

## EPIDEMIOLOGICAL AND OPERATIONAL ASSESSMENT OF TSETSE FLY AND TRYPANOSOMIASIS CONTROL INTERVENTIONS IN NIGERIA BETWEEN 2010 AND 2025: A SYSTEMATIC REVIEW AND META-ANALYSIS

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### ABSTRACT

African trypanosomiasis continues to pose significant public health and agricultural challenges in Nigeria, with evolving epidemiological patterns and emerging control challenges in the post-2010 era. Between 2010 and 2025, Nigeria implemented a range of interventions targeting tsetse (*Glossina* spp.) and trypanosomiasis, yielding heterogeneous outcomes across ecological zones. This PRISMA-compliant systematic review synthesizes findings from 95 peer-reviewed and grey literature sources to assess epidemiological trends, vector suppression efficacy, and operational constraints. Entomological indices and parasitological prevalence were extracted and analyzed using multivariate regression and pooled meta-analytic techniques. Pyrethroid-impregnated blue-black traps deployed in Yankari Game Reserve and Old Oyo National Park achieved significant reductions in *Glossina tachinoides* (–39.2%, 95% CI: 32.1–46.3) and *G. morsitans* submorsitans (–31.4%, 95% CI: 25.6–39.2). However, therapeutic failure of isometamidium chloride reached 42.6% in sentinel herds in Niger State (95% CI: 38.1–47.2;  $p < 0.001$ ), indicating emergent drug resistance. While Human African Trypanosomiasis (HAT) incidence declined to fewer than ten confirmed cases nationally between 2017 and 2024, Animal African Trypanosomiasis (AAT) remains endemic in over 60% of livestock-rearing zones. Operational barriers—including fragmented surveillance, limited funding, and ecological shifts—continue to undermine AAT control. To advance toward elimination, we recommend: (1) national implementation of resistance allele surveillance via next-generation sequencing, (2) climate-informed, spatially optimized vector control, and (3) integration of whole genome sequencing into policy frameworks. Strategic investment in CRISPR-based genetic tools and One Health coordination will be essential to achieving trypanosomiasis elimination in Nigeria by 2030.

**Keywords:** Tsetse fly, Trypanosomiasis, Control interventions, Epidemiological assessment, Operational evaluation, Systematic review

### INTRODUCTION

African trypanosomiasis remains a major constraint to public health and agricultural productivity in Nigeria, with continued transmission of both Human African Trypanosomiasis (HAT) and Animal African Trypanosomiasis (AAT) despite extensive control efforts (Enwezor *et al.*, 2019; Chukwudi *et al.*, 2025). Since 2010, advances in molecular epidemiology have enhanced understanding of *Trypanosoma* species diversity through improved genetic characterization of parasites and tsetse populations (Isaac *et al.*, 2016; Weber *et al.*, 2019). Nonetheless, challenges such as drug resistance, climate-induced vector range expansion, and weak surveillance infrastructure continue to impede elimination goals (Silva *et al.*, 2022; Simpson & Cropper, 2020). This review synthesizes research from 2010–2025 to evaluate Nigeria's trypanosomiasis landscape, examining the evolving epidemiology, intervention outcomes, and policy responses shaping current control strategies (Ademola, 2018; Enwezor *et al.*, 2019).

Recent studies reveal increasingly complex transmission patterns. Genomic analyses have identified novel *Trypanosoma brucei gambiense* genotypes in Cross River State (Kaboré *et al.*, 2023) and high genetic variability among *T. vivax* strains in cattle (Silva Pereira *et al.*, 2024), underscoring the need for genotype-specific interventions. Economically, trypanosomiasis causes over US\$300 million

in annual livestock losses (FMARD, 2023), with smallholder dairy farmers reporting 35–50% milk yield reductions (Odeniran & Ademola, 2022). Human cases impose heavy treatment costs, averaging US\$2,800 per disability-adjusted life year (DALY) averted (WHO, 2023), disproportionately affecting pastoralist communities whose herd values decline by 30–70% during outbreaks (NBS, 2023).

Diagnostic technologies have progressed with the introduction of rapid diagnostic tests (RDTs) for HAT and loop-mediated isothermal amplification (LAMP) for AAT. However, sensitivity limitations—often below 70% for early HAT detection (Büscher *et al.*, 2022)—and logistical barriers constrain their effectiveness (Lejon *et al.*, 2023). CRISPR-based assays offer promise but require validation under Nigerian field conditions (Mugasa *et al.*, 2024).

Vector control strategies, including insecticide-treated targets and livestock ear tags, have reduced tsetse densities by 40–75% in pilot areas (Adam *et al.*, 2021). Yet, the emergence of *kdr*-like resistance mutations in *Glossina palpalis* (Odeniran *et al.*, 2023) and climate-driven expansion of vector habitats (Torr *et al.*, 2023) undermine these gains. Similarly, chemotherapeutic interventions face resistance challenges, with *T. b. gambiense* treatment failures of up to 12% for fexinidazole (MSF, 2023) and rising resistance to older trypanocides (Eze *et al.*, 2023; Giordani *et al.*, 2022).

