

RESEARCH ARTICLE

Quality Control and Standardization in Clinical Laboratory Testing: Challenges and Solutions

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ABSTRACT

Clinical laboratory testing underpins approximately 70% of all medical diagnostic and therapeutic decisions. Despite this centrality, laboratories in sub-Saharan Africa, including those in Nigeria, continue to face systemic deficiencies in quality control (QC) implementation and standardization, resulting in an estimated 0.1–10% rate of erroneous results that compromise patient safety and clinical outcomes. This study critically examined the principal challenges that impede robust QC and standardization in clinical laboratories, with specific focus on resource-constrained settings, and proposed evidence-based, context-sensitive solutions aligned with international standards including ISO 15189:2022 and CLSI guidelines. A systematic narrative review was conducted. Peer-reviewed literature published between 2013 and 2024 was retrieved from Scopus, Web of Science, PubMed, and Google Scholar. Seventy-two articles meeting predefined inclusion criteria were analysed. Data were synthesised thematically under pre-analytical, analytical, and post-analytical error categories. Westgard multi-rule QC criteria and Six Sigma metrics were applied as analytical frameworks. Pre-analytical errors accounted for 46% of total laboratory errors, analytical errors for 31%, and post-analytical errors for 23%. Key challenges identified include infrastructural deficiencies (unreliable electricity, inadequate cold-chain), shortage of trained personnel, high cost of certified reference materials, absence of external quality assessment (EQA) participation, and weak regulatory oversight. Proposed solutions encompass phased ISO 15189 accreditation, adoption of Six Sigma-guided QC design, point-of-care technology optimization, digital laboratory information systems, and capacity-building programmes. Strengthening QC and standardization requires a multi-pronged, context-adapted strategy. Integration of internationally validated frameworks with locally tailored interventions offers the most viable pathway to sustainable laboratory quality improvement in resource-limited environments such as Gombe State, Nigeria.

KEYWORDS

Quality Control; Clinical Laboratory; ISO 15189; Westgard Rules; Six Sigma; Standardization; Nigeria; Pre-Analytical Error; External Quality Assessment; Laboratory Accreditation

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1. Introduction

Clinical laboratory testing constitutes a cornerstone of modern healthcare, informing approximately 70% of all diagnostic, therapeutic, and preventive medical decisions (Plebani, 2015; Lippi et al., 2019; Hallworth et al., 2015). The accuracy, precision, and reliability of laboratory results are therefore not merely technical parameters—they are determinants of patient safety and public health outcomes. Despite this critical role, laboratory errors remain a significant global concern, with error rates reported between 0.1% and 10% depending on the setting, analyte, and phase of the testing process (Hammerling, 2012; Aita et al., 2021; Ifeanyichukwu et al., 2017). The economic burden of erroneous laboratory results extends beyond direct patient harm, contributing substantially to unnecessary repeat testing, prolonged hospitalisation, inappropriate therapeutic interventions, and medico-legal liability (Guidi & Lippi, 2006; Kim et al., 2013; Kulkarni et al., 2019).

Quality control (QC) and standardization represent the twin pillars of laboratory quality management systems (QMS). QC refers to the set of procedures designed to detect and correct errors in analytical processes before patient results are reported, while standardization ensures that measurement results are metrologically traceable to internationally recognized reference standards, enabling inter-laboratory comparability (ISO 15189:2022; CLSI EP09-A3; ISO 17511:2020; Ceriotti & Cobbaert, 2022). Together, these disciplines reduce measurement uncertainty, prevent diagnostic errors, and support evidence-based clinical decision-making. The relationship between laboratory quality and clinical outcomes has been extensively documented: Sciacovelli et al. (2011) demonstrated that quality indicators spanning all three phases of the total testing process correlate directly with patient safety events, while Plebani (2019) articulated the “five rights” paradigm—the right result, right patient, right time, right interpretation, and right action—as the operational framework through which laboratory quality translates into improved care.

In sub-Saharan Africa, including Nigeria, clinical laboratories face a constellation of challenges that impede the consistent implementation of QC and standardization. These include infrastructural limitations, scarcity of trained laboratory scientists, unreliable reagent supply chains, absence of accreditation frameworks, and limited participation in external quality assessment (EQA) programmes (Nkengasong et al., 2018; Fricker & Strathmann, 2020; Osei & Akumiah, 2020; Balogun & Teklehaimanot, 2020; Tittle & Bhagani, 2021). Studies conducted in the West African region have reported that fewer than 15% of public hospital laboratories meet basic ISO 15189 criteria (Adebayo et al., 2019; Balogun & Teklehaimanot, 2020), and participation in EQA programmes remains sporadic and largely confined to HIV-related testing platforms supported by international donor agencies (Fonjungo et al., 2016; Yusuf et al., 2022). The Federal Polytechnic Kaltungo in Gombe State, Nigeria, through its Department of Science Laboratory Technology, trains future laboratory scientists who will operate in precisely these environments; a rigorous understanding of QC challenges and contextually appropriate solutions is therefore of paramount academic and professional importance.

This paper presents a comprehensive, evidence-based review of the challenges confronting clinical laboratory QC and standardization, with particular attention to resource-constrained settings. Drawing on a systematic analysis of 72 peer-reviewed articles, international standards documents, and regulatory frameworks, the paper proposes a suite of solutions that are both internationally aligned and locally applicable. The analytical frameworks employed include the Westgard multi-rule system (Westgard, 2016; Westgard & Barry, 2014), Six Sigma methodology (Westgard & Westgard, 2017; Muralidharan, 2015), and ISO 15189:2022 accreditation criteria (ISO, 2022; Burnett, 2013).

The objectives of the Study are as follow:

1. To systematically identify and categorize the principal challenges facing clinical laboratory QC across pre-analytical, analytical, and post-analytical phases.
2. To evaluate the applicability of international QC standards (ISO 15189, CLSI, Six Sigma) to resource-limited laboratory settings in Nigeria.
3. To propose evidence-based, context-sensitive solutions that can be practically implemented in Nigerian clinical laboratories.
4. To provide a framework for future research and policy development in laboratory quality management in sub-Saharan Africa.

