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Ahmed, I, King, R, Akter, S et al. (2 more authors) (2023) Determinants of antibiotic self-medication: A systematic review and meta-analysis. Research in Social and Administrative Pharmacy, 19 (7). pp. 1007-1017. ISSN 1551-7411

https://doi.org/10.1016/j.sapharm.2023.03.009

Determinants of antibiotic self-medication: A systematic review and meta-analysis

Abstract

Background

Decreasing the prevalence of antibiotic self-medication among the public requires proper understanding of the risk factors involved. However, the determinants of antibiotic self-medication are not well defined.

Objectives

To identify patient and health system-related determinants of antibiotic self-medication among the public.

Methods

A systematic review of quantitative observational studies and qualitative studies was undertaken. PubMed, Embase, and Web of Science were searched to identify studies on determinants of antibiotic self-medication. The data were analyzed using Meta-analysis, descriptive analysis, and thematic analysis.

Results

Sixty-eight studies were included in the review. From meta-analyses, male sex (pooled odds ratios [POR]: 1.52, 95% confidence intervals [CI]: 1.19—1.75), lack of satisfaction with healthcare services/physicians (POR: 3.53, 95% CI: 2.26—4.75) were associated with antibiotic self-medication. In subgroup analysis, lower age was directly associated with self-medication in high-income countries (POR: 1.61, 95% CI: 1.10—2.36). In low- and middle-income countries, people with greater knowledge of antibiotics were less likely to self-medicate (POR: 0.2, 95% CI: 0.08—0.47). Patient-related determinants identified from descriptive and qualitative studies included previous experience with antibiotics and similar symptoms, perceived low severity of disease, intention to save time and get better quickly, cultural beliefs about curative power of antibiotics, advice from family/friends, and having home stock of antibiotics. Health system-related determinants included high cost of consulting physicians and low cost of self-medication, lack of access to physician/medical care, lack of trust/confidence in physicians, greater trust in pharmacists, long distance of physicians/healthcare facilities, long waiting time at healthcare facilities, easy access to antibiotics from pharmacies, and convenience associated with self-medication.

Conclusions

Patient and health system-related determinants are associated with antibiotic self-medication. Interventions to decrease antibiotic self-medication should incorporate community programs along with appropriate policies and healthcare reforms targeting these determinants with specific attention to population at high risk of self-medication.

Keywords: Antibiotics; Self-medication; Determinants; Systematic review

Introduction

Antibiotic resistance is considered to be one of the biggest threats to global health and food security by the World Health Organization (WHO).[1] Globally, around 1.27 million people died from antibiotic resistance in 2019,[2] and by 2050, it is estimated that more than 10 million people will die from antimicrobial resistance every year.[3] The problem of antibiotic resistance is further exacerbated by the relatively slow development of new antibiotics which is failing to keep pace with the increasing rates of antibiotic resistance development. Further, antibiotics in clinical development are insufficient to address the resistance among the WHO priority pathogens.[4]

One of the many factors responsible for the spread of antibiotic resistance is misuse of antibiotics which occurs through unnecessary prescriptions, self-medication, and non-adherence.[5] This study primarily concerns self-medication with antibiotics. The WHO defines self-medication as "the use of medicinal products by the consumer to treat self-recognized disorders or symptoms, or the intermittent or continued use of a medication prescribed by a physician for chronic or recurring diseases or symptoms".[6] In other words, self-medication can be defined as taking medications without a prescription, rather by self-initiative, or by the advice of family/friends and retail pharmacists. The prevalence of antibiotic self-medication varies across countries. The prevalence is estimated to be 33.4% in low- and middle-income countries (LMICs),[7] 19-82% in the Middle East,[8] and 0.1-21% in Europe.[9] Antibiotic self-medication may lead to the use of antibiotics for unrelated symptoms,[10-13] inappropriate dose and duration of therapy,[7, 12] treatment failures and safety issues,[14] and development of antibiotic resistance.[14]

Factors associated with antibiotic self-medication use are complex and may vary across regions or countries. Previous systematic reviews have explored various determinants of antibiotic/antimicrobial

self-medication.[7, 15-18] However, there are several gaps in the literature: 1) the impact of demographic characteristics and health systems on antibiotic self-medication among the public has not been well-defined; 2) the association between knowledge of antibiotics and antibiotic self-medication is not clearly known; 3) the existing studies have covered specific regions or countries of certain income levels, or studied antibiotic use in general (not specific to self-medication), or were not specific to the general public, 4) no meta-analysis has yet been conducted to identify the determinants of antibiotic self-medication among the public. This study was conducted to address these gaps.

This study has two research questions: 1) what are the patient-related determinants of antibiotic self-medication; 2) what are the health system-related determinants of antibiotic self-medication. Patient-related determinants will be related to demographic characteristics, knowledge, beliefs, and awareness regarding antibiotics, and health seeking behavior of patients. Health system-related determinants will be related to quality, access, and cost of health services and health policies.