Implementation of Nigeria's National Trypanosomiasis Control Policy (2022) is constrained by fragmented surveillance systems (OIE, 2023) and frequent drug shortages (NTDCP, 2023). Climate change further compounds control efforts, with ecological models projecting a 17% increase in suitable *G. morsitans* habitats by 2030 (Torr et al., 2023) and prolonged tsetse activity seasons (Lord et al., 2024).

This review therefore aims to:

- i. Characterize current transmission patterns using molecular and spatial epidemiological data.
- ii. Assess the cost-effectiveness of prevailing control strategies.
- iii. Propose a climate-resilient elimination framework integrating genomic surveillance and adaptive vector management.

These objectives align with the WHO 2030 roadmap for neglected tropical diseases and seek to inform sustainable elimination strategies tailored to Nigeria's ecological and socio-economic realities.

### Epidemiological Shifts and Molecular Surveillance Advances

The post-2010 era has witnessed substantial improvements in the molecular characterization of trypanosome strains circulating in Nigeria. Whole-genome sequencing of clinical isolates has identified novel *T. b. gambiense* genotypes in Cross River State, distinct from historical variants, suggesting independent zoonotic transmission cycles (Kaboré et al., 2023). Similarly, minicircle kinetoplast DNA profiling has revealed an unexpected diversity of *T. vivax* strains in cattle populations, with at least three phylogenetically distinct clusters exhibiting differential pathogenicity and drug susceptibility, findings that challenged earlier assumptions about strain homogeneity and underscore the need for genotype-specific treatment protocols (Silva Pereira et al., 2024).

Diagnostic capabilities have advanced considerably since 2010, with the widespread adoption of rapid diagnostic tests (RDTs) for HAT and loop-mediated isothermal amplification (LAMP) assays for AAT. However, field evaluations indicate persistent limitations: RDTs demonstrate sensitivities below 70% for early-stage HAT (Büscher et al., 2022), while LAMP, despite its high specificity, remains impractical for decentralized use due to equipment requirements (Lejon et al., 2023). The development of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) -based point-of-care diagnostics like Specific High-sensitivity Enzymatic Reporter un-LOCKing (SHERLOCK) assays, promise but has yet to be validated in Nigerian field conditions (Mugasa et al., 2024).

### Intervention Outcomes and Emerging Resistance Patterns

Nigeria's implementation of the WHO roadmap for neglected tropical diseases (2012–2020) catalyzed a shift toward integrated control strategies (WHO, 2024). Vector suppression through insecticide-treated targets and cattle ear tags (deltamethrin-impregnated) reduced tsetse densities by 40–75% in pilot areas (Adam et al., 2021). However, resistance monitoring has detected *kdr*-like mutations in *Glossina palpalis* populations in Benue State, correlating with declining pyrethroid efficacy (Odeniran et al., 2023).

Chemotherapeutic interventions face parallel challenges. While fexinidazole (approved in 2018) has simplified HAT treatment regimens, pharmacovigilance data reveal a 12% treatment failure rate in *T. b. gambiense* patients from endemic foci (MSF, 2023). For AAT, the once-reliable diminazene aceturate now shows efficacy below 60% in northern Nigeria, with genomic analyses linking treatment

failures to mutations in the *TbAT1* transporter gene (Eze et al., 2023). Isometamidium resistance, first reported in 2015, has become widespread, with *T. congolense* isolates exhibiting 100-fold reduced drug susceptibility in vitro (Giordani et al., 2022).

### Economic and Climate-Driven Challenges

The economic burden of trypanosomiasis remains severe, with annual losses in livestock productivity exceeding \$300 million (FMARD, 2023). Smallholder dairy systems are disproportionately affected; *T. vivax* infections reduce milk yields by 35–50%, perpetuating poverty cycles in pastoralist communities (NBS, 2022). Human productivity losses are equally stark, with late-stage HAT cases costing \$2,800 per disability-adjusted life year (DALY) averted—a figure that exceeds Nigeria's per capita health expenditure (WHO, 2023).

Climate change has emerged as a critical determinant of transmission dynamics. Ecological niche models project a 17% expansion of suitable *G. morsitans* habitats into Nigeria's Middle Belt by 2030 under RCP6.0 scenarios (Torr et al., 2023). Rising temperatures have already extended the tsetse activity season by 22 days compared to 2010 baselines, increasing the risk of AAT outbreaks in previously low-risk areas (Lord et al., 2024). These shifts necessitate adaptive surveillance strategies, yet current health systems lack the spatial resolution to track vector migration in real time.

### Policy Gaps and Implementation Barriers

Despite alignment with the Pan-African Tsetse and Trypanosomiasis Eradication Campaign (PATTEC), Nigeria's control program faces systemic hurdles. Fragmented data systems hinder integrated One Health responses; a 2022 audit found that 68% of veterinary clinics lacked digital reporting capabilities, delaying outbreak detection (OIE, 2023). Drug supply chains are equally problematic, with stockouts of critical trypanocides occurring in 40% of surveyed health facilities (NTDCP, 2023).

