Prevalence and reasons associated with antibiotics misuse and self-medication among adults in Nigeria: A systematic review and meta-analysis [Protocol]

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Abstract

There is consistent increase in prevalence of antibiotics misuse and self-medication in Nigeria. The exact quality of information available in the public domain is unknown. There is no previous systematic review and meta-analysis that address antibiotics misuse and self-medication in Nigeria. Being the most populous country in Africa, understanding the drivers of antibiotics misuse and self-medication will impact in not only Nigeria, but Africa as a whole. The aim of this systematic review and meta-analysis is therefore to determine the prevalence and factors associated with antibiotics misuse and self-medication among adults in Nigeria. Attempt will be made to find and include published papers on prevalence and reasons associated with antibiotics misuse and self-medication among adults in Nigeria from 2011-2021. Systematic search for the literature will be conducted according to the Preferred Reporting Item for Systematic Reviews and Meta-Analysis (PRISMA) guidelines to identified published studies based on our predetermined inclusion and exclusion criteria in PubMed, EMBASE, PsychINFO, CINAHL and Web of Sciences. Two independent reviewers will assess all identified studies and another set of reviewers will extract data for analysis and evidence synthesis.

Introduction

Antibiotics are the most widely used drugs within the health care industry.[1] Of recent, studies have persistently reported rising trends in antibiotics misuse and self-medication globally.[2] As such, antibiotics misuse and self-medication has become one of the most serious public health challenges worldwide and arose significant interests among public health researchers.[3] Only about 20% of all antibiotics used are prescribed within the healthcare industry.[4] While about

80%-90% of all antibiotics are used in the community, majority of those antibiotics are used without prescription by trained health personnel.[5] Developing countries account for greater proportion of antibiotics misuse and self-medication.[6] Studies have reported higher prevalence of antibiotics misuse and self-medication in developing countries compared with developed countries.[7] Nigeria is the most populous country in Africa and has one of the highest prevalence of antibiotics misuse and self-medication compared with other African countries.[8] In addition, studies within Nigeria have reported poor knowledge about antibiotics use, poor understanding of effective use of antibiotics and poor antibiotics practices.[9,10] Antibiotics misuse and self-medication shows linear relationships with medical, social and economic consequences.[11] Resistance to common and cheaper antibiotics due to misuse and self-medication has been widely reported especially in otherwise resource limited African countries.[12] Delay in presentation for care due to antibiotics misuse and self-medication prolongs hospital stay and increases the cost of care and adds to financial strain on families in the African countries.[13]

Antibiotic misuse and self-medication also lead to adverse drug effects with serious negative outcomes as well as exposes higher generations of antibiotics to abuse and resistance.[14] The cumulative effects are increased morbidity and mortality as a result of antibiotics resistance and treatment failures for mostly infectious diseases.[15] Many factors have been reported as causes and associations of antibiotics misuse and self-medication. Significantly, studies have reported socioeconomic status,[16] peer influences, age,[17] gender,[18] literacy level, occupation, previous experiences, government policies among factors contributing to antibiotics misuse and self-medication. However, review of literature is widely used to provide better understanding of what is known and what is not known from the available knowledge in public domain. Systematic reviews play significant role in public policy development, clinical and in public health interventions. Unlike traditional narrative reviews, which lacks scientific rigors, systematic reviews methods which now increasingly gains popularity in medical research have "replicable, scientific and transparent process that aims to minimize bias using exhaustive literature search by providing the reviewer's audit trail of decisions, procedures and conclusions",[19] A recent systematic review investigated prevalence and reasons of antibiotics self-medication in Africa.[20]

Although this study provides significant insight on the causes of antibiotics self-medication in Africa, the study concluded among its limitations was included studies were lopsided with more than 80% of the studies coming from only 2 regions of Africa and only 3 countries provided 50% of the included studies.[20] This underscores the need for a robust systematic review to understand prevalence and causes of antibiotics misuse and self-medication in Nigeria which accounts for 20% population of Africa.[21] Contextualized evidence will enable identification of enabling factors for antibiotic misuse and self-medication, understanding research gaps, identify future research need and solutions. No previous

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review of the literature to the best of our knowledge has attempted to provide a systematic analysis of published papers on antibiotics misuse and self-medication confined to Nigeria. Beyond antibiotics resistance, Nigeria has the highest burden of infectious diseases in Africa, which can serve as trigger for antibiotics misuse and self-medication. This study will provide explicit objective evidence on what is known and what is not known about antibiotics misuse and self-medication in Nigeria by analyzing data from published studies that meet our sets of scientifically sound inclusion criteria. Findings from this study will have both therapeutic and policy implications at national, regional and continent levels.

