Antimicrobial Prescription patterns in East Africa: A systematic Review

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Research

Keywords: Antimicrobial, electronic databases, African countries

Posted Date: August 2nd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-722694/v1

Version of Record: A version of this preprint was published at Systematic Reviews on February 14th, 2023. See the published version at https://doi.org/10.1186/s13643-022-02152-7.

Abstract

Background

Antimicrobial resistance is currently a recognised global health problem stemming from poor antibiotic stewardship by health workers and inappropriate antimicrobial use by patients. Data showing the extent of poor antimicrobial stewardship in low- and middle-income countries are scanty though high incidences of antimicrobial resistance are increasingly reported in many settings across the globe. The objective of the present study was, therefore, to evaluate prescriptions for antimicrobials in East Africa.

Methods

A comprehensive literature search strategy that includes text words and medical subject headings was developed and applied to predefined electronic databases. Two authors independently screened the titles and abstracts of the outputs of the literature search. Full texts were then independently reviewed by the two researchers. Extracted data from included studies were pooled using meta-analysis

Results

Majority of the included studies (30.8%) were retrieved from Ethiopia, followed by Sudan, Kenya and Tanzania each contributing 19.2%. The overall proportion of encounter with antimicrobials reported was 57% (95%CI 42%; 73%). Ethiopia had an overall patient encounter with antimicrobials of 63% [95%CI: 50%, 76%] followed by Sudan with an overall encounter with antimicrobials of 62% [95%CI: 34%, 85%]. Studies from Kenya reported the overall encounter with antimicrobials of 54% [95%CI: 15%, 90%], whereas studies from Tanzania reported an overall patient encounter with antimicrobials of 40% [95%CI: 21%, 60%].

Conclusion

Prescription patterns demonstrated in this review significantly deviate from WHO recommendations suggesting inappropriate antimicrobial use in the East African countries. Further studies have to be pursued to generate more information on antimicrobial use in this region.

Introduction

Antimicrobial resistance is currently a recognised global health problem stemming from poor antibiotic stewardship by health workers and improper use of antimicrobial by patients [1]. Data showing the extent of poor antimicrobial stewardship in low- and middle-income countries is scanty though high incidences of antimicrobial resistance are increasingly reported in many settings across the globe [2]. Reports indicate that misuse of antimicrobials including over prescription and prescription without proper identification of offending pathogens in humans and animals are some of the main drivers of the currently witnessed antimicrobial resistance [3].

Studies revealed a more than 65% dramatic increase in antibiotic consumption between 2000 and 2015 fuelled by excessive antibiotic prescription in low- and middle-income countries [4]. One study reported the increasing trends of antimicrobial resistance due to the COVID-19 pandemic resulting from irrational antimicrobial treatment [5]. It is estimated that 10 million deaths will occur in Africa and Asia by 2050 if improper antimicrobial use is not tackled as a matter of emergency [5]. Several factors have attributed to the rise in antimicrobial use especially in Africa and other low- and middle-income countries: high burden of infectious diseases, poor antibiotic stewardship due to inadequate training of health professionals, lack of essential diagnostic equipment, widespread over the counter (OTC) sale of antibiotics, and weak antibiotic regulatory environment [6, 7].

Literature reporting on antibiotic use and prescription patterns is available in a lot of small studies with scanty synthesized evidence for Africa and other low- and middle-income countries [8, 9]. Yet devising interventions to combat the current global upsurge of antimicrobial resistance requires guidance from quality evidence whose availability is limited. This study is aimed to synthesize available data on this topic to avail policy relevant evidence on antimicrobial prescriptions in East Africa in order to guide decisions on antimicrobial resistance interventions.

Methods

The literature search strategy employed

We used the following key terms; “antimicrobial” or “antibiotic” or “anti-infective agent”. No time and language restrictions were applied during database searching. Eight electronic databases were searched (PubMed, EBSCOhost, Web of Science, Cochrane Library, Scopus, International Clinical Trials Registry Platform (ICTRP), Mednar) for relevant literature.

