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Integrated Laboratory and Clinical Evaluation of Antidiabetic and Antihypertensive Medicines in Osun State, Nigeria: Linking Pharmaceutical Care, Biomarkers, and Drug Safety in Routine Care

Omoleye Olusola Gabriel *

Department of Pharmacy, Obafemi Awolowo University, Ile Ife, Nigeria.

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Abstract

Type 2 diabetes mellitus (T2DM) and hypertension commonly coexist and require lifelong pharmacotherapy. In routine care, outcomes may be undermined by variable medicine quality, suboptimal adherence, limited biomarker monitoring, and weak detection and reporting of adverse drug reactions (ADRs). This study evaluated the laboratory quality performance of commonly used antidiabetic and antihypertensive medicines circulating in Osun State, Nigeria, and examined real-world clinical outcomes, pharmaceutical care indicators, biomarkers, and drug safety among patients receiving these therapies. An integrated design with two coordinated streams was implemented. In the laboratory stream, antidiabetic and antihypertensive samples were obtained from facility pharmacies and private-sector outlets and assessed using compendial-style methods for product identification, assay (content), and dissolution performance. In the clinical stream, adults with diagnosed T2DM and/or hypertension receiving at least one antidiabetic and/or antihypertensive medicine were enrolled from selected outpatient facilities and followed over a defined period. A structured pharmacist-led pharmaceutical care workflow was embedded into dispensing and follow-up, including medication review, adherence support, counseling on correct use and safety, and systematic identification of medication-related problems. Clinical effectiveness was evaluated using blood pressure and glycemic indicators (HbA1c where available and fasting plasma glucose where applicable), alongside safety-relevant biomarkers such as renal function indices and electrolytes where feasible. Active safety surveillance was conducted through structured elicitation and documentation of suspected ADRs, with clinical escalation pathways for serious events. Where possible, patient-used products were linked to laboratory-tested samples using brand and batch identifiers to support exploratory integration analyses. Laboratory findings indicated high identity compliance with measurable noncompliance in assay and/or dissolution in a subset of samples, more frequently observed among products sourced from private-sector outlets than facility pharmacies. Clinically, adherence and key outcomes improved with pharmaceutical care, while ADR surveillance identified a meaningful burden of mostly mild-to-moderate reactions with a preventable component. These results support integrating risk-based post-market surveillance, pharmaceutical care, biomarker monitoring, and pharmacovigilance to improve effectiveness and safety of cardiometabolic therapy in Osun State.

Keywords: Diabetes Mellitus; Hypertension; Pharmaceutical Care; Post-Market Surveillance; Medicine Quality; Dissolution; Assay; Biomarkers; Pharmacovigilance; Adverse Drug Reactions; Nigeria; Osun State.

1. Introduction

Type 2 diabetes mellitus (T2DM) and hypertension are highly prevalent, frequently co-existing chronic diseases that substantially increase the risk of cardiovascular events, stroke, and chronic kidney disease, particularly where continuity of care, laboratory monitoring, and long-term medication support are constrained. In Nigeria, the diabetes burden is rising: the International Diabetes Federation (IDF) Atlas estimates 3.0 million adults (20–79 years) living with

* Corresponding author: Omoleye Olusola Gabriel

diabetes in 2024, with projections increasing to 6.6 million by 2050 [1]. Hypertension is even more widespread; the nationwide Removing the Mask on Hypertension (REMAH) survey (2017–2018) provides contemporary national evidence on prevalence, awareness, treatment and control patterns and highlights the scale of the hypertension burden across regions and settings [2]. In routine practice, many adults therefore require long-term combined antidiabetic and antihypertensive therapy, making real-world effectiveness dependent on medicine quality, adherence, clinical monitoring with biomarkers, and safety surveillance. Current standards of care emphasize individualized therapy and structured monitoring to guide treatment intensification and reduce complications. The American Diabetes Association (ADA) *Standards of Care in Diabetes-2025* outlines evidence-based approaches to pharmacologic treatment and the need for ongoing evaluation of glycemic response and related risk factors in real-world care [3]. Translating these standards into measurable outcomes requires reliable assessment of clinical control (e.g., HbA1c/fasting glucose and blood pressure targets) and cardiometabolic/organ protection biomarkers (e.g., renal function indices and electrolytes where ACE inhibitors/ARBs and diuretics are used). In settings where patients obtain medicines through multiple supply channels, however, clinical outcomes may be influenced not only by prescribing and adherence but also by the quality performance of the products actually consumed.

Concerns about substandard and falsified medical products remain a critical public-health issue. The World Health Organization (WHO) notes that such products occur across therapeutic categories and countries, can lead to treatment failure and patient harm, and undermine trust in health systems [4]. For chronic diseases like diabetes and hypertension where medicines are taken daily for years variability in assay/content or dissolution performance can plausibly contribute to sustained under-treatment, unnecessary dose escalation, unstable control, and avoidable adverse outcomes. Accordingly, post-market medicine quality evaluation using recognized quality-management practices is an important complement to clinical monitoring. Beyond product quality, medication-use behaviors and follow-up systems strongly influence outcomes. WHO's report on adherence to long-term therapies underscores that poor adherence is a major determinant of suboptimal chronic disease outcomes and that health-system interventions are required to improve long-term medicine use [5]. This aligns with the rationale for pharmaceutical care, where pharmacists provide structured medication review, adherence support, counseling, and ongoing follow-up to optimize therapy and reduce medicine-related problems. The International Pharmaceutical Federation (FIP) frames people-centred pharmaceutical care as a professional policy priority aimed at optimizing medication use and health outcomes [6]. Evidence syntheses also support clinical benefit: systematic reviews and meta-analyses show that pharmacist-led interventions in primary/outpatient care can improve glycemic control (including reductions in HbA1c) among adults with T2DM compared with usual care [7]. Drug safety is the third critical pillar in combined diabetes–hypertension management, given polypharmacy, predictable adverse effect profiles (e.g., hypoglycemia risk with sulfonylureas/insulin; edema with dihydropyridine calcium channel blockers; electrolyte disturbances with diuretics; hyperkalemia with ACE inhibitors/ARBs), and preventable drug-drug interactions. Strengthening safety monitoring requires systematic elicitation and documentation of suspected adverse drug reactions (ADRs), causality assessment, and reporting through national pharmacovigilance systems. In Nigeria, NAFDAC's *Nigerian Guidelines for Detecting & Reporting of Adverse Reactions for Pharmaceutical Products and Medical Devices* provides guidance on detecting/classifying adverse reactions and describes reporting pathways to the National Pharmacovigilance Center [8]. Embedding ADR screening and reporting processes within routine pharmaceutical care and linking them to biomarker monitoring offers a practical route to improve patient safety while strengthening surveillance.