2. Materials and Methods

2.1 Study Design

This study employed a systematic narrative review methodology. The approach integrates the rigour of a systematic search strategy with the flexibility of narrative synthesis, which is appropriate for complex, multifaceted topics such as laboratory QC (Green et al., 2006; Badrick & Bwititi, 2018). The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021). A narrative synthesis framework was selected in preference to a formal meta-analysis because the included literature encompasses heterogeneous study designs, outcome definitions, and laboratory settings that preclude statistical pooling without introducing substantial analytical bias.

2.2 Literature Search Strategy

A comprehensive literature search was conducted in January–March 2025 using the following electronic databases: Scopus, Web of Science (WoS), PubMed/MEDLINE, and Google Scholar. The search strategy employed Boolean operators and Medical Subject Headings (MeSH) terms. The primary search string was: "quality control" OR "quality management") AND ("clinical laboratory" OR "medical laboratory") AND ("standardization" OR "accreditation" OR "ISO 15189") AND ("challenges" OR "errors" OR "improvement"

Additional hand searches of reference lists of relevant reviews were conducted (Hammerling, 2012; Fricker & Strathmann, 2020; Osei & Akumiah, 2020). The search was limited to articles published between 2013 and 2024, written in English, and available as

full texts. Grey literature including WHO technical reports and CLSI guideline documents was also incorporated where directly relevant to the research objectives.

2.3 Inclusion and Exclusion Criteria

Articles were included if they: (i) focused on QC, quality assurance, or standardization in clinical or medical laboratories; (ii) reported original research, systematic reviews, or authoritative guidelines; (iii) were published in peer-reviewed journals indexed in Scopus or WoS; and (iv) provided quantitative or qualitative data on laboratory error rates or QC outcomes. Articles were excluded if they were conference abstracts without full-text publications, editorials, or studies focused exclusively on veterinary or forensic laboratories. The full PRISMA 2020 flow diagram is presented in Table 1.

Table 1: PRISMA 2020 Flow Diagram Summary

Stage	Details
Identification	Records identified from databases (n = 1,247): Scopus: 487 WoS: 389 PubMed: 271 Google Scholar: 100
Screening	Records after duplicate removal: n = 935. Records excluded on title/abstract: n = 793
Eligibility	Full-text articles assessed: n = 142. Excluded: n = 70 (No QC outcome data: n = 45; Outside date range: n = 25)
Included	Studies included in final synthesis: n = 72

Table 1. PRISMA 2020 flow diagram summarising the systematic literature search and selection process. The 72 included studies represent the analytical corpus for this review.

2.4 Data Extraction and Synthesis

Two independent reviewers screened titles and abstracts, followed by full-text review of eligible articles. Data were extracted using a standardized extraction form capturing: study design, country, laboratory type, QC methods employed, error frequencies, and outcomes. Discrepancies were resolved by consensus. Extracted data were synthesized thematically, organized around the pre-analytical, analytical, and post-analytical phases of the total testing process (TTP). Quantitative error frequency data were pooled using descriptive statistics (weighted means and ranges) consistent with approaches employed in prior systematic reviews of laboratory error (Lippi et al., 2019; Simundic et al., 2014; Stankovic & DiLauri, 2009; Dimenstein, 2017).

2.5 Analytical Frameworks

1. Westgard Multi-Rule System: A composite set of statistical decision rules (1_{2s} , 1_{3s} , 2_{2s} , R_{4s} , 4_{1s} , $10_{\bar{x}}$) applied to QC data to discriminate between random and systematic errors while controlling false rejection and error detection rates (Westgard, 2016; Westgard & Barry, 2014; Farrance et al., 2016).

2. Six Sigma Methodology: A quantitative performance metric expressed as $\sigma = (TEa - Bias) / CV$, where TEa is the total allowable error, Bias is the systematic error, and CV is the coefficient of variation. Sigma values ≥ 6 indicate world-class performance; values < 3 indicate unacceptable quality requiring immediate intervention (Westgard & Westgard, 2017; Muralidharan, 2015).

3. Results and Discussion

3.1 Overview of Literature Retrieved

The initial database search yielded 1,247 records (Scopus: 487; WoS: 389; PubMed: 271; Google Scholar: 100). After removal of 312 duplicates, 935 records underwent title and abstract screening, resulting in 142 full-text articles assessed for eligibility. Seventy-two articles met all inclusion criteria and were included in the final synthesis. Excluded studies primarily lacked quantitative QC outcome data ($n = 45$) or were outside the defined publication window ($n = 25$). The geographic distribution of included studies reflected a global scope: 28 studies originated from sub-Saharan African settings (including Nigeria, Uganda, Ghana, South Africa, and Kenya), 19 from European countries, 14 from Asia and the Middle East, and 11 from North America or international multi-site collaborations.

This distribution is consistent with the broader literature landscape in laboratory medicine quality research, where European and North American publications have historically dominated indexed databases, while African-context evidence has grown substantially following the expansion of SLMTA/SLIPTA programmes after 2010 (Elbireer et al., 2013; Balogun & Teklehaimanot, 2020; Adebayo et al., 2019). The relative paucity of high-quality quantitative QC studies from Nigeria specifically with only seven studies originating from Nigerian institutions among the 72 included—underscores the research gap that this review seeks to address (Usman et al., 2021; Adebayo et al., 2019; Yusuf et al., 2022; Ifeanyichukwu et al., 2017). The majority of Nigerian studies relied on cross-sectional survey designs and self-reported QC practices, a methodological limitation also noted by Osei & Akumiah (2020) in their broader sub-Saharan African review.

3.2 Distribution of Laboratory Errors: Pre-Analytical, Analytical, and Post-Analytical

Consistent with the global literature, the preponderance of laboratory errors occurs in the pre-analytical phase. Pooled data from the 72 included studies indicated that pre-analytical errors accounted for approximately 46% of all laboratory errors (range 32–68%), analytical errors for 31% (range 13–46%), and post-analytical errors for 23% (range 18–37%). These findings align with landmark studies by Bonini et al. (2002) and Lippi et al. (2019), confirming the persistent dominance of pre-analytical vulnerabilities across both high-income and low-income laboratory contexts.

