

Protocol for a Structured, Health Policy and Systems–Oriented Scoping Review of Determinants of Single-Pill Combination Availability in Sub-Saharan Africa

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Abstract

Background: Although international guidelines recommend single-pill combinations (SPCs) as first-line therapy for hypertension, their availability and use remain limited. Evidence on access to essential medicines is largely not specific to SPCs, and the determinants influencing their availability are dispersed across heterogeneous sources that are not well captured by traditional systematic review approaches.

Objective: To describe the protocol for a structured, health policy and systems–oriented scoping review designed to map and synthesize the determinants of availability of antihypertensive SPCs in Sub-Saharan Africa (SSA) and to propose a transferable methodological framework applicable to other essential medicines and health system contexts.

Methods: A comprehensive scoping review of peer-reviewed literature, grey literature, and policy documents will be conducted in accordance with the PRISMA extension for scoping reviews (PRISMA-ScR). Searches will be performed across bibliographic databases, government repositories, and relevant non governmental organization (NGO) sources. Eligible sources will include empirical studies, policy analyses, and institutional reports addressing SPC availability. Two independent reviewers will screen studies and extract data. Evidence will be synthesized narratively and mapped to the World Health Organization (WHO) Health System Building Blocks and the Bigdeli access-to-medicines framework.

Expected results: The review will generate a structured mapping of regulatory, economic, health system, and sociocultural determinants influencing SPC availability in SSA and will identify key barriers, facilitators, and policy gaps relevant to hypertension management.

Conclusions: This protocol outlines a replicable methodological approach for synthesizing heterogeneous evidence on access to essential medicines. The framework may be adapted to other therapeutic areas and low- and middle-income contexts, potentially supporting more informed policy and implementation decisions to reduce cardiovascular morbidity and mortality.

Keywords: Hypertension; Drug Combinations; Africa South of the Sahara.

Introduction

Hypertension remains one of the leading modifiable risk factors for cardiovascular disease and premature mortality worldwide. In

2019, it was estimated that over 1.2 billion people were living with hypertension, with nearly two-thirds residing in low- and middle-income countries (LMICs).¹ Sub-Saharan Africa (SSA) bears a particularly heavy burden, characterized by high prevalence, low awareness, and poor blood pressure control, leading to increased cardiovascular morbidity and mortality.²

To address these challenges, international guidelines recommend the use of single-pill combinations (SPCs). These fixed-dose formulations combine two or more antihypertensive agents into a single tablet as first-line therapy for most individuals with hypertension.^{3–5} SPCs offer several advantages over monotherapy or multiple-pill regimens, including improved adherence, more rapid blood pressure control, and a reduced

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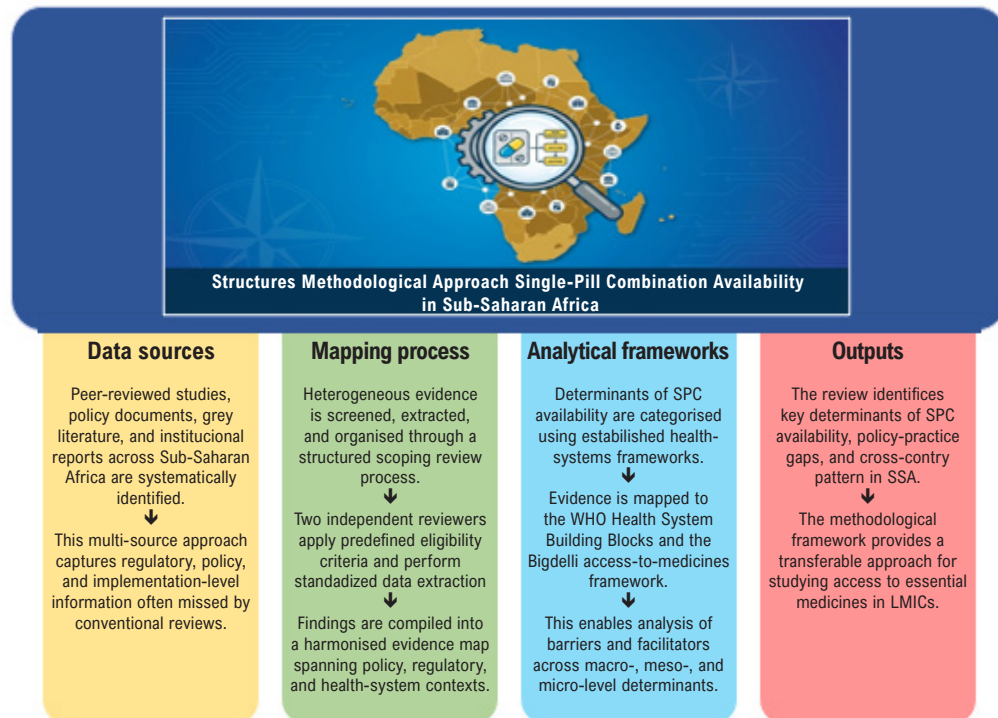
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Central Illustration: Protocol for a Structured, Health Policy and Systems–Oriented Scoping Review of Determinants of Single-Pill Combination Availability in Sub-Saharan Africa



