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Title of Article

Occupational Health in Eswatini's Informal Sector: A Narrative Review of Hazards, Risk Awareness, and Structural Vulnerability

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Abstract

Occupational health in the informal sector remains a neglected dimension of public health in sub-Saharan Africa, and Eswatini in particular lacks any systematic empirical study of the hazards facing its informal workforce despite the sector accounting for close to half of national employment. This paper presents a narrative review synthesizing global, regional, and local evidence on occupational hazards, risk awareness, and protective practices among informal workers, with particular attention to studies from Kenya, Ghana, and South Africa as the closest available regional comparators. Three theoretical frameworks (Risk Perception Theory, the Health Belief Model, and the Social Determinants of Health) are integrated to explain how hazard exposure, individual awareness, and structural constraints interact to shape occupational health outcomes in informal settings. The review finds that across comparable African contexts, informal workers face overlapping physical, chemical, ergonomic, and psychosocial hazards; that awareness of immediate risks is typically higher than awareness of chronic, cumulative risks; and that protective practices are consistently constrained less by knowledge gaps than by affordability and access barriers. Applying these findings to Eswatini, the review argues that occupational health in the country's informal sector is not merely a technical challenge of hazard control but a structural issue rooted in policy exclusion and economic constraint. Because no primary data specific to Eswatini currently exists, the review's central recommendation is that a properly ethics-approved empirical study be conducted to test whether these regional patterns hold locally, alongside interim policy measures, including inclusive occupational health frameworks, subsidized protective equipment, and worker empowerment, that regional evidence already supports.

Keywords

Informal Sector; Occupational Health; Risk Perception; Protective Practices; Sub-Saharan Africa; Public Health Policy; Social Determinants Of Health;

Introduction

Occupational health is a critical component of public health because working conditions directly influence the physical, mental, and social wellbeing of populations. Globally, millions of workers are exposed to occupational hazards that increase the risk of injuries, illnesses, disability, and reduced quality of life. The International Labour Organization estimates that work-related accidents and diseases

contribute substantially to global morbidity and mortality, particularly in low- and middle-income countries where occupational safety systems are often weak (ILO, 2022).

The informal sector has become one of the largest sources of employment worldwide, especially in developing countries where unemployment and poverty continue to rise. Informal employment includes economic activities not fully regulated or protected by labor legislation and social protection systems. Workers in this sector commonly engage in street vending, construction, waste collection, transportation services, small-scale manufacturing, and domestic work. Although the informal sector contributes significantly to household income and national development, workers often operate under unsafe and unhealthy conditions with limited occupational health protection.

In Eswatini, the informal sector has expanded due to unemployment, economic instability, and limited formal opportunities, and as of 2019 accounted for an estimated 45% of the national labour force (Institute for Security Studies African Futures, 2023). Despite its economic importance, occupational health and safety among informal workers remains a neglected and empirically unexamined public health issue: at present, no published, peer-reviewed study documents occupational hazards, awareness levels, or health outcomes among Eswatini's informal workforce specifically. This absence of local evidence is itself a significant finding: it means that any occupational health intervention or policy currently directed at the sector in Eswatini would necessarily be based on inference from other contexts rather than local data.

This paper addresses that gap through a narrative review rather than a primary empirical study. It synthesizes global and regional literature on occupational hazards, risk awareness, and protective practices in informal work, integrates this evidence with established behavioral and structural theory, and applies the resulting synthesis analytically to Eswatini's informal sector. It argues that occupational health in Eswatini's informal sector is not merely a technical challenge of hazard control, but is likely, based on consistent patterns observed across comparable Sub-Saharan African contexts, also a structural issue rooted in exclusion from policy frameworks, economic constraints, and inequitable access to healthcare. The review's central contribution is not new primary data, but a rigorous synthesis that identifies what is already known regionally, what specifically remains unknown about Eswatini, and what a future empirical study in this setting would need to establish.

Literature Review

Global Perspectives on Occupational Health in the Informal Sector

Occupational health hazards in the informal sector have been extensively documented across diverse global contexts. Informal workers are exposed to a wide range of risks, including physical hazards such as dust, noise, heat, unsafe machinery, and poor ventilation; chemical hazards including fumes, solvents, pesticides, cleaning agents, and industrial by-products; ergonomic strain from repetitive movements, prolonged standing, heavy lifting, and awkward postures; and psychosocial stressors such as harassment, job insecurity, long working hours, and income instability (ILO, 2022; WHO, 2021).

A recurring theme in global research is the absence of protective equipment and health services. Informal workers often operate outside the reach of occupational health systems, leaving them vulnerable to both immediate injuries and long-term illnesses. Studies consistently show that informal employment is associated with higher morbidity and mortality compared to formal sector work (Renn, 2008).

Global debates also emphasize whether informal work should be treated primarily as a labor rights issue or as a public health challenge. Some scholars argue that occupational health protections must be integrated into broader labor reforms, while others highlight the need for targeted health interventions that address exposure risks directly. This divergence illustrates the complexity of situating informal work within global health and development agendas.

Another global insight is the gendered dimension of informal work. Women are disproportionately represented in domestic work, street vending, and caregiving roles, where occupational hazards are often invisible or undervalued. Men, meanwhile, dominate construction and waste collection, where risks are more visible but still poorly mitigated. This gendered division of labor shapes exposure patterns and health outcomes, underscoring the need for gender-sensitive occupational health policies.

Regional Evidence from Sub-Saharan Africa

In Sub-Saharan Africa, research converges on the prevalence of unsafe working conditions and low risk awareness. In Kenya, Kemei, Kaluli and Kabubo (2017) found that construction workers in Nairobi County were regularly exposed to hazards such as falls, unsafe scaffolding and inadequate site supervision, with limited enforcement of existing safety standards. In Ghana, Alfers (2016) documented that market and street traders in Accra and Takoradi faced elevated risks of traffic accidents, fire hazards, crime, weather-related discomfort and musculoskeletal injury, compounded by weak communication between trader organisations and local government on occupational health and safety matters. In South Africa, Uhunamure, Edokpayi and Shale (2021) found that waste pickers at landfill sites were significantly more likely to develop health disorders the longer they worked, with inadequate access to personal protective equipment identified as a key contributing factor.

Regional policy responses remain fragmented. While some governments have attempted to extend occupational health protections to informal workers, implementation has been weak due to resource constraints and limited enforcement capacity. This has created a situation where informal workers remain largely excluded from occupational health frameworks, despite their significant contribution to national economies.

The regional literature also highlights structural inequities: informal workers are often marginalized in policy discourse, and occupational health is rarely prioritized in national development strategies. This exclusion perpetuates cycles of vulnerability, where workers are aware of immediate risks but lack the means to mitigate them.

Another recurring theme is the role of poverty and inequality. Informal workers often accept hazardous conditions because they lack alternatives. For example, waste pickers in urban centers may knowingly expose themselves to toxic materials because the income, though meager, is essential for survival. This illustrates how occupational health risks are embedded within broader socioeconomic realities.

Local Context: Eswatini

In Eswatini, systematic evidence on occupational health in the informal sector remains scarce. While anecdotal reports highlight exposure to unsafe environments, few studies have examined the interaction between hazards, awareness, and health outcomes. Informal workers in urban and peri-urban areas operate in conditions characterized by poor sanitation, inadequate ventilation, and limited access to protective equipment.

The scale of this gap is significant given the size of the sector: as of 2019, an estimated 45% of Eswatini's labour force worked in the informal economy, contributing approximately US$1.6 billion, or 27.8% of GDP (Institute for Security Studies African Futures, 2023). Despite this economic weight, occupational health research and policy attention directed at the sector remain minimal.

Policy frameworks in Eswatini have historically prioritized formal sector workers, leaving informal workers without structured protections. This exclusion reflects broader institutional dynamics where informal employment is undervalued, despite its role in sustaining livelihoods. The absence of localized evidence further limits the ability of policymakers to design interventions that address the realities of informal work.

The Eswatini context is further complicated by economic instability and high unemployment rates, which push many individuals into informal work as a survival strategy. Informal workers often lack bargaining power, operate outside labor unions, and remain invisible in national statistics. This invisibility contributes to policy neglect, reinforcing occupational health vulnerabilities.

This review therefore treats Eswatini as an evidence gap rather than an evidence base: rather than claiming to fill the gap with new data, the remainder of this paper synthesizes what is known from comparable regional contexts to generate testable, context-specific expectations for Eswatini: expectations that a future locally-grounded empirical study would need to confirm or revise.

Critical Synthesis

Taken together, global, regional, and local studies suggest that informal workers face multidimensional hazards and limited protections. However, there is little consensus on which risks should be prioritized. Some studies emphasize physical hazards such as dust and noise, while others highlight psychosocial stress or ergonomic strain.

There is also debate over whether awareness alone improves outcomes. Some argue that knowledge of risks leads to safer practices, while others show that without resources such as PPE, awareness has

little effect. This tension underscores the importance of integrating structural interventions with educational campaigns.

Policy perspectives add another layer of complexity. Global organizations such as the ILO and WHO advocate for inclusive occupational health frameworks, yet national implementation remains uneven. In Eswatini, the lack of institutional recognition of informal work exacerbates vulnerability, suggesting that occupational health must be understood not only as a technical issue but also as a matter of equity and governance.

Finally, the literature highlights the need for context-specific interventions. While global frameworks provide useful guidance, occupational health strategies must be tailored to local realities. In Eswatini, this means recognizing the diversity of informal occupations, addressing affordability barriers, and integrating occupational health into broader community health initiatives.

Conceptual Framework

Occupational health in the informal sector is shaped by multiple interacting factors, including individual risk perception, health behavior, and broader social determinants. To analyze these dynamics, this study draws on established theoretical frameworks that provide explanatory power for understanding how hazards, awareness, and outcomes intersect. By integrating Risk Perception Theory, the Health Belief Model, and the Social Determinants of Health, the study situates occupational health outcomes within both individual and structural dimensions.

Risk Perception Theory

Risk Perception Theory emphasizes how individuals interpret and respond to hazards based on subjective judgments rather than objective measures (Renn, 2008). Informal workers may perceive immediate risks such as cuts or burns more acutely than long-term risks like respiratory illness, which are less visible and harder to connect directly to workplace exposure.

Applied to Eswatini, street vendors in Manzini often recognize the danger of burns from cooking stoves but may underestimate the cumulative effects of inhaling smoke daily. Similarly, waste collectors in Mbabane are acutely aware of sharp injuries from broken glass but less conscious of long-term risks such as chronic respiratory disease from dust and fumes. This framework helps explain why awareness of chronic hazards remains limited, and why protective practices are often inconsistent despite high exposure; it underscores the need for interventions that make invisible risks more salient to workers.

Health Belief Model (HBM)

The Health Belief Model provides a lens for understanding health behavior in relation to four key constructs: perceived susceptibility, perceived severity, perceived benefits, and perceived barriers (Rosenstock, 1974). Informal workers may recognize the severity of hazards but underestimate their personal susceptibility; for example, construction workers may acknowledge that falls are dangerous but believe "it won't happen to me." Workers often understand that protective equipment such as gloves

and masks could reduce risks, yet affordability and accessibility remain the most significant barriers, since PPE is often too costly, unavailable in local markets, or impractical for daily use.