Example of the search strategy developed and on PubMed database

(("primary health care"[mesh] OR primary care[tw] OR primary health*[tw] OR community health*[tw] OR community care[tw] OR community worker*[tw] OR clinic[tw] OR clinics[tw] OR “general practitioners” [mesh] OR general practi*[tw] OR family medicine[tw] OR family practi*[tw] OR “physicians, family” [mesh] OR family physician*[tw] OR family doctor*[tw] OR "physicians, primary care"[mesh])) AND (("anti-bacterial agents"[Pharmacological Action] OR "anti-bacterial agents"[MeSH Terms] OR "anti-infective agents"[Pharmacological Action] OR "anti-infective agents"[MeSH Terms] OR antibiotic*[tw] OR antimicrobial*[tw] OR antibacterial*[tw] OR anti-bacterial*[tw] OR anti-infective*[tw])) AND ("therapeutic use"[sh] OR "drug prescriptions"[mesh] OR "drug utilization"[mesh] OR “inappropriate prescribing” [mesh] OR “drug utilization review” [mesh] OR "practice patterns, physicians'"[mesh] OR use[tiab] OR user*[tiab] OR used[tiab] OR overuse*[tiab] OR underuse*[tiab] OR misuse*[tiab] OR utiliz*[tiab] OR overutili*[tiab] OR underutili*[tiab] OR prescri*[tw] OR overprescri*[tiab] OR underprescri*[tiab])

Types of studies included in the review

We included studies conducted in East Africa that reported the proportion of patients receiving any antimicrobial prescription irrespective of facility setting or level. The study types included in the review were cross-sectional studies, cohort studies, and randomized controlled trials (RCTs) and non-RCTs.

Reviews of all kinds, economic evaluation studies, qualitative studies, mathematical modelling and non-primary research publications such as: commentaries, editorials and conference proceedings were not eligible for this review. Studies reporting antimicrobial use in animals i.e., those focused on veterinary use of antimicrobials, and those focused on special cohorts of patients such as surgical prophylaxis where use of antimicrobials biotics is justified, were excluded.

Data collection and analysis

Selection of studies

All outputs of electronic database search were imported into Rayyan Software for screening and selection (41). Two of the researchers independently screened 100% titles and abstracts for inclusion of potentially eligible studies obtained from the database searches. The first reviewer (JA), collected full-text articles/publications of potentially eligible studies and then JA and the second reviewer (PKO) independently screened 100% of full-text articles for inclusion. Where disagreement occurred between the two reviewers, the last reviewer (EM) was consulted. Each step of the study selection process was documented and where a study was excluded, the reason(s) for exclusion was recorded and entered the PRISMA flow diagram

Data extraction and management

Data were independently extracted in text, tables and figures of the included studies by the first and second researchers and recorded on a standardized, pre-designed extraction form. In the case of unclear data, corresponding author was contacted for clarifications. Data management was the duty of the first reviewer (JA) in consultation with the second reviewer (PKO). Completed data extraction forms were maintained on both a password secured laptop and USB memory stick and exported to STATA for analysis.

The following data points were extracted from the included studies:

Study characteristics: year(s) of data collection, study design, source of data, population or participants and objectives of the study.

Study setting: country, income level, health facility level.

Outcome measures: number of individuals receiving at least one antimicrobial prescription to the number of persons attending a given health facility within a specified time period.

Risk of bias assessment

The methodological quality of studies including risk of bias was assessed using a checklist to assess for internal and external validity. A modified check list originally developed by Hoy and colleagues (42) was used to score; sampling strategies used, outcome assessment, outcome measurement and statistical reporting and higher overall scores represented higher methodological quality. Each article was independently scored by the first and second reviewers (JA and PKO) in consultation with the research advisors (EM and GM).

Treatment of missing data

Authors of articles with missing data were contacted to provide the missing data points. In cases where the missing data were impossible to obtain, full descriptions are provided about the nature of the missing data and the implications on the results of this systematic review was described.

Assessment of Heterogeneity

Forest plots were used to assess the presence of statistical heterogeneity. We assessed heterogeneity by calculating Chi^2 (thresholdP>0.1) and | statistics (threshold $|^2$>40%). The values of $|^2$ were categorized for heterogeneity as follows: “not important” (0 to 40%), “moderate” (41 to 60%), “substantial” (61 to 80%), and “considerable” (81 to 100%). Where “not important” or “moderate” heterogeneity exists between studies ($|^2 \leq 40\%$), the outcomes were pooled in a meta-analysis and reported using forest plots. Where “substantial” or “considerable” heterogeneity exists between studies ($|^2 > 40\%$), the outcomes were pooled and reported in narrative form using forest plots.

Data synthesis

Data from the included studies were combined using random effects model to account for variability between studies. This is because substantial heterogeneity between-studies was anticipated considering the different study designs included in the systematic review. STATA software (College Station, Texas 77845 USA) was used to perform the meta-analysis. Subgroup analysis was done to assess antimicrobial use patterns in different East African countries.

Sensitivity analysis

Sensitivity analyses was performed to assess if methodological differences in outcome measurement influenced the review results.