The aim of this systematic review is to identify all published studies on antibiotics misuse and self-medication in Nigeria, to assess the qualities of the studies, extract data on prevalence, causes and factors associated with antibiotics misuse and self-medication in Nigeria. We will define and operationalize what constitutes antibiotics misuse and self-medication in the context of this study. We will then determine the specific prevalence of antibiotics misuse and self-medication, identify types of antibiotics for misuse and self-medication and the reasons for antibiotics misuse and self-medication. We will also identify sources of antibiotics misuse and self-medication.

Materials and Methods

This protocol describes the flow and approach of a systematic review and meta-analysis using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). The review combines both the Cochrane Collaborations guidelines for the conduct of systematic reviews and meta-analyses as well as the University of York's Center for Dissemination and Reviews guidelines (CRD). Being a systematic review that will use primary studies, an ethical approval is not deemed required for the study.

Inclusion and exclusion criteria

For a study to be eligible for inclusion in this study, it must have been conducted in Nigeria, it must be an observational (cross-sectional) study and subjects studied must be adults aged 18-65 years of age. All non-observational studies will be excluded so also when subjects are caregivers, a study conducted outside Nigeria and those thar uses non-human subjects. Editorial communications such as letters, opinions and comments will also be excluded.

Information sources

To identify all studies that satisfied our inclusion criteria, multiple databases relevant to our research questions will be searched. Multiple databases search has been shown to provide better outputs as compared with a single database search in systematic reviews.[22] In addition, references of identified studies will be assessed to identify other potential studies for inclusion. Multiple databases search combined with reference checking increases inclusion rates of systematic reviews.[23] The following databases will be searched from 2010-2021: MEDLINE(PubMed), EMBASE, PsycINFO, CINAHL, Web of Science.

Other potential sources that will be searched include conferences proceedings and abstracts books

Search strategy

In order to broaden the search strategy, both keywords and index/subject terms will be used. The Boolean operator "OR" will be used to broaden chances of retrieving more publications rather than "AND", that will enable greater sensitivity but at the expense of precision which is less favored to enable inclusion of more publications. To increase the precision of our search strategy, we will apply search filters with respect to the following fields: i) article/publication type (primary research articles in academic journal type of publication); ii) publication date (from 2010-2021); iii) language (to include only studies published in English language); iv) subject; iv) ages (participant included must be adults).

Search for "grey literature": we will attempt to search for all unpublished data on antibiotics misuse and self-medication in Nigeria by searching of the following sources: i) dissertations/thesis; ii) conference abstracts, presentations, proceedings; iii) government reports; iv) newsletters/bulletins.

We will limit our search terms to titles and abstracts only. We will search google and google scholar for grey literature, Scopus, Web of Sciences, SciFinder, ProQuest Dissertation & Theses, Ethos, NGOs and IGOs websites, OpenGrey and OpenDOAR websites.

Documenting our search strategies

To allow for reproducibility, we will document the following steps/actions taken during our systematic review search: i) databases searched; ii) database time covered; iii) search strategies applied; iv) date each search was conducted; v) number of results for each search strategy; vi) number of results after deduplicating.

Search terms

The following keywords search terms will be used as key words and subsequently with MeSH synonyms and respective databases vocabularies. #Antibiotics, #Antimicrobials, #Anti-bacterial agents, #Self-medication, #Self-prescription, #Misuse, #Non prescription, #Non-prescription,

#Over-the-counter, #Drugs, #Drug-misuse, #Drug misuse, #Inappropriate-use, #Antibacterial agents, #Self medication, #Self prescription, #Misuse, #Inappropriate use, #Factors, #Causes,

#Etiology, #Determinants, #Nigeria, #Northern Nigeria, #Northern-Nigeria, #South-West Nige- ria, #South-South Nigeria, #South-East Nigeria.

Selection process

Two reviewers will independently assess titles and abstracts of our search results for possible inclusion or exclusion based on our pre-established set of criteria. Where titles and or abstracts are adjudged for possible inclusion, the full texts of the articles will be retrieved for quality assessments prior to data extraction by a different set of two independent reviewers. Where are there are disagreements between two independent reviewers, it will be resolved by consensus. Where a consensus was not reached, a third reviewer will be used as tie-breaker as it is shown in methods of systematic reviews of prevalence studies.[24]

Data collection process

Two Reviewers will independently extract data from included studies using a Data Abstraction Form (DAF) to be developed priori. The reviewers will extract data on: corresponding author, year of publication, country, state, type of participants, study settings, sample size, sampling design, number of participants/response rate, prevalence period, prevalence rate, types of antibiotics being misused and self-medicated, reasons for self-medication and sources of antibiotics for self-medication.