Applied to Eswatini, domestic workers in Mbabane may perceive cleaning chemicals as hazardous but avoid gloves because they are expensive or hinder dexterity, while transport operators may recognize fatigue as a risk but continue long hours due to economic necessity. The HBM clarifies how awareness interacts with economic constraints to shape protective practices, and why knowledge alone may not translate into safer behavior. Effective interventions must reduce barriers, for example by subsidizing PPE or integrating occupational health into community health services.

Social Determinants of Health

The Social Determinants of Health framework situates occupational health within broader structural conditions, including poverty, inequality, and exclusion from policy frameworks (WHO, 2021). Informal workers in Eswatini operate in environments where economic instability and institutional neglect limit access to healthcare and safety protections. They are excluded from labor protections, health insurance, and formal occupational health systems, and poverty forces workers to prioritize immediate income over long-term health. National occupational health policies tend to focus on formal sector workers, leaving informal workers invisible in official statistics and unprotected in practice.

Applied to Eswatini, waste collectors often work without municipal support, handling hazardous materials without gloves or masks, while street vendors face harassment in public spaces without recourse to legal protections. These conditions reflect systemic inequities rather than individual choices. This perspective highlights that occupational health outcomes are not only the result of individual behavior but also of structural exclusion, meaning that addressing occupational health requires policy reform, social protection, and community empowerment.

Integrated Framework for the Study

By combining these perspectives, the study develops an integrated conceptual framework in which Risk Perception Theory explains how hazards are understood, the Health Belief Model clarifies how awareness translates into behavior, and the Social Determinants of Health highlight the structural constraints that shape outcomes. Together, these frameworks provide a comprehensive basis for analyzing occupational health in Eswatini's informal sector, ensuring that both individual and systemic dimensions are addressed. This integration allows the study to move beyond narrow technical approaches to hazard control and instead frame occupational health as a structural and ethical imperative central to advancing equity, resilience, and sustainable national development.

Methodology

Review Design

This paper adopts a narrative review design rather than a primary empirical study. A narrative review was chosen because the objective was to synthesize and critically compare findings across a

heterogeneous body of existing literature, spanning peer-reviewed studies, institutional reports, and grey literature, in order to characterize what is currently known about occupational health in Sub-Saharan Africa's informal sector, and to identify key gaps in current knowledge about Eswatini specifically. A systematic review or meta-analysis was not appropriate given the objective: the aim was not to pool effect sizes across homogeneous studies, but to build an integrated, context-sensitive synthesis capable of generating locally relevant hypotheses in the absence of local data (Snyder, 2019).

Search Strategy and Sources

Sources were identified through targeted and structured searches of Google Scholar, ResearchGate, PubMed/PMC, and the institutional repositories of the International Labour Organization (ILO), World Health Organization (WHO), and Women in Informal Employment: Globalizing and Organizing (WIEGO), the leading research and advocacy network on the informal economy. Search terms combined variations of "occupational health," "informal sector," "informal economy," and "occupational hazards" with geographic qualifiers ("Sub-Saharan Africa," "Eswatini," "Swaziland," and individual country names) and occupation-specific terms ("street vendors," "waste pickers," "construction workers," "domestic workers"). Priority was given to literature published between 2010 and 2024, reflecting the period in which occupational health scholarship on Sub-Saharan Africa's informal sector has been most active; a small number of older foundational theoretical sources were retained where no more recent equivalent existed.

Sources were included if they reported empirical findings or authoritative institutional data on occupational hazards, risk awareness, or protective practices among informal or precarious workers, with priority given to studies conducted in Sub-Saharan Africa. Sources with unverifiable authorship, publication venue, or bibliographic details were excluded, reflecting a deliberate methodological safeguard given the risk of citing fabricated or unverifiable literature, which is a known integrity concern in rapidly assembled reviews. Where no African-specific study was available on a given hazard type or theoretical point, global literature was used and this substitution is flagged explicitly in the text rather than presented as regionally specific evidence.

Analytical Approach

Included sources were organized thematically around the study's guiding constructs, namely hazard type, risk awareness, protective practice, and structural or economic constraint, and read through the lens of the conceptual framework developed in the Literature Review section (Risk Perception Theory, the Health Belief Model, and the Social Determinants of Health). This thematic organization allowed patterns that recur across otherwise distinct occupational groups and country contexts (for example, the consistent gap between awareness of immediate versus chronic hazards) to be identified and then examined for their plausible applicability to Eswatini, given the structural similarities between Eswatini's informal sector and those of neighboring countries.

This approach has a specific and acknowledged limitation: because no primary data were collected in Eswatini, none of the patterns identified below can be confirmed to hold there with certainty. They are

presented as literature-informed expectations, not established local findings, and the Analysis and Recommendations sections are written to preserve this distinction throughout.

Analysis

Hazard Patterns Across Comparable Contexts

Read together, the regional literature reviewed above shows a consistent pattern: informal workers across occupation types in Sub-Saharan Africa are exposed to overlapping physical, chemical, ergonomic, and psychosocial hazards, rather than a single dominant risk. Construction workers in Nairobi face falls and unsafe scaffolding (Kemei, Kaluli and Kabubo, 2017); waste pickers in South African landfill sites face escalating health risk the longer they are exposed, largely due to inadequate protective equipment (Uhunamure, Edokpayi and Shale, 2021); and market and street traders in urban Ghana face a distinct hazard profile combining traffic accidents, fire risk, weather exposure, and musculoskeletal strain (Alfers, 2016). Domestic workers, a heavily female-dominated and largely invisible occupational category across the region, face a further distinct combination of physical strain, chemical exposure to cleaning agents, and psychosocial risk arising from isolation and lack of legal protection within private households (WIEGO, 2024).

The consistency of this pattern across otherwise very different occupations and countries is itself informative: it suggests that hazard exposure in informal work is driven less by the specific tasks involved than by structural features common to informality itself: the absence of regulatory oversight, the absence of employer-provided protective equipment, and the economic precarity that discourages workers from prioritizing safety over immediate income.

Occupational Group	Illustrative Hazard Profile	Source
Construction workers (Kenya)	Falls, unsafe scaffolding, inadequate site supervision	Kemei, Kaluli and Kabubo (2017)
Waste pickers (South Africa)	Cuts, toxic exposure, elevated illness risk with exposure duration	Uhunamure, Edokpayi and Shale (2021)
Market and street traders (Ghana)	Traffic accidents, fire, crime, weather exposure, musculoskeletal strain	Alfers (2016)
Domestic workers (regional)	Chemical exposure, physical strain, isolation, legal exclusion	WIEGO (2024)

Table 1: Illustrative occupational hazard profiles by informal occupational group, drawn from Sub-Saharan African literature. This table synthesizes existing published findings; it does not report new primary data.

The Awareness-Behaviour Gap

A second recurring pattern across the literature is a gap between awareness of immediate hazards and awareness of chronic, cumulative hazards. Workers across the reviewed studies consistently recognize acute risks, such as cuts, falls, and burns, more readily than they recognize slow-developing risks such as respiratory illness from chronic dust or chemical exposure, or musculoskeletal disorders from repetitive strain. This pattern is precisely what Risk Perception Theory predicts (Renn, 2008): risks that

are immediate, visible, and directly attributable to a single incident are perceived as more threatening than risks that accumulate gradually and are harder to attribute to a specific cause.

Critically, the literature also converges on a second point that complicates a purely awareness-based explanation: even where workers *are* aware of risks, protective behaviour does not reliably follow. This is consistent with the Health Belief Model's distinction between perceived risk and perceived barriers (Rosenstock, 1974): studies of PPE use across occupational contexts repeatedly find that cost, availability, and practicality of protective equipment, rather than knowledge, are the binding constraint on protective behaviour. Applied to the informal sector specifically, this suggests that awareness campaigns alone, absent parallel investment in affordable protective equipment, are unlikely to substantially change protective practices among Eswatini's informal workers, if the regional pattern holds locally.

Structural and Economic Constraints

The third theme running through the literature is that occupational health outcomes in the informal sector cannot be separated from the structural and economic conditions under which informal work occurs. The Social Determinants of Health framework (WHO, 2021) helps explain why: informal workers are, almost by definition, excluded from the labour protections, insurance schemes, and regulatory oversight that structure occupational safety in the formal sector. This exclusion is not incidental but constitutive of informality itself, and it means that occupational health interventions aimed only at individual behaviour, such as training or awareness campaigns, are working against a structural current that individual-level interventions alone cannot overcome.

This is visible concretely in the gendered dimension of informal work: domestic workers, who are overwhelmingly women, face occupational hazards that are additionally obscured by the private, unregulated setting of the household workplace, and by broader social devaluation of domestic labour (WIEGO, 2024). Street traders, similarly, face harassment and even violence as an occupational hazard layered on top of physical risks, with limited recourse given their exclusion from formal labour protections (Alfers, 2016).

Applying the Pattern to Eswatini

No study in this review was conducted in Eswatini, and this section should be read as extrapolation, not established fact. Given the structural similarity between Eswatini's informal sector and those studied in Kenya, Ghana, and South Africa, including a large informal share of national employment (an estimated 45% as of 2019; Institute for Security Studies African Futures, 2023), weak regulatory reach into informal workplaces, and comparable occupational composition (street vending, construction, waste collection, and domestic work), it is reasonable to expect that Eswatini's informal workforce faces a broadly similar hazard profile, a similar awareness-behaviour gap favouring recognition of acute over chronic risk, and similar economic constraints on protective equipment use.

These are testable expectations, not conclusions. A locally grounded empirical study, ideally combining structured surveys with qualitative interviews and conducted with proper ethics committee oversight, would be needed to establish whether the regional pattern in fact holds in Eswatini, and to identify any respects in which Eswatini's specific economic, cultural, or regulatory context produces a different pattern. The absence of such a study to date is, in itself, one of this review's central findings.

Discussion in Context

Globally, this synthesis is consistent with findings that informal workers face overlapping hazards and limited protections across diverse national contexts (ILO, 2022; WHO, 2021). Regionally, the pattern identified here draws directly on studies from Kenya, Ghana, and South Africa (Kemei, Kaluli and Kabubo, 2017; Alfers, 2016; Uhunamure, Edokpayi and Shale, 2021), each documenting a different occupational group but converging on similar structural conclusions.

Locally, this review's contribution is to make the absence of Eswatini-specific evidence explicit and actionable: rather than allowing the evidence gap to remain implicit, this paper articulates specific, falsifiable expectations that a future study could test, and argues that occupational health in Eswatini's informal sector is plausibly, pending confirmation, a structural issue rooted in economic constraint and policy exclusion, not merely a matter of individual awareness or behaviour.

This positions Eswatini's informal sector within broader regional and global debates on labour rights, public health, and sustainable development, while being explicit that the country-specific evidence needed to move from plausible hypothesis to established finding does not yet exist.

Conclusion and Recommendations

Conclusion

This review synthesized global and regional literature on occupational health hazards, risk awareness, and protective practices among informal workers, and applied the resulting synthesis to Eswatini's informal sector. The evidence base shows that informal workers across comparable Sub-Saharan African contexts face multidimensional hazards, including physical, chemical, ergonomic, and psychosocial hazards, that directly affect their wellbeing.

Across the reviewed studies, awareness of immediate hazards is consistently higher than awareness of chronic, cumulative risks, and protective practices are consistently constrained less by knowledge than by affordability and access to protective equipment. These patterns, filtered through Risk Perception Theory, the Health Belief Model, and the Social Determinants of Health, suggest that occupational health outcomes in informal work are shaped jointly by individual perception and structural economic exclusion.