Results

Process of selection of included studies

The literature search resulted in 4284 records from the searched 8 databases and the process followed to arrive at the final studies included in the review are summarized in Figure 1. From PubMed database, 224 records were retrieved. Results from other databases searched include: EBSCOhost, 1018 records,

Web of Science, 458 records, Cochrane Library, 1118 records, Scopus, 1452 records, International Clinical Trials Registry Platform (ICTRP), 11 records and from, Mednar, 3 records were retrieved.

After removal of 1224 duplicates, 3060 records were screened by reading the title and abstract of each record, 3010 studies were excluded for failure to meet the inclusion criteria. The excluded studies included 204 Review articles, 905 studies from non-target regions, 1161 non-primary research studies and 70 records excluded for other reasons.

Fifty studies were eligible for a full text screening, of which 26 studies met the inclusion criteria, and they were then subjected to full text review, data extraction and systematic review**. Figure 1** shows the process followed to select eligible articles.

Characteristics of included studies

Eight studies (30.8%) that met the final inclusion criteria were conducted in Ethiopia (43-50). Fifteen studies were from Sudan (51-55), Kenya (56-60) and Tanzania (61-65), each country contributing 5 studies (19.2%)

Two studies (7.7%) were conducted in Eritrea (66-67), whereas 1 (3.9%) study was retrieved from Uganda (68). The included studies reported antimicrobial use among

various population segments including, adult in-patients, adults attending outpatient

department and children admitted in paediatric wards. In terms of study settings, included studies reported results from tertiary level (45-55) and primary level (43-44, 48-67) care settings. Characteristics of the studies included in the review are summarized in **Table 1**.

Patterns of antimicrobial prescriptions in East Africa

The patterns of antimicrobial prescriptions assessed in this systematic review followed the recommended WHO metrics for assessing prescriptions of drugs which include; the proportion of patient encounters with antimicrobials prescriptions, proportion of patient encounters with injectable antimicrobials prescriptions, proportion of patient encounters with antimicrobial prescriptions from the essential medicines list and proportion of encounters with antimicrobial prescriptions in generic names.

Proportions of patient encounters with antimicrobials prescriptions in East African countries

The overall proportion of encounter with antimicrobial reported in the studies was 57% [95%CI: 42%-73%]. Ethiopia had an overall patient encounter with antimicrobials of 63% [95%CI: 50%-76%] followed by Sudan with an overall encounter with antimicrobials of 62% [95%CI: 34%-85%]. Studies from Kenya reported the overall encounter with antimicrobials of 54% [95%CI: 15%- 90%], whereas studies from Tanzania reported an overall patient encounter with antimicrobials of 40% [95%CI: 21%-60%]. Studies from Uganda and Eritrea reported patient encounters with antimicrobials of 79% [95%CI: 76%-82%] and

37% [95%CI: 34%-40%], respectively. **Figure 2** shows the proportion of patient encounters with antimicrobial prescriptions in East African countries.

Proportion of patient encounters with injectable antimicrobials prescriptions in East African countries

Eighteen studies reported patient encounters with injectable antimicrobials. Overall, patient encounter with injectable antimicrobials was 28% CI [16%- 41%] for all the East African states. Heterogeneity among the included studies in the meta-analysis was 99.6%, p-value 0.000. The forest plot in **Figure 3**, shows a summary of studies reporting proportions of patient encounters with injectable antimicrobial agents.

Proportion of patient encounters with antimicrobial prescriptions from the essential medicines list

Eight out of the 26 studies that met the inclusion criteria reported patient encounter with antimicrobial prescriptions from the essential medicines list. Overall, the proportion of prescriptions from the essential medicines list was 90% [95% CI: 81%- 96%]. **Figure 4** summarises the results from studies reporting antimicrobial prescriptions from essential medicines list.

Proportion of encounters with antimicrobial prescriptions in generic names

Eleven studies reported patient encounters with antimicrobial prescriptions in generic names. Overall, prescriptions in generic names were 79% CI [58%-94%]. **Figure 5** provides a summary of proportions of patient encounters with antimicrobial prescriptions in East Africa.

Appropriateness of Antimicrobial prescriptions in East Africa

To assess appropriateness of antimicrobial prescriptions in East Africa, systematic review findings were compared with WHO recommended values. The systematic review findings and the WHO recommended values are summarised in **Table 1**.

