



## Systematic review

## Non-biomedical factors affecting antibiotic use in the community: a mixed-methods systematic review and meta-analysis

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## ARTICLE INFO

## Article history:

Received 18 August 2021

Received in revised form

24 October 2021

Accepted 25 October 2021

Available online 10 November 2021

Editor: L. Leibovici

## Keywords:

Antibiotics

Antimicrobial resistance

Drug policy

Drug use

Health Belief Model

Meta-analysis

One Health

Socio-ecological Model

Systematic review

## ABSTRACT

**Objectives:** In the past two decades, human antibiotic consumption has increased globally, contributing to the emergence and spread of antimicrobial resistance and needing urgent effective actions. Our objectives were to systematically identify and collate studies exploring non-biomedical factors influencing healthcare consumers' antibiotic use globally, in order to inform future interventions to improve practices in antibiotic use.

**Methods:** Data sources were PubMed, EMBASE, PsycINFO, and Cochrane. Study eligibility criteria were original and empirical studies that identified factors for healthcare consumers' antibiotic use. Participants were healthcare consumers. Assessment of risk of bias used adapted BMJ survey appraisal tools, the Critical Appraisal Skills Programme checklist, and the Mixed Methods Appraisal Tool for quality assessment. Methods of data synthesis employed the Social Ecological Framework and Health Belief Model for data synthesis. We did random-effects meta-analyses to pool the odds ratios of risk factors for antibiotic use.

**Results:** We included 71 articles for systematic review and analysis; 54 were quantitative, nine were qualitative, and eight were mixed-methods studies. Prevalent non-prescription antibiotic use and irresponsible prescriptions were reported globally, especially in low-to-middle-income countries. Barriers to healthcare—wait time, transportation, stigmatization—influenced people's practices in antibiotic use. Further, lack of oversight and regulation in the drug manufacturing and a weak supply chain have led to the use of substandard or falsified antibiotics. Knowledge had mixed effects on antibiotic use behaviours. Meta-analyses identified pro-attitudes towards self-medication with antibiotics, relatives having medical backgrounds, older age, living in rural areas, and storing antibiotics at home to be risk factors for self-medication with antibiotics.

**Conclusions:** Non-prescription antibiotic use and irresponsible prescriptions in the community are prevalent in all WHO regions and are driven largely by a mixed collection of non-biomedical factors specific to the respective setting. Future antimicrobial resistance strategies should incorporate an implementation science approach for community-based complex interventions that address drivers of the target behaviours tailored to local contexts. **Ruyu Sun, Clin Microbiol Infect 2022;28:345**

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## Introduction

Excessive use of antibiotics directly contributes to the emergence and spread of antimicrobial resistance (AMR) [1] which occurs when bacteria, parasites, viruses and fungi develop the ability to resist antimicrobials [2]. In 2019, the World Health Organization (WHO) listed AMR as one of the ten threats to global health [3], calling for urgent effective actions.

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Antibiotics used for human health account for a considerable proportion of total antibiotic consumption [4,5]. In the past two decades, human antibiotic consumption has increased globally. There has been a 65% increase in antibiotic consumption from 2000 to 2015 [6], and the majority of these increases have occurred in low-to-middle income countries (LMICs) [6,7] where the challenges of antibiotic overuse and underuse exist concurrently. Dr Ramanan Laxminarayan, the Director of the Center for Disease Dynamics, Economics & Policy (CDDEP), highlighted in a new report entitled “Access Barriers to Antibiotics” that a lack of consistent access to antibiotics—because of weak drug supply chains or affordability—is still responsible for a large portion of preventable deaths in LMICs [8].

In non-clinical settings, high volumes of antibiotic consumption are largely attributed to easy access to over-the-counter (OTC) antibiotics and non-prescription antibiotic use. A study reported a prevalence of 62% non-prescription antibiotic sales in community pharmacies globally, with the highest prevalence (78%) observed in South America [9]. Self-medication with antibiotics is also widely reported. In Asia, 58% of antibiotic use was non-prescription, and in Africa, where 76% of antibiotics were obtained at community pharmacies, 100% of the use was non-prescription [10].

In primary care and outpatient settings, the over-prescription of antibiotics remains a critical issue around the world. Studies reported high rates of prescription of antibiotics in outpatient sectors both in high income countries (HICs)—such as South Korea (80.9%) [11], the US (59.1%) [12] and European countries (approximately 90%) [13]—and in LMICs such as China (50.3%) [14] and India (69.4% among patients with acute infections) [15]. According to previous studies, 11.3–33.5% of these prescriptions were inappropriate [16,17], and half of the antibiotic prescriptions used for acute respiratory tract infections were unnecessary [18,19].

With the increasing prevalence of global antibiotic use in the community, it is vital to investigate non-biomedical drivers influencing these behaviours for developing mitigation policies and intervention programmes to educate the public and promote prudent antibiotic use. Therefore, we conducted a global mixed-methods systematic review and meta-analysis to identify, synthesize, and analyse the non-biomedical factors of healthcare consumers' (i.e. the general public, child caregivers, patients, etc.) antibiotic use in the community.

## Methods

### *Search strategy and selection criteria*

We conducted this systematic review and meta-analysis following the PRISMA guidelines [20]. Four databases—PubMed, EMBASE, PsycINFO, and Cochrane Library—were systematically searched with a combination of the key terms ‘antibiotic’, ‘anti-microbial’, ‘use’, ‘consumption’ and ‘behaviour’ to obtain relevant publications before July 2020. No language or geographical restrictions were applied. Full search strategies are shown in the [Supplementary Material Table S1](#).