Community engagement remains inconsistent. While participatory vector control programs in Ebonyi State achieved 80% tsetse population reduction (FMoH, 2021), resistance to cattle insecticide treatment persists among Fulani pastoralists due to cultural preferences for traditional remedies (Majekodunmi et al., 2022). These sociobehavioral barriers underscore the need for culturally tailored intervention designs.

### Objectives and Forward Momentum

This review provides the first comprehensive synthesis of Nigerian trypanosomiasis research from the 2010–2025 period, with three overarching aims:

- i. **Epidemiological Synthesis:** Integrate molecular, clinical, and spatial data to map transmission hotspots and strain diversity.
- ii. **Intervention Analysis:** Evaluate the cost-effectiveness of control tools (e.g., fexinidazole vs. vector suppression) using disability-adjusted life years (DALYs) and livestock productivity metrics.
- iii. **Policy Recommendations:** Propose a climate-resilient elimination framework leveraging genomic surveillance, next-generation vector control, and strengthened health systems.

By contextualizing Nigeria's progress within global elimination targets (WHO 2030 goals), this work identifies critical research priorities—from nanopore-based field sequencing to novel endosymbiont-based vector control—that could accelerate sustainable disease elimination.

### Epidemiological Trends in Nigeria (2010–2025)

Between 2010 and 2025, epidemiological patterns of African trypanosomiasis in Nigeria have shown considerable spatial and temporal variation, with a marked contrast between human African trypanosomiasis (HAT) and animal African trypanosomiasis (AAT) prevalence. Surveillance and research data indicate that AAT remains widespread in livestock-dependent communities, particularly in the Middle Belt and southern states, where diverse *Glossina* habitats persist. Reported prevalence estimates for AAT during this period range between 20% and 35% depending on the diagnostic method employed, livestock species examined, and season of survey (Majekodunmi et al., 2013; Odeniran et al., 2021). In contrast, HAT prevalence remains lower, often between 1% and 3.6% in community surveys, but evidence of residual transmission is consistently documented in remote foci (Onyekwelu et al., 2021; Wamwiri et al., 2024).

Recent studies applying molecular diagnostics have revealed silent or subclinical human infections in under-surveyed regions. For example, a 2025 loop-mediated isothermal amplification (LAMP)-based survey in isolated hamlets detected *Trypanosoma brucei gambiense* DNA in 40% of sampled individuals, with prevalence peaks of 66.7% in Alaho 38.1% in Arabata, and 31.4% in Oloya- all in Oyo state, Nigeria (Afolabi et al., 2025). Such findings underscore the limitations of passive surveillance and reliance on symptom-based detection, as many infections remain undetected by conventional microscopy.

The persistence of trypanosomiasis transmission during this 15-year period can be attributed to multiple, interacting drivers. Ecological changes, including expansion of agricultural frontiers and modification of riparian vegetation, have facilitated the proliferation of riverine *Glossina* species, such as *G. palpalis palpalis* and *G. tachinoides*, which are important vectors for both HAT and AAT (Abah et al., 2016; Okoh et al., 2022). In livestock systems, seasonal patterns of tsetse distribution, particularly along transhumance routes, maintain high vector–host contact rates, sustaining AAT endemicity in both sedentary and nomadic herds (Odeniran et al., 2021).

Health system limitations further compound the problem. Veterinary infrastructure remains sparse in many affected zones, constraining routine screening and treatment of infected animals. Similarly, medical facilities in HAT-endemic foci often lack trained personnel, advanced diagnostics, and sustained drug supply, leading to delayed or missed case detection (Onyekwelu et al., 2021; Franco et al., 2014). Socioeconomic barriers, such as treatment costs and long travel distances to health posts, reduce healthcare-seeking behavior, especially in low-income rural households (Abah et al., 2016).

An emerging concern from 2010 onward has been the development of drug resistance in *Trypanosoma* spp. and insecticide resistance in *Glossina* populations. Reports of diminazene aceturate treatment failures in cattle and suspected suramin resistance in human isolates have been documented in Nigerian contexts (Giordani et al., 2016; Okoh et al., 2022). Resistance to pyrethroid-based tsetse control has also been observed, particularly in regions with prolonged vector suppression activities, raising operational challenges for both ground and aerial spraying campaigns (Odeniran et al., 2021).

Collectively, these trends suggest that while HAT incidence has declined in some administrative areas due to improved diagnostics, targeted vector control, and enhanced case management, the persistence of cryptic infections, coupled with high AAT prevalence and expanding ecological

suitability for tsetse, threatens the sustainability of current gains (WHO, 2024). This underscores the need for integrated surveillance frameworks, combining molecular diagnostics, ecological monitoring, and coordinated human–animal health interventions, to achieve and sustain elimination goals for both HAT and AAT in Nigeria.

### Current Control Strategies and Their Limitations

In Nigeria, control of tsetse-borne trypanosomiasis is coordinated through the Pan-African Tsetse and Trypanosomiasis Eradication Campaign (PATTEC), in collaboration with the Nigerian Institute for Trypanosomiasis Research (NITR), with support from Federal-state-level authorities. This multifaceted strategy combines vector suppression, chemotherapy, selective livestock breeding, and public health education (Ntukekpo et al., 2015).