Table 1. Comparison of systematic review findings on patterns of antimicrobial use and WHO recommended ideal values

Patterns of drug use (including antimicrobials)	Systematic review finding estimate 95% CI	WHO recommendation [39]
% Encounters with antimicrobials	57% [42%-72%]	20% or less
%Encounter with injection prescriptions	28% [16%-41%]	10% or less
% Generic name prescribing	79% [58%-94%]	100%
%Drugs prescribed from EML	90% [81%-96%]	100%

Discussion

According to available literature, we found the patterns of antimicrobial prescriptions across East Africa countries to be heterogenous. Majority of the studies (30.8%) included in this review originated from Ethiopia, followed by Sudan, Kenya and Tanzania each contributing 19.2% of the included studies. In addition, Ethiopia, Sudan, Kenya and Uganda had patient encounters with antimicrobial prescriptions greater than 50%. The least number of included studies was retrieved from Uganda (3.9%). This review showed that East African countries were not at the same level regarding the research-based evidence of antimicrobial resistance patterns. The results from this review demonstrates how much research is being carried in each country represented in the review regarding antimicrobial use patterns. Considering the global threat posed by antimicrobial resistance, perhaps countries with few researches being carried out on use patterns and antimicrobial resistance should focus more on this research agenda as a matter of public health priority. Studies on antimicrobial use audits and implementation of interventions should be done in order to combat this global emergency that has far reaching health implications on the economy and health of the people in these countries.

Overall, patient encounter with antimicrobial agents in East Africa was 57%. This percentage of antimicrobial encounter is higher than the WHO recommended value of 20% or less (69). Furthermore, none of the countries represented in the systematic review reported lower antimicrobial prescription encounters less than the WHO recommended value of 20% or less. Several countries from East Africa were included with the hope to make meaningful comparison. The overall patient encounter with injectable antimicrobials prescriptions was found to be 28%. This is also a deviation from the ideal WHO recommended value of 10% or less for injectable prescriptions (69). Prescription of antimicrobials by generic names and prescriptions of antimicrobials from the essential medicines list were found to be lower than the recommended value of 100%. Countries in LMIC including East African countries have limited antimicrobial drugs in their essential drugs list. The increased inappropriate antimicrobial use in low-income countries might be attributes to inappropriate drug policies, poor health systems, a few skilled workforces and few diagnostics coupled with few of antimicrobial agents listed in their essential drug lists.

Conclusion

Prescription patterns observed in this review shows significant deviation in the region from what WHO recommends. This suggests existence of inappropriate antimicrobial use in the region leading to antimicrobial resistance. Because of the high-level of heterogeneity among included studies in this systematic review, the reliability of pooled estimate as a measure of poor antimicrobial stewardship in East African countries was considered less reliable. The findings of this study highlight the areas for action to improve antimicrobial prescription practices. As the high level of hetrogeneity observed in the present study made the meta-analysis not credible, further studies need to be conducted to determine the extent of the poor antimicrobial stewardship in East Africa.

Declarations

Ethics approval and consent to participate

Was not necessary for this type of study. Data publicly available.

Consent for publication

Not applicable.

Availability of data

All data generated during review of included studies are reported in this published article and the supplementary information files.

Competing interests

None to declare

Funding

This study was conducted without funding support

Authors' contributions

Research idea conceptualisation: JA. Protocol development: JA, PKO, EM, GM. Duplicate screening, study selection, quality assessment and data collection: PKO and JA. Data analysis and interpretation: JA, PKO. First draft of the manuscript JA. Provision of critical insights and refinement of the manuscript: JA, EM, GM. All listed authors read and approved the final draft of the manuscript.

Acknowledgements

The authors acknowledge Center for Innovative Drug Development and Therapeutic Trials for Africa (CDT-Africa) for the provision of resources for conducting the study and for the human resource support.