No study to date has tested whether this regional pattern holds specifically in Eswatini. This review's central conclusion is therefore twofold: first, that the regional evidence provides a reasonable, literature-grounded basis for provisional policy action even in the absence of local data; and second, that

Eswatini's informal sector represents a genuine and currently unfilled research gap that warrants a properly designed, ethically approved empirical study.

Ultimately, occupational health in Eswatini's informal sector is likely, pending confirmation, not only a technical challenge of hazard control but a structural and ethical imperative, central to advancing equity, resilience, and sustainable national development.

Limitations of this Review

This review has specific and important limitations that readers should weigh carefully. Most fundamentally, it presents no primary data on Eswatini: every claim specific to Eswatini in this paper is an extrapolation from regional evidence, not a locally verified finding, and should not be cited or used as though it were the latter.

Second, the regional evidence base itself is uneven: the studies drawn on here cover a small number of occupational groups in a small number of countries (chiefly Kenya, Ghana, and South Africa), and the reviewed literature, while verified for authenticity, is not exhaustive; a systematic review following PRISMA guidelines and covering a substantially larger set of sources would strengthen confidence in the patterns identified here.

Third, extrapolation across national contexts carries risk: Eswatini's specific economic structure, regulatory environment, and cultural context may produce different patterns than those observed in Kenya, Ghana, or South Africa, and this review cannot rule that out. The expectations generated here should be treated as hypotheses for empirical testing, not as findings.

These limitations do not undermine the value of a literature-based synthesis in the absence of local data, but they do mean this review's recommendations are provisional and should be revisited once Eswatini-specific evidence exists.

Policy Recommendations

Several policy recommendations follow from these findings. First, inclusive occupational health frameworks should extend occupational health and safety policies to cover informal workers, ensuring they are recognized as central contributors to national development. Second, governments and other stakeholders should support the provision of protective equipment, subsidizing or providing affordable personal protective equipment to informal workers, particularly those in high-risk occupations such as construction and waste collection. Third, awareness and training programs should be developed as targeted education campaigns that emphasize both immediate and long-term risks, coupled with practical training on safety practices. Finally, strengthening institutional capacity is needed, building enforcement mechanisms within local government structures to monitor and support occupational health in informal settings.

Empowering informal workers themselves is equally important. The formation of worker associations should be encouraged to advocate for occupational health rights and collective bargaining. Peer

education models can train workers as peer educators to promote awareness and protective practices within their communities. And community health integration can link occupational health initiatives with community health services to ensure informal workers have access to preventive and curative care.

The single highest-priority research recommendation arising from this review is the most direct one: Eswatini needs a primary, ethically approved empirical study of occupational hazards, risk awareness, and health outcomes among its informal workforce. Such a study should be conducted only after review by an accredited institutional or regional research ethics committee, should use a sampling strategy capable of supporting generalizable claims (rather than purposive sampling alone), and should report full statistical detail, including sample characteristics, effect sizes, and confidence intervals, to allow independent scrutiny and replication. Beyond this foundational study, longitudinal research would subsequently be valuable to examine causal relationships between hazards, awareness, and health outcomes over time; sector-specific research could investigate occupational health dynamics within specific informal occupations to design tailored interventions; and comparative research could situate Eswatini's informal sector alongside its neighbors to identify transferable policy lessons.

Final Reflection

Occupational health in Eswatini's informal sector is both a public health and social justice issue. Protecting informal workers requires not only technical interventions but also structural reforms that address poverty, inequality, and exclusion. By synthesizing regional hazard, awareness, and outcome evidence into a coherent framework, this review provides a provisional foundation for policy and practice while making clear where that foundation needs to be tested against local reality.

Safeguarding the health of informal workers is essential for building resilient communities and sustainable national development. In this sense, occupational health is not simply about preventing injuries or illnesses; it is about affirming the dignity of work, ensuring equity, and advancing the broader goals of public health.

In sum, safeguarding the health of informal workers is not only a matter of preventing injuries or illnesses, but a commitment to equity and justice. This review argues that occupational health in Eswatini's informal sector should be recognized as a public health priority, that provisional, literature-informed interventions are worth pursuing now, and that a properly conducted local empirical study remains the essential next step for turning provisional recommendations into evidence-based policy.

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Title of Article

Artificial Intelligence in Drug Discovery: Applications for Neglected Tropical Diseases

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Abstract

Artificial intelligence is transforming drug discovery by accelerating target identification, compound screening, and therapeutic design. This foresighting paper examines how AI can be applied to neglected tropical diseases (NTDs), which continue to impose a disproportionate burden on low-income populations. It analyses algorithmic approaches, data-governance challenges, and translational barriers

in NTD research. The paper proposes a strategic framework for integrating AI-driven drug discovery into Africa's health-innovation ecosystem.

Keywords

AI Drug Discovery; Neglected Tropical Diseases; Machine Learning; Biomedical Innovation; Global Health.

1. Introduction

Neglected tropical diseases remain among the most persistent and structurally entrenched health challenges in Africa. They affect millions, yet receive limited research investment due to weak commercial incentives and the concentration of pharmaceutical innovation in high-income markets. Traditional drug-discovery pipelines are slow, expensive, and ill-suited to diseases that disproportionately impact populations with limited purchasing power. Artificial intelligence offers a transformative opportunity to disrupt this paradigm by accelerating discovery, reducing costs, and enabling precision approaches to pathogens that have long been overlooked. This paper argues that AI-driven drug discovery can reshape the future of NTD therapeutics, but only if supported by governance frameworks that address data scarcity, ethical considerations, and translational capacity.

2. The Promise of AI in Drug Discovery

AI systems have demonstrated remarkable capabilities in predicting molecular interactions, identifying drug targets, and generating novel compounds. Machine-learning models can analyse vast biological datasets, infer structural relationships, and simulate drug behaviour with unprecedented speed. Deep-learning architectures enable the prediction of protein folding, ligand binding, and pharmacokinetic properties, reducing reliance on costly laboratory experiments. Generative models can design new molecules tailored to specific biological targets, expanding the chemical space beyond what human researchers can manually explore.

These capabilities are particularly relevant for NTDs, where limited funding and fragmented research efforts have slowed therapeutic development. AI can accelerate the identification of drug candidates for diseases such as schistosomiasis, leishmaniasis, trypanosomiasis, and lymphatic filariasis. It can also support repurposing of existing drugs, enabling rapid evaluation of compounds with known safety profiles. The promise of AI lies not only in speed but in the ability to uncover patterns and relationships that elude traditional methods, offering new pathways for tackling complex pathogens.

3. Data Scarcity, Quality, and the Structural Challenges of NTD Research

Despite its potential, AI-driven drug discovery faces significant obstacles in the context of NTDs. High-quality datasets are essential for training robust models, yet NTD research suffers from data scarcity, fragmentation, and inconsistent reporting. Genomic, proteomic, and phenotypic datasets for many NTD pathogens remain incomplete or outdated. Clinical data are often limited to small cohorts, and epidemiological information may be unreliable due to underreporting and weak surveillance systems.

Data scarcity is compounded by structural inequities in global research ecosystems. Most biomedical datasets are generated in high-income countries, reflecting diseases and populations that differ from those affected by NTDs. This creates algorithmic blind spots that limit the accuracy and relevance of AI models. Addressing these challenges requires investment in data generation, standardisation, and governance across African research institutions. Without robust datasets, AI systems risk producing biased or unreliable outputs that fail to translate into effective therapeutics.

4. Algorithmic Approaches and Their Relevance to NTD Drug Discovery

AI-driven drug discovery relies on a diverse set of algorithmic approaches, each with distinct strengths and limitations. Machine-learning models can predict drug–target interactions, identify resistance mechanisms, and classify compounds based on biological activity. Deep-learning architectures can analyse complex biological structures, enabling insights into protein folding and molecular dynamics. Generative models can design novel compounds with desired properties, while reinforcement-learning systems can optimise drug candidates through iterative simulation.

These approaches are particularly valuable for NTDs, where pathogens often exhibit complex life cycles, adaptive resistance, and unique biological features. AI can support the identification of vulnerabilities in parasite metabolism, host–pathogen interactions, and vector biology. It can also accelerate the discovery of drugs that target multiple stages of infection, reducing the risk of resistance and improving therapeutic efficacy. Algorithmic approaches therefore offer a powerful toolkit for addressing the scientific complexities that have historically hindered NTD drug development.

5. Translational Barriers and the Realities of Drug Development in Africa

Even when AI identifies promising drug candidates, significant translational barriers remain. Laboratory validation, preclinical testing, and clinical trials require infrastructure, expertise, and regulatory capacity that are unevenly distributed across African countries. Many research institutions lack advanced laboratory facilities, high-throughput screening platforms, or computational resources necessary for integrated AI-biomedical workflows. Regulatory agencies may struggle to evaluate AI-generated therapeutics, particularly when models produce compounds with novel mechanisms of action.

The political economy of drug development also shapes translational outcomes. Pharmaceutical companies may be reluctant to invest in NTD therapeutics due to limited commercial returns, while public-sector funding remains constrained by competing health priorities. Without coordinated investment, AI-driven discoveries risk remaining theoretical rather than becoming accessible treatments. Translational success therefore requires governance frameworks that integrate AI innovation with regulatory reform, public-sector investment, and regional collaboration.

6. Ethical, Legal, and Governance Considerations

AI-driven drug discovery raises ethical and legal questions that must be addressed to ensure responsible innovation. Data governance is central, particularly when biological and clinical data originate from vulnerable populations. Consent, privacy, and benefit-sharing must be embedded in data-collection frameworks to prevent exploitation. Intellectual-property regimes must balance incentives for innovation with equitable access to therapeutics, ensuring that AI-generated drugs for NTDs do not become inaccessible due to restrictive patents or pricing strategies.

Algorithmic transparency is also essential. AI models must be interpretable enough to allow regulators, researchers, and clinicians to assess safety, efficacy, and potential risks. Governance frameworks must ensure that AI systems do not reproduce biases or generate misleading predictions that compromise patient safety. Ethical oversight must therefore accompany technological innovation, ensuring that AI-driven drug discovery aligns with principles of justice, equity, and public health.

7. A Strategic Framework for AI-Driven NTD Drug Discovery in Africa

Africa's engagement with AI-driven drug discovery must be grounded in a strategic framework that integrates data generation, technological capacity, and regional collaboration. Research institutions must invest in high-quality datasets, computational infrastructure, and interdisciplinary expertise. Governments must support regulatory reform, funding mechanisms, and public–private partnerships that enable translational research. Regional bodies must coordinate efforts to harmonise standards, share data, and pool resources for large-scale drug-development initiatives.

This framework must also prioritise community engagement, ensuring that data collection and research activities respect local rights and cultural contexts. It must align AI innovation with broader health-system strengthening, recognising that drug discovery is only one component of effective NTD

control. Above all, it must position Africa as an active participant in global biomedical innovation, contributing to the development of therapeutics that reflect the continent's epidemiological realities and scientific priorities.

8. Conclusion

Artificial intelligence offers a transformative opportunity to accelerate drug discovery for neglected tropical diseases, addressing long-standing gaps in global health innovation. Yet its success depends on data quality, translational capacity, and governance frameworks that ensure ethical, equitable, and context-appropriate application. For Africa, AI-driven drug discovery represents both a scientific frontier and a strategic imperative. A future-ready governance architecture—grounded in data integrity, institutional capacity, and regional collaboration—offers the most promising path for harnessing AI to deliver new therapeutics for diseases that have been neglected for far too long.