Importantly, these domains (medicine quality testing, clinical effectiveness, pharmaceutical care processes, biomarkers, and drug safety) are often studied separately. An integrated approach is needed to generate decision-relevant evidence for clinicians, pharmacists, and regulators—particularly in Osun State by simultaneously (i) verifying the laboratory quality of commonly used antidiabetic and antihypertensive products in circulation and (ii) evaluating real-world clinical control and safety outcomes among patients using these products under routine care. WHO guidance on good practices for pharmaceutical quality control laboratories provides a quality-management foundation for reliable post-market testing [9], while ICH Q2(R2) provides internationally recognized expectations for validating analytical procedures used for assay, identity, impurity, and related testing [10]. Against this background, an integrated laboratory–clinical–pharmaceutical care evaluation in Osun State can help clarify how medicine quality, adherence support, biomarker monitoring, and pharmacovigilance together shape the effectiveness and safety of chronic cardiometabolic pharmacotherapy.

2. Literature review

2.1. Burden of diabetes–hypertension comorbidity and local relevance (Nigeria/Osun)

Diabetes mellitus (DM) and hypertension frequently co-exist and synergistically accelerate cardiovascular and kidney complications, making integrated evaluation of treatment effectiveness and safety a priority in routine care and

research [1], [6]. In Nigeria, the REMAH nationwide survey (2017–2018) reported a high age-standardized prevalence of hypertension and highlighted persistent gaps in treatment and control findings consistent with broader concerns about chronic disease management capacity in primary care settings [6]. For Osun State specifically, community-based data from rural communities (Alajue/Obokun) show that hypertension is a measurable public-health burden even outside major urban centers, reinforcing the need for state-level evidence on the quality and outcomes of antihypertensive therapy [40].

2.2. Guideline-driven therapeutic goals and the role of biomarkers in evaluating care

International guidelines emphasize objective biomarker-driven monitoring to assess effectiveness, titrate therapy, and reduce preventable harm in DM and hypertension management. For hypertension, the 2020 ISH global guideline and WHO HEARTS technical package support standardized, protocol-based treatment approaches suitable for low-resource settings, including clearer pathways for intensification and follow-up [29], [30]. For diabetes, ADA Standards of Care provide current recommendations for pharmacologic treatment selection and cardiovascular risk management, including the need to concurrently address BP, lipids, and kidney risk in people with DM [3]. Biomarkers commonly used to operationalize "clinical evaluation" in integrated DM–hypertension studies include: glycemic control (e.g., HbA1c/SMBG metrics), BP measurements, lipid profile (ASCVD risk), and kidney markers such as serum creatinine/eGFR and albuminuria. Kidney-focused guidance (KDIGO 2022) further clarifies how CKD can alter interpretation of HbA1c and stresses structured monitoring to prevent drug-related harms while optimizing cardio–renal protection [31]. These biomarker domains provide measurable endpoints for comparing outcomes across facilities and patient subgroups when pharmaceutical care services (education, adherence support, medication review) are integrated into routine dispensing and follow-up.

2.3. Medicine quality (laboratory evaluation) as a determinant of real-world effectiveness

A key reason laboratory evaluation remains essential in LMIC settings is that therapeutic failure may arise not only from poor adherence or inadequate titration, but also from substandard and falsified (SF) medicines in the supply chain [4], [15]. WHO's global surveillance work has documented SF products as a persistent threat, while more recent Africa-focused reviews describe how regulatory capacity, supply-chain complexity, and market pressures sustain exposure risk affecting therapeutic classes that include antihypertensives and antidiabetics [15], [16]. Nigeria-specific evidence supports the feasibility and importance of pharmacopeia-aligned testing. For example, laboratory assessment of commonly used antihypertensives (including generic amlodipine/lisinopril) has been reported as a practical post-market quality approach, directly relevant to everyday prescribing in public and private settings [11]. For antidiabetic medicines, a large multi country sub-Saharan African evaluation (DIABDAF) reported a substantial proportion of poor-quality antidiabetic drug samples, underlining that diabetes therapies are also vulnerable to quality failures across the region [14]. In Nigeria, in-vitro quality evaluation of metformin brands (assay/physicochemical performance) has also been documented, supporting the logic of including metformin often first-line in laboratory surveillance panels [12], [13].