Provenance and peer review: Not commissioned; externally peer reviewed

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Figures

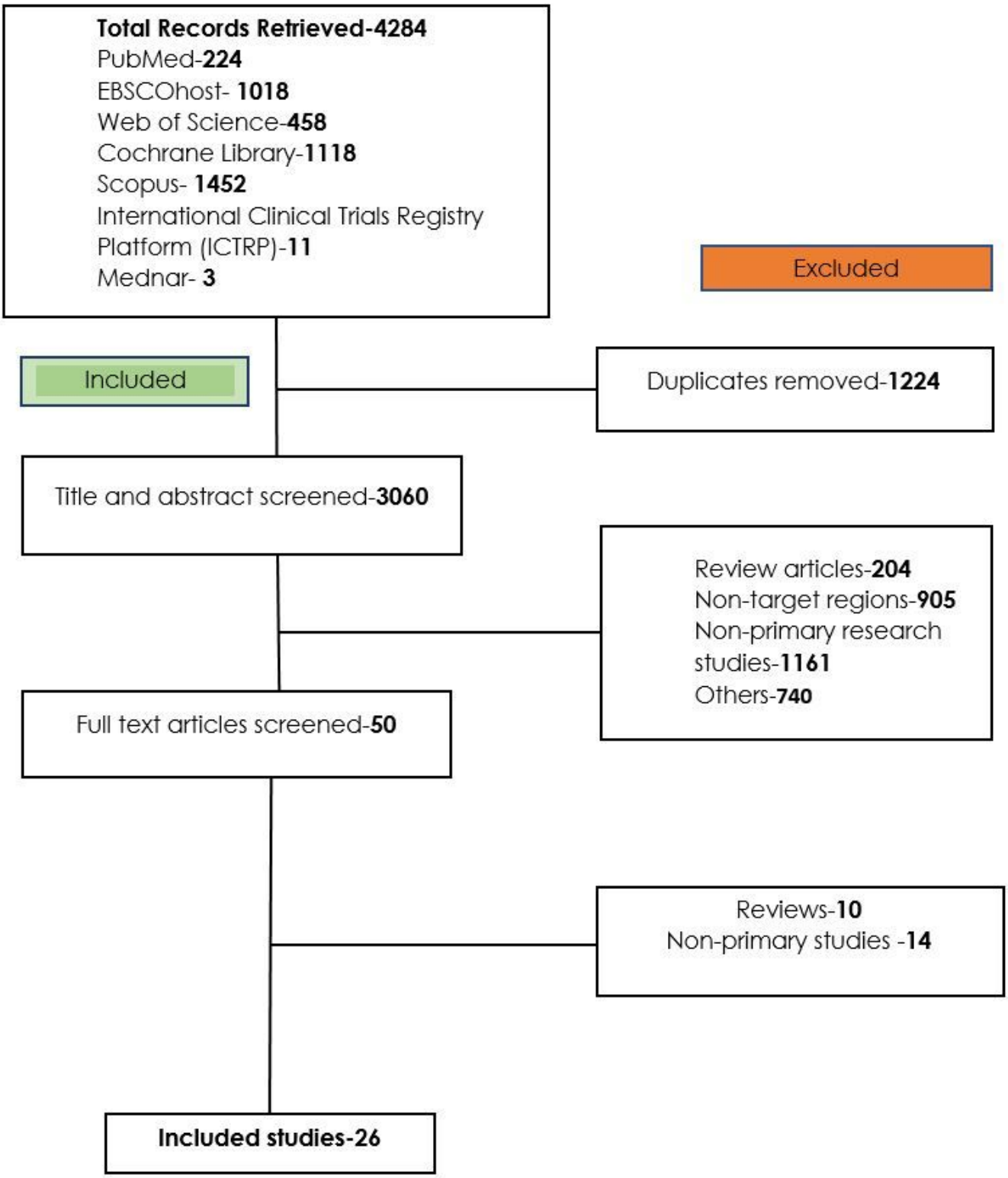

Figure 1

