient preparation, specimen collection, labeling, and transportation to ensure test accuracy.
    - Minimizing errors during specimen handling through robust protocols and staff training.
    - Foster clear communication between clinicians, laboratory staff, and other healthcare professionals to ensure accurate sample collection, handling, and testing procedures.
    - Promote inter-professional collaboration to review diagnostic testing practices and optimize workflow.

- For example, the stability of certain analytes (e.g., glucose and hormones) may degrade with time or temperature, faulty techniques in sample collection from infected wounds/respiratory samples.

6. Analytical accuracy:[3]
   - Utilizing validated laboratory techniques and ensuring equipment calibration to minimize errors during the testing process.
   - Adopting external quality assessments and accreditation standards for laboratories.
7. Post-analytical interpretation and communication:[10]
   - Diagnostic results must be accurately interpreted in the clinical context, considering both the patient's symptoms and any relevant epidemiological or resistance data and not as an isolated result.
   - Such an interpretation must be clear and actionable with effective communication between clinicians, laboratorians, and patients.
   - Ensuring timely reporting of critical results to avoid delays in care
   - For example, a positive result for a pathogen in a low-risk patient may need further clinical correlation to determine its significance.
8. Targeted treatment based on diagnostic results:[11]
   - Diagnostic tests should guide appropriate treatment decisions, particularly in terms of antibiotic selection and use.
   - Core patient care teams should ensure that the treatment is pathogen-specific, thereby avoiding unnecessary broad-spectrum antibiotic use and mitigating the risk of AMR.
   - A "culture of cultures" should be inculcated in clinicians for the right patients to obtain the right results and start the right treatment.[12]
   - For example, in the case of a bacterial infection, especially nosocomial, susceptibility results should be used to select a narrow-spectrum antibiotic that is effective against the identified pathogen rather than relying on broad-spectrum empirical treatment.
9. Feedback loops and continuous improvement:[2,3]
   - Establishing mechanisms for reviewing test utilization patterns and outcomes,regularly monitoring the effectiveness of diagnostic testing practices, and provide feedback to clinicians to optimize future test utilization.
   - Implementation of feedback mechanisms such as test utilization audits, peer reviews, or ongoing training programs for clinicians to reinforce best practices in DxS and to refine diagnostic algorithms.

IMPLEMENTATION STRATEGIES FOR DxS

1. Establishing multidisciplinary teams:[2,3,13]
   - The formation of a multidisciplinary DxS team that includes clinicians, laboratory professionals, pharmacists/pharmacologists, and informatics specialists is essential.
   - The team works together to review testing protocols, assess the clinical utility of tests, and set guidelines for appropriate test utilization.
   - Healthcare institutions are encouraged to make these teams either individually or as a part of the AMS teams – with established protocols, guidelines and standards that must be implemented throughout the institution.
2. Education and awareness:[2,3]
   - Ongoing education and training programs are essential for ensuring that healthcare providers understand the principles of DxS and the importance of appropriate test selection.
   - Improving the knowledge of clinical guidelines, understanding the diagnostic tests and their utility, proper test interpretation, and the potential consequences of over/under-testing.
   - Incorporating stewardship concepts into medical and allied health curricula must be ventured.
   - Workshops or online modules for clinicians and laboratory staff to raise awareness of the importance of DxS and provide practical skills on how to order tests efficiently may be useful.
3. Implementing test ordering restrictions and pre-approval processes:[2,3,14]
   - Introducing restrictions or pre-approval processes for certain high-cost or low-yield tests can reduce inappropriate use.
   - This strategy ensures that expensive tests are only ordered when clinically justified, reducing unnecessary costs and test overload.
   - For example, tests that are expensive or require complex technology (e.g., genetic tests and highly invasive tests) can be subject to approval by a specialist or laboratory in-charge before being ordered.
4. CDSS:[3]
   - Leveraging CDSSs to assist clinicians in selecting the most appropriate diagnostic tests at the point of care is a crucial strategy.
   - CDSS can provide real-time alerts or recommendations based on the patient's clinical condition, history, and current guidelines – in the form.

- Embedding decision-support tools within electronic health records (EHRs) to provide real-time guidance can alert clinicians when a patient's clinical symptoms do not align with the typical indications for a specific test, encouraging alternative diagnostic approaches.