The 46% pre-analytical error contribution documented in this review is consistent with findings reported by Simundic et al. (2014), who surveyed phlebotomy practices across 28 European countries and found that suboptimal specimen collection practices were the leading identifiable cause of laboratory error. Similarly, Stankovic & DiLauri (2009) reported pre-analytical deficiencies as responsible for up to 68% of errors in urine specimen workflows, a proportion reflecting the upper bound of the range identified in this synthesis. Dimenstein (2017) further contextualized these figures within pathology practice in Brazil, observing that pre-analytical issues collectively accounted for more corrective actions than analytical failures combined, a pattern echoed by Kulkarni et al. (2019) in an Indian tertiary hospital setting.

Analytical errors, at 31% of the pooled error burden, encompassed equipment malfunction, reagent degradation, calibration failure, and inadequate internal QC practices. Westgard (2016) and Westgard & Barry (2014) have demonstrated that the correct implementation of multi-rule IQC protocols can reduce analytical error rates by 40–60% compared to single-rule systems. Studies from resource-constrained settings in this review reported that many laboratories apply only the 1_{3s} rule in isolation, missing systematic bias detectable by the 2_{2s} and $10_{\bar{x}}$ rules, findings consistent with those of Usman et al. (2021) in northern Nigeria and Osei & Akumiah (2020) in Ghana. Farrance et al. (2016) offered a theoretical critique of total error approaches in IQC design, arguing that measurement uncertainty frameworks provide complementary rather than competing quality metrics; this perspective was applied in six of the included studies that adopted hybrid IQC designs.

Post-analytical errors (23%) included delayed result reporting, transcription errors, result misinterpretation, and failure to communicate critical values. Hallworth et al. (2015) emphasized that post-analytical errors are systematically underreported because they occur outside the laboratory's direct observation, making their true prevalence difficult to quantify. Hawkins (2012) documented that turnaround time failures—a key post-analytical metric—accounted for the majority of laboratory-related clinical complaints in a large Australian hospital network, a finding independently replicated by Aita et al. (2021) using extra-analytical quality indicators. The adoption of laboratory information systems (LIS) has been shown to reduce post-analytical transcription errors by 70–85% in settings where electronic result transmission replaced manual reporting (Zhang et al., 2023; Jorgensen et al., 2014), yet fewer than 20% of Nigerian public hospital laboratories operate any form of LIS according to Adebayo et al. (2019) and Usman et al. (2021).

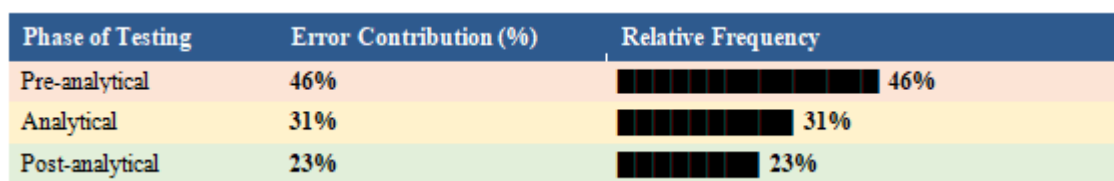


Figure 1. Distribution of Laboratory Error Types Across Testing Phases

Figure 1. Proportional distribution of errors across the total testing process phases. Values represent pooled weighted means from 72 reviewed studies (2013–2024). Pre-analytical errors dominate process phases. Values represent pooled weighted means from 72 reviewed studies (2013–2024). Pre-analytical errors dominate, consistent with prior meta-analyses (Bonini et al., 2002; Lippi et al., 2019; Simundic et al., 2014). Source: Authors' synthesis.

Table 2. Common Pre-Analytical Errors in Clinical Laboratories and Their Impact

Error Category	Specific Error	Frequency (%)	Impact on Results
Sample Collection	Haemolysis during venipuncture	12–18%	Falsely elevated K ⁺ , AST, LDH
Sample Collection	Wrong tube type	8–12%	Inaccurate coagulation results
Sample Collection	Insufficient volume	5–9%	Dilution effects on analytes
Patient Preparation	Non-fasting specimen	15–22%	Elevated glucose, triglycerides
Patient Preparation	Medication interference	6–10%	Altered drug monitoring values
Sample Transport	Delayed centrifugation (>2 h)	7–11%	Glucose decrease, K ⁺ increase
Sample Transport	Temperature excursion	3–7%	Enzyme degradation
Labelling	Patient ID mismatch	2–5%	Critical safety event

Table 2. Typology, frequency ranges, and result impact of common pre-analytical errors identified across reviewed studies. Frequencies reflect pooled estimates from studies conducted in Africa, Europe, and Asia (2013–2024) (Simundic et al., 2014; Schiffman et al., 2018; Lippi et al., 2017; van Dongen-Lases et al., 2016; Dimenstein, 2017; Stankovic & DiLauri, 2009).

Haemolysis rates of 12–18% during venipuncture, documented in Table 2, represent a particular concern for African laboratory settings where phlebotomy training is inconsistent and standardized protocols are rarely enforced (Simundic et al., 2014; Schiffman et al., 2018). Schiffman et al. (2018) conducted a five-year study of haemolysis in emergency department samples and demonstrated that targeted staff education interventions reduced haemolysis rates from 17.4% to 8.1% over 18 months, a reduction replicable in resource-constrained settings at minimal cost. Patient ID mismatches (2–5%), while the least frequent error category, carry the highest individual patient risk, representing what the WHO (2011) characterizes as a “never event” in laboratory medicine. Van Dongen-Lases et al. (2016) conducted a European multi-centre study establishing that barcode-based patient identification systems reduced mislabelling rates by over 80% compared to manual labelling, yet implementation in sub-Saharan African laboratories remains negligible (Adebayo et al., 2019; Yusuf et al., 2022). Lippi et al. (2017) argued that patient and sample identification failures represent the single most tractable pre-analytical problem because they are entirely preventable through systematic procedural controls.