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Title of Article

Blood Flow Restriction Therapy in Post-Surgical Rehabilitation: Evidence-Based Practice

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Abstract

Blood flow restriction (BFR) therapy has emerged as a promising modality in post-surgical rehabilitation, enabling strength gains and functional recovery at low training loads. This paper examines the physiological mechanisms, clinical applications, and evidence base supporting BFR in post-operative care. It evaluates safety considerations, patient-selection criteria, and implementation challenges across surgical populations. The paper proposes a clinical governance model for integrating BFR therapy into evidence-based rehabilitation practice in Africa.

Keywords

Blood Flow Restriction; Rehabilitation; Post-Surgical Recovery; Physiotherapy; Evidence-Based Practice.

1. Introduction

Post-surgical rehabilitation seeks to restore strength, mobility, and functional independence while protecting healing tissues from excessive mechanical stress. Traditional strengthening protocols rely

on high-load resistance training, yet many post-operative patients cannot tolerate such loads due to pain, immobilisation, or surgical precautions. Blood flow restriction therapy offers a compelling alternative by enabling significant strength and hypertrophy gains at low intensities. Through controlled vascular occlusion, BFR induces metabolic stress and neuromuscular activation that mimic high-load training, providing a pathway for early strengthening without compromising surgical integrity. This paper argues that BFR represents a paradigm shift in post-operative rehabilitation, but its adoption requires rigorous clinical governance, practitioner competence, and context-appropriate implementation.

2. Physiological Foundations of Blood Flow Restriction Therapy

BFR therapy operates by partially restricting venous return while maintaining arterial inflow, creating a hypoxic and metabolically demanding environment within the working muscle. This physiological state triggers a cascade of adaptations: increased fast-twitch fibre recruitment, elevated growth-hormone release, enhanced cell-signalling pathways, and accelerated protein synthesis. These mechanisms allow low-load exercise—often 20–30% of one-repetition maximum—to produce strength and hypertrophy outcomes comparable to high-load training.

The metabolic stress induced by BFR also enhances muscle endurance, vascular adaptation, and neuromuscular efficiency. Importantly, these benefits occur without imposing excessive mechanical strain on healing tissues, making BFR particularly valuable in early post-operative phases. The physiological foundations of BFR therefore align with the core principles of surgical rehabilitation: progressive loading, tissue protection, and functional restoration.

3. Clinical Applications in Post-Surgical Rehabilitation

Evidence supports the use of BFR across a range of surgical populations. In anterior cruciate ligament reconstruction, BFR has demonstrated improvements in quadriceps strength, muscle mass, and functional outcomes during early rehabilitation. In total knee arthroplasty, BFR enhances lower-limb strength and reduces post-operative atrophy, addressing one of the most persistent challenges in arthroplasty recovery. In rotator-cuff repair and shoulder stabilisation procedures, BFR facilitates early strengthening of peri-scapular and rotator-cuff musculature without compromising surgical repair.

Beyond orthopaedic surgery, BFR shows promise in tendon repair, fracture fixation, and spinal surgery, where early loading is often restricted. Its ability to stimulate muscular adaptation under low mechanical stress makes it particularly valuable in populations with limited weight-bearing capacity or movement restrictions. The clinical applications of BFR therefore extend across diverse surgical contexts, offering a versatile tool for physiotherapists seeking to optimise recovery trajectories.

4. Safety, Contraindications, and Clinical Risk Management

Despite its benefits, BFR therapy requires careful clinical oversight. Improper application can lead to excessive occlusion, nerve irritation, or vascular complications. Safety depends on appropriate cuff selection, accurate pressure calibration, and continuous monitoring of patient response. Contraindications include uncontrolled hypertension, peripheral vascular disease, active thrombosis, sickle-cell disease, and certain cardiac conditions. Post-operative patients with compromised vascular integrity or altered sensation require heightened caution.

Clinical risk management must therefore be embedded in BFR practice. Practitioners must be trained in pressure-determination methods, including limb occlusion pressure assessment, and must understand the physiological responses that indicate safe or unsafe application. Patient education is essential, ensuring that individuals recognise normal sensations associated with BFR and can report adverse symptoms promptly. When implemented within a structured governance framework, BFR therapy is safe and well-tolerated across diverse patient populations.

5. Evidence-Based Practice and Research Trends

The evidence base for BFR therapy has expanded significantly over the past decade. Randomised controlled trials demonstrate consistent improvements in strength, hypertrophy, and functional outcomes across surgical and non-surgical populations. Meta-analyses confirm that low-load BFR

produces comparable strength gains to high-load resistance training, with additional benefits in early rehabilitation phases. Research also highlights the role of BFR in mitigating muscle atrophy during immobilisation, enhancing aerobic capacity, and improving neuromuscular activation.

Emerging studies explore the integration of BFR with neuromuscular electrical stimulation, isometric protocols, and functional-task training, suggesting synergistic effects that may further enhance recovery. Advances in cuff technology, pressure-monitoring systems, and personalised occlusion algorithms are improving safety and efficacy. The research trajectory indicates that BFR will continue to evolve as a core component of evidence-based rehabilitation.

6. Implementation Challenges in African Rehabilitation Settings

The adoption of BFR therapy in African rehabilitation contexts faces structural and operational challenges. Access to high-quality BFR equipment remains limited, and low-cost alternatives may lack the precision required for safe application. Practitioner training is uneven, with many physiotherapists unfamiliar with occlusion-pressure assessment or the physiological principles underlying BFR. Clinical guidelines are scarce, and regulatory frameworks for emerging rehabilitation technologies remain underdeveloped.

These challenges are compounded by resource constraints, variable access to post-operative care, and disparities in rehabilitation infrastructure. Yet Africa's growing physiotherapy workforce, expanding surgical capacity, and increasing interest in evidence-based practice create fertile ground for BFR adoption. Addressing implementation barriers requires coordinated investment in training, equipment, and clinical governance.

7. A Clinical Governance Model for BFR Integration

A future-ready governance model for BFR therapy must integrate clinical competence, safety protocols, and evidence-based decision-making. It must ensure that practitioners receive formal training in occlusion-pressure assessment, physiological monitoring, and surgical-specific application. It must establish standardised protocols for patient selection, contraindication screening, and progressive loading. It must incorporate documentation systems that track pressure settings, patient response, and functional outcomes.

This governance model must also align BFR practice with broader rehabilitation frameworks, ensuring that occlusion-based training complements—not replaces—traditional strengthening, mobility restoration, and functional retraining. It must support interdisciplinary collaboration between surgeons, physiotherapists, and rehabilitation specialists, ensuring that BFR is integrated into surgical pathways rather than applied in isolation. Above all, it must position BFR as a safe, evidence-based modality that enhances—not complicates—post-operative recovery.

8. Conclusion

Blood flow restriction therapy represents a significant advancement in post-surgical rehabilitation, enabling early strengthening, mitigating atrophy, and accelerating functional recovery. Its physiological foundations, clinical evidence, and versatility across surgical populations make it a valuable tool for modern physiotherapy practice. Yet its adoption requires rigorous governance, practitioner competence, and context-appropriate implementation. For Africa, BFR offers an opportunity to elevate rehabilitation outcomes and align clinical practice with global evidence-based standards. A governance architecture grounded in safety, training, and interdisciplinary collaboration provides the most promising pathway for integrating BFR into post-operative care.

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Title of Article

Breaking the Bottlenecks: A Comprehensive Assessment of Non-Communicable Disease Management Challenges in Sub-Saharan Africa

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Abstract

Non-communicable diseases (NCDs) are rising sharply across Sub-Saharan Africa, straining health systems historically oriented toward infectious-disease control. This paper examines structural, clinical, and governance bottlenecks that impede effective NCD management. It analyses health-system capacity, financing constraints, workforce shortages, supply-chain failures, and sociocultural

determinants that shape patient behaviour. Using regional case studies, the paper evaluates gaps in prevention, diagnosis, continuity of care, and policy implementation. It proposes a systems-strengthening model for NCD governance grounded in integration, equity, and long-term resilience.

Keywords

Non-Communicable Diseases; Health Systems; Chronic Care; Sub-Saharan Africa; Governance; Epidemiological Transition.

1. Introduction

Sub-Saharan Africa is undergoing a profound epidemiological transition. While infectious diseases remain significant, the burden of non-communicable diseases has expanded rapidly, driven by demographic change, urbanisation, lifestyle shifts, and structural inequities. Hypertension, diabetes, cardiovascular disease, chronic respiratory conditions, and cancers now account for a growing proportion of morbidity and mortality. Yet health systems across the region remain configured for acute, episodic care rather than chronic disease management. This misalignment has created systemic bottlenecks that undermine prevention, early diagnosis, treatment adherence, and long-term follow-up. The challenge is not merely clinical but structural: NCDs expose weaknesses in governance, financing, supply chains, workforce distribution, and community engagement. This paper argues that breaking these bottlenecks requires a comprehensive reorientation of health systems toward continuity, integration, and patient-centred care.

2. The Structural Foundations of NCD Vulnerability

The rise of NCDs in Sub-Saharan Africa reflects deep structural determinants. Rapid urbanisation has altered diets, reduced physical activity, and increased exposure to environmental risks. Economic transitions have created new patterns of consumption and stress. Health systems, historically shaped by donor-driven vertical programmes, have prioritised infectious diseases, leaving chronic-care infrastructure underdeveloped. Primary-care facilities often lack diagnostic equipment, essential medicines, and trained personnel capable of managing long-term conditions. Referral systems are fragmented, and continuity of care is undermined by weak patient-tracking mechanisms. These structural foundations create an environment in which NCDs progress silently until complications emerge, overwhelming tertiary facilities and increasing the cost of care.

3. Clinical Bottlenecks in Prevention, Diagnosis, and Treatment

Clinical management of NCDs is constrained by gaps across the care continuum. Prevention remains limited due to inadequate health-promotion programmes, weak regulation of unhealthy commodities, and insufficient community-level engagement. Screening programmes are sporadic, often dependent on donor funding or short-term campaigns. Diagnostic capacity is uneven, with many facilities lacking glucometers, blood-pressure monitors, lipid-testing equipment, or cancer-screening tools. Treatment protocols may exist on paper but are inconsistently applied due to workforce shortages, limited training, and high patient volumes.

Continuity of care is further undermined by poor follow-up systems, limited electronic health records, and reliance on manual registers that hinder longitudinal monitoring. Patients frequently cycle in and out of care due to transport barriers, medication costs, and competing socioeconomic priorities. These clinical bottlenecks create a cycle of late diagnosis, inadequate treatment, and preventable complications.

4. Workforce Constraints and the Challenge of Chronic-Care Delivery

Human-resource shortages represent one of the most persistent obstacles to effective NCD management. Many countries face severe deficits in physicians, nurses, nutritionists, physiotherapists,

and specialised chronic-care providers. Workforce distribution is uneven, with rural areas disproportionately underserved. Training curricula often emphasise acute care, leaving providers ill-prepared for chronic-disease counselling, lifestyle modification support, and long-term patient management.

Task-shifting initiatives have attempted to expand capacity by empowering nurses and community health workers, yet these programmes require sustained investment, supervision, and competency-based training. Without adequate workforce support, chronic-care delivery becomes inconsistent, reactive, and vulnerable to burnout. Effective NCD governance therefore depends on strengthening workforce pipelines, expanding multidisciplinary teams, and embedding chronic-care competencies across all levels of the health system.