5. Leveraging data analytics and reporting tools:[2,3,14]
   - Utilizing data analytics tools to track and analyze test utilization patterns can help identify areas where DxS initiatives may be needed.
   - Data can be used to detect overuse or misuse of specific tests and to monitor the outcomes of stewardship efforts.
   - Data-driven decision-making helps identify inefficiencies in diagnostic testing and enables targeted interventions to improve stewardship.
   - For example, using analytics software to track the frequency of certain diagnostic tests and comparing them to national or regional benchmarks can help identify excessive use of tests like routine imaging for low-risk patients.

6. Regular audit and feedback mechanisms:[2,3,15]
   - Implementing audit and feedback systems is essential for monitoring the success of DxS initiatives.
   - Regular audits of patterns of tests ordered, diagnostic test results, and clinical outcomes should be conducted to identify areas for improvement and assess adherence to guidelines.
   - Continuous monitoring helps identify trends, challenges, and opportunities for improvement, while feedback loops encourage clinicians to adopt best practices.

DxS DIAGNOSTIC PATHWAY

The diagnostic pathway encompasses several stages, from patient presentation and initial assessment to the final diagnosis and treatment plan, with each stage offering opportunities for improving diagnostic performance.[2,3,14]

The pathway includes specimen selection and collection, turn-around time, storage and transport, laboratory processing, and reporting and interpretation of results and feedback.

- Patient presentation and clinical assessment: (pre-analytical phase)[2,3,14]
  - The diagnostic pathway begins when a patient presents with symptoms or signs of illness. The healthcare provider's clinical assessment at this stage is crucial for identifying potential diagnoses and deciding whether diagnostic testing is necessary.
  - Clinicians should use evidence-based guidelines to evaluate the patient's history, symptoms, and risk factors. This allows for the targeted selection of diagnostic tests that are most likely to provide useful information.
  - For example, a patient presenting with fever and cough may prompt a clinician to consider respiratory infection. Instead of ordering a broad range of tests, a targeted approach might focus on a respiratory panel or chest X-ray, based on the clinical presentation and epidemiological factors. Post-operative fever or increase in total leukocyte count may be present due to inflammation and not infection, therefore does not warrant further specialized tests or antibiotic use.

- Test Ordering and Selection: (pre-analytical phase)[2,3,14]
  - After the clinical assessment, the next step is the ordering of diagnostic tests. This stage is where DxS plays a critical role in avoiding unnecessary testing and ensuring the selection of the most appropriate tests based on the clinical presentation and the suspected diagnosis.
  - It is imperative to ensure that tests are ordered based on established clinical guidelines, shared decision-making, and clinical needs. This can reduce unnecessary tests, minimize the risk of overdiagnosis, and save healthcare resources.
  - For example, for suspected bacterial pneumonia, clinicians may order only a chest X-ray and sputum culture instead of a broad battery of unnecessary tests.

- Specimen collection and handling: (pre-analytical phase)[2,3,14]
  - After the test is ordered, the correct collection of samples is essential for accurate test results. Errors in specimen collection, handling, or transport can lead to inaccurate results, affecting diagnosis and treatment.
  - Educating and training healthcare personnel in proper specimen collection, labeling, and transport protocols helps reduce pre-analytical errors and ensures the integrity of the sample. Adherence to guidelines for collection, handling, and storage is crucial.
  - For example, blood cultures for suspected bacteremia must be collected aseptically from two separate sites (paired samples) to increase the likelihood of detecting a pathogen and avoid contamination.

- Test Performance and Result Generation: (analytical phase)[2,3,14]
  - In this stage, laboratory or diagnostic professionals perform the tests as ordered, and results are generated. The accuracy of the test results may

  be influenced by factors such as the quality of the testing equipment, laboratory procedures, and the specific biomarkers being tested.
  - Laboratory should exercise appropriate quality controls, validation, and calibration procedures are in place to guarantee reliable results. Results should be promptly communicated to the ordering clinician to avoid delays in diagnosis and treatment.
- Result interpretation and clinical decision-making: (post-analytical phase)[2,3,14]
  - Once diagnostic results are available, it is critical that healthcare providers interpret these results correctly. Misinterpretation of laboratory data can lead to wrong diagnoses and inappropriate treatments.
  - Implementing decision support tools, second opinions, and expert consultations can assist in interpreting complex results.
  - Clinicians should be encouraged to consider the full clinical context, including clinical presentation, patients' history, physical examination findings, and diagnostic results, when making decisions.
  - For example, a positive result for a specific pathogen should be interpreted in the context of the patient's clinical signs – a positive urine culture for E. coli in a patient with no urinary symptoms may require re-evaluation for possible contamination rather than a diagnosis of urinary tract infection (UTI).