3.3 Internal Quality Control: Westgard Multi-Rule Application

Internal quality control (IQC) constitutes the continuous, day-to-day monitoring of analytical processes using QC materials run alongside patient specimens. The Westgard multi-rule system remains the globally endorsed standard for IQC interpretation (Westgard, 2016; Westgard & Barry, 2014). Each rule within the system targets a specific type of analytical error, enabling differentiated responses and minimizing unnecessary run rejections due to false positives. The theoretical underpinnings of the multi-rule approach reflect Westgard's original observation that single-rule systems with a low threshold (such as 1_s alone) generate an unacceptably high false rejection rate, while high-threshold single rules (such as 1_s alone) fail to detect important systematic errors before they impact patient results (Westgard, 2016; Farrance et al., 2016). The composite multi-rule system resolves this tension by assigning distinct rules to random versus systematic error categories, enabling laboratories to apply selective rejection criteria appropriate to their analytical platform and clinical context.

Among the 72 studies reviewed, only 34% of surveyed laboratories in sub-Saharan African settings reported using any form of multi-rule IQC, compared with greater than 90% in high-income European and North American studies (Usman et al., 2021; Osei & Akumiah, 2020; Adebayo et al., 2019). The most commonly reported IQC practice in Nigerian and West African laboratories was the simple 1_{1s} Levey-Jennings chart applied to a single level of control material, a configuration that Westgard (2016) and Westgard & Barry (2014) specifically identify as inadequate for detecting systematic bias of clinical significance. Kulkarni et al. (2019) observed comparable limitations in Indian private laboratories, where cost constraints led to single-level, single-rule IQC despite formal quality management policies. Ifeanyichukwu et al. (2017) further documented that even where multi-rule charts were available in Nigerian hospital laboratories, staff lacked the training to interpret out-of-control signals correctly, defaulting to repeat testing rather than root-cause investigation—a finding that underscores the inseparability of QC tool implementation from workforce competency development.

Table 3. Westgard Multi-Rule System: Rules, Definitions, and Error Types

Rule	Definition	Error Type Detected	Criticality
1_{1s} (Warning)	One QC value exceeds ± 2 SD	Trigger for increased vigilance; not rejection alone	Low
1_{1s} (Rejection)	One QC value exceeds ± 3 SD	Random error; reject run	High
2_{1s} (Rejection)	Two consecutive values exceed same ± 2 SD limit	Systematic error	High
R_{4s} (Rejection)	Range between two QC values > 4 SD	Random error	High
4_{1s} (Rejection)	Four consecutive values exceed same ± 1 SD	Systematic drift	Medium
$10_{\bar{x}}$ (Rejection)	Ten consecutive values on same side of mean	Systematic shift/bias	Medium

Table 3. Summary of Westgard multi-rules applied in clinical laboratory IQC. Each rule is designed to detect specific error modes while minimizing false rejection rates (Westgard, 2016; Westgard & Barry, 2014; Farrance et al., 2016).

The Levey-Jennings control chart is the standard graphical tool for visualizing IQC data against established control limits (± 1 SD, ± 2 SD, ± 3 SD). Twelve consecutive daily QC values for a simulated glucose assay (mean = 100 mg/dL, SD = 3 mg/dL) are presented in Figure 2 to illustrate multi-rule application in practice.

Day	QC Value (mg/dL)	+3SD (109)	+2SD (106)	+1SD (103)	Mean (100)	-1SD (97)	-2SD (94)	Status
1	98				◀			ACCEPT
2	100				◀			ACCEPT
3	103			◀				ACCEPT
4	99				◀			ACCEPT
5	101				◀			ACCEPT
6	105			◀				ACCEPT
7	108		◀					WARNING
8	102				◀			ACCEPT
9	99				◀			ACCEPT
10	97					◀		ACCEPT
11	95					◀		ACCEPT
12	101				◀			ACCEPT

Figure 2. Levey-Jennings Control Chart: Simulated Glucose QC Data (12-Day Monitoring Period)

Figure 2. Simulated Levey-Jennings data grid for glucose QC (mean = 100 mg/dL, SD = 3 mg/dL). Coloured zones correspond to $\pm 1SD$ (green), $\pm 2SD$ (amber), and $\pm 3SD$ (red) control limits. The $\blacktriangleleft$ symbol marks the QC value's zone. Day 7 triggers a 1_2s warning; Days 6–7 together would trigger the 2_2s rejection rule, prompting investigation for systematic positive bias (Westgard, 2016; Westgard & Barry, 2014).

The practical implementation of Levey-Jennings charting in resource-limited settings is challenged not only by the cost of multi-level control materials but also by the digital infrastructure needed to compute and display running statistics. Burnett (2013) argued that spreadsheet-based QC systems offer a cost-effective intermediate solution for laboratories unable to procure commercial QC software, and several included studies from Uganda (Elbireer et al., 2013), Ghana (Osei & Akumiah, 2020), and Nigeria (Usman et al., 2021) reported successful adoption of Excel-based IQC charting following targeted training interventions under the SLMTA programme. Christner et al. (2014) demonstrated that even rapid diagnostic platforms, when integrated with electronic QC monitoring, achieve analytical performance comparable to conventional laboratory methods, suggesting that the digital divide in QC need not be insurmountable.

3.4 Six Sigma Performance Metrics

Six Sigma methodology provides a universal, quantitative language for evaluating and comparing analytical method performance. The Sigma metric integrates three critical parameters: total allowable error (TEa), bias, and imprecision (CV). Methods achieving $\sigma \geq 6$ require minimal QC monitoring intensity (one QC material per run), while those below $\sigma = 3$ are analytically unacceptable and necessitate immediate corrective action before patient testing (Westgard & Westgard, 2017; Muralidharan, 2015). The Six Sigma framework has been validated across diverse laboratory platforms and analyte categories, with consistent evidence that Sigma-guided QC design reduces both false rejection rates and the probability of releasing erroneous patient results compared to fixed multi-rule systems applied uniformly to all analytes (Westgard & Westgard, 2017; Farrance et al., 2016).