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AJOL: African Journals Online; EMLs: National Essential Medicines Lists; JBI: Joanna Briggs Institute; LMICs: Low- and middle-income countries; PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols; SPC: Single-pill combination; WHO: World Health Organization.

risk of cardiovascular events.^{6,7} The World Health Organization (WHO) and the International Society of Hypertension have strongly endorsed the use of SPCs to optimize hypertension management, particularly in LMICs.^{3,8} More recently, in September 2025, the WHO further reinforced this position by adding a triple SPC therapy to the WHO Model List of Essential Medicines, underscoring the growing global consensus on simplified and intensified treatment strategies.⁹

Despite robust clinical evidence and clear recommendations, the availability and routine use of SPCs in SSA remain limited. Global assessments indicate that only a small number of African countries include SPC antihypertensive medications in their National Essential Medicines Lists (EMLs), and even fewer ensure their consistent availability within public-sector supply systems.¹⁰ While barriers to access to essential medicines in African countries have been broadly described, existing evidence largely addresses essential medicines as a general category rather than focusing specifically on SPCs for hypertension. As a result, the determinants of SPC availability remain insufficiently characterized and poorly synthesized for this therapeutic class.¹¹

This gap is not only empirical but also methodological. Evidence relevant to SPC availability is dispersed across

heterogeneous sources, including observational and qualitative studies, policy documents, and program reports. Additionally, mapping the availability of SPC antihypertensive medications requires a methodological approach capable of capturing evidence across multiple levels of the health system, including regulatory environments, procurement mechanisms, supply chains, clinical practice, and sociocultural contexts. Given the heterogeneity of data sources and the predominance of non-comparative, policy-oriented evidence, traditional systematic reviews are not the most suitable design for addressing this type of evidence. A structured, health policy and systems–oriented scoping review offers a suitable methodological strategy to map this fragmented body of evidence, identify key determinants across different levels of the health system, and highlight areas requiring further investigation. The integration of the WHO Health System Building Blocks and the Bigdelli access-to-medicines framework further enables the structured categorization of determinants across macro-, meso-, and micro-levels,^{12,13} which is essential for informing actionable policy responses in SSA.

Therefore, this protocol aims to describe and justify a structured, health policy and systems–oriented methodological

approach to mapping the determinants of availability of SPC antihypertensive medications in SSA. By integrating scoping review methods with established health system and access-to-medicines frameworks, this approach seeks to provide a replicable strategy for synthesizing heterogeneous evidence relevant to policy and implementation decision-making in LMICs.