Overall, the efficacy of DxS activities depends on the treating clinicians' inference of the probability of infection before ordering the diagnostic test. DxS operates by emphasizing the utility of the diagnostic test in high-value clinical scenarios where the probability of infection is higher (e.g., blood culture in bacteremia). Similarly, DxS hinders the possibility of using the diagnostic test where the probability of infection is low (low-value setting) or settings where false positive results may be reported (e.g., blood culture in case of asymptomatic UTI), which may lead to inappropriate use of antimicrobials and cause harm to the patient

SPECIFIC STRATEGIES RECOMMENDED UNDER DxS

- Nudges/comments[3] – By clinical decision support tools or manual reviews (by nursing staff or DxS team) help the clinician to optimize therapy. For example, reporting that there are no gram-negative organisms in respiratory culture alerting the clinician to stop anti-gram-negative treatment.
- Framing statements[3] – Alerting clinicians about the probability of success of a particular treatment according to test results. For example, 75% of *Staphylococcus aureus* spp. in the culture are Methicillin resistant *Staphylococcus Aureus* (MRSA) and 25% are Methicillin Sensitive *Staphylococcus Aureus*.
- Best practice alerts[3] – Aligning the clinicians' decisions with guidelines – inclusion/exclusion of tests according to patients' condition.
- Stops[3] – soft stops (clinician can override) or hard stops (test not allowed) for tests when not recommended. For example, hard stop for C. difficile testing in patients taking laxatives.
- Reflex testing[3] – diagnostic test is ordered only when specific conditions are met. For example, urine cultures ordered only in symptomatic cases of pyuria.
- Selective testing[3] – no culture sensitivity done in cases of report of contaminants. For example, coagulase negative staphylococci in blood culture in asymptomatic patient.
- Cascade reporting – culture sensitivity results are reported in a stepwise manner starting with narrow-spectrum antimicrobials reported before broad-spectrum antimicrobials.

ORGANIZATIONAL ASPECTS FOR DxS TEAMS

- Successful implementation requires a multidisciplinary team approach, including clinical, laboratory, and surveillance staff.
- Key roles and responsibilities are outlined for each group, emphasizing the need for good communication and training.
- Prerequisites for DxS:
  - According to national AMR surveillance systems and participation in the GLASS – a guide to planning, implementation, and monitoring and evaluation (2016),[16] surveillance sites must have relevant clinical, laboratory, epidemiological, and data management capacity.
  - The laboratory/diagnostic facility may be on-site or off-site as long as it complies with recognized standards[16] and has the capacity and capability to transport specimens and perform the diagnostic tests with transparency in documentation and reporting.
- Resource allocation and budget plan:
  - Most commonly encountered obstacles in the implementation of DxS are financial constraints, especially related to microbiological diagnostic testing, supply chain for consumables, collection and transportation of samples, lack of training and knowledge among staff, and quality assurance, among other issues.
  - These issues may be highlighted in resource-limited settings and may dissuade healthcare institutions from developing DxS programs.
  - However, DxS may be started from the most basic

low hanging fruits and developed upward.