Flow diagram showing selection of eligible articles

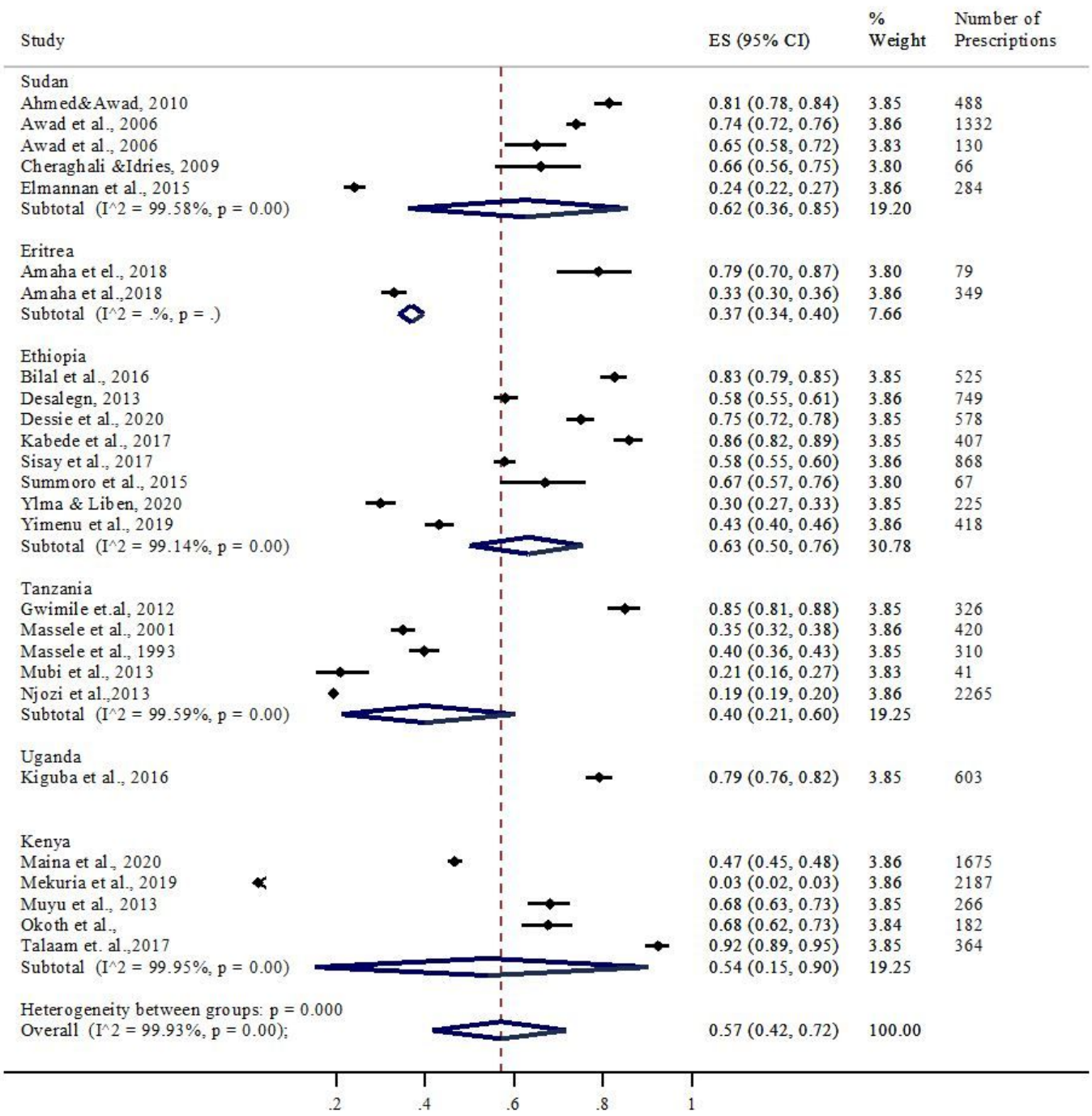

Figure 2

Forest plot showing proportions of patient encounter with antimicrobials in east African countries

