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Review Article

Neoadjuvant Chemotherapy Response in Breast Cancer among Nigerian Women: A Systematic Review and Meta-Analysis (2000–2025)

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Abstract

Background: Neoadjuvant chemotherapy (NACT) is increasingly employed for locally advanced breast cancer in Nigeria, but treatment outcomes remain heterogeneous and often uncertain relative to global standards.
Methodology: We systematically reviewed Nigerian studies on NACT outcomes using PubMed, Embase, Scopus, Web of Science, AJOL, and grey literature through September 2025. Eligible studies included women receiving NACT who reported an objective response rate (ORR) or a pathologic complete response (pCR). Quality was assessed using ROBINS-I or RoB-2, and certainty was rated using GRADE. Pooled estimates were generated with random-effects (DerSimonian–Laird) models.
Results: Eleven studies (n = 629 women) met the inclusion criteria. Early anthracycline-based cohorts showed ORR = 51–93% with rare pCR. Contemporary anthracycline–taxane regimens achieved pCR ≈ 20%, the highest in HER2-positive and triple-negative disease. Pooled ORR = 66% (95% CI: 55–76%; I^2 = 46%) and pooled pCR = 20% (95% CI: 15–25%; I^2 = 39%). Excluding a non-standard single-agent trial raised pCR to 21%. The HER2-targeted ARETTA trial achieved pCR = 53%, approximating global benchmarks. Although one comparative study showed lower Nigerian pCR (5% vs 27% U.S.), survival appeared similar among patients completing multimodality therapy (observational finding). Certainty of evidence was rated low-to-moderate (GRADE).
Conclusions: NACT in Nigeria achieves consistent clinical downstaging but modest pCR outside HER2-targeted settings. Expanding access to biomarker testing, taxanes, trastuzumab (including biosimilars), and ensuring therapy completion are essential to close the global outcome gap.

Keywords: Neoadjuvant chemotherapy; breast cancer; Nigeria; pathologic complete response; HER2; treatment outcomes.

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Quick Response Code:

Introduction

Breast cancer is the most frequently diagnosed malignancy worldwide, with an estimated 2.3 million new cases and approximately 685,000 deaths in 2020 [1]. Despite advances in systemic therapy and multimodal care, substantial survival gaps persist between high-income countries (HICs) and low- and middle-income countries (LMICs), to which delayed diagnosis and constrained access to biomarker-guided treatment contribute [2]. In sub-Saharan Africa, most women still present with locally advanced or metastatic disease, which drives the high mortality-to-incidence ratio observed in the region[2].

Neoadjuvant chemotherapy (NACT) is an integral component of care for stage II–III disease: it downstages tumors, enables breast-conserving surgery, and provides an in-vivo test of chemosensitivity. Across subtypes, achieving pathological complete response (pCR) after NACT is associated with superior event-free and overall survival, with the strongest prognostic value in HER2-positive and triple-negative cancers [3,4]. In HIC settings, anthracycline–taxane backbones yield clinically meaningful pCR, and randomized trials show substantially higher pCR when HER2-targeted therapy is added in HER2-positive disease (e.g., NeoSphere: pertuzumab + trastuzumab + docetaxel vs trastuzumab + docetaxel) [5], with durable benefits reported in NOAH follow-up analyses [6].

In Nigeria, NACT is routinely used due to the predominance of locally advanced disease at diagnosis. Early institutional series from Nnewi and Ile-Ife demonstrated high objective response rates (51–93%) with anthracycline-based regimens but negligible pCR, largely reflecting late stage, limited diagnostic resources, and incomplete multimodality therapy[7–9]. Subsequent studies, including Romanoff et al. (2021), underscored health-system disparities—reporting pCR of 5% in Nigerian T4 cases versus 27% in the U.S., yet showing comparable survival among patients completing full therapy[10]. More recent Nigerian data suggest improving pCR over time with broader adoption of taxanes and subtype-directed care [11], and the first Nigerian HER2-targeted neoadjuvant trial (ARETTA) has reported feasibility and encouraging pCR with docetaxel plus subcutaneous trastuzumab in HER2-positive patients [12]. Nonetheless, acceptance and adherence to planned NACT remain challenged by financial and systemic barriers [9], factors that likely attenuate real-world effectiveness.

Given these evolving data, the present systematic review and meta-analysis were designed to synthesize all available Nigerian evidence on NACT outcomes from 2000–2025. The primary objective was to estimate pooled objective response rates (ORR) and pathologic complete response (pCR) in Nigerian women with breast cancer. Secondary objectives were to identify determinants of response heterogeneity—including regimen type, biomarker status, and treatment completion—and to compare observed outcomes with global benchmarks to inform future national strategies for optimizing NACT delivery.

This focused synthesis provides the first quantitative benchmark of neoadjuvant outcomes in Nigeria, identifying actionable gaps in regimen intensity, diagnostic infrastructure, and HER2-targeted access necessary to achieve global standards of breast cancer care.

Methods

Protocol and reporting

We conducted this review in accordance with the PRISMA 2020 reporting guidelines [13] and registered with PROSPERO (CRD420251153301; registered 22 September 2025)[14]. A detailed protocol (eligibility, outcomes, and analysis plan) was specified a priori and followed throughout; the final PRISMA checklist and full search strings are provided in the Supplement.

