

Biomedical Science

Molecular Genetics



BMS 302 | Fall 2026-2027

Professional Practice Skills

Sensitivity, Specificity & Phases of Diagnostic Test

جميع الأوراق والمحتويات التابعة للمنصة محمية بموجب حقوق الملكية الفكرية. يُمنع منعاً باتاً نسخ، أو نشر، أو مشاركة أي محتوى أو مستندات تخص المنصة بأي شكل دون إذن مسبق. ويُعد أي تجاوز أو مخالفة لهذا القرار خرقاً قانونياً يعرض مرتكبه للمساءلة والملاحقة القانونية الفورية

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PART 1 OF 3

Why Diagnostic Tests Matter

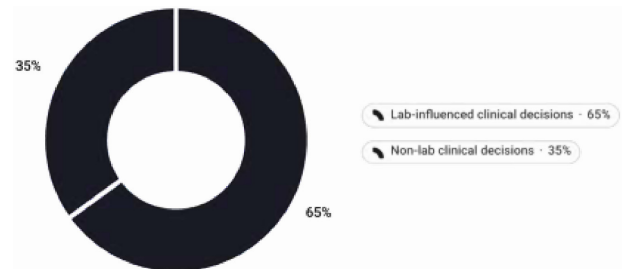
Establishing the clinical and statistical foundations of medical laboratory science.



The Engine of Clinical Decision-Making

Medical laboratory science uses clinical laboratory tests to **diagnose, treat and prevent disease** — the backbone of modern healthcare.

Between **60–70% of all clinical decisions** are influenced by laboratory medicine results.



Core functions of diagnostic testing span the full patient journey:

1

Confirming or Ruling Out Disease

Establishing a definitive diagnosis from the range of clinical possibilities.

2

Monitoring Progression & Treatment

Tracking disease trajectory and evaluating the effectiveness of therapeutic interventions over time.

3

Identifying Side Effects of Therapy

Detecting adverse drug reactions and organ toxicity before they become clinically serious.

CONDITIONS ROUTINELY MONITORED

Cardiovascular disease

Blood glucose (diabetes)

Pregnancy

HIV/AIDS

Cholesterol levels

Liver function

94% of all objective data recorded in medical records originates from laboratory tests — making lab medicine the **single largest source of clinical evidence.**

PART 2 OF 3

Sensitivity & Specificity

The two core statistical pillars for evaluating diagnostic test performance.

**The Two Pillars of Test Performance**

Sensitivity and specificity are the two core statistical measures used to assess diagnostic test performance against a **"gold standard" benchmark test.**

They mathematically describe the accuracy of a test that reports the presence or absence of a medical condition.

**Sensitivity — True Positive Rate**

The proportion of subjects correctly given a **positive** assignment out of all subjects who are **actually positive.**

- ◆ Indicates how well a test classifies subjects who **truly have** the outcome of interest
- ◆ Measures the probability of a positive test result, conditioned on the individual truly being positive
- ◆ A highly sensitive test rarely misses true cases — a negative result powerfully **rules OUT disease**

**Specificity — True Negative Rate**

The proportion of subjects correctly given a **negative** assignment out of all subjects who are **actually negative.**

- ◆ Indicates how well a test classifies subjects who **truly do not have** the outcome of interest
- ◆ Measures the probability of a negative test result, conditioned on the individual truly being negative
- ◆ A highly specific test rarely raises false alarms — a positive result powerfully **rules IN disease**



The 2×2 Contingency Table

Every diagnostic test compared against a gold standard produces one of **four possible outcomes**.

These four outcomes form the foundation for calculating sensitivity, specificity, and all derived diagnostic metrics.

	Test Positive	Test Negative
Disease Positive	True Positive ✓ TP Sick → correctly identified as sick	False Negative ✗ FN Sick → incorrectly identified as healthy — a missed diagnosis
Disease Negative	False Positive ✗ FP Healthy → incorrectly identified as sick — an unnecessary alarm	True Negative ✓ TN Healthy → correctly identified as healthy



Understanding the Four Outcomes

TP**True Positive ✓**

Correct identification of disease presence.

The test correctly flags a sick patient as sick.

The **desired outcome** for diseased patients.

FN**False Negative ✗**

Missed diagnosis.

The test incorrectly clears a sick patient as healthy.