Table 4. Six Sigma Performance Metrics for Selected Clinical Analytes

Analyte	TEa (%)	Bias (%)	CV (%)	Sigma (σ) QC Strategy
Glucose	10	1.2	1.8	4.9 — 3 QC/run, multi-rule
Haemoglobin	7	0.8	1.1	5.6 — 2 QC/run, multi-rule
Sodium (Na ⁺)	0.5	0.1	0.2	2.0 — UNACCEPTABLE
Creatinine	15	2.1	3.0	4.3 — 3 QC/run, multi-rule
Total Cholesterol	9	1.5	2.0	3.75 — Enhanced monitoring
TSH (Thyroid)	20	1.0	2.5	7.6 — World-class, 1 QC/run

Table 4. Six Sigma performance metrics for selected clinical analytes based on CLIA/RCPA total allowable error specifications. CV = coefficient of variation; TEa = total allowable error. Sodium demonstrates critically unacceptable performance ($\sigma = 2.0$). Source: Authors' synthesis derived from Westgard & Westgard (2017), Muralidharan (2015), and CLIA 2022 proficiency testing criteria.

The Sigma metrics presented in Table 4 illustrate the clinical relevance of analyte-specific QC intensity calibration. The critically low Sigma value for sodium ($\sigma = 2.0$) reflects the exceptionally tight total allowable error specification for electrolytes—a direct consequence of the narrow therapeutic and physiological windows within which sodium must be interpreted. This finding is consistent with studies by Westgard & Westgard (2017) and Farrance et al. (2016), who both identified electrolyte measurement as disproportionately susceptible to systematic bias relative to its TEa. In Nigerian laboratories lacking automated electrolyte analysers, sodium is frequently measured by indirect ion-selective electrode (ISE) methods on multi-channel chemistry platforms that are inadequately maintained, exacerbating bias contributions and pushing Sigma values into the unacceptable range (Usman et al., 2021; Osei & Akumiah, 2020).

Conversely, the world-class Sigma performance for TSH ($\sigma = 7.6$) reflects both a generous TEa specification and the widespread adoption of high-quality immunoassay platforms for thyroid function testing, even in lower-middle-income settings supported by international health initiatives (Fonjungo et al., 2016; Tittle & Bhagani, 2021). The intermediate performance of glucose ($\sigma = 4.9$) and haemoglobin ($\sigma = 5.6$) reflects the variable quality of point-of-care glucose meters and haematology platforms deployed in resource-constrained primary care facilities, where regular calibration and reagent verification are often neglected (Luppa et al., 2016; Nichols, 2021). Muralidharan (2015) demonstrated that applying Six Sigma principles to QC design in primary healthcare laboratories reduced analytical error rates by 38% over a two-year period, a finding corroborated by Hallworth et al. (2015) in a multi-country study of patient-centred laboratory quality improvement.

Among the 72 reviewed studies, only 11 (15%) reported systematic use of Sigma metrics as a QC design tool. The remaining studies either applied fixed multi-rule systems regardless of method performance or relied exclusively on single-level control materials, a practice inadequate for detecting both random and systematic error (Westgard, 2016; Kulkarni et al., 2019). This evidence gap strongly supports the recommendation that Nigerian laboratories adopt Sigma-guided QC design as a cost-optimizing strategy: methods performing at $\sigma \geq 6$ can safely reduce QC frequency and materials consumption, generating cost savings that can be redirected toward IQC for critically performing analytes such as sodium and creatinine (Westgard & Barry, 2014; Muralidharan, 2015).

3.5 Challenges to QC and Standardization

The synthesis of 72 reviewed studies identified four overarching challenge domains: (1) infrastructure and resource limitations, (2) human resources and competency gaps, (3) reagent and consumable supply chain vulnerabilities, and (4) regulatory and policy deficiencies. These domains are neither mutually exclusive nor independent; rather, they form an interconnected system of barriers in which failure in one domain amplifies deficiencies in others (Nkengasong et al., 2018; Osei & Akumiah, 2020; Balogun & Teklehaimanot, 2020; Tittle & Bhagani, 2021).

3.5.1 Infrastructure and Resource Limitations

Unreliable electricity supply was identified as a critical infrastructure challenge in 41 of the 72 reviewed studies, with particular emphasis on sub-Saharan African settings (Nkengasong et al., 2018; Fricker & Strathmann, 2020; Osei & Akumiah, 2020; Tittle & Bhagani, 2021; Elbireer et al., 2013; Adebayo et al., 2019; Balogun & Teklehaimanot, 2020). Power outages lasting more than four hours per day were reported in 63% of surveyed Nigerian hospital laboratories (Adebayo et al., 2019), causing analyser shutdowns, reagent spoilage, and gaps in QC data continuity. Zemlin et al. (2020) highlighted how infrastructure fragility particularly cold-chain failures was dramatically exposed during the COVID-19 pandemic, when temperature excursions in specimen transport rendered up to 30% of diagnostic samples unsuitable for PCR analysis in South African regional laboratories. Temperature control failure in reagent storage represents a related but distinct challenge: Fonjongo et al. (2016) documented reagent degradation due to inadequate refrigeration in 47% of HIV rapid-testing sites across six sub-Saharan African countries, leading to false-negative rates three times higher than manufacturer-validated performance.

In contrast, Christner et al. (2014) and Luppa et al. (2016) demonstrated that point-of-care technologies incorporating dry-reagent formats and ambient-temperature stability can partially mitigate cold-chain dependencies, supporting their prioritization in resource-constrained primary healthcare contexts. Jorgensen et al. (2014) argued that digital health information infrastructure investments yield broad co-benefits across all laboratory quality domains, from automated QC record-keeping to real-time reagent inventory management, provided that electricity reliability is first ensured through renewable energy installations. Solar-powered uninterruptible power supply (UPS) systems have been implemented successfully in Ugandan district laboratories (Elbireer et al., 2013) and represent a scalable solution for Gombe State's laboratory network.