Original and empirical studies that identified non-biomedical factors for antibiotic use in community settings (e.g. self-medication with antibiotics for treatment or prophylaxis, storing antibiotics at home, and OTC purchases) and clinical settings (e.g. demanding/pressuring for antibiotic prescriptions and receipt of antibiotic prescriptions for self-limiting illnesses) were eligible for inclusion. For the purpose of our study, ‘non-biomedical factors’ are defined as ‘factors that are outside the person’s body and are not clinical conditions or biomedical indicators’ such as sociodemographic characteristics, personal knowledge, prior experience, etc. [21]. Quantitative, qualitative, and mixed-methods studies were

included. Specifically, we included (a) quantitative components from quantitative and mixed-methods studies where confounders were accounted for, and (b) qualitative studies with explicit methods used for data collection and analysis. We manually searched the reference lists of included studies for additional relevant publications. Studies that merely reported healthcare consumers' knowledge, perception, beliefs, or attitudes towards antibiotic use without actual practices of antibiotic use were excluded. Detailed inclusion and exclusion criteria are presented in the [Supplementary Material Table S2](#).

All citations identified from the search were imported into Endnote, and two authors (LL and TY or RS) independently screened titles and abstracts to select potentially relevant citations. For citations considered relevant or for which the title/abstract was deemed insufficient for inclusion or exclusion, full texts were retrieved and evaluated independently by two authors (TY and RS). Discrepancies and uncertainties were resolved through discussion with a third author (LL) until consensus was reached.

### *Data extraction and quality assessment*

A purpose-built data collection form based on Cochrane Review and behavioural theories, including the Health Belief Model and Social Ecological Framework, was utilized for data extraction. The Health Belief Model was consulted to identify factors that could explain and predict individual antibiotic uptakes [22], and the Social Ecological Framework assisted us with the incorporation of the complex interplay between individual, interpersonal, community, and societal factors during data synthesis and analysis [23]. Data from the included studies were double-extracted independently by two authors (TY and RS). Disagreements were discussed with a third author (LL) until consensus was reached. We extracted data on study characteristics, methods, target population, sample size, and antibiotic use and associated factors, including numerical data (numbers or percentages) from the quantitative component and themes relevant to factors influencing antibiotic use from the qualitative component.

Three authors (LL, TY, and RS) independently performed quality assessment of all included studies and resolved disagreements through discussion. Quantitative components were evaluated by adapted BMJ survey appraisal tools [24]; qualitative components were assessed by the Critical Appraisal Skills Programme (CASP) checklist [25], and mixed-methods studies were appraised by the Mixed Methods Appraisal Tool (MMAT) [26].

### *Data analysis*

Quantitative components that reported prevalence of and factors of antibiotic use were included in the analysis, categorized by the WHO regions (i.e. African Region, Region of the Americas, South-East Asia Region, European Region, Eastern Mediterranean Region, and Western Pacific Region) [27], World Bank economic development levels (i.e. low-income, lower-middle-income, upper-middle-income, and high-income countries, the first three of these being categorized as LMICs to make the classification more concise) [28], and types of healthcare facility used (community or clinical settings).

Considering the heterogeneity between the studies, we performed random-effects (DerSimonian Laird method) meta-analyses to calculate summary odds ratios of major non-biomedical factors for antibiotic use. We carefully contrasted publications whose data came from the same study. We included those with the largest sample size or contributing the most comprehensive results; only factors that shared similar definitions and were explored in at least two studies via multivariate analysis were

incorporated for meta-analysis [29]. All meta-analyses were performed using Stata version 16.0.

### Registration

The study protocol is registered with PROSPERO, protocol number CRD42019139591.

### Results

Our literature search returned 3212 records, and 86 additional records were retrieved from other sources (Fig. 1). We assessed 152

full-text articles, of which 71 studies met our inclusion criteria, including 54 quantitative, nine qualitative, and eight mixed-methods studies. Apart from one experimental study [30], all included studies used a cross-sectional design and covered 52 countries and territories with a total of 138 490 adult healthcare consumers and 773 juvenile school students (Fig. 2, Supplementary Material Table S5). More than half were published after 2016 ( $n = 42$ , 59.1%) and were conducted in LMICs ( $n = 40$ , 57.1%). Only one article was published in German [31]; the others were in English. Non-biomedical risk factors of antibiotic use in the community were identified, analysed, and synthesized according to the modified Health Belief Model (Fig. 3, Supplementary Material Table S6).