The **most dangerous error** in high-stakes conditions — disease goes untreated.

FP**False Positive ✗**

Unnecessary alarm.

The test incorrectly flags a healthy patient as sick.

Triggers **costly or invasive follow-up** in healthy individuals.

TN**True Negative ✓**

Correct clearance.

The test correctly clears a healthy patient as healthy.

The **desired outcome** for non-diseased patients.



Calculating Sensitivity — PSAD

FORMULA

$$\text{Sensitivity} = \text{TP} \div (\text{TP} + \text{FN})$$

Measures the proportion of truly positive subjects who are correctly identified by the test.

PSA DENSITY (PSAD)

Serum PSA level (ng/mL) ÷ prostate gland volume (mL), measured via TRUS and MRI.

WORKED EXAMPLE — PROSTATE CANCER SCREENING

- **True Positives (TP): 489**
subjects with prostate cancer correctly identified
- **False Negatives (FN): 10**
subjects with prostate cancer incorrectly identified as negative

$$489 \div (489 + 10) = 489 \div 499 \\ = 0.98 = 98\%$$

INTERPRETATION

PSA density correctly identified **98% of all subjects** with clinically significant prostate cancer.

This places it firmly in the category of high-sensitivity diagnostic tests. Of every 100 patients who truly have prostate cancer, only **2 would be missed**.

A negative result from a **high-sensitivity test** is powerful for **"ruling OUT" disease**.

When sensitivity is near 100%, a negative test result gives strong reassurance that the condition is absent.

This is the **"SnNout"** rule: high **Sensitivity**, **Negative** result rules **out**.

CLINICAL SIGNIFICANCE

Missing a true case (false negative) carries serious consequences — delayed treatment, disease progression, and poorer long-term outcomes.

A sensitivity of 98% makes PSAD a highly valuable screening tool for this purpose.



Calculating Specificity — PSAD

FORMULA

$$\text{Specificity} = \text{TN} \div (\text{TN} + \text{FP})$$

Measures the proportion of truly negative subjects who are correctly identified by the test.

WORKED EXAMPLE — PROSTATE CANCER SCREENING

- **True Negatives (TN): 263**
subjects without prostate cancer correctly identified as negative
- **False Positives (FP): 1,400**
subjects without prostate cancer incorrectly identified as positive

$$263 \div (263 + 1,400) = 263 \div 1,663$$
$$= 0.16 = 16\%$$

THE "SPPIN" RULE

A positive result from a high-specificity test is powerful for "**ruling IN**" disease. High **Specificity**, Positive result rules **in**.

INTERPRETATION

A negative PSA density correctly identified only **16% of subjects** without clinically significant prostate cancer — a very low specificity.

Of every 100 healthy patients tested, **84 would receive a false-positive result**, triggering unnecessary clinical alarm, anxiety, and potentially invasive biopsy procedures.

⚠ CLINICAL BURDEN

Despite its excellent sensitivity (98%), a specificity of just **16%** generates an overwhelming number of false positives.

The ratio of false positives to true negatives here is **approximately 5.3:1**, a significant clinical burden.

When specificity is near 100%, a positive test result confirms the condition is almost certainly present.

98%

Sensitivity of PSAD

16%

Specificity of PSAD



Choosing Between Sensitivity & Specificity

Sensitivity and specificity are **inversely related** — as one increases, the other generally decreases.

The clinical context must guide cutoff selection, weighing the consequences of each error type carefully.



Prioritise High Sensitivity When:

- ✓ The consequence of failing to treat the condition is serious — e.g. **Ebola, HIV, sepsis**
- ✓ Treatment is highly effective with minimal side effects
- ✓ A negative result must definitively rule out disease
- ✓ **Example:** rapid Ebola POC diagnostics — missing an infected patient risks epidemic spread



Prioritise High Specificity When:

- ✓ A false positive leads to **invasive, expensive or stigmatising** follow-up testing
- ✓ Patients identified as positive face significant psychological or social consequences
- ✓ A positive result must definitively rule in disease

CUTOFF DECISION RULES



High Specificity Cutoff

When confirmatory testing is expensive or invasive — minimise false positives to avoid unnecessary procedures.



High Sensitivity Cutoff

When disease is fatal with available treatment, or is easily spread — maximise true positive detection above all else.