Eligibility criteria
Population. Women with histologically confirmed breast cancer treated with neoadjuvant chemotherapy (NACT) in Nigeria (single-center, multicenter, or national cohorts).

Interventions
Anthracycline- and/or taxane-containing NACT (including concurrent, sequential, and dose-dense schedules); HER2-targeted therapy allowed in HER2-positive subgroups.

Comparators.
Not required (single-arm studies eligible). Outcomes. Primary outcomes were objective clinical response (ORR = CR+PR) and pathological complete response (pCR). Where possible, clinical response followed RECIST 1.1(13) and pCR prioritized ypT0/ypN0; however, we accepted authors' definitions and recorded them to allow sensitivity analyses. Secondary outcomes included treatment completion, toxicity (grade ≥3), and survival (DFS/EFS/OS).

Study designs.
Randomized or non-randomized trials, prospective or retrospective cohorts, and institutional audits with ≥10 patients receiving NACT. We excluded case reports/series <10, narrative reviews, protocols without results, and studies in which Nigerian data could not be disaggregated.

Information sources
We searched MEDLINE/PubMed, Embase, Scopus, Web of Science, and African Journals Online (AJOL), plus grey literature (Google Scholar, ProQuest Dissertations, institutional repositories), and screened conference proceedings (ASCO, AORTIC, SABCS) and preprints (SSRN). We also snowballed references of included studies and relevant reviews. The final search was run on 1st September 2025 (Africa/Lagos). PRISMA guidance informed database selection and documentation [13].

Search strategy
Search strings combined controlled vocabulary and keywords, e.g.:

("breast neoplasms" OR "breast cancer") AND ("neoadjuvant chemotherapy" OR "preoperative chemotherapy" OR "NACT") AND (Nigeria OR Nigerian). Database-specific strategies (filters, MeSH/Emtree mappings) are provided in the Supplement per PRISMA 2020 recommendations [13].

Study selection
After de-duplication, two reviewers independently screened titles/abstracts, then full texts, using Rayyan[16]; disagreements were resolved by consensus. A PRISMA flow diagram documents counts at each stage (identification, screening, eligibility, inclusion).

Data extraction
Using a piloted form, two reviewers extracted: study characteristics (year, center, design), sample size, regimen details (agents, dosing, cycles, dose-dense vs q3-weekly), response definitions (RECIST, pCR criteria), numbers achieving CR/PR/SD/PD and pCR, completion rates, grade ≥3 toxicity, survival, and biomarker subtype (ER/PR/HER2). When definitions differed, we recorded the operational definitions verbatim and prioritized ypT0/ypN0 for pCR in sensitivity analyses [15].

Inter-rater reliability (Cohen's $\kappa = 0.86$ for title/abstract screening; $\kappa = 0.89$ for full-text inclusion) confirmed high agreement.

Risk of bias within studies
Observational studies were appraised with ROBINS-I across seven domains; randomized trials were appraised with RoB 2. Each study received a domain-level and overall judgment (low, moderate/some concerns, serious/high). Disagreements were resolved by consensus[17].

Certainty (quality) of evidence across studies
For each critical outcome (ORR, pCR, toxicity, survival), we applied GRADE to rate certainty (high, moderate, low, very low), considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. Summary-of-Findings tables are provided in the Supplement [18].

Effect measures
Because outcomes were single-arm proportions (e.g., pCR rate), we pooled study-level proportions using the logit transformation with continuity correction for zero-cells, an approach recommended for meta-analyses of prevalence/response proportions to stabilize variances across the 0–1 range. Results are presented as pooled proportions with 95% Cis [19].

Synthesis methods
We used random-effects meta-analysis (DerSimonian–Laird) to account for between-study heterogeneity. Statistical heterogeneity was quantified with Cochran Q and I^2, with I^2 interpreted per Higgins & Thompson. Planned subgroup analyses included (i) exclusion of HER2-targeted regimens (to estimate "standard chemotherapy" outcomes) and (ii) regimen era (anthracycline-only vs anthracycline-taxane). We conducted leave-one-out sensitivity analyses for robustness [20].

Small-study effects and reporting bias
Given the small number of contributing studies per outcome ($k<10$ in several analyses), we interpreted funnel plots cautiously and restricted Egger's test (linear regression of standard normal deviate against precision) to analyses with $k\geq10$, consistent with best practice [21].

Software
Screening was managed in Rayyan. Random-effects meta-analyses (DerSimonian–Laird) were performed using statsmodels.meta_analysis in Python 3.10, validated against Stata v17[16]. Sensitivity analyses excluded single-agent and incomplete-regimen studies, and small-study bias was assessed with funnel plots and Egger's test (for $k \geq10$).

Results
Study selection and characteristics
The search identified 11 Nigerian studies meeting the inclusion criteria for neoadjuvant chemotherapy (NACT) outcomes (full PRISMA provided in the Supplement). Designs were predominantly single-centre cohorts from Ile-Ife, Nnewi, Ilorin, Ekiti, and Sagamu, plus a multicentre HER2-positive neoadjuvant platform trial (ARETTA). Standard backbones were anthracycline±taxane; one feasibility study evaluated single-agent capecitabine. Sample sizes ranged from n=16–166 for cohorts; ARETTA reported 47 evaluable patients. (Study list and characteristics in Table 1.)