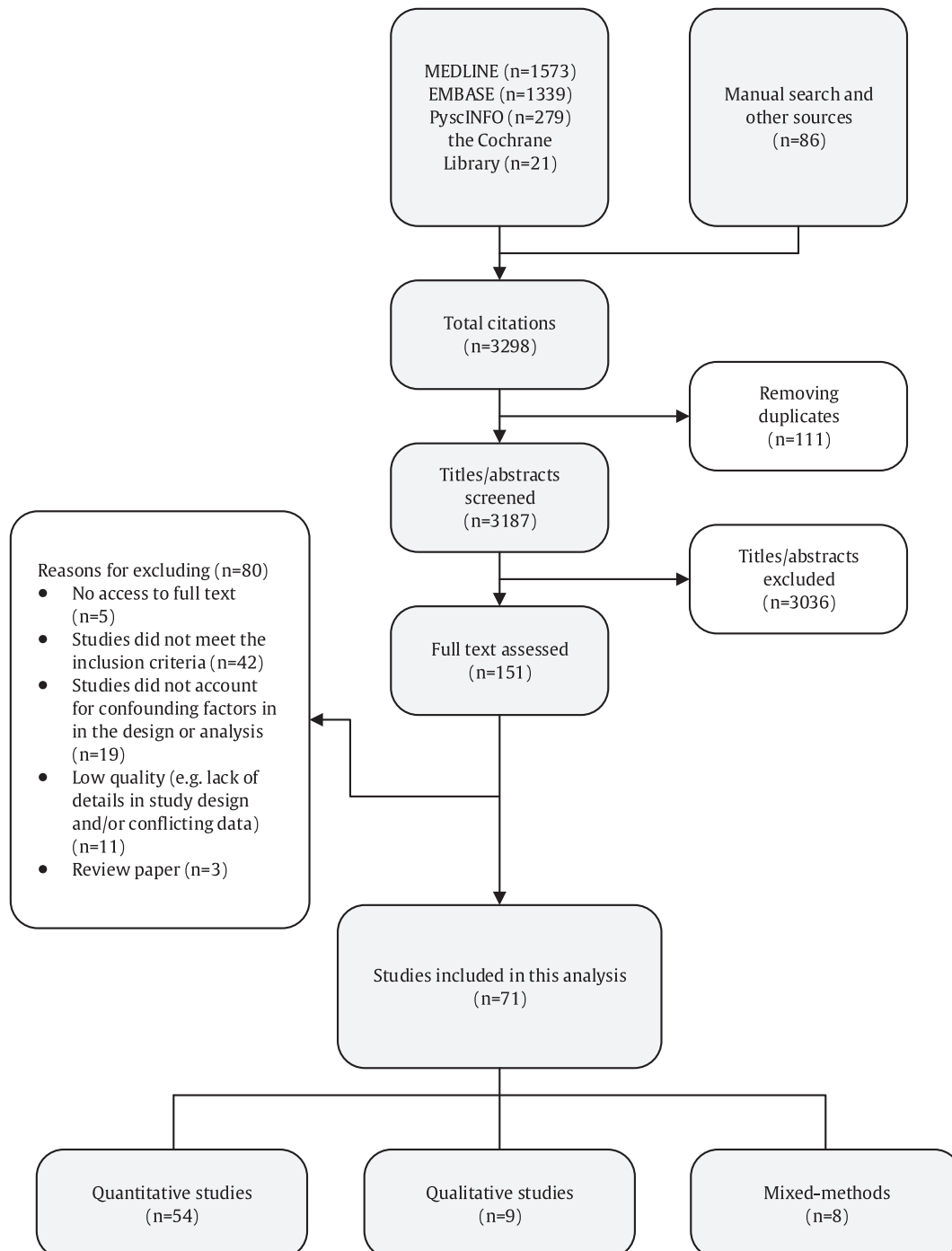


Fig. 1. The literature search methodology.

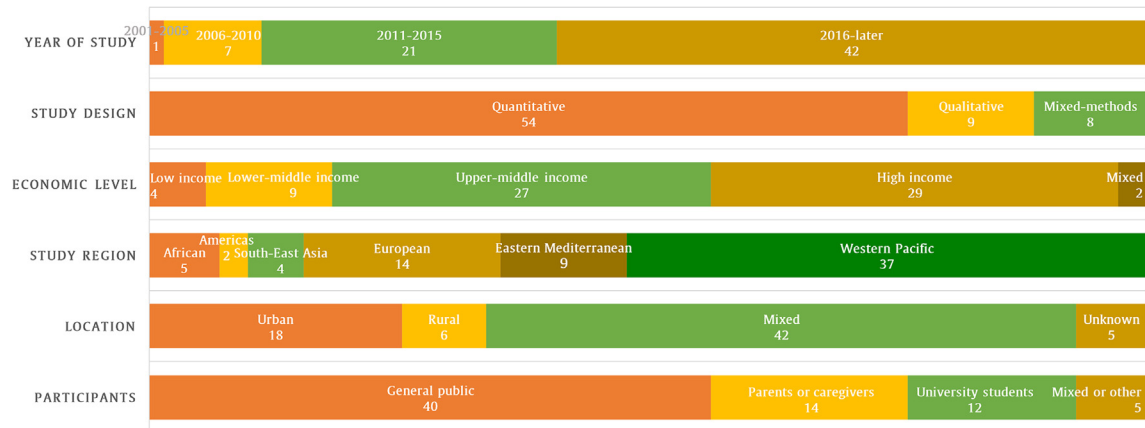


Fig. 2. Summary of selected studies.