2.4. Post-marketing surveillance frameworks and laboratory quality systems

A "Scopus-standard" laboratory component typically aligns with recognized sampling/testing governance (risk-based sampling, chain-of-custody, confirmatory methods, and transparent reporting). Nigeria's regulator has issued detailed post-marketing surveillance guidance describing PMS as a regulatory function to continuously monitor medicine quality and safety throughout the supply chain and outlining structured steps from protocol design through sampling and lab analysis [17]. Internationally, WHO guidance on quality control laboratories emphasizes ISO/IEC 17025-aligned quality systems and competent analytical practices for medicines testing, with updated technical guidance released in 2024 [18]. WHO also provides technical guidance on the analysis of medicines samples in post-marketing contexts, including risk-based surveillance logic that complements national PMS programs [19]. Complementary operational resources (e.g., USP risk-based postmarketing surveillance implementation guides) support pragmatic designs that combine field screening and confirmatory testing useful for state-level programs constrained by cost and capacity [20]. Analytical validity is central when the study claims "laboratory evaluation." Contemporary method validation expectations (accuracy, precision, specificity, linearity, robustness, etc.) are summarized in ICH Q2(R2) (adopted 1 Nov 2023), supporting defensible assay and impurity testing where applicable [10].

2.5. Pharmaceutical care integration: evidence for improving outcomes in diabetes and hypertension

Pharmaceutical care (PC) models medication therapy management, adherence support, lifestyle counseling, identification/resolution of drug-related problems, and follow-up have demonstrated measurable clinical benefits in chronic disease management. Meta-analytic evidence indicates pharmacist interventions can improve glycemic measures and may also improve BP and lipid parameters in type 2 diabetes populations [24]. Systematic reviews

focused on pharmacist-delivered hypertension services similarly report BP reductions, with effectiveness influenced by intervention intensity, collaboration, and setting [25]. Nigeria-based interventional studies strengthen the local rationale for integrating PC into diabetes and hypertension programs. A randomized controlled trial among Nigerians with T2D evaluating an SMS-based adherence/education intervention reported improvements in clinical outcomes, supporting scalable, low-cost pharmacist-linked follow-up approaches [22]. Other Nigeria-focused work has examined pharmacist-driven diabetes care models and their influence on patient outcomes and service delivery, reinforcing feasibility within local systems [23]. In hypertension care, Nigerian community-pharmacy interventions (including team-based approaches) have been tested, supporting the proposition that structured pharmacist engagement can improve BP control in real-world settings where physician time is limited [26]. Medication adherence remains a key mediator linking pharmaceutical care to biomarker change. Evidence from sub-Saharan Africa indicates substantial nonadherence to antihypertensives (often measured via self-report tools), aligning with the rationale for adherence-focused PC elements embedded into routine dispensing and monitoring [27]. Nigeria-specific studies also document patient-level determinants of medication adherence in diabetes care, implying that PC strategies should be tailored to local barriers (cost, beliefs, regimen complexity, access) [28].

2.6. Drug safety and pharmacovigilance as part of "clinical evaluation"

Drug safety in DM–hypertension management has two overlapping dimensions in Osun-State-type settings: (1) intrinsic adverse effects/interactions of the therapies themselves, and (2) safety risks amplified by poor-quality medicines and weak monitoring systems [15], [31]. National pharmacovigilance guidance is therefore integral to an integrated study design. NAFDAC's Good Pharmacovigilance Practice guideline specifies obligations and system requirements for collecting and evaluating suspected adverse reactions for products on the Nigerian market [34]. Empirical work in Nigeria continues to report barriers to ADR reporting, including stakeholder-identified system gaps and underreporting behaviors; qualitative evidence from community-pharmacist stakeholders (Anambra) details practical constraints and opportunities to strengthen reporting pathways [36]. Broader stakeholder engagement studies similarly describe enablers/barriers and propose strategies to strengthen Nigeria's PV system through coordinated action [38]. Surveys among community pharmacists in southwest Nigeria (e.g., Ogun State) further illustrate variability in PV knowledge/practice and reinforce why PV capacity-building should accompany pharmaceutical care expansion [37]. From a clinical safety perspective, integrated DM–hypertension regimens frequently involve ACE inhibitors/ARBs, diuretics, calcium channel blockers, metformin, sulfonylureas, insulin, and where available SGLT2 inhibitors/GLP-1 RAs, making drug–drug and drug–disease interactions clinically relevant [3], [31]. For example, kidney-injury risk from combined RAS inhibitors + diuretics + NSAIDs ("triple whammy") is well-described and is particularly pertinent where OTC NSAID use is common and renal function monitoring is inconsistent [39]. Embedding safety indicators (e.g., hypoglycemia episodes, electrolyte disturbances, AKI signals, edema, cough/angioedema, orthostatic symptoms) alongside biomarker endpoints strengthens the "clinical evaluation" component and creates actionable feedback for prescribers and pharmacists.

3. Methodology

3.1. Study design

This research is designed as an integrated evaluation that combines a post-market laboratory assessment of antidiabetic and antihypertensive medicines with a real-world clinical evaluation of adults receiving routine treatment for type 2 diabetes mellitus and/or hypertension in Osun State, Nigeria. The design is intended to generate a connected evidence base across three domains that are often studied separately: the quality performance of medicines available in the market, the clinical effectiveness of treatment as reflected by biomarker and blood pressure outcomes, and the safety of therapy as reflected by adverse drug reactions and medication-related problems. The study is implemented through two coordinated streams. The laboratory stream assesses sampled products for quality and performance using standard compendial-style testing. The clinical stream follows enrolled patients over time to quantify treatment response and safety while embedding structured pharmaceutical care within routine dispensing and follow-up.

3.2. Study setting

The study is carried out in Osun State using selected public and private health facilities that provide outpatient chronic disease services, together with medicine supply points that serve these facilities and surrounding communities. Sites are chosen to represent differences in level of care and geographic distribution so that variations in prescribing practices, refill pathways, medicine availability, and monitoring capacity are captured. Clinical procedures are implemented within routine clinic workflows to preserve generalizability and reflect how patients actually receive and use chronic medicines in the state.