Methods

Study design and methodological framework (protocol)

This protocol describes a health policy and systems-oriented scoping review methodology designed to map determinants of the availability of essential medicines, focusing on antihypertensive SPCs in SSA. The approach integrates scoping review principles with structured document analysis and established health system and access-to-medicines frameworks, with the intention of providing a replicable model for synthesizing heterogeneous evidence relevant to policy and implementation decision-making in low- and middle-income settings (Central Illustration). The methodological approach follows the framework proposed by Arksey and O'Malley (2005),¹⁴ further refined by Levac et al. (2010),¹⁵ and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines.¹⁶ The protocol was prospectively registered on the Open Science Framework to ensure transparency and methodological rigor.¹⁷

Identifying the research question

The guiding research question is: "What regulatory, economic, health system, and sociocultural factors influence the availability of SPC antihypertensive medications in SSA?" This question was intentionally framed broadly to allow the mapping of diverse types of evidence across health policy, pharmaceutical systems, and service delivery domains.

Information sources and search strategy

In line with the proposed health policy and systems-oriented scoping review framework, the search strategy will be designed to capture evidence across multiple levels of the health system, including regulatory, policy, and implementation domains. It will be applied across peer-reviewed literature, grey literature, and policy documents. Databases to be searched include:

- I. Primary databases: MEDLINE (via PubMed), Embase, Scopus, Web of Science, Cumulative Index to Nursing and Allied Health Literature, and Global Index Medicus;
- II. Local and regional databases: African Journals Online (AJOL), African Index Medicus, Nigeria Journals Online, and Uganda Health Information Digest;
- III. Grey literature: Google Scholar, OpenGrey, and Open Access Theses and Dissertations (OATD);
- IV. Government and NGO sources: Ministries of Health (Nigeria and Uganda), national reports on hypertension, access to medicines, health policy documents, health product supply chain strategies, and annual health

assessments; WHO; World Bank; African Development Bank (ADB); WHO Health InterNetwork Access to Research Initiative (HINARI); Clinton Health Access Initiative (CHAI); National Agency for Food and Drug Administration and Control; Noncommunicable Disease (NCD) Multisectoral Action Plan; National Drug Authority (NDA, for SPC registrations and availability); Medicines Transparency Alliance (MeTA) Uganda; UNICEF Supply Division; and Global Health Supply Chain (GHSC).

No language or date restrictions will be applied. The full search strategy is available in Supplementary Material 1.

Additionally, to increase sensitivity, the reference lists of all included publications will be manually screened to identify any relevant sources not captured in the initial search. Supplementary identification of potentially relevant materials may also be conducted through non-indexed academic networking platforms. Any records identified through such supplementary mechanisms will undergo the same eligibility assessment and screening procedures as those retrieved through the formal database and grey literature searches. These supplementary sources will not constitute part of the structured search strategy and will be transparently documented. Consistent with scoping review methodology, search strategies may be refined iteratively as familiarity with the literature evolves, with any modifications documented to ensure transparency and reproducibility.

We anticipate that a significant portion of the relevant data will come from grey literature, particularly official government and health organization documents.

Study selection

Study selection criteria will be deliberately broad to reflect the exploratory and mapping purpose of scoping reviews, prioritizing sources that inform system-level, policy, and contextual determinants of SPC availability rather than clinical effectiveness. Included sources will encompass observational studies, policy analyses, qualitative research, systematic or scoping reviews, and relevant government or institutional reports, provided they examine the availability of SPCs for hypertension treatment in SSA or the factors influencing it. Excluded sources will include those focusing solely on countries outside SSA, unrelated clinical contexts (e.g., pediatric or pregnancy-only populations without a focus on hypertension), lacking clear outcomes related to SPC availability, or narrative reviews. In such cases, the original studies will be assessed for inclusion.

Availability of SPCs for hypertension treatment will be defined as the presence of SPCs in healthcare facilities (public and private), pharmacies, and supply chains. Availability will be assessed through reported access, stock levels, and distribution data from government and institutional reports, as well as published studies. Barriers and facilitators of SPC availability will be defined as the factors identified as influencing SPC availability, such as regulatory policies, supply chain infrastructure, pricing, and prescriber preferences.