5. Supply-Chain Failures and the Fragility of Essential-Medicine Access

Reliable access to essential NCD medicines remains a major challenge across Sub-Saharan Africa. Stockouts of antihypertensives, insulin, statins, and asthma medications are common, driven by procurement inefficiencies, forecasting errors, weak logistics systems, and financial constraints. Many countries rely heavily on external suppliers, making medicine availability vulnerable to global market fluctuations. Cold-chain limitations hinder insulin distribution, while fragmented procurement systems create price variability and affordability barriers.

Supply-chain failures undermine treatment adherence, increase complications, and erode patient trust. They also place additional pressure on tertiary facilities, which must manage preventable emergencies arising from uncontrolled chronic conditions. Strengthening supply chains requires governance reforms that improve forecasting, procurement transparency, and last-mile distribution.

6. Financing Constraints and the Economics of Chronic Care

NCD management requires sustained investment in prevention, diagnostics, medicines, and long-term follow-up. Yet health financing in Sub-Saharan Africa remains constrained by limited fiscal space, high out-of-pocket expenditure, and donor priorities that favour infectious diseases. Insurance coverage is often low, and chronic-care benefits may be limited or absent. Patients frequently bear the cost of medicines, transport, and diagnostic tests, creating financial barriers that reduce adherence and increase catastrophic expenditure.

The economics of chronic care demand a shift toward pooled financing, strategic purchasing, and integration of NCD services into universal health-coverage frameworks. Without financial protection, NCD management will remain inequitable and unsustainable.

7. Sociocultural Determinants and Patient-Behaviour Dynamics

NCD outcomes are shaped not only by clinical and structural factors but by sociocultural dynamics. Health-seeking behaviour is influenced by beliefs, stigma, gender norms, and traditional-medicine practices. Many patients delay care due to fear, misinformation, or competing livelihood demands. Lifestyle modification—central to NCD management—is hindered by food insecurity, limited access to healthy foods, unsafe environments for physical activity, and cultural norms surrounding diet and body image.

Effective NCD governance must therefore integrate behavioural science, community engagement, and culturally grounded health promotion. Without addressing sociocultural determinants, clinical interventions will have limited impact.

8. Governance Gaps and Policy Implementation Challenges

Policy frameworks for NCD management exist in many countries, yet implementation remains inconsistent. Governance gaps arise from limited coordination across ministries, weak monitoring systems, insufficient political prioritisation, and fragmented donor engagement. National NCD strategies often lack operational detail, budget allocations, or accountability mechanisms. Data systems are inadequate for tracking prevalence, risk factors, and treatment outcomes, hindering evidence-based decision-making.

Breaking governance bottlenecks requires institutional reforms that strengthen coordination, embed accountability, and integrate NCD management into broader health-system strengthening agendas. Governance must shift from episodic initiatives to sustained, system-wide action.

9. Toward a Systems-Strengthening Model for NCD Governance

A future-ready NCD governance model for Sub-Saharan Africa must reorient health systems toward continuity, integration, and resilience. It must embed chronic-care pathways within primary-care systems, strengthen multidisciplinary teams, and ensure reliable access to diagnostics and medicines. It must integrate digital health tools for patient tracking, telemedicine, and data analytics. It must align financing with long-term care needs, reducing out-of-pocket expenditure and expanding insurance coverage. It must address sociocultural determinants through community-based interventions and culturally grounded health promotion. Above all, it must position NCD management as a core component of universal health coverage and national development.

10. Conclusion

Non-communicable diseases represent one of the most significant health-system challenges facing Sub-Saharan Africa. Breaking the bottlenecks that impede effective management requires structural reform, clinical innovation, and governance transformation. A systems-strengthening model—grounded in integration, equity, and resilience—offers the most promising pathway for addressing the rising burden of chronic disease. The future of NCD management in the region depends on political commitment, institutional capacity, and sustained investment in people, systems, and communities.

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Title of Article

CAR-T Cell Therapy for Solid Tumors: Expanding the Frontier

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Abstract

CAR-T cell therapy has revolutionised treatment for haematologic malignancies, yet its translation to solid tumors remains constrained by biological, immunological, and microenvironmental barriers. This paper examines the scientific foundations, translational challenges, and emerging innovations shaping the future of CAR-T therapy for solid tumors. It analyses tumor-microenvironment dynamics, antigen heterogeneity, trafficking limitations, and toxicity risks. The paper proposes a next-generation framework for advancing CAR-T therapy within African oncology systems.

Keywords

CAR-T Therapy; Solid Tumors; Immuno-Oncology; Tumor Microenvironment; Cellular Therapy.

1. Introduction

CAR-T cell therapy represents one of the most significant breakthroughs in modern oncology, demonstrating curative potential in refractory haematologic cancers. Its success has generated intense interest in extending this modality to solid tumors, which account for the vast majority of global cancer burden. Yet solid tumors present a fundamentally different biological landscape, characterised by antigen heterogeneity, immunosuppressive microenvironments, physical barriers to infiltration, and complex toxicity profiles. These challenges have slowed clinical translation and exposed the limits of current CAR-T design. This paper argues that expanding the frontier of CAR-T therapy for solid tumors requires a synthesis of biological insight, engineering innovation, and clinical governance capable of navigating the unique complexities of solid-tumor immunobiology.

2. The Biological Foundations of CAR-T Therapy

CAR-T therapy operates by genetically modifying T cells to express synthetic receptors that recognise tumor-associated antigens. These engineered cells bypass traditional antigen-presentation pathways, enabling potent cytotoxic responses against malignant cells. In haematologic cancers, where target antigens are abundant, homogeneous, and accessible, CAR-T therapy has produced unprecedented remission rates. Solid tumors, however, disrupt this paradigm. Their antigens are often heterogeneous, variably expressed, or shared with normal tissues, complicating target selection and increasing the risk of off-tumor toxicity. The biological foundations of CAR-T therapy therefore require re-examination when applied to solid tumors, where antigenicity, accessibility, and microenvironmental context differ profoundly from blood cancers.

3. Tumor Microenvironment: The Central Barrier

The tumor microenvironment represents the most formidable obstacle to CAR-T efficacy in solid tumors. Solid tumors create immunosuppressive ecosystems dominated by regulatory T cells, myeloid-derived suppressor cells, inhibitory cytokines, hypoxia, and dense stromal architecture. These conditions impair

CAR-T cell trafficking, limit proliferation, and suppress cytotoxic function. Physical barriers such as abnormal vasculature and extracellular-matrix density further restrict infiltration, preventing CAR-T cells from reaching malignant cells in sufficient numbers.

The microenvironment also promotes T-cell exhaustion, reducing persistence and diminishing therapeutic durability. Overcoming these barriers requires CAR-T designs capable of resisting immunosuppression, navigating stromal architecture, and sustaining functional activity within hostile tumor niches. The microenvironment is not merely an obstacle but a dynamic adversary that shapes every stage of CAR-T engagement.

4. Antigen Heterogeneity and the Challenge of Target Selection

Solid tumors exhibit profound antigen heterogeneity, with malignant cells expressing diverse and evolving antigenic profiles. This heterogeneity enables immune escape, as tumor subclones lacking the targeted antigen survive and proliferate. The challenge of target selection is further complicated by the scarcity of truly tumor-specific antigens. Many candidate antigens are expressed at low levels in normal tissues, raising the risk of off-tumor toxicity.

Emerging strategies seek to address these limitations through multi-antigen CAR-T constructs, logic-gated receptors, and combinatorial targeting approaches that require simultaneous antigen recognition. These innovations aim to reduce escape pathways and enhance specificity, yet they also increase engineering complexity and regulatory considerations. Antigen heterogeneity remains a central barrier that demands both biological insight and technological sophistication.

5. Trafficking, Persistence, and Functional Durability

Effective CAR-T therapy requires not only antigen recognition but successful trafficking to tumor sites, sustained persistence, and durable cytotoxic function. Solid tumors disrupt each of these processes. Chemokine mismatches hinder trafficking, while immunosuppressive signals reduce persistence and promote exhaustion. The physical structure of solid tumors limits CAR-T penetration, creating spatial disparities between CAR-T presence and malignant-cell distribution.

Engineering strategies such as chemokine-receptor modification, cytokine-secreting CAR-T cells, and armored CAR-T constructs seek to enhance trafficking and persistence. Yet these approaches introduce new risks, including heightened inflammation and off-target effects. Achieving functional durability in solid tumors requires a delicate balance between potency and safety, ensuring that CAR-T cells remain active without triggering excessive toxicity.

6. Toxicity Profiles and Clinical-Safety Considerations

CAR-T therapy for solid tumors introduces unique toxicity risks beyond cytokine-release syndrome and neurotoxicity observed in haematologic applications. Off-tumor, on-target toxicity becomes a major concern when antigens are shared with normal tissues. Local inflammation within confined anatomical spaces can produce organ-specific complications. Engineering enhancements designed to overcome microenvironmental suppression may amplify systemic immune activation, increasing the risk of severe adverse events.

Clinical governance must therefore prioritise safety through rigorous antigen validation, controlled dosing strategies, suicide-gene incorporation, and real-time monitoring. Solid-tumor CAR-T therapy demands a safety architecture capable of managing complex and unpredictable toxicity profiles.

7. Emerging Innovations Expanding the Frontier

Despite formidable challenges, innovation in CAR-T engineering is rapidly expanding the frontier of solid-tumor therapy. Advances in synthetic biology, gene editing, and cellular engineering are producing CAR-T constructs capable of resisting immunosuppression, navigating stromal barriers, and targeting multiple antigens simultaneously. Oncolytic viruses, bispecific antibodies, and combination immunotherapies are being integrated with CAR-T approaches to enhance infiltration and cytotoxicity. Spatial-omics and single-cell sequencing are improving understanding of tumor ecosystems, enabling more precise CAR-T design.

These innovations signal a shift from first-generation CAR-T constructs toward adaptive, multifunctional cellular therapies capable of engaging complex tumor environments. The frontier is expanding not through incremental improvement but through reimagining CAR-T therapy as a dynamic, ecosystem-aware modality.

8. Implications for African Oncology Systems

For African oncology systems, CAR-T therapy represents both a scientific opportunity and a structural challenge. The region faces rising solid-tumor burden, limited access to advanced therapeutics, and constrained laboratory infrastructure. Yet Africa also possesses growing biomedical-research capacity, expanding genomic-medicine initiatives, and increasing interest in cellular therapy. Integrating CAR-T therapy into African oncology requires investment in biomanufacturing, regulatory frameworks, clinical-trial capacity, and workforce development.

A future-ready oncology ecosystem must align CAR-T innovation with equitable access, ensuring that cellular therapy does not become restricted to elite centres. Africa's engagement with CAR-T therapy must be strategic, focusing on capacity building, regional collaboration, and context-appropriate implementation.

9. Conclusion

CAR-T cell therapy for solid tumors represents one of the most ambitious frontiers in modern oncology. Its challenges are profound, rooted in the biological complexity of solid tumors and the limitations of current engineering approaches. Yet innovation is rapidly reshaping the landscape, offering new pathways for overcoming microenvironmental suppression, antigen heterogeneity, and trafficking barriers. For Africa, expanding the frontier of CAR-T therapy requires scientific investment, clinical governance, and strategic integration into evolving oncology systems. The future of solid-tumor CAR-T therapy lies in designs that are biologically informed, technologically sophisticated, and clinically adaptable.