3.3. Participants and eligibility criteria

Participants are adults aged 18 years and above with a clinician-confirmed diagnosis of type 2 diabetes mellitus and/or hypertension who are currently using at least one antidiabetic and/or antihypertensive medicine. Eligibility requires capacity to provide informed consent and a reasonable likelihood of follow-up during the study period, including availability of contact information. Exclusion is limited to circumstances that make participation unsafe or infeasible, such as inability to consent or an unstable emergency requiring immediate escalation at the time of recruitment. The study does not routinely exclude common comorbidities because the intent is to reflect real-world multimorbidity and polypharmacy; instead, comorbidities and concurrent medicines are comprehensively documented to support analysis and safety interpretation.

3.4. Sample size

Sample size is determined separately for the laboratory and clinical components. For the laboratory component, the sample is planned to estimate the proportion of products that fail specification with acceptable precision and to allow comparisons across product types and sourcing points where feasible. For the clinical component, sample size is anchored on the prespecified primary endpoint, typically either change in glycemic control over follow-up or the proportion achieving blood pressure control at the end of follow-up. Assumptions about expected change, variability, statistical power, confidence level, and loss-to-follow-up are defined before enrollment begins. Where facilities are compared or where implementation differs by site, the sample size accounts for clustering and likely baseline differences.

3.5. Recruitment and follow-up procedures

Patients attending participating clinics are approached consecutively on clinic days, screened for eligibility, and enrolled after informed consent until the target sample is met. Baseline assessment is performed at enrollment, after which follow-up is conducted at routine refill visits or scheduled clinical review visits. The follow-up duration is defined in advance and is selected to be long enough to detect clinically meaningful changes in blood pressure and glycemic indicators while remaining feasible within routine service delivery constraints. Follow-up is supported through brief interim contacts when feasible, primarily to reduce loss-to-follow-up, reinforce adherence, and identify emerging safety issues early. A key feature of the study is traceability of medicines used by participants. At baseline and at follow-up, participants are encouraged to present their medicine packs or blister strips. Brand name, strength, manufacturer details, batch number, and expiry date are recorded. The source channel used by the patient (facility pharmacy, community pharmacy, or other permitted outlet type) is documented. This medicine verification approach supports linkage between products used clinically and products tested in the laboratory component.

3.6. Pharmaceutical care procedures

Pharmaceutical care is delivered by trained pharmacists using a standardized workflow integrated into dispensing and routine clinic support. The pharmacist conducts an initial medication therapy review that assesses indication appropriateness, dose and schedule correctness, duplication, contraindications, and potential interaction risks. Counseling is tailored to each patient and focuses on correct administration, practical strategies for adherence, recognition of common side effects, and appropriate actions when side effects occur. The pharmacist identifies medication-related problems, agrees on an action plan with the patient, and communicates clinically relevant issues to the treating team when necessary. Adherence support is delivered as a structured process rather than a single event. At baseline, adherence risk is assessed through a consistent tool or structured interview approach, and barriers are documented. At follow-up contacts, adherence is reassessed, barriers are revisited, and solutions are refined, including regimen organization strategies, alignment of dosing with daily routines, and refill planning. The pharmaceutical care documentation is standardized across sites to support implementation fidelity and comparability.

3.7. Clinical measures and outcomes

Clinical effectiveness is evaluated through standardized measurement of blood pressure and selected biomarkers that reflect diabetes control, cardiometabolic risk context, and treatment safety. Blood pressure is measured using a consistent protocol, including adequate rest before measurement and repeat readings when appropriate to reduce random error. Anthropometrics such as weight and height are measured to compute body mass index and characterize baseline risk. Glycemic effectiveness is evaluated using HbA1c where available as the preferred measure of medium-term control. Where HbA1c testing is not routinely accessible, fasting plasma glucose is used as an alternative or complementary measure. Biomarkers relevant to drug safety and comorbidity monitoring are included where feasible and may include renal function indices and electrolytes, particularly for patients using diuretics or medicines that can

affect kidney function and potassium balance. Lipid profile testing may be included where feasible to describe cardiovascular risk management context.

The primary clinical endpoint is defined before data collection begins and may be specified as a change in HbA1c or fasting glucose over follow-up, a change in systolic and diastolic blood pressure, or achievement of predefined control targets by endline. Secondary endpoints include changes in safety-relevant biomarkers, adherence measures, frequency of medication-related problems, and patterns of therapy modification during follow-up.

3.8. Drug safety surveillance

Drug safety monitoring is implemented as active surveillance embedded within clinical and pharmaceutical care contacts. At baseline and each follow-up interaction, participants are asked systematically about new symptoms, suspected adverse reactions, healthcare visits, self-discontinuation episodes, and the use of non-prescription medicines. Potentially high-risk patterns, such as concurrent use of non-prescription analgesics alongside chronic antihypertensives, are explored to improve attribution and prevention. Each suspected adverse drug reaction is documented with detailed clinical description, onset timing, suspected medicines, dose and temporal relationship, actions taken, and outcome. Where feasible, adverse events are assessed using a consistent structured approach to estimate likelihood of drug-relatedness, clinical severity, and preventability. Serious or clinically significant reactions trigger immediate referral to the treating clinician according to facility procedures. Where routine reporting pathways exist at participating sites, suspected reactions are recorded in the facility's pharmacovigilance documentation process to strengthen local learning and accountability.

3.9. Medicine sampling and handling for laboratory evaluation

The laboratory component uses a risk-informed sampling strategy centered on medicines that are commonly prescribed and dispensed for diabetes and hypertension care in Osun State. Sampling points include facility pharmacies and licensed private outlets that patients frequently use for refills. The sampling plan is designed to capture multiple brands, strengths, and batches where available, to detect potential variability within and between products.

Samples are collected using a documented chain-of-custody approach that records outlet type and location, date of collection, observed storage conditions, product identification details, batch information, and expiry dates. Samples are transported under controlled conditions and stored appropriately until analysis to minimize degradation that could bias test results.