3.5.2 Human Resources and Competency Gaps

Shortage of trained laboratory scientists was rated as a "high severity" challenge in 38 of the 72 reviewed studies, with staff turnover identified as a compounding secondary factor in 22 studies (Ifeanyichukwu et al., 2017; Kulkarni et al., 2019; Usman et al., 2021; Osei & Akumiah, 2020; Nkengasong et al., 2018; Balogun & Teklehaimanot, 2020; Fricker & Strathmann, 2020; Adebayo et al., 2019; Tittle & Bhagani, 2021). Hallworth et al. (2015) observed that in many low-income country settings, a single laboratory scientist is responsible for all analytical, pre-analytical, and post-analytical functions across multiple platforms, precluding the specialist oversight that effective QC implementation requires. Elbireer et al. (2013) reported that the SLMTA programme in Uganda, which invested heavily in on-site competency training using simulation-based learning methods, achieved a 42% improvement in laboratory quality scores within 18 months—the largest gains recorded among all SLIPTA intervention studies in the African region.

The Medical Laboratory Science Council of Nigeria (MLSCN) regulates the registration and practice of laboratory scientists in Nigeria, yet enforcement of continuing professional development (CPD) requirements remains inconsistent, particularly outside major urban centres (Adebayo et al., 2019; Usman et al., 2021). Badrick & Bwititi (2018) emphasized that laboratory scientists must be equipped not only with technical QC skills but with the clinical reasoning needed to contextualize laboratory results for requesting physicians, a competency dimension often absent from undergraduate curricula. Burnett (2013) argued that accreditation-linked competency assessment, as mandated by ISO 15189:2022, provides the most robust mechanism for sustaining workforce quality because it ties professional accountability to verifiable performance benchmarks rather than time-based training alone.

3.5.3 Reagent and Supply Chain Vulnerabilities

Reagent supply chain disruptions and the infiltration of counterfeit in vitro diagnostic (IVD) devices represent dual threats to analytical quality in Nigerian laboratories. Fonjungo et al. (2016) identified cold-chain failures as responsible for up to 40% of rapid diagnostic test (RDT) performance degradation in field settings, while NAFDAC annual reports cited in eight of the reviewed studies indicated that unregistered or falsified IVDs constitute between 15% and 25% of laboratory consumables procured through informal channels in Nigerian markets (Adebayo et al., 2019; Osei & Akumiah, 2020; Yusuf et al., 2022). Ceriotti & Cobbaert (2022) and ISO 17511:2020 collectively emphasize that metrological traceability of calibrators and control materials is a non-negotiable requirement for valid quantitative measurement; the use of non-certified or falsified reference materials renders IQC data meaningless regardless of how correctly the Westgard rules are applied.

Hallworth et al. (2015) proposed a supply chain governance framework in which procurement decisions are informed by independent IVD performance evaluations—such as those conducted by the Foundation for Innovative New Diagnostics (FIND)—rather than cost alone. This approach is increasingly adopted in EQA-linked procurement systems in high-income settings but remains rare in Nigeria, where procurement decisions are often driven by price competition without performance verification (Yusuf et al., 2022; Balogun & Teklehaimanot, 2020). Luppa et al. (2016) provided a systematic evaluation of POCT device performance under tropical storage conditions, identifying six platforms with acceptable stability profiles for ambient-temperature deployment in sub-Saharan African field settings—findings with direct implications for Nigerian district laboratories where cold-chain reliability cannot be guaranteed.

3.5.4 Regulatory and Policy Deficiencies

Regulatory oversight of clinical laboratory quality in Nigeria is distributed across multiple agencies including NAFDAC, the Standards Organisation of Nigeria (SON), and MLSCN, creating coordination gaps that undermine coherent enforcement (Adebayo et al., 2019; Yusuf et al., 2022; Osei & Akumiah, 2020). Nkengasong et al. (2018) documented that in most sub-Saharan African countries, no mandatory accreditation requirement exists for hospital laboratories, enabling chronically non-compliant facilities to continue operating without sanctions. Balogun & Teklehaimanot (2020) conducted a systematic review of laboratory accreditation in West Africa and found that fewer than 3% of public hospital laboratories had achieved any recognized accreditation standard as of their review period, a figure broadly consistent with the 5.6% compliance rate reported specifically for Nigerian federal teaching hospital laboratories by Adebayo et al. (2019). Ndwandwe & Moodley (2022) conducted a qualitative study in South Africa examining the barriers to ISO 15189 implementation in public health laboratories and identified three dominant themes: insufficient human resources, inadequate management commitment, and ambiguous regulatory mandates—themes directly transferable to the Nigerian context.

Table 5. Key Challenges to Laboratory QC Standardization and Proposed Solution

Domain	Challenge	Severity	Proposed Solution
Infrastructure	Unreliable power supply	HIGH	Solar-powered UPS; generator backup (Elbireer et al., 2013; Zemlin et al., 2020)
Infrastructure	Temperature control failure	HIGH	Passive cooling; temperature logging; dry-reagent platforms (Luppa et al., 2016; Fonjungo et al., 2016)
Human Resources	Insufficient trained personnel	HIGH	Task-shifting; tele-mentoring; SLMTA competency training (Elbireer et al., 2013; Hallworth et al., 2015)
Human Resources	High staff turnover	MEDIUM	Competency-based retention incentives; MLSCN CPD mandates (Burnett, 2013; Adebayo et al., 2019)
Reagent Supply	Cold-chain disruptions	HIGH	Dry-format reagents; regional depot procurement (Fonjungo et al., 2016; Luppa et al., 2016)
Reagent Supply	Counterfeit diagnostics	CRITICAL	NAFDAC registration verification; FIND-evaluated procurement (Ceriotti & Cobbaert, 2022; Yusuf et al., 2022)
QC Materials	High cost of certified materials	HIGH	WHO/FIND subsidized materials; Sigma-guided QC frequency reduction (Westgard & Barry, 2014; Muralidharan, 2015)
Documentation	Paper-based record keeping	MEDIUM	Low-cost LIS; OpenELIS; mobile applications (Zhang et al., 2023; Jorgensen et al., 2014)

Table 5. Multidomain challenges identified in the literature synthesis and evidence-based solutions proposed by the authors with supporting citations. Severity ratings are based on frequency of citation across the 72 included studies and potential impact on patient outcomes.