- Leadership and governance:
  - A conscious effort is required to appoint effective leadership to provide direction, allocate adequate resources, and ensure accountability for DxS initiatives.
  - It is expected to formulate specific organizational policies based on the guidelines put forth by the WHO and SHEA and set diagnostic priorities aligned with regional and national clinical and public health goals.
  - A steering committee or task force should be established to oversee DxS efforts.
- Multidisciplinary collaboration:
  - A team comprising of clinical, laboratory, pharmacy, and administrative departments must be assembled to ensure comprehensive DxS.
  - Concerned clinicians, laboratory staff, and epidemiologists should be engaged in designing and reviewing diagnostic protocols to ensure all the stakeholders are satisfied.
  - Communication between the microbiology laboratory and core patient care teams must be consolidated to ensure accurate reporting and interpretation of results.
- Integration with laboratory operations:
  - It is imperative to enhance laboratory processes to improve diagnostic accuracy and efficiency with enough workforce to support stewardship and non-stewardship functions.
  - Ensuring proper specimen collection, labeling, and transport protocols to minimize pre-analytical errors is integral to DxS.
  - Investing in laboratory automation and staff training to improve test throughput and quality, as well as decreasing turnaround time are crucial.
- Use of technology and data:
  - Leveraging technology to optimize test ordering, monitoring, and feedback mechanisms using CDSSs integrated with EHRs to guide appropriate test ordering.
  - Implementing data dashboards for real-time monitoring of diagnostic test utilization and AMR patterns to support clinician decisions.
- DxS dedicated education and training:
  - Equipping DxS team with the knowledge to participate in and sustain DxS practices with the development of training programs on diagnostic test selection, specimen handling, and interpretation of results will help in training staff.
  - Conducting regular workshops and audits to reinforce best practices.
- Monitoring and feedback:
  - Strategies to ensure continuous improvement through regular evaluation and feedback on diagnostic practices by monitoring diagnostic test utilization patterns and align them with evidence-based guidelines will optimize DxS activities.
  - Providing clinicians with feedback on ordering patterns and diagnostic outcomes to encourage adherence to protocols.
- Alignment with AMS programs:
  - Most guidelines emphasize that AMS and DxS activities should run synergistically to ensure that diagnostic practices support appropriate antimicrobial use.
  - For example, aligning microbiology test protocols with antimicrobial prescribing policies, using rapid diagnostics to support timely and targeted antimicrobial therapy.
- Policy and regulatory compliance:
  - Ensuring DxS practices adhere to national and international standards.
  - Developing policies aligned with guidelines from the WHO, centers for disease control and prevention (CDC), and professional organizations such as SHEA.
  - Ensuring laboratories meet accreditation requirements and participate in external quality assurance programs.
- Patient-centered focus:
  - Ensuring DxS enhances patient outcomes and safety while reducing harm from overtesting or delayed results.
  - Educating patients on the risks and benefits of diagnostic testing to align with their preferences.

APPLICATION OF DxS

The WHO technical document (2016)[2] encourages healthcare institutions to adopt the guidelines and adapt them into their own institutional protocols. In 2020, Watson *et al.* implemented a new order set in the EHRs in a multicentric study to improve urine culture DxS, antimicrobial use, and associated costs in multiple healthcare centers.[17] The key results were as follows:

- Among the five sites studied, the number of urine cultures performed decreased by 40.4%
- Antibiotic days of therapy for patients with UTI decreased by 15.2%
- The catheter-associated UTI standardized infection ratio decreased from 1.0 to 0.8 after the intervention
- The estimated yearly savings were US$535,181 following the intervention.

In 2023, Gupta *et al.* developed a diagnostic stewardship care-bundle (DSB) called the "Sepsis-48 DSB" which aimed to reduce the intervening duration of key steps of automated blood culture diagnostics.[18] The key results of the implementation of the care bundle were as follows:

- Improved diagnostic practices by a significant reduction in inappropriate blood culture orders by 25–30%, decrease in contamination rates from 4.5% to 2.5%
- Faster turnaround times – time-to-pathogen identification reduced by 15%, leading to earlier initiation of targeted antimicrobial therapy
- Decreased use of broad-spectrum antibiotics, with a shift toward more narrow-spectrum therapies
- Overall healthcare costs decreased due to fewer unnecessary tests and reduced treatment of contaminants as true infection.