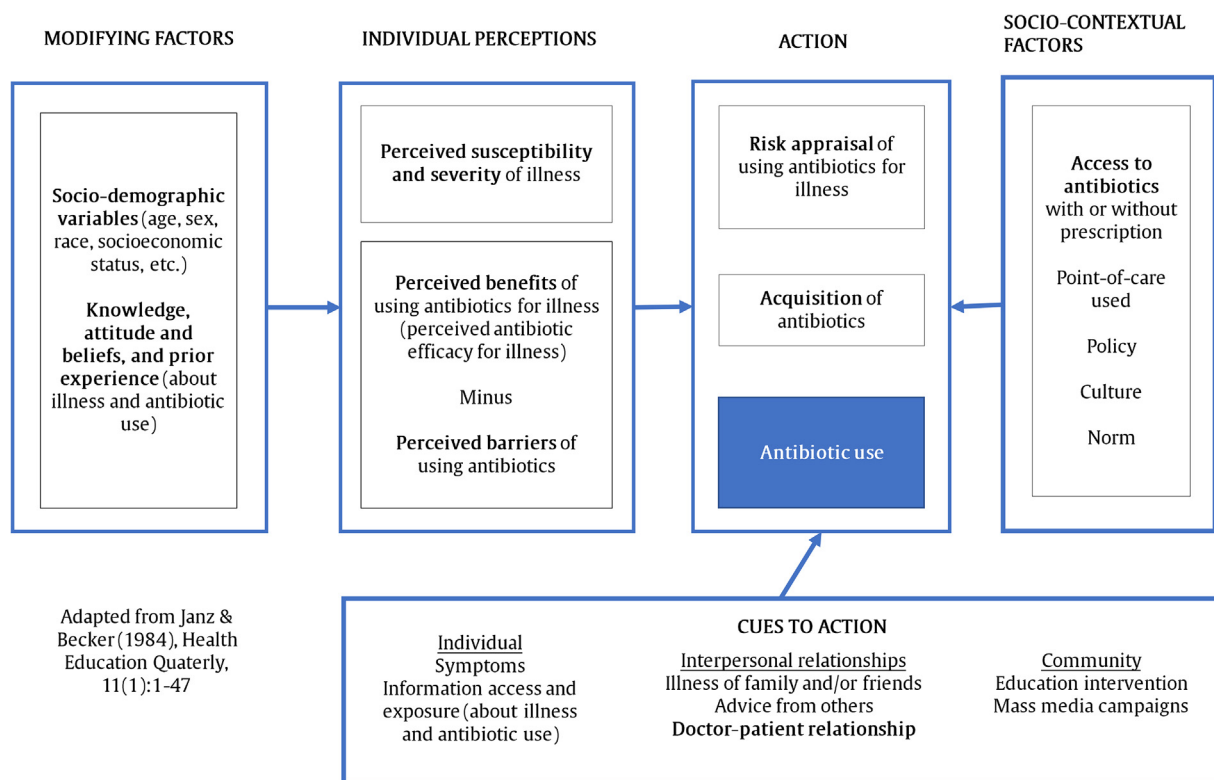


Fig. 3. Non-biomedical risk factors of antibiotic use in the community identified, analysed, and synthesized according to the modified Health Belief Model.

### Quantitative synthesis

We extracted measures (e.g. denominator, numerator, and recall period) of antibiotic use practices and synthesized the data by study region and income group (Figs. 4 and 5). Boxes with different colours in Figs. 4 and 5 show the prevalence range of different antibiotic use behaviours. In total, 57 studies quantitatively explored risk factors for antibiotic use practices. We summarize the identified factors in the Supplementary Material Table S7.1–S7.18.

### Community settings

Self-medication with antibiotics for therapeutic purposes was reported in 48 studies from 40 countries and territories, with a prevalence from 3.1% (19 European countries) [32] to 82.0% (Qatar) [33] among adults and 3.3% (the US) [34] to 62% (mainland China)

[35] among children. Seven studies identified knowledge as a factor for self-medication with antibiotics [36–42], usually assessed by a combined score with mixed results [36,37,39,41,42]. Having a medical background had mixed effects [43–50]. Prior experiences of antibiotic use were consistently found to be a risk factor [32,47,51]. Awareness of prescription-only regulations for antibiotic sales [43] or pharmacies controlling the number of antibiotic tablets dispensed [52] decreased the likelihood. Accessibility to GP consultation [53,54] and a satisfying experience with the GP [54] lowered the risk. The associations between self-medication with antibiotics and age [31,35,38,45,48,55], gender [38,41–43,47,48,55], education [35,38,43,50], income [38,45,50] or urbanicity [35,38,44,55,56] were inconsistent. Living in highly economically developed regions was consistently associated with less self-medication with antibiotics [32,43,46,50,52,56,57].