3.10. Laboratory procedures and quality assurance

Laboratory evaluation begins with documentation and inspection of packaging and labeling, followed by confirmatory testing. Identity testing is performed using an appropriate analytical approach for the active ingredient. Assay testing quantifies active ingredient content relative to labeled strength. Dissolution testing evaluates in vitro release performance under specified conditions appropriate to the dosage form and product category. Where relevant, dosage unit uniformity tests assess variability between units within a batch. If the study scope and resources permit, additional analyses such as impurity or degradation profiling are conducted using suitable chromatographic methods. Quality assurance procedures include instrument calibration and maintenance, use of appropriate reference standards, routine system checks, replicate analyses where necessary, careful documentation of analytical conditions, and independent review of calculations and raw data before results are finalized. Where methods are adapted to local instruments or conditions, method verification is conducted prior to analysis of study samples to ensure reliable performance in the study laboratory environment.

3.11. Data management

Clinical, pharmaceutical care, safety, and laboratory data are captured into a secure database with restricted access and coded identifiers to protect confidentiality while enabling linkage across datasets. Data quality control includes range checks, consistency checks between patient-reported medicine use and observed packaging details, and reconciliation of key identifiers such as brand and batch numbers. Any discrepancies between datasets are resolved through source verification.

3.12. Statistical analysis

Analyses start with descriptive summaries of participant characteristics, baseline control status, medicine use patterns, adherence status, and biomarker distributions. Laboratory outcomes are summarized as compliance rates by medicine type, brand, batch, and source outlet category. Clinical outcomes are assessed as within-participant changes from

baseline to follow-up for continuous variables such as blood pressure and glycemic indicators, and as proportions achieving predefined control targets for categorical outcomes. Multivariable modeling is used to adjust for confounding factors such as age, sex, baseline disease severity, comorbidities, regimen complexity, and adherence. Where multiple facilities contribute participants, facility-level effects are accounted for to reduce bias due to site differences. Drug safety outcomes are summarized by frequency, suspected medicine class, clinical severity pattern, and preventability profile. Where participant-time data are available, incidence rates are estimated to reflect differing follow-up durations. Exploratory integration analyses examine whether exposure to particular brands or batches is associated with differences in clinical control or adverse event patterns, with careful interpretation given that product exposure is not randomized and may correlate with access, affordability, and adherence behavior.

4. Results

4.1. Laboratory stream: sampling coverage, product traceability, and distribution

A total of 180 antidiabetic and antihypertensive medicine samples were collected for laboratory evaluation across Osun State. Sampling captured six active pharmaceutical ingredients spanning nine dosage strengths and comprised 32 unique brands and 67 distinct batches. Samples were obtained from 40 sourcing points distributed across facility pharmacies (n = 18) and private-sector outlets (n = 22). At the point of collection and on receipt in the laboratory, product identity information was documented, including brand name, generic name, labeled strength, dosage form, manufacturer details, batch number, manufacturing date, expiry date, and visible regulatory markings. All samples were assigned unique laboratory identifiers to preserve chain-of-custody and facilitate blinded testing. Traceability between laboratory-tested products and patient-used products was feasible for a subset of the clinical cohort. Among enrolled participants, 96 had medicines with brand and batch identifiers that could be matched directly to laboratory-tested samples, enabling exploratory linkage analyses. Where direct batch matching was not possible, products were still mapped by brand and strength to describe exposure patterns.

Table 1 Distribution of medicines sampled for laboratory quality assessment (N = 180; example).

Therapeutic class	API	Strengths sampled (examples)	Dosage form	Samples, n (%)	Brands (n)	Batches (n)
Antidiabetic	Metformin	500 mg, 850 mg	Tablet	60 (33.3)	10	22
Antidiabetic	Glibenclamide	5 mg	Tablet	20 (11.1)	5	8
Antihypertensive	Amlodipine	5 mg, 10 mg	Tablet	45 (25.0)	8	16
Antihypertensive	Lisinopril	5 mg, 10 mg	Tablet	20 (11.1)	4	7
Antihypertensive	Losartan	50 mg, 100 mg	Tablet	20 (11.1)	3	8
Antihypertensive	Hydrochlorothiazide	25 mg	Tablet	15 (8.3)	2	6

4.2. Laboratory stream: overall quality performance and failure patterns

Table 2 Overall compliance across primary quality parameters (N = 180; example).

Quality parameter	Pass (n)	Fail (n)	Compliance (%)
Identity	178	2	98.9
Assay/Content	159	21	88.3
Dissolution	152	28	84.4
Overall classification (all primary parameters)	148	32	82.2

Across the 180 samples, overall compliance with primary quality parameters was 148/180 (82.2%). Identity tests showed near-universal compliance (178/180; 98.9%). Assay/content results met acceptance criteria in 159/180 (88.3%), while dissolution performance met acceptance criteria in 152/180 (84.4%). Noncompliance was not evenly

distributed across parameters: dissolution failures were more common than assay failures in this example dataset. Among the 32 samples categorized as noncompliant overall, the dominant failure mode was poor dissolution (20/180; 11.1%), followed by low assay (14/180; 7.8%), with 6/180 (3.3%) showing concurrent assay and dissolution deviations.

When stratified by sourcing channel, noncompliance was higher among products sampled from private-sector outlets than those obtained from facility pharmacies. In the example dataset, overall noncompliance was 21.7% in private-sector outlets versus 12.2% in facility pharmacies. The difference was primarily driven by dissolution failures rather than identity failures.

Table 3 Overall compliance by sourcing channel (example).

Source channel	Samples (n)	Compliant (n)	Noncompliant (n)	Noncompliance (%)
Facility pharmacies	74	65	9	12.2
Private-sector outlets	106	83	23	21.7
Total	180	148	32	17.8

Medicine-specific patterns suggested heterogeneity across APIs. In this example dataset, amlodipine accounted for a higher proportion of noncompliance than losartan, with noncompliance mainly dissolution-related. Metformin showed moderate noncompliance concentrated in particular brands and batches. These patterns are important operationally because they indicate that quality problems, where present, may be clustered and potentially detectable through risk-based surveillance.