The inverse relationship means there is **no universally "perfect" cutoff**. Clinical judgment, prevalence of disease, and cost of errors must all inform the decision.

PART 3 OF 3

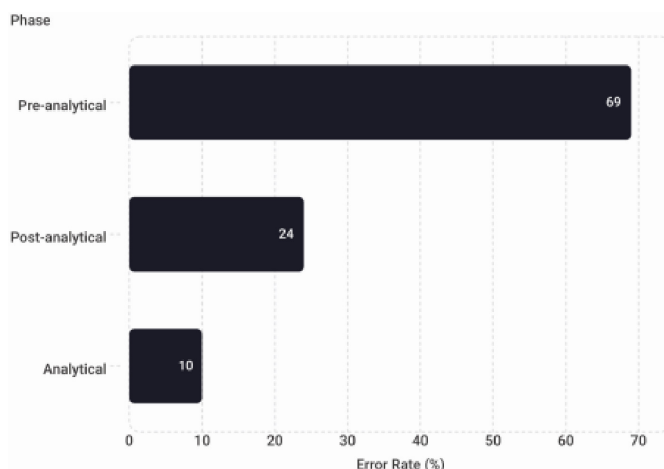
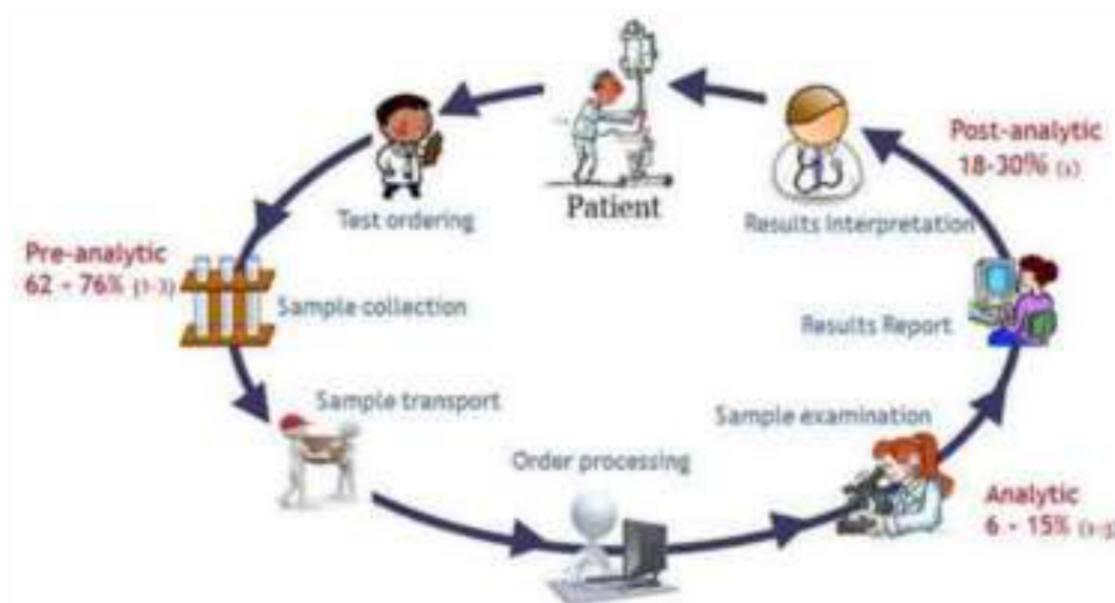
The Three Phases of Diagnostic Testing

Pre-analytical, analytical, and post-analytical — understanding where errors occur and how quality systems govern each stage.



The Total Laboratory Testing Process

The entire diagnostic testing process is governed by **Quality Management Systems (QMS)** and broken into three critical phases — each with distinct error rates and responsibilities.



Pre-analytical 62–76%

of errors — test ordering → sample collection → transport

Analytical 6–15%

of errors — order processing → sample examination

Post-analytical 18–30%

of errors — results reporting → interpretation



Phase 1 — Pre-analytical

DEFINITION · 62–76% OF ERRORS

All steps from the initial **test ordering** decision to **preparation of the sample** immediately before analysis.

This phase consistently accounts for **the majority of laboratory errors** across healthcare systems worldwide.



01 Test Ordering

Selecting the appropriate test for the clinical question — errors here **cascade through the entire process**.