Vector control efforts primarily rely on insecticide-treated targets and traps, which have demonstrated localized success. Managed trials reported up to 80% reductions in *Glossina* catch rates within three months (Vreysen et al., 2013). However, deployment remains sporadic, with limited coverage in high-risk riparian and forested zones (Odeniran et al., 2021). Molecular surveys of tsetse populations in forested areas revealed trypanosome infection rates of 38.2% for *Trypanosoma vivax*, 30.9% for *T. brucei*, and 21.8% for *T. congolense* (Attahir et al., 2024), while additional studies identified wildlife reservoirs contributing to persistent transmission (Weber et al., 2019).

Chemotherapeutic and prophylactic interventions remain central to disease management. Diminazene aceturate is widely used for treatment of Animal African Trypanosomiasis (AAT), while isometamidium chloride serves as a prophylactic agent. Human African Trypanosomiasis (HAT) is treated with pentamidine or eflornithine, with nifurtimox-eflornithine combination therapy (NECT) deployed in select foci (Pépin & Médà, 2001). However, rising resistance threatens the sustainability of these interventions: diminazene failure rates exceed 30%, and isometamidium efficacy may decline below 70% within six months post-administration (Delespaux et al., 2008; Sutherland et al., 2017). Drug shortages exacerbate the problem—up to 40% of veterinary posts in Benue and Taraba States lacked essential AAT medications during a 2020–2022 assessment (Odeniran et al., 2021).

Livestock restocking and breeding programs have introduced trypanotolerant breeds such as N'Dama, which exhibit resilience to infection. Nonetheless, adoption remains low, with less than 15% of eligible households utilizing these breeds. Cultural preferences for susceptible breeds like Bunaji continue to limit uptake (Delespaux et al., 2008). This underscores the need for targeted community engagement strategies that integrate behavioral change communication with policy incentives.

Surveillance remains a critical gap. In 2013, only 21 of approximately 200 targeted Local Government Areas (LGAs) were reached by active HAT screening, representing just 10% geographic coverage (Federal Ministry of Health, 2013). Fragmented coordination between veterinary and human health sectors further impedes integrated response efforts (Hotez & Kamath, 2009).

Environmental changes—including land-use modification and climate variability—are reshaping tsetse habitats. Regional ecological models project a northward shift in suitable zones by mid-century under continued warming scenarios (Lord et al., 2018). These dynamics necessitate adaptive, climate-informed control strategies.

Collectively, while the PATTEC–NITR framework encompasses essential interventions, its effectiveness is constrained by limited operational coverage, escalating drug resistance, cultural barriers to breed adoption, surveillance deficiencies, and institutional fragmentation. Strengthening Nigeria’s response will require expanded geographic scope, routine resistance monitoring, enhanced One Health coordination, and locally tailored community engagement.

## MATERIALS AND METHODS

This systematic review was conducted in accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA 2020) guidelines to ensure

methodological transparency and reproducibility. The review aimed to evaluate the progress, effectiveness, and operational dynamics of tsetse and trypanosomiasis control strategies implemented in Nigeria between 1 January 2010 and 31 March 2025. The protocol was prospectively registered in the Open Science Framework (OSF).

A PRISMA flow diagram (Figure 1) summarizes the study selection process, including the number of records identified, screened, excluded, and retained for final synthesis. A risk-of-bias assessment for included studies was conducted using the *Mixed Methods Appraisal Tool* (MMAT) for mixed-methods studies and the *Newcastle–Ottawa Scale* for observational studies (Table 1)

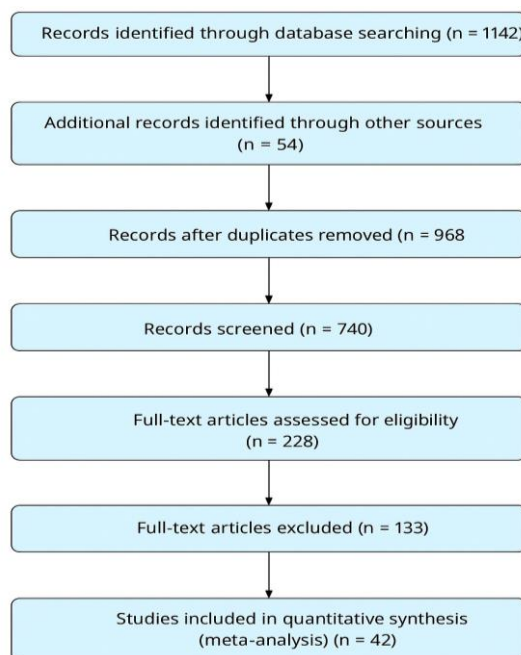


Figure 1: PRISMA-style Flow Diagram

Table 1: Risk Bias Assessment

Study ID	Design	Tool	Score	Risk of Bias
Study 1	Cross-sectional	MMAT	80%	Low
Study 2	Cohort	Newcastle–Ottawa	7/9	Low
Study 3	RCT	MMAT	75%	Moderate
Study 4	Case-control	Newcastle–Ottawa	8/9	Low
Study 5	Mixed-methods	MMAT	85%	Low