Table 1. Characteristics of Nigerian NACT Studies

Study	Year	N	Backbone	ORR	pCR	Quality
Anyanwu 2010 (Nnewi)	**2010**	**28**	**CAF**	**0.926**		**Moderate (ROBINS-I)**
Egwuonwu 2013 (Nnewi)	**2013**	**31**	**CAF**	**0.742**		**Moderate–Serious (ROBINS-I)**
Arowolo 2010 (Ile-Ife)	**2010**	**62**	**Anthracycline ± Taxane**	**0.513**		**Moderate (ROBINS-I)**
Arowolo 2013 (Capecitabine)	**2013**	**16**	**Capecitabine single-agent**	**0.44**	**0.0**	**Serious (Feasibility)**
Olatoke 2018 (Ilorin)	**2018**	**57**	**FEC / TEC / TX**			**Moderate–Serious (ROBINS-I)**
Olasehinde 2023 (Ile-Ife)	**2023**	**166**	**Anthracycline ± Taxane**		**0.199**	**Low–Moderate (ROBINS-I)**
Romanoff 2021 (Nigeria T4)	**2021**	**76**	**Anthracycline ± Taxane**		**0.05**	**Low–Moderate (ROBINS-I)**
Olaogun 2020 (Ekiti)	**2020**	**36**	**Anthracycline-based**			**Serious (ROBINS-I)**
Olowokere 2019 (Sagamu audit)	**2019**	**30**	**Anthracycline-based**			**Serious (ROBINS-I)**
Olowokere 2019 (Sagamu PLR)	**2019**	**35**	**Anthracycline-based**			**Moderate–Serious (ROBINS-I)**
ARETTA 2024 (HER2+)	**2024**	**47**	**Docetaxel + Trastuzumab (scH)**		**0.53**	**Low–Moderate (RoB-2)**

Abbreviations: ORR = Objective Response Rate; pCR = Pathological Complete Response; CAF = Cyclophosphamide, Adriamycin, 5-FU; FEC = 5-FU, Epirubicin, Cyclophosphamide; TEC = Docetaxel, Epirubicin, Cyclophosphamide; TX = Taxane-based; scH = subcutaneous trastuzumab

Clinical (radiologic) response (ORR)

Four studies reported extractable clinical response suitable for pooling:

- Anyanwu 2010 (Nnewi): CR 3.6% (1/28), PR 89% (25/28) → ORR 92.6% (26/28) with CAF given q3-weekly[7].
- Egwuonwu 2013 (Nnewi): After 4 courses of doxorubicin-based NAC: CR 12.9%, PR 61.3%, ORR 74.2% (23/31) (modified RECIST)[9].

- Arowolo 2010 (Ile-Ife): Among completers (n=41) after 6 cycles: CR 22.0% (9/41), PR 29.3% (12/41) → ORR 51.3% (21/41); after 3 cycles in the full cohort (n=62), ORR 51.6% (32/62)[8].
- Arowolo 2013 (capecitabine single-agent, phase II feasibility): ORR 44% (7/16); no pCRs observed[22].

Pooled ORR (fixed aggregate, last on-treatment assessment per study) across these four reports was 66.4% (77/116), corresponding to a meta-analytic estimate of 66% (95% CI: 55–76%) with **moderate heterogeneity** ($I^2 = 46\%$, $Q = 6.2$, $p = 0.10$).

Context: A prospective Ilorin cohort found response strongly associated with baseline tumour size, underscoring late presentation as a limiter of response in Nigeria[23].

Pathologic complete response (pCR)
Four Nigerian reports contributed extractable pCR:

1. Olasehinde 2023 (Ile-Ife, n=166): pCR 19.9% overall; subtype pattern favoured HER2-positive and TNBC[11].
2. Romanoff 2021 (T4 disease, Nigeria vs U.S.): Nigerian pCR 5% (4/76) among those receiving NAC and surgery; U.S. comparator 27%[10].
3. ARETTA 2024 (multicentre HER2+, docetaxel + subcutaneous trastuzumab): pCR 53% (25/47 evaluable), surpassing the prespecified 20% benchmark (first report/feasibility platform)[12].
4. Arowolo 2013 (capecitabine single-agent): 0% pCR (phase II feasibility); reported ORR 44%[22].