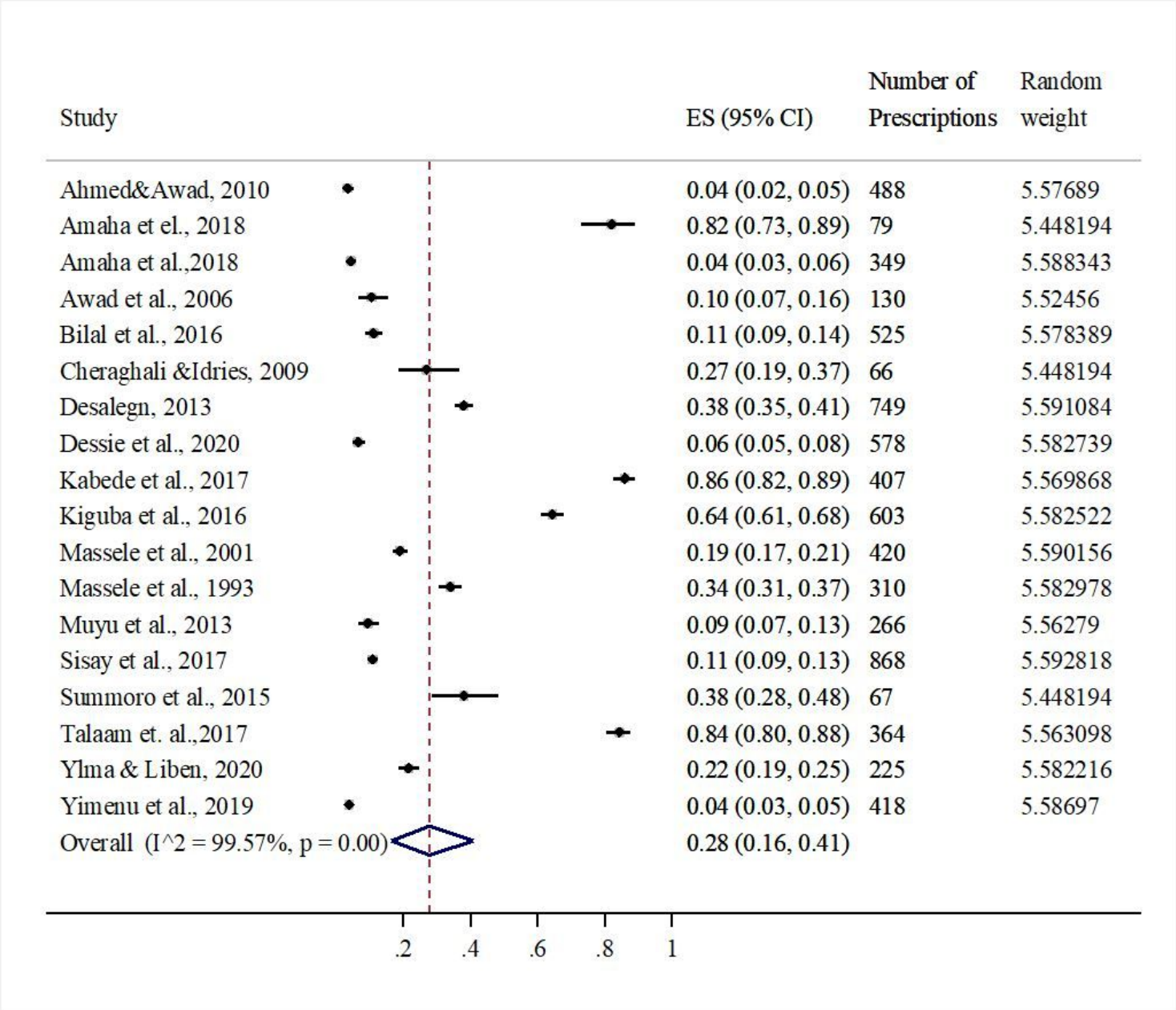

Figure 3

Proportion of encounters with injectable antimicrobials in East Africa

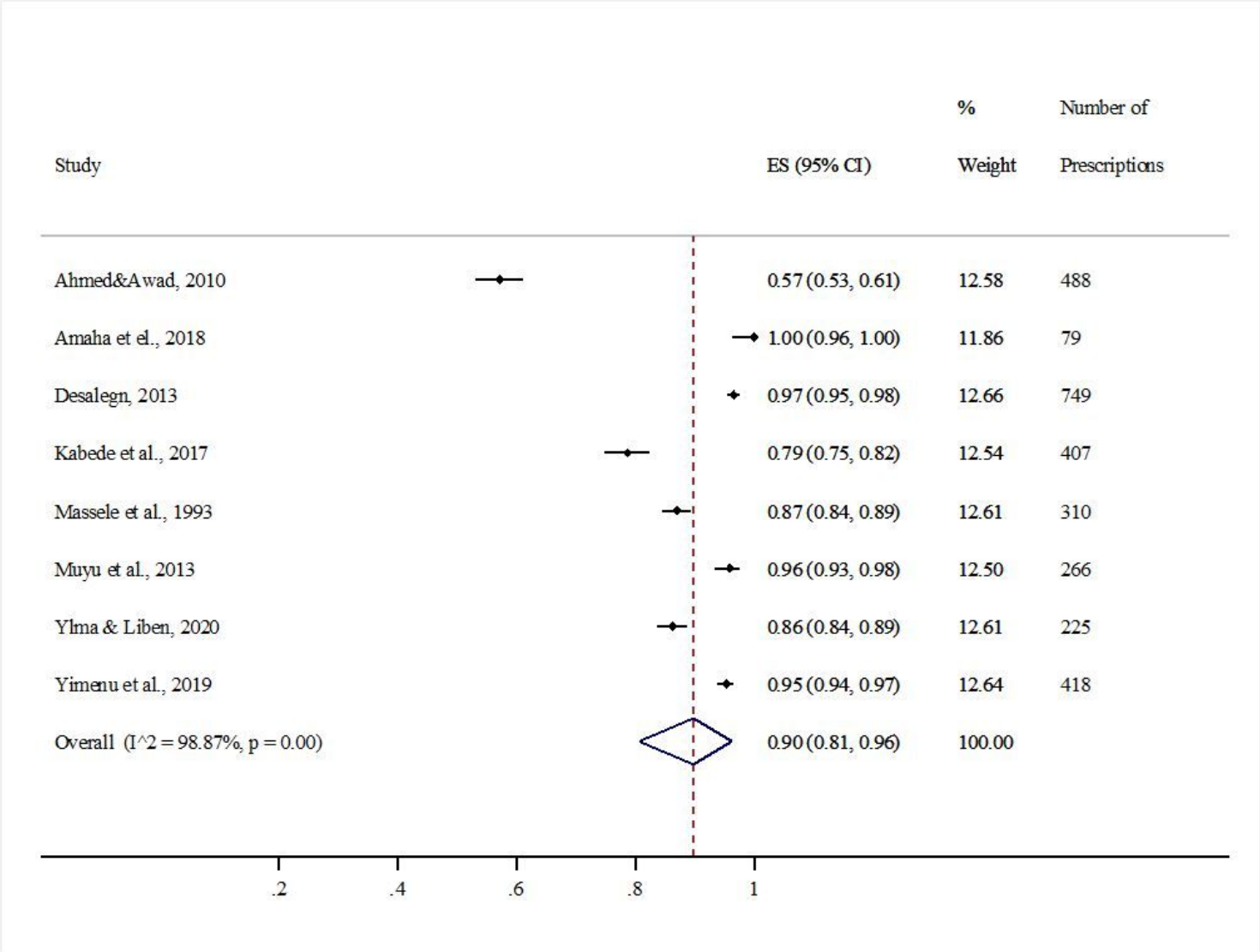

Figure 4

Proportion of encounters with antimicrobial prescriptions from essential medicines list