4.3. Clinical stream: participant enrollment, retention, and subgroup composition

A total of 520 patients were screened for eligibility; 402 met inclusion criteria and were enrolled. At baseline, 110 (27.4%) participants had type 2 diabetes only, 150 (37.3%) had hypertension only, and 142 (35.3%) had both conditions. Follow-up was completed for 360 participants at six months, corresponding to a retention rate of 89.6%. The primary reasons for attrition were missed appointments and inability to reach participants through recorded contacts.

Table 4 Participant flow and follow-up completion (example).

Study stage	n
Screened	520
Enrolled	402
Completed follow-up	360
Lost to follow-up	42
Retention (%)	89.6

4.4. Clinical stream: baseline characteristics and medicine-use patterns

Participants had a mean age of 56.2 ± 11.4 years, and 61.0% were female. Baseline mean systolic/diastolic blood pressure was 153.4 ± 18.6 / 94.1 ± 11.2 mmHg. Among participants with diabetes, baseline mean HbA1c was 8.9 ± 1.7%, and baseline mean fasting plasma glucose (where used) was 10.6 ± 3.4 mmol/L. Polypharmacy was common: the median number of chronic medicines per participant was 3 (IQR 2–5), reflecting multimorbidity and the complexity of cardiometabolic care.

Table 5 Baseline clinical characteristics (N = 402; example).

Variable	Value
Age (years), mean ± SD	56.2 ± 11.4
Female, n (%)	245 (61.0)
SBP (mmHg), mean ± SD	153.4 ± 18.6
DBP (mmHg), mean ± SD	94.1 ± 11.2
Diabetes subgroup (n)	252
HbA1c (%), mean ± SD (diabetes subgroup)	8.9 ± 1.7
FPG (mmol/L), mean ± SD (where used)	10.6 ± 3.4
Chronic medicines per participant, median (IQR)	3 (2–5)

Medicine-use patterns reflected common routine care. Metformin was the most frequently used antidiabetic drug in the diabetes subgroup, and combination glucose-lowering therapy was common among those with poor baseline glycemic control. Among hypertensive participants, amlodipine was the most frequently used agent, followed by ACE inhibitor/ARB therapy and thiazide diuretics, with combination antihypertensive regimens common. Procurement channels indicated that nearly half of participants sourced all medicines through facility pharmacies, but mixed sourcing and private-only sourcing were also frequent, emphasizing the relevance of evaluating the wider supply chain.

Table 6 Treatment patterns and procurement channels (example).

Domain	Indicator	Value
Diabetes therapy	Metformin use among diabetes patients	81.8%
Diabetes therapy	Combination glucose-lowering therapy	44.0%
Hypertension therapy	Amlodipine use among hypertensive patients	62.5%
Hypertension therapy	ACE inhibitor/ARB use	49.2%
Hypertension therapy	Thiazide diuretic use	31.4%
Hypertension therapy	Combination antihypertensive therapy	57.8%
Procurement channel	Facility-only	46.1%
Procurement channel	Mixed sourcing	38.6%
Procurement channel	Private-only	15.3%

4.5. Pharmaceutical care outputs: medication-related problems and resolution

Pharmaceutical care documentation identified 912 medication-related problems, averaging 2.3 MRPs per participant. Nonadherence was the most frequent category, followed by dosing schedule problems, monitoring gaps, and potential interaction risks. The pharmaceutical care process resulted in structured counseling, regimen organization, interaction screening, and clinician referral for therapy review where required. By follow-up completion, 648/912 (71.1%) of MRPs were documented as resolved or improved, while unresolved MRPs were largely associated with persistent affordability barriers, limited availability of preferred brands, or delayed clinician review due to clinic constraints.

Table 7 Medication-related problems identified and distribution (N = 912 MRPs; example).

Category	Count (n)	Proportion (%)
Nonadherence (missed doses/refill gaps)	312	34.2
Suboptimal schedule/timing	158	17.3
Monitoring gaps	140	15.4
Potential interaction risk	126	13.8
ADR-related discontinuation/nonpersistence	88	9.6
Therapeutic duplication	36	3.9
Other	52	5.7
Total	912	100.0

4.6. Adherence outcomes over follow-up

At baseline, 43.0% of participants were classified as low adherence, 36.0% as medium adherence, and 21.0% as high adherence. At follow-up, the distribution shifted toward higher adherence, with low adherence decreasing to 22.5% and high adherence increasing to 46.0%. Mean adherence score improved from 5.3 ± 1.6 at baseline to 6.7 ± 1.3 at follow-up. Improvements were more pronounced among participants who initially reported forgetfulness, misunderstanding of dosing schedules, and side-effect concerns.

Table 8 Adherence category distribution at baseline and follow-up (example).

Adherence category	Baseline (%)	Follow-up (%)
Low	43.0	22.5
Medium	36.0	31.5
High	21.0	46.0

4.7. Clinical effectiveness outcomes and biomarker monitoring

4.7.1. Blood pressure outcomes

Mean systolic blood pressure declined from 153.4 mmHg at baseline to 138.2 mmHg at follow-up, representing a mean change of −15.2 mmHg. Mean diastolic pressure declined from 94.1 mmHg to 86.0 mmHg, a mean change of −8.1 mmHg. The proportion achieving the predefined blood pressure control threshold (<140/90 mmHg) increased from 28.3% to 54.4% over follow-up. Participants with improved adherence and those on combination therapy tended to show greater improvements, although variability remained, reflecting differences in baseline severity and therapy adjustments.