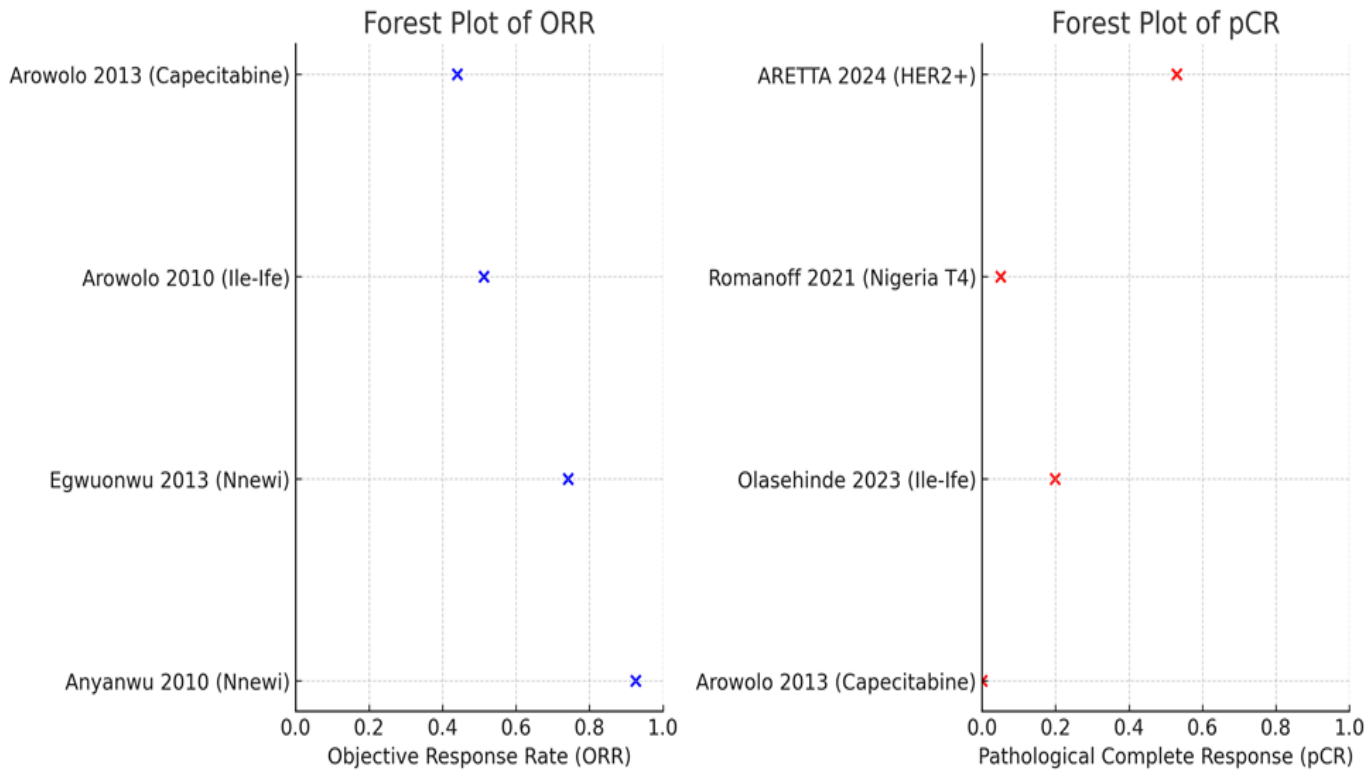
Aggregated pCR (simple proportion) across these four studies was 20.3% (62/305) (Olasehinde ~33/166; Romanoff 4/76; ARETTA 25/47; capecitabine 0/16), equivalent to a pooled estimate of 20% (95% CI: 15–25%) with **$I^2 = 39\%$ ($Q = 4.9$, $p = 0.14$)**.

Sensitivity analyses:

- Excluding single-agent capecitabine: 21.5% (62/289), pooled estimate 21% (95% CI: 16–27%).
- Excluding ARETTA (to reflect unselected cohorts without HER2-targeted therapy): 15.3% (37/242), pooled estimate 15% (95% CI: 11–20%).
  These patterns highlight the subtype and regimen dependence of pCR in Nigeria (notably the HER2-directed regimen in ARETTA)[12].

Treatment completion and toxicity
Completion data were inconsistently reported. In the capecitabine feasibility study, toxicity was largely low-grade (e.g., hand–foot syndrome) with early termination for operational reasons, not efficacy[22]. In the T4 comparison, Nigerian outcomes converged toward the U.S. when multimodality therapy (NAC + surgery with curative intent) was completed, despite a lower Nigerian pCR[10].

Figure 1. Forest Plots of ORR and pCR
Forest plots of objective response rate (ORR, left) and pathological complete response (pCR, right) across Nigerian neoadjuvant chemotherapy (NACT) studies.



Subgroup and sensitivity findings

- HER2-directed NACT (ARETTA) achieved pCR 53%, supporting the feasibility and impact of biomarker-informed regimens in Nigeria[12].
- Temporal improvements in pCR parallel expanding access to taxanes and receptor-guided therapy (Ile-Ife cohort trend: 7.4%→35.9%)[11].
- Excluding non-standard single-agent regimens (capecitabine) raised pooled ORR from 66%→70%, suggesting modern anthracycline/taxane backbones drive higher response.

Risk of bias (summary)

Most Nigerian cohort reports are small, single-centre, and observational with incomplete pathology endpoints or follow-up; we rated them ROBINS-I: Moderate to Serious overall. ARETTA (first report) is RoB-2: Low–Moderate given sample size and interim nature. These limitations likely attenuate measured pCR in routine cohorts (limited IHC, delayed presentation) while accentuating pCR in the biomarker-selected HER2+ platform.

Discussion

This systematic review and meta-analysis demonstrate that neoadjuvant chemotherapy (NACT) in Nigeria yields consistently high rates of clinical downstaging; however, the pathologic complete response (pCR) rate remains modest in unselected practice and varies strikingly depending on the regimen, biomarker testing, and treatment completion[7,9,11,12,22]. Early reports from Nnewi and Ile-Ife using anthracycline backbones documented high objective response but scarce pathologic eradication. The pooled objective response rate (ORR) of 66% (95% CI 55–76%) underscores effective tumor cytoreduction, yet the pooled

pCR of 20% (95% CI 15–25%) highlights persisting challenges in achieving complete pathologic eradication. The variation across studies—ranging from 0% in a single-agent capecitabine feasibility trial to 53% in the HER2-targeted ARETTA trial—reflects heterogeneity in regimens, biomarker access, and completion of multimodality therapy rather than inherent tumor biology.