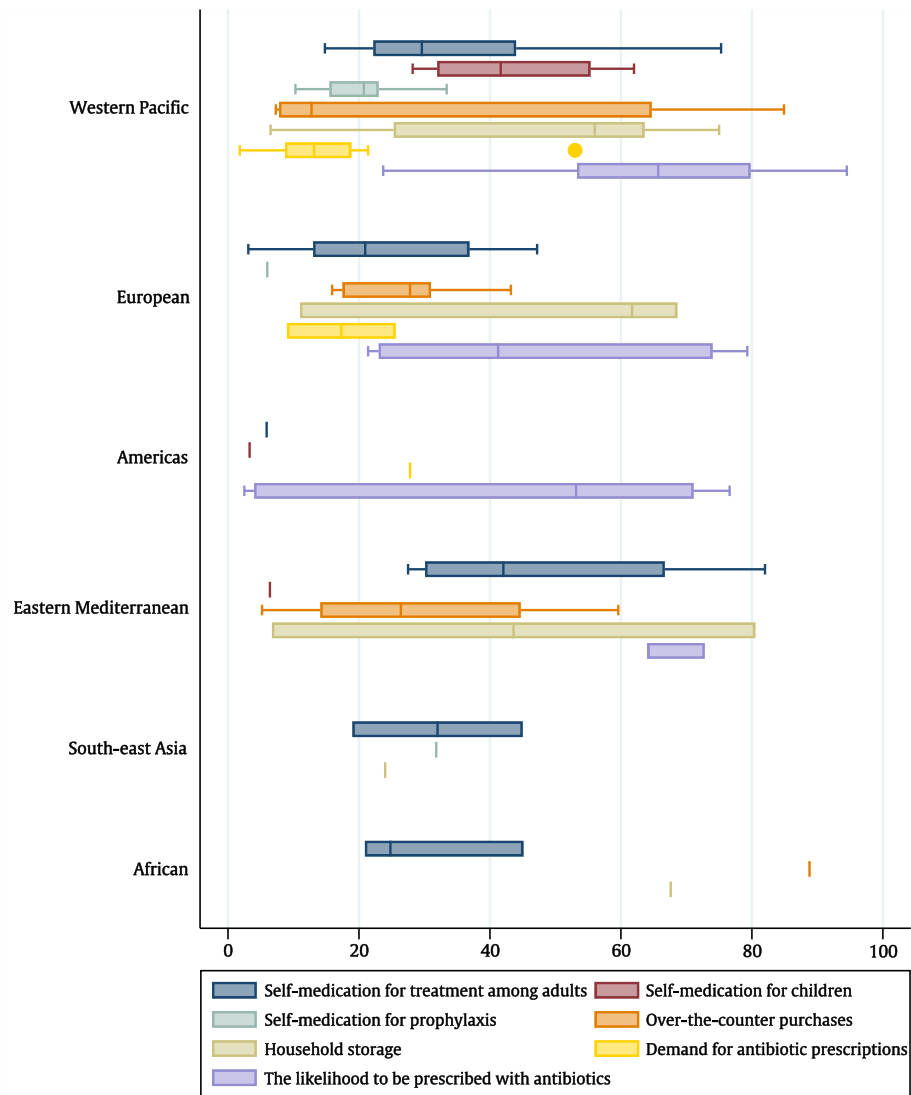


Fig. 4. Antibiotic use practices and synthesized the data by study region.

Self-medication with antibiotics as prophylaxis was assessed by 14 studies from four countries, with a prevalence ranging from 6.0% (Serbia) [36] to 31.8% (Nepal) [58] and 33.4% (mainland China) [44]; it was especially common in mainland China [35,39,44,46,56,59]. Eight studies [39,40,46,50,56,57,59,60], all conducted in mainland China, investigated the risk factors and found that living in urban areas [56,59] or in highly economically developed regions [46,50,56,57,60] lowered the risk.

Overall, having easy access to non-prescription antibiotics—including perceiving an easy access to OTC purchasing [52], obtaining it successfully [35,42,50,56], household storage [35,39,42,43,50,56,61] or leftover prescriptions [50,56]—contributed to both therapeutic and prophylactic self-medication.

OTC purchasing of antibiotics was reported in 34 studies from 35 countries and territories, and ranged from 5.2% (Lebanon) [62] and 7.3% (Hong Kong, China) [63] to 84.9% (mainland China) [64] and 88.8% (Tanzania) [65]. Among the 34 studies, six investigated potential influencing factors [46,47,53,66–68]. Prior experience of antibiotic use [47] and perceiving long waiting time before getting necessary medical care [53] contributed to OTC purchasing of antibiotics. Additionally, a survey conducted in Lao further investigated

public use of substandard or falsified antibiotics when purchased OTC; in the study, no falsification was found among the antibiotic samples obtained by mystery shoppers, while laboratory analyses showed that 79.8% of the samples were substandard [30].

Household storage of antibiotics was measured in 37 studies from 36 countries, ranging from 6.5% (Hong Kong, China) [66] to 80.5% (Pakistan) [69]. Ability to recognize antibiotics [70] and pro-attitudes to use leftover antibiotics [70] were associated with storing antibiotics at home. Being female [46,50,56,57,59], higher socioeconomic positions [46,50,56,57,59], living in urban areas [46,56,59] or economically developed regions [50,56,57], having a medical background [46,47,50,56,57,59] and prior experience of antibiotic use [47,70] all increased the risk. Immigrants from countries or regions where non-prescription purchasing and use were prevalent were likely to continue those habits [66,67]. OTC purchases were also a risk factor [67].

Only one study explored antibiotic use from One Health perspective; it reported that antibiotic use for humans was associated with that for animal use: having bought OTC antibiotics for pigs in the previous year increased backyard pig farmers' OTC purchases of antibiotics for humans [64].