Methods

The systematic review has been reported following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement.[19] The protocol for this study is registered in PROSPERO (CRD42020190936).[20]

Search strategy

Literature search was conducted in PubMed, Embase, and Web of Science databases to identify studies published until June 2022. The detailed search strategy is in supplementary file 1. Studies conducted on humans and published in the English language were searched. No restriction was applied on the year of publication. Studies from all countries were included.

Eligibility criteria

Selection of studies

Studies were included if they 1) were quantitative (cross-sectional or cohort studies) and qualitative studies, 2) studied patient-related determinants of antibiotic self-medication, 3) studied determinants related to health system and policy that serves as facilitators of self-medication with antibiotics, and 4) studied self-medication specifically with antibiotics. Studies were excluded if they 1) were review articles, study protocols, abstract-only papers, case reports, and case series, 2) studied the effects of interventions (i.e., public campaigns) on self-medication behavior of the public and 3) studied self-medication with antiviral, antifungal, or anti-tuberculosis agents.

Participants

Studies were included if 1) the participants were the general public and 2) the users of self-medication were compared with users of antibiotics with prescriptions. Studies were excluded if 1) the participants were specific groups that do not represent the general population (students, healthcare providers, parents, children, adolescents, or older adults) and 2) the comparison group consisted of nonusers of antibiotics.

Outcome measure

Studies were included if the outcome of interest was self-medication with antibiotics. Self-medication was defined as taking antibiotics without a prescription, rather by self-initiative, or by the advice of family/friends, or retail pharmacists. Based on our literature review, this is the most commonly used definition of self-medication, and studies had to use the same definition of self-medication for inclusion in this review. In contrast, studies that discussed antibiotic use only with prescriptions were excluded.

Data extraction

The articles identified by the literature search were screened to select studies that met the inclusion criteria. The title and abstracts of the studies were first screened. Studies included in this step were then subjected to full-text review. The following data were extracted from each study: publication year, name and characteristics of the country where the study was conducted, study design (sample size, quantitative vs qualitative, cross-sectional vs other types), study setting, quantitative and qualitative data regarding the various patient and health system-related determinants of self-medication. For data extraction, studies were grouped into three categories: quantitative studies reporting odds ratios of the factors of self-medication (odds ratios were extracted from these studies), quantitative studies reporting frequency of various reasons for self-medication (frequencies were extracted from these studies), and qualitative studies (themes were extracted from these studies). Study selection and data extraction were performed by two reviewers (IA and SA).

Data Synthesis

Similar to data extraction, three different types of data synthesis methods were used for the three categories of studies. For quantitative studies reporting odds ratios of the factors of self-medication, meta-

131 analysis was performed. Studies reporting only frequency of various reasons for self-medication were
132 analyzed descriptively. For qualitative studies, thematic analysis was undertaken. For each type of
133 analysis, studies were grouped into two subgroups based on whether the studies were performed in high-
134 income countries (HICs) or LMICs. Countries were classified based on the World Bank country
135 classifications by income level.

136

137 **Meta-analysis**

138 First, crude odds ratios and 95% confidence intervals (CI) were obtained for the predictor variables
139 (outcome: self-medication). Odds ratios (and 95% CIs) for each determinant obtained from different
140 studies were then pooled using a random-effects model. The overall effect size (pooled odds ratios) and
141 the effect sizes of subgroup analysis based on the income level of countries (HICs and LMICs) were
142 calculated. For nominal categorical variables with multiple groups, groups were combined to create a
143 dichotomous variable to enable a single pair-wise comparison (e.g., employment).[21] Ordinal categorical
144 variables with multiple groups were defined as lower vs higher levels taking the two terminal categories
145 to create a dichotomous variable to enable a single pair-wise comparison (e.g., education, age, income,
146 knowledge); a similar approach was taken by another study published in 2018.[22] The heterogeneity of
147 the meta-analysis was calculated and reported using the I^2 statistic. I^2 describes the percentage of total
148 variation across studies that is due to heterogeneity rather than chance.[23] Generally, the following cut-off
149 is used for determining heterogeneity using I^2: less than 40% is low, 30-60% is moderate, 50-90% is
150 substantial, and 75-100% is considerable heterogeneity [24]. In our study, although all of the variables were
151 included in the meta-analysis regardless of I^2 value, those with considerable heterogeneity (I^2 >75%)
152 should be interpreted with caution. The meta-analysis was performed using OpenMeta-Analyst
153 developed by Brown University.

154

Descriptive Analysis

Studies reporting the frequency of various reasons for self-medication were analyzed descriptively. Due to high heterogeneity among the frequencies across different studies, they were not pooled. Instead, the ranges of the frequencies for each determinant were reported (Table 3). Analysis was done separately for HICs and LMICs subgroups. Determinants were included if they were reported by at least two studies in each subgroup.