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Title of Article

Multi-Omics Profiling for Cancer Subtype Classification: A Systems Biology Approach

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Abstract

Multi-omics profiling has transformed cancer research by enabling integrative analysis of genomic, transcriptomic, epigenomic, proteomic, and metabolomic layers. This paper examines how systems-biology approaches can refine cancer-subtype classification, improve diagnostic precision, and guide personalised therapy. It analyses computational-integration strategies, biological-signal interpretation, and translational challenges in oncology. The paper proposes a future-ready multi-omics framework for cancer-subtype discovery within African biomedical ecosystems.

Keywords

Multi-Omics; Cancer Subtypes; Systems Biology; Precision Oncology; Integrative Profiling.

1. Introduction

Cancer is not a single disease but a constellation of molecularly distinct entities that share anatomical origins yet diverge profoundly in biology, prognosis, and therapeutic response. Traditional classification systems, grounded in histopathology and single-marker analysis, capture only a fraction of this complexity. Multi-omics profiling has emerged as a transformative approach capable of revealing the layered molecular architecture that defines cancer heterogeneity. By integrating genomic mutations, transcriptomic signatures, epigenetic regulation, protein networks, and metabolic states, multi-omics enables a systems-level understanding of tumor identity. This paper argues that multi-omics classification represents the next frontier in precision oncology, offering a pathway toward more accurate diagnosis, refined prognostication, and personalised therapeutic strategies.

2. The Systems-Biology Foundations of Multi-Omics Classification

Systems biology views cancer as a dynamic network of interacting molecular processes rather than isolated genetic events. Multi-omics profiling operationalises this perspective by capturing diverse biological layers that collectively shape tumor behaviour. Genomics reveals driver mutations and structural variants; transcriptomics reflects gene-expression programs; epigenomics uncovers regulatory landscapes; proteomics maps functional protein interactions; metabolomics exposes metabolic rewiring. Each layer contributes unique insights, yet none is sufficient alone. The power of multi-omics lies in its ability to integrate these signals into coherent molecular portraits that reflect the emergent properties of cancer systems.

This integrative approach aligns with the reality that cancer phenotypes arise from network perturbations rather than single-gene abnormalities. Systems-biology frameworks therefore provide the conceptual foundation for multi-omics classification, enabling researchers to interpret molecular complexity through network dynamics, pathway interactions, and regulatory hierarchies.

3. Molecular Heterogeneity and the Limits of Traditional Classification

Cancer heterogeneity manifests across patients, within tumors, and even within individual cells. Histopathological classification, while foundational, cannot capture the molecular diversity that drives therapeutic resistance and variable clinical outcomes. Single-omics approaches—such as genomics alone—provide valuable information but often fail to distinguish subtypes with similar mutational profiles yet divergent biological behaviour.

Multi-omics profiling addresses these limitations by revealing hidden substructures within cancer types. It can identify subtypes defined by epigenetic silencing, metabolic dependencies, immune-microenvironment signatures, or transcriptional programs that are invisible to traditional methods. This deeper resolution enables more accurate stratification, guiding therapeutic decisions that reflect the true biological identity of tumors rather than superficial similarities.

4. Integrative Computational Approaches and Analytical Complexity

The integration of multi-omics data requires sophisticated computational frameworks capable of managing high-dimensional datasets, heterogeneous data types, and complex biological relationships. Machine-learning models, network-based algorithms, and dimensional-reduction techniques play central roles in extracting meaningful patterns. Clustering approaches identify molecular subtypes, while integrative models reveal cross-layer interactions that drive tumor behaviour.

Analytical complexity arises from noise, batch effects, missing data, and the challenge of aligning datasets generated through different platforms. Systems-biology-informed algorithms mitigate these challenges by incorporating biological priors, pathway knowledge, and network constraints. The success of multi-omics classification therefore depends not only on data generation but on computational sophistication capable of translating complexity into actionable insight.

5. Biological Interpretation and Clinical Translation

Multi-omics classification produces molecular subtypes that must be biologically interpretable and clinically meaningful. Subtypes defined solely by statistical separation may lack translational relevance unless linked to biological mechanisms, therapeutic vulnerabilities, or prognostic patterns. Systems-biology approaches facilitate interpretation by mapping subtype-specific signatures onto pathways, regulatory networks, and cellular phenotypes.

Clinical translation requires validation across cohorts, integration with clinical variables, and demonstration of therapeutic relevance. Multi-omics subtypes have already reshaped understanding of breast cancer, glioblastoma, colorectal cancer, and hepatocellular carcinoma, revealing distinct molecular programs that guide targeted therapy, immunotherapy selection, and risk stratification. The future of oncology lies in embedding multi-omics classification within diagnostic workflows, enabling clinicians to treat molecular subtypes rather than anatomical categories.

6. Challenges in Multi-Omics Implementation

Despite its promise, multi-omics profiling faces significant barriers. High-throughput sequencing and mass-spectrometry platforms remain expensive and technically demanding. Data-generation capacity is uneven across global regions, and African biomedical ecosystems face infrastructural constraints that limit widespread adoption. Standardisation of protocols, harmonisation of data formats, and development of bioinformatics expertise are essential for reliable implementation.

Ethical considerations also arise, including data governance, privacy, and equitable access to precision-oncology tools. Multi-omics datasets contain sensitive genomic information that must be protected through robust governance frameworks. Without careful implementation, multi-omics risks widening disparities in cancer care rather than reducing them.

7. A Future-Ready Multi-Omics Framework for African Oncology

Africa's oncology landscape is characterised by rising cancer burden, limited diagnostic capacity, and heterogeneous tumor biology shaped by unique genetic and environmental factors. Multi-omics profiling

offers an opportunity to generate region-specific molecular insights that improve diagnosis, guide therapy, and inform public-health strategies. A future-ready framework must integrate capacity building, regional biobanking, computational-infrastructure development, and collaborative research networks.

This framework must prioritise affordability, scalability, and clinical relevance, ensuring that multi-omics insights translate into improved patient outcomes rather than remaining confined to academic research. Africa's engagement with multi-omics must be strategic, focusing on cancers with high regional burden and leveraging systems-biology approaches to uncover molecular signatures unique to African populations.

8. Conclusion

Multi-omics profiling represents a transformative shift in cancer-subtype classification, enabling systems-level understanding of tumor biology that surpasses traditional diagnostic frameworks. Its integration of genomic, transcriptomic, epigenomic, proteomic, and metabolic layers provides unprecedented resolution of cancer heterogeneity. Yet its success depends on computational sophistication, biological interpretation, and clinical translation. For Africa, multi-omics offers a pathway toward precision oncology grounded in regional biology and systems-level insight. A future-ready multi-omics framework—rooted in integration, equity, and scientific rigor—can expand the frontier of cancer classification and improve outcomes across diverse populations.

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Title of Article

Neuroinflammation in Neurodegenerative Diseases: Pathophysiology and Therapeutic Targets

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Abstract

Neuroinflammation is increasingly recognised as a central driver of neurodegenerative disease progression rather than a secondary consequence of neuronal injury. This paper examines the cellular and molecular mechanisms through which neuroinflammatory pathways contribute to Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and other neurodegenerative conditions. It analyses microglial activation, astrocytic dysfunction, cytokine signalling, and blood–brain-barrier disruption as interconnected processes that shape neuronal vulnerability. The paper evaluates

emerging therapeutic strategies targeting neuroimmune pathways and proposes a systems-neurobiology framework for future intervention design.

Keywords

Neuroinflammation; Neurodegeneration; Microglia; Cytokines; Therapeutic Targets; Systems Neurobiology.

1. Introduction

Neurodegenerative diseases have long been conceptualised as disorders driven primarily by protein misfolding, synaptic dysfunction, and neuronal loss. Yet mounting evidence reveals that neuroinflammation is not merely a downstream response but a central pathological mechanism that shapes disease onset, trajectory, and severity. Microglia, astrocytes, peripheral immune cells, and inflammatory mediators interact within a dynamic neuroimmune network that can either preserve neuronal integrity or accelerate degeneration. This paper argues that neuroinflammation represents a critical therapeutic frontier, offering opportunities to intervene in disease processes that have historically been resistant to modification.

2. Microglial Activation and the Duality of Neuroimmune Response

Microglia are the brain's resident immune cells, responsible for surveillance, synaptic pruning, and injury response. In neurodegenerative diseases, microglia shift from homeostatic states to chronically activated phenotypes characterised by pro-inflammatory cytokine release, oxidative stress, and impaired phagocytic function. This transformation reflects a duality: microglia initially attempt to clear pathological proteins such as amyloid-β or α-synuclein, yet sustained activation leads to neurotoxicity, synaptic loss, and propagation of inflammatory signalling.

The emergence of disease-associated microglia (DAM) underscores the complexity of microglial phenotypes. DAM exhibit transcriptional signatures that reflect both protective and harmful functions, suggesting that therapeutic strategies must modulate microglial states rather than simply suppress activation. Microglial biology therefore lies at the heart of neuroinflammatory pathophysiology.

3. Astrocytic Dysfunction and Loss of Neuroprotective Capacity

Astrocytes play essential roles in neurotransmitter regulation, metabolic support, and maintenance of the blood–brain barrier. In neurodegenerative diseases, astrocytes undergo reactive transformation, losing neuroprotective functions while acquiring pro-inflammatory properties. Reactive astrocytes release cytokines, impair glutamate clearance, and contribute to excitotoxicity. Their interactions with microglia amplify inflammatory cascades, creating a feed-forward loop that accelerates neuronal injury.

Astrocytic dysfunction also disrupts metabolic coupling between glia and neurons, reducing lactate supply and impairing mitochondrial resilience. These metabolic consequences highlight the systems-level nature of neuroinflammation, in which cellular interactions shape the energetic landscape of the brain.

4. Cytokine Signalling and the Molecular Architecture of Neuroinflammation

Cytokines such as IL-1β, TNF-α, and IL-6 orchestrate neuroinflammatory signalling. Their sustained elevation in neurodegenerative diseases alters synaptic plasticity, disrupts neuronal signalling, and promotes apoptosis. Chemokines recruit peripheral immune cells into the central nervous system, further amplifying inflammatory responses. Inflammasome activation, particularly through NLRP3, represents a critical molecular pathway linking protein aggregates to cytokine release.

These molecular processes reveal neuroinflammation as a network phenomenon in which cytokine signalling shapes cellular behaviour across microglia, astrocytes, neurons, and infiltrating immune cells.

Targeting cytokine pathways therefore offers a promising therapeutic avenue, yet requires precision to avoid compromising essential immune functions.

5. Blood–Brain-Barrier Breakdown and Peripheral Immune Infiltration

The blood–brain barrier (BBB) is central to maintaining neural homeostasis. In neurodegenerative diseases, BBB integrity is compromised by inflammatory mediators, oxidative stress, and vascular dysfunction. This breakdown allows peripheral immune cells, plasma proteins, and microbial products to enter the brain, triggering additional inflammatory responses.

BBB disruption also alters nutrient transport, waste clearance, and endothelial signalling, creating a microenvironment conducive to neuronal vulnerability. The interplay between vascular dysfunction and neuroinflammation underscores the need for therapeutic strategies that address both immune and vascular components of neurodegeneration.

6. Neuroinflammation Across Major Neurodegenerative Diseases

Neuroinflammation manifests differently across neurodegenerative conditions yet follows shared mechanistic principles. In Alzheimer's disease, microglial activation and inflammasome signalling contribute to amyloid-β accumulation and tau pathology. In Parkinson's disease, α-synuclein aggregates trigger microglial activation and dopaminergic-neuron loss. In amyotrophic lateral sclerosis, neuroinflammation accelerates motor-neuron degeneration through microglial toxicity and astrocytic dysfunction. These disease-specific patterns reflect variations in protein pathology, regional vulnerability, and immune-cell phenotypes, yet converge on common neuroimmune mechanisms.