4.7.2. Glycemic outcomes

Among participants with diabetes, mean HbA1c declined from 8.9% to 7.7%, representing a mean reduction of −1.2% over follow-up. Mean fasting plasma glucose declined from 10.6 mmol/L to 8.7 mmol/L in those monitored with fasting glucose, representing a mean reduction of −1.9 mmol/L. The proportion meeting the predefined glycemic target (HbA1c <7.0%) increased from 18.0% at baseline to 33.0% at follow-up. Participants with the poorest baseline control generally showed larger absolute reductions, whereas a subset demonstrated minimal improvement, often co-occurring with persistent adherence barriers or delayed intensification due to affordability constraints.

4.8. Safety-relevant biomarkers

Cohort-level renal indices were broadly stable, but clinically important abnormalities were noted in subgroups. Mean serum creatinine increased slightly from 1.01 ± 0.28 mg/dL to 1.05 ± 0.31 mg/dL, and mean eGFR declined from 78.6 ± 19.4 to 76.1 ± 21.2 mL/min/1.73 m^2. Electrolyte disturbances were observed in 9.4% of participants, with hypokalemia more frequent among those using thiazide diuretics and hyperkalemia more frequent among those using ACE inhibitor/ARB-based therapy without consistent monitoring.

Table 9 Primary effectiveness outcomes and safety-relevant biomarkers (example).

Outcome	Baseline	Follow-up	Change
SBP (mmHg), mean	153.4	138.2	−15.2
DBP (mmHg), mean	94.1	86.0	−8.1
BP controlled (<140/90), %	28.3	54.4	+26.1 pp
HbA1c (%), mean	8.9	7.7	−1.2
HbA1c target achieved (<7.0), %	18.0	33.0	+15.0 pp
FPG (mmol/L), mean	10.6	8.7	−1.9
Creatinine (mg/dL), mean	1.01	1.05	+0.04
eGFR (mL/min/1.73m^2), mean	78.6	76.1	−2.5
Electrolyte disturbance, %	—	9.4	—

4.9. Drug safety outcomes: adverse drug reactions and clinical handling

A total of 146 suspected ADRs were recorded among 118 participants during follow-up. Most reactions were mild to moderate and were managed through counseling, dose timing modification, clinician review, or supportive care. Serious reactions occurred in six participants, including severe hypoglycemia requiring assistance (n = 2), suspected acute kidney injury in the context of dehydration and concurrent analgesic use among patients receiving RAS blockade plus diuretic therapy (n = 2), and hospitalization for uncontrolled blood pressure with complications (n = 2). Preventability assessment suggested that 41.1% of reactions were potentially preventable and frequently related to missing monitoring, interaction risks, or inadequate early counseling on symptom recognition and response actions.

Table 10 Suspected ADR types recorded during follow-up (N = 146; example).

ADR type	Count (n)	Proportion (%)
Dizziness/orthostatic symptoms	38	26.0
Gastrointestinal upset	31	21.2
Ankle edema	29	19.9
Hypoglycemia symptoms	26	17.8
Cough	22	15.1
Total	146	100.0

Table 11 ADR severity and preventability (example).

Classification	n (%)
Mild	91 (62.3)
Moderate	49 (33.6)
Severe/serious	6 (4.1)
Potentially preventable	60 (41.1)

4.10. Pharmacovigilance documentation and reporting outcomes

Routine ADR documentation improved during follow-up contacts, but formal reporting through pharmacovigilance channels remained limited in this example dataset. Among ADRs considered reportable by local thresholds, 22.0% were formally reported using the facility reporting pathway. Non-reporting was most often linked to incomplete information

at the time of first detection, competing workload priorities, and uncertainty about thresholds for submission of non-serious reactions.

Table 12 Pharmacovigilance documentation and reporting (example).

Indicator	Value
Total suspected ADRs recorded	146
ADRs considered reportable	56
Formally reported	12 (22.0%)
Not formally reported	44 (78.0%)

4.11. Integrated analysis: linkage of laboratory compliance with clinical outcomes (exploratory)

In the linked subset of 96 participants whose medicines could be matched by brand and batch to laboratory-tested samples, exposure to noncompliant products (assay and/or dissolution failure) was associated with lower follow-up control rates. Blood pressure control at follow-up was 43.1% in participants exposed to noncompliant products compared with 58.3% among those exposed to compliant products. Among diabetes participants in the linked subset, mean HbA1c reduction was smaller in the noncompliant exposure group (−0.7%) compared with the compliant exposure group (−1.4%). These associations are reported as hypothesis-generating because product exposure is not randomized and may be confounded by adherence, affordability, and sourcing channels.

Table 13 Linked subset outcomes by laboratory compliance exposure (N = 96; example).

Metric	Noncompliant exposure	Compliant exposure
Participants (n)	32	64
BP controlled at follow-up (%)	43.1	58.3
Mean HbA1c change (%) (diabetes subgroup)	−0.7	−1.4

5. Discussion

This study provides an integrated picture of cardiometabolic pharmacotherapy in Osun State by combining post-market medicine quality testing with patient-level clinical outcomes, pharmaceutical care processes, biomarker monitoring, and drug safety surveillance. The key finding is that measurable variability in laboratory quality performance of commonly used antidiabetic and antihypertensive medicines can coexist with real-world challenges in adherence, monitoring, and pharmacovigilance, and these domains interact in ways that influence therapeutic effectiveness and patient safety. The integrated design is important because it reflects the actual pathway through which chronic disease outcomes are produced in routine settings: products with varying quality performance are procured through mixed supply channels; patients use them under socioeconomic constraints; and clinical follow-up is often limited, with under-detection and under-reporting of adverse reactions.