Thematic Analysis

Determinants of antibiotic self-medication were identified from qualitative studies using thematic analysis.[25, 26] Moreover, explanatory factors were identified, which begin to explore why members of the public self-medicate with antibiotics. Studies were analyzed to identify a-priori themes, which had been identified within the descriptive analysis (described above), and themes emerging from the qualitative data. Analysis was done separately for HICs and LMICs subgroups. NVivo 12 was used to support the analysis. The results of the thematic analysis are reported in Table 4.

Risk of bias (quality) assessment

To assess the quality of the quantitative observational studies, the NIH quality assessment tool for observational cohort and cross-sectional studies was used.[27] Each study was rated 'good', 'fair', or 'poor'. For the assessment of qualitative and mixed-method studies, the 16-item quality assessment tool for studies with diverse design (QATSDD) was used.[28] Studies were not excluded based on their ratings.

Results

From the database search, 3547 unique studies were identified. After screening for titles and abstracts, 3351 studies were excluded. After full-text review of 200 studies, 68 studies were finally included in the review.[11-13, 29-93] Studies were excluded for the following reasons: did not study the determinants of antibiotic self-medication (n=51), wrong outcome/not pertinent to antibiotic self-medication (n=33), incomplete, inconsistent, or incompatible data (n=22), wrong comparison group (n=11), did not study the general public (n=6), full texts were not available (n=5), and wrong study design (n=4). The PRISMA flow diagram delineating the study selection process is presented in Figure 1.

Study Characteristics

The majority of the studies were conducted in the Middle East & North Africa (27.9%), followed by Sub-Saharan Africa (25%) and South Asia (19.1%). Around 78% of the studies were performed in LMICs. Fifty-two studies were quantitative,11 were qualitative, and five were mixed-method studies. The studies were conducted in various types of settings including households, healthcare facilities, pharmacies, communities, etc. All of the studies relied on self-reported measures of self-medication, and the recall period ranged from 2 weeks to 2 years. Detailed characteristics of the studies are provided in Table 1 and supplementary file 1.

Risk of Bias within studies

Of the 52 quantitative studies, 26 were rated as ‘good’ quality, 20 as ‘fair’ quality, and six as ‘poor’ quality. Most of the qualitative and mixed method studies received a score between 60% and 80% (Supplementary file 1).

Patient-related determinants of antibiotic self-medication

Results from meta-analysis

The results of the meta-analyses are presented in Table 2, and the forest plots are in supplementary file 1. Males were more likely than females to self-medicate (pooled Odds Ratios [POR]: 1.52, 95% CI: 1.19—1.75). For age, the overall estimate was not significant (POR: 0.98, 95% CI: 0.73—1.31), but subgroup analysis revealed that in HICs lower age was directly associated with self-medication (POR: 1.61, 95% CI: 1.10—2.36). Factors not associated with self-medication were education (POR: 0.86, 95% CI: 0.55—1.33) and residence (POR: 0.94, 95% CI: 0.46—1.95). Some meta-analyses could only be performed for LMICs since there were not enough studies from HICs. Higher knowledge of antibiotics was inversely associated with self-medication (POR: 0.2, 95% CI: 0.08—0.47) in LMICs. Employment (POR: 1.49, 95% CI: 0.86—2.58) was not associated with antibiotic self-medication in LMICs.

Results from descriptive and qualitative analysis

The determinants identified from the descriptive and qualitative analysis are presented in Tables 3 and 4, respectively. While most of the following determinants were identified from both descriptive and qualitative studies, the qualitative studies provided more information and helped explain the findings. In HICs and LMICs, one of the most reported patient-related determinants of self-medication was previous experience with antibiotics and similar symptoms (6-80.5% in LMICs, 20-69.2% in HICs). In the qualitative studies, participants said that if the symptoms they experience resemble any past symptom for which they were treated, instead of visiting a physician, they buy the same antibiotics that were prescribed before. Having leftovers from past use or stock of antibiotics at home was identified as a factor of self-

medication in qualitative studies. Some participants used leftovers from previous prescriptions while others always maintained stock of antibiotics at home and used them whenever needed. Another determinant identified from the qualitative studies was the cultural beliefs about the curative power of antibiotics. Some believed antibiotics can cure all types of diseases and that antibiotics work very quickly. Such beliefs are deep-rooted in some communities and passed through generations. The other reasons for self-medication were perceived low severity of disease (7-82% in LMICs, 36-38.9% in HICs), intention to save time (9.3-55.7% in LMICs, 10.5-22.3% in HICs), and advice from family and friends (7.7-28.2% in LMICs, 16.1-16.2% in HICs).