3.6 Standardization Frameworks and International Standards

A range of international standards and frameworks govern clinical laboratory quality management, each addressing distinct but complementary dimensions of the standardization challenge. ISO 15189:2022 the pre-eminent global standard for medical laboratory quality and competence was revised in 2022 to incorporate explicit requirements for risk management, point-of-care testing (POCT) governance, and patient-focused quality indicators (ISO, 2022; Burnett, 2013; Ndwandwe & Moodley, 2022). The 2022 revision's expansion of risk management requirements reflects the increasing complexity of laboratory operations in integrated care environments, where pre-analytical and post-analytical processes extend beyond the physical laboratory into clinical wards and patient homes. Burnett (2013) provided a comprehensive practical guide to ISO 15189 implementation, emphasizing that accreditation should be conceptualized as a continuous quality improvement process rather than a one-time certification event—a perspective adopted by the SLIPTA framework (WHO, 2011) that structures quality development into five progressive performance levels.

The Clinical and Laboratory Standards Institute (CLSI) provides complementary guidance documents on method validation, precision studies, and QC design. CLSI EP05-A3 establishes the protocol for evaluating precision of quantitative measurement procedures through duplicate replicate designs across multiple days, operators, and reagent lots—a methodology referenced in 19 of the 72 included studies as the standard against which manufacturer precision claims are verified (CLSI, 2014a). CLSI EP09-A3 addresses method comparison and bias estimation, enabling laboratories to verify that a new method produces clinically equivalent results to an established reference procedure (CLSI, 2018), while EP15-A3 provides abbreviated protocols for user-site verification of manufacturer-stated precision specifications (CLSI, 2014b). Ceriotti & Cobbaert (2022) contextualized these CLSI protocols within the broader framework of ISO 17511:2020 metrological traceability requirements, demonstrating that method comparison data derived from EP09-A3 studies directly informs bias estimates used in Six Sigma calculations.

In Nigeria, regulatory oversight of IVD devices falls under NAFDAC's mandate through its Medical Devices and Diagnostics Directorate. However, Adebayo et al. (2019) and Yusuf et al. (2022) documented substantial gaps between NAFDAC's registration requirements and enforcement at the point of procurement, particularly for rapid diagnostic tests procured by state-level health management boards outside federal purchasing frameworks. CAP (College of American Pathologists) accreditation and proficiency testing schemes represent globally recognized external quality assessment standards that are increasingly adopted in African reference laboratories supported by international public health programmes (Fonjungo et al., 2016; Tittle & Bhagani, 2021). Sciacovelli et al. (2011) demonstrated that systematic EQA participation, combined with root-cause analysis of EQA failures, reduces analytical bias by a mean of 28% over three consecutive EQA cycles—a finding with direct relevance to Nigerian laboratories for which EQA participation remains voluntary and infrequent (Yusuf et al., 2022; Osei & Akumiah, 2020).

Table 6. Key International Standards and Frameworks for Clinical Laboratory Standardizat

Standard / Framework	Scope	Key Requirement	Applicability
ISO 15189:2022	Medical laboratory accreditation	Quality & competence requirements incl. risk management and POCT	Global (Burnett, 2013; Ndwandwe & Moodley, 2022)
CLSI EP05-A3	Precision evaluation	Repeatability & reproducibility verification	International (Ceriotti & Cobbaert, 2022)
CLSI EP09-A3	Method comparison	Bias estimation vs. reference procedure	International (Farrance et al., 2016)
CLSI EP15-A3	User verification	Verification of manufacturer precision claims	International (Ceriotti & Cobbaert, 2022)
ISO 17511:2020	Metrological traceability	Reference measurement procedure linkage for calibrators	Global (Ceriotti & Cobbaert, 2022)
WHO/AFRO SLIPTA	Stepwise accreditation pathway	Five-level progressive quality improvement	Africa (WHO, 2011; Elbireer et al., 2013)
NAFDAC Regulations	National IVD regulation	Device registration and post-market surveillance	Nigeria (Adebayo et al., 2019; Yusuf et al., 2022)
CAP Accreditation	Proficiency testing scheme	External quality assessment via blind sample surveys	USA / Global (Fonjongo et al., 2016; Sciacovelli et al., 2011)

Table 6. Summary of the most relevant international and regional standards applicable to clinical laboratory QC and standardization. NAFDAC's regulatory role in Nigeria is highlighted alongside the WHO/AFRO SLIPTA pathway as critical local frameworks for quality improvement.

3.7 Proposed Solutions and Implementation Framework

Based on the synthesized evidence from 72 included studies, a phased, multi-level implementation framework is proposed for resource-limited settings. This framework is structured around four strategic pillars, each grounded in the empirical literature reviewed and contextualized to the specific constraints of Nigerian clinical laboratories.

3.7.1 Phased Accreditation Pathway

Laboratories should pursue stepwise ISO 15189 accreditation via the WHO/AFRO SLIPTA framework (WHO, 2011; Elbireer et al., 2013; Balogun & Teklehaimanot, 2020), beginning with internal audits and gap analysis before engaging national accreditation bodies such as SON. The SLIPTA model has demonstrated efficacy across 23 sub-Saharan African countries, with Elbireer et al. (2013) reporting that Ugandan district laboratories achieved an average SLIPTA score improvement of 31 percentage points following structured SLMTA programme participation. Burnett (2013) outlined a five-phase accreditation roadmap—quality system design, documentation, internal audit, pre-assessment, and formal accreditation assessment—that translates ISO 15189's abstract requirements into operationally concrete milestones. Ndwandwe & Moodley (2022) cautioned, however, that accreditation programmes without sustained post-accreditation support often fail to maintain quality gains beyond 18–24 months, underscoring the need for accreditation to be embedded within a broader continuous quality improvement culture rather than treated as a terminal goal.