All identified records will be imported into a reference management system, and duplicates will be removed. Two

reviewers will independently screen titles and abstracts to assess eligibility. Full texts of potentially eligible studies will be retrieved and assessed in duplicate. Discrepancies will be resolved by a third reviewer. The entire process will be documented in a PRISMA flow diagram.

Data extraction and management

A standardized extraction form will capture study characteristics (authors, year, country, design, methods), healthcare context (public/private sector, rural/urban), type of SPCs, and factors influencing availability. For qualitative and document-based sources, information on the theoretical framework, intervention levels (macro, meso, micro), and stakeholder perspectives will be collected. Systematic and scoping reviews will be included as documents for synthesis, and relevant primary studies cited within these reviews may be extracted separately to avoid duplication.

A codebook with clear definitions of each variable was developed (Supplementary Material 2), and all researchers involved in data extraction will be trained in advance to ensure consistency.

Data synthesis

Given the anticipated heterogeneity of study designs and outcomes, a narrative and descriptive mapping synthesis will be used to integrate findings from empirical studies, reviews, and policy documents. The structured mapping planned in this protocol is intended to enable the systematic organization of heterogeneous evidence across macro-, meso-, and micro-level determinants.

Data will be mapped to the WHO Health System Building Blocks and the Bigdeli access-to-medicines framework to categorize regulatory, economic, health system, and sociocultural determinants of SPC availability.^{12,13} Where possible, prevalence and trends in SPC availability from observational studies will be summarized descriptively. Particular attention will be paid to differences and similarities across countries in terms of policies, health system constraints, and SPC access. Quantitative data extracted from studies (e.g., prevalence rates, policy impact assessments) will be summarized descriptively where applicable.

Additionally, a review of the National EMLs of all SSA countries will be conducted to verify whether SPC antihypertensive medications are included and to identify which specific combinations are listed. In parallel, national hypertension treatment guidelines available for each country will also be reviewed to determine whether and how SPCs are mentioned or recommended as therapeutic options. This integrated document and literature mapping allows for the assessment of alignment between governance instruments and on-the-ground availability and provides a comprehensive view of regulatory and programmatic barriers to SPC adoption. .

Ethical considerations

All data used will be derived from published documents; no primary data will be collected. Therefore, the systematic

review does not require ethical approval. The authors commit to reporting all results, including unexpected findings, to ensure credibility and transparency.

Expected results

The planned scoping review is expected to generate a comprehensive and structured mapping of the determinants influencing the availability of antihypertensive SPCs in SSA. Specifically, the review will identify and categorize regulatory, economic, health system, and sociocultural factors affecting SPC availability across different country contexts.

The synthesis is expected to include:

- I. a description of the volume and types of evidence available, including peer-reviewed studies, policy documents, and grey literature;
- II. a structured mapping of identified determinants according to the WHO Health System Building Blocks and the Bigdeli access-to-medicines framework;
- III. identification of key barriers and facilitators influencing SPC availability; and
- IV. an assessment of alignment between national policies (e.g., EMLs and treatment guidelines) and reported availability in practice.

In addition, the review is expected to highlight gaps in the existing literature and policy landscape, particularly in relation to implementation challenges and health system constraints. These findings will support the identification of priority areas for future research and inform policy and implementation strategies aimed at improving access to SPCs in low- and middle-income settings.

Discussion

The availability of SPC antihypertensive medications in SSA remains a critical yet understudied component of effective hypertension management. Despite consistent international recommendations endorsing SPCs as the preferred treatment for most patients with hypertension,^{3-5,8} real-world access to these therapies across the region is constrained by fragmented regulatory environments, inconsistent inclusion in national formularies, and limited procurement mechanisms.^{10,11}

This protocol outlines a structured, health policy and systems-oriented approach to mapping the determinants of availability of essential medicines, focusing on SPC antihypertensive therapies in SSA. While the limited availability of SPCs remains a critical barrier to effective hypertension management in the region, the primary contribution of this work lies in proposing a systematic strategy for identifying, organizing, and interpreting heterogeneous, policy-relevant evidence in complex health systems.