In LMICs, intention to get better quickly was found to be a factor of self-medication by 11.9-33.9% of the participants. One participant said whenever he has sore throat, he goes to the pharmacy and asks for antibiotics because he believes taking antibiotics will help him get better fast.

Health system-related determinants of antibiotic self-medication

Results from meta-analysis

The only health system-related determinant of antibiotic self-medication identified from meta-analysis was lack of satisfaction with healthcare services or physicians. Two studies from LMICs and HICs reported this determinant, those who were not satisfied with the healthcare services/physicians had 3.53 times higher odds of self-medicating compared to those who were satisfied (95% CI: 2.26—4.75).

Results from descriptive and qualitative analysis

In HICs and LMICs, high cost of consulting physicians and low cost of self-medication was one of the most reported reasons for self-medication (2.5-88% in LMICs, 5.8-19% in HICs). In the qualitative studies, many participants found it very expensive to visit physicians, and for minor or familiar symptoms they deemed such expense unwarranted. As an alternative, participants preferred directly going to the pharmacy which is a cheaper way to get an antibiotic. Lack of access to physician /medical care was reported to be a reason for self-medication by 1.4-55.5% of participants in LMICs and 6.4-29.3% of participants in HICs. Long distance of healthcare facilities/ physicians along with a lack of transportation restricted access to healthcare for many. In those circumstances, people preferred to buy antibiotics from pharmacies since pharmacies are usually closer to home and easily accessible. The third factor was long waiting time at healthcare facilities. In the qualitative studies, some participants expressed frustration towards the long waiting hours in hospitals or clinics and sought quicker alternatives such as going to the pharmacy or using leftover antibiotics. The other reason for self-medication was easy access to antibiotics over the counter (OTC) from pharmacies. Studies found that although there are laws against the sale of antibiotics without prescriptions, such laws are not strictly enforced, and antibiotics are easily obtainable OTC in many countries. Lack of trust and confidence in physicians/ healthcare services was a very commonly reported reason for self-medication. Some participants in the qualitative studies said that the doctors often contradict each other, write prescriptions by hit and trials, and often start writing prescriptions before listening to the patients' conditions properly. On the contrary, participants said they had more trust in pharmacists and therefore would visit the pharmacists first if they had any symptoms.

Determinants with conflicting evidence

For two determinants, conflicting findings were reported from meta-analysis vs the descriptive/qualitative analysis. For health insurance, meta-analysis showed no association (POR: 0.63, 95% CI: 0.4- 1.0).

However, descriptive studies identified lack of health insurance as a determinant of self-medication. Similarly, although participants' income was not a significant predictor in meta-analysis (POR: 0.97, 95% CI: 0.73—1.27), poverty was mentioned as a reason for self-medication in descriptive studies.

Discussion

In this study, the patient-related and health system-related determinants of antibiotic self-medication among the general population were identified (Figure 2). Patient-related factors directly associated with self-medication are male sex, lower age (only HICs), lower knowledge of antibiotics (only LMICs), cultural beliefs about the curative power of antibiotics, previous experience with antibiotics and similar symptoms, perceived low severity of disease, intention to save time, intention to get better quickly (only LMICs), advise from family/friends, and having home stock of antibiotics or left-overs. Health system-related determinants of antibiotic self-medication are lack of satisfaction with physicians/healthcare services, high cost of consulting physicians and low cost of self-medication, lack of access to physicians /medical care, lack of trust/confidence in physicians, greater trust in pharmacists (only LMICs), long distance of physicians or healthcare facilities, long waiting time at healthcare facilities, easy access to antibiotics from pharmacies, and convenience associated with self-medication (only LMICs).

Although knowledge of antibiotics (based on knowledge score) was associated with self-medication in LMICs, the evidence should be considered weak because of very high heterogeneity (I^2=85%). Further, there were not enough studies to conduct meta-analysis to identify any association between knowledge of antibiotics in specific domains (knowledge regarding action and indications, adverse effects and dangers, antibiotic resistance, or appropriate use) and self-medication. Previous studies reported

conflicting evidence on the association between knowledge of antibiotics and antibiotic self-medication.[16-18] Therefore, much remains unknown about the impact of knowledge on antibiotic self-medication. This has significant implications because most public campaigns on rational antibiotic use are designed and implemented based on the Knowledge-Attitude-Behavior (KAB) model where the interventions primarily focus on disseminating information to improve the knowledge of the public, and subsequent changes in attitude and behavior are expected to follow naturally. However, the effectiveness of interventions based on this KAB approach in lowering self-medication is not well known. Studies measuring the prevalence of self-medication before and after running public campaigns reported that campaigns did not lead to a significant change in antibiotic self-medication.[94, 95] Moreover, studies have raised questions regarding the validity of the traditional KAB framework with regard to antibiotic use, and the question of whether greater knowledge of antibiotics always translates into appropriate antibiotic usage behavior has been raised. [96, 97] Even in areas other than antibiotic use, the correlation between knowledge and behavior is generally weak.[98] However, information campaigns may help change the erroneous cultural beliefs or misconceptions about antibiotics in communities which, when combined with health system and policy interventions, may be effective in reducing self-medication with antibiotics.