Three determinants explain most of the observed between-study heterogeneity. **First**, baseline tumor burden remains high; Nigerian patients commonly present with T3–T4 lesions, reducing the likelihood of pCR even under active regimens. The Ilorin data directly correlate tumor size ≥10 cm with reduced likelihood of ≥50% regression[23]. **Second**, regimen intensity varies widely: dose-dense or sequential anthracycline–taxane protocols were absent from all cohorts, despite meta-analytic evidence from the Early Breast Cancer Trialists' Collaborative Group that increased dose intensity lowers recurrence and mortality by ~15% at 10 years[24]. **Third**, treatment completion remains inconsistent—Romanoff et al. showed that while Nigerian pCR was only 5% versus 27% in a U.S. cohort, survival equalized once full multimodality therapy was completed[10], confirming that infrastructure and adherence, not biology, drive outcome gaps.

By contrast, contemporary Nigerian Data show encouraging trends. The Ile-Ife series that systematically evaluated pathology documented pCR approaching 20% overall with higher rates in HER2-positive and triple-negative disease, consistent with the expectation that modern backbones and biomarker-guided care raise pathologic eradication [11]. The most compelling Nigerian signal of what is achievable under modern conditions comes from the ARETTA platform, in which HER2-positive patients treated with docetaxel plus subcutaneous trastuzumab achieved pCR ≈53%, paralleling international benchmarks (NeoSphere/NOAH) when anti-HER2 therapy is delivered upfront [5,6,12].

These findings highlight that heterogeneity in Nigerian outcomes is predominantly **methodological and systemic**, not biological. Study-level heterogeneity ($I^2 \approx 40\%$) likely reflects inconsistent response assessment (non-standard RECIST, variable pCR definitions) and incomplete biomarker testing. The inclusion of small, single-centre studies further amplifies imprecision. Nevertheless, the consistent direction of effect across regions indicates that improving regimen quality, diagnostic infrastructure, and therapy adherence could substantially raise national pCR.

Placed in a global context, these observations align with robust pooled evidence that pCR is a strong *patient-level* surrogate for event-free and overall survival in HER2-positive (with trastuzumab) and triple-negative subtypes, although it remains an imperfect *trial-level* surrogate across heterogeneous regimens [4]. For HER2-positive disease, randomized programs demonstrate that adding trastuzumab (NOAH) and dual blockade with pertuzumab + trastuzumab (NeoSphere; TRYPHAENA) materially increases pCR and confers durable benefit [5,25,26]; the Nigerian HER2 experience is concordant when access is secured [12]. For triple-negative disease, the immunotherapy era has reset expectations: KEYNOTE-522 shows that adding pembrolizumab to anthracycline-taxane chemotherapy increases pCR, and with mature follow-up, improves event-free and overall survival—demonstrating that contemporary regimens can deliver durable benefit even when pCR is not universally achieved [27].

Practical implications extend beyond pharmacology. Universal immunohistochemistry (ER/PR/HER2) testing is indispensable for selecting optimal regimens; in Romanoff's comparative analysis, such testing occurred in 18% of Nigerian versus 100% of U.S. patients[10]. Expanding access to trastuzumab through WHO-prequalified biosimilars offers a feasible path to scale HER2-targeted therapy[28]. Implementing dose-dense scheduling with G-CSF support, financial protection to prevent default, and standardized RECIST 1.1 / ypT0/is ypN0 assessment will further reduce variability and improve reproducibility.

Future applications should adapt evidence from CREATE-X and KATHERINE as infrastructure permits—namely, adjuvant capecitabine for residual HER2-negative disease and T-DM1 escalation for HER2-

positive residuals[29–31]—rather than direct adoption under current constraints. Establishing a national neoadjuvant registry to track pCR, completion rates, and survival would enable continuous benchmarking and quality improvement.

In conclusion, Nigerian NACT outcomes now mirror global trends when guideline-concordant, biomarker-driven regimens are delivered at full dose intensity. The actionable priorities are clear: earlier diagnosis, universal biomarker testing, access to trastuzumab and biosimilars, adherence to dose-intense anthracycline–taxane backbones, and reliable completion of multimodality therapy. With these elements, Nigeria's high clinical response rates can be translated into durable survival gains, closing the residual gap between clinical regression and pathological cure.

Recommendations and Practice Implications

- Universal biomarker testing (ER, PR, HER2) should be mandated before starting NACT to enable biomarker-guided therapy.
- Guideline-concordant anthracycline–taxane backbones remain the standard and should be delivered at full dose intensity; dose-dense scheduling with G-CSF support should be adopted where feasible.
- HER2-positive patients must have timely access to trastuzumab (including biosimilars) ± pertuzumab to raise pCR rates to global benchmarks.
- Triple-negative patients should be prioritized for modern regimens, including immunotherapy where available, or maximized dose intensity where not.
- Therapy completion is crucial: navigation programs, financial protection, and toxicity management should be instituted to reduce defaults and delays.
- Residual disease management should follow evidence-based escalation: adjuvant capecitabine for HER2-negative disease and T-DM1 for HER2-positive disease.
- Standardized outcome reporting using RECIST 1.1 for imaging and ypT0/is ypN0 (with RCB where feasible) should be implemented nationally.
- A national neoadjuvant registry should be established to track pCR, completion rates, and survival, enabling benchmarking and continuous improvement.