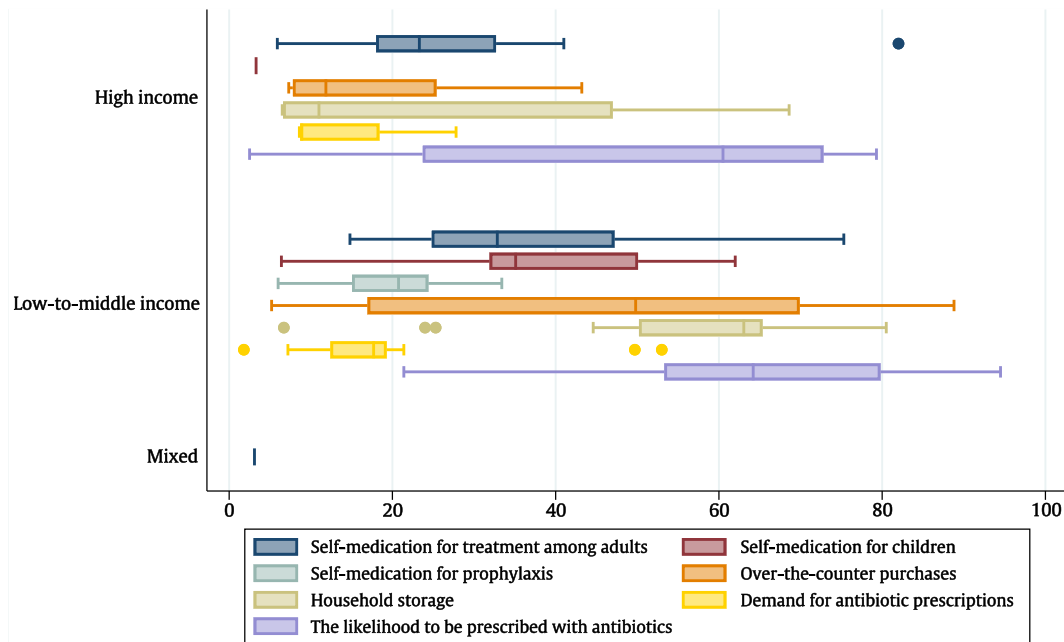


Fig. 5. Antibiotic use practices and synthesized the data by income group.

### Clinical settings

The prevalence of receipt of antibiotic prescriptions for different illnesses (mostly self-limiting illnesses) was reported in 18 studies from 11 countries and territories, ranging from 21.4% (the UK) [71] to 94.5% (mainland China) [72]. Three studies [35,39,59] conducted in mainland China reported that 31.7% [39] to about half [35] of the prescribed antibiotics were administered through intravenous injection. A higher combined knowledge score [39,72] and having a medical background [46] lowered the risk of being prescribed antibiotics by doctors. People who believed they needed an antibiotic and who self-diagnosed themselves with a bacterial infection were more likely to be prescribed one [34]. Living in rural or less economically developed areas was associated with a higher risk [46,57]. Masculinity, one of Hofstede's five cultural dimensions that is more assertive and competitive, was positively correlated with outpatient antibiotic prescriptions, hence a higher antibiotic prescription rate [73].

Demand for antibiotic prescriptions were reported in 22 studies from nine countries and territories, with a prevalence ranging from 1.8% (mainland China) [43] to 53% (mainland China) [35]. Of the 11.2% [74] to 26% [75] of participants who reported asking for antibiotics, most [74,75] or even all of them [39] were prescribed one with or without discussion. Students taking antibiotics as anti-inflammatory drugs were more likely to demand antibiotics [40], and a higher combined knowledge score stopped this behaviour [39]. Older age [46,57,59] and living in less economically developed areas [46,60] were risk factors, yet the results for education level were mixed [46,57,60,76,77].

### Combined measure of antibiotic use behaviours

Ten studies assessed antibiotic use practices with a combined measurement, either combined (mis)uses together as antibiotic (mis)use behaviours, or a combined behaviour score [49,58,62,63,65,71,78–81]. Four reported that a higher combined knowledge score led to better antibiotic use behaviours [62,65,71,80]. People who had seen or heard about antibiotic resistance and who agreed with the seriousness of AMR were not more likely to behave

correctly [80]. Consistently, older age was identified as a protective factor for better practices [71,78–80].

For meta-analyses, factors for self-medication with antibiotics for treatment and storing antibiotics at home were included (Table 1). For self-medication with antibiotics for treatment, nine factors were included in analyses, with five identified to be significant. Pro-attitudes towards self-medication with antibiotics, relatives having medical backgrounds, older age, living in rural areas, and storing antibiotics at home were risk factors. The effects of pro-attitudes towards self-medication with antibiotics were consistent in both HICs and LMICs, while older age was a risk factor only in LMICs. Six factors were included in the meta-analyses for storing antibiotics at home, and two were identified to be significant. Relatives having medical backgrounds and prior experience of antibiotic use were risk factors, and the effect of relatives having medical backgrounds was consistent in both HICs and LMICs. Meta regressions were conducted and revealed no significant statistical difference in effects of these risk factors between HICs and LMICs.

### Qualitative synthesis

Factors identified from 17 qualitative and mixed-methods studies generally supported the quantitative findings and provided critical perspectives regarding antibiotic use driven by non-biomedical factors. Five studies conducted in Saudi Arabia [82], Romania [83], Pakistan [69], Malawi [61] and Ghana [84] reported having difficulty accessing healthcare when getting ill as a reason for self-medication with antibiotics; this included the long waiting time for an appointment [69,82,84], transportation issues [61,69,82,84] (e.g. women in Saudi were not allowed to drive), or a lack of financial resources for formal consultations [68,69,83,84]. Previous experiences of antibiotic use drove people to self-medicate [61,69,83]. Barriers in doctor–patient communications induced self-medication with antibiotics among patients [61,82,83]. The cultural norm of stigmatizing infections prevented Saudi residents from seeking formal health care and led to self-medication with antibiotics, despite knowing it was against