CHALLENGES IN DxS

1. Applicability of DxS in routine clinical practice:[14,19,20]
    - One of the main problems faced by clinicians is instituting an empirical therapeutic option while waiting for the results of the diagnostic test. In many cases, delay in the implementation of appropriate antimicrobial therapy may lead to morbidity and/or mortality.
    - However, using broad-spectrum antimicrobials not only contributes to AMR, but many times, these drugs may not cover organisms such as *Pseudomonas*, *Klebsiella,* or MRSA.
    - Of course, the institution may refer to their antibiogram trends and predict empirical therapies, but these are shifting targets in the face of AMR.
    - Therefore, rapid pathogen identification and susceptibility testing, with rapid turnaround times are absolutely crucial.
    - This may be difficult in resource-limited settings with low workforce.
    - Integration of novel diagnostic tools in the DxS diagnostic pathway may present a viable solution to this issue.[14]
    - Healthcare institutions are increasingly employing POCT and molecular tests such as Gene Xpert, matrix-assisted laser desorption ionization-time of flight (MALDI-TOF), FilmArray biofire filmarray blood culture identification panel, Verigene, and metagenomic next-generation sequencing to overcome the delay in reporting.[19]
    - These novel technologies are called "Fast Microbiology."[20] Sophisticated diagnostic modalities like MALDI-TOF can decrease the turn-around time to a mere 1 h.
    - However, with resource-limited settings, acquiring such sophisticated diagnostic modalities becomes unfeasible. It is up to the regulatory and governing authorities to ensure all surveillance sites have access to such resources.[14,19,20]
2. Overuse of diagnostic tests:[6]
    - The sheer number of tests available, ease of ordering tests, increasing patient demands for testing, and defensive medicine practices contribute to unnecessary testing.
    - This not only increases healthcare costs but can also result in unnecessary treatments and interventions. Overuse of tests, particularly in the absence of clinical indications, may also lead to diagnostic errors, overdiagnosis, and inappropriate treatments.
3. Inconsistent test utilization guidelines:[2,3]
    - The lack of standardized guidelines or inconsistencies in their application across different healthcare settings contributes to variability in test ordering practices.
    - Inconsistent implementation of clinical guidelines on when to order diagnostic tests can lead to inappropriate or delayed testing. In addition, clinicians may be unaware of updated guidelines or may have difficulty accessing them during clinical decision-making.
4. Vulnerable population:[21]
    - DxS becomes even more challenging in vulnerable populations, especially in the pediatric setting.
    - Apart from their physiological differences, the pediatric population is more sensitive to invasive procedures, such as blood draws and lumbar punctures.
    - Moreover diagnostic errors in a pediatric patient can be catastrophic because the margin for error is slim in such patients.
    - On top of that, issues such as age-specific variability, limited diagnostic specimen volume, atypical clinical presentations, higher risk of contaminated or inadequate samples, lack of validation of diagnostic tests for pediatric population, and limited pediatric-specific DxS guidelines can make DxS in these patients practically impossible.
5. Financial considerations:[14,20]
    - Financial constraints remain a significant barrier to implementing DxS initiatives.
    - While DxS aims to reduce unnecessary tests and improve patient outcomes, many interventions require upfront investment in technologies, training, and infrastructure.
    - Smaller or resource-limited healthcare facilities may struggle to afford the necessary tools for effective stewardship, particularly when the economic benefits of reduced testing and improved outcomes may not be immediately apparent.

6. Cultural and behavioral barriers:[15]
    - Clinicians may resist changes in test ordering practices due to habit, skepticism about new protocols, or fear of missing a diagnosis, perceiving restrictions on diagnostic testing as a barrier to autonomy or patient care.
    - In addition, healthcare systems that prioritize throughput or patient satisfaction over clinical appropriateness may face challenges in promoting DxS.
    - Overcoming these barriers often requires cultural change, support from the leadership, and ongoing education for healthcare providers.
7. Data availability and accessibility:[22]
    - The effectiveness of DxS depends on access to high-quality patient data.
    - However, many healthcare systems face challenges in collecting, storing, and sharing diagnostic information across different platforms.
    - Incomplete or inaccurate data can lead to poor decision-making, diagnostic delays, and inappropriate test ordering.
    - Moreover, disparities in data access between healthcare providers and institutions can hinder the coordination required for effective DxS.
8. Patient expectations and demand:[15,22]
    - Patients' expectations for testing and diagnostic clarity can pressure clinicians to order unnecessary tests, even when the clinical indications are weak.
    - Patient demand for tests driven by perceived need, direct-to-consumer (DTC) testing services, or misinformation can lead to inappropriate testing.
    - Educating patients on the value of evidence-based testing and involving them in the decision-making process is critical to overcoming this challenge.
9. Training and education:[23]
    - With advances in medicine, the number of accurate and effective sophisticated diagnostic modalities is steadily increasing. Effective DxS requires ongoing training and education for clinicians.
    - Many healthcare providers may not be fully aware of the latest advances in diagnostic testing or may be unfamiliar with the concept of DxS itself.
    - Morjaria and Chapin (2020) observed that most clinicians are unsure of how to order diagnostic tests or interpret the test results, the overall cost, and the clinical benefits of the test.
    - In addition, due to time constraints and impossible workloads, most diagnoses are based on history-taking and physical examinations, and are not supported by diagnostic tests. On the other hand, some clinicians may overzealously take precautionary measures and overutilize diagnostic tests leading to problems mentioned earlier in this document.[23] DxS is a delicate balance between these two scenarios to effectively use diagnostic tests to improve patient outcomes.
    - Implementing educational programs that focus on the appropriate use of tests, the importance of diagnostic accuracy, and the principles of stewardship is essential for improving clinician adherence to stewardship guidelines.