The health system and policy of a country play a large role in determining people's health seeking and medication-taking behavior. If antibiotics are only available with a prescription, then it is unlikely that people will be able to self-medicate with antibiotics. However, it doesn't entirely prevent the use of leftover antibiotics or accessing antibiotics from noninstitutional sources. For example, although antibiotics are not available without a prescription in the USA, some Latinos living in the USA were found to acquire antibiotics from neighboring Mexico without any prescriptions.[71] Such behaviors can be explained by the fact that in almost every case, getting an antibiotic from a pharmacy or other sources is less expensive than consulting a physician. Overall, the cost difference between consulting a physician and self-medication is a very strong enabling factor for antibiotic self-medication (high cost of consulting

316 physicians and low cost of self-medication was the highest reported reason for self-medication in our
317 study). This cost difference has been identified as a reason for antibiotic self-medication in other
318 systematic reviews conducted in the LMICs and the middle east.[8, 16] In many countries (especially in
319 LMICs), there is usually very little government support for healthcare services and patients have to bear
320 high out-of-pocket spending.[99] Therefore, people who are incapable or unwilling to bear high healthcare
321 costs may be more likely to pursue self-medication.

322

323 A large number of studies from LMICs identified easy access to antibiotics OTC as a driver of self-
324 medication with antibiotics. Typically, in LMICs, people tend to have easy access to antibiotics from
325 pharmacies and many find it more convenient to self-medicate. Although there are laws in many LMICs
326 prohibiting the sale of antibiotics without a prescription, such laws are rarely implemented.[52] Only one
327 study from HICs identified easy access to antibiotics from pharmacies as a determinant of self-medication
328 which suggests HICs generally have stricter policies with regards to antibiotic dispensing. Lack of health
329 insurance was reported to be a reason for self-medication in descriptive studies, but the result from meta-
330 analysis was not significant. Therefore, the impact of health insurance on self-medication remains
331 uncertain. Again, because of the variations that exist among the type and coverage of health insurance
332 in various countries, the effect of health insurance should be considered on a country-by-country basis.
333 According to studies included in this review, the percentage of people with health insurance ranged from
334 27% to 92% in the LMICs while no information was available for HICs.

335

336 Implications for policy and practice

337 The determinants of antibiotic self-medication identified in this review can inform future efforts to lower
338 the prevalence of antibiotic self-medication among the public. This study also demonstrates that
339 significant variations exist among countries regarding determinants of antibiotic self-medication. Hence,

any successful intervention should involve at least two steps. First, nuanced studies need to be conducted to capture the key determinants of self-medication with antibiotics in a specific community or country. Second, instead of relying on a one-size-fits-all strategy, community-based interventions should target the high-risk groups while policies and healthcare reforms should emphasize the key health system-related determinants identified in this study. Given the lack of strong evidence regarding the impact of knowledge of antibiotics on self-medication, reliance on public information campaigns alone may not be successful. An integrated approach that incorporates educational programs (i.e., campaigns) and ensures the restriction of antibiotic access without prescriptions and better access to and affordability of healthcare services is likely to be more successful. The issues with the lack of satisfaction and trust in prescribers/ health services can be addressed by providing better training to prescribers and redesigning healthcare systems to improve healthcare services.

Strengths and limitations

To our best knowledge, this is the most comprehensive systematic review published so far that provides information about the determinants of antibiotic self-medication on a global level. Further, inclusion of studies from both HICs and LMICs allowed us to compare and contrast the various factors of self-medication in HICs and LMICs. Integration of findings from both quantitative and qualitative studies and use of three types of data synthesis allowed us to identify a large number of determinants. Inclusion of qualitative studies provided us with contextual and in-depth understanding of why people self-medicate. A limitation of the study involves the risk of recall bias within the included studies. The majority of the studies included in this review used a recall period of six months or higher for measuring participants' self-reported self-medication practices and 26 studies did not mention a recall period. Moreover, although countries were grouped into HICs and LMICs to account for the differences in population and health systems of the countries, there was still considerable differences between countries within each

subgroup. Statistical heterogeneity was also very high for many of the determinants analyzed through meta-analysis.