**Table 1**  
Factors associated with antibiotic use behaviours

	Number of studies	Sample size	OR (95%CI)
<b>Factors for self-medication with antibiotics for treatment:</b>			
Factor 1: pro-attitudes towards self-medication with antibiotics			
Worldwide	5	6296	2.37 (1.48–3.26)
HICs	1	1090	2.13 (1.65–2.61)
LMICs	4	5206	2.68 (1.30–4.06)
Factor 2: respondents having medical background			
Worldwide	5	6329	1.44 (0.88–1.99)
LMICs	5	6239	1.44 (0.88–1.99)
Factor 3: relatives having medical background			
Worldwide	3	6119	1.27 (1.00–1.53)
HICs	1	1050	1.45 (0.95–1.96)
LMICs	2	5069	1.21 (0.85–1.57)
Factor 4: female gender			
Worldwide	12	52195	0.99 (0.86–1.12)
HICs	4	3111	0.95 (0.58–1.32)
LMICs	8	49084	1.02 (0.88–1.16)
Factor 5: older age			
Worldwide	5	6648	1.10 (1.02–1.18)
HICs	1	1050	1.01 (0.95–1.07)
LMICs	4	5592	1.12 (1.02–1.23)
Factor 6: university education			
Worldwide	3	40755	0.74 (0.46–1.02)
HICs	2	1531	0.97 (0.28–1.67)
LMICs	1	39224	0.60 (0.55–0.66)
Factor 7: living in urban area			
Worldwide	7	46162	0.79 (0.63–0.95)
HICs	1	942	0.50 (0.30–0.70)
LMICs	6	45220	0.85 (0.68–1.01)
Factor 8: health insurance			
Worldwide	2	4212	1.22 (0.94–1.51)
LMICs	2	4212	1.22 (0.94–1.51)
Factor 9: storing antibiotics at home			
Worldwide	4	7850	4.63 (3.09–6.17)
LMICs	4	7850	4.63 (3.09–6.17)
<b>Factors for storing antibiotics at home</b>			
Factor 1: respondents having medical background			
Worldwide	2	20718	1.28 (0.78–1.78)
LMICs	2	20718	1.28 (0.78–1.78)
Factor 2: relatives having medical background			
Worldwide	2	12242	1.60 (1.37–1.83)
HICs	1	1050	1.80 (1.26–2.34)
LMICs	1	11192	1.56 (1.30–1.81)
Factor 3: prior experience of antibiotic use			
Worldwide	2	1519	2.29 (1.77–2.81)
HICs	2	1519	2.29 (1.77–2.81)
Factor 4: female gender			
Worldwide	4	22541	1.08 (0.79–1.37)
HICs	1	1050	0.90 (0.66–1.14)
LMICs	3	21491	1.14 (0.81–1.47)
Factor 5: older age			
Worldwide	3	21768	1.00 (0.95–1.05)
HICs	1	1050	0.92 (0.88–0.97)
LMICs	2	20718	1.04 (1.01–1.07)
Factor 6: living in urban area			
Worldwide	3	21491	1.32 (0.91–1.74)
LMICs	3	21491	1.32 (0.91–1.74)

LMICs, low–middle-income countries; HICs, high-income countries.

regulations [82]. Similarly, workplace cultures that expect staff to fight minor ailments without taking days off led to the decision to apply self-medication with antibiotics [85]. Poor regulatory enforcement around OTC antibiotic purchases were associated with prevalent self-medication with antibiotics in LMICs, including Saudi Arabia [82], China [86] and Romania [83]. Studies reported a mixed use of antibiotics and traditional herbs [84,87].

Difficulties in accessing healthcare facilities (e.g. inconvenience, high fees) drove residents to purchase antibiotics OTC in mainland China [87,88]. Moreover, in Malawi, lack of sufficient antibiotic stocks in hospitals increased OTC purchases [61]. In India, patients

pressured pharmacy shopkeepers for antibiotics due to their wish for a ‘quick cure’ [89]. Sources of antibiotics stored at home were mostly leftovers from delayed prescriptions [75,85] or previous prescriptions [66,67], and people usually prepared them for future use [66,67,75,82,85] or sharing with family members [82]. Trust in doctors stopped some patients from asking for antibiotics [67], while others demanded specific antibiotics according to their prior treatment experience [86,87,90]. Parents in mainland China even demanded intravenous antibiotics for children, thinking this would help recovery [90].

## Discussion

This systematic review shows that non-prescription antibiotic use and irresponsible antibiotic prescriptions are prevalent across the world and are influenced largely by multifaceted non-biomedical factors. In consultation with the Health Belief Model, we found antibiotic uses were influenced by individual's socio-demographic variables [32,43,46,50,52,56,57], perceptions of vulnerability and susceptibility to the infections [34,43,51,62,91,92], and access to drugs [50,56]. Knowledge was found to have mixed effects on antibiotic use behaviours [56,62,65,71,80]. Qualitative studies also showed that social–contextual factors such as barriers to health care could interfere with people's care-seeking behaviours, resulting in avoiding medical interactions while purchasing antibiotics over the counter and self-medication with antibiotics [61,69,82–84]. Lack of consistent access to antibiotics was reported in LMICs [82,87], with the proportion of falsified or substandard antibiotics remaining high in some regions [30]. Effective doctor–patient relationships could cue people to act appropriately; it had a direct impact on people's healthcare-seeking behaviours and antibiotic use decisions [54,61,67,82,83]. Meta-analyses further identified older age, living in rural areas, storing antibiotics at home, having relatives with medical backgrounds, and having a positive attitude towards self-medication with antibiotics to be risk factors for self-medication with antibiotics; having relatives with a medical background and prior experience of antibiotic use were risk factors for storing antibiotics at home.