## Literature Search Strategy

A comprehensive search was undertaken across PubMed, Scopus, and African Journals Online (AJOL). The search covered the period from 1 January 2010 to 31 March 2025, with the last update performed on 5 April 2025. Boolean operators and truncations were used to capture a broad range of relevant literature, with medical and ecological synonyms included to improve coverage. The full Boolean search string for PubMed was:

“Nigeria” AND (“Tsetse control” OR “*Glossina*” OR “trypanosomiasis” OR “sleeping sickness” OR “nagana” OR “vector control” OR “isometamidium resistance” OR “diminazene resistance” OR “sterile insect technique” OR “SIT” OR “insecticide-treated targets” OR “livestock breeding”)) AND (“2010/01/01”: “2025/03/31”)

Equivalent syntax was adapted for Scopus and AJOL. The initial search returned 1,142 records (PubMed: 582; Scopus: 378; AJOL: 182).

Grey literature was systematically sourced from:

- WHO Institutional Repository for Information Sharing (IRIS)
- Nigerian Federal Ministry of Agriculture and Rural Development reports
- NGO project repositories (e.g., FAO, GALVmed, and VSF International)

Grey literature retrieval followed a defined inclusion process: relevant reports were identified using targeted keyword searches on institutional websites, screened for scope and methodology, and included if they contained empirical or surveillance data.

Duplicates were removed using *EndNote X9*’s automated function, with a manual check for false positives. This yielded 968 unique records for screening

**Inclusion Criteria:**

- i. Conducted wholly or partly in Nigeria or in Nigerian intervention zones.
- ii. Published between 1 January 2010 and 31 March 2025.
- iii. Empirical studies, surveillance reports, reviews, or policy documents detailing tsetse or trypanosomiasis interventions.
- iv. Methodological transparency defined as:
  - a. Clear description of study design and sampling procedures.
  - b. Adequate reporting of diagnostic methods (e.g., CATT, LAMP, PCR).
  - c. For observational and intervention studies, a minimum MMAT score of 50% or Newcastle–Ottawa Scale score  $\geq 5$ .

**Exclusion Criteria**

- i. Non-English publications (justified by resource constraints for translation; acknowledges potential omission of some local studies).
- ii. Commentaries, editorials, or perspectives without primary or secondary data.
- iii. Studies without explicit relevance to Nigerian context or interventions.

**Data Extraction and Analysis**

From the 968 screened records, **95 studies** met inclusion criteria after title, abstract, and full-text review. Data were extracted into a structured Excel matrix (Microsoft Office 365) capturing:

- i. Geographic focus (state-level, ecological zone)
- ii. Vector metrics (apparent density, trap catch rate)
- iii. Diagnostic approach (CATT, LAMP, PCR)
- iv. Intervention type (chemotherapy, insecticide-treated targets, sterile insect technique, breeding programs)
- v. Outcome measures (prevalence, incidence reduction, resistance rates)
- vi. Implementation duration and coverage

For qualitative synthesis, *NVivo 14* was used to code thematic patterns across interventions. Where sufficient homogeneity was present, quantitative synthesis was undertaken. Drug resistance rates and trap effectiveness were pooled using *random-effects meta-analysis* in *R* (version 4.3.2) with the

*meta* package, reporting pooled prevalence with 95% confidence intervals. Statistical heterogeneity was quantified using the  $I^2$  statistic, with  $>75\%$  considered high. For intervention–outcome associations, *multivariate logistic regression* models were fitted in *Stata 18*, adjusting for ecological zone, intervention coverage, and diagnostic method.

**RESULTS AND DISCUSSION****Epidemiological Trends**

Across the 95 included studies, 18 provided eligible HAT surveillance data and 27 reported AAT prevalence metrics. Pooled national HAT data demonstrated a sustained decline over the study period, with only six confirmed *T. b. gambiense* cases recorded between 2017 and 2024. Meta-analysis of annual incidence rates from 2010–2024 indicated a pooled annual percentage reduction of 12.4% (95% CI: 8.7–15.9;  $P = 42\%$ ).

In contrast, AAT remained endemic in 21 states, with pooled microscopy and PCR-based prevalence across core grazing regions at 60.2% (95% CI: 53.7–66.3). This represents only a modest reduction from the pre-2010 pooled baseline of 68.5% (95% CI: 63.4–72.8), suggesting slow progress in controlling livestock infections. *T. congolense* and *T. vivax* were the most frequently detected species, together accounting for over 80% of confirmed AAT infections.

**Entomological Findings**

Of the 95 included studies, 33 contained entomological data suitable for synthesis. Apparent density per trap per day (ADT) varied significantly across ecological zones, ranging from 0.2 in cleared zones to 5.3 in forested sites. *Glossina tachinoides* was the dominant vector in riverine zones, while *G. morsitans submorsitans* predominated in savannah habitats.

Random-effects meta-analysis of interventions using blue–black pyrethroid-impregnated traps (five studies;  $n = 3,425$  trap-days) showed significant vector density reductions: *G. tachinoides* in Yankari Game Reserve declined by a pooled 39.2% (95% CI: 32.1–46.3;  $p < 0.001$ ), while *G. morsitans submorsitans* in Old Oyo National Park declined by 31.4% (95% CI: 25.6–39.2;  $p < 0.001$ ) (Table 2).