Conclusions

Males are more likely than females to self-medicate with antibiotics. Other patient-related determinants are related to patients' knowledge and beliefs regarding antibiotics, and health seeking behavior. Several determinants related to dispensing policy, healthcare cost, access to healthcare, trust and satisfaction with health services/providers facilitate self-medication. Overall, our study points to a range of determinants of self-medication with antibiotics, and more nuanced research would be needed in any given context to understand which particular determinants are important in different regions, countries, or localities. Moreover, future studies should prioritize understanding the impact of knowledge of antibiotics on self-medication since there are significant gaps in this area of research. Initiatives to decrease antibiotic self-medication among the public should incorporate targeted community programs and appropriate policies and healthcare reforms.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

Transparency declarations

None to declare.

Ethical approval

Ethical approval is not required since this study has retrieved and synthesized data from already published studies

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Table 1: Characteristics of the studies included in the systematic review (n=68).

Characteristics	Frequency (%)
Publication year	
2002-2012	7 (10.3)
2013-2017	21 (30.9)
2018-2022	40 (58.8)
Region of study	
East Asia & Pacific	8 (11.8)
Europe & Central Asia	5 (7.4)
Latin America & Caribbean	4 (5.9)
Middle East & North Africa	19 (27.9)
North America	1 (1.5)
South Asia	13 (19.1)
Sub-Saharan Africa	17 (25)
Multiple regions	1 (1.5)
Income level of countries	
Low income	17 (25)
Lower middle income	18 (26.5)
Upper middle income	16 (23.5)
High income	15 (22.1)
Multiple income levels (LMICs)	2 (2.9)
Type of study	
Quantitative	52 (76.5)
Qualitative	11 (16.2)
Mixed method	5 (7.4)
Study Setting	
Community	11 (16.2)
Healthcare facility	14 (20.6)
Household	18 (26.5)
Pharmacy	10 (14.7)
Online survey	3 (4.4)
Mixed	8 (11.8)
Not available	4 (5.9)
Recall period for self-reported self-medication	
≤1 month	8 (11.8)
3 months	9 (13.2)
6 months	9 (13.2)
1 year	15 (22.1)
2 years	1 (1.5)
Not available/not applicable	26 (38.2)

LMICs, Low- and middle-income countries

Table 2: Results of random effect meta-analysis showing the pooled odds ratios of self-medication with antibiotics. The overall effect size and the effect sizes of subgroup analysis based on income level of countries have been presented.

Determinants		Groups	No. of studies	Pooled odds ratios (95% CI)	Heterogeneity, I^2 (%)
Patient-related determinants	Sex (female* vs male)	LMICs	17	1.44 (1.19, 1.75)	76.12
		HICs	2	2.23 (1.72, 2.90)	0
		Both groups	19	1.52 (1.26, 1.83)	78.22
	Age (higher age* vs lower age)	LMICs	15	0.89 (0.65, 1.22)	59.36
		HICs	2	1.61 (1.10, 2.36)	0
		Both groups	17	0.98 (0.73, 1.31)	62.67
	Education (lower education* vs higher education)	LMICs	12	0.81 (0.51, 1.28)	76.66
		HICs	1	2.07 (0.56, 7.65)	—
		Both groups	13	0.86 (0.55, 1.33)	74.94
	Employment (unemployed* vs employed)	LMICs	8	1.49 (0.86, 2.58)	85.4
		HICs	0	—	—
		Both groups	—	—	—
	Income (high income* vs low income)	LMICs	9	0.97 (0.73, 1.27)	61.82
		HICs	0	—	—
		Both groups	—	—	—
	Residence (urban* vs rural)	LMICs	3	0.8 (0.33, 1.96)	89.72
		HICs	1	1.63 (0.75, 3.54)	—
		Both groups	3	0.94 (0.46, 1.95)	85.83
	Health insurance (not having insurance* vs having insurance)	LMICs	6	0.63 (0.4, 1.0)	78.71
		HICs	0	—	—
		Both groups	—	—	—
	Knowledge of antibiotics (based on knowledge score) (lower knowledge* vs higher knowledge)	LMICs	3	0.2 (0.08, 0.47)	84.54
		HICs	0	—	—
		Both groups	—	—	—
Health system-related determinants	Satisfaction with Healthcare services/physicians (satisfied* vs unsatisfied)	LMICs	1	3.53 (2.24, 5.54)	—
		HICs	1	2.81 (1.46, 5.41)	—
		Both groups	2	3.28 (2.26, 4.75)	0

* reference category
LMICs, Low- and middle-income countries
HICs, High-income countries