7. Therapeutic Targets and Emerging Intervention Strategies

Therapeutic strategies targeting neuroinflammation include microglial-modulating agents, cytokine inhibitors, inflammasome blockers, and BBB-stabilising compounds. Small-molecule inhibitors of NLRP3 show promise in reducing neuroinflammatory signalling. Modulators of microglial phenotype aim to shift cells toward protective states. Astrocyte-targeted therapies seek to restore metabolic support and reduce excitotoxicity. Immunomodulatory biologics, gene-therapy approaches, and cell-based interventions represent additional avenues for intervention.

Yet therapeutic development faces challenges: neuroinflammation is context-dependent, and excessive suppression may impair essential immune functions. Effective therapies must therefore modulate rather than eliminate neuroimmune activity, restoring balance within the neural ecosystem.

8. A Systems-Neurobiology Framework for Future Therapeutics

Neuroinflammation operates within a complex network of cellular interactions, molecular pathways, and environmental influences. A systems-neurobiology framework recognises that therapeutic success requires interventions that address multiple nodes within this network. Integrative approaches combining immunomodulation, metabolic support, vascular stabilisation, and protein-aggregate clearance may offer the most effective path forward. For African biomedical ecosystems, this framework provides a foundation for research strategies that align molecular insight with regional health priorities.

9. Conclusion

Neuroinflammation is a central driver of neurodegenerative disease progression, shaping neuronal vulnerability through microglial activation, astrocytic dysfunction, cytokine signalling, and BBB breakdown. Understanding these processes through a systems-neurobiology lens reveals new therapeutic opportunities capable of modifying disease trajectories. The future of neurodegenerative-disease intervention lies in precision modulation of neuroimmune networks, guided by molecular insight and translational innovation.

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Title of Article

Platelet-Rich Plasma vs Corticosteroids in Osteoarthritis: Comparative Efficacy

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Abstract

Platelet-rich plasma (PRP) and corticosteroid injections represent two widely used intra-articular therapies for osteoarthritis (OA), yet their mechanisms, therapeutic trajectories, and clinical durability differ profoundly. This paper examines the comparative efficacy of PRP and corticosteroids across symptomatic relief, structural modification, and long-term functional outcomes. It analyses biological mechanisms, patient-selection considerations, and evidence from controlled trials. The paper argues that PRP offers superior long-term benefit in mild-to-moderate OA, while corticosteroids retain value for short-term analgesia in acute inflammatory flares. A systems-orthopaedic framework is proposed for integrating both modalities into evidence-based OA management.

Keywords

Platelet-Rich Plasma; Corticosteroids; Osteoarthritis; Intra-Articular Therapy; Regenerative Medicine.

1. Introduction

Osteoarthritis remains one of the most prevalent and disabling musculoskeletal conditions worldwide, characterised by progressive cartilage degeneration, synovial inflammation, and structural joint deterioration. Intra-articular therapies have long been used to modulate symptoms and delay surgical intervention. Corticosteroids, historically the mainstay of injection therapy, provide rapid analgesia through potent anti-inflammatory effects but offer limited structural benefit and short-lived relief. Platelet-rich plasma, emerging from regenerative-medicine paradigms, seeks to harness autologous growth factors to modulate inflammation, enhance chondrocyte activity, and promote tissue repair. This paper examines the comparative efficacy of these modalities, arguing that their therapeutic profiles reflect fundamentally different biological mechanisms and clinical trajectories.

2. Biological Mechanisms Underpinning Therapeutic Action

Corticosteroids exert their effects through suppression of inflammatory mediators, inhibition of phospholipase A2, and down-regulation of cytokines such as IL-1 and TNF-α. This mechanism produces rapid pain relief but does not address underlying cartilage degeneration. Repeated corticosteroid exposure may impair chondrocyte metabolism, reduce collagen synthesis, and accelerate structural deterioration in susceptible joints.

PRP operates through a regenerative paradigm. Concentrated platelets release growth factors including PDGF, TGF-β, VEGF, and IGF-1, which modulate synovial inflammation, enhance chondrocyte proliferation, and support extracellular-matrix synthesis. PRP also influences macrophage phenotype, shifting synovial biology toward reparative states. These mechanisms produce slower onset of relief but more durable improvement, particularly in early-stage OA where biological responsiveness remains intact.

3. Clinical Trajectories and Symptomatic Outcomes

Corticosteroids provide rapid analgesia, often within days, making them valuable for acute inflammatory flares or severe pain that limits mobility. However, relief typically wanes within four to six weeks, and repeated injections show diminishing returns. Their short-term efficacy is therefore offset by limited durability and potential structural risks.

PRP demonstrates a different trajectory. Symptomatic improvement emerges gradually over several weeks, reflecting biological modulation rather than immediate anti-inflammatory suppression. Controlled trials consistently show superior outcomes at three, six, and twelve months compared with corticosteroids, particularly in mild-to-moderate OA. Patients report improved pain, enhanced function, and reduced stiffness, with benefits sustained beyond one year in some cohorts. PRP therefore aligns with long-term disease-modifying goals rather than short-term symptom suppression.

4. Structural and Functional Implications

Corticosteroids do not modify disease progression and may accelerate cartilage loss when used frequently. Their value lies in symptomatic control rather than structural preservation. PRP, by contrast, demonstrates potential for biological modulation of cartilage metabolism. Imaging studies reveal improved cartilage thickness, reduced synovial hypertrophy, and enhanced joint biomechanics in selected patients. While PRP is not a cure, its capacity to influence structural biology positions it closer to disease-modifying therapy than corticosteroids.

Functional outcomes reflect these differences. PRP improves gait parameters, quadriceps activation, and joint loading patterns over time. Corticosteroids improve function transiently but do not alter long-term biomechanical deficits.

5. Patient-Selection Considerations

Therapeutic efficacy depends on patient phenotype. Corticosteroids benefit individuals with acute synovitis, severe pain, or advanced OA where regenerative potential is limited. PRP is most effective in early-to-moderate OA, younger patients, and those with preserved joint alignment. Obesity, severe varus deformity, and end-stage cartilage loss reduce PRP responsiveness. Understanding these phenotypes is essential for evidence-based selection.

6. Safety Profiles and Risk Considerations

Corticosteroids carry risks including cartilage toxicity, accelerated degeneration, hyperglycaemia, and systemic effects in susceptible individuals. PRP, being autologous, has an excellent safety profile with minimal adverse events. Post-injection soreness is common but transient. The safety differential reinforces PRP's suitability for repeated use, whereas corticosteroids require cautious dosing intervals.

7. Comparative Evidence from Controlled Trials

Randomised trials consistently demonstrate that corticosteroids outperform PRP in the first two to three weeks due to rapid anti-inflammatory action. Beyond six weeks, PRP shows superior outcomes, with sustained benefit at six and twelve months. Meta-analyses confirm PRP's superiority in pain reduction, functional improvement, and patient satisfaction. Corticosteroids retain value for short-term rescue therapy but do not match PRP's long-term efficacy.

8. A Systems-Orthopaedic Framework for Integrated Use

A future-ready OA-management framework must integrate both modalities strategically. Corticosteroids should be reserved for acute inflammatory flares, severe pain crises, or patients unsuitable for regenerative therapy. PRP should be deployed for long-term symptom control, biological modulation, and functional restoration in early-to-moderate OA. This integrated approach aligns therapeutic choice with biological mechanism, patient phenotype, and long-term goals.

9. Conclusion

PRP and corticosteroids represent distinct therapeutic paradigms in osteoarthritis management. Corticosteroids offer rapid, short-term relief but lack durability and carry structural risks. PRP provides slower onset but superior long-term outcomes, enhanced functional recovery, and potential biological modulation. Comparative evidence supports PRP as the preferred modality for sustained management of mild-to-moderate OA, while corticosteroids retain value for acute symptom control. A systems-orthopaedic framework grounded in mechanism, phenotype, and evidence offers the most effective pathway for integrating these therapies into modern OA care.

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Synthetic Biology in Vaccine Development: Next-Generation Platforms

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Abstract

Synthetic biology is reshaping vaccine development by enabling programmable platforms, modular antigen design, and rapid manufacturing pipelines. This paper examines how synthetic-biology tools—including genetic circuits, engineered viral vectors, self-amplifying RNA systems, and cell-free biomanufacturing—are redefining the speed, precision, and scalability of modern vaccinology. It analyses molecular-engineering principles, platform innovations, and translational challenges in global health. The paper proposes a future-ready synthetic-biology framework for vaccine development tailored to African biomedical ecosystems.

Keywords

Synthetic Biology; Vaccines; Genetic Circuits; RNA Platforms; Biomanufacturing; Immuno-Engineering.

1. Introduction

Vaccinology is undergoing a profound transformation driven by synthetic biology, a discipline that merges engineering principles with molecular design to create programmable biological systems. Traditional vaccine platforms—attenuated pathogens, inactivated organisms, and protein subunits—have delivered historic successes yet remain constrained by slow development cycles, complex manufacturing, and limited adaptability to emerging pathogens. Synthetic biology offers a new paradigm in which vaccines are designed, assembled, and optimised using modular genetic components, computational tools, and cell-free systems. This paper argues that synthetic-biology-enabled vaccine platforms represent the next frontier in global immunisation, capable of accelerating response to outbreaks, enhancing antigen precision, and expanding access across diverse health systems.

2. Molecular-Engineering Foundations of Synthetic-Biology Vaccines

Synthetic biology enables rational design of vaccine components through programmable genetic circuits, modular promoters, engineered RNA structures, and synthetic antigens. These tools allow precise control over antigen expression, immune-system engagement, and intracellular signalling. Genetic circuits can modulate dose, timing, and localisation of antigen production, creating vaccines that behave as engineered biological devices rather than passive formulations. Codon optimisation, epitope engineering, and computational antigen design further enhance immunogenicity while reducing off-target effects.

These molecular-engineering foundations shift vaccine development from empirical trial-and-error toward predictable, model-driven design. Synthetic biology therefore provides the conceptual and technical infrastructure for next-generation vaccine platforms capable of rapid adaptation and high-fidelity immune activation.

3. RNA Platforms and the Rise of Programmable Immunogens

RNA vaccines, particularly mRNA and self-amplifying RNA (saRNA), exemplify the power of synthetic biology in vaccinology. mRNA platforms allow rapid antigen design, scalable manufacturing, and precise control over protein expression. saRNA systems extend these capabilities by incorporating replicase machinery that amplifies RNA within host cells, enabling lower doses and prolonged antigen presentation.

Synthetic-biology tools enhance RNA stability, translation efficiency, and immunogenicity through engineered untranslated regions, modified nucleotides, and lipid-nanoparticle formulations. These innovations produce vaccines that are not only fast to develop but highly tunable, allowing modulation of immune pathways with unprecedented precision. RNA platforms therefore represent a cornerstone of next-generation vaccinology.

4. Engineered Viral Vectors and Modular Immuno-Delivery

Synthetic biology has revitalised viral-vector vaccinology by enabling modular engineering of adenoviruses, lentiviruses, and poxviruses. Engineered vectors can be customised to enhance tropism, reduce pre-existing immunity, and optimise antigen presentation. Synthetic promoters and regulatory elements allow fine-tuned expression, while capsid engineering improves stability and immune engagement.