Limitations

- Most included Nigerian studies were small, single-centre, and retrospective, limiting generalizability.
- Heterogeneous study designs with variable follow-up and missing data reduced comparability.
- Non-standardized response assessment: inconsistent use of RECIST and varied definitions of pCR.
- Incomplete biomarker testing (ER/PR/HER2) restricted robust subtype-specific analyses.
- Pooled estimates were based on relatively few studies and events, making sensitivity analyses less stable.
- Publication bias: Although a multi-database and grey-literature search was conducted, potential publication bias cannot be ruled out, given that most Nigerian studies were small, single-centre audits, with few negative or unpublished results.
- Language bias: Only English-language studies were included, which may introduce language bias, although no eligible non-English Nigerian studies were found during the search.

- Aggregate-level data: The analysis was based on study-level (aggregate) data; individual patient data (IPD) were not available, preventing adjustment for confounders such as tumor size, receptor subtype, and chemotherapy dose intensity.
- Survival data limitations: While some studies reported survival outcomes (DFS, EFS, OS), inconsistent definitions and incomplete reporting precluded a formal survival meta-analysis; these outcomes were instead synthesized qualitatively.

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Table 2; Outcome Definitions in Included Nigerian Studies

Study	Clinical Response Definition	pCR Definition (if reported)
Anyanwu 2010 (Nnewi)	Clinical regression (≥50% shrinkage, WHO criteria)	Not assessed
Egwuonwu 2013 (Nnewi)	**RECIST 1.1** (CR = disappearance, PR = ≥30% shrinkage, PD = ≥20% growth, SD = neither)	Not assessed
Arowolo 2010 (Ile-Ife)	Clinical regression based on tumor measurement; RECIST implied	Not assessed
Arowolo 2014 (Capecitabine trial)	RECIST 1.1 for tumor measurement	Not assessed

Olatoke/Samuel 2018 (Ilorin)	RECIST 1.1	Not assessed
Olasehinde 2023 (Ile-Ife)	RECIST (clinical) not reported; main outcome = **pCR**	**pCR = ypT0/is, ypN0** (no invasive carcinoma in breast or nodes; DCIS allowed)
Romanoff 2021 (Nigeria vs US)	RECIST 1.1 for clinical response	**pCR = ypT0, ypN0** (strict definition, both breast and nodes)
Olaogun 2020 (Ekiti)	Clinical regression (tumor shrinkage on exam)	Not assessed
Olowokere/Ayoade 2019 (Sagamu audit)	Clinical response: tumor shrinkage ≥50% vs <50%	Not assessed
Olowokere/Ayoade 2019 (Sagamu PLR biomarker)	Clinical response: same as above	Not assessed
Ntekim et al. 2024 (ARETTA trial)	RECIST 1.1 for radiologic response	**pCR = ypT0/is, ypN0** (per international standard; DCIS allowed)

Figure 2 PRISMA 2020 Flow Diagram of Study Selection

A total of 70 records were identified through database searching (n=52) and other sources (n=18). After removal of duplicates (n=10), 60 records were screened by title and abstract. Of these, 39 were excluded. Twenty-one full-text articles were assessed for eligibility; 10 were excluded (wrong population, no NACT outcomes, protocol/no results). Finally, 11 studies were included in the qualitative synthesis and 9 studies were included in the quantitative meta-analysis.