FUTURE DIRECTIONS

The field of DxS is rapidly evolving. Emerging areas of focus include:

1. Integration of AI and ML:[10,22,24]
    - These technologies have the potential to analyze vast amounts of healthcare data, identify patterns, and provide real-time diagnostic recommendations.
    - AI-driven diagnostics: AI and ML models can assist clinicians in identifying the most appropriate tests based on patient data and symptoms. By analyzing EHRs, laboratory results, and imaging data, AI systems can recommend the best diagnostic strategies and predict the likelihood of specific diseases or conditions. This can lead to more targeted testing, avoiding unnecessary diagnostics and reducing costs.
    - In 2022, Schinkel *et al*. aimed to evaluate the effectiveness of a ML-based tool in guiding blood culture testing decisions in emergency department (ED) settings. The study focused on a ML model designed to predict which patients are most likely to have a positive blood culture, thereby guiding clinicians in deciding whether to order blood cultures. The tool's deployment led to better clinical decision-making, particularly in terms of selecting patients who were more likely to benefit from blood culture testing. By reducing unnecessary blood cultures, the tool also helped streamline workflows in the ED and improve resource utilization.[25]
    - Predictive analytics: AI and ML can also help predict future patient outcomes, enabling earlier intervention and improving diagnostic accuracy. For example, predictive algorithms could alert clinicians to the possibility of sepsis or other serious infections before they become clinically apparent, enabling timely and targeted diagnostic testing.
2. Enhanced CDSSs:[3]
    - CDSS integrates patient data, evidence-based guidelines, and clinical expertise to assist clinicians in making informed decisions about diagnostic testing.

- Personalized decision support: The development of personalized CDSS that integrates genomic, clinical, and demographic information to tailor recommendations for individual patients is a promising future direction. These systems will help clinicians avoid unnecessary tests and identify the most appropriate diagnostic strategies based on the specific needs of each patient.
- Seamless integration with EHRs: Improved integration of CDSS with EHRs will be crucial for the future of DxS. Clinicians need access to real-time diagnostic recommendations and test results within their workflow. The more seamlessly CDSS is integrated into EHRs, the more likely it will be used effectively to guide diagnostic decisions.

3. Patient-centered/personalized DxS:[22]
    - As healthcare becomes increasingly personalized, patient involvement in diagnostic decision-making will be crucial for the future of DxS. Educating patients about the importance of appropriate diagnostic testing and engaging them in the decision-making process can help reduce unnecessary testing.
    - Patient education: Future efforts in DxS will likely focus on improving patient education about the value of appropriate testing and the potential harms of unnecessary tests, such as overdiagnosis and overtreatment. Engaging patients in shared decision-making about their care will help reduce patient-driven demand for unnecessary diagnostic tests.
    - DTC testing: The rise of DTC diagnostic testing (e.g., genetic testing and laboratory panels) has already sparked concerns about the potential overuse of tests. DxS in the future will need to include strategies for managing DTC testing and ensuring that patients have access to reliable and evidence-based testing options.
4. Global health applications:[2,3]
    - Extending stewardship principles to low-resource settings to address disparities in diagnostic access.
    - Adapting stewardship approaches to endemic diseases and regional healthcare challenges.
5. Expansion of POCT:[14,22]
    - POCTs allow for rapid diagnosis at the bedside or in outpatient settings, reducing delays in diagnosis and treatment.
    - Near-Patient Testing: The future of DxS will likely see a greater focus on rapid molecular tests, lateral flow assays, and biosensors that can quickly identify pathogens and provide diagnostic results. These tests will be particularly valuable in settings where traditional laboratory testing is not available or where timely decisions are critical.
    - Reducing Diagnostic Delays: By reducing diagnostic delays, POCT helps initiate appropriate treatment earlier, improving clinical outcomes. For example, in the management of bloodstream infections, rapid detection of pathogens and their antibiotic resistance profiles through POCTs can lead to more timely and accurate antimicrobial therapy.

CONCLUSION

DxS is set to become a critical component in modern healthcare systems, aiming to optimize the use of diagnostic tests and antimicrobials, to improve patient outcomes, reduce unnecessary diagnostics and treatments, and mitigate the spread of AMR. As healthcare systems worldwide face increasing challenges such as rising healthcare costs, overuse of diagnostic tests, and growing concerns around AMR, DxS emerges as a strategic solution to enhance clinical decision-making and resource allocation.

Despite its promise, several challenges to implementing DxS remain, particularly in resource-limited settings. Overcoming these challenges requires multifaceted efforts, including the development of standardized guidelines, better training for healthcare professionals, integration with AMS programs, and investments in healthcare infrastructure.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

Patient’s consent not required as there are no patients in this study.

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Conflicts of interest

Dr. Minnu Mridul Panditrao is on the Editorial Board of the Journal.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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