02 Patient Identification

Ensuring correct patient–sample matching — misidentification is a leading cause of **serious adverse events**.



03 Specimen Collection

Aseptic phlebotomy; correct tube selection and fill volume; avoiding **haemolysis, lipaemia** and other integrity-compromising factors.



04 Specimen Transport

Transferring samples from collection site to laboratory — significant challenges in **remote and resource-limited settings**.



05 Specimen Processing & Storage

Accessioning, centrifugation, reagent preparation, tissue preservation; maintaining proper conditions to preserve **sample viability and integrity**.



Pre-analytical Errors & Their Prevention



Consequences of Pre-analytical Errors

Errors in this phase lead to **misdiagnosis, delayed treatment, inappropriate therapy** — and in the most severe cases, **loss of human life**.

Because the sample is compromised before it even reaches the analyser, analytical-phase quality controls cannot detect or correct these upstream errors.



POCT Advantage

Point-of-Care Testing can eliminate **specimen transport, blood collection tubes and centrifugation**.

It reduces pre-analytical risk significantly by bringing the test directly to the patient, rather than the patient's sample to the laboratory.

WHY THESE ERRORS ARE INSIDIOUS

Pre-analytical errors are particularly insidious because they are **invisible to automated quality-control systems**.

A perfectly calibrated analyser will faithfully report an incorrect result from a compromised specimen.



Pre-analytical Quality Assurance

Systematic quality assurance requires coordinated effort across **governance, training and procedural frameworks** — addressing every activity from test ordering through to specimen storage.



A Standard Operating Procedures (SOPs)

Development and strict adherence to protocols for every pre-analytical step, from test ordering to specimen storage. SOPs standardise practice across all staff and shifts, **removing individual variation as a source of error**.



B Training & Competency Assessment

All personnel — including non-laboratory staff performing POCT at the bedside — must be adequately trained in specimen handling and quality control. Competency must be **demonstrated and documented, not assumed**.



C Quality Management Systems (QMS)

Comprehensive systems of policies, procedures and records that direct and control quality throughout the pre-examination process. QMS governs pre-examination, examination and post-examination processes to ensure **sustainable and repeatable outcomes**.



Point-of-Care Testing (POCT)

POCT brings diagnostic testing **directly to the patient**, bypassing many pre-analytical steps and reducing delays in diagnosis.

The inventory below illustrates the scale of POCT deployment across a single **NHS Trust (LGI & SJUH)**.



POCT EQUIPMENT INVENTORY – ONE NHS TRUST

**40**

Blood Gas Analysers

**70+**

Urinalysis Analysers

**300+**

Glucose/Ketone Meters

**17**

CoaguChek INR Meters

**6**

i-STAT Analysers

**5**

Flu/COVID Analysers

WHAT POCT REDUCES OR ELIMINATES

Specimen transport

Blood collection tubes

Centrifugation

Particularly critical in **remote and resource-limited settings** where transport delays compromise sample integrity.

Rapid Ebola POC diagnostics are actively being developed to reduce diagnosis delays and infection risk.



Phase 2 — Analytical

DEFINITION · 6–15% OF ERRORS

The actual **performance of the laboratory test** — the sample is analysed to detect the presence or absence of a condition, or to measure specific analytes.

Although this phase carries **the lowest error burden**, it remains subject to rigorous quality standards.

KEY DIAGNOSTIC TECHNIQUES APPLIED

Macroscopic & Microscopic Examination — visual and microscopic assessment of specimens for morphological abnormalities.

Histopathological Staining & Tissue Sectioning — preparation and staining of tissue sections for pathological evaluation.

Manual & Automated Full Blood Counts (FBC) — haematological analysis of cellular components of blood.

Antimicrobial Susceptibility Testing — determining pathogen sensitivity to antibiotics to guide therapeutic decisions.

Molecular Techniques (e.g., PCR) — highly sensitive detection of infectious disease agents at the nucleic acid level.

QUALITY ASSURANCE FRAMEWORKS



Automation & Robotics

Automated systems improve efficiency and accuracy, and reduce human error in high-volume testing environments — a critical advancement in modern laboratory practice.



IQC & EQA

Internal Quality Control and **External Quality Assurance** provide standardised methods for continuous quality monitoring throughout the analytical process.