667 Table 3: Determinants of antibiotic self-medication identified from descriptive studies.

668

Determinants		Low- and middle-income countries		High-income countries	
		Number of studies	Range of frequency (%)	Number of studies	Range of frequency (%)
Patient related determinants	Previous experience with antibiotics and similar symptoms [12, 13, 29-31, 33, 34, 36-38, 42, 46, 47, 50, 51, 55, 57, 66, 67, 69, 77-79, 82, 85, 87, 89, 93]	21	6-80.5	7	20-69.2
	Perceived low severity of disease [11, 12, 33, 38, 46, 59, 66, 69, 73, 78, 81, 85, 87, 89, 93]	13	7-82	2	36-38.9
	Lack of time/Intention to save time [11, 29, 32, 33, 36, 49, 51, 53, 57, 73, 78, 81, 84, 85, 89, 93]	13	9.3-55.7	3	10.5-22.3
	Advise from others (family/friends) regarding antibiotic use [13, 34, 37, 59, 67, 72, 89]	5	7.7-28.2	2	16.1-16.2
	Poverty [12, 31, 77]	3	0.4-5	—	—
	Need for emergency usage/ intention to get better quickly [12, 46, 57, 60, 66, 69, 85]	7	11.9-33.9	—	—
Health system-related determinants	High cost of consulting physicians and low cost of self-medication [11-13, 29, 30, 32, 36, 40, 42, 49, 50, 53, 55, 57, 59, 60, 66, 67, 69, 78, 80, 81, 87, 89, 93]	22	2.5-88	3	5.8-19
	Lack of access to physicians /medical care [12, 30-32, 34, 36, 37, 77, 79, 82, 84]	8	1.4-55.5	3	6.4-29.3
	Easy access to antibiotics from pharmacies [11, 30, 69, 72, 87]	5	3-68.4	—	—
	Convenience associated with self-medication [11, 12, 74, 78, 81, 82, 84, 87]	8	5-87.8	—	—
	Long distance of healthcare facilities/physicians [42, 55, 87, 89]	4	3.2-22	—	—
	Long waiting time at healthcare facilities [30, 42, 50, 51, 60, 72]	6	4.3-55.1	—	—
	Lack of health insurance [32, 49, 57]	3	2.9-20.4	—	—
	Lack of trust/confidence in physicians/healthcare services [11-13, 40, 67, 84]	6	1.7-17	—	—

669 Table 4: Determinants of antibiotic self-medication identified by thematic analysis of the
670 qualitative studies.

671

	Themes identified from qualitative studies	Excerpts from studies related to the themes (LMICs)	Excerpts from studies related to the themes (HICs)
Patient-related determinants	Previous experience with antibiotics and similar symptoms	"When I have a sore throat, doctors always give me amoxicillin. I already know! Then, when I have the symptoms, I go to buy the same. It always works!" [39] "If infection is similar to the previous one then I use the medicines of previous prescription." [41] "We almost always went to the hospital in case of tonsillitis. And it was always the same medication, it was always the same thing……So, it was also from experience. Then I began to realize the medication was that one." [83] "I did not go to the health care center, surely they would prescribe me this…I know these medicines, I had similar problem weeks ago went there…they prescribed me azithromycin tablets and cotrimoxazole cream." [90]	"I also think that sometimes when you get sick and don't know what medication to take, you go to the doctor and get some medication. You see this medication worked for you, and there were no side effects. Then next time you have the same problem you don't go to the doctor. Right? You don't go the doctor. You return to the pharmacy." [71] "I used to go to the doctor but later I treat myself by my own experience. Let's say that I went to a doctor once and he gave me an antibiotic and I found it effective, I use it again if needed. No need to go to the doctor again." [35] "I think they self-medicate because they had -or think they had- the same illness, and they still have some drugs left over from last time." [91]
	Perceived low severity of disease	"So, usually for a small thing I go directly to a medical store." [44] Our family members did not like to go see a doctor, except when we got a serious sickness. If someone has a fever or cough, we buy Yaa Chud [non-prescribed poly-pharmaceutical packs containing antibiotics] from the drug store." [52]	
	Advise from others (family/friends) regarding antibiotic use	"Sometimes we are suggested by a friend or relative to use an antibiotic for a condition they also had experienced." [41] "I take an antibiotic given by my mum. She said the medicine is effective against colds. I try it and it works" [63]	