By integrating scoping review methods with structured document analysis and established conceptual frameworks, the proposed approach seeks to address a recurring methodological challenge in access-to-medicines research: the dispersion of relevant evidence across peer-reviewed

studies, grey literature, policy documents, and institutional reports. The structured mapping strategy described in this protocol is intended to enable the synthesis of determinants operating across regulatory, economic, health system, and sociocultural domains, while preserving contextual specificity at national and subnational levels.

The planned application of the WHO Health System Building Blocks and the Bigdeli access-to-medicines framework provides a transparent and replicable structure for organizing evidence across macro-, meso-, and micro-level determinants.^{12,13} In the case of antihypertensive SPCs, this framework is expected to facilitate the identification of barriers that may span multiple system components simultaneously. This includes medicine registration and regulation, inclusion in EMLs, procurement and financing mechanisms, supply chain capacity, and prescriber practices. Importantly, the methodological framework may support the identification of misalignment between global clinical recommendations and national policy instruments, a pattern that is likely relevant not only to SPCs but also to other essential medicines in LMIC settings.

Beyond its intended substantive outputs, this protocol contributes to the broader field of health policy and systems research. The explicit integration of document review, grey literature, and framework-based mapping allows researchers and policymakers to move beyond inventories of barriers toward a more structured understanding of how governance, market dynamics, and health system design interact to shape access to medicines.

From a policy perspective, the proposed approach may support Ministries of Health, regulatory authorities, and implementation partners in identifying leverage points for intervention, prioritizing reforms, and aligning national policies with international guidance. While this protocol focuses on antihypertensive SPCs in SSA, the methodology is adaptable to essential medicines for other NCDs and therapeutic areas, regions, and policy questions.

Limitations and future directions

As a protocol for a scoping review, several limitations should be acknowledged. First, the availability and quality of evidence on SPCs in SSA are likely to be uneven and heterogeneous, with substantial reliance on grey literature and government policy documents that may not be systematically archived or publicly accessible. The potential for reporting bias in policy documents must be acknowledged, which may also contribute to difficulties in comparing variables across countries. This reflects a broader limitation of access-to-medicines research in low-resource settings rather than a shortcoming of the methodological approach itself.

Second, while the structured mapping framework is designed to enhance transparency and comparability, it does not aim to quantify or infer causal relationships or to measure the relative contribution of individual determinants. Future research building on the findings of the planned review may integrate quantitative policy analyses, implementation studies, or country-level case studies to strengthen causal inference.

Importantly, future applications of this methodology could test its utility in other regions and therapeutic areas, as well as explore

its integration with participatory methods involving policymakers and stakeholders. This would further strengthen its relevance for implementation-oriented research and policy development.

Conclusion

This protocol outlines a structured, health policy and systems-oriented methodological approach for synthesizing heterogeneous evidence on the availability of essential medicines. By proposing the application of this framework to antihypertensive SPCs in SSA, it describes how scoping review methods, combined with established access-to-medicines frameworks, may generate policy-relevant insights while maintaining transparency and replicability. Beyond its intended outputs, this protocol presents a transferable framework for synthesizing heterogeneous evidence on access to essential medicines and supporting more informed policy, planning, and implementation decisions to reduce cardiovascular morbidity and mortality.

Author Contributions

Conception and design of the research and obtaining financing: Marcolino MS, Dalakoti M, Liu H, Njohjam MN; writing of the manuscript and critical revision of the manuscript for intellectual content: Marcolino MS, Costa MR, Schettini I, Dalakoti M, Liu H, Njohjam MN.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

Use of Artificial Intelligence

The authors did not use any artificial intelligence tools in the development of this work.

Availability of Research Data

The underlying content of the research text is contained within the manuscript.

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