ISO 15189

Provides specific technical requirements for clinical laboratories to ensure competence in performing medical laboratory tests.



Lean & Six Sigma

Frameworks used to reduce waste and variation, improving overall quality performance and throughput in laboratory settings.



Phase 3 — Post-analytical

DEFINITION · 18–30% OF ERRORS

All processes **after analytical testing is completed** — from interpretation of results to communication and impact on patient management.

This phase bridges the laboratory and the clinical team, making **communication quality as important as analytical accuracy.**



01 Interpretation & Validation

Critically evaluating results; making decisions on the most appropriate procedures; medically assessing findings in clinical context.



02 Identifying Abnormal Results

Recognising unexpected or critical values requiring prompt clinical attention — and escalating appropriately.



03 Report Generation

Accurately maintaining records and generating comprehensive laboratory reports suitable for **clinical and medicolegal purposes.**



04 Communication

Effectively delivering results to clinicians, patients and caregivers via spoken, written and electronic methods; correlating laboratory findings with clinical presentation.



Data Management & Connectivity



Electronic Health Records

Centralised digital records enable better data management, longitudinal tracking and care coordination across clinical teams.



Automated Data Transmission

Direct transmission from central labs to clinic sites — reduces turnaround time and eliminates transcription errors.



Patient-Facing Online Reports

Remote monitoring and enhanced patient engagement through accessible, patient-friendly result portals.

Together, these digital tools reduce post-analytical error by **minimising manual transcription,** accelerating result delivery, and keeping patients actively engaged in their own care.



Post-analytical Quality Assurance

Given that laboratory medicine influences **60–70% of all clinical decisions**, the post-analytical phase carries an ethical and professional weight that extends well beyond technical accuracy.

QMS governance, ethical frameworks and communication protocols must work in concert.



A Professionalism & Ethics

Biomedical scientists must uphold **patient autonomy, dignity and confidentiality**, and work collaboratively with clinical colleagues.

Data privacy, security and appropriate use of patient information are **non-negotiable ethical obligations**.



B Communication Protocols

Ensuring **clarity, sensitivity and effectiveness** when delivering results — especially for critical or complex diagnoses.

Patient engagement through immediate and clear communication fosters deeper understanding and active participation in treatment plans.



C Continuous Quality Monitoring

Post-market surveillance and continuous quality monitoring programs ensure diagnostic quality is maintained from manufacture to delivery.

QMS governs all post-examination processes to ensure **sustainable, repeatable and fully auditable** outcomes across the entire testing cycle.



To Summarise...

Part 1 — principles synthesising the foundational and statistical elements of the lecture. **Part 2** — principles covering the operational realities of the three-phase testing cycle and quality governance.

PART 1 60–70%

Laboratory Medicine Drives Clinical Decision-Making

- ▶ 60–70% of clinical decisions originate from laboratory tests
- ▶ 94% of objective medical record data comes from the lab
- ▶ Accuracy is non-negotiable and directly linked to patient outcomes

PART 1 $Sn \leftrightarrow Sp$

Sensitivity and Specificity Are Inversely Related

- ▶ Sensitivity rules OUT disease — the SnNout rule
- ▶ Specificity rules IN disease — the SpPin rule
- ▶ Cutoff selection must be guided by clinical context

PHASE 1 62–76%

Pre-analytical Carries the Highest Error Burden

- ▶ Rigorous SOPs, staff training and POCT adoption are essential mitigations
- ▶ Errors are invisible to downstream quality controls
- ▶ A compromised specimen reaching the analyser cannot be corrected

PHASE 2 6–15%

Analytical Phase Demands Formal Quality Frameworks

- ▶ Lowest error share, but requires ISO 15189 compliance
- ▶ IQC and EQA programs for continuous monitoring
- ▶ Lean and Six Sigma maintain consistent, reliable performance

PHASE 3 18–30%

Post-analytical Requires Communication & Ethics

- ▶ Clear communication protocols and EHR integration
- ▶ Patient engagement and strict ethical standards
- ▶ As critical as technical accuracy in driving correct clinical action

GOVERNANCE QMS

QMS Governs the Entire Testing Cycle

- ▶ Spans all three phases of diagnostic testing
- ▶ Ensures sustainable, repeatable and patient-safe outcomes
- ▶ From test ordering to final clinical communication