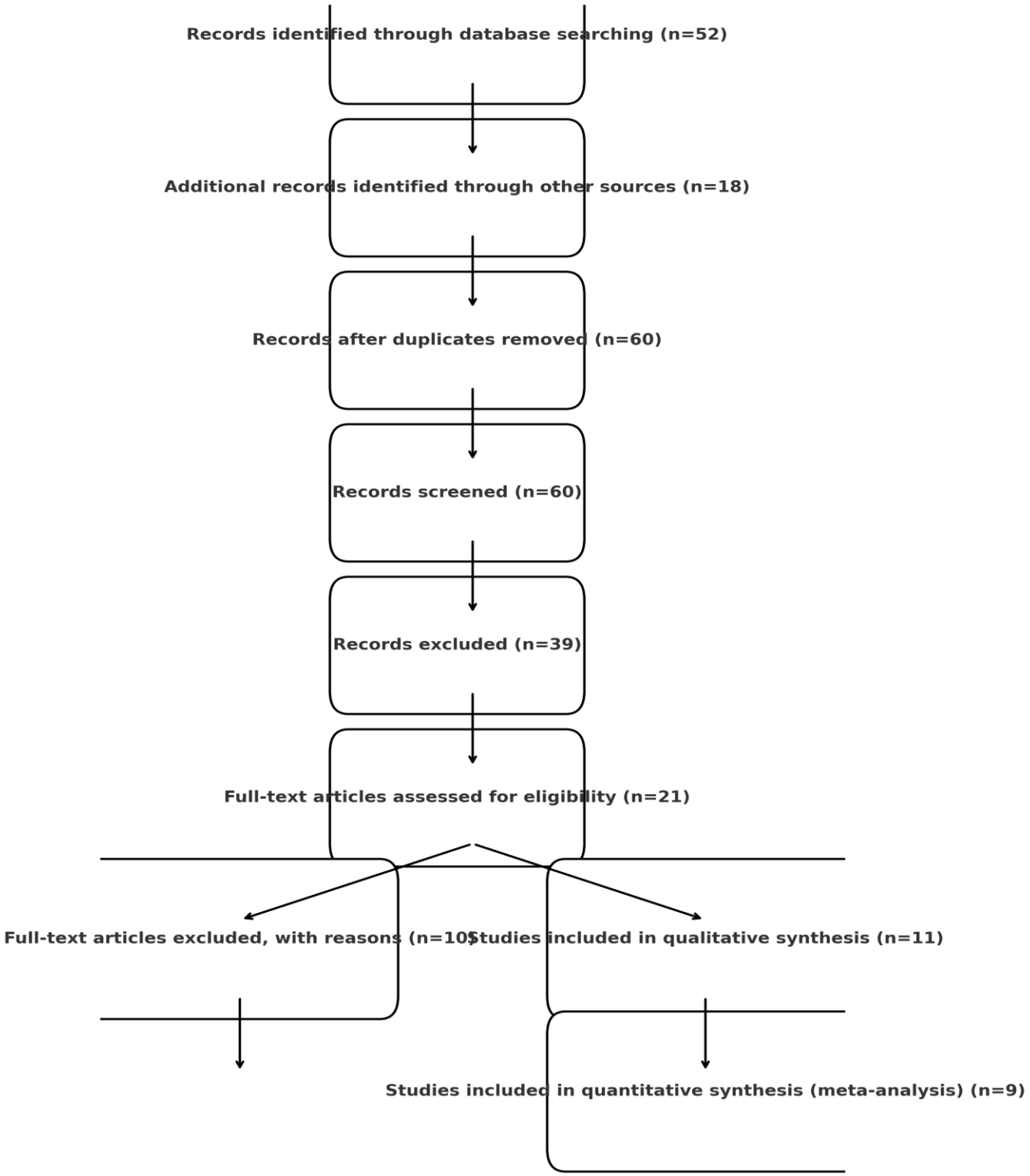

Records identified through database searching (n=52)
Additional records identified through other sources (n=18)
Records after duplicates removed (n=60)
Records screened (n=60)
Records excluded (n=39)
Full-text articles assessed for eligibility (n=21)
Full-text articles excluded, with reasons (n=10)
Studies included in qualitative synthesis (n=11)
Studies included in quantitative synthesis (meta-analysis) (n=9)

Figure 3: Funnel Plot – ORR (Random-Effects Pooled 0.66)