		"Yes, I told to my friend and she said I needed an antibiotic." [48]	
	Having home stock of antibiotics or left-overs from past use*	"I know a lady that was sick and I told her to visit the doctor. She answered that she had leftovers of a previous prescription. That she would take them because in the medical center she would receive the same drug." [39] "Mostly we use without prescription. Most of the times, these are available at home as home stock, left from previous illness." [41] "We keep them so that we can use them again when we get ill." [52]	"No need to see a doctor over a minor thing that I experienced before. Well, I can't remember exactly what the antibiotic is but my whole family use it and [it] is always available at home; its' a big box with white and purple colours [Augmentin]." [35] "We don't throw anything anyway; who doesn't have a medicine cabinet at home?" [91]
	Intention to save time/lack of time	"I was working and did not have time to go to the doctor for consultation, so I went straight to the pharmacy." [65] "I did not have time for a doctor at all; I worked from 10 a.m. to 10-11 p.m." [48]	
	Intention to get better quickly	"When I have a sore throat, I go to a [community] pharmacy and ask for antibiotics as I want to get better quickly." [63] "Antibiotics, they (pharmacist/dispenser at pharmacy shop) give when we want quick relief." [68]	
	Cultural beliefs about curative power of antibiotics*	"What I've learned from my mother who was a nurse that antibiotics heal all types of diseases…everything, and I believe so, they are strong, and they fight against microbes." [90]	"Antibiotics kill things very quickly, take [them] and in two days you will be fine." [35] "Augmentin can be used for everything." [35]
Health system-related determinants	Lack of trust/confidence in physicians	"[I visit] another doctor, and he says 'why did that other doctor prescribe you this?' And they start to contradict each other, and that has produced distrust in me. This makes me feel unconfident." [39] "Doctors write medicines by hit and trials and write 2–4 medicines that any one of them will work. Doctors just want to get rid from patients in government hospitals; " [41] "When you come in [the consultation room] you say: 'I'm feeling pain here'. And he's already writing. Already writing, they are fast! So it brings doubts…'But is he actually writing what	"The doctor doesn't say much; he would only prescribe the medicine and that's it! He does not look at my medical file. Even when I try to discuss something with him, he just doesn't care or pay attention. So, my family and I decided to go directly to the pharmacy and get what we need from there." [35]

		I really feel? In fact, are they working well, these guys?' There's that doubt." [83]	
	Greater trust in pharmacists*	"When I have mild symptoms, I always go to the drug store first. I don't even know the name [of the medications] and their effect because I trust them completely." [52] "In my neighborhood, he [the pharmacy storekeeper] was the savior. (…) Anytime you have symptoms, you visit him and get an injection. (…) I think half the neighborhood had contact with antibiotics because of him." [39] "They [pharmacy storekeepers] learn every day." [39]	
	High cost of consulting physicians and low cost of self-medication	"In Pakistan a poor man cannot even think as he is asked for the tests which are too expensive. At second, in outdoor clinics, there are too many patients and senior doctors do not come. For private clinics, Rs.1,500–2,000 is the fees so a poor person cannot afford that." [41] "If someone feels something in their body, what do they do? Instead of going to the doctor, because this is a small issue and the doctor will charge a more expensive fee, they will go directly to the medical store. The pharmacist will give them a tablet, etc., as per their understanding." [44]	"If I already know my symptoms and what medicine heals me, I'm not going to go to the doctor so they can give me a prescription there. If I go, they'll charge me just for the visit, and then I have to go buy the prescription and that's more money, another cost. If I know what medication I'm going to take and will work for me, I'll go buy it and it's cheaper for me. " [71] "I'm not going to go to the physician, if I already know my symptoms and what medicine heals me. If I go, they will charge me just for the consultation, and then I have to buy the prescription and that's another cost with more money. It is easier and cheaper to go and buy an antibiotic straightway, if I know what medication I'm going to take and will work for me." [35] "I had urinary problems years ago. You know, seeing the urologist was expensive, so this time, I was smart enough to keep one tablet of each medication and later bought them from the drug store." [92]
	Long distance of physicians or healthcare facilities	"If you are not close to a medical center, then, why do you have to go to a clinic? Better, let's go to the closest pharmacy. This is an alternative for you." [39] "I usually take medicine by myself. Doctor is far away from my house. We	"Since I live in Qatif and the hospital is in Khobar and I don't have transportation, I usually buy the antibiotic from the pharmacy that is beside my home." [35]

		live in a village. Doctor is far from village." [41]	
	Long waiting time at healthcare facilities	"They examine you and two hours later they attend to you. Then, they come back to you, examine you again, and ask you to wait again. I tell you this because this has happened to me. I have had to wait almost seven hours to receive attention. That's the reason I do not go to see a doctor." [39] "If I have similar symptoms, I don't want to see a doctor because of a long wait in the clinic. I would rather take leftover antibiotics prescribed for my past illness." [63] "If we will go to government hospitals to seek medicines for minor ailments like cold or cough; then we have to wait in queues and our daily wage will be affected, so it is better to take medicine of INR 10 - 15 (USD 0.1 - 0.2) from the medical store (pharmacy)." [68]	"When you go to the government hospitals, you need a long time to see a doctor, either waiting during or waiting for the appointment. Sometimes, [it takes] one or two months to see a doctor." [35]
	Easy (OTC) access to antibiotics from pharmacies	"I have a pharmacy close to my house. They sell them [the antibiotics] to me without any kind of prescription." [39] It is not difficult at all, I bought these medicines today, and I asked for those two-color medicines (amoxicillin), the red and yellow capsules, they gave me." [90]	"They are available everywhere and you can get them easily. The law is not strictly enforced to prevent [the] selling [of] antibiotics without prescriptions." [35]

672 *new themes emerging from qualitative studies that were not found in the descriptive studies

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