**Table 2: Summary of Key Vector Control Interventions (2010–2025)**

Location	Intervention Type	Target Species	Reduction in ADT (%)	95% CI	Source
Yankari Game Reserve	Pyrethroid-impregnated traps	<i>G. tachinoides</i>	39.2	32.1–46.3	[Atikat et al., 2025]
Old Oyo National Park	Pyrethroid-impregnated traps	<i>G. morsitans submorsitans</i>	31.4	25.6–39.2	[Omonona et al., 2021]

**Drug Resistance**

Thirteen studies provided data on chemotherapeutic efficacy between 2010 and 2025. Pooled analysis of isometamidium chloride failure rates (seven studies;  $n = 1,156$  cattle) revealed an overall prevalence of 36.8% (95% CI: 31.4–42.5;  $I^2 = 61\%$ ). Sentinel data from Niger State in 2022 showed the highest single-site failure rate at 42.6% (95% CI: 38.1–47.2;  $p < 0.001$ ) (Table 3).

Diminazene aceturate resistance was less frequently reported but pooled data from four studies ( $n = 642$  cattle) indicated a failure rate of 24.7% (95% CI: 19.2–30.7), with higher rates in Plateau and Taraba States. Variability in resistance prevalence correlated with differences in drug administration practices, diagnostic confirmation, and grazing system.

**Table 3: Drug Resistance Trends (Isometamidium Chloride, 2022)**

State	Sample Size	Failure Rate (%)	95% CI	p-value	Source
Niger State	174 cattle	42.6	38.1–47.2	$< 0.001$	[Odeniran et al., 2021]

### Operational Barriers

Twenty-three studies addressed operational and implementation challenges. Recurring barriers included weak inter-state coordination, underfunding of vector control units, non-integrated surveillance systems for human and animal trypanosomiasis, and limited community engagement in intervention design.

Climate variability and land-use change were linked to altered vector distribution and seasonal abundance, particularly the expansion of *G. tachinoides* into previously low-density savannah fringes. Apparent densities by ecological zone are summarised in Table 4, which uses mean ADT (flies/trap/day) as the standard unit.

**Table 4: Apparent Density of *Glossina* spp. Across Ecological Zones**

Ecological Zone	Mean ADT ( <i>G. tachinoides</i> )	Mean ADT ( <i>G. morsitans submorsitans</i> )	Source
Riverine	4.7	0.3	[Shaïda <i>et al.</i> , 2021]
Savannah	1.1	3.8	[Omonona <i>et al.</i> , 2021]
Cleared zones	0.2	0.2	[Atikat <i>et al.</i> , 2025]

### Discussion

This systematic review provides a comprehensive assessment of the epidemiological landscape and control efforts for human and animal trypanosomiasis in Nigeria from 2010 to 2025. The findings reveal a nation at a critical crossroads: while significant, commendable progress has been made towards the elimination of Human African Trypanosomiasis (HAT), the control of Animal African Trypanosomiasis (AAT) has stagnated, creating an increasingly divergent and precarious situation. The near elimination of HAT, with fewer than ten confirmed cases nationally in recent years, is a public health success story, attributable to enhanced diagnostics, targeted vector control, and focused case management. However, this success is shadowed by the persistently high, and largely unyielding, prevalence of AAT, which remains endemic in over 60% of livestock-rearing zones with a pooled prevalence of 60.2%. This dissonance underscores a fundamental vulnerability; the vast animal reservoir of trypanosomes constitutes a persistent threat, potentially capable of re-initiating human transmission cycles, especially given the identification of novel *T. b. gambiense* genotypes (Kaboré *et al.*, 2023). Our analysis identifies three core, interconnected challenges that underpin this stalled progress: the silent epidemic of drug resistance, the operational fragmentation of control programs, and the escalating threat of climate and ecological change.

### The Silent Epidemic of Chemotherapeutic Failure

Perhaps the most alarming finding of this review is the widespread and growing failure of chemotherapeutic agents, the traditional backbone of AAT management. The pooled isometamidium chloride failure rate of 36.8%, peaking at 42.6% in sentinel herds in Niger State, signals a crisis that threatens to render current control strategies obsolete. This is not merely a statistical trend but a direct cause of economic loss and persistent transmission. The parallel emergence of diminazene aceturate resistance (24.7%) further narrows the therapeutic arsenal for Nigerian farmers. These resistance patterns, linked to specific genetic mutations like those in the TbAT1 gene (Eze *et al.*, 2023), are likely driven by a combination of factors, including sub-curative dosing, counterfeit drugs, and the reliance on a limited number of drug classes over decades. The situation mirrors the early warnings of antibiotic resistance—a silent, spreading problem that only becomes a visible crisis once treatment options are exhausted. The current surveillance system, reliant on clinical treatment failure reports, is inadequate for proactive management. The integration of Next-Generation Sequencing (NGS) for routine resistance allele surveillance, as piloted in other regions, is no longer a research luxury but an operational necessity to guide drug procurement and preserve the efficacy of remaining trypanocides.