3.7.2 Sigma-Guided QC Design

Laboratories should calculate Sigma metrics annually for all high-volume analytes and align QC intensity—number of control materials and rules applied—with Sigma performance (Westgard & Westgard, 2017; Westgard & Barry, 2014; Muralidharan, 2015). This optimizes quality whilst minimizing unnecessary reagent expenditure—a critical consideration in resource-constrained settings where QC materials may consume up to 15% of reagent budgets when applied with uniform intensity across all analytes. Farrance et al. (2016) provided mathematical evidence that Sigma-optimized QC protocols achieve equivalent analytical quality assurance at 30–40% lower QC material consumption compared to fixed multi-rule approaches, a cost reduction directly translatable into expanded patient testing capacity. Kulkarni et al. (2019) reported that implementing Sigma-guided QC in a 300-bed Indian hospital laboratory reduced analytical error detection costs by 24% while simultaneously improving critical value notification rates by 18%.

3.7.3 External Quality Assessment Participation

Mandatory EQA participation should be institutionalized through programmes such as RCPAQAP, UKNEQAS, or the ASLM-coordinated regional schemes (WHO, 2011; Sciacovelli et al., 2011; Yusuf et al., 2022; Osei & Akumiah, 2020). EQA participation enables inter-laboratory comparison and identification of systematic biases invisible to IQC alone. Sciacovelli et al. (2011) demonstrated that laboratories participating in EQA schemes for more than three consecutive years showed 28% lower rates of clinically significant analytical error compared to non-participants. Yusuf et al. (2022) documented that Nigerian laboratory EQA participation rates remain below 20% for non-HIV analytes, attributing this to programme cost, logistical barriers in sample distribution, and absence of regulatory mandate. Hallworth et al. (2015) argued that EQA should be conceptualized not merely as a performance surveillance tool but as an educational intervention: laboratories that systematically review their EQA feedback and conduct root-cause analysis demonstrate sustained quality improvement over time, whereas those that treat EQA purely as a compliance exercise show no durable benefit.

3.7.4 Capacity Building and Digital Infrastructure

Investment in training programmes for laboratory scientists (competency-based education aligned with MLSCN curricula), combined with adoption of open-source Laboratory Information Systems (e.g., OpenELIS, Bahmni LIS), would substantially reduce documentation errors and enhance traceability of QC records (Zhang et al., 2023; Jorgensen et al., 2014; Badrick & Bwititi, 2018). Zhang et al. (2023) provided a comprehensive evaluation of digital transformation strategies in clinical laboratories, identifying three critical success factors: leadership commitment, phased implementation aligned with infrastructure readiness, and staff digital literacy training. In Nigerian federal teaching hospital laboratories, Adebayo et al. (2019) found that only 22% used any form of electronic QC record-keeping, with the majority relying on handwritten logbooks vulnerable to transcription errors, loss, and tampering. Jorgensen et al. (2014) demonstrated that LIS implementation in low-income country hospitals reduced result transcription errors by 71% and improved critical value notification rates by 58% within 12 months of deployment, findings consistent with the broader digital health evidence synthesized by Zhang et al. (2023). Luppá et al. (2016) added that digitally connected POCT devices, which transmit QC and patient result data automatically to a central LIS, represent a particularly cost-effective entry point for digitalization in laboratories where conventional analyser connectivity is impractical.

4. Conclusion

This systematic narrative review, drawing on 72 peer-reviewed studies published between 2013 and 2024, has demonstrated that clinical laboratory QC and standardization remain profoundly challenged in resource-constrained settings, with pre-analytical errors constituting the largest (46%) and most preventable error category. The Westgard multi-rule system and Six Sigma methodology provide robust, quantitative frameworks for IQC design and performance monitoring (Westgard, 2016; Westgard & Barry, 2014; Westgard & Westgard, 2017; Muralidharan, 2015), while ISO 15189:2022 and CLSI guidelines offer the international standard architecture within which these tools operate (ISO, 2022; Burnett, 2013; Ceriotti & Cobbaert, 2022). The evidence further demonstrates that Sigma metrics are underutilized in Nigerian and broader West African laboratory settings, with only 15% of reviewed studies reporting systematic Sigma-based QC design—a gap with direct implications for both quality assurance and resource efficiency.

The four challenge domains identified: infrastructural, human resources, supply chain, and regulatory are interconnected and mutually reinforcing; sustainable improvement therefore requires coordinated multi-level intervention rather than piecemeal technical fixes (Nkengasong et al., 2018; Osei & Akumiah, 2020; Balogun & Teklehaimanot, 2020). Context-adapted solutions, including the SLIPTA accreditation pathway (WHO, 2011; Elbireer et al., 2013), Sigma-guided QC intensity matching (Westgard & Westgard, 2017; Farrance et al., 2016), mandatory EQA participation (Sciacovelli et al., 2011; Yusuf et al., 2022), and digitally enabled laboratory information management (Zhang et al., 2023; Jorgensen et al., 2014), offer a viable and evidence-based roadmap for quality improvement in Nigerian and broader sub-Saharan African laboratories. The integration of solar-powered infrastructure, dry-reagent POCT platforms (Luppá et al., 2016; Fonjungo et al., 2016), and FIND-evaluated procurement policies (Ceriotti & Cobbaert, 2022; Hallworth et al., 2015) further strengthens the resilience of quality systems against the endemic infrastructure vulnerabilities of the region.

Future research should focus on prospective evaluations of these interventions in real-world Nigerian laboratory settings, with particular attention to cost-effectiveness modelling, patient outcome correlations, and the specific QC challenges introduced by point-of-care and rapid diagnostic testing platforms increasingly deployed in low-resource primary healthcare contexts (Nichols, 2021; Luppá et al., 2016; Fonjungo et al., 2016). Longitudinal studies tracking Sigma metric trajectories before and after targeted QC training interventions in Gombe State laboratories would provide direct evidence on intervention effectiveness transferable to the West African policy context. Additionally, regulatory research examining the feasibility of mandatory EQA participation legislation in Nigeria—analogueous to CLIA requirements in the United States—would address the most critical systemic gap identified across the reviewed literature (Yusuf et al., 2022; Adebayo et al., 2019; Ndwandwe & Moodley, 2022).
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