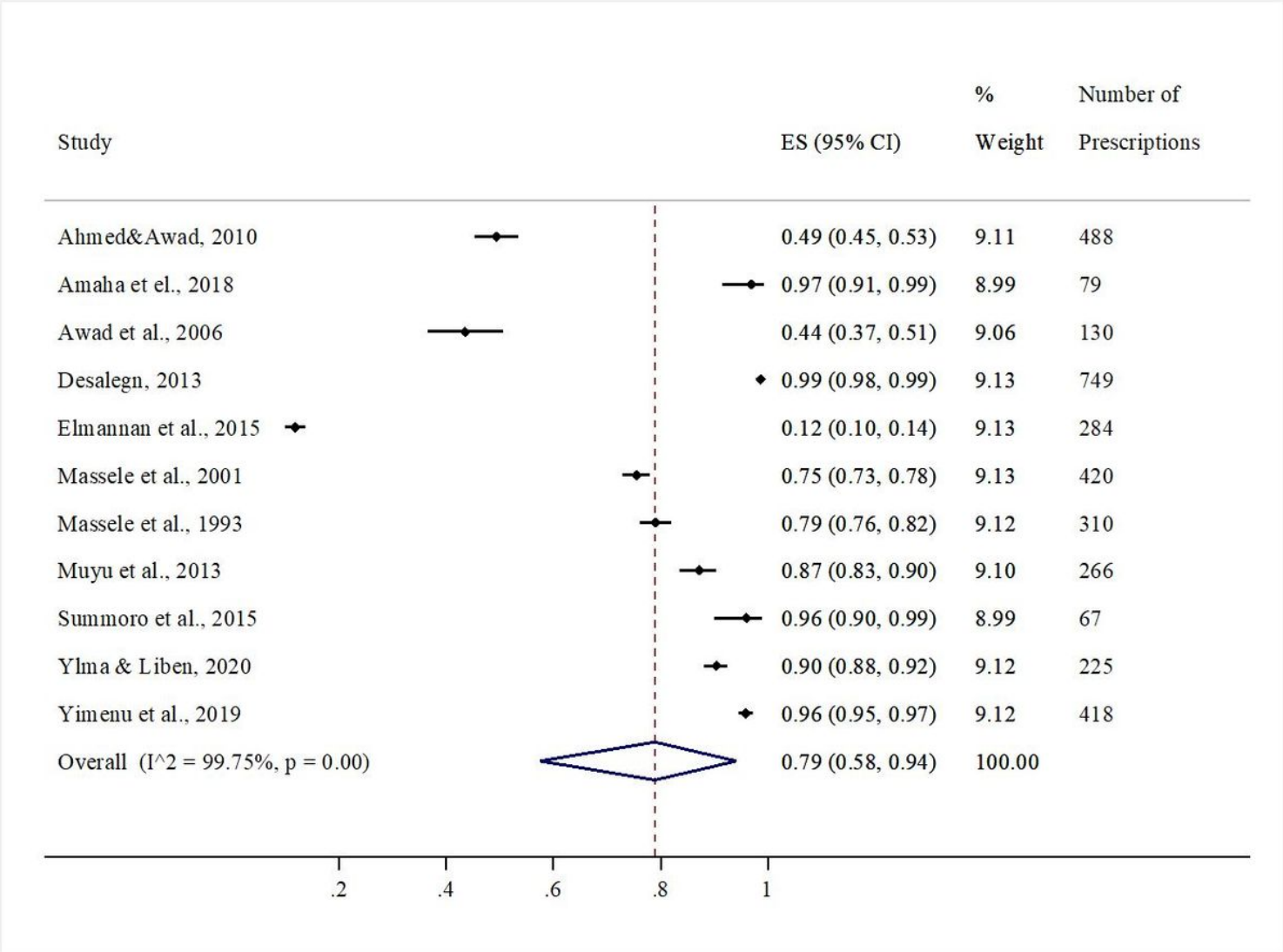

Figure 5

Proportion of encounters with antimicrobial prescriptions in generic names

Supplementary Files

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- Appendices1.docx
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