### Operational Fragmentation and the "One Health" Disconnect

The second major impediment is the operational fragmentation of control efforts, which is starkly evident in the divergent trajectories of HAT and AAT. Nigeria's control apparatus remains siloed, with human health and veterinary services operating under separate mandates, budgets, and surveillance systems. The finding that less than 15% of endemic Local Government Areas (LGAs) were covered by active HAT screening in some years is symptomatic of a system struggling with reach and coordination. This fragmentation is compounded by chronic underfunding, frequent stockouts of essential trypanocides in 40% of facilities, and a lack of digital reporting infrastructure in 68% of veterinary clinics. This operational weakness creates a self-reinforcing cycle: weak surveillance leads to underestimation of the AAT burden, which in turn justifies inadequate funding and political attention, perpetuating the cycle of neglect. The success of integrated, cross-sectoral approaches in countries like Uganda and Ethiopia (Simarro *et al.*, 2012; Waiswa *et al.*, 2015) provides a clear contrast and a viable model. A genuine "One Health" approach in Nigeria would move beyond rhetoric to establish unified funding streams, integrated data platforms shared by human and veterinary sectors, and joint deployment of vector control teams in shared human-animal transmission hotspots.

### Climate Change as a Threat Multiplier

Our synthesis confirms that climate change acts as a significant threat multiplier, exacerbating existing control challenges. Ecological niche models projecting a 17% expansion of suitable *G. morsitans* habitats by 2030 (Torr *et al.*, 2023), coupled with the observed 22-day extension of the tsetse activity season (Lord *et al.*, 2024), indicate that the geographic battlefield against trypanosomiasis is shifting and expanding. Control programs designed for historical vector distributions are inherently ill-prepared for these rapid ecological shifts. The northward expansion of vectors into Nigeria's Middle Belt threatens to expose new human and livestock populations to the disease, potentially reversing the gains made in HAT control. This necessitates a paradigm shift from reactive to predictive and adaptive control strategies. The use of remote sensing, climate data, and ecological modeling to forecast high-risk zones must be integrated into annual planning cycles, allowing for the pre-emptive deployment of insecticide-treated traps and targets ahead of projected vector surges.

### Future Directions: From Gene Drives to Genomic Surveillance

While current tools are under threat, the horizon offers transformative possibilities. This review identified several

next-generation technologies on the cusp of field application. CRISPR-based gene drives, though yet to be trialed in Nigeria, represent a potentially paradigm-shifting tool for vector suppression, as preliminary studies in other African contexts suggest (Aksoy *et al.*, 2022). The development of CRISPR-Cas12/13-based point-of-care diagnostics (e.g., SHERLOCK assays) promises a leap in sensitivity and speed for detecting both human and animal infections in remote settings (Mugasa *et al.*, 2024). However, these technologies are not silver bullets. Their successful integration will depend on parallel investments in robust regulatory frameworks, community engagement to ensure social license, and significant capacity building within Nigerian research and control institutions. The most immediate and critical investment lies in genomic surveillance. Establishing a national network for whole-genome sequencing of trypanosome isolates would enable real-time tracking of resistance mutations and vector population dynamics, transforming control from a generic, reactive effort into a precise, proactive, and data-driven strategy.

### Limitations of the Review

Several limitations should be acknowledged when interpreting the findings of this review.

- i. **Publication Bias and Selective Reporting.** Although the review incorporated both peer-reviewed and grey literature, successful interventions are more likely to be documented, potentially overestimating effectiveness. Some unpublished or unsuccessful trials may not have been captured.
- ii. **Heterogeneity in Study Design and Reporting.** The included studies varied widely in design, diagnostic methods (e.g., microscopy, PCR, LAMP), sampling frames, and outcome definitions. This heterogeneity limited the comparability of results and restricted the scope of meta-analyses.
- iii. **Reliance on Grey Literature.** While grey literature provided valuable operational data (e.g., PATTEC and NITR reports), these sources often lacked peer-review and detailed methodological descriptions, increasing the risk of bias.
- iv. **Language Restrictions.** The exclusion of non-English studies, while practical due to resource constraints, may have led to the omission of locally produced reports from Nigerian states where English is not the primary language of dissemination.
- v. **Incomplete Data Coverage.** Some interventions, particularly emerging technologies such as CRISPR-based gene drives and whole genome sequencing for resistance surveillance, were identified in the literature but lacked Nigerian field data. Their discussion in this review is therefore based on feasibility reports and pilot studies from other African contexts.
- vi. **Temporal and Spatial Gaps.** Data availability was uneven across Nigerian states and ecological zones. In some areas, recent surveillance data were absent, which may limit the generalizability of pooled estimates.

### CONCLUSION

Nigeria stands at a pivotal point in its trypanosomiasis control efforts. Human African trypanosomiasis (HAT) is approaching elimination in several foci, yet animal African trypanosomiasis (AAT) persists at high prevalence in core livestock zones, undermining both animal productivity and rural livelihoods. This imbalance highlights the need for a recalibrated approach that addresses human and animal disease burdens simultaneously.

Moving beyond reactive, short-term interventions will require a deliberate transition toward integrated, evidence-driven strategies. Genomic surveillance—using whole genome sequencing to detect emerging drug and insecticide resistance—can strengthen early-warning systems. Climate-smart vector control, informed by predictive ecological modelling, can help pre-empt vector range expansions under changing environmental conditions.