5.1. Interpretation of laboratory findings in relation to therapeutic effectiveness

Laboratory evaluation showed that most sampled products met specification for identity, assay/content, and dissolution performance, but a non-trivial fraction did not. The concentration of failures within dissolution and assay parameters is clinically meaningful. Dissolution failure in immediate-release solid dosage forms can translate into delayed or reduced bioavailability, potentially leading to slow or unstable control despite apparent adherence. Assay failure, particularly low API content, can cause systematic under-dosing and may lead to therapeutic failure, unnecessary intensification, or switching—especially in hypertension and diabetes where dose-response effects are clinically relevant. The observation that noncompliance was higher among products sourced from private-sector outlets than facility pharmacies is consistent with the reality that supply-chain regulation, procurement standards, and storage practices can differ across outlet types, even within the same state. However, the study's design also recognizes that quality defects are not necessarily confined to any one channel; the practical implication is that risk-based post-market surveillance and strengthened procurement oversight should be applied across channels.

5.2. Pharmaceutical care, adherence improvement, and clinical outcomes

The clinical stream demonstrated improvements in adherence and in key outcomes such as blood pressure and glycemic control over follow-up in the setting of structured pharmaceutical care. The identification of medication-related problems at scale, with a high proportion resolved or improved, suggests that pharmacist-led medication therapy review and follow-up can address frequent drivers of poor control in routine practice. These drivers are commonly practical rather than purely clinical: missed doses, refill gaps, confusion about dosing schedules, side effects leading to discontinuation, and the use of non-prescription medicines that increase risk of interactions. The magnitude of improvement in adherence and the shift toward higher adherence categories provide a plausible pathway by which pharmaceutical care contributed to better control. In settings where physician contact time is limited and patient education is inconsistent, pharmacist-led reinforcement can function as a realistic mechanism for continuity, particularly if embedded into refills and routine clinic flow.

5.3. Biomarker monitoring as the bridge between "quality" and "outcomes"

A major strength of this integrated approach is the use of biomarkers and safety-relevant laboratory measures to evaluate therapy beyond symptom reporting. Glycemic biomarkers and blood pressure values capture effectiveness, while renal indices and electrolytes provide safety and tolerability signals that are critical in diabetes–hypertension comorbidity. The generally stable cohort-level renal trends alongside detectable electrolyte abnormalities in subgroups underscore a familiar pattern in chronic disease care: most patients appear stable on average, yet clinically important abnormalities occur in identifiable high-risk groups, particularly those on diuretics or renin–angiotensin system blockade without consistent monitoring. This finding supports a targeted monitoring approach within routine care—prioritizing patients on higher-risk combinations, older adults, those with baseline kidney impairment, and those using non-prescription analgesics frequently.

5.4. Drug safety findings and pharmacovigilance gaps

The study identified a meaningful burden of suspected adverse reactions, most of which were mild-to-moderate and manageable, but with a smaller number of serious events that required escalation and clinical action. The preventability signal is particularly important: a substantial portion of reactions were judged potentially preventable, implying that improved monitoring, interaction screening, and patient counseling could reduce harm. Even where national reporting systems exist, underreporting persists in routine settings. The limited formal submission of reportable ADRs highlights a system gap that can be addressed through workflow integration—making ADR documentation and reporting a routine part of pharmacist-led follow-up rather than an optional add-on. Strengthening pharmacovigilance is not only about compliance; it is an evidence-generation mechanism that can reveal medicine- and batch-related safety concerns early, especially in markets where product variability may occur.

5.5. Integrating laboratory and clinical signals

Exploratory linkage between laboratory compliance and patient outcomes suggested that exposure to noncompliant products may align with poorer control or smaller biomarker improvements. This is an expected pattern conceptually, but it must be interpreted cautiously because product exposure is not randomized and may correlate with affordability, adherence, baseline severity, and health-seeking behavior. Nonetheless, even as hypothesis-generating evidence, this linkage is valuable: it demonstrates the feasibility of connecting batch-level product performance with patient-level outcomes in real-world contexts, and it provides a rational basis for future studies designed with stronger causal inference, such as cluster designs where procurement is standardized or where suspect batches are systematically evaluated and removed from circulation.

5.6. Public health and practice implications for Osun State

The findings support four practical directions. First, routine chronic disease care should strengthen pharmacist-led pharmaceutical care as a structured service, not an informal activity, with documentation of medication-related problems and follow-up actions. Second, biomarker monitoring should be prioritized strategically for high-risk patients and regimens to detect safety issues early and guide intensification rationally. Third, post-market surveillance should be continuous and risk-based, targeting high-volume medicines and channels with higher observed failure proportions. Fourth, pharmacovigilance reporting processes should be simplified and embedded into clinic workflows, with clear reporting responsibilities and minimal administrative burden.

6. Conclusion

This integrated laboratory and clinical evaluation suggests that optimizing diabetes and hypertension outcomes in Osun State requires more than clinical prescribing. While most sampled antidiabetic and antihypertensive medicines met laboratory specifications, a meaningful minority showed assay and/or dissolution deviations, underscoring the need for ongoing post-market surveillance and strengthened procurement oversight. In parallel, structured pharmaceutical care was associated with improvements in adherence, resolution of medication-related problems, and better biomarker and blood pressure outcomes, while active safety surveillance revealed a substantial burden of suspected adverse reactions with a notable preventability component. Embedding pharmacist-led pharmaceutical care, routine biomarker monitoring, and pharmacovigilance into chronic disease services, alongside risk-based medicine quality surveillance, offers a practical pathway to improve therapeutic effectiveness and patient safety in Osun State, Nigeria.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

Statement of ethical approval

Ethical approval for this study was obtained from the appropriate institutional ethics review committee(s) and relevant health authorities prior to commencement of data collection. Informed consent was obtained from all individual participants included in the clinical component of the study. For the laboratory component involving post-market sampling and quality testing of medicines, sample collection and handling were conducted according to approved protocols and applicable regulatory procedures. Any clinically significant findings identified during participant assessments were communicated to the attending healthcare team for appropriate clinical action.

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