In this review we found that sociodemographic characteristics were included in almost all studies as risk factors for antibiotic use; however, they are less modifiable when it comes to behavioural change. On the other hand, important factors such as knowledge and perceptions were not studied critically or comprehensively. For instance, antibiotic-use-related knowledge items (e.g. antibiotic literacy, antibiotic efficacy, etc.) are often added up as a combined score [36,37,39,41,42,51,62,65,71,80,93,94], neglecting the heterogeneity and complexity in the associations between different antibiotic knowledge items and various antibiotic use practices, and vice versa [58,62,63,65,71,78–81]. This could also explain why studies reported inconsistent associations between combined antibiotic-use-related knowledge and prudent antibiotic use. Further, we found that individual antibiotic use behaviours were heavily influenced by external factors specific to the local context, which are critical to explain patients' antibiotic use practices and habits in community settings, yet few studies investigated this beyond simple knowledge–attitude–practice surveys. Future studies should address these research gaps by exploring factors influencing antibiotic use across various dimensions in depth. Data from this review also showed that the likelihood of being prescribed antibiotics (mostly for self-limiting illnesses) appears to be high in all WHO regions (Western Pacific, European, Eastern Mediterranean regions and the regions of the Americas) except in Southeast Asia and African regions, where previous studies have reported irresponsible antibiotic prescriptions [95–97] with only very limited social or behavioural data available.

Findings of this review provide multifaceted evidence based on the Social Ecological Framework for future interventions to reduce public non-prescription antibiotic use. At the individual level, knowledge was complicatedly associated with behaviours. Future AMR awareness campaigns need to consider the complexities, and rigorous and evidence-based evaluation designs should be embedded in the intervention design to assess its effectiveness, which is also suggested in a recent review that conducted a global survey to examine the characteristics of antibiotic awareness campaigns conducted in different countries/regions [98]. At the interpersonal level, doctor–patient relationships and communications were important factors [54,61,67,82,83]. At the organizational level, meta-analyses revealed that relatives having medical backgrounds increased self-medication with antibiotics and antibiotic household storage. At the community level, local culture and norms exerted effects on antibiotic use; public-targeted education interventions are therefore urgently needed [73,82]. At the structural level, a high prevalence of self-medication with antibiotics and OTC antibiotic purchases was found in some LMICs due to their easy access to antibiotics [35–37,39,43,46,53,65,94]. Since evidence suggested that responsible antibiotic dispensing might effectively reduce antibiotic use without clinical indication [52], future regulations or policies could emphasize this strategy. However, in LMICs with limited access to formal medical care or medications, the public demands to be able to store antibiotics at home, to make OTC purchases, and to self-medicate with antibiotics to treat diseases; yet under many circumstances, they might improperly take antibiotics for viral infections/self-limiting illnesses without professional instructions [84]. In some LMICs there is reportedly a high prevalence of falsified or substandard antibiotics; the public might use them unknowingly, which could lead to severe health outcome [8,30,99,100]. Interventions in these regions should focus not only on promoting prudent antibiotic use but also on how to properly treat self-limiting illnesses, and should increase international efforts towards antimicrobial stewardship actions in LMICs [101]. All the evidence revealed in this review points to a need for multifaceted and context-tailored interventions.

To date, there is no standardized measure to assess the prevalence of antibiotic use behaviours. When extracting the prevalence data from the published studies, wide discrepancies were found among the survey designs. Different recall periods and populations of the numerator and denominator decreased the comparability. Besides, only four of the 71 included studies were from low-income countries [41,42,61,84]. Risk factors influencing public antibiotic use in these countries remain largely unexplored. Only one study explored risk factors for antibiotic use under the One Health framework [64]. More research is needed to inform One Health interventions.

This study has several limitations. First, there was certain heterogeneity among studies included in the meta-analyses, which might result from the differences in study participants and study regions. However, high heterogeneity could also indicate that there is a wide variation in factors affecting antibiotic use behaviours across different populations or regions. Second, comprehensive meta-regressions were not conducted because not enough studies were eligible.

In conclusion, non-prescription antibiotic use and irresponsible antibiotic prescriptions in the community are alarmingly prevalent in all WHO regions, warranting immediate action. This study identified the non-biomedical factors that drive antibiotic use in the community within different cultural contexts, highlighting the complexity of the challenge. Future AMR strategies that aim to reduce antibiotic use without clinical indication should incorporate a multifaceted community-based design that addresses non-biomedical drivers tailored to local contexts. For instance, in

regions where antibiotic use is heavily affected by local culture or norms, educational campaigns can be targeted to both the public and providers to influence the deep-rooted misconceptions. In LMICs with deficient healthcare resources, access to antibiotics is life-saving and should be guaranteed; educating the public to use antibiotics correctly should be the priority. In countries with sufficient antibiotic supplies, the dispensing through community pharmacies need to be supervised or restricted—e.g. prohibiting antibiotic sales without a validated prescription, or dispensing exact numbers of antibiotic pills according to the treatment course—so as to prevent occurrence of leftover medication. Strict selective testing of antibiotic drug quality can be integrated into interventions in LMICs where falsified or substandard antibiotics are rampant. Health policy reforms that remove financial incentives for prescribing antibiotics or outpatient antibiotic infusions should also be considered.

### Author contributions

LL conceptualized the study, designed the methods, and supervised the project. RS and TY searched the literature. RS and TY extracted and coded the data. RS completed the meta-analysis. RS and TY completed the visualization. LL, RS and TY interpreted the results. RS prepared the original draft with important contributions from LL and TY. XZ and SH commented on drafts, and provided edits and feedback. All authors had full access to all the data and have approved the final version of the paper.

### Transparency declaration

The authors declare that they have no conflicts of interest. This research was funded in whole, or in part, by the UK Foreign, Commonwealth and Development Office and Wellcome [Grant number 215373/A/19/Z]. For the purpose of open access, the author has applied a CC BY public copyright licence to any Author Accepted Manuscript version arising from this submission.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cmi.2021.10.017>.

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