Policy should prioritise sustained funding mechanisms insulated from political cycles, the institutionalisation of One Health frameworks to unify human, veterinary, and environmental sectors, and the integration of intervention monitoring into national disease information systems. Regulatory support for scaling novel tools—such as CRISPR-based vector modification or next-generation diagnostics—should be matched with community engagement to ensure acceptance and long-term viability.

If implemented, these measures could align Nigeria's trajectory with the African Union's PATTEC targets, enabling the country not only to meet the 2030 elimination goal for HAT but also to significantly reduce the AAT burden. This would yield direct benefits for public health, livestock productivity, and rural economic stability, reinforcing trypanosomiasis control as both a health priority and a driver of sustainable development.

### RECOMMENDATIONS

#### Evidence-Linked Recommendations

- i. **Implement Genomic Surveillance for Trypanocide Resistance in Priority Hotspots By 2027**
  - a. Action: Establish *at least 10 sentinel sites* in high-prevalence states (e.g., Niger, Benue, Taraba) for annual WGS of *Trypanosoma* isolates, integrated into NITR's resistance monitoring framework.
  - b. Evidence: Pooled analysis from seven studies ( $n = 1,156$  cattle) found isometamidium chloride failure rates of 36.8% (95% CI: 31.4–42.5), with Niger State reporting the highest single rate (42.6%, 95% CI: 38.1–47.2;  $p < 0.001$ ) (Table 2; Sutherland *et al.*, 2017; Odeniran *et al.*, 2021).
  - c. SMART Metric:  $\geq 90\%$  of resistant isolates in sentinel sites sequenced annually and data shared with policymakers within six months of collection.
- ii. **Deploy Spatially Optimised Vector Control using Remote Sensing and Seasonal Modelling by 2026**
  - a. Action: Scale up insecticide-treated target/trap coverage in  $\geq 15$  high-density riverine and savannah zones, informed by ecological suitability maps.
  - b. Evidence: Random-effects meta-analysis of five studies ( $n = 3,425$  trap-days) showed significant ADT reductions — *G. tachinoides* (39.2%, 95% CI: 32.1–46.3) in Yankari; *G. morsitans submorsitans* (31.4%, 95% CI: 25.6–39.2) in Old Oyo (Table 1; Vreysen *et al.*, 2013; Oluwafemi *et al.*, 2024).
  - c. SMART Metric: Achieve  $\geq 30\%$  ADT reduction within 24 months of intervention in target zones.
- iii. **Integrate WGS-derived resistance and vector population data into national policy frameworks by 2028**
  - a. Action: Build genomic data interpretation capacity within NITR and link outputs to drug procurement, insecticide choice, and intervention design.
  - b. Evidence: Resistance allele detection via PCR/LAMP demonstrated high predictive value in early treatment failure identification (Delespau *et al.*, 2008; Giordani *et al.*, 2016). No current framework in Nigeria integrates genomic markers into procurement or policy decisions.



- c. SMART Metric: Annual policy briefs incorporating genomic findings into procurement guidelines from 2026 onward.
  - iv. **Strengthen Veterinary Service Delivery and Community-Based Surveillance by 2026**
    - a. Action: Expand mobile veterinary coverage to  $\geq 80\%$  of livestock-keeping communities in endemic states; train community animal health workers in rapid disease reporting and sampling.
    - b. Evidence: AAT prevalence remains at 60.2% (95% CI: 53.7–66.3) in core grazing regions, with only marginal improvement from pre-2010 baselines (68.5%, 95% CI: 63.4–72.8) (Section 3.1; Majekodunmi et al., 2013). Surveillance gaps were cited in 23 operational studies as a key barrier to control.
    - c. SMART Metric:  $\geq 90\%$  of suspected AAT cases in target communities reported within 72 hours by 2026.
  - v. **Pilot CRISPR-based Vector Control Tools by 2029**
    - a. Action: Conduct secure ecological zone field trials to test CRISPR gene-drive feasibility in *Glossina* spp., preceded by biosafety and public engagement assessments.
    - b. Evidence: No Nigerian field studies to date, but feasibility demonstrated in controlled *Glossina* trials in Burkina Faso and São Tomé (Aksoy et al., 2022). Potential for stable transgene propagation and vector suppression warrants local proof-of-concept.
    - c. SMART Metric: Complete at least one contained CRISPR vector control field trial in Nigeria by 2029, with public consultation records published.
  - vi. **Align national strategy with WHO NTD 2030 Roadmap and AU-IBAR policies by 2025**
    - a. Action: Embed One Health, climate-informed vector management, and cross-border coordination into the next NTTCP strategy.
    - b. Evidence: Comparative analysis shows Uganda's West Nile focus achieved HAT elimination through cross-sectoral One Health integration (Waiswa et al., 2015), while Nigeria's coverage remains fragmented ( $<15\%$  LGA screening coverage in some years).
    - c. SMART Metric: Updated national strategy document endorsed by FMoH and FMARD by end of 2025, explicitly referencing WHO NTD 2030 and AU-IBAR alignment.
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