Data items

Outcomes for which data would be sought include: i) pooled antibiotics misuse and self-medication prevalence (pooled prevalence of antibiotics misuse and self-medication across all included studies); ii) rates of types of antibiotics misuse and self-medication (pooled rates of specific types of antibiotics being misused and self-medicated across all included studies); iii) rates of reasons for antibiotics misuse and self-medication (pooled rates of specific reasons for antibiotics misuse and self-medication across all included studies); iv) Rates of

sources of antibiotics for self-medication (pooled rates of sources of antibiotics for misuse and self-medication across all included studies). Other variables for which data will be sort include age of participants, sex, place of residence. Where there is missing information, attempts will be made to contact the authors using the address of corresponding authors.

Study risk of bias assessment

All included studies will be assessed for presence of bias. We will use the checklist for assessment of bias in systematic review of prevalence studies developed by Damian Hoy in

2012.[25] The Hoy checklist is the most widely used tool for assessment of bias in systematic reviews of prevalence studies. The checklist has 10 components divided into two sections. Four components (items 1-4) assess external validity (domains are selection and non-response bias) while 6 components assess internal validity (items 5 to 9 assess the domain of measurement bias, and item 10 assesses bias related to the analysis). Two reviewers will work independently to assess all included studies for existence of bias.

Effect measures

The primary outcome will be occurrence of event (antibiotics misuse and self-medication). The effect measure will be prevalence (proportion of the event within the sample population). Other outcomes to be measured will be sources of antibiotics and reasons for antibiotics misuse.

Data synthesis methods

The table of characteristics of included studies and the quality assessment will be used to assess whether a study is eligible for inclusion or not. Quantitative variables will be reported using mean and standard deviation and variance, while qualitative discreet variables will be reported using median and inter-quartile range. Where there is missing summary statistics attempt will be made to contact the authors for information or raw data to enable synthesis of the summary statistics. Non-normally distributed variables will be transformed by either Freeman-Turkey transformation[26] or by Logit transformation methods.[27] Results of meta-analysis will be displayed in forest plot. Graphs will be used to display publication bias assessment and heterogeneity. Tables will be used to summarize frequencies and percentages Results will be synthesized using the followings methods: i) narrative summary: this will include summary of types of antibiotics misuse, sources and reasons of antibiotics misuse; ii) tables: this will include frequencies and percentages of types of antibiotics misuse, sources and reasons of antibiotics misuse; iii) graphs: this will include bar graphs and pie-charts to summarize types of antibiotics misuse, sources and reasons of antibiotics misuse; iv) meta-analysis: this will include weighted effects sizes of individual studies as well as pooled summary of effect size combined in a meta-analysis. Also, sub-group analysis based on certain characteristics such as study settings, gender and age will be carried out.

Heterogeneity

We will explore presence of heterogeneity to enable us to know whether there are significant variations in the characteristics of our included studies. Clinical heterogeneity will be assessed by examining the table of included studies to assess participants characteristics, study settings, samples sizes and effects sizes. Statistical heterogeneity will be assessed by first examining forest plot of the meta-analysis using "eye-bowling" approach. Presence of overlaps in confidence intervals margins of included studies will suggest lack of heterogeneity. Quantitative measurements of heterogeneity will be done by using chi-squared test and I2 tests. A p-value greater than 0.05 signifies lack of heterogeneity. I2 test of 25% will mean low heterogeneity, 50% will mean moderate heterogeneity and 75% will mean high heterogeneity. If there is significant heterogeneity, we will use subgroup analysis (such as subset of studies or subset of participants) and meta- regression to explore sources of heterogeneity across the included studies. Also, we will use fixed effect model for our meta-analysis if significant heterogeneity exists

Sensitivity analyses

We will assess the robustness of our synthesized results using sensitivity analyses. This will enable us to assess our decision on included studies and on the quality of the included studies. We will carry out sensitivity assessment using the following approaches: i) forest plot by precision; ii) egger's regression; iii) finding/removing outliers; iv) leave-one-out.

Reporting bias

We will assess presence of bias in reporting results of our included studies using the following methods: i) examination of funnel plot appearance: absence of asymmetry of the funnel plot by presence of outliers will indicate presence of bias in the reporting of result of our included studies; ii) Egger's regression test: this will test Y-Intercepts with p-value. If the p-value is greater than 0.05 it shows lack of reporting bias; iii) standardized residual histogram: this test will also show a symmetry of included studies when there is no reporting bias; iv) galbraith plot; v) normal quintile plot; vi) Rosenthal fail safe test; vii) Glasser and Olkin fail safe test; viii) Trim and Fill test.

Certainty (confidence) assessment

We will assess the methodological quality of our included studies using the Newcastle- Ottawa Scale (NOS) recommended by the Agency for Healthcare Research and Quality (AHRQ).[28] This scale uses a star system to assess the quality of a study in three domains: selection of study groups; comparability of groups; and ascertainment of outcomes.[29]

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