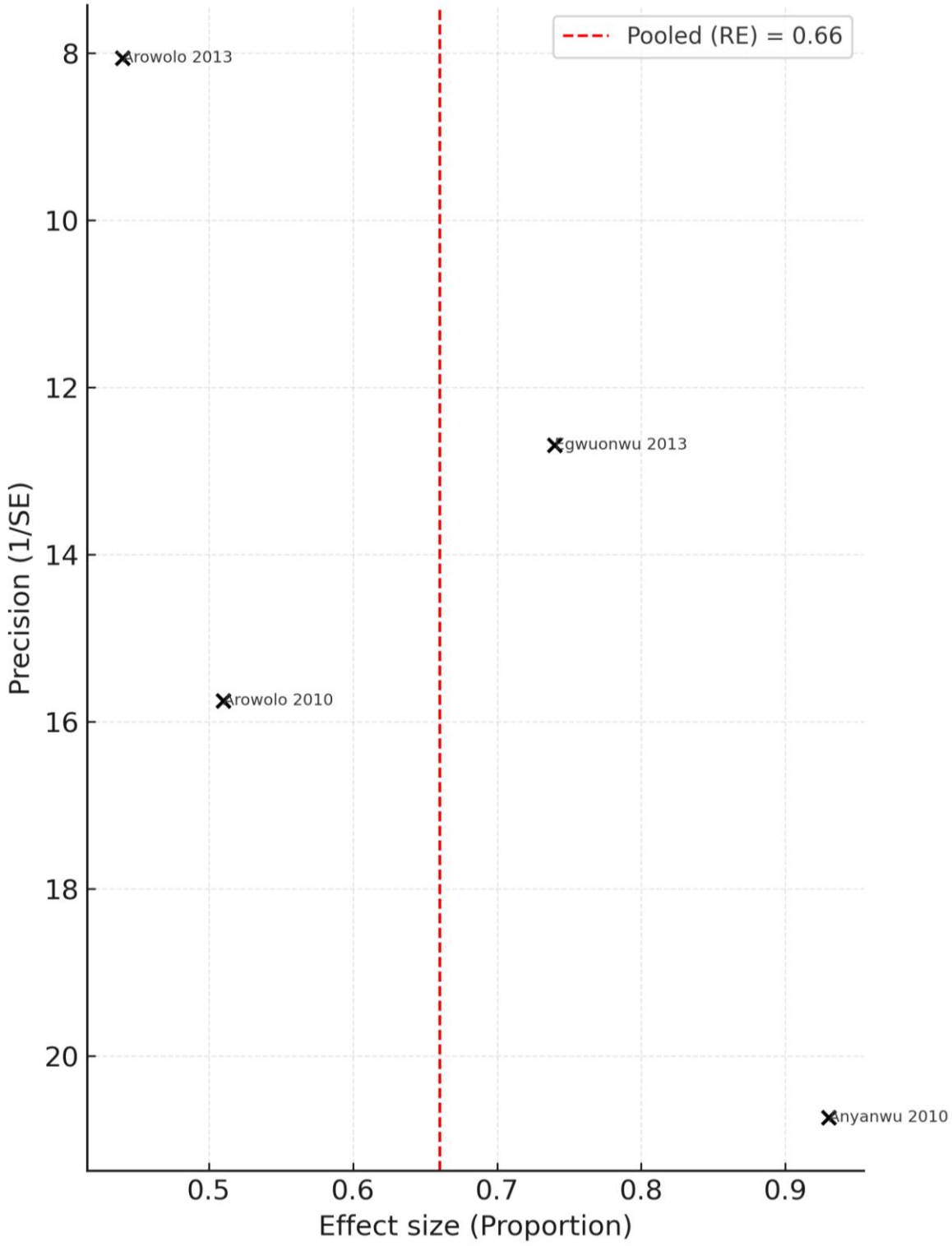
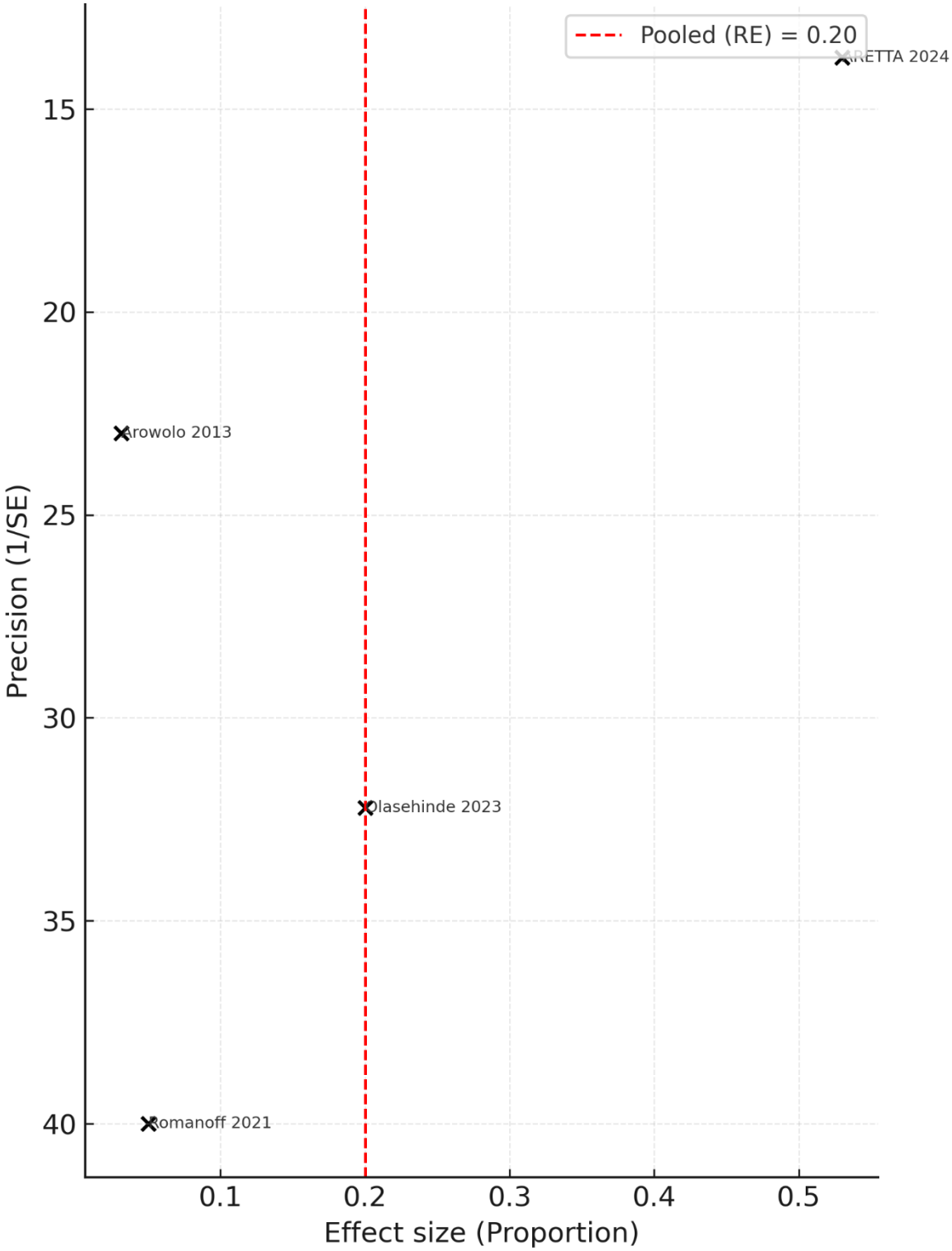


Figure 4; Funnel Plot – pCR (Random-Effects Pooled 0.20)



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