These vectors serve as programmable delivery vehicles capable of transporting complex genetic payloads, including multi-antigen constructs and immunomodulatory circuits. Their modularity enables rapid redesign in response to emerging pathogens, making them valuable tools for outbreak preparedness and personalised immunotherapy.

5. Protein and Peptide Vaccines Through Synthetic-Biology Design

Synthetic biology enables precision engineering of protein and peptide vaccines through computational epitope mapping, scaffold design, and modular assembly. Synthetic antigens can be constructed to mimic conformational epitopes, enhance stability, and optimise immune recognition. Nanoparticle scaffolds, virus-like particles, and self-assembling protein structures provide platforms for multivalent antigen display.

These engineered proteins offer high safety profiles and tunable immunogenicity, making them suitable for chronic infections, cancer vaccines, and pathogens requiring complex antigenic structures. Synthetic-biology-driven protein design therefore expands the landscape of subunit vaccinology beyond traditional recombinant approaches.

6. Cell-Free Biomanufacturing and Rapid-Response Vaccine Production

Cell-free systems represent one of the most transformative synthetic-biology innovations in vaccine manufacturing. By removing reliance on living cells, cell-free platforms enable rapid, scalable, and decentralised production of RNA, proteins, and viral components. These systems can be freeze-dried, transported, and reactivated on demand, offering unprecedented flexibility for outbreak response and low-resource settings.

Cell-free biomanufacturing aligns with global health priorities by reducing infrastructure requirements, accelerating production timelines, and enabling distributed manufacturing networks. For Africa, this technology offers a pathway toward regional vaccine autonomy and resilience.

7. Immuno-Engineering and Precision Modulation of Immune Pathways

Synthetic biology enables vaccines that not only present antigens but actively modulate immune pathways. Engineered adjuvants, synthetic cytokine circuits, and immunomodulatory genetic elements allow precise control over innate and adaptive responses. Vaccines can be designed to enhance T-cell activation, promote mucosal immunity, or bias responses toward specific immunological phenotypes.

This precision immuno-engineering transforms vaccines into programmable immune interventions capable of addressing complex pathogens, chronic infections, and cancer. It also opens avenues for personalised vaccinology tailored to individual immune profiles.

8. Governance, Safety, and Ethical Considerations

Synthetic-biology vaccines introduce new governance challenges related to biosafety, genetic-material handling, and regulatory oversight. Engineered constructs require rigorous evaluation to ensure stability, containment, and predictable behaviour. Ethical considerations arise around genetic manipulation, equitable access, and intellectual-property frameworks that shape global vaccine distribution.

A future-ready governance architecture must balance innovation with safety, ensuring that synthetic-biology platforms are deployed responsibly and equitably across diverse health systems.

9. A Synthetic-Biology Framework for African Vaccine Innovation

Africa's vaccine landscape is shaped by limited manufacturing capacity, dependence on external suppliers, and vulnerability to global supply disruptions. Synthetic biology offers a strategic opportunity to build regional autonomy through modular platforms, cell-free biomanufacturing, and rapid-response technologies. A future-ready framework must integrate capacity building, regulatory reform, regional collaboration, and investment in computational and molecular-engineering expertise.

This framework positions Africa not merely as a consumer of global vaccine technologies but as an active innovator capable of developing next-generation platforms tailored to regional pathogens and health priorities.

10. Conclusion

Synthetic biology is redefining vaccine development by enabling programmable platforms, modular antigen design, and rapid manufacturing systems. Its integration of molecular engineering, computational design, and cell-free biomanufacturing offers unprecedented speed, precision, and adaptability. For global health—and for Africa in particular—synthetic-biology vaccines represent a transformative opportunity to build resilient, responsive, and equitable immunisation systems. The future of vaccinology lies in platforms that are engineered, modular, and capable of evolving alongside emerging pathogens.

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The Long-Term Metabolic Consequences of Antiretroviral Therapy: Forecasting the Future Burden of Non-Communicable Diseases Among Adults Living with HIV in Sub-Saharan Africa

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Abstract

As antiretroviral therapy (ART) transforms HIV from a fatal infection into a chronic, manageable condition, a new epidemiological frontier is emerging across Sub-Saharan Africa: the rising burden of non-communicable diseases (NCDs) among adults living with HIV. This paper examines the long-term metabolic consequences of ART, analysing dyslipidaemia, insulin resistance, adipose-tissue dysfunction, chronic inflammation, and accelerated cardiometabolic ageing as interconnected processes shaping future disease trajectories. It evaluates demographic transitions, treatment-era effects, and health-system vulnerabilities that will influence the scale of the coming NCD burden. The paper proposes a forecasting framework for anticipating and managing the metabolic consequences of lifelong ART within African health systems.

Keywords

Antiretroviral Therapy; Metabolic Syndrome; Non-Communicable Diseases; HIV; Sub-Saharan Africa; Epidemiological Forecasting.

1. Introduction

The success of antiretroviral therapy has fundamentally altered the natural history of HIV infection. Millions of adults across Sub-Saharan Africa now live longer, healthier lives, with viral suppression enabling near-normal life expectancy. Yet this triumph has revealed a new epidemiological challenge: the emergence of metabolic disorders and NCDs linked to chronic HIV infection, long-term ART exposure, and ageing. As the region's HIV-positive population grows older, the interplay between viral persistence, immune activation, and ART-induced metabolic alterations is reshaping disease patterns. This paper argues that the long-term metabolic consequences of ART represent one of the most significant—and least prepared for—public-health challenges facing African health systems.

2. ART, Chronic HIV Infection, and the Metabolic Reconfiguration of the Body

ART suppresses viral replication but does not eliminate chronic immune activation. Even in virally suppressed individuals, low-grade inflammation persists, altering lipid metabolism, insulin signalling, endothelial function, and adipose-tissue biology. These changes interact with ART-specific effects to create a metabolic landscape characterised by dyslipidaemia, insulin resistance, visceral adiposity, and mitochondrial dysfunction.

Older ART regimens, particularly thymidine analogues and protease inhibitors, produced profound metabolic disturbances. Newer regimens—especially integrase inhibitors—have reduced toxicity but introduced new concerns, including weight gain, altered fat distribution, and increased risk of diabetes.

The metabolic consequences of ART therefore reflect both historical exposure and contemporary treatment patterns, creating heterogeneous risk profiles across cohorts.

3. Dyslipidaemia and the Cardiovascular Consequences of Lifelong ART

Dyslipidaemia is one of the most consistent metabolic effects of ART. Elevated triglycerides, reduced HDL cholesterol, and altered LDL particle composition create a pro-atherogenic profile that increases cardiovascular risk. Protease inhibitors disrupt lipid regulation through interference with hepatic lipid metabolism, while integrase inhibitors appear to influence adipocyte differentiation and weight gain.

In Sub-Saharan Africa, where baseline cardiovascular risk is rising due to urbanisation, dietary transitions, and sedentary lifestyles, ART-associated dyslipidaemia amplifies existing vulnerabilities. The convergence of HIV, ART, and lifestyle-driven metabolic change is likely to accelerate the region's cardiovascular-disease burden over the next two decades.

4. Insulin Resistance, Weight Gain, and the Emerging Diabetes Burden

Insulin resistance arises from chronic inflammation, adipose-tissue dysfunction, and ART-specific effects. Integrase inhibitors, particularly dolutegravir, have been associated with significant weight gain, especially among women. This weight gain is not merely cosmetic; it reflects metabolic shifts toward visceral adiposity, impaired glucose tolerance, and increased risk of type 2 diabetes.

As African HIV cohorts age, diabetes prevalence is expected to rise sharply. The combination of ART-associated metabolic changes, genetic predisposition, and environmental risk factors creates a perfect storm for accelerated diabetes incidence. Without proactive intervention, diabetes will become a major driver of morbidity among adults living with HIV.

5. Adipose-Tissue Dysfunction and the Legacy of Lipodystrophy

Lipodystrophy—characterised by abnormal fat loss or accumulation—was historically associated with older ART regimens. While its prevalence has declined, adipose-tissue dysfunction remains a central metabolic consequence of HIV and ART. Altered adipocyte signalling contributes to insulin resistance, dyslipidaemia, and chronic inflammation.

Even in the absence of overt lipodystrophy, subtle adipose-tissue abnormalities persist, influencing metabolic risk. These changes interact with ageing, lifestyle factors, and ART exposure to shape long-term NCD trajectories.

6. Chronic Inflammation, Immune Activation, and Accelerated Ageing

Chronic immune activation persists despite viral suppression, driving endothelial dysfunction, oxidative stress, and accelerated biological ageing. This inflammatory milieu contributes to hypertension, cardiovascular disease, frailty, and neurocognitive decline. ART reduces but does not eliminate inflammatory signalling, meaning that adults living with HIV experience ageing processes that differ from HIV-negative populations.

The interaction between chronic inflammation and metabolic dysfunction creates a synergistic risk environment that will shape future NCD patterns across the region.

7. Forecasting the Future Burden of NCDs Among Adults Living with HIV

Forecasting the future burden of NCDs requires integrating demographic trends, treatment patterns, metabolic-risk trajectories, and health-system capacity. Sub-Saharan Africa's HIV-positive population is ageing rapidly, with millions expected to reach older adulthood within the next decade. As ART exposure lengthens, metabolic complications will accumulate, producing rising prevalence of hypertension, diabetes, cardiovascular disease, chronic kidney disease, and obesity.

Urbanisation, dietary change, and reduced physical activity will amplify these trends. Health systems designed for acute infectious-disease management will face increasing demand for chronic-care services, long-term monitoring, and integrated HIV-NCD management. Without strategic planning, the region will confront a dual epidemic of HIV and NCDs that strains already limited resources.

8. Health-System Vulnerabilities and the Coming Strain on Chronic-Care Infrastructure

African health systems remain oriented toward vertical HIV programmes that emphasise viral suppression rather than metabolic monitoring. Routine lipid testing, glucose screening, and cardiovascular-risk assessment are rare in many HIV clinics. Workforce shortages, limited diagnostic capacity, and fragmented care pathways hinder early detection and management of metabolic complications.

As the NCD burden grows, these vulnerabilities will become more pronounced. The region must transition from an HIV-centric model to an integrated chronic-care model capable of managing multimorbidity. This transition requires investment in diagnostics, workforce training, supply-chain reliability, and data systems that support longitudinal monitoring.

9. A Future-Ready Framework for Managing ART-Associated Metabolic Disease

A future-ready framework must integrate metabolic monitoring into routine HIV care, prioritise early detection, and adopt treatment strategies that minimise metabolic risk. It must incorporate lifestyle-modification support, community-based interventions, and culturally grounded health promotion. It must strengthen primary-care systems, expand chronic-care capacity, and embed NCD management within universal-health-coverage agendas.

This framework positions HIV care as a gateway to broader chronic-disease management, leveraging existing infrastructure to address emerging metabolic challenges.

10. Conclusion

The long-term metabolic consequences of antiretroviral therapy represent a major epidemiological shift in Sub-Saharan Africa. As adults living with HIV age, the burden of NCDs will rise sharply, driven by dyslipidaemia, insulin resistance, adipose-tissue dysfunction, chronic inflammation, and accelerated ageing. Forecasting this burden reveals an urgent need for integrated chronic-care systems capable of managing multimorbidity. The future of HIV care in Africa lies not only in viral suppression but in proactive management of metabolic health, ensuring that the gains of ART are not undermined by preventable chronic disease.

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